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agus Cáilíocht Sláinte

Potential impact of different testing scenarios to reduce the duration of restriction of movement for close contacts of a COVID-19 case

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About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is an independent statutory authority established to promote safety and quality in the provision of health and social care services for the benefit of the health and welfare of the public.

HIQA's mandate to date extends across a wide range of public, private and voluntary sector services. Reporting to the Minister for Health and engaging with the Minister for Children and Youth Affairs, HIQA has responsibility for the following:

- **Setting standards for health and social care services** — Developing person-centred standards and guidance, based on evidence and international best practice, for health and social care services in Ireland.
- **Regulating social care services** — The Chief Inspector within HIQA is responsible for registering and inspecting residential services for older people and people with a disability, and children's special care units.
- **Regulating health services** — Regulating medical exposure to ionising radiation.
- **Monitoring services** — Monitoring the safety and quality of health services and children's social services, and investigating as necessary serious concerns about the health and welfare of people who use these services.
- **Health technology assessment** — Evaluating the clinical and cost-effectiveness of health programmes, policies, medicines, medical equipment, diagnostic and surgical techniques, health promotion and protection activities, and providing advice to enable the best use of resources and the best outcomes for people who use our health service.
- **Health information** — Advising on the efficient and secure collection and sharing of health information, setting standards, evaluating information resources and publishing information on the delivery and performance of Ireland's health and social care services.
- **National Care Experience Programme** — Carrying out national service-user experience surveys across a range of health services, in conjunction with the Department of Health and the HSE.

List of abbreviations used in this report

CDC	Centers for Disease Control and Prevention
CI	confidence interval
COVID-19	Coronavirus disease 2019
EAG	Expert Advisory Group
ECDC	European Centre for Disease Prevention and control
HIQA	Health Information and Quality Authority
HSE	Health Service Executive
HTA	health technology assessment
NPHE	National Public Health Emergency Team
rRT-PCR	real time reverse transcription-polymerase chain reaction
RADT	rapid antigen detection test
R0	basic reproduction number
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SCOPI	Study to investigate COVID-19 Infection in People Living in Ireland
WHO	World Health Organization

Potential impact of different testing scenarios to reduce the duration of restriction of movement for close contacts of a COVID-19 case

Key points

- Public health interventions aim to minimise the burden of COVID-19 by reducing the spread of SARS-CoV-2. Important interventions that may be associated with specific durations of time include 'self-isolation' and 'restriction of movements'.
- 'Restriction of movements' is defined as separating and restricting the movements of people who may have been exposed to COVID-19. This is performed as a precautionary measure to prevent transmission should exposed individuals later become infected. It is distinct from isolation (or self-isolation) which is defined as separating those with symptoms of, or diagnosed with COVID-19, from people who are not infected.
- Currently in Ireland, the duration of restricted movements is 14 days for individuals identified as close contacts of a COVID-19 case. Testing of close contacts (first test - 'Day Zero', day of identification; second test - 'Day Seven' since last exposure) is for the purpose of contact tracing; a negative test (that is virus 'not detected') does not impact the recommended duration of restricted movements.
- This report modelled the potential impact of a number of different testing scenarios in reducing the current duration of restricted movements from 14 days. RT-PCR based testing is the current standard practice in Ireland; however, rapid antigen detection tests (RADTs) may offer benefits over RT-PCR based tests provided they meet the minimum performance criteria in clinical validation studies. Modelled scenarios therefore considered both testing options.
- Parameter estimates for the model were gathered from the recent literature, previous HIQA evidence summaries, and Irish data sources. The outcomes of interest from the model, included estimates of potential benefits (reduced person-days in restricted movements), potential risks (increased infectious person-days in the community), and organisational implications (number of tests conducted).

- On balance, relative to the current standard practice in Ireland, estimates from scenarios which included a condition of ending the period of restricted movements on receipt of a day 10 'not detected' test result were considered to present the largest benefit (in terms of reduced person-days in restricted movements), relative to the lowest risk (in terms of infectious person-days in the community). Scenarios which involved an end of restricted movements on receipt of a 'Day Seven' result were noted to have larger benefits, but had a considerably higher risk overall.
- The choice of test (RT-PCR or RADT) further influenced results, with an end of restricted movements on receipt of a 'Day 10' RADT having a larger benefit (in terms of reduced person-days in restricted movement), but also additional risk, relative to ending on receipt of a 'Day 10' RT-PCR based test.
- Scenarios that adopt a 'Day 10' test instead of the current 'Day Seven' test are associated with an increase in the total number of tests conducted. This increase is due to a larger number of individuals being eligible for a second test, because of the longer interval between this test and the day 0 test.
- Additional factors identified which could not be fully accounted for within the model, but should be considered in overall decision-making included: adherence to duration of restricted movements, adherence to testing regimens, and socioeconomic gradients.
- It must be noted that the model did not assess the impact of a change in testing scenario on the current contact tracing process in Ireland. Furthermore, estimates included within the model reflect the pandemic to date; recently, there has been a change in the demographic profiles of infected individuals, with a trend towards younger cases which could impact the overall estimates provided.
- Overall, the estimates presented from the model suggest that the use of RT-PCR tests on 'Day Zero' and 'Day 10' with an end of restricted movements on receipt of a 'not detected' result from the second test would present the largest benefit and lowest risk, relative to the current standard of practice in Ireland. The identification and validation of a suitable RADT test may offer further benefits; however this will likely be associated with an increase in risk. Consideration is required by policy makers as to what constitutes an overall acceptable level of risk, relative to current practice.

Potential impact of different testing scenarios to reduce the duration of restriction of movement for close contacts of a COVID-19 case

The Health Information and Quality Authority (HIQA) has developed a series of evidence syntheses to inform advice from HIQA to the National Public Health Emergency Team (NPHE). The advice will take account of expert interpretation of the evidence by HIQA's COVID-19 Expert Advisory Group. This evidence synthesis relates to the following policy question outlined by NPHE:

"Is there a rationale upon which to reduce the current period of restricted movement for close contacts from 14 days? If so, how will any change in guidance intersect with the current testing protocol (that is, a PCR test on day zero and a PCR test on day seven)?"

This current report summarises a modelling exercise to inform the following research question that formulated to inform the above policy question:

"What is the potential impact of different testing scenarios to reduce the duration of restriction of movement for close contacts of a COVID-19 case?"

Background

In the absence of effective treatment options or a vaccine for an infectious disease such as COVID-19, two non-pharmaceutical public health interventions are paramount to reducing transmission:⁽¹⁾

1. isolation of infected cases, and
2. tracing, testing and restricting the movements of their contacts.

Although intertwined in the collective public health strategy employed in the COVID-19 pandemic, these concepts are distinct. Isolation (or self-isolation) is defined as the separation of those diagnosed with, or suspected of having, COVID-19 from people who are not infected. 'Restriction of movements' (or self-quarantine, or quarantine) is defined as the separation, and restriction of movements, of people may have been exposed to SARS-CoV-2, as a precautionary measure because they may have the disease.^(2, 3)

In the context of the COVID-19 pandemic, the latter strategy of the restriction of movements carries particular weight in reducing potential onward transmission of the SARS-CoV-2 virus. However, ensuring an appropriate duration of restricted movements for those exposed to an infectious disease is crucial given the associated

personal and societal implications.^(4, 5) Durations which are too long will have implications for the quality of life of the individual, and contribute to absenteeism or availability for work, with implications for the economy. Durations that are too short risk those who are infectious re-entering the community.

The requirement for the restriction of movements may be due to an individual being identified as a close contact of a confirmed case of COVID-19, or due to potential travel-related exposure or a household member awaiting a test result.^(6, 7) In terms of close contact exposure, currently in Ireland a restriction of movements for a period of 14 days from the last point of exposure is recommended.⁽⁶⁾ Close contacts of a confirmed COVID-19 case are identified and tested as soon as possible, preferably on the same day of identification, representing a 'Day Zero' test. Of note, this 'Day Zero' reflects the time of identification and contact; it is not reflective of time since exposure. If a negative (that is, 'not detected') test is returned, a follow-up test is conducted seven days since the last identified exposure to the confirmed case ('Day Seven' test). However, if the scheduled 'Day Zero' and 'Day Seven' tests fall within 24 hours of each other, the second test is not conducted. The results of these 'Day Zero' and 'Day Seven' tests do not affect the duration of the restriction of movements, with an individual who returns two negative ('not detected') tests asked to continue to restrict their movements for the full 14-day period.⁽⁶⁾ Should an individual become symptomatic and or test positive at any point, they must enter a self-isolation period of 10 days with their contacts then traced.⁽⁶⁾

The 14-day duration of restriction of movements in Ireland is reflected in the World Health Organization (WHO) and US Centers for Disease Control and Prevention (CDC) guidance; both organisations outline significant caution when considering a reduction in this duration.^(8, 9) However, an option proposed by the European Centre for Disease Prevention and Control (ECDC), published 24 September 2020, allows the period of the restriction of movements to be reduced from 14 days if a PCR test taken on or after day 10 following last exposure to the case is negative (virus not detected).⁽¹⁰⁾ The cited evidence underpinning this recommendation is based on an upper bound estimate of the incubation period of 12 days and detectability of the virus 1-3 days prior to symptom onset (12 days minus two days resulting in the day 10 recommendation); however, the guidance notes that the potential residual risk of transmission associated with this scenario may not be acceptable depending on the context.^(10, 11) The report further points to modelling work on contact-tracing, quarantine and testing published as a pre-print article by a mathematical modelling team at the London School of Hygiene and Tropical Medicine.⁽¹²⁾

Of particular importance to any reduction in the duration of restricted movements based on testing is the accuracy and overall performance of the diagnostic test used.

Current standard practice for detection of SARS-CoV-2 RNA in Ireland is the use of laboratory-based real time reverse transcription polymerase chain reaction (rRT-PCR). This form of test is noted to have considerable accuracy, in terms of both sensitivity and specificity;^(13, 14) however, there are a number of pre-analytical factors that may impact performance, such as the timing of specimen collection, the population being tested, the type of clinical specimen obtained, the sampling and transport techniques, and the quality of particular test kits.⁽¹⁴⁻¹⁷⁾ Of particular relevance is the timing of the test relative to exposure to the case; a 'not detected' result due to low viral loads may be returned for tests conducted too early following exposure; or if conducted later in the disease course as viral load decreases.⁽¹⁵⁾ Typically viral loads for SARS-CoV-2 from the upper respiratory tract are thought to peak one to three days prior to symptom onset and during the early symptomatic phase.^(13, 18, 19) A further important consideration is the population being tested, with asymptomatic populations posing particular difficulty in the context of the COVID-19 pandemic, whereby the diagnostic test accuracy and validation in this group has yet to be established.^(14, 17) A rapid health technology assessment (HTA) undertaken by HIQA, noted an international trend towards the adoption of rapid antigen detection tests (RADTs), with a growing number of these coming to market.⁽¹⁴⁾ However, these RADTs are noted to vary considerably in terms of analytical performance. At present, the WHO denotes caution with their use, citing they should only be used when RT-PCR is unavailable or where prolonged turnaround times preclude clinical utility.⁽¹³⁾ Where RADTs are used, the WHO suggests that the tests must meet the minimum acceptable performance requirements of $\geq 80\%$ sensitivity and $\geq 97\%$ specificity relative to the reference standard, RT-PCR. As these reflect minimum standards, the WHO has suggested that the lower bound of their confidence intervals should exceed these values.^(13, 20) Should, a RADT be developed and validated meeting these performance thresholds, and those set out by each country individually, it could offer significant benefits in terms of turnaround times and testing capacity.⁽¹⁴⁾

A reduction in the duration of restricted movements based on a 'not detected' test result requires careful consideration of potential consequences and associated residual risk of disease transmission. The aim of this report is to assess the potential impact of a reduction in the duration of restricted movements based on a number of testing scenarios, for close contacts of a COVID-19 case.

Methods

A modelling exercise was undertaken to estimate the potential impact of a reduction in the duration of the restriction of movements based on a number of testing scenarios. Below is a summary of the four key elements underpinning the model: population, outcomes, testing scenarios considered and parameter estimates.

Population and setting

This modelling exercise considers close contacts of a confirmed COVID-19 case. All settings (for example, household and non-household) in the context of close contacts are considered relevant. The model does not consider individuals with potential travel-related exposure.

Outcomes of interest

The model estimates the following four clinical and organisational outcomes of interest to the policy question, relative to the base case comparator of the current standard of practice in Ireland:

- total number of person-days of restricted movement.
- total number of person-days for infected individuals not in restricted movement.
- potential number of additional infections arising directly from infectious individuals re-entering the community following a test result of 'not detected'.
- number of tests conducted.

Base case analysis and testing scenarios

As a base case analysis, the model considers the current standard of practice in Ireland (comparator), and a reduction in the current duration of restricted movements based on eight testing scenarios. These scenarios are summarised in Table 1, and outlined in full below. A number of additional scenarios were modelled which will not be discussed in detail in the context of this report, but are provided in Appendix 1 for information.

- Scenario one (comparator): the base case scenario is the current standard practice in Ireland. For close contact exposure, a restriction of movements for a period of 14 days is recommended. Close contacts of a confirmed COVID-19 case are identified and tested as soon as possible, preferably on the same day of identification, representing a 'Day Zero' test. Of note, this 'Day Zero' reflects the time of identification and contact, it is not reflective of time since exposure. If a negative ('not detected') test is returned, a follow-up test is conducted seven days since the last identified exposure to the confirmed case ('Day Seven' test). If the 'Day Zero' and 'Day Seven' test fall within 24 hours of each other, the second test is not conducted. The results of these tests have no effect on the duration of the restriction of movements, with an individual who returns two negative ('not detected') tests asked to continue to restrict their movements for the full 14-day period.

- Scenario two: ending the period of restricted movements of an individual conditional on receipt of a 'not detected' RT-PCR test result from the current test conducted seven days post-exposure ('Day Seven' test).
- Scenario three: using a rapid antigen detection test (of pre-specified lower limits of test sensitivity and specificity), as an alternative to the 'Day Seven' RT-PCR test while maintaining the 'Day Zero' RT-PCR test. Ending of restricted movements on receipt of a 'not detected' test result from the 'Day Seven' test.
- Scenario four: using a rapid antigen detection test (of pre-specified lower limits of sensitivity and specificity) as an alternative to the 'Day 10' RT-PCR test while maintaining the 'Day Zero' RT-PCR test. Ending of restricted movements on receipt of a 'not detected' test result from the 'Day 10' test.
- Scenario five: replacing the current 'Day Seven' RT-PCR test with a 'Day 10' RT-PCR test, and ending the period of restricted movements on receipt of a 'not detected' result from the 'Day 10' test.
- Scenario six: using a rapid antigen detection test (of pre-specified lower limits of sensitivity and specificity) on 'Day Zero', as an alternative to a 'Day Zero' RT-PCR test while maintaining the 'Day Seven' RT-PCR test. Ending of restricted movements on receipt of 'not detected' test result from the 'Day Seven' test.
- Scenario seven: using a rapid antigen detection test (of pre-specified lower limits of sensitivity and specificity) on 'Day Zero', as an alternative to a 'Day Zero' RT-PCR test and using a 'Day 10' RT-PCR test. Ending of restricted movements on receipt of 'not detected' test result from the 'Day 10' test.
- Scenario eight: using a rapid antigen detection test (of pre-specified lower limits of sensitivity and specificity) as an alternative to 'Day Zero' and 'Day Seven' RT-PCR tests. Ending of restricted movements on receipt of a 'not detected' test result from the 'Day Seven' test.
- Scenario nine: using a rapid antigen detection test (of pre-specified lower limits of sensitivity and specificity) on 'Day Zero' and 'Day 10' as an alternative to RT-PCR testing. Ending of restricted movements on receipt of a 'not detected' test result from the 'Day 10' test.

Table 1. Scenarios considered within model

Scenario	First test*	Second test^	End of restriction of movements
1 (comparator)	Day 0 - RT-PCR	Day 7 - RT-PCR	Day 14
2	Day 0 - RT-PCR	Day 7 - RT-PCR	Receipt of ND day 7 test
3	Day 0 - RT-PCR	Day 7 - RADT	Receipt of ND day 7 test
4	Day 0 - RT-PCR	Day 10 - RADT	Receipt of ND day 10 test
5	Day 0 - RT-PCR	Day 10 - RT-PCR	Receipt of ND day 10 test
6	Day 0 - RADT	Day 7 - RT-PCR	Receipt of ND day 7 test
7	Day 0 - RADT	Day 10 - RT-PCR	Receipt of ND day 10 test
8	Day 0 - RADT	Day 7 - RADT	Receipt of ND day 7 test
9	Day 0 - RADT	Day 10 - RADT	Receipt of ND day 10 test

Key: ND- Not Detected; RT-PCR- real time reverse transcription polymerase chain reaction; RADT- Rapid Antigen Detection Test

*First test on 'Day Zero' indicates time of contact identification and testing, it does not infer time since exposure

^Second test infers time since last exposure to a COVID-19 case

Model parameters

The model required a range of input parameters that describe disease, person, testing, and organisational factors. Parameter estimates are typically defined by statistical distributions that reflect the uncertainty in their true values.

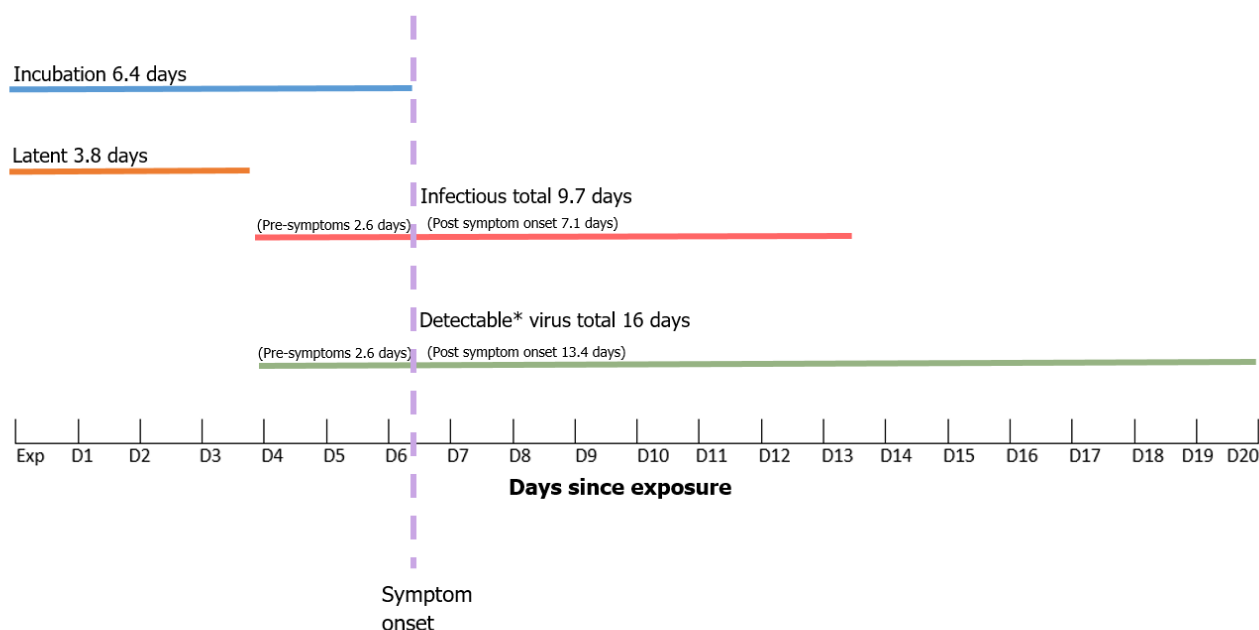
The focus of the model is to estimate the 'on average' effects, and does not consider superspreaders. The term superspreader describes individuals who infect disproportionately more secondary contacts, in comparison to the majority of others with the disease, typically described as a 20/80 rule.⁽²¹⁾ This phenomenon is acknowledged as likely occurring within the COVID-19 pandemic, with a small proportion of individuals responsible for a considerable number of overall cases, and has been noted within previous disease outbreaks.⁽²¹⁾ However, the predictive and contextual factors which facilitate superspreader events are poorly understood at present with a shortage of available literature;⁽²²⁾ hence, this present model does not consider this group.

Of note, given a shortage of identified data for estimating the disease process within asymptomatic populations, an assumption was made within the model that the course of disease is the same in symptomatic and asymptomatic cases, with the exception of symptom onset. This is likely reflective of a conservative approach given evidence to suggest viral shedding time is similar, if not shorter, for asymptomatic populations,^(23, 24) and a lower transmission potential for this population overall.⁽²⁵⁾

Disease factors

A summary of the parameter estimates for each relevant disease factor is provided in Table 2. Figure 1 illustrates the key disease parameter estimates for an average symptomatic COVID-19 case.

Figure 1. Disease parameter estimates for an average symptomatic COVID-19 case



*Detectable by PCR based testing; RADT assumed to be the same as PCR for detectability in pre-symptomatic and infectious period

- Incubation period

The incubation period denotes the period from exposure to symptom onset. It is frequently reported as the time from last known exposure. The incubation period is not used explicitly in the model, but rather used along with the latent period to determine the infectious period prior to symptom onset. The estimate of the incubation period is derived from a systematic review of relevant studies.⁽²⁶⁾

- Latent period

The latent period is the period from exposure to becoming infectious. During this period the individual is asymptomatic or pre-symptomatic and will not transmit the infection to others. There are very limited data to support an estimate of the latent period, and as such there is substantial uncertainty around the estimate.

- Duration of infectiousness (pre-symptom onset)

The period prior to becoming symptomatic when an infected individual's viral load is sufficient to transmit infection to others. Managing the period during which an individual is infectious is critical to controlling transmission of SARS-CoV-2. It is also assumed that a person will not test positive prior to the infectious period. The pre-symptomatic infectious period is modelled as the difference between the incubation time and the latent period.

- Duration of infectiousness (post-symptom onset)

This denotes the period that an infected individual is infectious after symptom onset. It was assumed in the model that symptomatic individuals would self-isolate and thereby minimise the onward transmission of COVID-19.

Asymptomatic individuals were assumed to have an equivalent period during which they were infectious, but not symptomatic. Furthermore, the model accounts for a reduction in the number of infectious individuals over time. While it was assumed that a person was equally likely to transmit COVID-19 over the duration of being infectious, it is highly likely that the profile of infectivity changes over time. This is partly implicit in the data, as the duration of infectivity is estimated from an evidence of transmission over time. The available data also suggest that a disproportionate amount of transmission occurs before symptom onset, but this may be a reflection of reduced opportunity after symptom onset due to self-isolation of the index case. The reduced opportunity to transmit is explicit in the model as we assume all symptomatic and test-detected cases adhere to restricted movements.

- Detectable virus (post-infectious state)

While viral load and detectability increase rapidly at the start of infection, viral load diminishes slowly over time at the end of the infection.⁽²⁷⁾ As such, an individual tested late in the infection may return a positive test result, but no longer be infectious.

- Proportion of close contacts infected

In determining the impact of different strategies of testing and restricted movement, it is essential to consider the risk of infection in the target population. With a low likelihood of infection, the benefit to harm balance of some control measures will shift. With a very low risk, for example, a large group of people will be required to restrict movement with little gain in terms of reduced infection. Conversely, in a group with a high risk of infection there will be a substantial health gain from restricted movement. In this model, the

probability that a close contact of a confirmed case is infected was derived from the Irish contact tracing data.

- Proportion of asymptomatic infections

Infected individuals may experience a range of symptoms of varying severity. Some individuals will experience no notable symptoms at all, and therefore may be unaware that they are infected unless detected through testing. Asymptomatic individuals can, however, transmit disease, creating challenges for the control of transmission. The parameter values here are based on the findings of a systematic review,⁽²⁵⁾ and are consistent with the proportion of asymptomatic cases estimated in an Irish sero-prevalence study.⁽²⁸⁾

Table 2. Parameter estimates for disease factors

Parameter	Description	Source(s)	Estimate
Incubation period	The time duration (in days) from exposure to symptom onset	HIQA evidence summary of incubation period ⁽²⁶⁾	Mean: 6.4 95% CI (0.95 to 14.8)
Latent period	The time duration (in days) from exposure to becoming infectious	HIQA evidence summary of incubation period combined with LSHTM modelling estimate of latent period ^(12, 26)	Mean: 3.8 95% CI (1.4 to 8.4)
Duration of infectiousness (pre-symptomatic)	The time duration (in days) from becoming infectious to symptom onset	HIQA evidence summary of duration of infectiousness ⁽²⁹⁾ combined with LSHTM modelling estimate of latent period ⁽¹²⁾	Mean: 2.6 95% CI (0.3 to 9.5)
Duration of infectiousness (symptomatic)	The time duration (in days) from symptom onset to no longer being infectious. Adjusted for proportional reduction in infectious individuals over time.	HIQA evidence summary of duration of infectiousness ⁽²⁹⁾ Singanayagam et al. ⁽³⁰⁾	Mean: 7.1 95% CI (2.7 to 11.5)
Detectable virus (post-infectious state)	The time period (in days) that an individual has detectable disease after they are no longer infectious	Inferred with consideration of estimates of false negative tests from Kucirka et al., ⁽¹⁵⁾ viral load estimates from Walsh et al., ⁽¹⁸⁾ and duration of infectiousness estimates from Byrne et al. ⁽²⁷⁾	Mean: 6.3 95% CI (5.7 to 6.9)
Percentage of close contacts infected	The percentage of close contacts who subsequently test positive for SARS-CoV-2 RNA	HSE COVID-19 CMP data	Mean: 15% 95% CI (11% to 20%)
Percentage of asymptomatic infections	The percentage of all infected cases which remain asymptomatic (that is they do not show symptoms at any point). The confidence bounds are based on the reported prediction interval in the underlying study.	Buitrago-Garcia et al. ⁽²⁵⁾	Mean: 31% 95% CI (26% to 37%)

Person factors

A summary of the parameter estimates for each relevant person factor is provided in Table 3.

- Mean number of close contacts

This refers to the average number of close contacts generated by each infected individual. Although not explicitly used in the model, it has been used to put estimates in context in relation to the numbers of new cases per day.

- Rate of onward infection (with and without restricting movements)

The reproductive number, or R_0 , refers to the number of individuals infected, on average, by an index case. An R_0 value of less than one implies that the infection will diminish, whereas a value of greater than one implies an increasing number of cases. The reproductive number in Ireland has varied over time between a high of between four and five at the start of the epidemic to a low of between 0.4 and 0.5 in April and May. The reproductive number is affected by individual and societal control measures in place, such as physical distancing. For the purposes of the model, values of R_0 were inferred separately for those restricting and not restricting movements. The values used in the model are expressed as infections per day. The value for someone who remains in restricted movement for the entire infectious period is 0.2, while for someone not in restricted movement, it is equivalent to 1.6 infections. It is intended that these values are only indicative and account for the variety of control measures in place.

- Adherence to testing

An important aspect of managing contact tracing is identifying those who have been infected with COVID-19. Identification is contingent on testing or through symptomatic presentation. Approximately 58% of individuals are not referred for a second test; this is due to the contact testing positive prior to the second test (11%) the second test falling within 24 hours of the first (17%), or due to identification on at least day six since last known exposure to the index case (72%). Data from the contact tracing programme demonstrates a high uptake of the first test, but a low uptake of the 'Day Seven' test. There may be a number of reasons for the apparent poor uptake of 'Day Seven' tests, particularly in relation to proximity to the first test and the lag between testing and receiving results. While the test is provided free, there may be cost or practical barriers to accessing testing. It is possible that delaying the second test from seven to ten days post-exposure may improve uptake, although in the absence of any evidence to support this, we have assumed that the uptake for a 'Day 10' test would be the same as for a 'Day Seven' test.

- Estimated proportion of individuals adherent to restriction of movement

Individuals may be adherent to restricting movement, but not avail of testing. There are limited international or Irish data that examine adherence to

restricting movement. Some of the evidence available has taken a strict two-part approach to measuring adherence, with individuals considered to be either fully adherent or not at all. Such a narrow definition is unrealistic in practice, and we have assumed that the majority of people asked to restrict movement will enter into the spirit of the request as far as is possible. On the basis that more than 80% of individuals avail of the first test, we have assumed that 90% of close contacts are compliant with restricting movements at the outset, declining over time to an average of 65% ten days following exposure (Figure 2).⁽³¹⁾ It was assumed that all those who become symptomatic or are test-detected will restrict movements. It was also assumed that those who avail of testing will restrict movements while awaiting their test results.

Figure 2. Estimated adherence to restricted movement over time

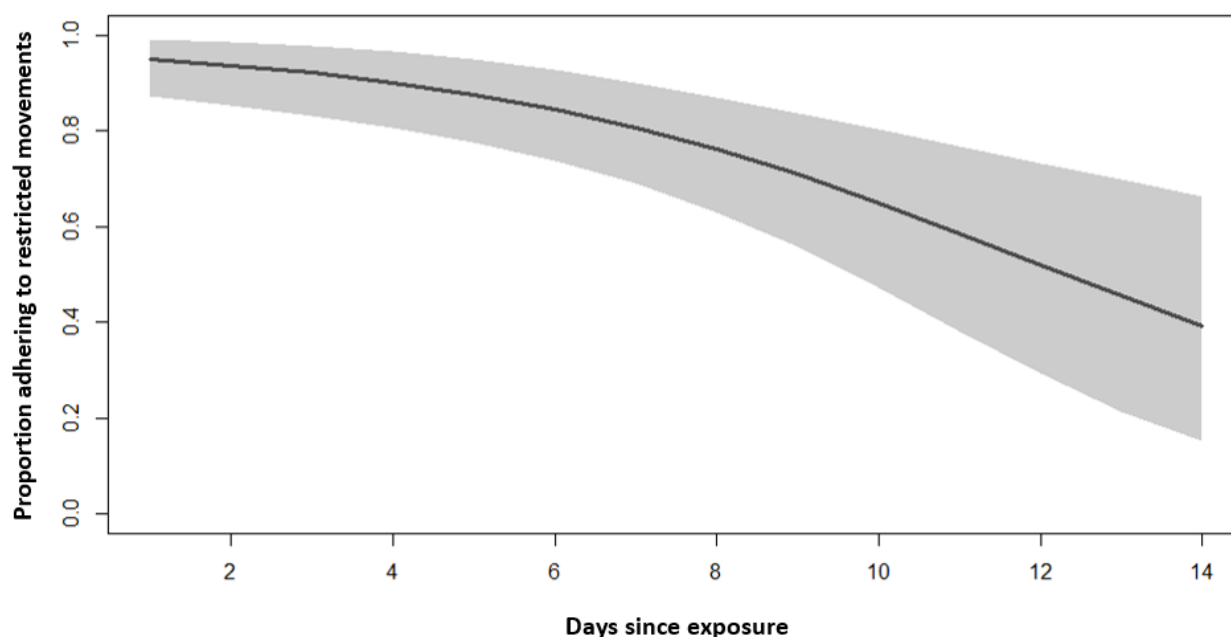


Table 3. Parameter estimates for person factors

Parameter	Description	Source(s)	Estimate
Mean number of close contacts	The average number of close-contacts for a COVID-19 case in Ireland	HSE COVID-19 CMP data	Mean: 6.0 95% CI (4.4 to 8.0)
Rate of onward infection (not restricting movements)	Reproductive number (per day) for an infectious individual not restricting movements	Inferred from a simulation exercise assuming overall R_0 1 to 1.1.	Mean: 0.17 95% CI (0.11 to 0.24)
Rate of onward infection (restricting movements)	Reproductive number (per day) for an infectious individual who is restricting movements	Inferred from a simulation exercise assuming overall R_0 1 to 1.1.	Mean: 0.022 95%CI (0.001 to 0.078)
Uptake of first test	The proportion of close contacts that present for 'Day Zero' testing	HSE COVID-19 CMP data	Mean: 82% 95% CI (73% to 90%)
Uptake of second test (in eligible individuals)	The proportion of close contacts that present for 'Day Seven' testing.	HSE COVID-19 CMP data	Mean: 57% 95% CI (40% to 74%)

Test factors

A summary of the parameter estimates for each relevant test factor is provided in Table 4.

- Sensitivity and specificity of RT-PCR testing for SARS-CoV-2

RT-PCR is generally considered the gold standard for detection of SARS-CoV-2. As such, there are challenges to assessing the diagnostic test accuracy of the test. While high sensitivity and specificity are achievable, accuracy is affected by the stage of infection and the quality of the sample, among other factors. At early or late stages of infection, the viral load may be insufficient to trigger a positive test result. Swabbing from a single site or issues with storage and transportation of swabs can also impact on diagnostic test accuracy. For modelling purposes we adopted an average sensitivity of 90%, but allowed wide uncertainty to explore the impact on the results.

- Sensitivity and specificity of RADT for detection of SARS-CoV-2

As RT-PCR is the gold standard, the sensitivity and specificity for the rapid antigen detection tests (RADT) are considered relative to RT-PCR. While the tests being considered for use in Ireland are noted to have high sensitivity and specificity in an ideal setting, it is assumed that they will be less accurate in practice. For this analysis, it is assumed that relative to RT-PCR, RADT tests will have the minimum acceptable sensitivity of 80% as set out by the WHO. This translates to a parameter estimate of 72% (80% of 90%).

Table 4. Parameter estimates for test factors

Parameter	Description	Source(s)	Estimate
Clinical sensitivity of RT-PCR testing for SARS-CoV-2	Proportion of individuals with COVID-19 correctly identified as infected with SARS-CoV-2 by RT-PCR testing, subject to pre-analytical factors.	HIQA Rapid HTA of diagnostic tests; ⁽¹⁴⁾ Inferred as high sensitivity when appropriate pre-analytical time factors satisfied	Mean: 90% 95% CI (83% to 95%)
Clinical specificity of RT-PCR testing for SARS-CoV-2	Proportion of individuals who do not have COVID-19 correctly identified as negative by RT-PCR testing for SARS-CoV-2	HIQA Rapid HTA of diagnostic tests; ⁽¹⁴⁾ Inferred as high	Mean: 99% 95% CI (98% to 100%)
Sensitivity of RADT for detection of SARS-CoV-2	Proportion of individuals with COVID-19 correctly identified as infected by RADT for SARS-CoV-2. Considered relative to RT-PCR as reference standard.	Minimum acceptable performance criteria set out by the WHO ^(13, 20) and considered relative to RT-PCR as reference standard	Mean: 72%* 95% CI (63% to 80%)
Specificity of RADT for detection of SARS-CoV-2	Proportion of individuals who do not have COVID-19 correctly identified as negative by RADT for SARS-CoV-2. Considered relative to RT-PCR as reference standard.	Minimum acceptable performance criteria set out by the WHO ^(13, 20) and considered relative to RT-PCR as reference standard	Mean: 98% 95% CI (96% to 99%)

*Using the WHO minimum accepted sensitivity of $\geq 80\%$ relative to RT-PCR (80% of 90% = 72%)

Organisational factors

A summary of the parameter estimates for each relevant organisational factor is provided in Table 5.

- Time lag between exposure to day 0 test
Although referred to as the 'Day Zero' test, it is in reality the first test and may occur ten days or more after exposure. Data from the contact management programme provided evidence on the range of days on which the first test was undertaken.
- Time lag between test and result
After a sample is collected from an individual, there is an average lag of two days to receiving the test results. The lag arises for a variety of reasons, including the time taken for transportation to the laboratory and processing.
- Capacity for RT-PCR testing

The capacity to carry out RT-PCR testing was not explicitly included in the model, but used for considering the logistical feasibility of different testing scenarios.

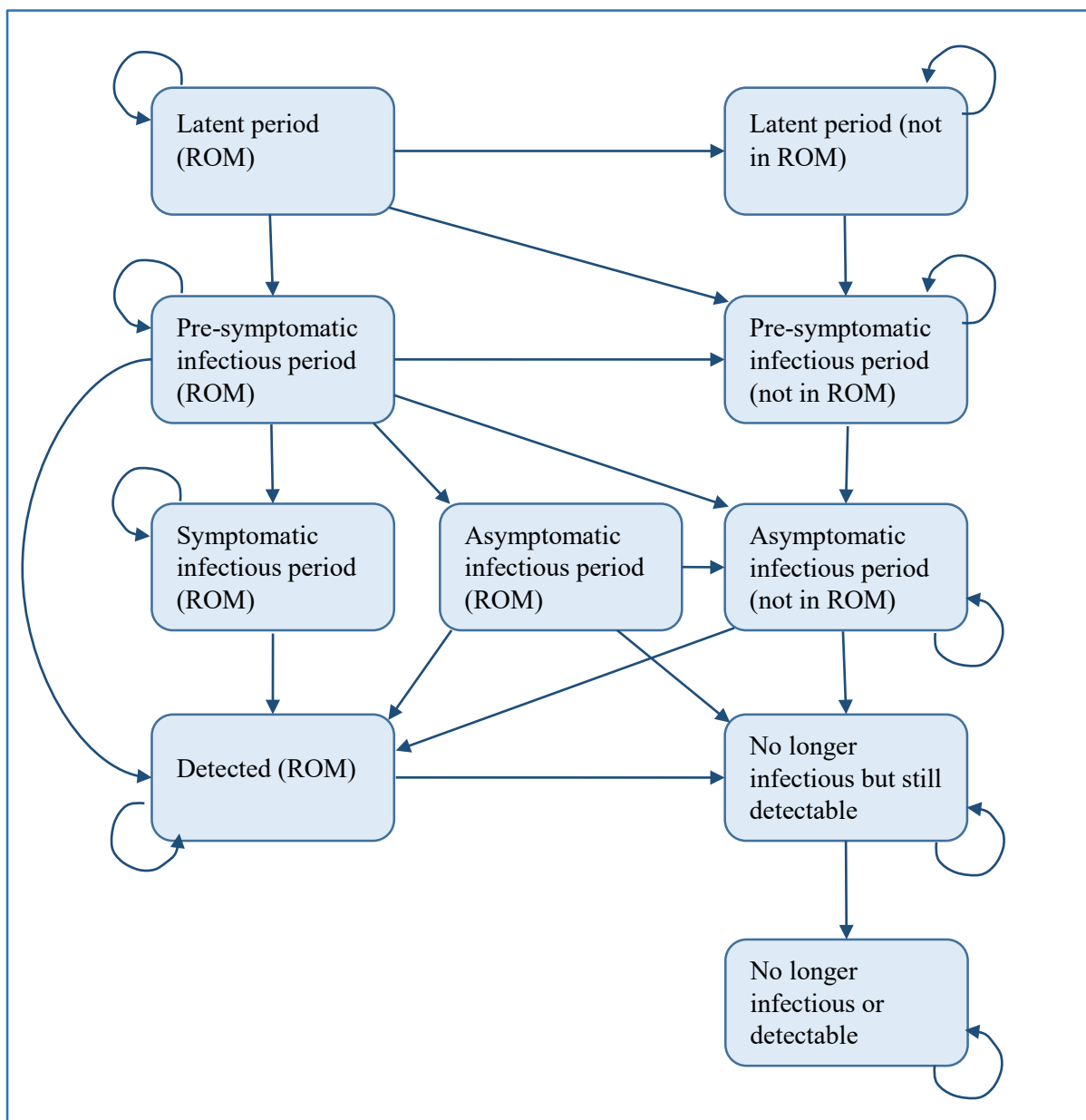
Table 5. Parameter estimates for organisational factors

Parameter	Description	Source(s)	Estimate
Time lag between exposure to 'Day Zero' test	The time period (in days) from the point of exposure to COVID-19 case and the close contact having 'Day Zero' test	Estimated from HSE Test and Trace data (week 22-28 September)	Mean 4.2 95% CI (1.5 to 9.7)
Time lag between negative test and result	The time period (in days) from specimen collection from the close contact and a negative test result.	Estimated from HSE Test and Trace data (week 6-12 October)	Mean 1.5 95% CI (1.0 to 3.0)
Capacity for RT-PCR testing	Current numbers of weekly RT-PCR tests completed in Ireland and overall capacity	HSE Test and Trace data	Weekly capacity on island: 100,000 Weekly capacity off-shore: 15,000 Tests completed week 4-10 October: 99,269

Model structure

The model classified close contacts infected with COVID-19 into a series of mutually exclusive states based on the progression of infection (Figure 3). Close contacts with undetected disease could also adhere to restriction of movement or not, in which case it is assumed they were moving freely in the community. After the infectious period is complete there was an extended period during which the viral load was sufficiently high that a case can return a positive test result. The model did not use explicit transition probabilities as transitions were based on duration of each period which could be shortened through testing or a close contact ceasing to adhere to restriction of movement. Once a close contact ceased adhering to restriction of movement, they would only return to restriction of movement while awaiting a test result or once confirmed positive for COVID-19.

Figure 3. State transition model for infected close contacts



The model was structured as a series of functions. One function was used to generate the parameter values for use in the model. Parameters were split into individual-level and simulation-level variables. Individual-level parameters captured the variability in infection characteristics across cases. Simulation-level parameters captured population-level variables, such as test uptake and test performance. A separate function took the generated parameter data as an input and estimated the number of close contacts in each state by days since exposure. The state matrix was generated for 10,000 simulated infected close-contacts. For each of the modelled scenarios, cases could change states in different ways depending on the timing and accuracy of testing. An equivalent state matrix was maintained for 10,000 uninfected close contacts which had three states: uninfected and observing restriction of

movement, uninfected and not observing restriction of movement, and self-isolating having received a false-positive test result. The relative contribution of infected and uninfected cases was calculated using the estimated proportion of close-contacts that are infected.

The so-called 'Day Zero' test can occur at any point after last exposure, although the 95% confidence interval runs from two to 10 days following last exposure. It was assumed that a second test would not be conducted unless it arose more than a day after the first test.

All computations were carried out in R (4.0.2).

Results

Model results

The results of this analysis are presented by each of the four outcomes of relevance considering each scenario. An additional outcome of the number of false positive tests is provided in Appendix 2.

Person-days in restricted movement

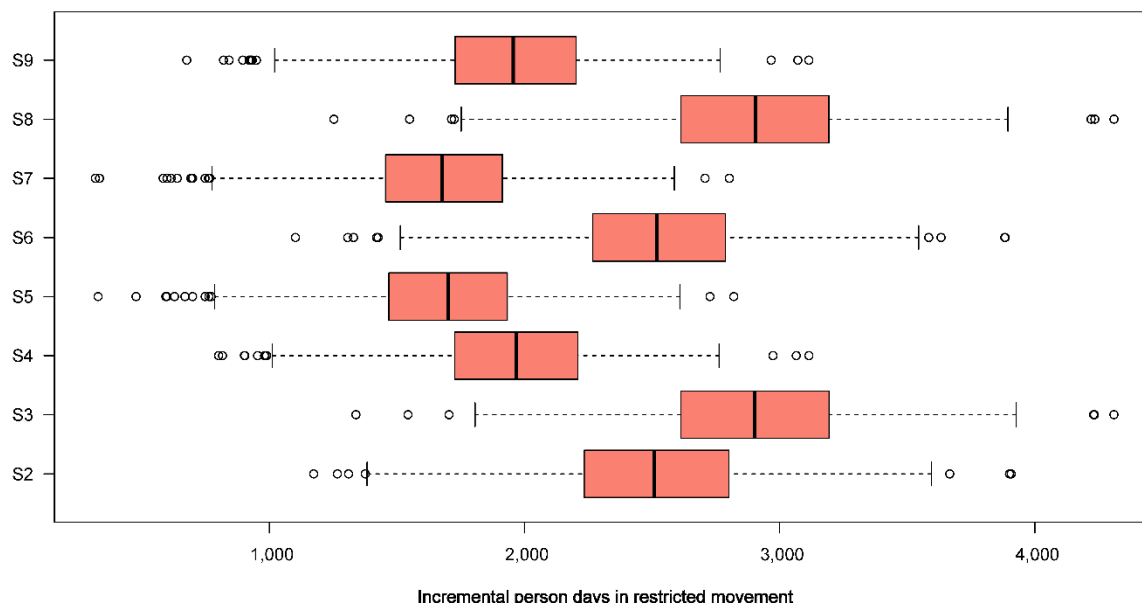
The total number of person-days in restricted movement is a measure of the burden of the control measure. The highest burden of restricted movement, 7,346 days per 1,000 close contacts of a confirmed case, is under the currently applied strategy of 14 days irrespective of test results (Table 6). The lowest burden (of 4,451 days) is for scenarios three and eight; that is, a rRT-PCR first test on 'Day Zero' and a RADT on 'Day Seven' with release on receipt of a 'Day Seven' 'not detected' test result, and a RADT first test on 'Day Zero' and a RADT on 'Day Seven' with release on receipt of a 'not detected' test result. Figure 4 outlines the distribution of incremental person days in restricted movement relative to current practice by each scenario assessed.

Table 6. Total person days in restricted movement (per 1,000 close contacts of confirmed cases)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	7,346	(6,039 to 8,594)	-	-
2	4,834	(3,925 to 6,028)	-2,512	(-3,362 to -1,690)
3*	4,451	(3,565 to 5,731)	-2,895	(-3,700 to -2,108)
4	5,385	(4,579 to 6,463)	-1,961	(-2,584 to -1,265)
5	5,657	(4,835 to 6,661)	-1,690	(-2,340 to -929)
6	4,822	(3,924 to 6,010)	-2,524	(-3,323 to -1,730)
7	5,677	(4,850 to 6,692)	-1,669	(-2,312 to -890)
8	4,451	(3,559 to 5,741)	-2,895	(-3,694 to -2,098)
9	5,934	(4,577 to 6,460)	-1,953	(-2,579 to -1,246)

*shading indicates scenario with lowest burden in terms of person days in restricted movement

Figure 4. Distribution of incremental person days in restricted movement relative to current practice by scenario



Footnotes for Figure 4: in a box and whisker plot, the box represents the interquartile range of values, with the vertical line indicating the median. Values beyond the ends of the whiskers (dotted lines) are generally classified as statistical outliers.

Person-days of infectious individuals in community

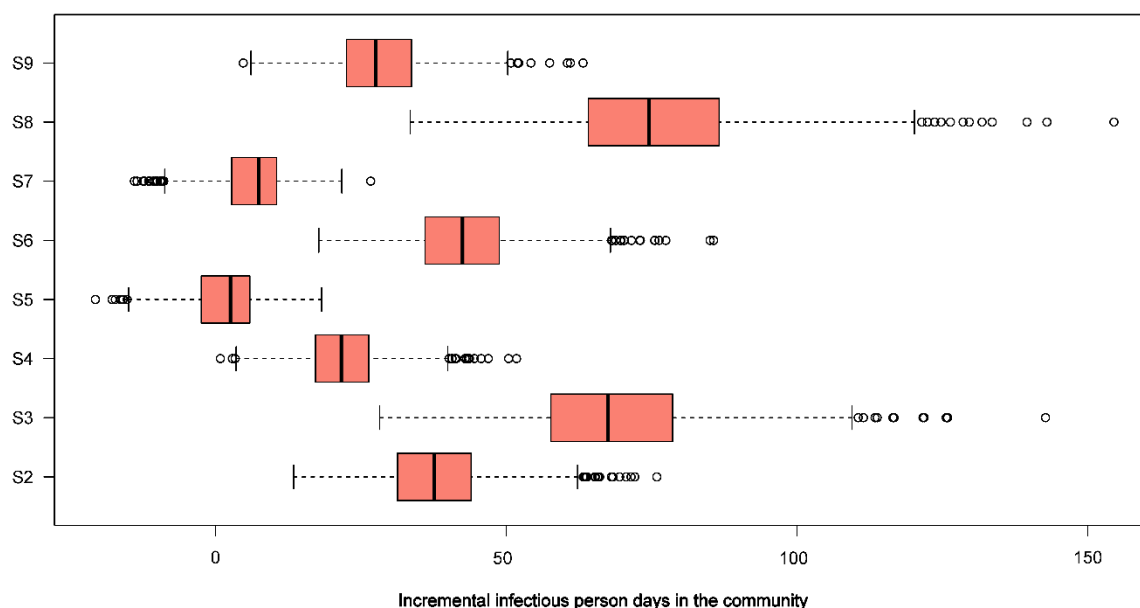
The reduction in days in restricted movement is counterbalanced with an increased risk of individuals out of restricted movement while infectious. This can arise through individuals who are yet to become symptomatic or those who will remain asymptomatic. The more time an infectious individual is in the community, the greater the risk of onward transmission, and as such it can be interpreted as a measure of risk. As shown in Table 7, the lowest total risk is for the currently applied strategy with the lowest additional risk for scenario five. That is, an RT-PCR first test on 'Day Zero' and a RT-PCR on 'Day 10' with release on receipt of a 'not detected' test result. Figure 5 outlines the distribution of infectious person-days in the community relative to current practice by each scenario assessed.

Table 7. Total person days for infected individuals not in restricted movement (per 1,000 close contacts of confirmed cases)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	189	(123 to 270)	0	-
2	227	(152 to 320)	38	(21 to 59)
3	258	(174 to 361)	69	(43 to 103)
4	211	(142 to 296)	22	(9 to 38)
5*	191	(125 to 268)	2	(-12 to 11)
6	232	(154 to 327)	43	(25 to 66)
7	196	(128 to 279)	7	(-9 to 17)
8	265	(178 to 374)	76	(48 to 111)
9	218	(145 to 309)	28	(14 to 46)

*shading indicates scenario with lowest additional risk in terms of infectious person days in community

Figure 5. Distribution of incremental infectious person days in the community relative to current practice by scenario



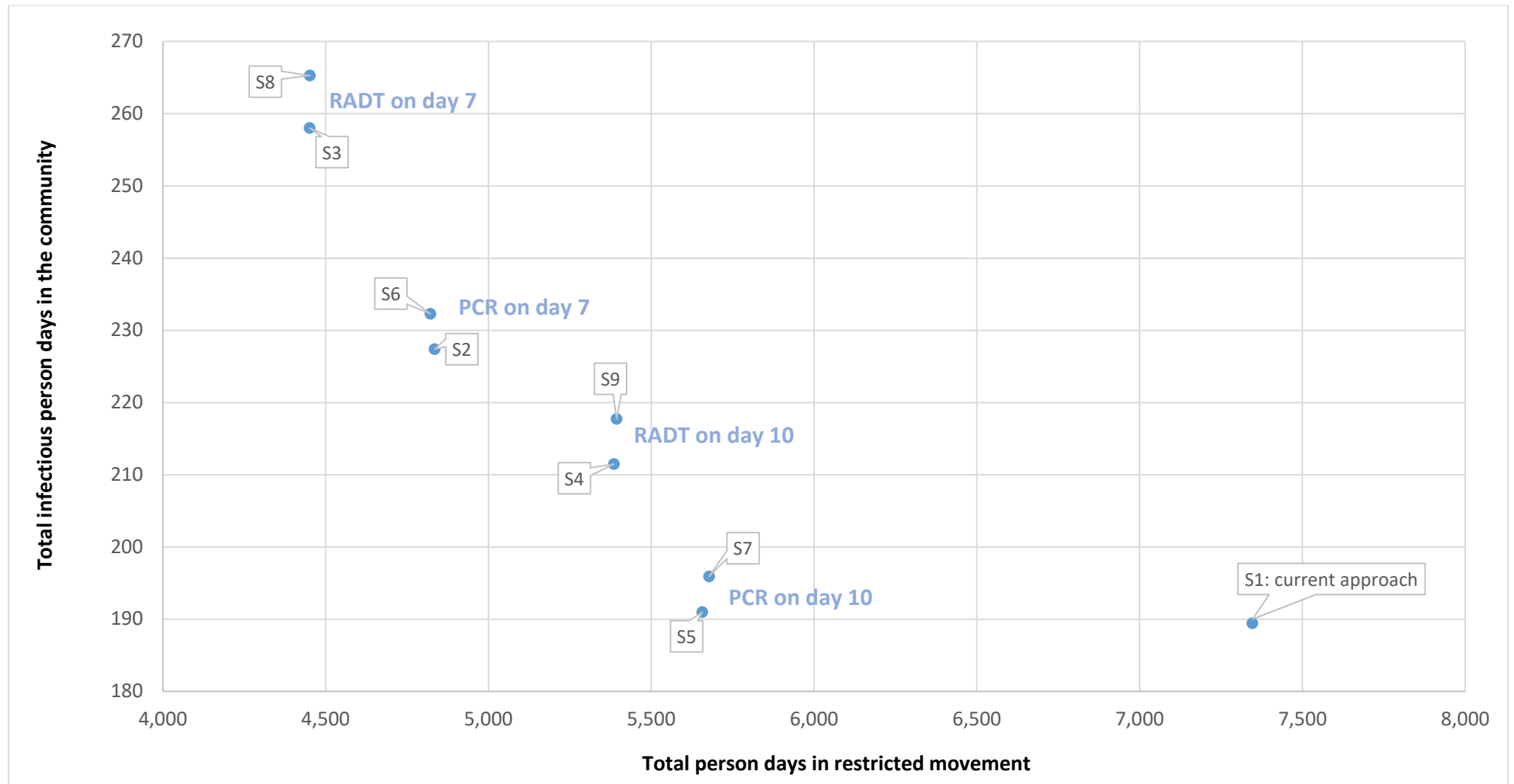
Footnotes for Figure 5: in a box and whisker plot, the box represents the interquartile range of values, with the vertical line indicating the median. Values beyond the ends of the whiskers (dotted lines) are generally classified as statistical outliers.

Person days in restricted movements versus infectious person-days in community

To provide a balanced view of the above results it is useful to consider these two estimates simultaneously. Figure 5 below presents each scenario plotted with

respect to the estimated number of person-days in restricted movements and the estimated infectious person-days in the community upon ending the restriction of movements. As highlighted across all the considered scenarios, there is a strong negative correlation between total person-days in restricted movement and total person-days of infected individuals in the community. On balance, it can be seen that relative to the comparator, those scenarios which involve an end of restricted movements on receipt of 'Day 10' 'not detected' test result provide the largest benefit (in terms of reduced number of person-days in restricted movement), relative to the lowest additional risk (in terms of infectious days in the community). The choice of test further influences results, with RT-PCR-based testing highlighting a lower risk with a lower benefit compared with RADT-based testing, which shows higher benefit, but also a higher risk. Scenarios considering an end of restricted movements on receipt of a 'Day Seven' 'not detected' test result present notably higher estimates of overall risk. It is noted within the analysis that the use of a RT-PCR or RADT as the first test ('Day Zero') has a relatively small increase in risks with little impact on the benefits (see Figure 6; scenarios five versus seven, and scenarios four versus nine). These overall results can further be considered in terms of a proportionate plane considering an increase in infectious person-days in the community relative to reduction in person-days in the restricted movements, as shown in Appendix 3.

Figure 6. Person-days of infected individuals in the community versus total person-days in restricted movement (per 1,000 close contacts of confirmed cases)



Estimation of the number of COVID-19 infections

The risk caused by infected individuals can be expressed as an approximate number of COVID-19 infections arising directly from the group of infected close contacts. The additional incremental impact of a number of the strategies is small, but it can be seen that some scenarios have a higher impact and a wider range of uncertainty (Table 8). The estimates are subject to the estimates of the reproductive number for those in restricted movement and for those who are not. The impact of varying the reproductive number on the estimates for the comparator and scenario five is presented in Appendix 4.

Table 8. Estimated new COVID-19 cases directly infected by close contacts (per 1,000 close contacts of confirmed cases)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	89	(36 to 157)	-	-
2	96	(38 to 168)	7	(1 to 15)
3	103	(42 to 177)	13	(2 to 28)
4	94	(37 to 165)	4	(1 to 10)
5	90	(36 to 157)	0	(-2 to 3)
6	98	(39 to 170)	8	(1 to 17)
7	91	(36 to 159)	1	(-1 to 4)
8	104	(43 to 180)	15	(2 to 32)
9	95	(38 to 167)	6	(1 to 13)

Number of tests carried out

Alternative strategies will have implications for the number of tests carried out. Of the scenarios modelled, the highest number of tests are generated by those which utilise a 'Day 10' test (Table 9; scenarios four, five, seven and nine). It should be noted that moving the second test from 'Day Seven' to 'Day 10' increases the number of tests, as additional individuals become eligible for a second test. Currently individuals are not referred for a second test if it falls within 24 hours of their first test; an increase in the time between these two tests is estimated to increase the number of individuals eligible for a second test.

Table 9. Total tests performed as part of contact tracing (per 1,000 close contacts of confirmed cases)

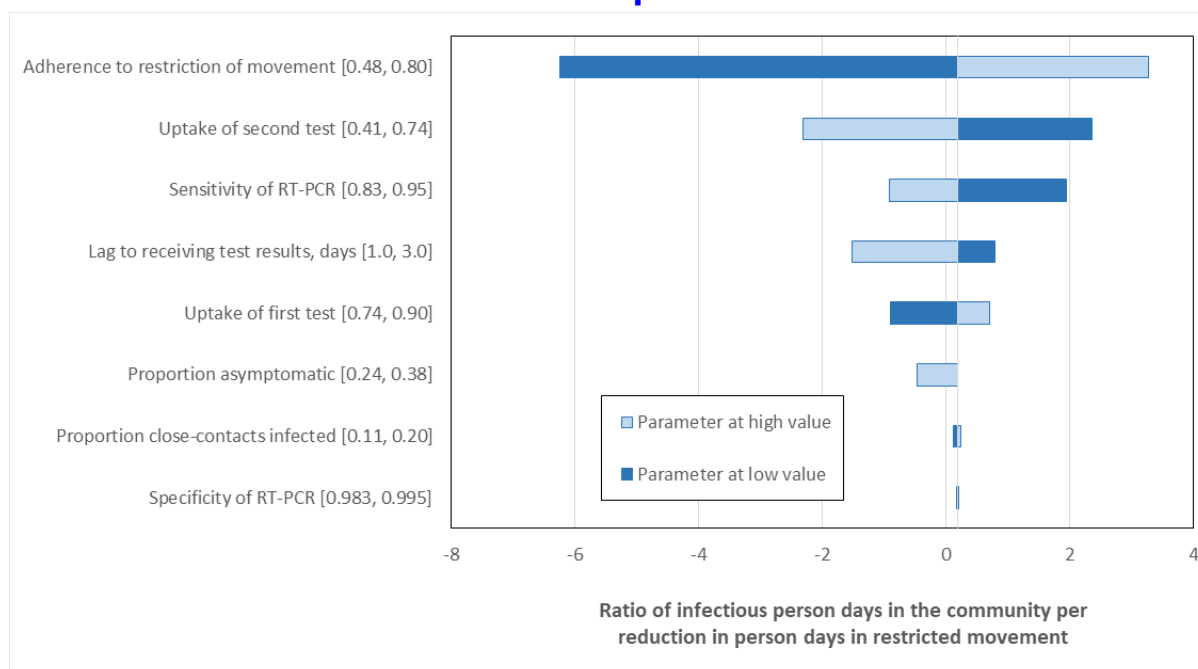
Scenario	Total RT-PCR tests		Total RADT tests		Total (combined)	
	Mean	95% CI	Mean	95% CI	Mean	95% CI
1 (comparator)	1,249	(1,097 to 1,401)	0	-	1,249	(1,097 to 1,401)
2	1,249	(1,097 to 1,401)	0	-	1,249	(1,097 to 1,401)
3	807	(722 to 879)	443	(308 to 578)	1,249	(1,097 to 1,401)
4	807	(722 to 879)	498	(346 to 651)	1,305	(1,135 to 1,469)
5	1,305	(1,135 to 1,469)	0	-	1,305	(1,135 to 1,469)
6	440	(305 to 576)	807	(722 to 879)	1,247	(1,095 to 1,397)
7	497	(344 to 651)	807	(722 to 879)	1,304	(1,136 to 1,467)
8	0	-	1,247	(1,095 to 1,397)	1,247	(1,095 to 1,397)
9	0	-	1,304	(1,136 to 1,467)	1,304	(1,136 to 1,467)

Sensitivity analysis

A one-way univariate sensitivity analysis was undertaken in which each parameter in turn was set at its upper and lower bound value while all other parameters were held at their mean value. This form of analysis can highlight the importance of parameter uncertainty on overall decision uncertainty. In all cases, scenario five (RT-PCR tests on 'Day Zero' and on 'Day 10' with end of restricted movements on receipt of a 'not detected' result from the second test) remained as the most efficient alternative to current practice in terms of minimising the increase in infectious person days in the community per reduction in person days in restricted movement.

The model is based on an underlying assumption that, in the absence of evidence or the contrary, adherence to restriction of movement is not impacted by adherence to testing, that is, that those who do not attend for testing are assumed to be no more or less likely to adhere to restriction of movements than those who do attend. Similarly, there is an assumption that those who undergo a test are fully adherent to restricted movement while awaiting the test results. When adherence to the second test is low, current practice is favoured (as cases not test detected may remain in restricted movement until day 14) while where adherence to the second test is high, scenario five is favoured (as more cases will be test detectable on 'Day 10' than on 'Day Seven', and fewer will be ineligible due to receiving their 'Day Zero' test within 24 hours of the scheduled second test). This favouring of scenario five when adherence to restricted movement is low, reflects an interaction with the timing of the second test. The parameter of lag to receiving test result has an impact on the findings (Figure 7), but is likely affected by the assumption that those who undergo a test are fully adherent to restricted movement while awaiting the test results.

Figure 7. Ratio of infectious person days in the community to reduction in person days in restricted movement for scenario 5 versus current practice



Footnotes to Figure 7: Values in brackets indicate lower and upper bounds used in sensitivity analysis. For adherence to restricted movements, the 'Day 10' figure is given for illustrative purposes. In all instances, scenario 5 leads to reduced person days in restricted movement compared to current practice. A negative ratio indicates that scenario 5 results in fewer infectious person days in the community than current practice.

Additional considerations

A number of additional considerations are outlined below which could substantially affect the model estimates provided. These considerations could not be fully accounted for through the quantitative analysis undertaken by the model. These factors should be taken into account when considering the model estimates, during decision-making processes.

Adherence to restriction of movements

An analysis was conducted within the model considering the influence of an individual's adherence to the overall duration of the period of restricted movements. Firm data related to this form of adherence is limited in the context of the COVID-19 pandemic. Adherence relates to the extent to which an individual follows the recommendations of an outlined regimen.⁽³²⁾ Adherence is typically described as a multifactorial concept possessing considerable levels of complexity in its structure.⁽³²⁾ Given this complexity, it is likely unreasonable to consider adherence to be a binary outcome of success or failure. Estimates from a UK survey of 405 individuals who

were advised to restrict movements secondary to being close contacts of a confirmed COVID-19 case, indicate that when a singular non-adherent event is factored as overall non-adherence, adherence was 10.9% (95% CI 7.8 to 13.9).⁽³¹⁾ The reasons for non-adherence provided within this survey are outlined in Appendix 5. The reasons highlighted for non-adherence outline a number of diverse influencers, including beliefs about the disease, emotional coping, and life circumstances. Conversely, from the same survey 65% of individuals highlighted an intention to restrict movements; inferring that while not fully adherent, a majority are receptive of such a recommendation. Considering the results of this survey, it must be reasoned that adherence is influenced by a range of personal, societal and behavioural factors which will vary substantially between individuals.

Time-dependent adherence to the restriction of movements

Time-dependent adherence is a potentially important concept to consider. In the context of the COVID-19 pandemic, this relates to a potential population-level decline in adherence to public health measures as the pandemic evolves. The theoretical basis for such decline has been noted by the WHO in terms of 'pandemic fatigue', defined as de-motivation to follow recommended protective behaviours, emerging gradually over time and affected by a number of emotions, experiences and perceptions.⁽³³⁾ Time-dependent results were presented within the survey by Smith et al.,⁽³¹⁾ with results remaining consistent throughout the pandemic to date; that is to say, no evidence of a decline in adherence was presented. In contrast, results from a study of adherence to self-isolation and or quarantine in Norway, suggest a time-dependent reduction in adherence as the COVID-19 pandemic has progressed.⁽³⁴⁾ The authors note that such fatigue may explain findings, but further suggest that the findings may also be explained by perceived risk; that is, as the perceived risk reduces due to a reduction in the number of cases, so does adherence to protective behaviours. Similar results have been presented from Irish data suggesting a trend relative to overall risk within the community;^(35, 36) rather than a consistent decline expected if associated with general pandemic fatigue. These findings appear in line with a systematic review of factors affecting adherence to quarantine⁽³⁷⁾, in which knowledge of disease and quarantine procedure, social norms, perceived benefits of quarantine and perceived risk of the disease were outlined as the primary influencing factors.

Adherence to testing regimen

International literature suggests disparities may exist in terms of access to testing during the COVID-19 pandemic.^(38, 39) Minority groups may be particularly susceptible to disparity in access to testing-based surveillance or screening.⁽³⁸⁾ In Ireland, testing is available free of charge with all identified close contacts of a COVID-19 case referred for testing. However, there may be disparity in the ability of individuals

to comply with testing (for example, due to difficulty getting to the testing site), and with subsequent adherence to the testing regimen. Within the model, estimates from the HSE COVID-19 CMP were used as an indicator of overall test adherence; however, adherence to a testing regimen is also likely sensitive to similar factors outlined for adherence to the restriction of movements above, such as beliefs and attitudes towards the disease and caring responsibilities. As noted this may be further influenced by aspects, such as access to transport (in Ireland transport is provided where needed however this may be associated with a delay in testing) and experience or timing of the previous test. In this way, adherence to a testing regimen is likely to vary considerably between individuals. Equally, it is likely biased to use estimations of adherence to a testing regimen as indication of adherence to restriction of movements; as an individual may not be able to attend testing, but may be restricting movements, which would underestimate adherence overall.

Socioeconomic gradient

Adherence to the duration of the restriction of movements and testing regimens may be further compounded by a socioeconomic gradient. This gradient appears well acknowledged in terms of infection rates and outcomes within the COVID-19 pandemic.⁽⁴⁰⁾ However, at present, there is limited literature when considering socioeconomic differences in adherence to public health guidance overall, and specifically to restricted movements or testing for close contacts.

Discussion

This assessment aimed to model the potential impact of a reduction in the current duration of restricted movements from 14 days, considering a number of potential testing scenarios. Overall, the results of the model indicate that compared with the current standard practice in Ireland, scenarios which permit ending the duration of restricted movements conditional on receipt of a 'not detected' RT-PCR test conducted ten days since last exposure offer the most balanced view when considering benefit (in terms of reduced person-days in restricted movement) and risk (in terms of potential infectious person-days in the community). This form of scenario would be in keeping with the updated recommendations published by the ECDC on 24 September 2020.⁽¹⁰⁾ The choice of the type of test elicits further benefit in terms of reducing person-days of restricted movement with RADT providing larger gains than RT-PCR overall, although with an increase in associated risk; however, at present this remains a hypothetical scenario as clinical validation studies of RADTs for this purpose have yet to be completed for the national Test and Trace programme in Ireland. A change to the use of a "Day 10" RT-PCR test, instead of the current 'Day Seven' test, would have further organisational implications as the number of people eligible for a second test would increase, thereby increasing the overall number of tests conducted. Currently the number of 'Day Seven' tests is

substantially reduced as their timing falls within 24 hours of the first test. A number of additional considerations that could impact adherence with either testing or restriction of movements which could not be fully accounted for within the model are also outlined which should be considered within any decision-making processes: adherence to restricted movements, adherence to testing, time-dependent factors, and potential socioeconomic gradients.

It is useful to consider the use of a 'Day 10' test in terms of its overall meaning in real world practice. With regards to a 'Day 10' RT-PCR test, and release on receipt of a 'not detected' result, the receipt of this test result is likely to take approximately two days from the time the swab is taken; therefore the actual duration of restricted movements would only be reduced, on average, to 12 days. The use of a validated RADT would mean a near instantaneous result, with an end of restriction of movements on the same day as the test is taken. However, given the lower anticipated sensitivity of such tests, there is a notable increase in the risk associated with this scenario in terms of the number of potentially infectious days for individuals re-entering the community.

It must further be considered that this modelling exercise did not explicitly estimate the impact on the contact tracing processes in Ireland. Should close contacts of an index case test positive, in turn, their close contacts must be identified and tested. The use of a 'Day 10' test as opposed to a 'Day Seven' test could delay this process and potentially have negative implications for contact tracing. However, as the close contact should already be restricting their movements, the influence of this longer interval between tests may not be significant. Conversely, lengthening the time duration between the first and second tests would increase the number of people receiving a second test. Current HSE CMP COVID-19 data suggests that the majority of individuals not referred for a second test is due to this test (current 'Day Seven') falling within 24 hours of the first test, or contacts not being identified until at least six days post-exposure.

Decisions regarding the appropriate duration of restricted movements for a close contact of a COVID-19 must be carefully considered in relation to the personal, societal and disease impact. A longer duration than needed can have negative impacts on the person in terms of psychological impact, while work absenteeism will further impact societal outcomes.⁽⁵⁾ Conversely, durations which are too short may increase potential transmission risk with individuals re-entering the community while infectious, or pre-infectious. Recommendations put forward for a 14-day duration of restricted movements for a close contact of COVID-19 are largely inferred from estimates of the upper bound of the incubation period of the disease; that is, when a growing proportion of people are likely to develop symptoms and be identified.^(26, 41) However, such recommendations are made on the basis of disease epidemiology alone without consideration of testing strategies which could influence this duration.

Naturally, any change from the current duration will carry an inherent residual risk given limitations of the available tests for SARS-CoV-2 detection (that is, they are not 100% sensitive).⁽¹⁰⁾ The decision regarding what constitutes an acceptable rate of potentially missed cases, and possibly infectious individuals re-entering the community, is one which requires a balance between the potential impact of the disease and the impact on the person and society.^(4, 42) Such decisions should reflect a form of risk-based assessment with careful consideration of all elements. The scenarios highlighted above, that include the use of a 'Day 10' test, constitute those which present the least risk (in terms of potential onward transmission) balanced with the most benefit (in terms of reduced person-days restricting movement) from the options presented. Policy decision-making could infer that a larger risk is merited on the grounds of a greater overall benefit for the individual; or equally that the residual risk associated with any of the presented scenarios is unjustified in the context of the turbulent disease course, inferring no change to the current approach. Further attention should also be given to particular groups and circumstances where any residual risk may not be considered acceptable, such as in high-risk congregated settings or for healthcare workers.

As noted, in Ireland RADTs are not currently being used for the diagnosis of COVID-19. However, a recent HIQA rapid HTA outlined potential benefits in their use, in terms of time and resources, should an appropriate test be sourced and validated.⁽¹⁴⁾ The WHO has set out minimum acceptable performance criteria of $\geq 80\%$ sensitivity and $\geq 97\%$ specificity; in reference to the lower bound of their confidence intervals;^(13, 20) a higher desired minimum may be defined as acceptable by individual countries. These performance measures are relative to the reference standard, RT-PCR, therefore reflecting a larger risk overall as returned within the present model. Use of RADTs infers a near instantaneous end of restricted movements given a rapid return of results which is beneficial in terms of person-days; however, it further considers a higher risk. Should a suitable RADT be identified for potential use in Ireland, the blended scenarios with both RADT and RT-PCR presented within this report may offer opportunities to support validation and to assess the logistical impact of their use.

Within the current model, estimates were included to enable analysis of the scenarios with consideration of adherence both to the testing regimen and the overall duration of restricted movements. Previous modelling studies have neglected these elements and considered complete, or near complete, adherence with both aspects which does not decline or vary over time.^(12, 43, 44) These assumptions result in a potential bias which overestimates the benefit and underestimates the overall risk. In terms of adherence to testing, data from the HSE COVID-19 CMP highlights that although there is reasonable adherence to the first test, this declines sharply for a second test. The reason for this is not clear; however, an increased duration in the

timeframe between tests may theoretically improve adherence, as for a proportion of individuals the timing of this second test is relatively soon after the first test, or in receiving first test results. Furthermore, the incentive of a potentially reduced period of restricted movements may further improve second test attendance. As noted within the additional considerations of this report, it is doubtful that there is full or near full adherence to the duration of restricted movements, with a large variation in adherence within the population likely. There is limited evidence to suggest that a shorter duration of restricted movements would directly influence adherence.⁽³⁷⁾

There is, however, evidence to suggest that factors such as knowledge of the disease, knowledge about quarantine (restricted movements) procedure, social norms, perceived benefits of quarantine (restricted movements) and perceived risk of the disease influence adherence during disease outbreaks.⁽³⁷⁾ Additionally, practical issues such as the financial consequences of being out of work are further highlighted as related to non-adherence. Irish data regarding motivations for adherence and non-adherence to public health recommendations during the COVID-19 pandemic are lacking at present. However, there are data to suggest that generally there is ongoing support from the majority of the population for recommendations provided.^(35, 36, 45) For the scenarios presented within this report, clear communication of the reasoning behind the testing procedure coupled with the accompanying incentive of a reduced duration of restricted movements, and further proximity from a first test, may therefore promote and increase overall adherence.

Finally, it must be stressed that the results of this report are contingent on the use of testing and therefore adherence to the testing regimens presented. Should the scenarios within this report be considered viable alternatives to the current approach, an individual who does not adhere to testing should continue to restrict their movements for the full 14-day duration. That is to say, a reduction in the duration of restricted movements in the absence of testing should not be recommended. This reasoning is outlined in a previous HIQA evidence synthesis indicating that it takes 14 days for approximately 95% of individuals who will become symptomatic to do so, alongside supporting evidence from international public health guidance, and the views of the HIQA COVID-19 Expert Advisory Group.

Limitations

Context of data

The model incorporates parameter data in a manner intended to capture uncertainty in the true values. While variability across patients is modelled, there is an averaging effect in aggregating results to a group level. The data are a mixture of international and Irish-specific estimates and reflect what is known at this point in time. It is evident that there have been quite substantial shifts over time in the demographic characteristics of those infected with SARS-CoV-2 in Ireland. As such, the

characteristics of infection may differ from what is understood from the available data, which largely reflects the older group affected by the first wave. This changing pattern may have a substantial impact over time on the estimates presented within this report.

Of note, it may be highlighted that a conservative estimate of the basic reproductive number, R_0 , was included within the model to generate estimates of potential direct onward infections. However, this estimate is only used to provide a numerical representation and any increase in the R_0 would have a proportioned increase in numbers of infection across all scenarios, including the base case comparator scenario of current practice in Ireland. Furthermore, the model only considered direct onward infections from an infected case, this in turn could result in a considerable amount of wider community level transmission with further onward infection from those infected by this index case.

Data quality

The model included numerous parameters. The data supporting the parameter estimates came from a wide range of heterogeneous sources. Many were derived from observational studies which were not always designed to estimate the parameter of interest. A key distinction that frequently occurs is the difference between the last date of exposure and the date of exposure that lead to the infection. The difference between the two may be a matter of a day or two, but that becomes important in understanding the latent period, incubation period and critically the point at which an infected individual becomes infectious. It is also important to note that the available data describes the course of infectious individuals in a wide range of settings and population groups, not all of which may be applicable to an Irish setting. While characteristics of the infection itself should perhaps be similar across populations, those aspects that are affected by human behaviour could vary immensely. Of particular relevance are adherence to control measures and testing. The model presented here used uncertainty around parameter estimates to explore uncertainty in the relative effects of the different scenarios modelled.

Infectivity

An important consideration in the spread of COVID-19 is the period and magnitude of infectivity in an index case. The estimates of duration of infectivity implicitly acknowledge that viral load declines over time to the extent that an individual may no longer be infectious, but can still test positive with RT-PCR. It is plausible that peak infectiousness may occur early in the infection, as demonstrated by the proportion of onward infections that occur prior to symptom onset.⁽⁴⁶⁾ However, it is worth considering that the propensity to infect and the opportunity to infect are distinct, and that symptomatic cases will typically self-isolate, reducing the

opportunity to transmit disease. The reported data likely reflect the fact that both propensity and opportunity to infect decreases over time. In the absence of data on the magnitude of infectiousness, we have modelled uniform infectiousness for an individual over the period for which they are considered infectious. In the event that infectiousness is greater prior to and at the point of symptom onset than after symptom onset, the impact is that the model may have overestimated the benefits of 'Day 10' testing, relative to 'Day Seven'. However, in the absence of good supporting data, we have taken a conservative approach and assumed that propensity to infect is constant, but the opportunity is reduced by restricted movement or self-isolation.

Uptake and adherence

The extent to which close contacts adhere to restricted movement and can avail of the offered tests is clearly a significant factor. We could not identify applicable data on adherence to restricted movement. The uptake of the so-called "Day Zero" test indicates a large proportion of people present for testing, and may be reflective of a high willingness to follow guidance. The large drop from 'Day Zero' to 'Day Seven' may be suggestive of poor adherence, or it may reflect a range of factors, including proximity to the first test. Another aspect to consider is that the demographics of cases and close contacts has changed over time, and is likely to continue changing. The balance of benefits and harms associated with adhering to restricted movement will be interpreted differently by people depending on their perception of the risk of poor outcomes and the impact on daily activities, such as work. Setting adherence to restricted movement and uptake to testing at high and low values did not change the interpretation that a move to 'Day 10' RT-PCR testing would lead to a substantial reduction in the burden of person-days in restricted movement and a modest increase in the number of infectious person-days in the community.

Characterisation of the pathway

Describing the management pathway of close contacts of confirmed cases is challenging. There is substantial variation across individuals in terms of when they are identified and undergo the 'Day Zero' test, whether they present for testing, whether they present for a second test, and how long it takes to get test results. It is not possible at this point to determine the extent to which there are associations between different characteristics. For example, is it possible to predict which cases are unlikely to present for 'Day Seven' testing based on the interactions up to 'Day Seven'? It is also a dynamic situation because of changes to the system, such as reductions in the time from testing to the receipt of results, or capacity constraints on the numbers of contacts that can be followed up. We have attempted to characterise the management pathway based on recent activity in the contact management programme, but acknowledge that the findings from this point in time

may no longer be applicable if there are substantive changes to the contact management programme.

Correlation between variables

As the various parameter estimates were each derived independently, we have assumed that they are not correlated. That is, that an individual with a long latent period may also have a long pre-symptomatic infectious period. Certain correlations could be important, such as if asymptomatic cases had a longer infectious period, as this would imply that in the absence of being test-detected or adhering to restricted movement that they could infect many individuals. In terms of future research and potentially to aid understanding of individuals described as superspreaders, it would be useful for studies to consider the extent to which infection characteristics are correlated.

Conclusion

This report aimed to estimate the potential impact of reducing the duration of restricted movements, through a number of testing scenarios and for individuals identified as close contacts of a COVID-19 case. Overall, relative to the current standard of practice in Ireland, the estimates presented within this report suggest that the use of RT-PCR tests on 'Day Zero' and 'Day 10' with an end of restricted movements on receipt of a 'not detected' result from the second test would present the highest benefit (in terms of reduced person-days in restricted movements) and lowest risk (in terms of infectious person-days in the community) of the scenarios considered. The identification and validation of a suitable RADT test may offer further benefits overall, although with a noted increase in risk relative to a 'Day 10' RT-PCR test. Such 'Day 10' test scenarios were associated with an increase in the total number of tests conducted relative to the current standard practice in Ireland. Scenarios which involve an end of restricted movements on receipt of a 'Day Seven' result were noted to have a high benefit, but were associated with a notably higher risk overall.

Additional factors identified which could not be fully accounted for within the model, but should be considered in overall decision-making included: adherence to duration of restricted movements, adherence to testing regimens, and socioeconomic gradients. It should be further noted that the model did not assess the impact of a change in testing scenario on the current contact tracing process in Ireland. Policy decision-making as to what constitutes an acceptable level of risk overall could dictate the preferred use of other scenarios examined, or equally an unjustifiable risk associated with any scenario presented relative to current practice.

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Appendix 1. Additional scenarios and model estimates

A number of additional scenarios were included within the model which may be of interest to the reader. An outline of these scenarios, and the resulting estimates from model are outlined below.

Additional scenario descriptions

- Scenario 10: the addition of a 'Day 10' RT-PCR test to the current testing regimen, maintaining the 'Day Zero' and 'Day Seven' RT-PCR tests, with ending of the period of restricted movements on receipt of a 'not detected' result from the test conducted on 'Day 10'
- Scenario 11: ending the period of restricted movements on 'Day 10' with receipt of a 'not detected' RT-PCR test result from the test conducted on 'Day Seven' post-exposure.
- Scenario 12: using a rapid antigen detection test (of pre-specified lower limits of test sensitivity and specificity) on day eight as an alternative to the 'Day Seven' RT-PCR test while maintaining the 'Day Zero' RT-PCR test. Ending of restricted movements on receipt of 'not detected' test result on day eight.
- Scenario 13: using a rapid antigen detection test (of pre-specified lower limits of test sensitivity and specificity) on day nine, as an alternative to the 'Day Seven' RT-PCR test while maintaining the 'Day Zero' RT-PCR test. Ending of restricted movements on receipt of 'not detected' test result on day nine.

Table App1.1. Scenarios descriptive

Scenario	First test*	Second test^	Third Test	End of restriction of movements
10	Day 0- RT-PCR	Day 7- RT-PCR	Day 10- RT-PCR	Receipt of ND day 10 test
11	Day 0- RT-PCR	Day 7- RT-PCR		Day 10
12	Day 0- RT-PCR	Day 8- RADT		Receipt of ND day 8 test
13	Day 0- RT-PCR	Day 9- RADT		Receipt of ND day 9 test

Table App1.2. Total person-days in restricted movement (per 1,000 close contacts of confirmed cases)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	7,346	(6,039 to 8,594)	0	-
10	5,899	(4,856 to 7,237)	-1,447	(-1,965 to -949)
11	4,852	(3,945 to 6,037)	-2,494	(-3,332 to -1,682)
12	4,659	(3,822 to 5,881)	-2,687	(-3,464 to -1,929)
13	4,991	(4,190 to 6,124)	-2,355	(-3,053 to -1,635)

Table App1.3. Total person-days for infected individuals not in restricted movement (per 1,000 close contacts of confirmed cases)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	189	(123 to 270)	0	-
10	187	(124 to 262)	-2	(-20 to 6)
11	216	(144 to 302)	27	(16 to 41)
12	239	(161 to 335)	49	(30 to 75)
13	222	(150 to 310)	32	(17 to 51)

Table App1.4. Estimated new COVID-19 cases directly infected by close contacts (per 1,000 close contacts of confirmed cases)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	89	(36 to 157)	0	-
10	89	(35 to 156)	0	(-5 to 2)
11	94	(37 to 165)	5	(1 to 10)
12	98	(39 to 171)	9	(1 to 19)
13	96	(38 to 167)	6	(1 to 14)

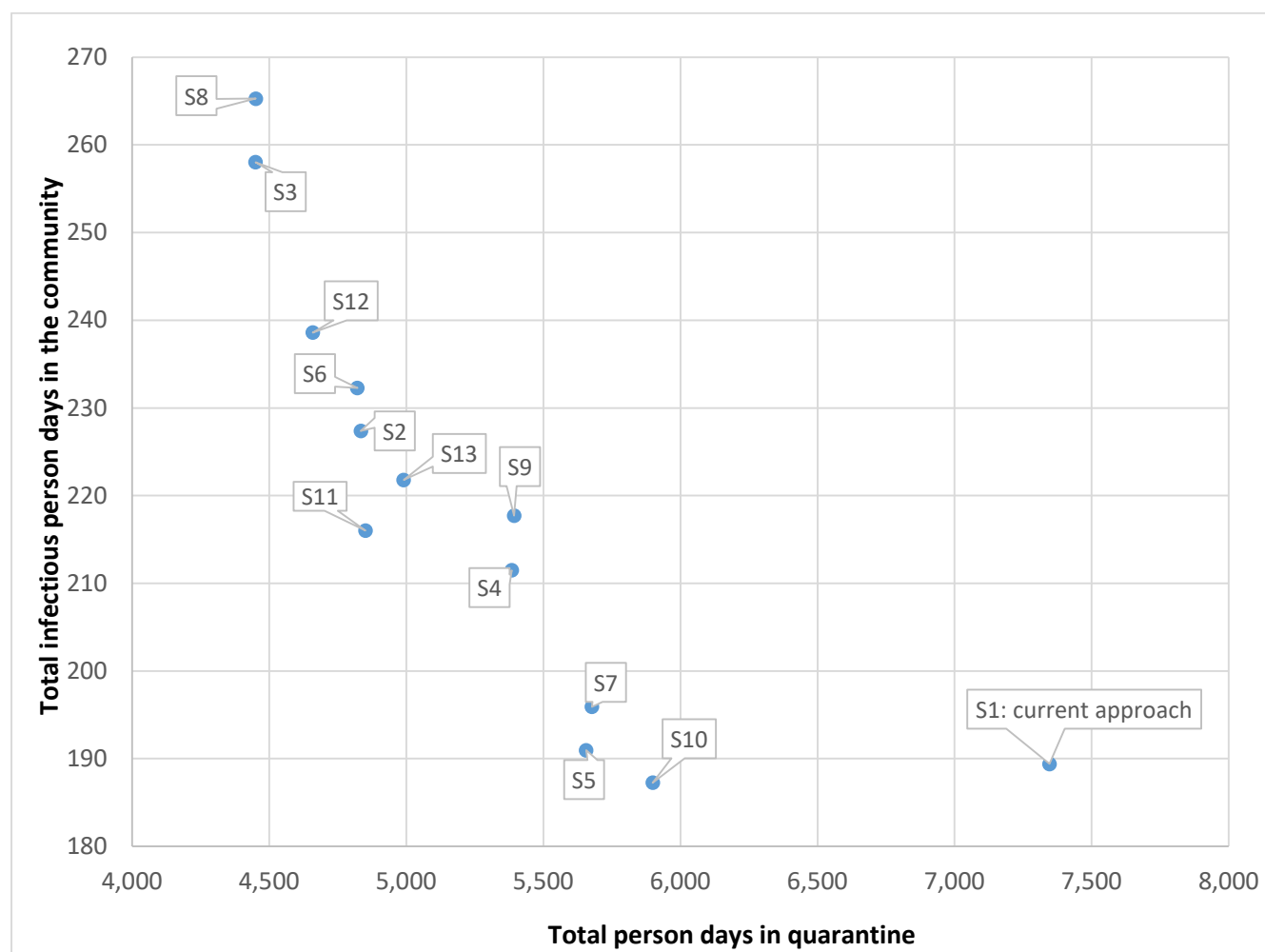
Table App1.5. Total tests performed as part of contact tracing (per 1,000 close contacts of confirmed cases)

Scenario	Total RT-PCR tests		Total RADT tests	
	Mean	95% CI	Mean	95% CI
1 (comparator)	1,249	(1,097 to 1,401)	0	-
10	1,586	(1,395 to 1,772)	0	-
11	1,249	(1,097 to 1,401)	0	-
12	807	(722 to 879)	470	(326 to 614)
13	807	(722 to 879)	487	(339 to 638)

Table App1.6. False-positive test results (per 1,000 close contacts of confirmed cases)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	11	(5 to 19)	0	-
10	14	(7 to 24)	3	(1 to 6)
11	11	(5 to 19)	0	-
12	14	(7 to 27)	3	(0 to 13)
13	14	(7 to 27)	3	(0 to 14)

Figure App.1. Person-days of infected individuals in the community versus total person-days in restricted movement (per 1,000 close contacts of confirmed cases)



Appendix 2. False-positive test results

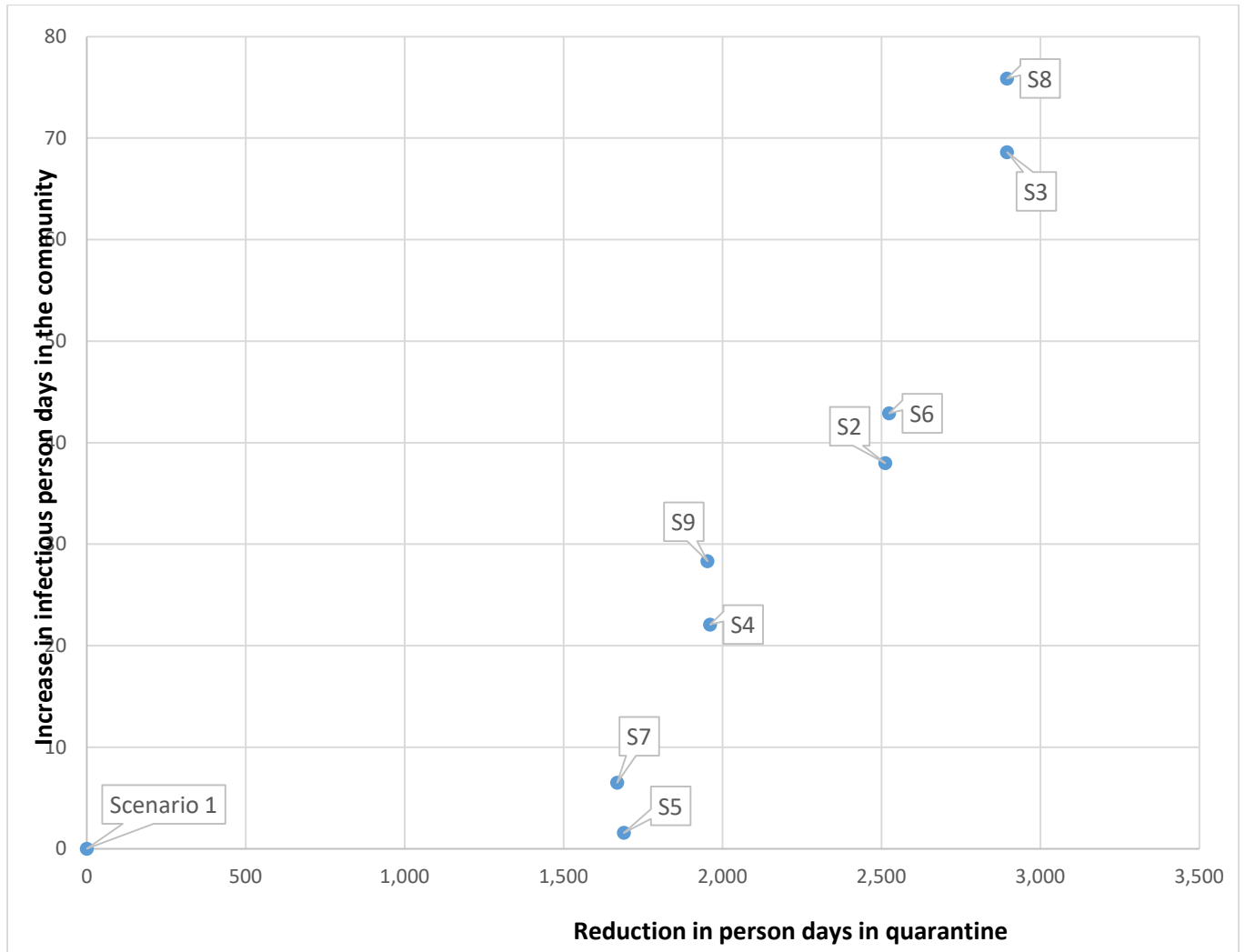
For every 1,000 close contacts of a confirmed COVID-19 case, it is anticipated that approximately 150 will be infected and 850 will not. Although both of the tests are quite specific, (that is, they perform well at identifying people who are not infected), there will be false-positives associated with testing. That is, people who do not have COVID-19 will be notified that they are infected and should self-isolate. The expected number of false-positives is low, ranging from an average of 11 to 19 across all scenarios modelled (Table 1).

Table App2.1. False-positive test results (per 1,000 close contacts of confirmed cases)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	11	(5 to 19)	0	-
2	11	(5 to 19)	0	-
3*	13	(6 to 25)	2	(0 to 12)
4*	14	(7 to 28)	4	(1 to 14)
5	11	(6 to 20)	1	(0 to 1)
6*	15	(6 to 32)	4	(0 to 20)
7*	16	(7 to 33)	5	(1 to 21)
8*	18	(7 to 42)	7	(0 to 31)
9*	19	(7 to 45)	8	(1 to 34)

*scenario includes RADT

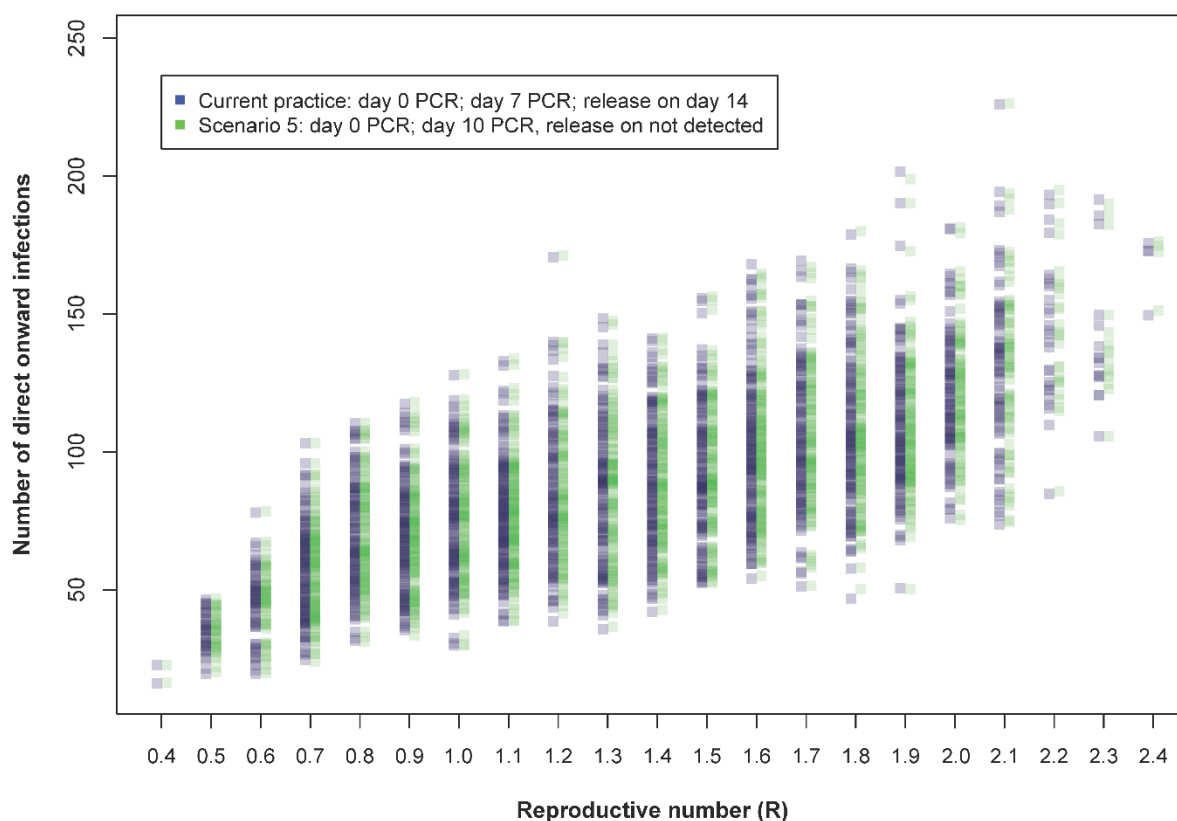
Appendix 3. Plane - increase in infectious person-days in the community relative to reduction in person-days in the restricted movements



Appendix 4. Estimates of direct onward infection with variations in the reproduction number

Based on the contact tracing data, approximately 15% of close contacts are infected. The model simulated a cohort of 1,000 close contacts, so on average 150 of those close-contacts would be individuals infected with COVID-19. The mean number of direct onward infections under the current scenario was 89 – that is, 150 infected close contacts will directly infect 89 people. That implies a reproductive number (R) of 0.59 for infected close contacts, taking into account adherence to restriction of movement, asymptomatic cases, and other factors. The calculation of onward infections used separate values for R for those restricting and not restricting movement, assuming that all symptomatic cases restrict movement on symptom onset. The values used implied an overall R of approximately 1.1 which is higher than that observed when extensive infection control measures are in place, but lower than was observed at the outset of the epidemic. We explored a wider range of R values to determine the impact on onward infections. Clearly, doubling the value of R will on average double the number of onward infections. There is substantial variation in the number of onward infections for a given R value, which is influenced the difference between R for those restricting and not restricting movement. Scenarios one (current practice) and five (day zero and day 10 PCR with release on not detected) generate an almost identical number of onward infections and that is consistent for a range of R values (Figure 4.1).

Figure App 4.1. Impact of varying R on the number of onward infections.



Appendix 5. Self-reported reasons for not adhering to quarantine as a close contact from UK survey*

Self-reported reasons for not quarantining in the 14 days after being contacted by the NHS contact tracing service (participants could select multiple response options)	%
I couldn't stay away from other people in my household, so didn't think it was necessary for me to stay away from people outside my household	14.3
I didn't develop any symptoms	11.9
To go to the shops, for groceries/pharmacy	10.9
To go to the shops, for things other than groceries/pharmacy	10.6
I had just finished self-isolating because I had been in contact with a different confirmed coronavirus case	10.9
To go for a walk or some other exercise	10.6
For a medical need (other than coronavirus)	10.4
I thought I have already had coronavirus and thought I was immune	10.4
To help or provide care for a vulnerable person	9.9
I didn't think it was necessary for me to self-isolate (not leave the home at all)	9.9
I thought it was unlikely that I had coronavirus	9.9
It had been 7 days or more since I had seen the person with a confirmed coronavirus case	9.9
I thought 14 days is too long	9.4
To go out to work	8.9
I was too depressed or anxious	8.4
I was too bored	8.4
To meet up with friends and/or family	7.4
I only developed mild symptoms	7.4
I was too lonely	6.9
I have a child and needed to look after them	6.7

*Results from Smith et al.⁽³¹⁾

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