Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Potential impact of different testing scenarios and durations of mandatory home quarantine for people travelling to Ireland from non-designated states

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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, Equality, Disability, Integration and Youth, 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

CI	confidence interval
CIDR	Computerised Infectious Disease Reporting
COVID-19	Coronavirus disease 2019
HIQA	Health Information and Quality Authority
HSE	Health Service Executive
HPSC	Health Protection Surveillance Centre
HTA	health technology assessment
NCPP	National Clinical Programme for Pathology
NPHET	National Public Health Emergency Team
RADT	rapid antigen detection test
RT-PCR	reverse transcription-polymerase chain reaction
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2

DRAFT: Potential impact of different testing scenarios and durations of mandatory home quarantine for people travelling to Ireland from non-designated states

Key points

- A number of travel restrictions have been implemented in Ireland to protect public health and mitigate against the risk of SARS-CoV-2 from entering the country. With the exception of certain exemptions, anyone arriving into the country is subject to a mandatory 14 day quarantine. For people who have not travelled through a designated country in the previous 14 days, the quarantine period may be reduced on receipt of a 'not detected' RT-PCR test result if the test is taken no less than five days after arriving in the country.
- This analysis, in the form of a modelling exercise, aimed to assess the potential impact of different testing scenarios and durations of mandatory home quarantine. For individuals travelling to Ireland from non-designated states, these scenarios included increasing the minimum duration of quarantine from five to ten days for those who avail of testing and receive a 'not detected' RT-PCR test result.
- The estimates presented within this analysis suggest that increasing the minimum duration of quarantine to ten days will result in a substantially increased burden of days in quarantine (from 5,100 to 8,800 days per 1,000 people) with a limited benefit in terms of a reduction in infectious person-days in the community (from 25 down to 17 days).
- The addition of a 'Day 0' test, either RT-PCR or a rapid antigen detection test, would provide little or no additional benefit in terms of reducing the number of infectious person-days in the community.
- There is substantial uncertainty in relation to three key factors:
    - the uptake of the existing 'Day 5' test; the reported uptake of testing is very low at 35%, although this is likely an underestimate of actual uptake as a proportion of passengers will transit through the state before Day 5, while others will either be exempt from quarantine or avail of testing through alternative means.

  - adherence to quarantine; no evidence was identified for the adherence to mandatory quarantine
  - and the timing of exposure when abroad or in transit.

- For those who wish to avail of testing (to test out of quarantine), any decision to increase the minimum duration of quarantine from five days should be informed by evidence on the adherence to quarantine and uptake of testing among people travelling into Ireland from non-designated states. Since the end of November 2020, there has been a trend of increasing risk of infection in people travelling to Ireland, and this should also be monitored to determine if a change in practice is required.

DRAFT: Potential impact of different testing scenarios and durations of mandatory home quarantine for people travelling to Ireland from non-designated states

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 (NPHET) and the Health Service Executive (HSE). The advice takes 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 the NPHET:

> "To examine whether a single test at Day 5 post arrival in Ireland remains the most appropriate approach to testing for those travelling from non-designated states, who are subject to home quarantine"

This report summarises a modelling exercise that estimates the potential impact of different testing scenarios and durations of quarantine for passengers arriving in Ireland (by sea and air) from non-designated states, who are subject to home quarantine.

The output of the analysis will be provided for consideration by the National Clinical Director for Health Prevention to inform her advice to NPHET.

Background

A number of travel restrictions have been implemented in Ireland to protect public health and mitigate against the risk of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) from entering the country. All non-essential international travel is currently advised against,[(1)] while anyone arriving in the country must complete a Coronavirus disease 2019 (COVID-19) Passenger Locator Form for the purposes of contact tracing and ensuring passengers adhere to mandatory quarantine requirements.[(2)] Passengers must also provide evidence of a negative or 'not detected' pre-departure COVID-19 reverse transcription polymerase chain reaction (RT-PCR) test result, which must have been carried out up to 72 hours before arriving in the country – although some exemptions have been made for international transport workers, patients travelling for urgent medical care, children aged six and under, among some other groups (see Appendix 1).[(2)]

Upon arriving in Ireland, anyone who has been overseas in the 14-days prior to entering the country is subject, by law,[(3)] to mandatory quarantine requirements, with some limited exemptions (Appendix 1). Since 4 February 2021, it has been a

legal requirement that passengers complete 14 days 'home quarantine' at an address specified on the passenger locator form. Passengers arriving overland from Northern Ireland are also required to quarantine, unless their journey originated there.[2] During the quarantine period, it is only possible to leave the place of residence for unavoidable reasons such as an emergency situation which involves protecting a person's health or welfare, or to leave the State.[2] The quarantine period may be reduced on receipt of a 'not detected' RT-PCR test result if the test is taken no less than five days after arriving in the country. If a positive or 'detected' test result is obtained, passengers must begin a period of self-isolation, in line with Irish guidelines for laboratory-confirmed cases of COVID-19 (that is, self-isolate for 10 days from onset of symptoms with last five days without a fever, or from date of test if asymptomatic).[4] Passengers that do not comply with home quarantine regulations can be fined up to €5,000 or serve a prison sentence of up to six months, or both.[5]

The requirement to quarantine at home is currently in effect until 9 June 2021 for most passengers arriving in Ireland. However, stricter mandatory quarantine requirements were introduced on 26 March 2021 to mitigate against the risk of importing SARS-CoV-2 from countries particularly exposed to the virus, as well as new variants of concern (VOCs),[6] which have been shown to be more transmissible and which may reduce the effectiveness of COVID-19 vaccines.[7] Initially, 31 countries were designated as high risk due to the high incidence levels of the disease and VOCs in these countries (referred to as 'Category 2' countries), although this increased to 71 countries on 4 May 2021.[1] On 8 May, two additional countries/territories were added to the list (effective from 12 May), while 11 designations were revoked with immediate effect. The list is frequently revised to reflect the changing situation with respect to incidence and VOCs worldwide (the complete list of designated states, as of 17 May 2021, is provided in Appendix 2).[1]

Passengers that have spent time in a designated state at any time in the previous 14 days, or travelled through an airport or port in a designated state are required to complete 14 days 'mandatory hotel quarantine'.[6] Mandatory hotel quarantine must be completed at a designated facility, which must be booked and paid for in advance of travelling to Ireland. Similar to 'home quarantine', the duration of quarantine may be reduced on receipt of a 'not detected' RT-PCR test result, but only if the test is taken no less than 10 days after arriving in the country. Passengers that arrive from non-designated states (referred to as 'Category 1' countries) without a 'not detected' RT-PCR test result are also subject to mandatory hotel quarantine, but can complete their quarantine at home on receipt of a 'not detected' test result, which is typically taken on the first day in quarantine.[8] In the event that a 'detected' test result is obtained, passengers must complete a period of self-isolation in the designated facility.[6] Anyone that resists being brought to quarantine or leaves a designated

facility without authorisation may be fined up to €2,000, imprisoned for one month, or both.[5]

A limited number of exemptions from mandatory hotel quarantine have been made to recognise fully vaccinated people, for example, as well as families travelling with new-born babies (no more than 28 days old), including those arriving from designated states for the purpose of surrogacy.[6] However, in these situations, passengers must still provide evidence of a 'not detected' pre-departure RT-PCR test result and complete a period of self-quarantine at an address specified on the passenger locator form. (Details of all travel restriction exemptions are provided in Appendix 1.)

For passengers arriving from non-designated States, who are subject to a minimum duration of five days home quarantine, the proportion of infected passengers that may be detected either during the quarantine period or following testing on day five may be low. However, prolonged durations of home quarantine, with minimal oversight, may be associated with diminished adherence. The aim of this report is to assess, through a modelling exercise, the potential impact on transmission risk and resource requirements of different testing scenarios and durations of quarantine for people travelling to Ireland (by sea and air) from non-designated states, who are subject to home quarantine.

Methods

A modelling exercise was undertaken to estimate the potential impact of different testing scenarios and durations of mandatory home quarantine based on a range of pre-specified scenarios. Below is a summary of the four key elements underpinning the model: population, outcomes, scenarios considered, and estimates for included parameters.

Population and setting

This modelling exercise considers outcomes for individuals travelling to Ireland from non-designated states, by sea or air, who are infected or become infected during transit. In the base case analysis it was assumed that the transmission of SARS-CoV-2 occurred during transit, rather than before departure. A separate scenario analysis was conducted where it was assumed infection occurred prior to travel.

Outcomes of interest

The model estimates the following clinical and organisational outcomes of interest, relative to the base case comparator of test on day five with release from quarantine on receipt of a 'not detected' test result:

- probability of undetected cases being released from quarantine
- total number of infectious-person days in the community
- total number of person days in self-isolation or quarantine
- number of RT-PCR tests carried out
- number of false positives
- resource requirements in terms of support staff to manage or supervise testing.

Base case analysis and testing scenarios

The model considers the currently implemented test on day five with release from quarantine on receipt of a 'not detected' RT-PCR test result as the base case (comparator). The analysis considers a number of other potential approaches for those entering the country from non-designated states, including a test on day ten with release on receipt of a 'non-detected' test result as is the requirement for people travelling from designated states. In all scenarios, RT-PCR tests are considered.

Specifically, six core scenarios are modelled:

- Scenario one (comparator): test on day five with release on receipt of a 'not detected' test result, release on day 14 otherwise.

- Scenario two: test on day six with release on receipt of a 'not detected' test result, release on day 14 otherwise.
- Scenario three: test on day seven with release on receipt of a 'not detected' test result, release on day 14 otherwise.
- Scenario four: test on day eight with release on receipt of a 'not detected' test result, release on day 14 otherwise.
- Scenario five: test on day nine with release on receipt of a 'not detected' test result, release on day 14 otherwise.
- Scenario six: test on day ten with release on receipt of a 'not detected' test result, release on day 14 otherwise.

For each scenario, an alternative approach is modelled that additionally includes a day zero test (that is, test on arrival in Ireland, which is consistent with the approach taken for passengers arriving from designated states).[4, 5] The use of a day zero test assumes that exposure to infection occurred a number of days before travel. Scenarios involving a day zero test were further split into the day zero test being either an RT-PCR test or a rapid antigen detection test (RADT) followed by a confirmatory RT-PCR for those returning a positive test result on the RADT.

Model parameters

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

Disease factors

A summary of the parameter estimates for each relevant disease factor is provided in Table 1.

- 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 (symptomatic cases)

  The duration of infectiousness is split into two periods: pre- and post-symptom onset. These two periods are 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 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 period and the latent period. The post-symptom onset infectious period is the duration of infectiousness once symptoms have developed. While it was assumed that a person was equally likely to transmit SARS-CoV-2 throughout the infectious period, it is highly likely that the profile of infectiousness changes over time. This is partly implicit in the data, as the duration of infectiousness is estimated from 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 self-isolation. A recent analysis of duration of the proliferation and clearance phases in COVID-19 cases with and without the alpha variant suggests a longer period of infectiousness; however, this study comprised 65 participants, only seven of whom had the alpha variant, so there is substantial uncertainty with respect to these estimates.[9] A sensitivity analysis was undertaken to incorporate the potentially longer duration of infectiousness reported in that study.

- Duration of infectiousness (asymptomatic cases)

  This denotes the period that an asymptomatic individual is infectious, which commences once the latent period ends. The total infectious period for asymptomatic individuals was assumed to be equivalent to sum of the pre-symptomatic and the post-symptom onset infectious periods in symptomatic individuals.

- 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 are based on the findings of a systematic review,[10] and are consistent with the proportion of asymptomatic cases estimated in an Irish sero-prevalence study.[11]

- Rate of infection in people travelling to Ireland

  To determine the impact of different strategies of testing and release from quarantine, it is essential to consider the risk of infection in people travelling into Ireland. 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 may be required to quarantine with little gain in terms of reduced disease transmission. Conversely, in a group with a high risk of infection there could be a substantial health gain from quarantine. In this model, the probability that a person travelling to Ireland is infected was estimated from data in the HPSC's Computerised Infectious Disease Reporting (CIDR) system and travel data from the Central Statistics Office (CSO) and the Department of Health. COVID-19 notifications in CIDR include the country of origin of the infection. Considering all data since March 2020, the country of infection is not reported in 17% of cases; however, reporting has improved over time with country of infection not reported in only 11% of cases in 2021. The age profile of cases infected abroad is distinct from those infected in Ireland, with fewer children and older people, and an overrepresentation of those aged 20 to 49 years. Cases with no reported country of infection have an age profile that closely matches those infected in Ireland, giving some reassurance that they are likely to have been infected in Ireland. The proportion of cases missing country of infection is consistent across age groups, ranging between 13% (for those aged 85 years and older) to 19% (for those aged 15 to 19 years).

Inward travel data by country of origin were collated. Flight data records the numbers of passengers landing in Irish airports. The data do not facilitate distinction between direct and indirect flights and therefore only capture the last flight taken on an indirect route. Due to the inability to adequately capture numbers of passengers entering Ireland by the country in which transit started, a global figure of inward passengers was used. Data on travel from countries where indirect travel was unlikely, for example Germany, were used to estimate whether there is an association between local incidence and risk of infection for people travelling. Data on all those arriving in Ireland was analysed for the period March 2020 to November 2020, indicating that 91% of people arrive by air. The percentage was at its lowest in May 2020 when only 69% arrived by air, but that also coincided with a period of very low passenger volumes. For the last three months of available data, the percentage of arrivals by air was stable at approximately 88% despite declining numbers of arrivals.

Data on numbers of people arriving in Ireland and numbers of infections that originated outside of Ireland were analysed by week for the 20 weeks starting 30 November 2020 to determine the mean and variance in the estimates. Across the 20 week period, one in 429 (i.e., 0.0023) travellers entering the country were infected prior to arrival in Ireland. The risk of infection ranged from one in 153 (i.e., 0.0065) to one in 1,925 (i.e., 0.00052). For the

purposes of modelling, the proportion of people infected was estimated to be 0.0058 (95% CI: 0.0024 to 0.0122) based on the estimated risk in the week starting 12 April 2021. A sensitivity analysis was carried out using the projected risk for the week starting 10 May 2021 (mean 0.0085; 95% CI: 0.0031 to 0.0198).

It was assumed that people travelling to Ireland undergo an RT-PCR test 72 hours of starting travel. Given the lack of clarity in relation to the timing of infectious exposure, there were insufficient data to support an analysis of alternative timings for the pre-travel test (e.g., 48 hours before travel).

Table 1. Parameter estimates for disease factors

Parameter	Description	Source(s)	Estimate*
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, 13]	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[14] combined with LSHTM modelling estimate of latent period[12]	Mean: 2.6 95% CI (0.3 to 9.8)
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[14] Singanayagam et al.[15]	Mean: 7.1 95% CI (2.8 to 11.5)
Duration of infectiousness (asymptomatic)	The time duration (in days) over which an asymptomatic case is infectious.	HIQA evidence summary of duration of infectiousness[14]	Mean: 10.9 (95% CI: 5.2 to 18.7)
Proportion of asymptomatic infections	The proportion of all infected cases which remain asymptomatic (that is they do not show symptoms at any point).	Buitrago-Garcia et al.[10]	Mean: 0.31 95% CI (0.24 to 0.38)
Rate of infection in people travelling to Ireland	Proportion of passengers arriving in Ireland that are infected.	Notifications of travel-related infections (source: CIDR) combined with travel data (source: CSO).	Mean: 0.0058 (95% CI: 0.0024 to 0.0122)

Key: CIDR, Computerised Infectious Disease Reporting; CSO, Central Statistics Office; LSHTM London School of Hygiene and Tropical Medicine; NCPP National Clinical Programme for Pathology
*Percentage estimates rounded to nearest whole number

Test characteristics

A summary of the parameter estimates for relevant test factors is provided in Table 2.

- **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.

- **Sensitivity and specificity of RADT testing for SARS-CoV-2**

  The sensitivity and specificity of RADT is considered relative to that of RT-PCR. The parameters utilised reflect the results of validation work undertaken by the National Clinical Programme for Pathology (NCPP) with variability in the estimates dependent on whether a case is symptomatic or asymptomatic.

Table 2. 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;[16] inferred as high sensitivity when appropriate pre-analytical time factors satisfied.	Mean: 0.90 95% CI (0.83 to 0.95)
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;[16] inferred as high.	Mean: 0.99 95% CI (0.98 to 1.00)
Clinical sensitivity of RADT for SARS-CoV-2: symptomatic populations	Proportion of symptomatic individuals with SARS-CoV-2 correctly identified as infected with SARS-CoV-2 by RADT.	NCPP RADT validation results.[17]	Mean: 77% (95% CI: 69% to 85%)
Clinical sensitivity of RADT for SARS-CoV-2: asymptomatic populations	Proportion of asymptomatic individuals with SARS-CoV-2 correctly identified as infected with SARS-CoV-2 by RADT.	NCPP RADT validation results.[17]	Mean: 47% (95% CI: 36% to 56%)
Clinical specificity of RADT for SARS-CoV-2	Proportion of individuals who do not have SARS-CoV-2 correctly identified as negative by RADT.	NCPP RADT validation results.[17]	Mean: 99% (95% CI: 98% to 99%)

Key: NCPP National Clinical Programme for Pathology

*Percentage estimates rounded to nearest whole number

Person factors

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

- **Uptake of testing**

  The rules regarding quarantine for those travelling from a non-designated state stipulate that quarantine can be ended on receipt of a 'not detected' test result taken on or after day five. Clearly not everyone will avail of the option to test out of quarantine before day 14. Some people may not be in a position to avail of testing or may choose to complete the full 14 days of quarantine. It is also possible that some people will not avail of testing and will not adhere to quarantine. The HSE began offering free post-arrival testing in April 2021 to people coming into the country. The tests can be accessed through the GP referral service and walk-in test centres. At present, people entering Ireland can opt-in to SMS reminders about presenting for testing. Based on data linked to the text reminders, an estimated 35% of passengers have availed of testing. This may be an underestimate due to those who travel out of the country within five days of arrival or may access testing through other means. An alternative source of test uptake data are data relating to those identified as close contacts of cases. Close contacts of confirmed cases are asked to restrict movements and are offered two tests, with recent uptake being 87% for the first test and 85% for the second. Given the uncertainty around the applicability of the uptake rate estimate, alternative mean values of 50% and 65% were also modelled as part of sensitivity analyses.

- **Adherence to quarantine**

  Individuals may adhere to quarantine yet choose not to avail of testing. Equally, they may avail of testing, but not adhere to quarantine. There are limited Irish or international data that examine adherence to restricting movements or quarantine. Some of the evidence available has taken a strict approach to measuring adherence, with individuals considered to be either fully compliant or not at all. Such a narrow definition is unrealistic in practice, and we have assumed that the majority of people asked to go into quarantine will enter into the spirit of the request as far as is possible. Based on a previous analysis of close contacts of confirmed cases, we assumed that 90% of people entering Ireland are compliant with quarantine at the outset. In the earlier analysis it was assumed that adherence to restriction of movements on day ten was 75%.[18] This assumption was applied in the current analysis, but a scenario analysis was used to explore the impact of lower adherence. It was assumed that all those who become symptomatic or are test-detected will self-isolate, and that adherence to quarantine is unaffected by attendance at

testing. That is, a person who adheres to quarantine will do so irrespective of attending testing.

The adherence to quarantine was modelled as a curve of waning adherence connecting between initial adherence and adherence on day ten, with extrapolation out to day 14. Substantial uncertainty was applied to account for the very limited data available on adherence to quarantine, particularly among those who return a 'not detected' test result. Given the apparent low uptake of day five testing, sensitivity analyses were undertaken to evaluate the impact of substantially reduced adherence figures.

Table 3. Parameter estimates for person factors

Parameter	Description	Source(s)	Estimate*
Uptake of testing	Proportion of people who present for scheduled testing.	HSE/DoH data on uptake of testing among people arriving into Ireland.	Mean: 0.35 (95% CI: 0.26 to 0.44)
Adherence to quarantine at outset	Proportion of people who adhere to quarantine.	Estimated using contact tracing data.[18]	Mean: 0.90 (95% CI: 0.80 to 0.97)
Adherence to quarantine on day 10	Proportion of people who adhere to quarantine.	Estimated using contact tracing data.[18]	Mean: 0.75 (95% CI: 0.62 to 0.86)

*Percentage estimates rounded to nearest whole number

Organisational factors

A summary of the parameter estimates for relevant organisational factors is provided in Table 4.

Table 4. Parameter estimates for organisational factors

Parameter	Description	Source(s)	Estimate*
Swabs per hour	The number of swabs a HCW or appropriately qualified staff can collect per hour.	HIQA evidence synthesis of serial testing of employees in meat processing plants.[19]	Mean: 7.2 (95% CI: 5.9 to 8.7)

Key: HCW healthcare worker

Model structure

A natural history model was used that simulates individuals on arrival in Ireland, through to reaching day 14 since arrival. It was assumed that all individuals had a RT-PCR test within the 72 hours before travel and which reported a 'not detected'

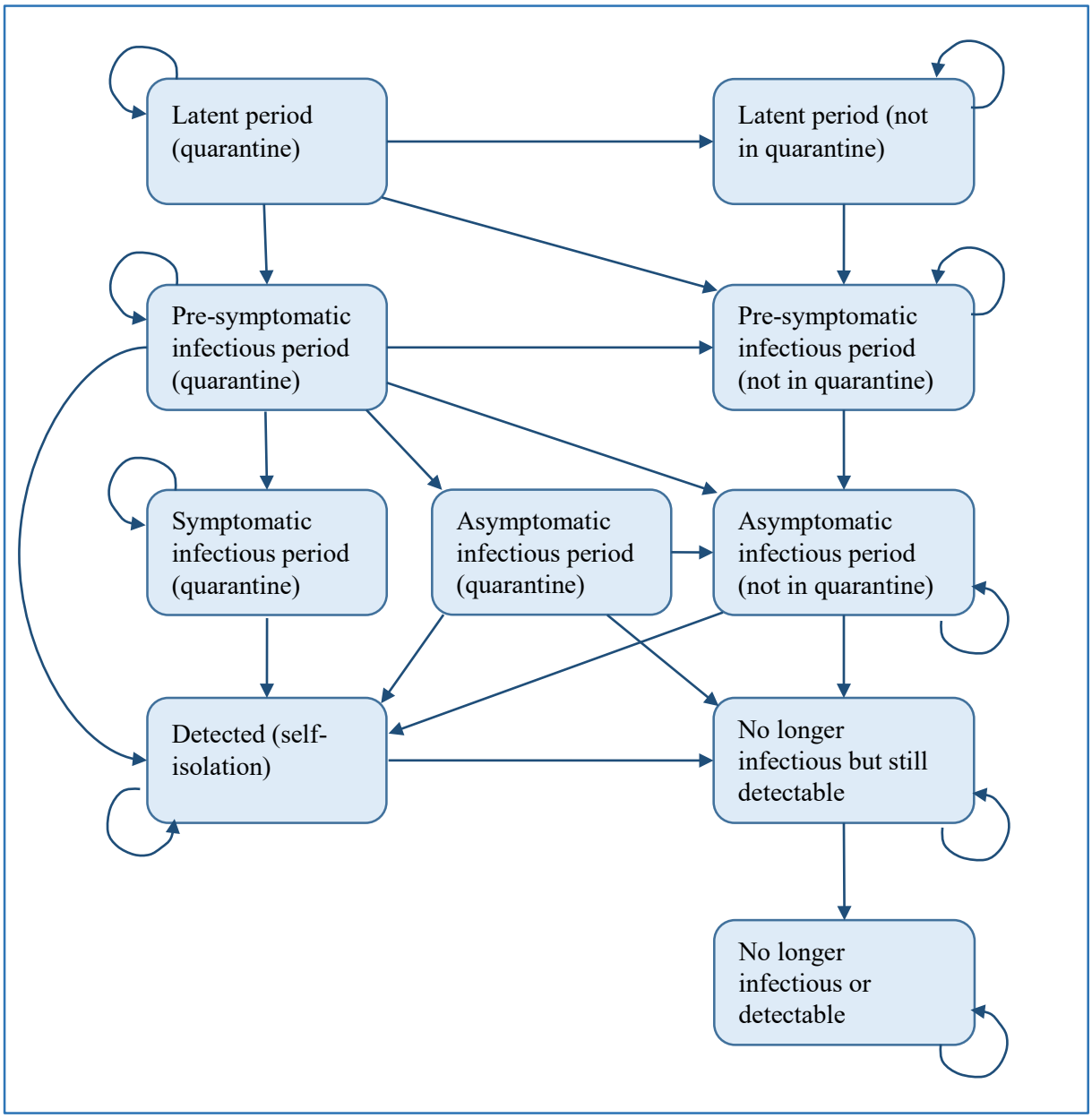
finding. Individuals were classified into a series of mutually exclusive states based on the progression of infection (Figure 1). After the infectious period is complete, there is an extended period during which a positive test result is still obtained, but the individual is no longer infectious (for example, low viral load or detection of non-viable viral remenants). The model did not use explicit transition probabilities, as transitions were based on the duration of each period, which could be shortened through testing or passengers ceasing to adhere to quarantine. While individuals could cease adhering to quarantine, the model assumed that they would adhere to self-isolation if informed of a positive test result. Individuals that were not infected had three states: uninfected and observing quarantine requirements, uninfected and not observing quarantine requirements, and self-isolating having received a false-positive test result.

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 model generated 20,000 individuals, with a cohort of 1,000 randomly sampled for each simulation. For each of the modelled scenarios, individuals could change states in different ways depending on the timing and accuracy of testing.

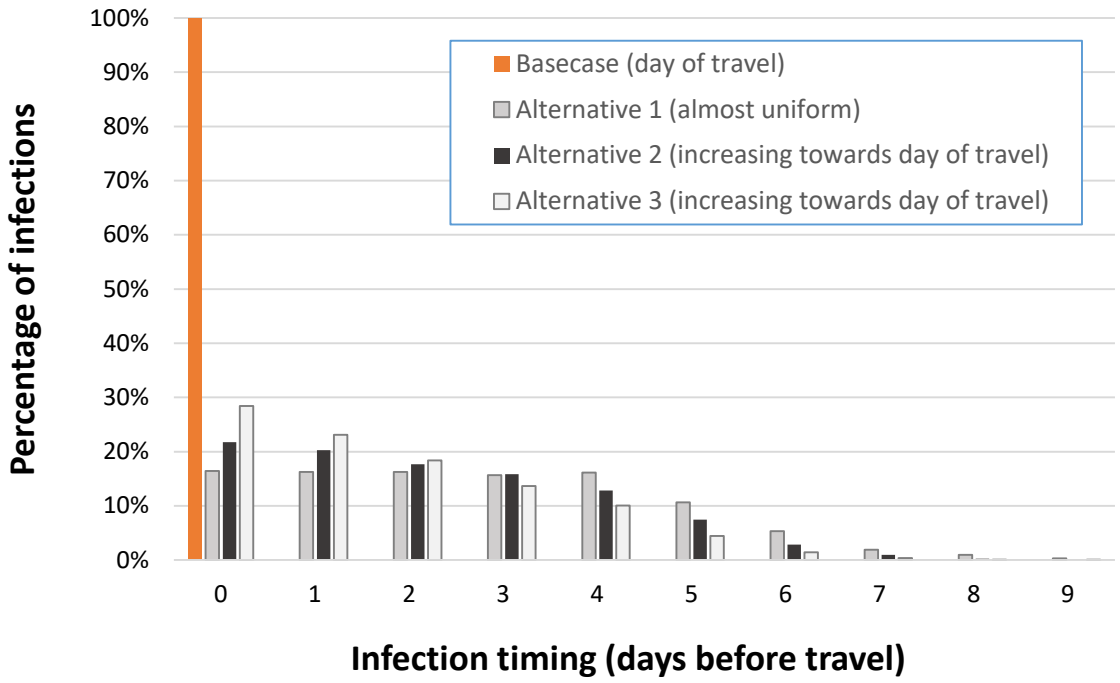
Individuals that become symptomatic were assumed to get tested and or be clinically diagnosed. Once symptomatic and test-detected, cases were assumed to self-isolate. Asymptomatic cases could only be test identified if they attended for the specified test. It was assumed that not all individuals would adhere to quarantine. Any testing strategy that reduces identification of cases is likely to lead to an increase in infectious person-days in the community due to undetected cases that do not adhere to quarantine.

Figure 1. State transition model for infected cases



For the base case analysis, it was assumed that exposure resulting in transmission of disease occurred in the course of travel. That is, infection occurred on the day of arrival in Ireland. Under this conservative assumption, a day zero test will not be of benefit as infected individuals will not have developed sufficient viral load to be detectable by RT-PCR or RADT testing. The alternative of being infected prior to the day of entering the country was also modelled. Three alternative approaches to distributing the timing of infection were also tested, all of which incorporated the assumption that all individuals were tested within the 72 hours prior to travel and tested negative at that point (Figure 2).

Figure 2. Timing of infectious exposure prior to travel

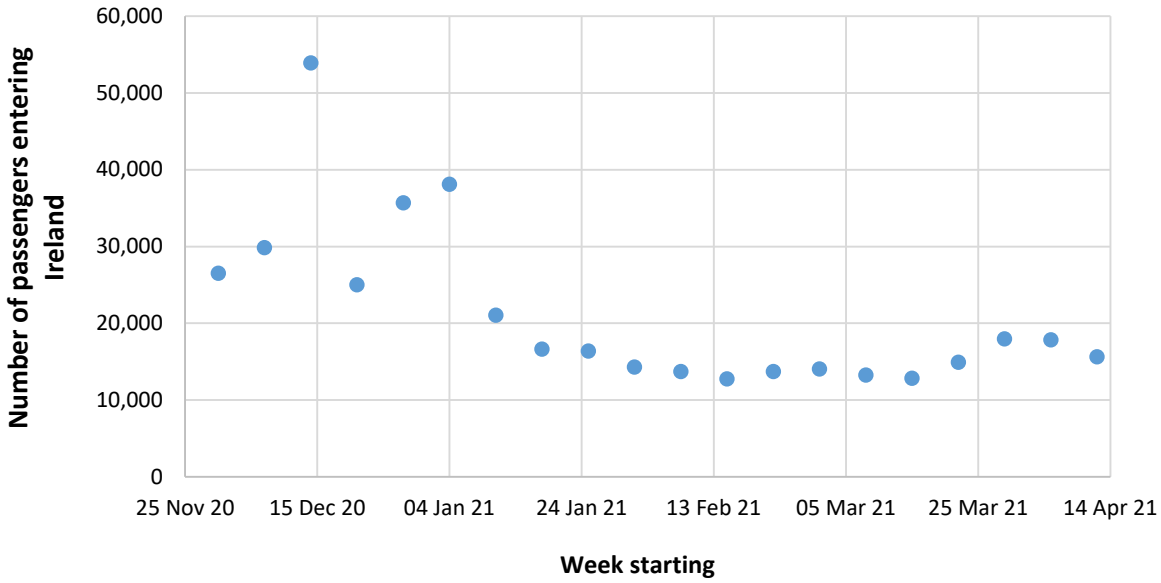


All computations were carried out in R (4.0.2). Results are presented for a hypothetical cohort of 1,000 individuals. The model allowed parameters to vary for all the outlined parameters. A series of sensitivity analyses were conducted to test structural assumptions in the model.

Results

Since the end of November 2020, there has been fluctuation in the number of people travelling to Ireland, mostly influenced by travel into the country in mid to late December (Figure 3). Since mid-January the number of people travelling into Ireland has been between 13,000 and 18,000 each week.

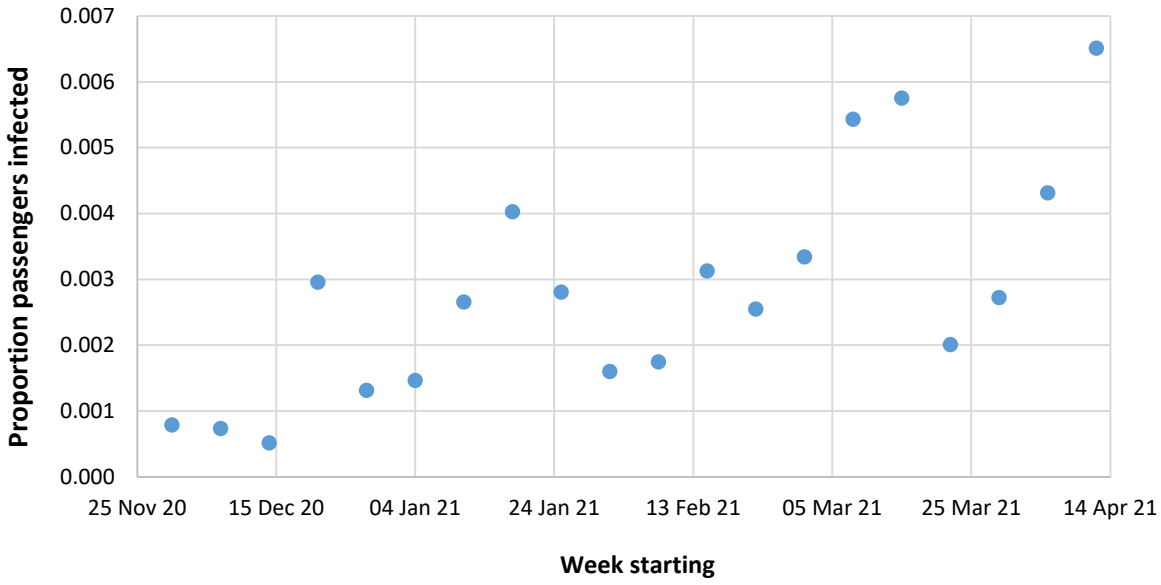
Figure 3. Numbers of people travelling to Ireland by week



Since the start of the epidemic until 4 May 2020, a total of 1,758 notified cases were infected during travel or while abroad. By that date, there had been 250,672 total notifications, indicating a risk of one in 143 (i.e., 0.007) for a case to be an infection that originated during travel or while abroad.

The proportion of people travelling to Ireland that have been notified as infected during travel has increased since late November 2020 (Figure 4). In late November 2020, the risk was less than one in a thousand people travelling being infected. The most recent week of data (week starting 12 April 2021) indicate a risk of infection of almost seven in a thousand.

Figure 4. Risk of infection in people travelling to Ireland by week



Model results

The results of the analysis are presented by each of the key outcomes considering each scenario. The results presented here are based on alternative quarantine durations and testing days (single RT-PCR test) as an alternative to the current approach of an RT-PCR test on day five with ending of quarantine on receipt of a 'not detected' test result. Results are presented for a hypothetical cohort of 1,000 people travelling into Ireland.

Expected number of detected cases by scenario

In the base case analysis, it was assumed that on average, there would be six infected individuals for every thousand people travelling into Ireland. The data suggest that only one of those will be test detected through the referred testing programme (Table 5). Extending the timing of the test is not associated with improved detection of cases.

Table 5. Total cases detected by scheduled test (per 1,000 people travelling into Ireland)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator): 'day 5' RT-PCR	1	[0 to 5]	-	-
2: 'day 6' RT-PCR	1	[0 to 5]	0	[-1 to 1]
3: 'day 7' RT-PCR	1	[0 to 5]	0	[-2 to 1]
4: 'day 8' RT-PCR	1	[0 to 4]	0	[-2 to 1]
5: 'day 9' RT-PCR	1	[0 to 4]	0	[-3 to 1]
6: 'day 10' RT-PCR	1	[0 to 3]	-1	[-3 to 1]

Person-days of infectious individuals circulating in the community

An increased duration of quarantine is associated with a reduced number of infectious person-days circulating in the community (Table 6). Testing on day ten with release on a 'not detected' test result is associated with a 32% reduction in the number of infectious person-days circulating in the community. However, in absolute terms the reduction is nine infectious person-days (95% CI: 0 to 30) per 1,000 people travelling into Ireland.

Table 6. Total infectious person-days in the community (per 1,000 people travelling into Ireland)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator): 'day 5' RT-PCR	25	[0 to 77]	-	-
2: 'day 6' RT-PCR	23	[0 to 69]	-3	[-11 to 0]
3: 'day 7' RT-PCR	21	[0 to 65]	-5	[-16 to 0]
4: 'day 8' RT-PCR	19	[0 to 62]	-6	[-21 to 0]
5: 'day 9' RT-PCR	18	[0 to 57]	-8	[-26 to 0]
6: 'day 10' RT-PCR	17	[0 to 55]	-9	[-30 to 0]

Total number of person-days in self-isolation or quarantine

On the basis of an assumed high adherence to quarantine (90% on day zero declining to 75% on day 10), extending to test out on day ten results in a 70% increase in the number of person days in quarantine or self-isolation (Table 7). Given the results in Table 6, this would mean, for example, that testing out on day 10 instead of day five means an extra 402 days in self-isolation or quarantine per 1,000

people travelling are required to prevent one infectious person-day in the community.

Table 7. Total person-days in self-isolation or quarantine (per 1,000 people travelling into Ireland)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator): 'day 5' RT-PCR	5,134	[4,595 to 5,605]	-	-
2: 'day 6' RT-PCR	5,916	[5,299 to 6,456]	782	[654 to 894]
3: 'day 7' RT-PCR	6,676	[5,979 to 7,311]	1,542	[1,308 to 1,744]
4: 'day 8' RT-PCR	7,404	[6,592 to 8,143]	2,271	[1,919 to 2,590]
5: 'day 9' RT-PCR	8,097	[7,176 to 8,921]	2,964	[2,501 to 3,383]
6: 'day 10' RT-PCR	8,753	[7,739 to 9,657]	3,620	[3,028 to 4,146]

Number of false positives generated

Due to the low proportion of people infected, the likelihood of a false-positive exceeds the likelihood of a true positive (Table 9). However, changes to the day of testing have no substantive impact on false positives.

Table 9. Number of false-positive test results (per 1,000 people travelling into Ireland)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator): 'day 5' RT-PCR	3	[0 to 9]	-	-
2: 'day 6' RT-PCR	4	[0 to 10]	1	[-4 to 5]
3: 'day 7' RT-PCR	4	[0 to 8]	0	[-5 to 5]
4: 'day 8' RT-PCR	3	[0 to 8]	0	[-5 to 5]
5: 'day 9' RT-PCR	3	[0 to 8]	0	[-5 to 5]
6: 'day 10' RT-PCR	3	[0 to 7]	0	[-6 to 5]

Cost of testing

The cost of testing is largely unaffected by the timing of testing due to the limited impact on the number of tests conducted (Table 10).

Table 10. Cost of testing (per 1,000 people travelling into Ireland)

Scenario	Total (€)		Incremental (relative to comparator) (€)	
	Mean	95% CI	Mean	95% CI
1 (comparator): 'day 5' RT-PCR	29,167	[20,489 to 38,932]	0	[0 to 0]
2: 'day 6' RT-PCR	29,164	[20,489 to 38,932]	-3	[-73 to 0]
3: 'day 7' RT-PCR	29,149	[20,412 to 38,932]	-18	[-97 to 0]
4: 'day 8' RT-PCR	29,132	[20,412 to 38,836]	-34	[-174 to 0]
5: 'day 9' RT-PCR	29,116	[20,410 to 38,836]	-51	[-244 to 0]
6: 'day 10' RT-PCR	29,100	[20,410 to 38,836]	-67	[-264 to 0]

Scenario analysis

For the main analysis, it was assumed that infectious exposure would occur on the day of travel. An alternative approach was applied, in which exposure could occur up to nine days prior to travel, although the probability of exposure was weighted in favour of being closer to the day of travel. In the scenario presented here, 28% of infections occurred on the day of travel, 23% the day before travel, 18% two days before travel, 14% three days before travel, and the remaining 15% occurred four or more days before travel. For this analysis, strategies including a day zero test were also included. The day zero test could either be RT-PCR or RADT with a confirmatory RT-PCR test for individuals that were positive on the RADT test.

Assuming that a 35% uptake would also apply to the day zero test, the impact of an additional test is negligible in terms of reducing the number of infectious person-days circulating in the community (Table 11).

Table 11. Infectious person-days circulating in the community (per 1,000 people travelling into Ireland) for a range of single and two-test strategies

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator): 'day 5' RT-PCR	21	[0 to 60]	0	[0 to 0]
7: 'day 0' RT-PCR + 'day 5' RT-PCR	22	[0 to 62]	1	[-6 to 9]
13: 'day 0' RADT + 'day 5' RT-PCR	21	[0 to 60]	0	[0 to 5]
2: 'day 6' RT-PCR	19	[0 to 55]	-2	[-10 to 2]
8: 'day 0' RT-PCR + 'day 6' RT-PCR	19	[0 to 57]	-2	[-10 to 2]
14: 'day 0' RADT + 'day 6' RT-PCR	19	[0 to 57]	-2	[-10 to 2]
3: 'day 7' RT-PCR	17	[0 to 52]	-4	[-14 to 2]
9: 'day 0' RT-PCR + 'day 7' RT-PCR	17	[0 to 51]	-4	[-14 to 1]
15: 'day 0' RADT + 'day 7' RT-PCR	17	[0 to 51]	-4	[-14 to 1]
4: 'day 8' RT-PCR	16	[0 to 49]	-5	[-18 to 1]
10: 'day 0' RT-PCR + 'day 8' RT-PCR	16	[0 to 49]	-5	[-18 to 0]
16: 'day 0' RADT + 'day 8' RT-PCR	16	[0 to 49]	-5	[-18 to 1]
5: 'day 9' RT-PCR	15	[0 to 46]	-7	[-20 to 0]
11: 'day 0' RT-PCR + 'day 9' RT-PCR	14	[0 to 46]	-7	[-20 to 0]
17: 'day 0' RADT + 'day 9' RT-PCR	14	[0 to 46]	-7	[-20 to 0]
6: 'day 10' RT-PCR	14	[0 to 44]	-8	[-23 to 0]
12: 'day 0' RT-PCR + 'day 10' RT-PCR	14	[0 to 44]	-8	[-23 to 0]
18: 'day 0' RADT + 'day 10' RT-PCR	14	[0 to 44]	-8	[-23 to 0]

Sensitivity analysis

A number of sensitivity analyses were undertaken to explore the impact of choices of parameter values on the results. The results presented here are limited to the main strategies of interest: testing out of quarantine on days five and 10. The outcomes considered here are the person-days in self-isolation or quarantine, and the number of infectious person-days in the community (Table 12).

The only parameter that substantially impacted on the number of person-days in self-isolation or quarantine was adherence to quarantine. Low adherence reduced the difference between testing out on day five compared with day 10. However, low adherence to quarantine eliminated the benefit of reduced infectious person-days in the community.

In terms of infectious person-days circulating in the community, the total person-days is correlated with the risk of infection in people travelling to Ireland. The benefits of extended quarantine are most noticeable if the risk of infection is high or if infections occur earlier before travel. However, with the exception of there being a

very high risk of infection, the absolute reduction in infectious person days remains modest relative to the increase in person-days in self-isolation or quarantine.

The impact of no testing and no quarantine is shown in Table 13.

Removing quarantine requirements for people travelling to Ireland from a non-designated country would reduce the number of person-days in self-isolation or quarantine by 5,112 (95% CI: 4,585 to 5,587) days per 1,000 persons travelling relative to the current approach of a 14 day quarantine with the possibility of testing out on day five. The number of infectious person-days circulating in the community would increase by 22 (95% CI: 0 to 63) days relative to the current approach.

Table 12. Sensitivity analyses to assess the impact on person days in quarantine or self-isolation and infectious person-days in the community (per 1,000 people travelling into Ireland)

Scenario	Person-days in self-isolation or quarantine			Infectious person-days in the community		
	Day 5	Day 10	Difference	Day 5	Day 10	Difference
Main analysis	5,134	8,753	3,620	25	17	-9
High RT-PCR sensitivity (95%)	5,134	8,753	3,619	25	17	-8
Higher test uptake (50%)	5,487	9,071	3,583	22	16	-6
Higher test uptake (65%)	5,839	9,287	3,448	18	15	-3
Low quarantine adherence on day 10 (start at 90%, finish at 65%)	5,052	8,328	3,276	23	16	-7
Low quarantine adherence throughout (start at 75%, finish at 50%)	4,069	6,140	2,071	25	23	-2
Lower quarantine adherence throughout (start at 50%, finish at 35%)	2,582	3,432	850	37	39	2
Infection risk = 0.0083 (projected for week starting 10 May 2021)	5,162	8,788	3,626	31	20	-11
Infection risk = 0.0031 (low value)	5,102	8,714	3,612	11	9	-2
Infection risk = 0.0198 (high value)	5,181	8,752	3,571	76	47	-29
Estimated infection duration for alpha variant	5,107	8,721	3,614	33	20	-13
Timing of infectious exposure (average 2.7 days before travel)	5,499	9,323	3,824	15	8	-7
Timing of infectious exposure (average 2.2 days before travel)	5,347	9,040	3,693	13	7	-6
Timing of infectious exposure (average 1.8 days before travel)	5,296	8,982	3,686	15	9	-6

Note: confidence bounds are not presented here.

Table 13. Impact on person days in quarantine or self-isolation and infectious person-days in the community (per 1,000 people travelling into Ireland)

Scenario	Person-days in self-isolation or quarantine				Infectious person-days in the community			
	Total		Incremental		Total		Incremental	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
Exposure on day of travel								
'Day 5' RT-PCR	5,134	[4,595 to 5,605]	0	[0 to 0]	25	[0 to 77]	0	[0 to 0]
'Day 10' RT-PCR	8,753	[7,739 to 9,657]	3,620	[3,028 to 4,146]	17	[0 to 55]	-9	[-30 to 0]
No test and no quarantine	21	[0 to 59]	-5,112	[-5,587 to -4,585]	47	[0 to 135]	22	[0 to 63]
Exposure before and on day of travel								
'Day 5' RT-PCR	5,274	[4,721 to 5,743]	0	[0 to 0]	21	[0 to 60]	0	[0 to 0]
'Day 10' RT-PCR	8,921	[7,866 to 9,711]	3,647	[3,093 to 4,132]	14	[0 to 44]	-8	[-23 to 0]
No test and no quarantine	35	[0 to 88]	-5,239	[-5,696 to -4,678]	45	[4 to 114]	24	[1 to 62]

Discussion

This analysis aimed to model the potential impact on alternative test and quarantine strategies for people travelling to Ireland from non-designated states. The estimates presented within this analysis suggest that increasing the duration of quarantine will lead to a modest absolute reduction in the number infectious person-days in circulation, but a potentially large increase in the number of person-days in quarantine or self-isolation.

Key issues in relation to the analysis are the apparently low uptake of testing by people travelling to Ireland and the low risk of infection. The low uptake of testing may also be associated with a low adherence to quarantine, although no data were available to determine whether this is the case. If test uptake reflects adherence to other measures then these data are concerning given that there is a legal obligation to quarantine. Adherence to restriction of movements for close contacts of confirmed cases has been noted to be high at the outset, and it is possible that the low uptake of testing is not indicative of adherence to quarantine. The low uptake of testing may be biased by people entering and leaving the country within five days, a proportion of passengers what are exempt from mandatory quarantine and potentially people availing of testing without being recorded as someone being tested due to travel into the country.

The current estimated risk of infection (as of end-April 2021) for people travelling to Ireland is approximately six in a thousand. This risk is for all those travelling (designated and non-designated countries) as it was not possible to estimate a risk of infection specific to those travelling from non-designated countries. The low level of risk stands in contrast to HSE data for close contacts of confirmed cases where there is a risk of infection of 146 per thousand on the first test and a further 67 per thousand on the second test. The risk of infection could be an underestimate as there are a large number of COVID-19 notifications with no record for country of infection. However, it must be noted that there has been steady trend for increasing risk since the end of November 2020. Due to the lack of detailed data on countries from which people travelled to Ireland, it was not possible to reliably estimate the association between risk of infection and incidence of COVID-19 in the origin country. An increasing trend could reflect increased testing of people travelling into Ireland or changes to the type of travel people are engaging in. With increasing vaccine coverage globally, the risk of travel-related infection is likely to diminish, but it is advisable that the situation is monitored.

Similar risk mitigation strategies have been considered in the literature.[20-23] Using simulation models, similar to the one developed for this analysis, previous analyses

modelled different combinations of testing and durations of quarantine, as well as symptom monitoring, for passengers arriving in a destination country. A study in the UK modelled several risk mitigation scenarios representing 'low', 'moderate', 'high', and 'maximum' levels of stringency and found a moderate strategy with a quarantine period of eight days from day of arrival with a RT-PCR test on day seven (with a one day delay for test results) can reduce the number of infectious arrivals released into the community by a median 94% compared to a no quarantine, no test scenario.[20] A shorter quarantine period in which passengers spent five days in quarantine was also found to substantially reduce the risk of transmission (by a median 88%), provided a negative RT-PCR test result was obtained before passengers were released from quarantine. A separate study in the US found that a seven-day quarantine duration with testing on exit from quarantine, or testing on entry to and exit from quarantine, provided the same or slightly lower probabilities of post-quarantine transmission as a more stringent 13-day quarantine period with testing on entry only.[23] Another study in the US found pre-departure testing, such as on the day of departure, can reduce the risk of transmission by 44-72%, even if the sensitivity of the test (such as a RADT) was lower than an earlier test (for example, RT-PCR) taken up to seven days prior to travel.[21] On arrival, a 14-day quarantine duration, without symptom monitoring or testing, was found to reduce the risk of post-travel transmission by 96–100% on its own. However, a shorter quarantine period of seven days combined with symptom monitoring and a test on day five or six after arrival achieved comparable results with a reduction in the risk of transmission by 97-100%.

In most of these studies, however, the analyses assumed perfect adherence to quarantine, which is an oversimplification of reality. Imperfect adherence (50%) was considered in one study, in which a seven day quarantine, combined with a test in the first three days of arrival and symptom monitoring reduced the risk of transmission by 77-86% (which was lower than with perfect adherence and a test on exit from quarantine, at 96-100%).[21] However, the strategy was more effective than a 14-day quarantine strategy with 50% adherence and no test, which reduced the risk of transmission by 71-77%. In this analysis, a range of values were applied in the model to investigate the impact of adherence to quarantine requirements on the total number of person-days of infectious individuals circulating in the community, as well as the total number of person-days in quarantine or self-isolation. Low adherence naturally reduced the number of person-days in quarantine or self-isolation and increased the number of infectious person-days in the community. For example, assuming 50% adherence on day one (compared with 90% in the base case analysis) and 35% adherence on day five (versus 70%), the number of person-days in quarantine or self-isolation decreased from 5,134 to 2,582 per 1,000 passengers arriving in Ireland, while the number of infectious person-days

in the community increased from 25 days to 37. These findings highlight the importance of adherence on potential transmission risk.

A further oversimplification of reality that was assumed in these studies was the uptake rate of testing. Each of the studies assumed perfect uptake of testing, which has not been the experience of passengers arriving in Ireland who are subject to home quarantine. In this analysis, 35% of passengers arriving in Ireland were tested on day five, as per national data on testing. A higher uptake of 50% and 65% were considered in sensitivity analyses, which reduced the number of infectious person-days in the community and increased the number of person-days in quarantine or self-isolation.

Another study, partly funded by EasyJet, considered the implications of international travel across Europe.[22] Unlike the previous studies, the analysis compared different combinations of testing and durations of quarantine against a travel ban, rather a stringent duration of quarantine, in an effort to identify strategies that were equivalent to strict border closures. It incorporated prevalence, daily incidence, vaccine coverage, immunity, age demographics, and travel flow for 31 European countries in its evaluation and compared infection rates and hospitalisations arising from travel.[22] The study found that for some country pairs, short-term infection rates would remain unchanged if travel was permitted without the need for quarantine or testing of passengers on arrival. For most other country pairs, the study found a three-day or shorter quarantine duration with RT-PCR or antigen detection testing on exit did not increase infection rates or hospitalisations in the destination country. The authors also modelled the impact of VOCs, in particular the alpha (B.1.1.7) and beta (B.1.351) variant, in additional analyses and found that lengthier durations of quarantine and increased travel restrictions would generally be required for the beta variant, given its relatively low prevalence in Europe. In particular, a quarantine duration of median six days would be required.[22] In contrast, the impact of the alpha variant yielded similar results as for the nonspecific viral incidence due to its widespread prevalence across Europe. While the authors considered the impact of VOCs in its analysis, it is unclear to what extent the results can be generalised to new VOCs, such as the delta (B.1.617) variant, whose transmissibility, duration of infectiousness, and neutralising activity against vaccines, remains broadly under investigation. As with the previous studies,[20, 21, 23] the analysis assumed perfect adherence to quarantine and uptake of testing in passengers arriving in destination countries, which is an oversimplification of reality. However, the shorter durations of quarantine suggested in this study may be associated with increased adherence.

Limitations

Context of data

The model developed for this study is fully probabilistic, reflecting the uncertainty in the true values of the various included parameters. 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. It was assumed that the disease parameters used in the model are appropriate for the demographic group represented by people travelling into Ireland from a non-designated states.

Data quality

The model included a variety of parameters with values obtained from a wide range of heterogeneous sources. Some were derived from observational studies which were not always designed to estimate the parameter of interest. Of particular importance was the inability to estimate the risk of infection specifically for people travelling from non-designated states. Data on numbers of passengers entering Ireland was available by the country that the flight originated in. These data, however, do not take into account indirect flights. There are a number of countries that are an important source of infections that do not have any direct flights into Ireland. Information on countries that people have visited in the 14 days prior to arrival in Ireland are collected through the passenger locator forms (PLFs). The coverage and completeness of the data in these forms was not assessed, although they may provide useful evidence for a more detailed analysis of risk of infection by country of origin. However, it should be borne in mind that the list of designated states is frequently updated, and hence the estimation of risk of infection specific to non-designated state would also have to be updated regularly.

It is also important to note that the available data describes the course of COVID-19 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 are likely to be similar across populations, those aspects that are affected by human behaviour could vary immensely. The model presented here used uncertainty around parameter estimates to explore uncertainty in the relative effects of the different scenarios modelled.

Infectivity and time of exposure

An important consideration in the spread of COVID-19 is the period and scale 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.[24] However, it is worth considering that the ability to infect and the opportunity to infect are different, 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 scale 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 model may be impacted through the overestimation of the benefits of 'day 10' testing, relative to 'day five'. 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 mandatory quarantine or self-isolation.

Another important consideration in the spread of SARS-CoV-2 is the duration of infectiousness before symptom onset. Since it is not possible to identify the time of exposure, people travelling may be infected and unknowingly transmitting virus to others. To mitigate against the risk of this, passengers arriving in Ireland are required to provide evidence of a negative RT-PCR test taken up to 72 hours before arriving in the country. However, passengers may already be infected at the time of testing, but in the latent phase of the disease where the virus is undetectable, for example, such that by the time of travel the risk of transmission to others is high. There are no data available on the proportion of people who test positive on their pre-travel RT-PCR test. Such data would potentially provide some clarity about the timing of infectious exposure.

Since it is not possible to determine the time of exposure in people travelling, the base case analysis assumed the last exposure was during transit. As such, a test on day five after arriving in Ireland, or thereafter, should capture a substantial proportion of infected passengers. However, since the time of exposure may be in advance of travelling, a scenario analysis in which a test on day zero (or arrival in Ireland) was investigated, in addition to the test on exit from quarantine. For the scenario analysis, it was assumed that exposure could have occurred anywhere up to nine days in advance of arriving in Ireland. Alternative assumptions about the timing of infectious exposure had little impact on the findings of the analysis.

Uptake of testing and adherence to quarantine and self-isolation

As has already been noted, the available data suggests a low uptake of day five testing at present. In the absence of any data on adherence to quarantine, it was assumed that the levels of adherence would be similar to that observed in close contacts of confirmed cases. However, the high adherence to restriction of movements is also associated with a high uptake of testing. As such, the low uptake

in people travelling into Ireland may also be indicative of a low adherence to quarantine. Assessing the benefits of the current approach to quarantine, and hence any modifications to it, should ideally be supported by the collection of data on adherence, acceptability, and barriers to adhering to quarantine.

Correlation between variables

As the various parameter estimates were each found 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 movements 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.

Modelled scenarios

A selected group of different potential testing scenarios and durations of quarantine were modelled in this report. Other frequencies of testing may be feasible, or other approaches that might better facilitate the logistics of testing people travelling to Ireland from overseas (for example, use of alternative tests on departure, arrival, and/or during quarantine, including increased frequency of testing).

Variants of concern

The model did not incorporate any data on VOCs. The prevalence of VOCs in countries that people are travelling to Ireland from must be considered. Given that the prevalence of VOCs is likely to influence whether a country is designated, coupled with the low risk of infection in people travelling to Ireland, it may be considered that the risk of VOCs entering from non-designated states is low.

Conclusions

The low risk of infection coupled with the low adherence to testing suggest that increasing the duration of quarantine would result in a substantially increased burden of quarantine with a limited benefit in terms of a reduction in infectious person-days in the community. Any decision to increase the duration of quarantine should be informed by evidence on the adherence to quarantine and uptake of testing among people travelling to Ireland from non-designated states. Since the end of November 2020, there has been a trend of increasing risk of infection in people travelling to Ireland, and this should be monitored to determine if a change in practice is required.

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Appendix 1 – Travel restriction exemptions

The following people are exempt from requiring a pre-departure COVID-19 test on arrival in Ireland:

- people who are travelling in the course of their duties and are an international transport worker in possession of an annex 3 certificate, the driver of a heavy goods vehicle or are aviation crew or maritime crew
- patients travelling to Ireland for urgent medical reasons, and that reason is certified by registered medical practitioner or person holding an equivalent qualification outside the State
- children aged 6 and under
- passengers whose journey originated in Northern Ireland and have not been overseas in the 14-day prior to arrival
- a member of the Gardaí or Defence Forces personnel travelling to the State in the course of performing his or her duties
- a person who travels to the State pursuant to an arrest warrant, extradition proceedings or other mandatory legal obligation
- travel to perform the function of or provide services to an office holder or elected representative, where such travel to Ireland is required to continue providing such services or performing such functions
- if a citizen has a genuine humanitarian emergency requiring urgent travel, and might not be able to obtain the result of a pre-departure RT-PCR test in time, they should contact the nearest embassy or consulate immediately for advice and consular assistance before commencing their journey.

The following exemptions apply to mandatory quarantine:

- patients travelling to Ireland for urgent medical reasons
- international transport workers in possession of an Annex 3 Certificate; Drivers of Heavy Goods Vehicles; Aviation and maritime crew
- Gardaí/Defence Forces personnel, while carrying out their duties
- travel to the State pursuant to an arrest warrant, extradition proceedings or other mandatory legal obligation
- diplomats, or travel to perform the function of or provide services to an office holder or elected representative

- transit passengers who arrive for the purposes of travelling to another state, and who do not leave the port or airport.

The following may temporarily leave their place of quarantine when necessary to perform their essential function – and only for as long as strictly required:

- a person required to carry out essential repair, maintenance, construction or safety assurance of critical transport infrastructure, critical utility infrastructure, manufacturing services, information services, or communication services
- a member of staff of an international organisation, or person invited, carrying out functions required for the proper functioning of such organisations and which cannot be carried out remotely
- a passenger who is participating in a sporting event and has been provided with written certification by Sport Ireland
- journalists, carrying out their professional functions.

The following exemptions apply to mandatory hotel quarantine:

- People fully vaccinated* against COVID-19 do not have to complete mandatory hotel quarantine if they can provide evidence of vaccination. Any dependents travelling with them, including children, will also be exempted from the requirement to complete mandatory hotel quarantine.
    - All passengers still have to have a negative pre-departure RT-PCR test and complete a period of self-quarantine at an address specified on the passenger locator form.
- All families travelling with new-born babies (no more than 28 days old), including those who have travelled to a designated state for the purpose of surrogacy, do not have to complete mandatory hotel quarantine.
    - All passengers still have to have a negative pre-departure RT-PCR test and complete a period of self-quarantine at an address specified on the passenger locator form.
- The following categories of essential workers are exempt from mandatory hotel quarantine, as specified in The Health (Amendment) Act 2021:
    - arriving into the State in the course of duty and who hold a valid Annex 3 certificate (ensuring the availability of goods and essential services)

- arriving in the State in the course of duty and are drivers of a heavy goods vehicle
- airline pilots, aircrew, maritime master or maritime crew and who arrive in the State in the course of performing duties
- travelling to the State pursuant to an arrest warrant, extradition proceedings or other mandatory legal obligation
- a member of An Garda Síochána or Defence Forces (or their equivalents from another state) and travelling to the State in course of duty
- travelling to the State for unavoidable, imperative and time-sensitive medical reasons and these reasons are certified by a registered medical practitioner or person with equivalent qualifications outside the State
- having been outside of the State to provide services to or perform the functions of an office holder (under any enactment or the Constitution) or a member of either house of the Oireachtas or the European Parliament
- diplomats and certain other categories of persons entitled to privileges and immunities in the State.

* Fully vaccinated is defined as:

Full course of any one of the following vaccines:	Regarded as fully vaccinated after:
Pfizer-BioNtech Vaccine: BNT162b2 (Comirnaty®)	7 days
Moderna Vaccine: CX-024414 (Moderna®)	14 days
Oxford-AstraZeneca Vaccine: ChAdOx1-SARS-COV-2 (Vaxzevria® or Covishield)	15 days
Johnson & Johnson/Janssen Vaccine: Ad26.COV2-S [recombinant] (Janssen®)	14 days

Appendix 2 – Designated states

The following countries/territories were designated as high risk, as of 17 May 2021:

- **Africa**: Angola, Botswana, Burundi, Cape Verde, Democratic Republic of the Congo, Eswatini, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, Rwanda, Seychelles, Somalia, South Africa, Tanzania, Zambia, Zimbabwe.
- **Asia:** Bahrain, Bangladesh, Georgia, India, Kuwait, Maldives, Mongolia, Nepal, Oman, Pakistan, Qatar, The Philippines, United Arab Emirates.
- **Europe:** Andorra, Belgium, France, Georgia, Luxembourg, Turkey.
- **North America:** Canada, Costa Rica, Puerto Rico, United States of America.
- **South America:** Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, French Guiana, Guyana, Panama, Paraguay, Peru, Suriname, Uruguay, Venezuela.

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