



**Health
Information
and Quality
Authority**

An tÚdarás Um Fhaisnéis
agus Cáilíocht Sláinte

Protocol:

**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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Purpose and aim

The purpose of this protocol is to outline the process by which the Health Information and Quality Authority's (HIQA's) Health Technology Assessment (HTA) directorate will synthesise evidence to address a policy question posed by the National public Health Emergency Team (NPHE). The work will take account of expert interpretation of the evidence by HIQA's COVID-19 Expert Advisory Group (EAG). This evidence synthesis relates to the following policy question outlined by the NPHE to the Health Service Executive (HSE) and HIQA:

"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"

The following research questions were developed to inform this policy question:

1. What is the risk of SARS-CoV-2 infection in passengers arriving in Ireland (by sea and air)?
2. Is the risk of SARS-CoV-2 infection proportional to the incidence of COVID-19 in the origin country?
3. How do different choices for the duration of mandatory home quarantine and timing of testing of passengers arriving in Ireland from non-designated States impact on the number of infectious person-days in the community?

Process outline

Given the policy question under consideration, a model will be developed of the potential impact of different durations of quarantine and timing of testing for the detection of SARS-CoV-2 in people travelling into Ireland. Nine distinct steps in the process have been identified:

- 1.** Assess the risk of SARS-CoV-2 infection in passengers arriving in Ireland.
- 2.** Examine the association between risk of infection and incidence in the origin country.
- 3.** Outline the scenarios under consideration in the model and the outputs of interest.
- 4.** Outline the necessary parameters for identification and inclusion in the model.
- 5.** Develop and run the model for the different scenarios.
- 6.** Summarise the findings of the modelling exercise.

7. Consider additional factors not included in the model, but that may impact the overall outcomes (for example, prevalence of variants of concern).
8. Present collective findings to COVID-19 Expert Advisory Group (EAG) for expert interpretation.
9. Provide advice to the HSE for consideration based on the findings of the evidence synthesis and informed by expert interpretation by the COVID-19 EAG.

1. Assess the risk of SARS-CoV-2 infection in passengers arriving in Ireland

Using national data on notified cases of COVID-19 from the Health Protection Surveillance Centre (HPSC) Computerised Infectious Disease Reporting (CIDR) database, the risk of infection due to travel to Ireland from overseas will be assessed. Notifications include data on likely infection due to travel and the country of infection. The data on notified cases will be combined with monthly data (March 2020 to March 2021, or the most recent available month) on inward travel at air and sea ports by country of origin. Since the monthly flight data do not distinguish between direct and indirect flights (that is, the data only capture the last flight taken on an indirect route), it will not be possible to estimate a risk of infection for non-designated States only. Instead, a global risk of infection will be estimated for people travelling to Ireland from designated and non-designated States. Data on risk of infection will be pooled across all countries to obtain an average and conservative range of values.

2. Examine the association between risk of infection and incidence in the origin country

The basis for identifying designated countries can include consideration of local incidence of variants of concern (VOCs) and COVID-19 incidence generally in the origin country. Having estimated the risk of infection by country of origin, that risk will be compared to the incidence of COVID-19 in the country of origin at the time of travel.

3. Scenarios to be considered and outputs of interest

The modelling exercise will consider scenarios relating to the duration of quarantine and timing of testing of passengers arriving in Ireland from non-designated states. The intention of testing is to enable the detection of cases to minimise the transmission of SARS-CoV-2 and the introduction of VOCs.

The current national approach is RT-PCR testing no less than five days after entry into the country from non-designated states. Those who return a non-detected test result are allowed to cease quarantining while those who return a positive test result follow the standard procedure for confirmed cases. For those entering from a designated state, RT-PCR tests are carried out on day 0 and day 10 with release from mandatory hotel quarantine on receipt of a non-detected test result following the day 10 test.

The analysis will consider a number of potential approaches for those entering the country from non-designated states, including the existing approach (Scenario one) and that defined for people travelling from designated states (Scenario six).

Six core scenarios will be considered:

- Scenario one: test on day five with release on receipt of a 'non-detected' test result.
- Scenario two: test on day six with release on receipt of a 'non-detected' test result.
- Scenario three: test on day seven with release on receipt of a 'non-detected' test result.
- Scenario four: test on day eight with release on receipt of a 'non-detected' test result.
- Scenario five: test on day nine with release on receipt of a 'non-detected' test result.
- Scenario six: test on day ten with release on receipt of a 'non-detected' test result.

For each scenario an alternative approach will be modelled that also includes a day 0 test.

The outputs of interest from each modelled scenario to inform this policy question include the:

- 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.

4. Necessary parameters for identification and inclusion in the model

Table 1 outlines the necessary parameters for inclusion within the model, alongside the sources used to estimate these parameters. Where available, Irish data will be used to populate the model. Where parameters are identified from the research literature, a non-systematic search will be conducted with the aim of including the best available evidence, preferably from high quality systematic reviews, including evidence summaries previously conducted by HIQA.

For a range of parameters, typically only limited data are available for asymptomatic cases (for example, period of infectiousness). For the simulation model, it is assumed that the course of disease is the same in symptomatic and asymptomatic cases with the exception of symptom onset. It is assumed that RT-PCR test sensitivity is not related to whether the individual is symptomatic or asymptomatic.

The model will also incorporate a measure of adherence to quarantine and testing. There are limited international or Irish data that examine adherence to quarantine requirements. Some of the evidence available has taken a strict binary approach to measuring adherence, with individuals considered to be either fully adherent or not at all. A high level review of the available evidence will be undertaken to generate plausible parameter values for the model. Some individuals may not avail of testing. Irrespective of the reasons for not presenting for testing, if the individual is infected, it creates a risk that they will cease quarantining while infectious.

Data on timings for testing (e.g., delay to getting tested, time from providing sample to receiving test result) are adopted from previous work in relation to testing as part of contact tracing.⁽¹⁾

Table 1. Parameter estimates for inclusion in model

Parameter	Description	Source(s)	Estimate
<i>Disease factors</i>			
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 ^(2, 3)	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 ⁽⁴⁾ combined with LSHTM modelling estimate of latent period ⁽²⁾	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 ⁽⁴⁾ Singanayagam et al. ⁽⁵⁾	Mean: 7.1 95% CI (2.8 to 11.5)
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. ⁽⁶⁾	Mean: 0.31 95% CI (0.24 to 0.38)
Rate of infection in people travelling to Ireland	Proportion of passengers arriving in Ireland from non-designated countries that are infected.	Notifications of travel-related infections (source: CIDR) combined with travel data (source: CSO).	To be confirmed
Adherence to quarantine at outset	Proportion of people who adhere to quarantine.	Estimated using contact tracing data.	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.	Mean: 0.75 (95% CI: 0.62 to 0.86)
Uptake of testing	Proportion of people who present for scheduled testing.	To be confirmed	
<i>Test characteristics</i>			
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; ⁽⁷⁾ 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; ⁽⁷⁾ inferred as high	Mean: 0.99 95% CI (0.98 to 1.00)

Organisational factors			
Swabs per hour	of 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. ⁽⁸⁾	Mean: 7.2 (95% CI: 5.9 to 8.7)

5. Model development

The model will be based on an individual-level microsimulation to capture the variation in disease progression across individuals. Different testing scenarios and durations of quarantine will be simulated to determine the numbers of individuals for whom a false-negative test may be returned (including due to pre-analytical issues such as timing of test), thereby potentially ceasing quarantine and circulating in the community while infectious. In this context, a false positive occurs when RT-PCR test returns a positive test result in an individual who is not infected with SARS-CoV-2. A number of sensitivity analyses will be used to test the impact of the assumptions in both the model structure and the included parameters.

6. Additional factors for consideration

A number of additional factors that may affect overall outcomes, but are not feasible to include within the model will be outlined in the final report. These factors are likely to include the ability of people to fully adhere to quarantine requirements, timely access to testing and the impact of VOCs.

7. Summarise findings

A report will be produced summarising the findings of this analysis.

8. Quality assurance process

The analysis and modelling will be led by an experienced analyst. A small team of analysts will be assigned to assist. The model will be quality assured by a second analyst, who will check that the model is running as intended, that inputs to the model accurately reflect those in the report and that the summary report accurately reflects the outputs of the analysis. The report will be reviewed by a senior member of the team, to ensure processes are followed and quality maintained.

9. Present collective findings to HIQA's COVID-19 Expert Advisory Group for input

The collective findings of the modelling exercise will be presented to HIQA's COVID-19 EAG for consideration, clinical interpretation and input to the subsequent advice to the HSE.

10. Provide findings to the HSE for consideration

A document outlining the advice informed by the key findings of the modelling exercise and expert interpretation by the EAG will be provided to the HSE for consideration.

11. Timelines

This modelling exercise will be conducted in line with the processes and timelines outlined for Phase 2 of HIQA's COVID-19 response. Work will commence on 21 April 2021 and it is anticipated that a final draft will be circulated to HIQA's COVID-19 EAG for review and input on the 17 May 2021, with a view to providing advice and recommendations to the HSE on 21 May 2021. However, this timeframe is subject to agreement of the protocol and availability of the relevant data. Should delays be encountered, this timeline will be amended.

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