

# Risk management in the public health context

The COVID-19 experience of risk-based decision making in Ireland

## **Philip Nolan**

Director General, Science Foundation Ireland Chair, Irish Epidemiological Modelling Advisory Group

PDA Ireland – PRST TU Dublin Joint Seminar and Workshop

8 September 2022

# Approach



- Pharmaceutical quality systems as "a framework for delivering quality products to patients" 1
- Public health emergency responses as a framework for delivering quality public health interventions in populations
- "Science and risk-based decisions" (ICH Q10) require a mutually reinforcing relationship between risk management and knowledge management <sup>1</sup>
- "Knowledge", "science" and "evidence" are dynamic, contested and sometimes unstable



# Irish Epidemiological Modelling Advisory Group (IEMAG)

- Ireland had no formal national advanced biostatistics or disease modelling infrastructure
- 8-13 March 2020 *ad hoc* group mobilized from across university and public health system
  - Monitor and model pandemic in Ireland
  - Irish Epidemiological Modelling Advisory Group (IEMAG)
  - Applied mathematics, statistics, computer science, geospatial science, epidemiology, public health
  - Membership grew dynamically over time 50 members in 4 working groups
- IEMAG reported to a wider National Public Health Emergency Team (NPHET) which was also a very large group (>40)
- *"Monitor and model the COVID-19 outbreak in Ireland"* 
  - Knowledge management: data information insight action
  - Risk assessment



# Data infrastructures

PCR testing NVRL and HSE laboratory systems	<b>Positive tests and contacts</b> Contact Management Programme (CMP) COVID Care Tracker (CCT)	Antigen test portal Contact Management Programme (CMP)
	<b>Cases</b> Health Protection Surveillance Centre (HPSC) Computerised Infectious Disease Record (CIDR)	
Genotyping NVRL WGS and SGT data		Hospital admissions HSE-PMIU-SDU daily data HIPE
Vaccination HSE COVAX		ICU admissions NOCA ICU-BIS

Data incomplete, delayed, unlinked, not geocoded Slow negotiation of data sharing agreements Systems not integrated Failure to implement an individual health identifier and Eircode Data governance Societal questions of privacy, security and trust



# **Early exponential growth projections**



Exponential growth projections from 26 March 2020, at different growth rates

# **SEIR models**





I<sub>a</sub>: asymptomatic infected

I<sub>p</sub>: presymptomatic infected

I<sub>a</sub>: symptomatic infected quarantined

It: symptomatic infected quarantined and tested

In: symptomatic not quarantined



 $rac{\mathrm{d}S}{\mathrm{d}t} = -\lambda S$ 

and  $\frac{\mathrm{d}R}{\mathrm{d}t} = \frac{1}{D}I_a + \frac{1}{D-C+L}I_q + \frac{1}{D-C+L-T}I_{t_2} + \frac{1}{D-C+L}I_n,$ 



# **UCD CVERA evidence synthesis**

**Original research** 

### Centre for Veterinary Epidemiology and Risk Analysis

### Incubation period

### BMJ Open Incubation period of COVID-19: a rapid systematic review and meta-analysis of observational research

Conor McAloon O, 1 Áine Collins, 2 Kevin Hunt, 3 Ann Barber, Andrew W Byrne 0.4 Francis Butler.3 Miriam Casey 0.2 John Griffin 0.5 Elizabeth Lane,<sup>6</sup> David McEvoy <sup>9</sup>,<sup>7</sup> Patrick Wall,<sup>7</sup> Martin Green,<sup>8</sup> Luke O'Grady,<sup>1,8</sup> Simon J More

#### To cite: McAloon C. Collins A. ABSTRACT Objectives The aim of this study was to conduct a rapid

Hunt K. et al. Incubation period of COVID-19: a rapid systematic review and meta analysis of observational research. BMJ Open 2020:10:e039652. doi:10.1136/ bmiopen-2020-039652 Prepublication history and additional material for this paper are available online. Toview these files, please visit the journal online (http://dx.doi. org/10.1136/bmjopen-2020-039652). Received 22 April 2020 Revised 06 July 2020 Accepted 23 July 2020

Open access

or sufficient information to facilitate calculation of those values. After initial eligibility screening, 24 studies were selected for initial review, nine of these were shortlisted for meta-analysis. Final estimates are from meta-analysis of

eight studies. Primary outcome measures Parameters of a lognormal distribution of incubation periods.

Results The incubation period distribution may be modelled with a lognormal distribution with pooled mu and sigma parameters (95% Cls) of 1.63 (95% Cl 1.51 to 1.75) and 0.50 (95% CI 0.46 to 0.55), respectively. The corresponding mean (95% Cls) was 5.8 (95% Cl 5.0 to 6.7) days. It should be noted that uncertainty increases towards the tail of the distribution: the pooled parameter estimates (95% Cls) resulted in a median incubation period of 5.1 (95% Cl 4.5 to 5.8) days, whereas the 95th percentile was 11.7 (95% CI 9.7 to 14.2) days. Conclusions The choice of which parameter values are adopted will depend on how the information is used.

systematic review and meta-analysis of estimates of the

Design Rapid systematic review and meta-analysis of

Setting International studies on incubation period of

Participants Searches were carried out in PubMed.

Google Scholar, Embase, Cochrane Library as well as

selected for meta-analysis if they reported either the

parameters and CIs of the distributions fit to the data.

the preprint servers MedRxiv and BioRxiv. Studies were

incubation period of COVID-19.

observational research.

COVID-19.

the associated risks and the perceived consequences of decisions to be taken. These recommendations will need () Check for updates to be revisited once further relevant information becomes available. Accordingly, we present an R Shiny app that facilitates updating these estimates as new data become permitted under CC BY-NC. No available commercial re-use. See rights

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For numbered affiliations see Reliable estimates of the incubation period are important for decision-making around the control of infectious diseases in human the validation of the model. populations. Knowledge of the incuba-

### Strengths and limitations of this study

- > This study provides a pooled estimate of the distribution of incubation periods which may be used in subsequent modelling studies or to inform decision-making. Several studies used data that were publicly available, therefore there is potential that some of the
- data may be used for more than one study. This estimate will need to be revisited as sub
- data become available. Accordingly, we present an R Shiny app to allow the meta-analysis to be updated with new estin

decision-making around infectious disease control. For example, the maximum incubation period can be used to inform the duration of quarantine, or active monitoring periods of people who have been at high risk of exposure. Estimates of the duration of the incubation period, coupled with estimates of the latent period, serial interval or generation times, may help infer the duration of the presymptomatic infectious period, which is important in understanding both the transmission of infection and opportunities for control.1 Finally, decision-making in the midst of a pandemic often relies on predicted events, such as daily number of new infections, from mathematical models. Such models depend on key input parameters relevant to the transmission of the specific infectious disease. It is important that input parameters into such models are as robust as possible. Given that some models fit data to many parameters, only some of which are specifically of interest but all of which are interdependent, output estimates may be compared with the robust estimates as part of

Earlier work has shown that for models of tion period can be used directly to inform respiratory infections, statements regarding

Lauer et al., 202	0	⊢∎⊣		1.62 [1.50, 1.75]
Li et al., 2020a	-			1.42 [0.96, 1.89]
Bi et al., 2020	+	<b>.</b>	4	1.57 [1.09, 2.05]
Jiang et al. 202	0	⊢∎⊣		1.53 [1.40, 1.66]
Linton et al, 202	20	⊢∎⊣		1.61 [1.47, 1.75]
Zhang et al., 202	20	<b></b>		1.54 [1.36, 1.72]
Ma et al., 2020				1.86 [1.81, 1.90]
Leung, 2020	+			1.78 [1.09, 2.47]
RE Model		•		1.63 [1.52, 1.75]
1				
	0.5 1	1.5 2	2.5	

Observed Outcome

Figure 1 Forest plot of the random effects (RE) metaanalysis of mu parameter of the lognormal distribution of incubation period.



Figure 3 Probability density function of the pooled lognormal distribution of reported incubation period with mu=1.63 and sigma=0.50.

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end of article.

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Dr Conor McAloon:

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# **UCD CVERA evidence synthesis**

### Centre for Veterinary Epidemiology and Risk Analysis

### Presymptomatic transmission

transmission of SARS-CoV-2 infection that can occur, and

the timing of transmission relative to symptom onset.

Data sources Meta-analysis of COVID-19 incubation

time, which are published separately.

period and a rapid review of serial interval and generation

There is currently a pandemic of COVID-19,

a recently emerged and rapidly spreading

infectious disease that is caused by the novel

Setting/design Secondary analysis of internationa

### Open access **Original research BMJ Open** Presymptomatic transmission of SARS-CoV-2 infection: a secondary analysis using published data

Miriam Casey-Bryars <sup>(a)</sup>, <sup>1</sup> John Griffin <sup>(a)</sup>, <sup>1</sup> Conor McAloon <sup>(b)</sup>, Andrew Byrne <sup>(3)</sup>, <sup>3</sup> Jamie Madden, <sup>1</sup> David Mc Evoy <sup>(3)</sup>, <sup>4</sup> Áine Collins, Kevin Hunt,<sup>5</sup> Ann Barber,<sup>1</sup> Francis Butler,<sup>5</sup> Elizabeth Ann Lane O, <sup>6</sup> Kirsty O'Brien, Patrick Wall 8 Kieran Walsh 7 Simon John More

#### To cite: Casey-Bryars M, ABSTRACT Griffin J. McAloon C. et al. Objective To estimate the proportion of presymptomatic

ptomatic transm of SARS-CoV-2 infection: a econdary analysis using published data. BMJ Ope 2021-11:e041240 doi:10.1136/ bmjopen-2020-041240 Prepublication history and additional supplemental material for this paper are available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/ bmjopen-2020-041240). Received 11 July 2020 Accented 16 May 202

estimated presymptomatic transmission

published data

resymptomatic transmission ranged from 45.9% (95% Cl 42.9% to 49.0%) to 69.1% (95% Cl 66.2% to 71.9%). Conclusions There is substantial potential for Con Linked presymptomatic transmission of SARS-CoV-2 across a

range of different contexts. This highlights the need for http://dx.doi.org/10.1136 rapid case detection, contact tracing and guarantine bmiopen-2020-039652 http://dx.doi.org/10.1136. The transmission patterns that we report reflect the bmjopen-2020-040263 combination of biological infectiousness and transmission opportunities which vary according to context.

INTRODUCTION

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BMJ

Participants Data from China, the Islamic Republic of Iran, Italy, Republic of Korea, Singapore and Vietnam from December 2019 to May 2020. them Methods Simulations were generated of incubation period and of serial interval or generation time. From these, transmission times relative to symptom onset, and the proportion of presymptomatic transmission, were Outcome measures Transmission time of SARS-CoV-2 relative to symptom onset and proportion of Results Based on 18 serial interval/generation time estimates from 15 papers, mean transmission time relative to symptom onset ranged from -2.6 (95% Cl -3.0 to -2.1) days before infector symptom onset to 1.4 (95% Cl 1.0 to 1.8) days after symptom onset. The proportion of

transmission-pair level. is control measures such as rapid isolation symptomatic people may increase the proportion of presymptomatic transmission, we generated estimates based on single locations and did not poo 14% and 5% of cases were classified as severe and critical, respectively.2 There are also major indirect impacts of COVID-19 and its control measures on other aspects of healthcare<sup>3-3</sup> and on the economy.

Strengths and limitations of this study

on for different countries

We generated estimates of presymptomatic trans

As this is a secondary analysis of published es

imates, we did not analyse data at individua

In addition to vaccination, primary control measures entail reducing transmission from infectious individuals. These include case isolation, contact tracing and quarantine physical distancing, hygiene and ventilation measures.8 Infectious people are identified when they report symptoms, and are tested for SARS-CoV-2. Infectious people without symptoms may be identified when an active surveillance programme is in place In the absence of active surveillance, infec

tious people without symptoms may not be guarantined, and therefore may have more contacts with susceptible people resulting in increased SARS-CoV-2 transmission. Therefore, quantifying the transmission potential before or in the absence of symptoms will inform disease control measures and predic tions of epidemic progression.

Characteristics of presymptomatic and coronavirus, SARS-CoV-2. There are large direct impacts of COVID-19 among known asymptomatic transmission are potentiall cases. As of 19 April 2021, the WHO has different, and separate approaches may be reported 140, 886773 confirmed cases and required to understand them. In this paper 3012251 deaths due to COVID-19.1 In China, we capitalise on the considerable information

Casey-Bryars M, et al. BMJ Open 2021;11:e041240. doi:10.1136/bmjopen-2020-041240

### Asymptomatic infectiousness

### Open access Original research **BMJ Open** Relative infectiousness of asymptomatic SARS-CoV-2 infected persons compared with symptomatic individuals: a rapid scoping review

David McEvoy O, <sup>1</sup> Conor McAloon O, <sup>2</sup> Aine Collins, <sup>3</sup> Kevin Hunt, <sup>4</sup> Francis Butler.<sup>4</sup> Andrew Byrne <sup>0</sup>.<sup>5</sup> Miriam Casey-Bryars <sup>0</sup>.<sup>3</sup> Ann Barber <sup>0</sup>.<sup>3</sup> John Griffin <sup>6</sup>, <sup>3</sup> Elizabeth Ann Lane <sup>6</sup>, <sup>3,6</sup> Patrick Wall, <sup>7</sup> Simon John More <sup>6</sup>

#### To cite: McEvoy D, McAloon C, Collins A, et al. ABSTRACT

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BMJ

end of article.

Mr David McEwor

Objectives The aim of this study was to determine the Relative infectiousness of relative infectiousness of asymptomatic SARS-CoV-2 asymptomatic SARS-CoV-2 infected persons compared infected persons compared with symptomatic individuals based on a scoping review of available literature. with symptomatic individuals: a Design Rapid scoping review of peer-reviewed literature rapid scoping review. BMJ Open 2021;11:e042354. doi:10.1136/ from 1 January to 5 December 2020 using the LitCovid database and the Cochrane library. bmiopen-2020-042354 Setting International studies on the infectiousness of Prepublication history and individuals infected with SARS-CoV-2. additional supplemental ma Participants Studies were selected for inclusion if they for this paper are available defined asymptomatics as a separate cohort distinct online. To view these files, from presymptomatics and if they provided a quantitative please visit the journal online (http://dx.doi.org/10.1136 measure of the infectiousness of asymptomatics relative to bmiopen-2020-042354) symptomatics. Primary outcome measures PCR result (PCR studies).

Received 30 July 2020 the rate of infection (mathematical modelling studies) and secondary attack rate (contact tracing studies) - in each Accepted 21 April 2021 case from asymptomatic in comparison with symptomatic individuals.

Results There are only a limited number of published studies that report estimates of relative infectiousness of asymptomatic compared with symptomatic individuals. 12 studies were included after the screening process. Significant differences exist in the definition of infectiousness. PCR studies in general show no difference in shedding levels between symptomatic and asymptomatic individuals; however, the number of study subjects is generally limited. Two modelling studies estimate relative infectiousness to be 0.43 and 0.57, but both of these were more reflective of the infectiousness of undocumented rather than asymptomatic cases. The results from contact tracing studies includ estimates of relative infectiousness of 0, but with insufficient Check for updates evidence to conclude that it is significantly different from 1. C Author(s) (or their Conclusions There is considerable heterogeneity in employer(s)) 2021, Re-us estimates of relative infectiousness highlighting the need permitted under CC BY-NC. No commercial re-use. See rights for further investigation of this important parameter. It is not possible to provide any conclusive estimate of relative

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INTRODUCTION Correspondence to

The transmission potential of such asymptomatic individuals is likely to be differen from those who have clinical signs. On the one hand, they might shed lower quanti ties of the infectious agent; on the other The first case of COVID-19 was first reported hand, their potential for contacts might be from Wuhan, China, in December 2019, greater. Being unaware that they are infected

mate of relative

studies in this area.

within the population.

uals may never present with clinical signs (ie

symptomatic) yet still be infectious to other

The existence of this cohort of SARS-CoV-9

infected individuals is now well recognised.

McEvov D. et al. RMJ Open 2021:11:e042354. doi:10.1136/bmiopen-2020-042354

#### Collins Á, et al. Rapid revie Strengths and limitations of this study A strength of this study is that it only included pee This study also had a robust screening process that was used to ensure that the relative infectiousness of asymptomatic compared with symptomatic was defined properly. It ensured that each study properly distinguished asymptomatic and presympton Differences in the definition of infectiousness and the heterogeneity in results between studies negative the potential to provide a pooled quantitative esti-

The present study highlights the need for addition

The outbreak of COVID-19 was declared a Public Health Emergency of Internationa Concern on 30 January 2020 and a pandemi was declared on 11 March 2020.2 Since then many countries have sought to contain the spread of the virus through a range of measures aimed at limiting transmission At the outset of an epidemic, a key principl of control might be quarantining of individ uals with clinical symptoms fitting a particular case definition. However, for many infectiou diseases, a proportion of infected individ Check for updates

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#### of available evidence on the an infector-infectee pair. The generation time, also known serial interval and gene as the generation interval, is the time between infection time of COVID-19. BMJ Oper events in an infector-infectee pair. The serial interval and 2020:10:e040263. doi:10.1136/ the generation time are key parameters for assessing bmjopen-2020-040263 the dynamics of a disease. A number of scientific papers Prepublication history and reported information pertaining to the serial interval and/or additional material for this generation time for COVID-19. paper are available online. To Objective Conduct a review of available evidence to view these files, please visit advise on appropriate parameter values for serial interval the journal online (http://dx.do and generation time in national COVID-19 transmission org/10.1136/bmjopen-2020models for Ireland and on methodological issues relating 040263). to those parameters Received 18 May 2020 Reviewd 17 Sentember 2020

To cite: Griffin J. Casey M.

Open access

Methods We conducted a rapid review of the literature covering the period 1 January 2020 and 21 August 2020, Accepted 11 October 2020 following predefined eligibility criteria. Forty scientific papers met our inclusion criteria and were included in the

> Results The mean of the serial interval ranged from 3.03 to 7.6 days, based on 38 estimates, and the median from 1.0 to 6.0 days (based on 15 estimates). Only three estimates were provided for the mean of the generation time These ranged from 3.95 to 5.20 days. One estimate of 5.0 days was provided for the median of the generation Discussion Estimates of the serial interval and the

generation time are very dependent on the specific factors that apply at the time that the data are collected, including the level of social contact. Consequently, the estimates may not be entirely relevant to other environments Therefore, local estimates should be obtained as soon as possible. Careful consideration should be given to the methodology that is used. Real-time estimations of the serial interval/generation time, allowing for variations over time, may provide more accurate estimates of reproduction numbers than using conventionally fixed serial interval/generation time distributions

Serial interval/generation time

The serial interval is the time between symptom onsets in

of COVID-19

Simon More

ABSTRACT

BMJ Open Rapid review of available evidence on

the serial interval and generation time

John Griffin <sup>0</sup>, <sup>1</sup> Miriam Casey <sup>0</sup>, <sup>1</sup> Áine Collins, <sup>1,2</sup> Kevin Hunt, <sup>3</sup> David McEvoy,

Andrew Byrne <sup>(3)</sup>, <sup>5</sup> Conor McAloon <sup>(3)</sup>, <sup>6</sup> Ann Barber, <sup>1</sup> Elizabeth Ann Lane <sup>(3)</sup>

#### INTRODUCTION

Irish Epidemiological Modelling Advisory Group (IEMAG) for COVID-19 was established to assist the Irish National Public Health Emergency Team in their decision-making during the pandemic. A subcommittee from interval and generation time in national

ransmission model for Ireland

symptom onsets in an infector-infectee pair that is, the interval between the onset of symp toms in an infectee and its presumed infector. This can be a negative number if the onse of symptoms in the infectee occurs prior to the onset of symptoms in the infector. The generation time, also known as the genera tion interval, is the time between infection events in an infector-infectee pair. The serial interval and the generation time are key parameters for assessing the dynamics of an infectious disease, and the generation time. or its proxy the serial interval, is an essential quantity for estimating the reproduction number

A number of scientific papers reported information pertaining to the serial interval context of national control efforts in Ireland our objective was to conduct a rapid review of available evidence to advise the IEMAG on appropriate parameter values for serial

Griffin J, et al. BMJ Open 2020;10:e040263. doi:10.1136/bmjopen-2020-040263

rengths and limitations of this study The study provides timely information on serial in terval and generation time for those involved in th development of models and in the implementation of introl measures against COVID-19. This is a rapid review of available evidence in the scientific literature between 1 January 2020 and 21 ugust 2020 on the serial interval and the gener tion time and it contains the usual limitations as ciated with such a review.

The statistical methods used in the different paper were not analysed in detail. IEMAG was tasked with researching the various parameters, leading to the development of a series of synthesis documents rele

vant to the parameterisation of a COVID-19 The serial interval is the time between



Ireland For what's next

# **HIQA-EAG evidence synthesis**

Impact of HRB SPHeRE doctoral training programme

### Duration of immunity

Received: 1 July 2020 Revised: 16 August 2020 Accepted: 17 August 2020

DOI: 10.1002/mv.2162

REVIEW

WILEY

### Immune response following infection with SARS-CoV-2 and other coronaviruses: A rapid review

Eamon O Murchu<sup>1,2</sup> | Paula Byrne<sup>1</sup> | Kieran A. Walsh<sup>1</sup> | Paul G. Carty<sup>1</sup> | Máire Connolly<sup>3</sup> | Cillian De Gascun<sup>4</sup> | Karen Jordan<sup>1</sup> | Mary Keoghan<sup>5</sup> Kirsty K. O'Brien<sup>1</sup> | Michelle O'Neill<sup>1</sup> | Susan M. Smith<sup>6</sup> | Conor Teljeur<sup>1</sup> | Máirín Ryan<sup>1,7</sup> | Patricia Harrington<sup>1</sup>

were searched from 1/1/2000 until 26/5/2020.

In this review, we systematically searched and summarized the evidence on the immune

response and reinfection rate following SARS-CoV-2 infection. We also retrieved studies

on SARS-CoV and MERS-CoV to assess the long-term duration of antibody responses. A

protocol based on Cochrane rapid review methodoloev was adhered to and databases

Of 4744 citations retrieved, 102 studies met our inclusion criteria. Seventy-four stud-

ies were retrieved on SARS-CoV-2. While the rate and timing of IgM and IgG sero-

conversion were inconsistent across studies, most seroconverted for IeG within

2 weeks and 100% (N = 62) within 4 weeks, IgG was still detected at the end of

follow-up (49-65 days) in all patients (N = 24). Neutralizing antibodies were detected

in 92%-100% of patients (up to 53 days). It is not clear if reinfection with SARS-

CoV-2 is possible, with studies more suggestive of intermittent detection of

Twenty-five studies were retrieved on SARS-CoV. In general, SARS-CoV-specific IgG

was maintained for 1-2 years post-infection and declined thereafter, although one

study detected IgG up to 12 years post-infection. Neutralizing antibodies were

detected up to 17 years in another study. Three studies on MERS-CoV reported that

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Summary

residual RNA.

IgG may be detected up to 2 years.

Albreviations: CDC, Centers for Disease Control and Prevention: CJ. Confidence Interval: Covid-19, Coronavirus disease 2019; HQA, Health Information and Quality Authority; IzA.

Immandiata A.S., Chang and A.S., Chang and A.S. (2014) and

#### Earnon O Murchu, Health Information and Quality Authority, George's Court, Dublin

7. Ireland. Email: com

Funding information This research was funded in part by the Health search Board under grant no. HRB-CICER 2016-1871

### Duration of infectious period



#### Review

SARS-CoV-2 detection, viral load and infectivity over the course of an infection

#### Kieran A. Walsh \*\*, Karen Jordan \*, Barbara Clyne \*, Daniela Rohde \*, Linda Drummond \*, Paula Byrne<sup>a</sup>, Susan Ahern<sup>a</sup>, Paul G. Carty<sup>a</sup>, Kirsty K. O'Brien<sup>a</sup>, Eamon O'Murchu<sup>a</sup>, Michelle O'Neill<sup>a</sup>, Susan M. Smith<sup>b</sup>, Máirín Ryan<sup>a,c,1</sup>, Patricia Harrington<sup>a</sup>,

<sup>4</sup> Health Information and Quality Authority, Smithfield, Dublin 7, Ireland
<sup>6</sup> Health Research Board Centre for Primary Care Research, Department of General Practice, Royal College of Surgeons in Ireland, 123 St Stephens Green, Dublin 2. Ireland <sup>4</sup>Department of Pharmacology & Therapeutics, Trinity College Dublin, Trinity Health Sciences, James Street, Dublin 8, Ireland

ARTICLE INFO	S U M M A R Y
Article history: Accepted 26 June 2020 Available online 29 June 2020	Objectives: To summarise the evidence on the detection pattern and viral load of SARS-CoV-2 over the course of an infection (including any asymptomatic or pre-symptomatic phase), and the duration of in- fectivity.
Keywords:	Methods: A systematic literature search was undertaken in PubMed, Europe PubMed Central and EMBASE from 30 December 2019 to 12 May 2020.
COVID-19 SARS-CoV-2 Viral load Infectivity RNA	Results: We identified 113 studies conducted in 17 countries. The evidence from upper respiratory tract samples suggests that the viral load of SAMS-GoV-2 peaks around symptom onset or a few days thereafter, and becomes undetectable about two weeks after symptom onsets the owner, viral laads from systum samples may be higher, peak later and persist for longer. There is evidence of prolonged virus detection in stead assumes tables advances alloid namices and persist.
Review	No study was found that definitively measured the duration of inferitvity: however, patients may not be infections for the entite duration of virus detection, as the presence of viral ribonucleic acid may not represent transmissible line virus. Graduator: There is a relatively consistent trajectory of SMS-CoV-2 viral load over the course of COVID-
	19 from respiratory tract samples, however the duration of infectivity remains uncertain.

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Introd	iction
The lic heal numbe precede missibi mortali immun ment o and so evidene formati	Coronavirus Disease 2019 (COVID-19) pandemic is a pub- th emergency of international concern causing a substantial of cases and deshift globally. <sup>12</sup> COVID-19 presents an un- of cases and deshift globally. <sup>12</sup> COVID-19 presents an un- tily of the wires, the scale of its impact on morbidity and the uncertainty regarding the development of long-term by the uncertainty regarding the development of long-term ty in those infected, the current Lack of vaccine or trad- tions, and the impact on healthcare systems, economies icteg. <sup>1,4</sup> Much remains unknown about COVID-19: however e is emerging at a fast pace. <sup>2</sup> Dur term an the Health In- on and Quality Authority (HIQA) of Ireland has conducted a
• Com	sponding author at: Health Information and Quality Authority, Unit 1301, Mahon 112 Y2XT, Cork, Ireland.
E-ma	il address: kiwalsh@hiqa.ie (K.A. Walsh).
<sup>1</sup> Both	authors are co-senior authors.

#### series of rapid reviews on various public health topics relating to COVID-19 The rapid reviews arose directly from questions posed by policy makers and expert clinicians supporting the Irish Na tional Public Health Emergency Team (NPHET). Hence, the find ings of these reviews have informed the national response to the COVID-19 pandemic in Ireland.<sup>6</sup> and have implications for interna tional health policy as well as clinical and public health guidance Understanding the trajectory of severe acute respiratory syn drome coronavirus 2 (SARS-CoV-2), and the duration of infectiv ity is of critical importance to controlling the pandemic.7 As SARS CoV-2 is a novel virus in the human population, there is substan-tial uncertainty regarding virological levels (i.e. detection and viral load) in patients and how this relates to infectivity and dis ease severity. Information relating to SARS-CoV-2 detection and vi ral load at different time points of an infection, including in those without any symptoms, will aid with the clinical interpretation

of real-time reverse transcriptase polymerase chain reaction (rRT-PCR) test results. Furthermore, information pertaining to the dura-

0163-4453/0 2020 The British Infection Association. Published by Elsevier Ltd. All rights reserved

### Duration of immunity / risk of reinfection

Received: 27 April 2021 Revised: 17 May 2021 Accepted: 18 May 2021

DOI: 10.1002/rms 2260

REVIEW

### WILEY

Despite over 140 million SARS-CoV-2 infections worldwide since the beginning of the

pandemic, relatively few confirmed cases of SARS-CoV-2 reinfection have been re-

### Quantifying the risk of SARS-CoV-2 reinfection over time

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Funding information

Number: HRB-CICER-2016-1871

#### fection over time. A standardised protocol was employed, based on Cochrane methodology. Electronic databases and preprint servers were searched from 1 January 2020 to 19 February 2021. Eleven large cohort studies were identified that estimated the risk of SARS-CoV-2 reinfection over time, including three that enrolled healthcare workers and two that enrolled residents and staff of elderly care homes. Across studies, the total number of PCR-positive or antibody-positive participants at baseline was 615,777, and the maximum duration of follow-up was more than 10 months in three studies. Reinfection was an uncommon event (absolute rate 0%-1.1%), with no study reporting an increase in the risk of reinfection over time. Only one study estimated the population-level risk of reinfection based on whole genome sequencing in a subset of patients; the estimated risk was low (0.1% [95% CI: 0.08-0.11%]) with no evidence of waning immunity for up to 7 months following primary infection. These data suggest that naturally acquired SARS-CoV-2 immunity does not wane for at least

10 months post-infection. However, the applicability of these studies to new variants

KEYWORDS COVID-19. SARS-CoV-2. reinfection

or to vaccine-induced immunity remains uncertain

#### 1 | INTRODUCTION

countries worldwide have experienced epidemics of Covid-19. While much is yet unknown about the immune response following infection Following the emergence of a novel coronavirus (SARS-CoV-2) in with SARS-CoV-2, evidence is emergine at a fast pace. The Health China in December 2019 and the declaration by WHO of a public Information and Quality Authority (HIQA) of Ireland has conducted a health emergency of international concern on 30 January 2020, series of rapid reviews on various public health topics relating to

Abbreviations: Covid-19. contravirus disease 2019: CL confidence interval: CL cucle threshold: HIOA. Health Information and Quality Authority: IPG immunoslobulin G NAAT, nucleic add nology, RNA, ribonucleic Acid; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory s ndrome coronavirus type 2: WHO, Worl Health Organization

Patricia Harrington and Mäirin Ryan are co-senior authors.

Rev Med Virol. 2022;32:e2260.	wileyonlinelibrary.com/journal/rmv	© 2021 John Wiley & Sons Ltd.	1 of
https://doi.org/10.1002/rmv.2260			

Rev Med Virol. 2021;31:e2162 wileyonlinelibrary.com/journal/rmv https://doi.org/10.1002/mnv.2162

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ported. While immunity from SARS-CoV-2 infection is probable, at least in the short term, few studies have quantified the reinfection risk. To our knowledge, this is the first systematic review to synthesise the evidence on the risk of SARS-CoV-2 rein-

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# **SEIR models**







# **Communicating risk and uncertainty**

# A delay of weeks greatly attenuates any fourth wave

These model runs delay the low additional close contact scenario (initial Reff  $\approx$  1.5) by four weeks (B1) and eight (B2) weeks, reducing anticipated case numbers and risk by approximately 25% and 50% respectively.



### B. 199,000 (95,000-279,000) cases

### B1. 152,000 (69,000-185,000) cases



### B2. 96,000 (51,000-129,000) cases



Homogeneous population SEIR model scenario estimates of new cases per day; credible intervals generated from 1000 runs of the model with different assumptions. The solid line is the ensemble average of all runs, dark ribbon the interquartile range, and the light ribbon the 2.5 and 97.5 percentiles. The effect of vaccination included according to current vaccination plan, with average vaccine effectiveness assumed to be 85% 28 days from first dose and uptake 80-90%. The stated R<sub>eff</sub> applies on 5 April 2020 – transmissibility is held constant in the model from that point, but measured R<sub>eff</sub> will decrease as immunity increases; transmissibility is then increased from 3 May or 31 May, and the stated R<sub>eff</sub> is that which would have applied, for that level of transmissibility, on 5 April 2021. The actual measured R<sub>eff</sub> will be lower due to increased population immunity

Rialtas na hÉireann Government of Ireland



# The challenge of influencing policy



Responsible risk profile	Informed decisions	Risk management
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Minimise	Maximise	Knowledge
uncertainty	understanding	management



# The challenge of influencing policy



Scope to ease restrictions on golf and children's sport, immunologist claims

### Health expert accuses government of 'pandering' to pubs and slams vaccine certs 'catastrophe'

A leading immunology expert has called for an immediate public inquiry into NPHET and the government "while the players are still on the pitch"

# Covid-19 antigen tests should be free for everyone in Ireland says immunology expert

"This is Delta and we haven't dealt with Delta in a winter situation before"

Covid boosters should be rolled out to over 40s, immunologist says

# Immunology expert calls for rapid antigen tests for children

Regular Covid-19 vaccines similar to flu jab will be needed - immunologist



# The nature of knowledge

- Explicit / scientific knowledge is dynamic, contested and sometimes unstable
- Tacit / experiential knowledge essential, especially with instability or uncertainty
- Knowledge management and evidence synthesis are sophisticated disciplines – ongoing research and training are critical
- Large and diverse expert groups may be useful in achieving "knowledge and risk-based decisions"



# The challenge of influencing policy





# **Lessons and observations**

- The need for data infrastructures
  - and a national conversation on governance, privacy, security and trust
- The importance of knowledge management, systematic review and evidence synthesis
- The value of structured PhD programmes for key skills
- The management of population risks (explicit or implicit, direct or indirect) creates particular knowledge and risk management challenges



# **Lessons and observations**

- Science in the media can be confusing for the public
  - "follow the science" versus contested and contingent nature of scientific knowledge
- Independence of a public risk advisory structure is essential
  - but so are humility, empathy, trust, persistence, resilience ... and respect for the political system and the democratic mandate
- Difficult questions on governance, ethics and communication where professionals seek to manage risk on behalf of a community or population