



RESEARCH NOTE

REVISED **The second wave: estimating the hidden asymptomatic prevalence of COVID-19 in Ireland as we plan for imminent immunisation [version 2; peer review: 2 approved]**

Catherine Comiskey , Anne Snel, Prakashini Banka

School of Nursing and Midwifery, Trinity College Dublin, The University of Dublin, Dublin, 2, Ireland

V2 **First published:** 18 Feb 2021, 4:19
<https://doi.org/10.12688/hrbopenres.13206.1>
Latest published: 25 Feb 2022, 4:19
<https://doi.org/10.12688/hrbopenres.13206.2>



Abstract





Since the first case of COVID-19 in Ireland was recorded policy makers have introduced mitigation measures to control the spread of infection. Infection is spread by both known cases and hidden, undetected asymptomatic cases. Asymptomatic individuals are people who transmit the virus but display no clinical symptoms. Current evidence reveals that this population is a major contributing factor to the spread of the disease. There is little or no knowledge of the scale of the hidden prevalence of all infections both asymptomatic and symptomatic in Ireland. Furthermore, as governments plan for the roll out of imminent immunisation programmes, the need to know the scale of the hidden prevalence and hence knowledge of the level of immunisation required is essential.


We describe and analyse the numbers of reported cases of COVID-19 in Ireland from the first case in February 2020 to mid-December 2020. Using the method of back-calculation we provide estimates of the asymptomatic prevalence of cases from June to December 2020. The descriptive analysis highlighted two epidemic waves of known cases in the time period. Wave two from June to December included twice as many cases as wave one and cases were significantly younger. The back-calculation estimates of asymptomatic prevalence during this time period revealed that for every case known there was an additional unknown case and total prevalence in wave two was estimated to be approximately 95,000 as opposed to the reported 48,390 cases.


As prevalence in wave two is known to be spreading within and from younger age groups the role of mixing patterns on spread needs to be disseminated to the wider public to adequately inform them how personal modifications in behaviour can contribute to the control of the epidemic. While universally imposed lockdowns and mitigation measures may be essential, personal behavioural mixing choices are powerful protectors.

Open Peer Review

Approval Status  

	1	2
version 2 (revision) 25 Feb 2022		 view
version 1 18 Feb 2021	 view	  view

1. **Yoon Hong Choi** , Public Health England, London, UK

2. **Harapan Harapan** , Universitas Syiah Kuala, Banda Aceh, Indonesia

Any reports and responses or comments on the article can be found at the end of the article.

Keywords

COVID-19, prevalence, age, mixing, mitigation, lockdown, back-calculation, back-projection



This article is included in the [Coronavirus \(COVID-19\)](#) collection.

Corresponding author: Catherine Comiskey (catherine.comiskey@tcd.ie)

Author roles: **Comiskey C:** Conceptualization, Funding Acquisition, Investigation, Methodology, Resources, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing; **Snel A:** Formal Analysis, Investigation, Methodology, Validation, Writing – Review & Editing; **Banka P:** Formal Analysis, Investigation, Project Administration, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: Health Research Board Ireland and Irish Research Council [COV19-2020-010].

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Copyright: © 2022 Comiskey C *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Comiskey C, Snel A and Banka P. **The second wave: estimating the hidden asymptomatic prevalence of COVID-19 in Ireland as we plan for imminent immunisation [version 2; peer review: 2 approved]** HRB Open Research 2022, 4:19 <https://doi.org/10.12688/hrbopenres.13206.2>

First published: 18 Feb 2021, 4:19 <https://doi.org/10.12688/hrbopenres.13206.1>

REVISED Amendments from Version 1

Within this version we have provided some more detail explaining the back-calculation method. We have explained that we fitted models to the increasing and decreasing phase of each epidemic wave to improve models fits. Finally, we have included one further limitation explaining that it is also possible that some individuals may have been symptomatic and infectious and did not seek a test and were therefore not recorded in the data. For these reasons our estimates can be considered a minimum estimate.

Any further responses from the reviewers can be found at the end of the article

Introduction

Coronavirus disease 2019 or COVID-19 is a novel human respiratory disease caused by the SARS-CoV-2 virus and was first identified in 2019¹. The surveillance of COVID-19 cases in Ireland was integrated into the existing national Computerised Infectious Disease Reporting (CIDR) system when the notification of the disease was made mandatory in February 2020². Since the first case of COVID-19 in Ireland was recorded policy makers have introduced mitigation measures to control the spread of infection³. These measures included public health advice to stay and work at home, restrictions on travel, the closure of educational settings, the cancellation of routine hospital procedures and the isolation and contact tracing of cases identified through testing centres³. It has been observed that during these periods of increased and subsequent decreased mitigation measures the reported number of positive cases has decreased and increased in line with the implementation and removal of the measures. These increases and decreases are referred to as epidemic waves⁴ and their relationship to the mitigation measures have been clearly established and modelled in Ireland⁵.

Infection we know is spread by both known cases and hidden, undetected asymptomatic cases. Asymptomatic individuals in the context of COVID-19 are people who are carriers of the virus but display no clinical symptoms. Current evidence reveals that this population is a major contributing factor to the spread of the disease, while escaping detection by public health surveillance systems⁵. As a result of this lack of detection public health systems can record only the daily incidence of new known cases and there is little or no knowledge of the actual scale of the hidden cumulative prevalence of all infections both asymptomatic and symptomatic. Furthermore, as governments plan for the roll out of imminent national immunisation programmes, the need to know the scale of the hidden prevalence and hence knowledge of the level of immunisation required is essential to produce the so called ‘herd immunity’ defined as ‘the protection of populations from infection which is brought about by the presence of immune individuals’^{5,6}.

The aim of this research was to build on previous modelling work and provide an estimate of the hidden and asymptomatic prevalence of COVID-19 in Ireland during the second wave

of infection from October to December 2020. Methods while developed nationally are applicable globally. The objectives were to provide a descriptive and comparative analysis of the first and second waves; to use the back-calculation method to provide an estimate of total prevalence of cases during the second wave and an estimate of the ratio of unknown asymptomatic cases to known symptomatic recorded cases and finally to provide recommendations for future research to enable effective immunisation modelling and planning.

Methods

A plot of the five-day moving average of the reported numbers of COVID-19 cases from the first recorded case on the 29th of February 2020 to the 8th of December 2020 was prepared. Descriptive statistics illustrating the numbers of known cases, hospitalised cases, intensive care cases and deaths during this period were computed and cumulative cases by age group were derived. The Chi-squared test of association was used to test the independence of the relationship between the number of cases during an epidemic wave and the numbers of cases reported by age group. This statistic was also used to test the relationship between the number of cases during an epidemic wave the number of hospitalised cases by age group.

Following the statistical analysis of the known cases from the Irish reporting system the back-calculation method was implemented to estimate the numbers of asymptomatic and unknown cases. Working with observed symptomatic cases and the known incubation period, these models predict backwards in time through the incubation period distribution the total numbers of infected and asymptomatic cases these observed cases arose from.

The method of back-calculation also known as back-projection is well documented and implemented internationally for a wide variety of infectious and social epidemics, from HIV/AIDS to bio-terrorism to heroin use⁷⁻¹⁰. Previous use of the back-calculation model to predict the incidence and prevalence of disease, particularly AIDS, in the United States, the United Kingdom and Ireland is well documented¹¹⁻¹⁴. The method is known as an indirect method and working with observed symptomatic cases and the known incubation period, the model predicts minimum estimates of the hidden numbers of infected cases. The model is given by,

$$C_T(t) = \int_0^t C_U(t-s)f(s)ds$$

Where $C_T(t)$ describes the change in the incidence of the treated and known cases over a defined time period, $f(s)$ is the incubation period distribution of the disease and $C_U(t)$ is the unknown number of cases at time t we wish to solve for. The prevalence of the unknown cases over the defined time period is then given by,

$$\int_0^t C_U(t)dt$$

Given varying forms in the growth of the known cases $C_T(t)$ and the incubation period $f(s)$, the back-calculation model can be solved analytically as in Comiskey^{7,8}, Comiskey and Hay¹⁵, Dempsey and Comiskey^{10,16} or numerically as in Comiskey and Ruskin¹³. The details of the incubation period distribution for COVID-19 $f(t)$ are provided by Banka and Comiskey¹⁷ who in their international scoping review found a mean incubation period of 6.7 days with a standard deviation of 4.0 days. The mathematical solution of the back-calculation equation when $f(t)$ is described by the Gamma distribution as identified by Banka and Comiskey (2020) and given by $\Gamma(\alpha, \lambda)$ when $\alpha = 6$ and when $\alpha = 3$ were originally provided by Dempsey and Comiskey^{10,16} and latterly for early COVID-19 modelling in Ireland by Comiskey, Snel and Banka¹⁸. These solutions were implemented here with data on daily COVID-19 cases reported to the national Computerised Infectious Disease Reporting (CIDR) system and available at website https://covid-19.geohive.ie/datasets/d8eb52d56273413b84b0187a4e9117be_0

This research received ethical approval from the Faculty of Health Sciences at Trinity College Dublin, The University of Dublin, Ireland.

Results

A plot of the number of daily cases reported to the national system from the 29th of February to the 8th December 2020 are provided in Figure 1. From this we can clearly see that Ireland has recorded to date two epidemic waves each with an increasing and decreasing phase. As two epidemic waves were observed in the data, we study each wave separately. To improve the fit of the models to the data we fit the models separately to the increasing and decreasing part of the wave.

From the reported data we can see that during wave one and two a total of 74,439 cases were reported and perhaps more importantly we can also see that greater numbers of individuals were infected within wave two. A total of 25,189 cases were reported in wave one and this almost doubled and increased to 49,250 cases being reported in the second wave. A comparison of the reported cases by age distribution across the two waves is provided in Table 1.

A comparison of the distribution of known cases by age between wave one and wave two is provided in Table 2. We can see that there was a significant change in the age distribution of cases between the two time periods. Within wave one those aged over 65 years of age accounted for approximately between one fifth and one quarter of all reported cases while those under the age of 25 years approximately accounted for one tenth of all cases. Within wave two however this situation reversed with those over the age of 65 accounting for approximately one tenth of all cases and those under the age of 25 accounting for one third of all cases.

Clearly the dynamics of spread changed in wave two as societal mitigation measures were relaxed and prevention measures within older person settings were enhanced. Exploring wave two in more detail using the back-calculation method we initially fitted, using simple regression techniques, separate curves $C_T(t)$ to all of the known cases of COVID-19 during both the increasing and decreasing phase of wave two. This included cases where the age was unknown. These curves included exponential, logarithmic, quadratic and cubic models. Details of the best fitting curves amongst all curves fitted are provided in Table 3.

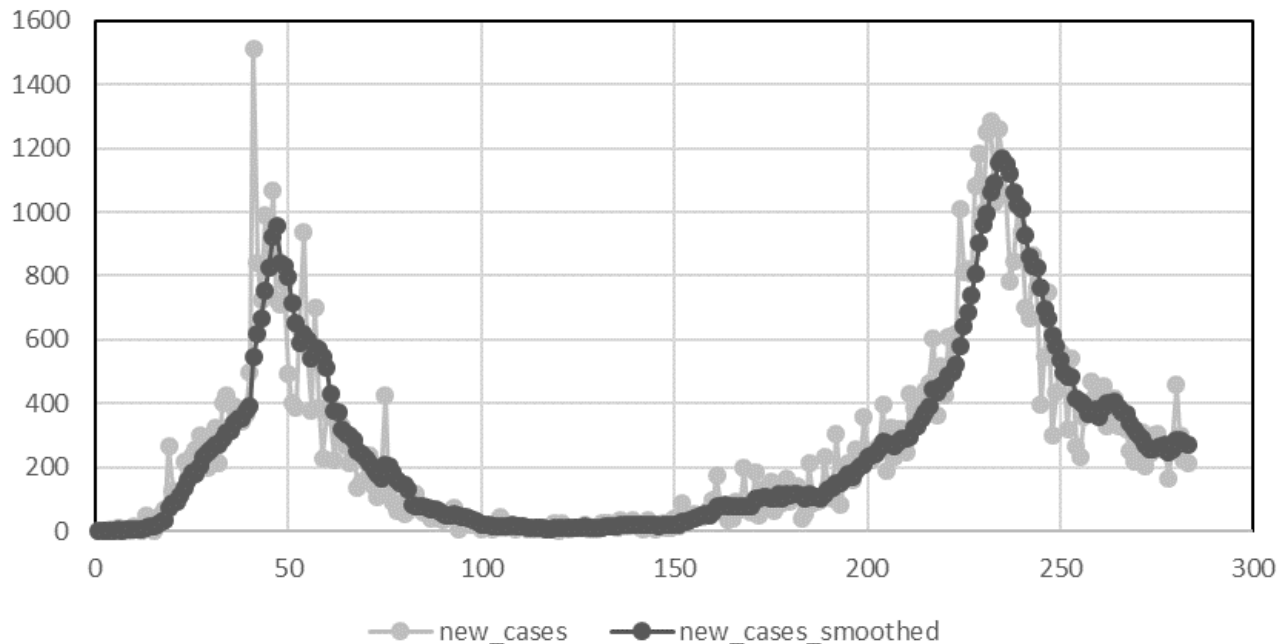


Figure 1. Daily reported incidence of COVID-19 from 29th February to 8th December 2020.

Table 1. COVID-19 cases in Ireland during the increasing and decreasing phases of epidemic wave 1 and wave 2, where the age of the case was known.

	Wave 1		Wave 2	
	Phase 1	Phase 2	Phase 1	Phase 2
	29 th Feb- 16 th Apr	17 th Apr - 10 th Jun	11 th Jun - 21 st Oct	22 nd Oct - 8 th Dec
Total Cumulative Cases	12,405	25,189	52,226	74,439
< 5 Years	72	161	1,013	1,972
5 - 14 Years	124	320	2,404	4,847
15 - 24 Years	809	1,861	8,667	12,976
25 - 34 Years	2,145	4,223	9,068	12,498
35 - 44 Years	2,315	4,438	8,370	11,673
45 - 54 Years	2,395	4,535	8,134	11,227
55 - 64 Years	1,806	3,232	5,841	7,935
> 65 Years	2,739	6,419	8,729	11,311
Total Cases Within the Time Period	12,405	12,784	27,037	22,213
< 5 Years	72	89	852	959
5 - 14 Years	124	196	2,084	2,443
15 - 24 Years	809	1,052	6,806	4,309
25 - 34 Years	2,145	2,078	4,845	3,430
35 - 44 Years	2,315	2,123	3,932	3,303
45 - 54 Years	2,395	2,140	3,599	3,093
55 - 64 Years	1,806	1,426	2,609	2,094
> 65 Years	2,739	3,680	2,310	2,582
Hospitalised Cumulative Cases	2,026	3,321	4,055	5,343
< 5 Years	13	20	42	58
5 - 14 Years	4	17	36	51
15 - 24 Years	43	71	123	171
25 - 34 Years	132	198	261	333

	Wave 1		Wave 2	
	Phase 1	Phase 2	Phase 1	Phase 2
	29 th Feb- 16 th Apr	17 th Apr - 10 th Jun	11 th Jun - 21 st Oct	22 nd Oct - 8 th Dec
35 - 44 Years	164	260	327	424
45 - 54 Years	298	445	528	668
55 - 64 Years	308	489	605	765
> 65 Years	1,062	1,819	2,130	2,871
Hospitalised Cases Within the Time Period	2,026	1,295	733	1,289
< 5 Years	13	7	22	16
5 - 14 Years	4	13	19	15
15 - 24 Years	43	28	52	48
25 - 34 Years	132	66	63	72
35 - 44 Years	164	96	67	97
45 - 54 Years	298	147	83	140
55 - 64 Years	308	181	116	160
> 65 Years	1,062	757	311	741
ICU Cumulative Cases	284	411	519	630
ICU Cases Within the Time Period	284	127	108	111
Healthcare Workers Cumulative Cases	3,090	8,099	10,012	12,302
Healthcare Workers Cases Within the Time Period	3,090	5,009	1,913	2,290
Total Cumulative Deaths	486	1,695	1,868	2,097
Total Deaths Within the Time Period	486	1,209	173	229

The solutions provided by Comiskey, Snel and Banka¹⁸ for the unknown number of cases $C_U(t)$ given the best fitting curve $C_T(t)$ were then applied and the results are provided in Table 4.

From Table 4, we can see that regardless of the exact nature of the Gamma distribution chosen for the incubation period, the model predicts that for each known infectious case reported

Table 2. Proportions of cases by age within each epidemic wave and Chi-square results.

	Wave 1		Wave 2		χ^2
	Phase 1	Phase 2	Phase 1	Phase 2	
	29 th Feb–16 th Apr	17 th Apr – 10 th Jun	11 th Jun – 21 st Oct	22 nd Oct – 8 th Dec	
Cases					
< 5 Years	0.58	0.70	3.15	4.32	$\chi^2 = 32.57$ $p \leq 0.001$ df = 21
5 – 14 Years	1.00	1.53	7.71	11.00	
15 – 24 Years	6.52	8.23	25.17	19.40	
25 – 34 Years	17.29	16.25	17.92	15.44	
35 – 44 Years	18.66	16.61	14.54	14.87	
45 – 54 Years	19.31	16.74	13.31	13.92	
55 – 64 Years	14.56	11.15	9.65	9.43	
> 65 Years	22.08	28.79	8.54	11.62	
Hospitalised Cases					
< 5 Years	0.64	0.54	3.00	3.00	$\chi^2 = 32.57$ $p \leq 0.001$ df = 21
5 – 14 Years	0.20	1.00	2.59	2.59	
15 – 24 Years	2.12	2.16	7.09	7.09	
25 – 34 Years	6.52	5.10	8.59	8.59	
35 – 44 Years	8.10	7.41	9.14	9.14	
45 – 54 Years	14.72	11.35	11.32	11.32	
55 – 64 Years	15.22	13.98	15.83	15.83	
> 65 Years	52.47	58.46	42.43	42.43	

Table 3. $C_T(t)$ details of the best fitting curve amongst all curves fitted to the known number of COVID-19 cases within wave two of the epidemic.

Epidemic Wave	Best fitting curve	R squared	F; df1, df2; p
Wave 2, increasing, 11 th June to 21 st October	$C_T(t) = 0.120 e^{0.037t}$	0.953	2645.790; 1, 131; $p \leq 0.001$
Wave 2, decreasing, 22 nd October to December 8 th	$C_T(t) = 0.622t^2 - 341.160t + 47039.209$	0.971	749.348; 2, 45; $p \leq 0.001$

Table 4. Estimates of the hidden prevalence of COVID-19 in Ireland during the second epidemic wave.

Epidemic Wave Given $\alpha = 3$	Estimated Hidden Prevalence, $C_h(t)$	Known Diagnosed Prevalence, $C_d(t)$	Estimated Total Prevalence	Ratio of Unknown to Known Cases
Wave 2, increasing phase 11 th June – 21 st October	28,155	28,184	56,339	1.00:1
Wave 2, decreasing phase 22 nd October–8 th December	18,764	20,206	38,970	0.93:1
Total 11th June – 8th December	46,919	48,390	95,309	0.97:1
Epidemic Wave Given $\alpha = 2$				
Wave 2, increasing phase 11 th June – 21 st October	28,026	28,184	56,210	0.99:1
Wave 2, decreasing phase 22 nd October–8 th December	18,544	20,206	38,750	0.92:1
Total 11th June – 8th December	46,570	48,390	94,960	0.96:1

there exists approximately one unreported asymptomatic infectious case contributing to infection within the population.

Discussion/conclusions

The principal finding from this study illustrates that in Ireland the true prevalence of the scale of the COVID-19 epidemic may be twice that which has been recorded through testing. Results for the period from early June 2020 to early December 2020 suggest that while the prevalence of known cases was approximately 48,000, the asymptomatic prevalence was estimated to be approximately a further 46,000 cases. Furthermore, a detailed analysis of the known number of cases illustrated that as of early December 2020 Ireland has experienced two COVID-19 epidemic waves. The second wave involved almost twice the numbers of cases as the first. Within the first wave most infections occurred among those aged 65 years and older. The age profile of the second wave was significantly different to the first and most cases were observed within those under the age of 25 years.

Results presented must be interpreted in light of their limitations. Reported numbers presented were not adjusted for potential reporting delays. In addition, results of the back-calculation method were computed solely for an incubation period described by a Gamma distribution and other distributions may be equally as applicable. It is also possible that some individuals may have been symptomatic and infectious and did not seek a test and were therefore not recorded in the data. For these reasons an estimate can be considered a minimum estimate.

However, given these limitations the results presented do provide new and additional knowledge on the scale of asymptomatic prevalence within Ireland. Given the estimates of the asymptomatic prevalence during the second wave, and given that known cases are significantly younger than previously, and according to one study directly related to increases in the movement of people⁵ there is a clear need to focus on transmission between and more importantly from those in younger age groups. The impact of mixing patterns on the spread of disease from one age group to another is well established and it is known that mixing *between* age groups carries far greater risk to the spread of disease than mixing *within* age groups¹⁹. It is these mixing patterns which need to be addressed while Ireland awaits vaccine roll out and avoids a potential third wave of a COVID-19 epidemic. Further research is needed on asymptomatic prevalence within age groups. Additional research illustrating the role of mixing patterns on spread needs to be disseminated to the wider public to adequately inform them how personal modifications in behaviour can contribute to the control of the epidemic. While universally imposed lockdowns and mitigation measures may be essential, personal behavioural mixing choices are powerful protectors.

Data availability

Publicly available data was accessed from Our World in Data webpage: <https://ourworldindata.org/coronavirus-data> and the Health Protection and Surveillance Centre (HPSC) Computerised Infectious Disease Reporting (CIDR) system and available at website https://covid-19.geohive.ie/datasets/d8eb52d56273413b84b0187a4e9117be_0

References

1. Zhu N, Zhang D, Wang W, *et al.*: **A novel coronavirus from patients with pneumonia in China, 2019.** *N Engl J Med.* 2020; **382**(8): 727–733.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
2. **Minister for Health signs regulations to make Covid-19 a Notifiable Disease.** [press release]. Ireland: Irish Government, 2020.
[Reference Source](#)
3. Kennelly B, O'Callaghan M, Coughlan D, *et al.*: **The COVID-19 pandemic in Ireland: An overview of the health service and economic policy response.** *Health Policy Technol.* 2020; **9**(4): 419–429.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
4. Atkinson C, Reuter G: **Deterministic epidemic waves.** *Mathematical Proceedings of the Cambridge Philosophical Society.* Cambridge University Press. 1976; **80**(2): 315–330.
[Publisher Full Text](#)
5. Cazelles B, Comiskey C, Van Yen BN, *et al.*: **Identical trends of SARS-Cov-2 transmission and retail and transit mobility during non-lockdown periods.** *International Journal of Infectious Diseases.* under review. 2020.
6. Mahase E: **Covid-19: Vaccine roll out could take a year and will require difficult prioritisation decisions.** *BMJ.* 2020; **371**: m3846.
[PubMed Abstract](#) | [Publisher Full Text](#)
7. Comiskey CM: **Improvements in Integral Equation Models for Estimates of the Level of HIV Infection in Ireland.** *J Roy Stat Soc D-Sta.* 1992; **41**(3): 329.
[Publisher Full Text](#)
8. Comiskey C: **Integral equations and estimating the incidence of HIV infection.** *Z Angew Math Mech.* 1996; **76**: 505–6.
[Reference Source](#)
9. Brookmeyer R, Blades N: **Statistical models and bioterrorism: Application to the U.S. anthrax outbreak.** *J Am Stat Assoc.* 2003; **98**(464): 781–8.
[Publisher Full Text](#)
10. Dempsey O, Comiskey CM: **Estimating the Prevalence of Illegal Drug Use.** *Math Popul Stud.* 2014; **21**(2): 65–77.
[Publisher Full Text](#)
11. Brookmeyer R, Damiano A: **Statistical methods for short-term projections of AIDS incidence.** *Stat Med.* 1989; **8**(1): 23–34.
[PubMed Abstract](#) | [Publisher Full Text](#)
12. Brookmeyer R, Gail MH: **A method for obtaining short-term projections and lower bounds on the size of the AIDS epidemic.** *J Am Stat Assoc.* 1988; **83**(402): 301–8.
[Publisher Full Text](#)
13. Comiskey CM, Ruskin HJ: **AIDS in Ireland: the reporting delay distribution and the implementation of integral equation models.** *Bioinformatics.* 1992; **8**(6): 579–81.
[PubMed Abstract](#) | [Publisher Full Text](#)
14. Isham V: **Mathematical modelling of the transmission dynamics of HIV infection and AIDS: a review.** *J R Stat Soc Ser A Stat Soc.* 1988; **151**(1): 5–30.
[Publisher Full Text](#)
15. Comiskey C, Hay G: **The method of back calculation as a means of estimating incidence.** *Modelling drug use: methods to quantify and understand hidden processes.* 2001; 105.
[Reference Source](#)
16. Dempsey O, Comiskey CM: **Estimating the incidence of hidden, untreated opiate use.** *Math Popul Stud.* 2011; **18**(3): 172–88.
[Publisher Full Text](#)
17. Banka P, Comiskey CM: **The incubation period of COVID-19: A scoping review and meta-analysis to aid modelling and planning.** *medRxiv.* 2020.
[Publisher Full Text](#)
18. Comiskey CS, Anne Banka P: **Indirect methods to produce the first back-calculation and infection fatality estimates of asymptomatic COVID-19 prevalence in Ireland.** *European Journal of Public Health.* under review. 2020.
19. Anderson R, May R: **Infectious Diseases in Humans.** Oxford University Press, United Kingdom, 1993.
[Reference Source](#)

Open Peer Review

Current Peer Review Status:  

Version 2

Reviewer Report 28 February 2022

<https://doi.org/10.21956/hrbopenres.14734.r31567>

© 2022 Harapan H. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Harapan Harapan 

Medical Research Unit, School of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia

The authors have responded and addressed my concerns adequately.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Public Health and Virology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 13 January 2022

<https://doi.org/10.21956/hrbopenres.14356.r30899>

© 2022 Harapan H. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Harapan Harapan 

Medical Research Unit, School of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia

1. It is not clear what does back-calculation method in this study. Should be explained more.
2. What was the justification to divide the wave into two phases?

3. Please also discuss the possibility that some of the individuals might be infected, symptomatic but did not seek healthcare and therefore not reported in the database.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Public Health and Virology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 11 Feb 2022

Catherine Comiskey, Trinity College Dublin, The University of Dublin, Dublin, Ireland

Thank you for your review and suggestions for improvements.

In response, I can confirm we have provided a further explanation of the back-calculation method. We have included the text:

Working with observed symptomatic cases and the known incubation period, these models predict backwards in time through the incubation period distribution the total numbers of infected and asymptomatic cases these observed cases arose from.

In response to your comment on the phases within the epidemic waves, we have included the text:

As two epidemic waves were observed in the data, we study each wave separately. To improve the fit of the models to the data, we fit the models separately to the increasing and decreasing part of these waves.

In response to your comment on symptomatic cases not being reported in the data we have included within the limitations section the text:

It is also possible that some individuals may have been symptomatic and infectious and did not seek a test and were therefore not recorded in the data. For these reasons our estimates can be considered a minimum estimate.

Thank you.

Competing Interests: No competing interests.

Reviewer Report 26 March 2021

<https://doi.org/10.21956/hrbopenres.14356.r28936>

© 2021 Choi Y. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Yoon Hong Choi 

Statistics and Modelling Economics Department, Public Health England, London, UK

Authors estimated the hidden asymptomatic prevalence of COVID-19 in Ireland using the known symptomatic cases and the back-calculation method. Their study is very interesting, important, and timely as the outcomes would provide the policy decision making bodies and public with valuable epidemiological information to implement various control measures to reduce the spread of SARS-CoV-2 in Ireland.

I have few comments and questions to authors:

1. The definition of the hidden prevalence being estimated is not clear. Authors wrote the following statement:

Infection we know is spread by both known cases and hidden, undetected asymptomatic cases.

It is not clear whether the result of the back-calculation is unknown asymptomatic cases or unknown both symptomatic and asymptomatic cases. Many of symptomatic cases are still not notified to the surveillance due to lack of testing facility availability or self-isolation due to close contacts or only having mild symptoms (no need to use hospital facility).

2. Justification of applying the back calculation method to COVID-19.

Since the asymptomatic cases do not develop any clinical symptoms, asymptomatic infections would be cleared without developing any symptoms after the incubation period unlike HIV/AIDS. Any comment on this issue would be helpful to justify using this method for the COVID-19 to estimate asymptomatic cases or prevalence.

3. The detection rate on symptomatic cases by different time periods was very dependent on the testing priority and facility availability of SARS-CoV-2 in Ireland.

This testing facility was poorly available during the first wave and the priority testing was given to only limited people such as who are in long-term care facilities and those with multiple major symptoms in Ireland. This prioritisation could force testing results to detect mainly older adults and very limited number in younger population. Authors need to mention about this time-dependent testing prioritisation and age dependency in different time periods before they suggested that mitigation and prevention measures during the second wave be responsible for the change of the dynamics.

4. Are there any seroprevalence studies to evaluate the estimations in this manuscript? Those studies showing antibody levels in the population would be an invaluable measure to evaluate the outcomes of this study as the vaccination was not introduced during the second wave.
5. Authors only present the estimation results during the second wave as the title described. Could you also show the results in the first wave as well? Or, is there any particular reason if not performed?
6. The objective authors mentioned at the end of the introduction is to provide recommendations for future research to enable effective immunisation modelling and planning.
It would be helpful for readers if authors discuss this matter with their findings.
7. It would be interesting to see authors' view on the impact of various control measures implemented by the Irish government and human behaviour change in different time periods during this pandemic.
8. It would be interesting to measure hidden symptomatic infections using the fatal cases. There is unignorable uncertainty around the "known" symptomatic infections during different periods through COVID-19. As the infection fatality rate became more measurable during the second wave, It might be interesting to estimate the overall number of symptomatic cases using this infection fatality rate and average time to death from infection.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: The first author, Professor Catherine Comiskey, was my PhD supervisor and we have published two papers together in the past. I have not worked with Professor Comiskey since 2003. I reviewed the manuscript impartially.

Reviewer Expertise: Mathematical modelling in infectious diseases, epidemiology.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
