How much is covid-19 spreading via asymptomatic versus symptomatic infections?

May 4, 2020

As we look at exit strategies from lockdown, these authors discuss how we can measure the spread of covid-19 and whether mathematical modelling helps

The covid-19 pandemic, caused by the SARS-CoV-2 virus, continues to spread worldwide [1]. To slow down the spread of the disease, flatten the epidemic curve and minimise morbidity and mortality due to the pandemic, governments across the world have enacted physical distancing measures. However, as countries across the globe begin plans to relax these measures, it is important to assess whether the phasing out of physical distancing measures and resumption of social mixing will lead the number of infections to increase again with a secondary covid-19 pandemic wave.

In the absence of immunisation and proactive testing strategies, a large portion of the population may remain susceptible to infection and at risk of exposure. To predict how the epidemic curve will behave when restrictions are lifted, it is crucial to gain a better understanding of the extent to which the virus is spreading asymptomatically as well as symptomatically, as recent studies from Italy [2] and China [3] have suggested.

There is mixed evidence on the proportion of cases that are asymptomatic. A scoping review suggests that between 5% and 80% of people with covid-19 experience mild or asymptomatic disease, with WHO suggesting that 80% of infections show mild symptoms, 15% exhibit severe symptoms, and 5% fall critically ill [1,4,5]. This implies that symptom-based control strategies are unlikely to be sufficient unless asymptomatic cases are significantly less infectious than symptomatic ones. New evidence from the Italian city of Vo' at the epicenter of the pandemic and from China indicates that the large majority of coronavirus infections do not result in symptoms, up to 75% and 80% respectively. [2,3] However, findings of other studies have suggested that the proportion of covid-19 cases that are asymptomatic is smaller: 10% among children, 18% among passengers on the Diamond Princess cruise ship and 42% among Japanese people evacuated from Wuhan. [6,7,8] Moreover, these studies typically have happened only at single points in time; other studies that have included later follow-up have shown that a significant proportion of people without symptoms upon first positive test later go on to develop symptoms. [9]

Although new information and findings are released daily on covid-19, the predominant focus has been on people who have shown symptoms, sought hospital care, had a test, and tested positive. Therefore, the reported number of cases does not include people that have asymptomatic infections, or those that have shown symptoms but self-isolated and did not seek care or testing. Consequently, we only know a fraction of the total covid-19 infections, and thus we do not know what proportion of covid-19 infections are symptomatic versus asymptomatic. This is different to previous epidemics, such as Severe Acute Respiratory Syndrome (SARS), where most of the infections were symptomatic and could be contact traced. [10]

Widespread antibody testing will tell us if people have had covid-19 and can therefore enable a better approximation of the total number of infections— which includes both asymptomatic and symptomatic cases. This will be key to inform effective decisions and plans to lift physical distancing measures. For example, if widespread antibody testing suggests that a large proportion of the population has already contracted covid-19, there is a smaller chance of asymptomatic and undiagnosed cases spreading the infection once restrictions are eased. On the other hand, if only a small proportion of the population has had the infection, then the lifting of physical distancing measures may have to be delayed until a vaccine, or potentially highly effective testing protocols and contact tracing strategies, become widely available.

There is therefore urgency around developing and rolling out antibody testing in the UK and worldwide. This has to be part of a continued strategy of testing, contact tracing, and isolation of infected people as the first step to relax physical distancing measures, once we are assured that the pandemic has been sufficiently suppressed. This is in alignment with the six point strategy to relax covid-19 restrictions recommended by the WHO recently [11].

Can mathematical modelling help?

Since the onset of this pandemic, mathematical modelling has been at the heart of informing decision making on mitigation and containment measures. For example, the enforcement of physical distancing measures has been attributed to the predicted outcomes from a mathematical model of a large number of deaths in the absence of such measures. [12] So what can mathematical modelling tell us about the proportion of asymptomatic and symptomatic infections that would be useful when we come out of isolation?

Mathematical modelling allows us to develop a framework to mimic reality using formulaic expressions and parameters based on what we know about the spread of the virus. The model can be refined (or calibrated) to replicate known aspects such as the number of reported infections and deaths due to covid-19. Then, with the model calibrated to data from the onset of the pandemic to the present day, it can be used to investigate various scenarios and predict likely trends.

A classic example of mathematical models used for infectious disease spread are SEIR models. These models track populations that are susceptible (S), exposed (E), infected (I), and that have recovered from the virus (R). The infected population group (I) can be split into asymptomatic and symptomatic populations, which can be modelled separately. In this case, the model is simply known as SEIIR, in other words it has two separate infected population groups or model "compartments."

Such a model can project the epidemic curve for the population that is infected and symptomatic, but also the epidemic curve for the population that is infected and asymptomatic. By calibrating the model based on what we already know—the epidemic curve of symptomatic infections and deaths from the pandemic onset to the present day—we can then predict the shape and behaviour of the epidemic curve for the population that is infected but asymptomatic.

Past studies on potential pandemic influenza outbreaks in the UK have investigated scenarios similar to the physical distancing measures currently adopted, and estimated a substantial negative shock on the economy with a loss of around 5% of GDP [13-14]. Modelling asymptomatic cases is therefore key as governments will find that prolonged physical distancing is economically and socially unsustainable. It is therefore crucial to understand how and when the physical distancing measures can be eased, while still ensuring that mortality due to covid-19 does not increase. Morbidity and mortality are not necessarily a fixed proportion of infections if health system capacity is effectively expanded to cope with a predicted pandemic spread, and predictions on the behaviour of the epidemic curve post-physical distancing can be generated using mathematical modelling.

Unfortunately, as the wide range of estimates listed above indicate, currently the greatest challenge to modelling asymptomatic cases is the large uncertainty in key model parameters. It is a common saying among mathematical modellers that "mathematical models are as good as the data they use". Data based only on new infections tested positive in the context of limited testing capacities, hospitalisations and deaths—all of which have large confounders and possible delay in reporting rates—are not sufficient to resolve the question of symptomatic versus asymptomatic transmission. To resolve this question, let us hope we start widespread antibody testing and contact tracing as soon as possible.

J.Panovska-Griffiths, Senior Research Fellow and and Lecturer in Mathematical modelling at UCL and Lecturer in Applied Mathematics at The Queen's College, Oxford University.

G.J. Abou Jaoude, Institute for Global Health, University College London.

A. Correa, Institute for Global Health, University College London; Section of Clinical Medicine, University of Surrey.

C.C.Kerr, Institute for Disease Modeling, Bellevue, Washington; School of Physics, University of Sydney, Sydney, Australia.

Competing interests: None declared.

References:

1. World Health Organization Coronavirus disease 2019 (COVID-19) Situation report -98, https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200427-sitrep-98-covid-19.pdf?sfvrsn=90323472_4m, assessed 28/04/2020.
2. E. Lavezzo, Franchin E, Ciavarella C, et al. Suppression of COVID-19 outbreak in the municipality of Vo', Italy. Preprint assessed on 28/04/2020 and available here https://www.medrxiv.org/content/10.1101/2020.04.17.20053157v1.full.pdf
3. Covid-19: four fifths of cases are asymptomatic, China figures indicate. BMJ2020;369:m1375 doi: https://doi.org/10.1136/bmj.m1375
4. COVID-19: What proportion are asymptomatic? Centre for Evidence-Based Medicine, University of Oxford, https://www.cebm.net/covid-19/covid-19-what-proportion-are-asymptomatic/, assessed 28/04/2020.
5. D. Thomas-Rüddel, J. Winning, P. Dickmann,D. Ouart, A. Kortgen, U. Janssens and M. Bauer.Coronavirus disease 2019 (COVID-19): update for anesthesiologists and intensivists March 2020. Anaesthesist. 2020 Mar 24 : 1–10. doi: 10.1007/s00101-020-00760-3
6. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study, Lancet Inf Dis, doi:10.1016/S1473-3099(20)30198-5 (epub ahead of print).
7. K.Mizumoto, K.Kagaya, A.Zarebski, G.Chowell.G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Euro Surveill.2020;25(10):pii=2000180. https://doi.org/10.2807/1560-7917.ES.2020.25.10.2000180

8. 8.H.Nishiura, T.Kobayashi, T.Miyama, A.Suzuki, et al.Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19). Preprint assessed 28th April 2020 and available here doi: https://doi.org/10.1101/2020.02.03.20020248.
9. 9.Centres for Disease Control and Prevention report, Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility — King County, Washington, March 2020, https://www.cdc.gov/mmwr/volumes/69/wr/mm6913e1.htm ,assessed 28/04/2020
10. A. Wilder-Smith,MD. Teleman MD, BH.Heng, A.Earnest, AE. Ling,YS. Leo YS. Asymptomatic SARS coronavirus infection among healthcare workers, Singapore. Emerg Infect Dis. 2005; 11: 1142-1145
11. WHO Director-General's opening remarks at the media briefing on COVID-19 – 13 April 2020, https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—13-april-2020, assessed 28/04/2020.
12. Ferguson NM, Laydon D, Nedjati-Gilani D, et al. Impact of non-pharmaceutical interventions (NPIs) to reduce COVID- 19 mortality and healthcare demand. Preprint assessed 26th March 2020 and available at https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-College-COVID19-NPI-modelling-16-03-2020.pdf.
13. R.D.Smith, MR Keogh-Brown, T.Barnett. Estimating the economic impact of pandemic influenza: An application of the computable general equilibrium model to the UK. Social Science & Medicine, 2011,73(2),235-244. https://doi.org/10.1016/j.socscimed.2011.05.025
14. RD.Smith, MR Keogh-Brown, T.Barnett, J.Tait. The economy-wide impact of pandemic influenza on the UK: a computable general equilibrium modelling experiment BMJ2009; 339doi: https://doi.org/10.1136/bmj.b4571

Guest writers

« Covid-19: an opportunity or risk to addressing health inequalities?

Containing covid-19: crucial role of nurses »