

Asymptomatic Transmission of COVID-19

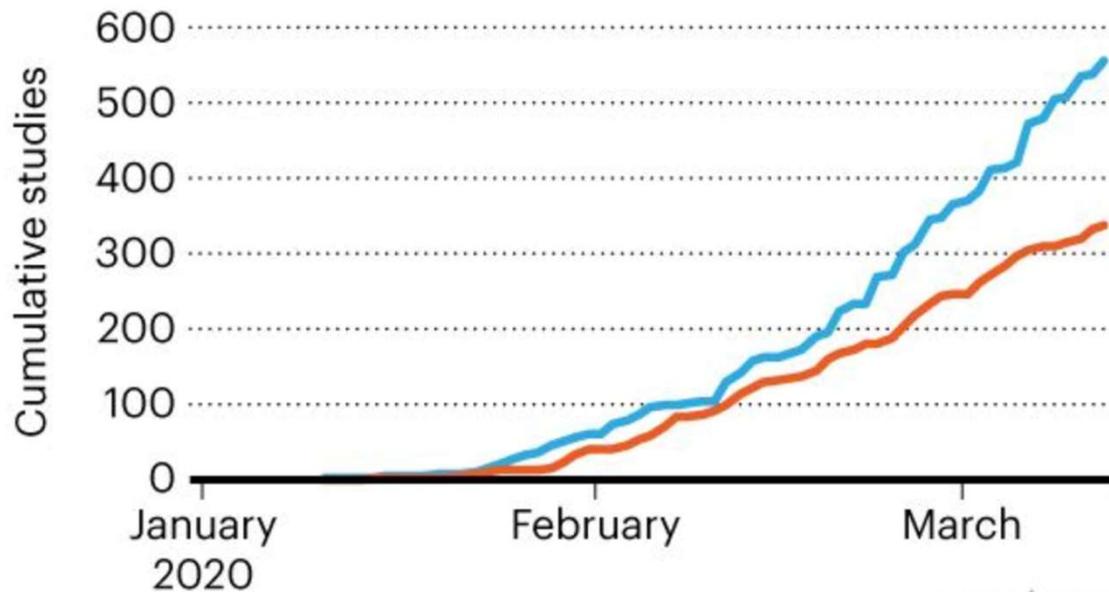
ID Grand Rounds

3/26/20

CORONAVIRUS RESEARCH

Hundreds of studies about the virus have been published since the outbreak began.

— Journal articles — Preprints



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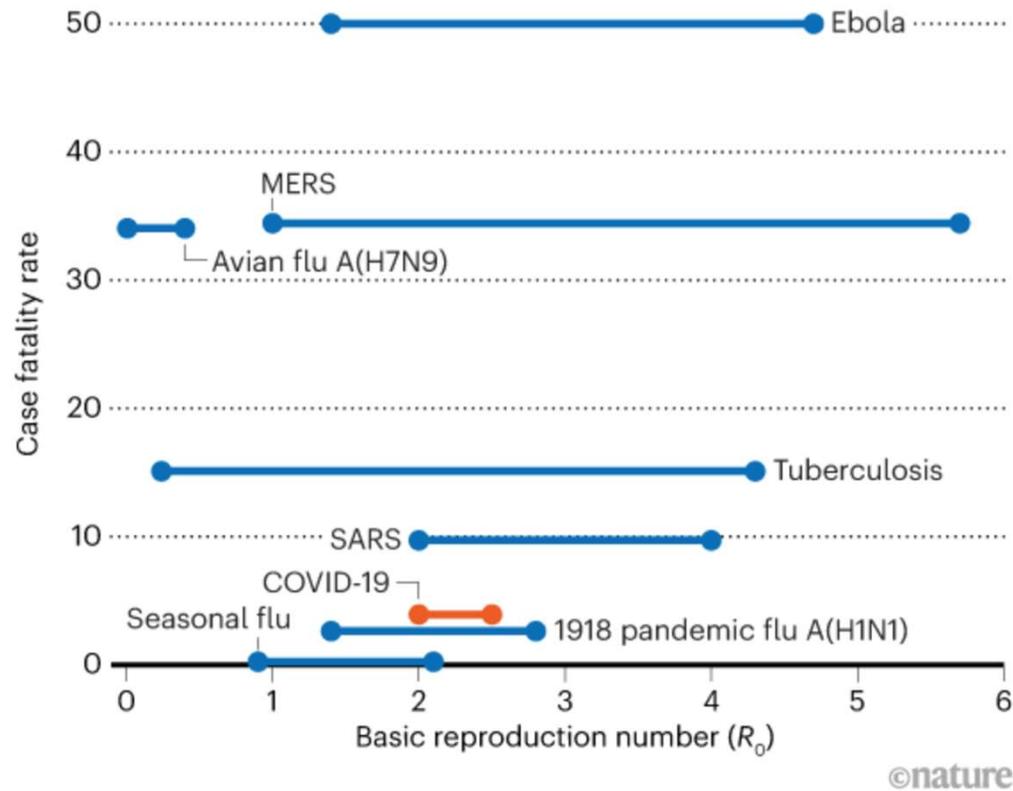
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1827 publications
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532 publications in
last one week

Nature News: Coronavirus in
five powerful charts. March
18, 2020.

COVID-19 VS OTHER DISEASES

Estimates suggest the COVID-19 coronavirus is less deadly than the related illnesses SARS or MERS, but more infectious (R_0) than seasonal influenza.



Nature News: Coronavirus in five powerful charts. March 18, 2020.

Outline

- Recent papers on asymptomatic transmission, background (Melisa Shah)
- Discussion of case fatality rate estimations and shortcomings (Eran Bendavid)
- Update on serology for COVID-19 (Scott Boyd)

Asymptomatic Proportion

- **What proportion of infected people have mild or no symptoms and might be passing the virus on to others?**
 - Informs public health policy, intensity and role of social distancing, true burden of disease
- **Can asymptomatic people transmit disease?**
 - NEJM study¹ measured SARS-COV-2 viral loads in upper respiratory specimens n=18 from China. 1 patient with asymptomatic infection had similar viral load to symptomatic patients.
 - Rothe, Camilla, et al. "Transmission of 2019-nCoV infection from an asymptomatic contact in Germany." *New England Journal of Medicine* (2020).

1. Zou, Lirong, et al. "SARS-CoV-2 viral load in upper respiratory specimens of infected patients." *New England Journal of Medicine* 382.12 (2020): 1177-1179.)

Studies examining asymptomatic proportion

- Study assessing asymptomatic infection among people in the **Diamond Princess** (Mizumoto et al)
- Study using **Japanese evacuees** from Wuhan n=565 to estimate the asymptomatic proportion (Nishiura et al)
- **Related Study:** Mathematical modelling study estimating undocumented infections (not only asymptomatic) using pre lock-down data from **China** and impact on transmission (Ruiyun et al)

RAPID COMMUNICATION

Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020

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Diamond Princess Cruise Ship

- On January 20, 2020, the Diamond Princess cruise ship departed Yokohama, Japan, carrying 3,711 passengers and crew.
- On January 25, a symptomatic passenger departed the ship in Hong Kong, where he was evaluated; testing confirmed SARS-CoV-2 infection.
- On February 3, the ship had returned to Japan and quarantine started.



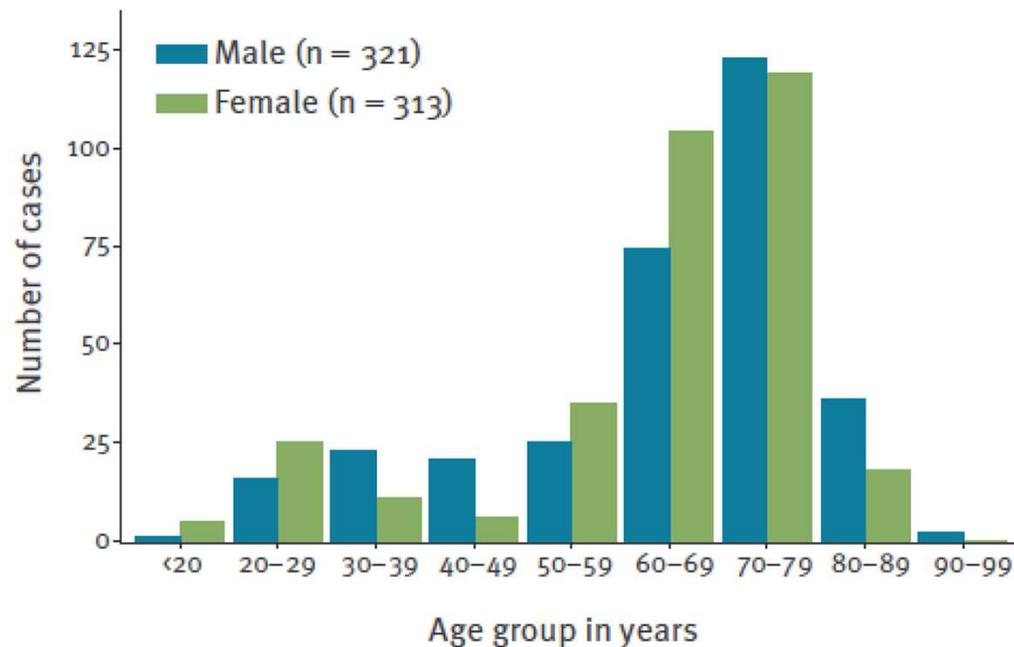
Mizumoto Study

- Tested passengers with PCR, prioritizing high risk and symptomatic cases. 3063 of 3711 received testing.
- Statistical modelling analysis to estimate the proportion of asymptomatic individuals among those tested
- Survival data with right censoring

Results

FIGURE

Age distribution of reported coronavirus disease 2019 cases on board the Diamond Princess cruise ship stratified by sex, Yokohama, Japan, 20 February 2020 (n = 634 cases)



Of 634 confirmed cases, 306 were symptomatic and 328 were asymptomatic.

Estimated asymptomatic proportion is 17.9% (95%CI: 15.5–20.2%)

Mizumoto, Kenji, et al. "Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020." *Eurosurveillance* 25.10 (2020): 2000180.

Other Studies

- Japanese nationals evacuated from Wuhan¹:
 - 565 people evacuated from Wuhan
 - 5 asymptomatic patients tested positive, and 7 symptomatic patients tested positive (**41.6%** asymptomatic ratio, **33.3%** if one asymptomatic developed symptoms after 14 days)
- Individual level data² on 25,961 cases through Feb 18, 2020 using SEIR model
 - “At least **59%** of infected cases were unascertained in Wuhan, potentially including asymptomatic and mild-symptomatic cases”

1. Nishiura, Hiroshi, et al. "Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19)." *medRxiv* (2020).
2. Wang, Chaolong, et al. "Evolving Epidemiology and Impact of Non-pharmaceutical Interventions on the Outbreak of Coronavirus Disease 2019 in Wuhan, China." *medRxiv* (2020).

Cite as: R. Li *et al.*, *Science*
10.1126/science.abb3221 (2020).

Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2)

Ruiyun Li^{1*}, Sen Pei^{2**†}, Bin Chen^{3*}, Yimeng Song⁴, Tao Zhang⁵, Wan Yang⁶, Jeffrey Shaman^{2†}

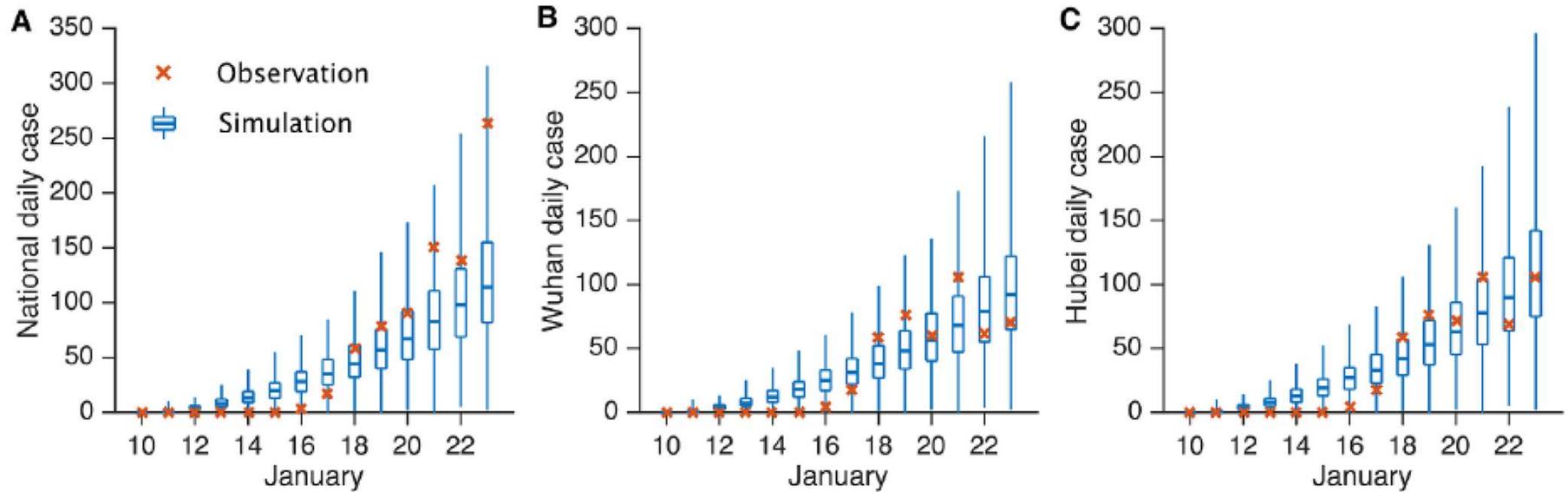
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Methods

- Mathematical model simulating the spatiotemporal dynamics of infections among 375 Chinese cities
 - Uses travel data estimations before and after the Wuhan lock-down
 - January 10-January 23 (period before travel restrictions)
 - Based on an SEIR model including latent period, infection duration, transmission reduction factor for undocumented infections, transmission rate for documented infections, travel multiplicative factors).
 - Found the best fitting model



86% of infections went undocumented from Jan 10-23, and undocumented infections were 55% as contagious ($u=0.55$) as documented infections.

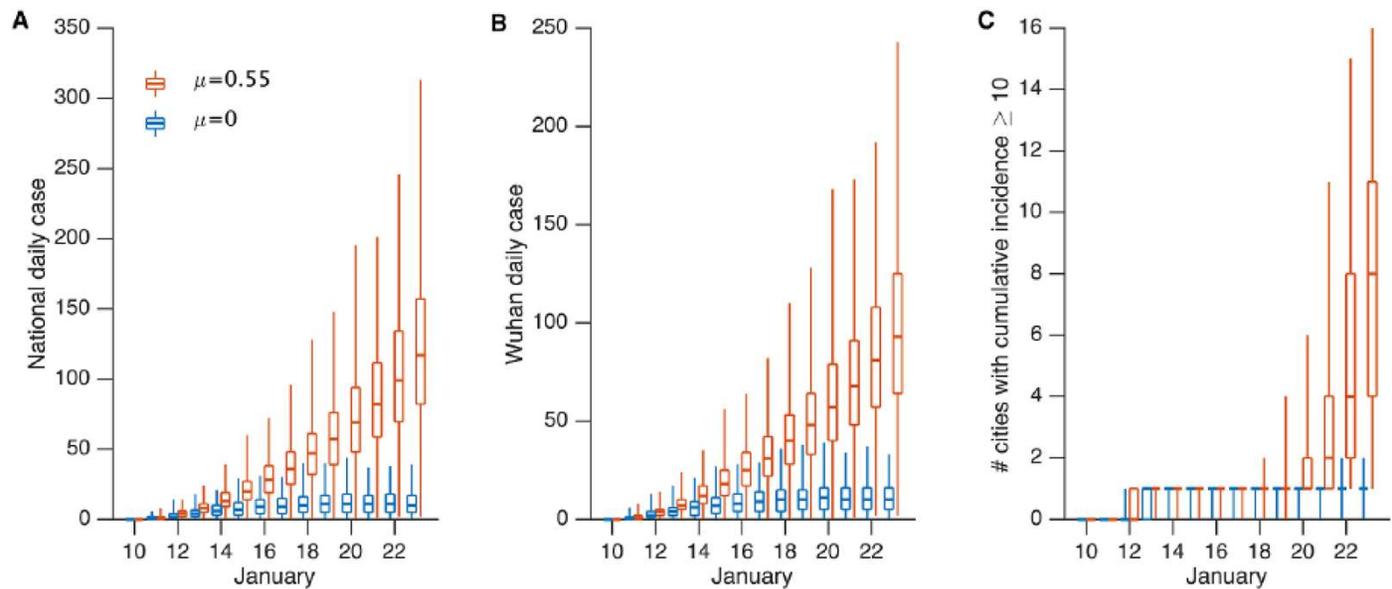


Fig. 2. Impact of undocumented infections on the transmission of SARS-CoV2. Simulations generated using the parameters reported in Table 1 with $\mu = 0.55$ (red) and $\mu = 0$ (blue) showing daily documented cases in all cities (A), daily documented cases in Wuhan city (B) and the number of cities with ≥ 10 cumulative documented cases (C). The box and whiskers show the median, interquartile range, and 95% credible intervals derived from 300 simulations.

“Overall, our findings indicate that a large proportion of COVID-19 infections were undocumented prior to the implementation of travel restrictions and other heightened control measures in China on 23 January, and that a large proportion of the total force of infection was mediated through these undocumented infections.”

Conclusions

- The asymptomatic fraction for COVID is likely significant (18-33?%) as indicated from these studies but more data is needed.
- What are the implications of an increased asymptomatic fraction for policy and planning?
- How can we use serology to help better inform these key epidemiological parameters?

OPINION | COMMENTARY

Is the Coronavirus as Deadly as They Say?

Current estimates about the Covid-19 fatality rate may be too high by orders of magnitude.

By Eran Bendavid and Jay Bhattacharya
March 24, 2020 6:21 pm ET

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Extra Slides

Methods

$$g(x, p) = \begin{cases} p + (1 - p)(1 - F_D(c - x)) & \text{if they do not have symptoms,} \\ F_D(c - x) & \text{if they do have symptoms,} \end{cases}$$

Figure S1. Heat maps of the density distribution of infection timing by individuals, Symptomatic cases (N= 306)

Vertical axis represents each individual from 1 to N. Cases disembarked after testing positive for the disease. Day 1 corresponds to January 20, 2020, when the first symptomatic case embarked. The vertical line corresponds to February 5, 2020 when the quarantine period started.

Heatmap of infection timing distribution by individual, Symptomatic case

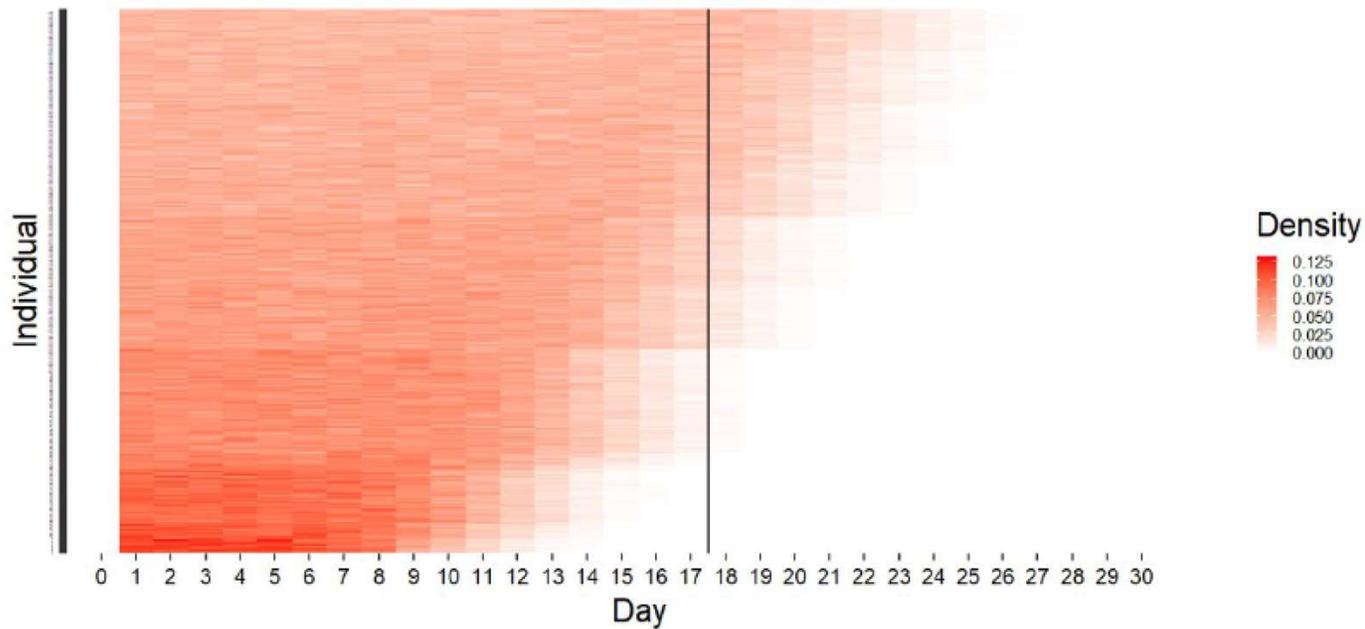


Figure S2. Heat maps of the density distribution of infection timing by individuals, Asymptomatic cases (N= 320)

Vertical axis represents each individual from 1 to N. Cases disembarked after testing positive for the disease. Day 1 corresponds to January 20, 2020, when the first symptomatic case embarked. The vertical line corresponds to February 5, 2020 when the quarantine period started.

