

Acknowledgments and disclaimer:

- 1. Synthesized high quality modelling from around the world
- 2. Highly influenced by post-SARS modelling efforts
- 3. This talk is like sushi



Globally confirmed cases: 8247 with 171 deaths. Mainland China: 8124; 171 deaths. Counts based on social media review of reportedly confirmed cases; may differ from tallies currently reported by official sources. Special Administrative Region abbreviated to SAR, and Autonomous Regions

The following countries have confirmed cases but do not appear on this map:

Country	Count
Australia	9
Finland	1
France	5
Germany	4
United Arab Emirates	4

Incidence data (Wuhan)

Huang et al, Lancet preprint (Jan 24); Liu et al, biorxiv 2020.01.25.919787 (Jan 25)

Incidence data (China)

- 9 deaths outside Hubei province (to Jan 31)
- Over 15,000 suspected cases and over 100,000 under observation

Wikipedia: Timeline of the 2019–20 Wuhan coronavirus outbreak (accessed Jan 31)

Incidence data (International)

<u>https://docs.google.com/spreadsheets/d/1jS24DjSPVWa4iuxuD4OAXrE3Qel8c9BC1hSlqr-NMiU/edit#gid=1187587451</u> (data of Dr Kaiyuan Sun, NIH) <u>https://docs.google.com/spreadsheets/d/1itaohdPiAeniCXNIntNztZ_oRvjh0HsGuJXUJWET008/</u>edit#gid=0 (data compiled by Kraemer et al...)

Clinical Progression

Retrospective study:

- 99 confirmed cases in Wuhan Jinyintan Hospital, January 1-20 (follow up to Jan 25)
- 67 men, 32 women,
- average age 55.5 (sd 13.1 so mostly over 40)
- 50% exposed to Huanan seafood market
- 50% had chronic disease
- Fever, cough, shortness of breath, pneumonia
- 31 patients discharged by Jan 25
- 17 patients had severe disease and 11 died

Chen et al, Lancet, January 29, 2020 (https://doi.org/10.1016/ S0140-6736(20)30211-7)

Coronavirus (CoV) infections

- Four circulating coronaviruses causing influenza-like illness (ILI)
 - CoV found in 12% of ILI-presenting patients in 2018 USA
 - Of 111 CoV+ patients, 1 day total of hospitalization
- Middle East Respiratory Syndrome (MERS)
 - Sporadically seen in people contacting dromedary camels
 - Occasional human-human transmission (larger outbreak in South Korea 2015)
 - Case fatality rate 30-40% (!!)
- Sudden Acute Respiratory Syndrome (SARS)
 - Large outbreak 2002-2003
 - Approx 8000 cases worldwide (mostly China/Taiwan/HK)
 - 10% case fatality (!)
 - 250 cases in Canada, 43 deaths

Bouvier et al, Influenza Other Respir Viruses (2018)

Evolution / phylogeny of nCoV in humans

• With 42 public nCoV genomes, estimate phylogeny (family tree)

Trevor Bedford et al, posted at nextstrain.org

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Evolution / phylogeny of nCoV in humans

 Minimal variation across samples points to single introduction into human population in November / early December

Trevor Bedford et al, posted at nextstrain.org

Questions to address through modeling / data:

- What is the rate of spread in and among different populations?
- How effective must public health measures be to stop the epidemic?
- What is the course of disease in an infected person?
- What is the predicted final size / end date of the epidemic?

The basic reproductive number: R₀

- R_0 is the *average* number of new infections caused by a single newly infected person at the beginning of the epidemic
- $R_0 > 1$: "exponential growth is possible"

A LOT A

• $R_0 < 1$: "extinction is guaranteed"

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- $R_0 > 1$: "exponential growth is possible"
- $R_0 < 1$: "extinction is guaranteed"
 - "Pandemic" influenza: $R_0 \sim 1.6$
 - Polio: $R_0 \sim 6$
 - SARS $R_0 \sim 2.5$
 - Measles: R₀ ~ 18
 Pertussis: R₀ ~15

• To find R_0 empirically requires contact tracing and is a lot of work. Modeling infection process is important.

The basic reproductive number: R₀

- Define:
 - average *contact* rate c (per day)
 - average *probability of infection* per contact p
 - average duration of infectiousness T (day)
- Then $R_0 = c p T$
- To control an epidemic, reduce c, p or T so $R_0 < 1$.
 - Reduce by $\left(1-\frac{1}{R_0}\right)$
- Influenza: $R_0 \sim 1.6$ so reduce contacts by 37%
- Measles: $R_0 \sim 18$ so reduce contacts by 94%
- Achieve by vaccination (*herd immunity*) or segregation
- R₀ tells us how strong must the public health response be

- Simple, useful: SEIR model
 - Susceptible Exposed Infectious Removed
 - assume non-infectious for an exponentially-distributed period (*exposed* class)
 - then infectious for an exponentially-distributed period (*infectious* class)

 σE

 σE

dt

$$I(t) \simeq I(0)e^{rt}$$

$$i(t) = \frac{dI}{dt} = rI(0)e^{rt}$$

$$i(t) = \int_0^\infty \beta(\tau)i(t-\tau) d\tau$$

$$0)e^{rt} = \int_0^\infty \beta(\tau)rI(0)e^{r(t-\tau)} d\tau$$

$$1 = \int_0^\infty \beta(\tau)e^{-r\tau} d\tau$$

$$1 = \int_0^\infty \beta_0 \frac{\sigma (e^{-\sigma\tau} - e^{-\alpha\tau})}{\alpha - \sigma} e^{-r\tau} d\tau$$

$$1 = \frac{\beta_0\sigma}{(r+\alpha)(r+\sigma)}$$

$$\frac{(r+\alpha)(r+\sigma)}{\alpha\sigma} = \frac{\beta_0}{\alpha} = R_0$$

Incidence-based R0 for nCoV

Using SARS estimates for serial interval, and SEIR or close variant:

Zhao: $2.7 < R_0 < 5.4$ (Jan 23) Liu: $2.3 < R_0 < 3.6$ (Jan 25)

Liu: also estimate of incubation period 4.8+/-2.6 days

Zhao et al, bioRxiv 2020.01.23.916395 Liu et al, bioRxiv 2020.01.25.919787

- Count "Infected people":
- Start with (e.g.) ONE infected person.
- Each infected person makes k new infections with probability q_k:

 R_0 = average number of new infections produced by one infected cell, at the start of the infection. R_0 = 1.5

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On average 41 /0 of all these epidemics go ex

"Super-spreader" model

• Consider more aborted infections but a small probability of 10 new infections.

k	0	1	2	3	4	••••	10

 q_k .5 .15 .15 .15 005 $R_0 = 1.5 \text{ (maintained)}$

- Imai et al:
 - Run many simulations with SARS-like new infection distribution and SARS generation time (8.4 days)
 - Include possible super-spreaders via wide distribution
 - Keep only those parameter sets where >5% of all simulations with those parameters match the data through 18 Jan.
 - Estimate $1.5 < R_0 < 3.5$
 - Note (baseline) 40 zoonotic infections (contradicts new info from nextstrain.org)
- Riou et al:
 - Similar approach
 - Obtain $1.4 < R_0 < 3.8$

Imai et al (<u>https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/news--wuhan-coronavirus/</u>, Jan 25) Riou et al (bioRxiv 2020.01.23.917351, Jan 24)

• Riou et al one parameter set:

Riou et al (bioRxiv 2020.01.23.917351, Jan 24)

• Riou: heat map and comparison with previous epidemics

Riou et al (bioRxiv 2020.01.23.917351, Jan 24)

Kucharski et al, https://cmmid.github.io/ncov/wuhan_early_dynamics/index.html (Jan 31)

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- Read et al:
 - Multi-location differential equation model
 - Cities in China, other countries, data to Jan 21
 - Each location has an SEIR model
 - Linkages according to commercial air traffic data
 - Predictions!

Read et al, medRxiv 2020.01.23.20018549 (Jan 24)

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Wu et al, Lancet, Jan 31 "Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study"

- •Data from Wuhan, Chinese cities and Int'l cases to Jan 28
- •SEIR-type model in each location
- •SARS estimates for serial interval
- •Int'l flights and human mobility data for China
- •Estimate $R_0 = 2.47 2.86$

•Chinese cities have large numbers of infections already and will see exponential growth, lagging Wuhan by 1-2 weeks

Wu et al, Lancet, Jan 31 "Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study"

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Backer et al, medRxiv 2020.01.27.20018986 (Jan 28)

•34 cases that were detected outside Wuhan with known travel dates

•Estimate incubation period 5.8 days (4.6-7.9 days)

•"findings of previous studies that have assumed incubation period distribution similar to MERS or SARS will not have to be adapted because of a shorter or longer incubation period"

R0 Summary

		R0_lowe			
study	RO	r	R0_upper	interval_type	approach
imai2020	2.6	1.5	3.5	uncertainty	branching process, NB offspring
riou2020	2.2	1.4	3.8	hpd	branching process, NB offspring
bedford2020		1.5	3.5	uncertainty	simple branching process
read2020	3.1	2.4	4.1	95% confidence	deterministic metapopulation SEIR transmission model
liu2020	2.9	2.3	3.6	95% confidence	regression
zhao2020	3.3	2.7	4	95% confidence	regression
majumder2020		2	3.1	uncertainty	regression (IDEA model)
kucharski2020		1.5	4	time-varying	stochastic SEIR fitted by sequential Monte Carlo
li2020	2.2	1.4	3.9	95% confidence	renewal equation
abbott2020		2	2.7	90% credible	branching process, NB offspring
wu2020	2.7	2.5	2.9	95% credible	deterministic metapopulation SEIR transmission model

Park et al (this afternoon) meta-analysis: "*median of 3.1, 95% CI 2.1-5.7*" Fred Brauer (yesterday): "*probably around 2*"

Simon Frost, Microsoft

https://docs.google.com/spreadsheets/d/1QP5vM62ctnMRYdkQ4J5IqaOmB3hISGvYqCvnB8rBmNY/edit#gid=0

Caveats and Notes

- Data is likely to be patchy and not up-to-date
- Almost certainly there are more cases than reported
 - How many asymptomatic cases?
- All studies have homogeneous populations
 - if travel correlates negatively with infection, intercity spread before quarantine was less
- Uncertainty around initial number of cases
- Changes in travel behaviour pre-restrictions
- Seasonality of infectiousness?

References - General and Updating

- BC CDC Coronavirus updates (updated daily M-F)
 - <u>http://www.bccdc.ca/about/news-stories/stories/2020/information-on-novel-coronavirus</u>
- Imperial college modelling group page (includes Imai preprint)
 - <u>https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/</u>
- Lancet coronavirus (includes Joe Wu preprint)
 - <u>https://www.thelancet.com/coronavirus</u>
- Modelling virus evolution at Fred Hutchinson (very good site)
 - <u>nextstrain.org</u>
 - Simon Frost model summary page
 - <u>https://docs.google.com/spreadsheets/d/</u> <u>1QP5vM62ctnMRYdkQ4J5IqaOmB3hISGvYqCvnB8rBmNY/edit#gid=0</u>
- Data repositories
 - <u>https://docs.google.com/spreadsheets/d/</u> <u>1jS24DjSPVWa4iuxuD4OAXrE3Qel8c9BC1hSlgr-NMiU/edit#gid=1187587451</u>
 - (data of Dr Kaiyuan Sun, NIH)
 - <u>https://docs.google.com/spreadsheets/d/</u> <u>1itaohdPiAeniCXNIntNztZ_oRvjh0HsGuJXUJWET008/edit#gid=0</u>
 - (data compiled by Kraemer et al...)

References - Preprints

- Bouvier et al 2018 (circulating coronavirus paper)
 - <u>https://onlinelibrary.wiley.com/doi/full/10.1111/irv.12538</u>
- Zhao and Lu regression-based estimates of R0:
 - <u>https://www.biorxiv.org/content/10.1101/2020.01.23.916395v2</u>
 - https://www.biorxiv.org/content/10.1101/2020.01.25.919787v1
- Rio simulation approach
 - <u>https://www.biorxiv.org/content/10.1101/2020.01.23.917351v1</u>
 - Kucharski and Read simulation models with geo spread
 - <u>https://cmmid.github.io/ncov/wuhan_early_dynamics/index.html</u>
 - <u>https://www.medrxiv.org/content/10.1101/2020.01.23.20018549v2</u>
- Park et al (McMaster/Princeton group) meta- and sensitivity- analysis
 - <u>https://github.com/parksw3/nCoV_framework/blob/master/v2/ncov.pdf</u>
 - https://www.biorxiv.org/content/10.1101/683326v1