Analysis of the early phase of COVID-19 outbreak in China

Yifan Zhu and Ying Qing Chen

Evolution of the 2019-nCoV outbreak (31 December 2019 – 10 February 2020)

Dec 31, 2019
Cluster of 27 pneumonia cases of unknown origin with 7 severe cases reported to China National Health Commission

Jan 1, 2020
Huanan Seafood Wholesale market closed

Jan 7, 2020
Novel coronavirus isolated

Jan 8, 2020
First confirmed case in **Thailand**

Jan 11, 2020
First fatal case in China

Jan 12, 2020
Named as 2019-nCoV; Whole genome sequence shared with WHO

Jan 13, 2020
First confirmed case in **Nepal**

Jan 14, 2020
First confirmed case in **Japan**

Jan 19, 2020
First confirmed case in **Republic of Korea**

Jan 20, 2020
Infection in health-care workers caring for 2019-nCoV Patients

First confirmed case in **USA**

China confirms human to human transmission

Jan 22-23, 2020
1st Emergency Committee

Jan 23, 2020
First confirmed case in **Singapore**

Shutdown of Wuhan City

Jan 24, 2020
First confirmed cases in **France** and **Viet Nam**

Jan 25, 2020
First confirmed cases in **Australia** and **Malaysia**

Jan 26, 2020
First confirmed case in **Canada**

Jan 27, 2020
First confirmed cases in **Cambodia** and **Sri Lanka**

WHO Director General in China

Jan 28, 2020
First confirmed case in **Germany**

Jan 29, 2020
First confirmed cases in **UAE**, **Finland** and **Italy**

Jan 30, 2020

2nd Emergency Committee – WHO declares a PHEIC

First confirmed cases in **India** and **Philippines**

Jan 31, 2020
First confirmed cases in **Russian Federation**, **Spain**, **Sweden** and **UK**

Feb 1, 2020
Index case on Princess Diamond cruise ship confirmed in Hong Kong SAR

Feb 2, 2020
First fatal case outside China

Feb 4, 2020
First confirmed case in **Belgium**

Feb 5, 2020
Press Release by Japanese government about 10 cases on cruise ship

World Health Organization

HEALTH EMERGENCIES programme

The Situation (as of 11 Feb, 6am Geneva time)

Updates from last 24 hours

China:

- 2,484 new confirmed cases: 84%, 2,097 cases from Hubei
- 849 new severe cases and 108 deaths: Hubei(103), Beijing(1), Tianjin(1), Heilongjiang(1), Anhui(1), Henan(1))
- 3,536 new suspected cases

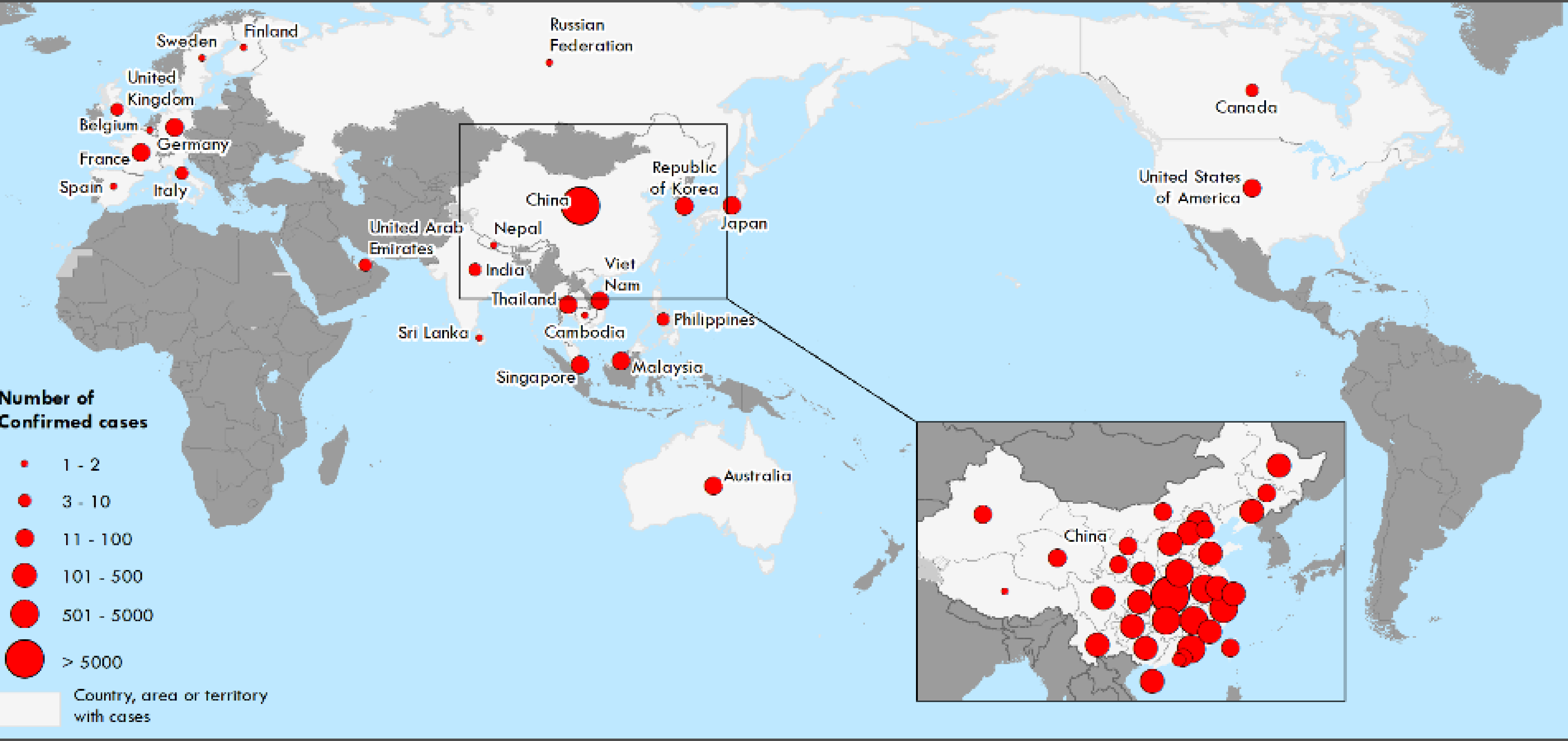
Outside China:

- 74 new confirmed cases: International conveyance (Japan)(65), The United Kingdom(4), Singapore(2), Viet Nam(1), United Arab Emirates(1), Republic of Korea(1)

- Between 31 Dec 2019 - 11 Feb 2020
  - In total, 43,101 confirmed cases including 1,018 deaths globally
- China
  - 42,708 confirmed cases
  - 7,333 severe cases
  - 1,017 deaths: Hubei(974), Heilongjiang(8), Henan(7), Anhui(4), Beijing(3), Hainan(3), Tianjin(2), Hebei(2), Chongqing(2), Gansu(2), Jilin(1), Shanghai(1), Jiangxi(1), Shandong(1), Hunan(1), Guangdong(1), Guangxi(1), Sichuan(1), Guizhou(1), Hong Kong SAR(1)
- Outside China
  - 393 cases from 24 countries
  - 1 death

Distribution of 2019-nCoV cases as of 10 February 2020

World Health Organization



***Data Source**: World Health Organization, National Health Commission of the People's Republic of China*
***Map Production**: WHO Health Emergencies Programme*

Not applicable

0 2,500 5,000 km

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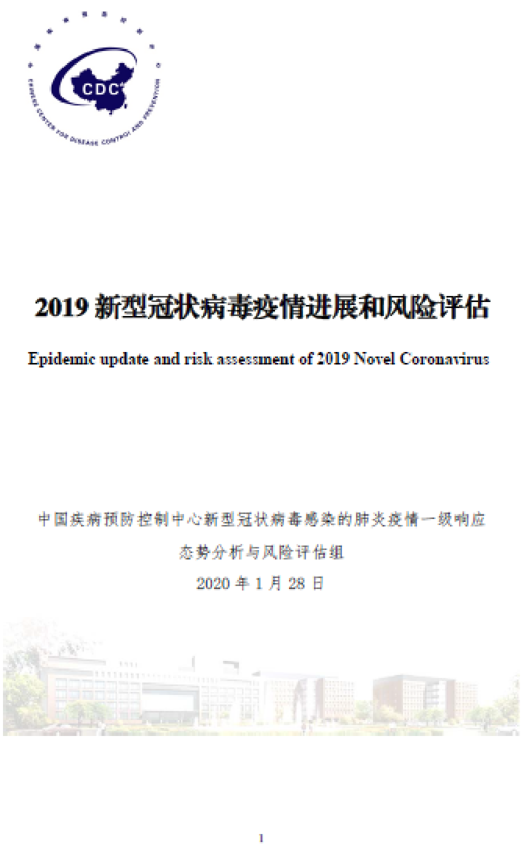
China CDC 1/28/2020 report



2019 新型冠状病毒疫情进展和风险评估

Epidemic update and risk assessment of 2019 Novel Coronavirus

中国疾病预防控制中心新型冠状病毒感染的肺炎疫情一级响应

态势分析与风险评估组

2020 年 1 月 28 日

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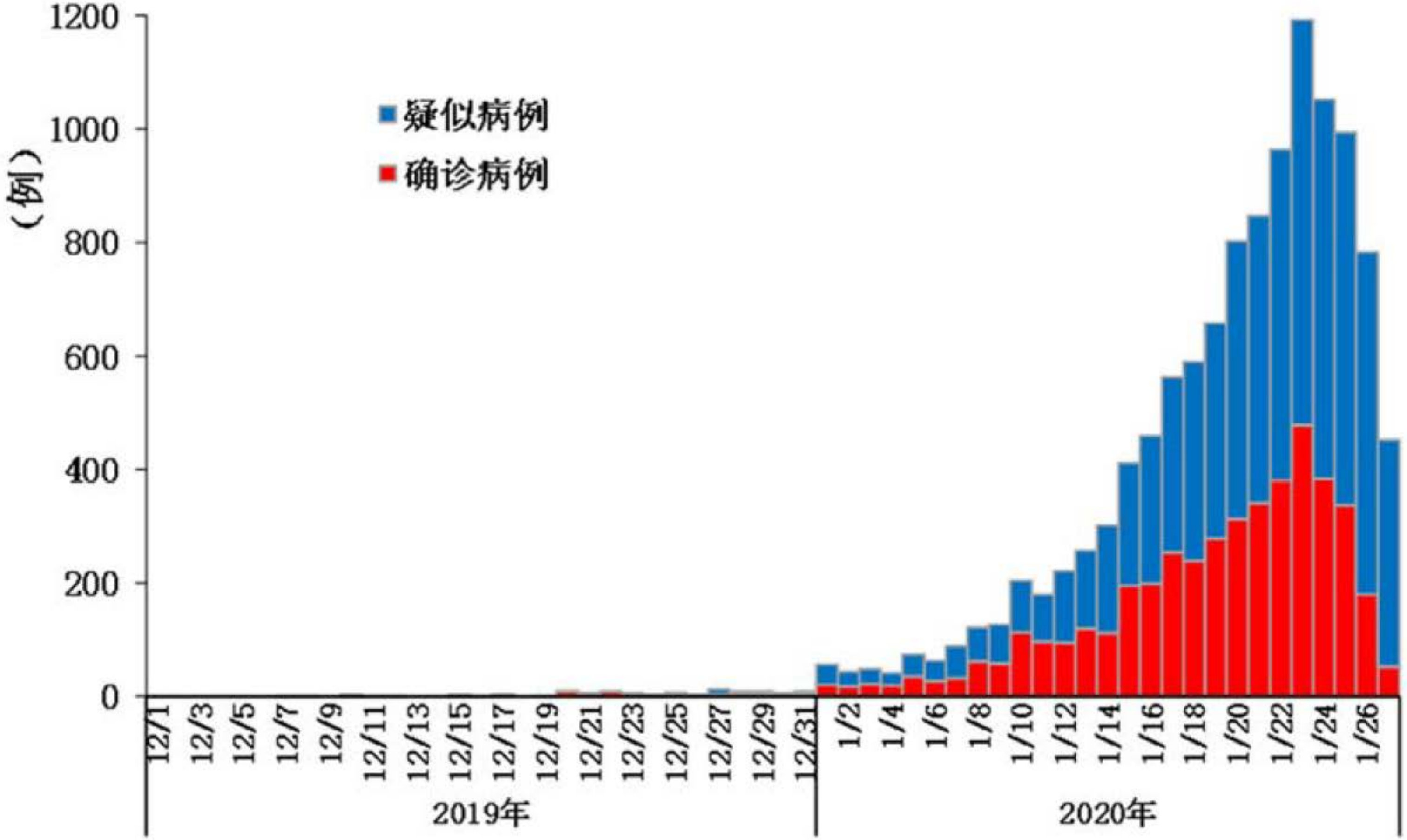

http://www.chinacdc.cn/jkzt/crb/zl/szkb_11803/jszl_11811/202001/P020200127544648420736.pdf

Updated data 12/8/2019 to 2/11/2020

中华流行病学杂志2020年2月第41卷第2期　Chin J Epidemiol, February 2020, Vol.41, No.2　· 145 ·

· 新型冠状病毒肺炎疫情防控 ·

新型冠状病毒肺炎流行病学特征分析

中国疾病预防控制中心新型冠状病毒肺炎应急响应机制流行病学组
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【摘要】 **目的** 新型冠状病毒肺炎在武汉暴发流行以来，已在全国范围内蔓延。对截至2020年2月11日中国内地报告所有病例的流行病学特征进行描述和分析。**方法** 选取截至2020年2月11日中国内地传染病报告信息系统中上报所有新型冠状病毒肺炎病例。分析包括：①患者特征；②病死率；③年龄分布和性别比例；④疾病传播的时空特点；⑤所有病例、湖北省以外病例和医务人员病例的流行病学曲线。**结果** 中国内地共报告72 314例病例，其中确诊病例44 672例(61.8%)，疑似病例16 186例(22.4%)，临床诊断病例10 567例(14.6%)，无症状感染者889例(1.2%)。在确诊病例中，大多数年龄在30～79岁(86.6%)，湖北省(74.7%)，轻/中症病例为主(80.9%)。确诊病例中，死亡1 023例，粗病死率为2.3%。个案调查结果提示，疫情在2019年12月从湖北向外传播，截至2020年2月11日，全国31个省的1 386个县区受到了影响。流行曲线显示在1月23—26日达到峰值，并且观察到发病数下降趋势。截至2月11日，共有1 716名医务工作者感染，其中5人死亡，粗病死率为0.3%。**结论** 新型冠状病毒肺炎传播流行迅速，从首次报告病例日后30 d蔓延至31个省(区/市)，疫情在1月24—26日达到首个流行峰，2月1日出现单日发病异常高值，而后逐渐下降。随着人们返回工作岗位，需积极应对可能出现的疫情反弹。

【关键词】 新型冠状病毒肺炎；暴发流行；流行特征
基金项目：国家科技重大专项 基于大数据的动物源性流感流行规律和相关影响因素研究(2018ZX10201002-008-002)；国家自然科学基金"一带一路"背景下公共卫生风险防范及其模式创新研究(71934002)
DOI：10.3760/cma.j.issn.0254-6450.2020.02.003

The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China

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【Abstract】 **Objective** An outbreak of 2019 novel coronavirus diseases (COVID-19) in Wuhan, China has spread quickly nationwide. Here, we report results of a descriptive, exploratory analysis of all cases diagnosed as of February 11, 2020. **Methods** All COVID-19 cases reported through February 11, 2020 were extracted from China's Infectious Disease Information System. Analyses included: 1) summary of patient characteristics; 2) examination of age distributions and sex ratios; 3) calculation of case fatality and mortality rates; 4) geo-temporal analysis of viral spread; 5) epidemiological curve construction; and 6) subgroup analysis. **Results** A total of 72 314 patient records—44 672 (61.8%) confirmed cases, 16 186 (22.4%) suspected cases, 10567 (14.6%) clinical diagnosed cases (Hubei only), and 889 asymptomatic cases (1.2%)—contributed data for the analysis. Among confirmed cases, most were aged 30-79 years (86.6%), diagnosed in Hubei (74.7%), and considered mild/mild pneumonia (80.9%). A total of 1 023 deaths occurred among confirmed cases for an overall case-fatality rate of 2.3%. The COVID-19 spread outward from Hubei sometime after December 2019 and by February 11, 2020, 1 386 counties across all 31 provinces were affected. The epidemic curve of onset of symptoms peaked in January 23-26, then began to decline leading up to February 11. A total of 1 716 health workers have become infected and 5 have died (0.3%). **Conclusions** The COVID-19 epidemic has spread very quickly. It only took 30 days to expand from Hubei to the rest of Mainland China. With many people returning from a long holiday, China needs to prepare for the possible rebound of the epidemic.

【Key words】 2019 Novel Coronavirus; Outbreak; Epidemiological characteristics

China CDC Weekly

Vital Surveillances

The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020

The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team

Opinion

VIEWPOINT

Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China
Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention

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Viewpoint

Related article

The Chinese Center for Disease Control and Prevention recently published the largest case series to date of coronavirus disease 2019 (COVID-19) in mainland China (72 314 cases, updated through February 11, 2020).[1] This Viewpoint summarizes key findings from this report and discusses emerging understanding of and lessons from the COVID-19 epidemic.

Epidemiologic Characteristics of the COVID-19 Outbreak

Among a total of 72 314 case records (Box), 44 672 were classified as confirmed cases of COVID-19 (62%; diagnosis based on positive viral nucleic acid test result on throat swab samples), 16 186 as suspected cases (22%; diagnosis based on symptoms and exposures only, no test was performed because testing capacity is insufficient to meet current needs), 10 567 as clinically diagnosed cases (15%; this designation is being used in Hubei Province only; in these cases, no test was performed but diagnosis was made based on symptoms, exposures, and presence of lung imaging features consistent with coronavirus pneumonia), and 889 as asymptomatic cases (1%; diagnosis by positive viral nucleic acid test result but lacking typical symptoms including fever, dry cough, and fatigue).[1]

Most case patients were 30 to 79 years of age (87%), 1% were aged 9 years or younger, 1% were aged 10 to 19 years, and 3% were age 80 years or older.

Box. Key Findings From the Chinese Center for Disease Control and Prevention Report

72 314 Cases (as of February 11, 2020)
- Confirmed cases: 44 672 (62%)
- Suspected cases: 16 186 (22%)
- Diagnosed cases: 10 567 (15%)
- Asymptomatic cases: 889 (1%)

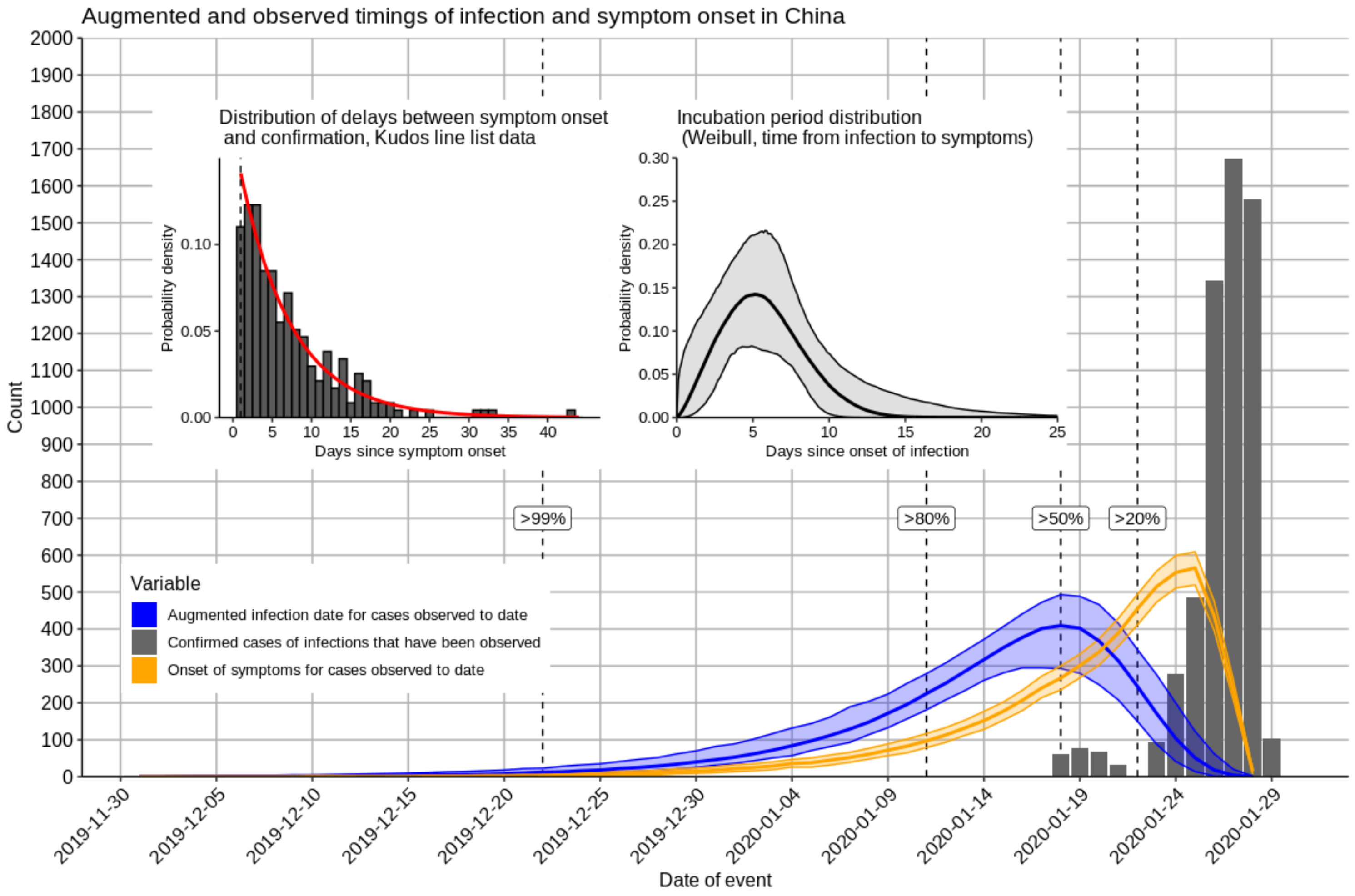
Age distribution (N = 44 672)
- ≥80 years: 3% (1408 cases)
- 30-79 years: 87% (38 680 cases)
- 20-29 years: 8% (3619 cases)
- 10-19 years: 1% (549 cases)
- <10 years: 1% (416 cases)

Spectrum of disease (N = 44 415)
- Mild: 81% (36 160 cases)
- Severe: 14% (6168 cases)
- Critical: 5% (2087 cases)

Case-fatality rate
- 2.3% (1023 of 44 672 confirmed cases)
- 14.8% in patients aged ≥80 years (208 of 1408)
- 8.0% in patients aged 70-79 years (312 of 3918)
- 49.0% in critical cases (1023 of 2087)

Health care personnel infected
- 3.8% (1716 of 44 672)
- 63% in Wuhan (1080 of 1716)
- 14.8% cases classified as severe or critical (247 of 1668)
- 5 deaths

Augmented Onset Time from Case Report Time



https://github.com/jameshay218/case_to_infection

Disease Natural History Assumptions

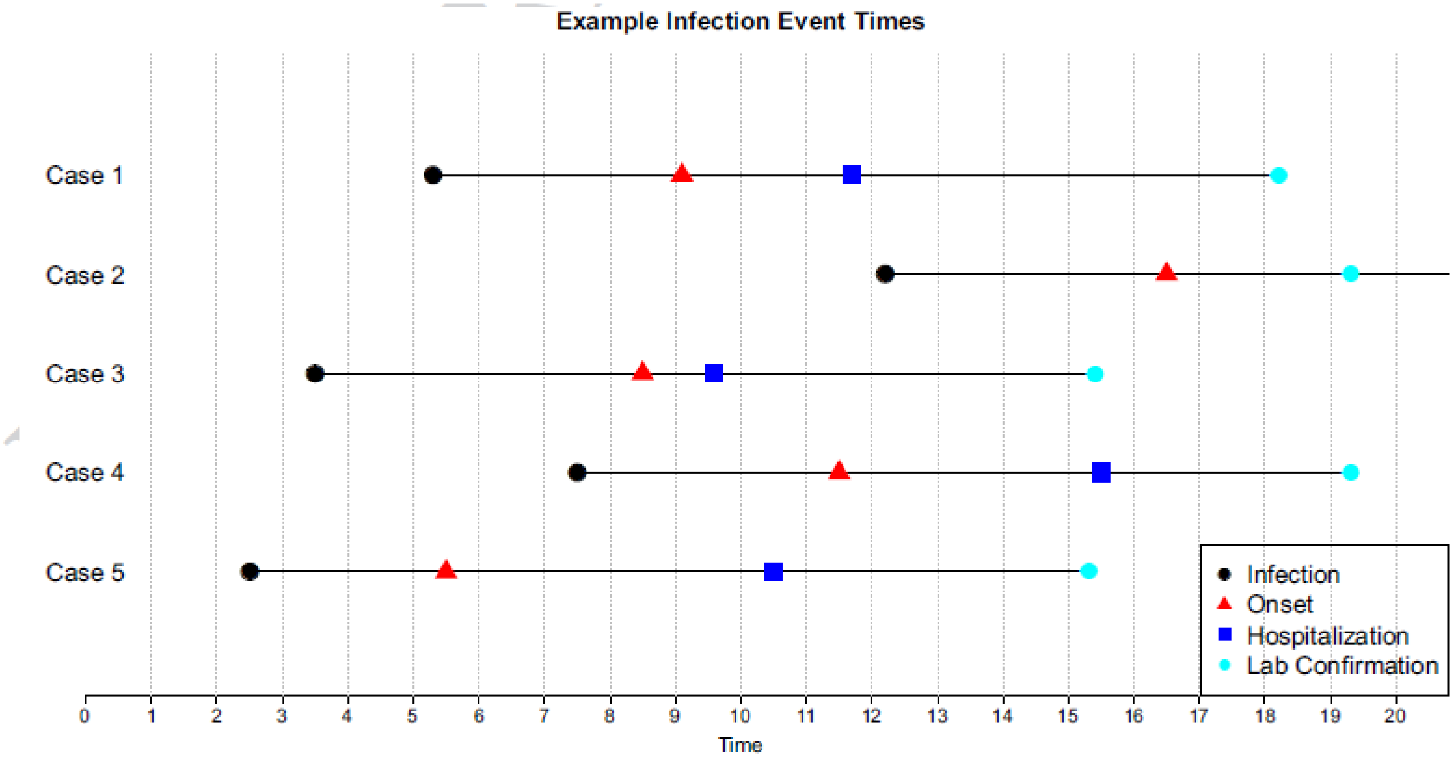


Fig. 1 Illustrative examples for infection, symptom onset, hospitalization and virus lab confirmation time

Incubation period distribution

$$p_{\mathrm{inc}}(t \mid \hat{t}) = f_{\mathrm{beta}}\left(\frac{t - \hat{t} - \mathrm{Inc}_{\mathrm{min}}}{\Delta_{\mathrm{inc}}} \mid \alpha_{\mathrm{inc}}, \beta_{\mathrm{inc}}\right),$$

$$t \in (\hat{t} + \mathrm{Inc}_{\mathrm{min}}, \hat{t} + \mathrm{Inc}_{\mathrm{min}} + \Delta_{\mathrm{inc}}),$$

Relative infectivity distribution
(symptomatic only/pre-symptomatic)

$$p_{\mathrm{inf}}(t \mid \tilde{t}) = f_{\mathrm{beta}}\left(\frac{t - \tilde{t}}{\Delta_{\mathrm{inf}}} \mid \alpha_{\mathrm{inf}}, \beta_{\mathrm{inf}}\right), \quad t \in (\tilde{t}, \tilde{t} + \Delta_{\mathrm{inf}}).$$

The Transmission Model

- Cases shedding infection intensity to others, homogeneous mixing assumption:

$$\hat{\lambda}(t) = \sum_{i:t\in[\tilde{t}_i,\tilde{t}+\Delta_{\text{inf}}]} p_{\text{inf}}(t|\tilde{t}_i)\Delta_{\text{inf}}\gamma. \quad (1)$$

- Infection intensity to onset intensity through incubation period, and likelihood of onset:

$$\tilde{\lambda}(t) = \int_{t-\text{Inc}_{\max}}^{t-\text{Inc}_{\min}} \hat{\lambda}(\tau)p_{\text{inc}}(t|\tau)\text{d}\tau.$$

$$p(\tilde{\mathbf{N}}|\gamma,\theta_{\text{inc}},\theta_{\text{inf}}) = \prod_{t=1}^{T} \frac{e^{-\tilde{\Lambda}(t)}\tilde{\Lambda}(t)^{\tilde{N}_t}}{\tilde{N}_t!}. \quad (2)$$

- Pre-symptomatic infection, modify the virus shedding formation:

$$\hat{\lambda}(t) = \sum_{i:t\in[\hat{t}_i,\hat{t}+\Delta^*_{\text{inf}}]} p^*_{\text{inf}}(t|\hat{t}_i)\Delta^*_{\text{inf}}\gamma. \quad (3)$$

City Lockdown Intervention

- A simple effect with two components -- immediate reduction and lasting effect for strengthening measures:

$$\theta(t) = \left(\theta_1 e^{-\theta_2 (t-t_0)}\right)^{I(t>t_0)}, \tag{4}$$

$$\hat{\lambda}(t) = \sum_{i:\, t \in [\tilde{t}_i, \tilde{t}+\Delta_{\text{inf}}]} p_{\text{inf}}(t|\tilde{t}_i)\Delta_{\text{inf}}\gamma\theta(t). \tag{5}$$

- Successful control of outbreak is reflected in time needed to reduce the effective R to below 1:

$$\hat{R}_0 = \hat{\gamma}\Delta_{\text{inf}}$$

$$R_{eff} = R_0\theta(t)$$

Natural History Assumptions Used in Analyses (Symptomatic infection only)

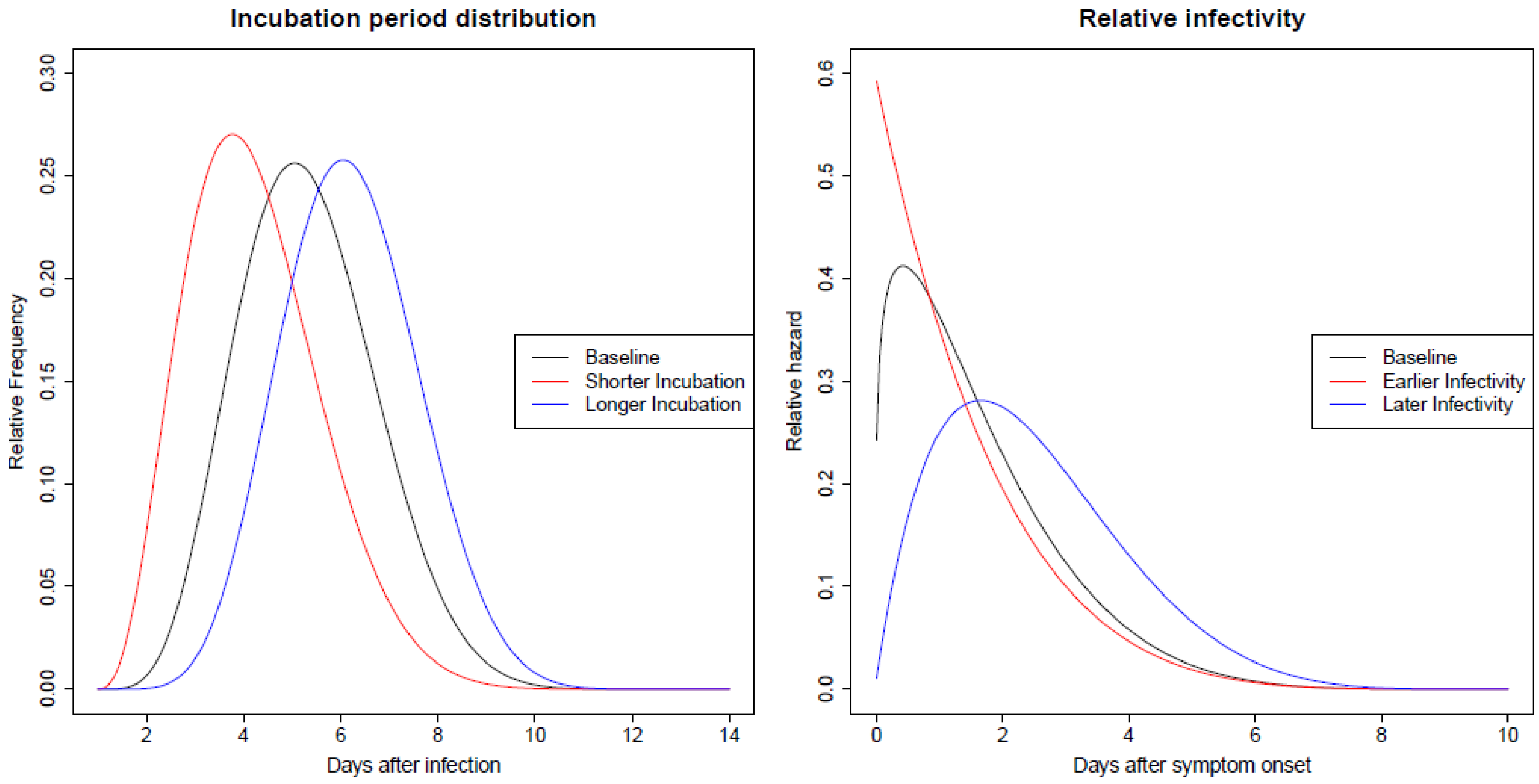


Fig. 2: Assumptions used to model the incubation period length distribution and relative infectivity following patient symptom onset for COVID-19 outbreak in China from Dec. 1, 2019 to Jan. 23, 2020. No asymptomatic infectiousness was possible in this model as cases may infect others only after symptom onset.

Natural History Assumptions Used in Analyses (Pre-symptomatic infection)

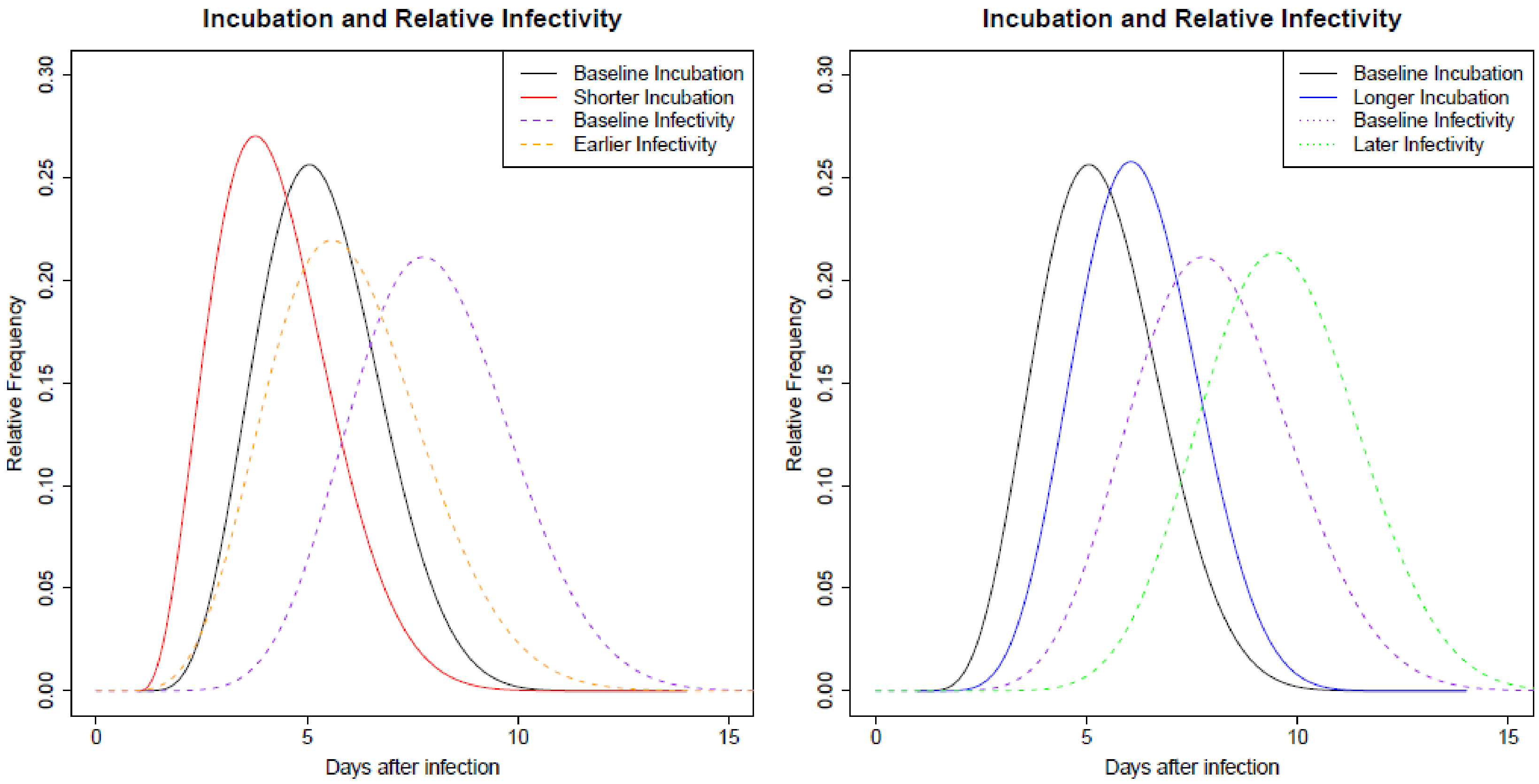


Fig. 3: Modified assumptions used to model the incubation period length distribution and relative infectivity following infection time for COVID-19 outbreak in China from Dec. 1, 2019 to Jan. 23, 2020. Asymptomatic infectiousness exist as the infectious period starts at time of infection.

Updated Results, onset until 2/11/2020, Wuhan*

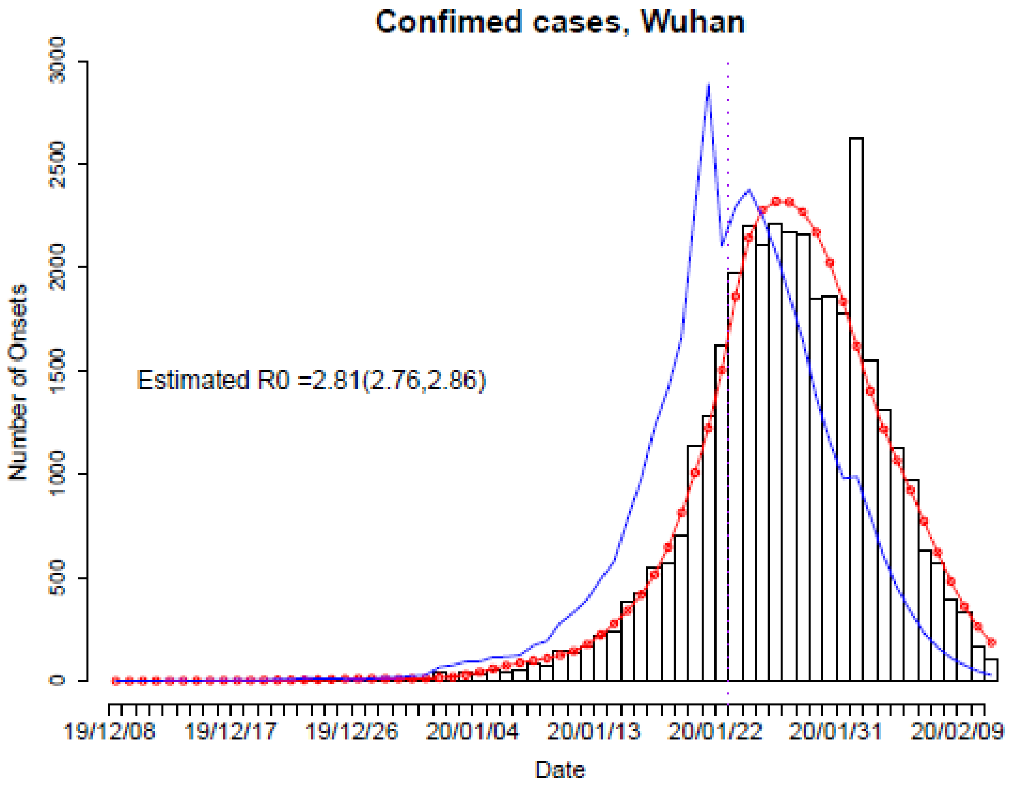
Table 2 Estimated model parameters and their 95% CIs for COVID-19 outbreak in Wuhan with updated data [12]

p_{inf}	Without asymptomatic infection		With asymptomatic infection	
	Baseline	Earlier	Baseline	Earlier
Confirmed cases, sWuhan[a]				
θ_1	0.579 (0.556, 0.599)	0.582 (0.563, 0.602)	0.635 (0.612, 0.659)	0.664 (0.640, 0.690)
θ_2	0.126 (0.122, 0.130)	0.121 (0.117, 0.125)	0.183 (0.179, 0.189)	0.137 (0.133, 0.142)
R_0	2.81 (2.76, 2.86)	2.70 (2.65, 2.75)	4.15 (4.07, 4.24)	2.73 (2.68, 2.79)
Days after intervention to $R_{eff} < 1$	3.85	3.74	5.29	4.35

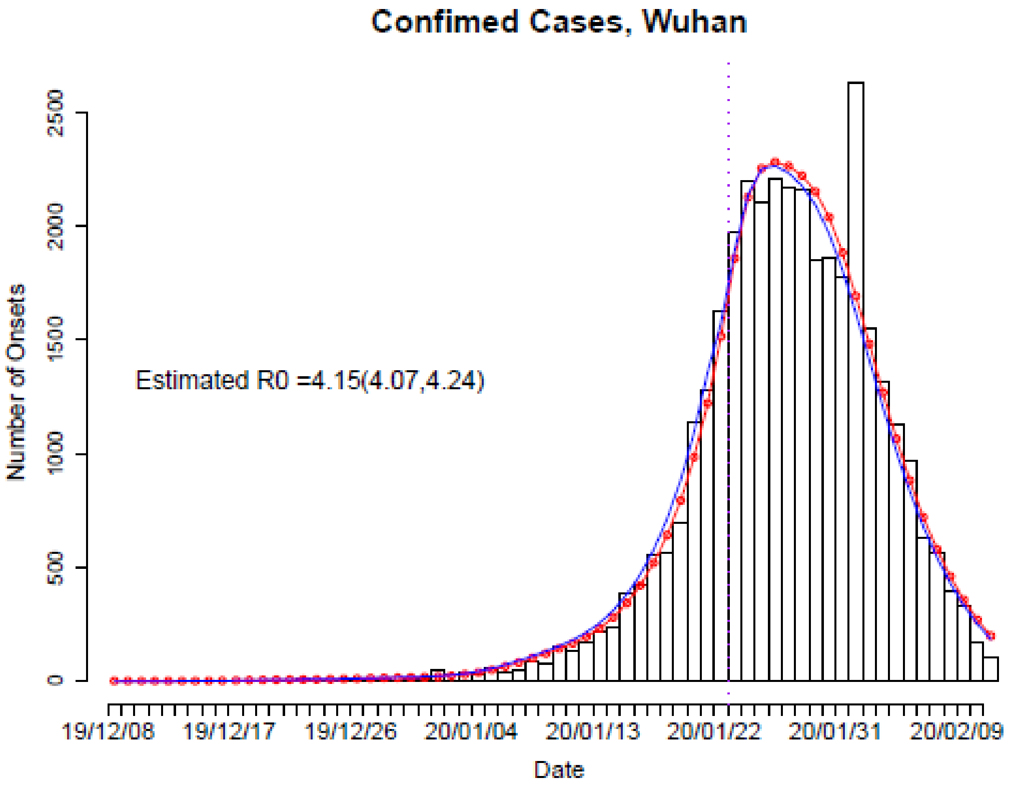
Shorter incubation period assumption used

[a]See the results from cases outside Wuhan in the Supplementary Material

Updated Results, onset until 2/11/2020, Wuhan*



(a) Cases in Wuhan, without asymptomatic infection.



(b) Cases in Wuhan, with asymptomatic infection.

Discussion

- The current model is based on homogeneous mixing assumption due to lack of data. The reported cases may be merely a reflection of available medical resources.
- We modelled the true epidemic curve instead of the case ascertainment report to avoid potential report bias. The intervention effect was shown to be effective relatively quickly in epidemic curve but much slower in the report curve.
- The estimated R0's from asymptomatic infectivity model were higher due to the extra window of viral shedding before onset. However it's not just more required effort to reduce R to below 1, but the whole extra set of intervention will be needed for effective control/mitigation.
- Testing! Testing! Testing! Contact tracing and quarantine of exposed individuals. The draconian measures in China seemed to effectively worked in 4-5 days after lockdown implementation, but in other places how to modify the strategies remain very challenging.
- A good YouTube video on the South Korean approach: https://www.youtube.com/watch?v=gAk7aX5hksU

Summary

- Bottom line: What is the question that you're trying to answer?
  - R0, with/without intervention, with/without asymptomatic transmission
- Significance: Why is this question important?
  - Understanding transmission mechanism, estimation from epi curve instead of ascertainment curve, differentiate natural history assumptions and their impact on model
- Data: What data are needed to answer your question?
  - Epi curve by onset time, better with subject level data including location, demographics, contact history etc. for more detailed modelling
- Methods: What statistical methods are needed? Have they already been developed?
  - Transmission model, MLE, potentially EM/Multiple imputation/MCMC for unobserved infection time. Model not complicated but restricted by available data
- Student Involvement: Are there opportunities for student involvement?
  - If someone could help collect data will be very helpful

Statistics in Biosciences
https://doi.org/10.1007/s12561-020-09277-0

On a Statistical Transmission Model in Analysis of the Early Phase of COVID-19 Outbreak

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Abstract

Since December 2019, a disease caused by a novel strain of coronavirus (COVID-19) had infected many people and the cumulative confirmed cases have reached almost 180,000 as of 17, March 2020. The COVID-19 outbreak was believed to have emerged from a seafood market in Wuhan, a metropolis city of more than 11 million population in Hubei province, China. We introduced a statistical disease transmission model using case symptom onset data to estimate the transmissibility of the early-phase outbreak in China, and provided sensitivity analyses with various assumptions of disease natural history of the COVID-19. We fitted the transmission model to several publicly available sources of the outbreak data until 11, February 2020, and estimated lock down intervention efficacy of Wuhan city. The estimated R_0 was between 2.7 and 4.2 from plausible distribution assumptions of the incubation period and relative infectivity over the infectious period. 95% confidence interval of R_0 were also reported. Potential issues such as data quality concerns and comparison of different modelling approaches were discussed.

AQ1

Keywords COVID-19 · Transmission model · Basic reproduction number · Emerging outbreak

- https://link.springer.com/article/10.1007/s12561-020-09277-0