Tracking and Predicting COVID-19 Pandemic with Varying Coefficient Epidemiological Models

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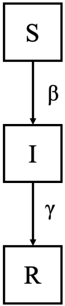
Classical SIR Model, Kermack and McKendrick (1927)

- Three compartments: Susceptible $S(t)$, Infectious $I(t)$ and Removed (cured and dead) $R(t)$.

$$\begin{aligned}\frac{dS(t)}{dt} &= -\beta I(t)s(t),\\ \frac{dI(t)}{dt} &= \beta I(t)s(t) - \gamma I(t)\\ \frac{dR(t)}{dt} &= \gamma I(t)\end{aligned}$$

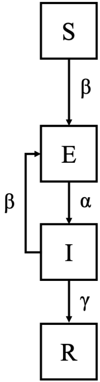


- Susceptible ratio $s(t) = S(t)/N$ and N is the population size.
- β–the infection rate; γ – the removal rate.

SEIR Model with Four Compartments, Hethcote (2000)

- Add Exposed E between S and I, infected **but not infectious**.

$$\frac{dS(t)}{dt} = -\beta I(t)s(t)$$
$$\frac{dE(t)}{dt} = \beta I(t)s(t) - \alpha E(t)$$
$$\frac{dI(t)}{dt} = \alpha E(t) - \gamma I(t)$$
$$\frac{dR(t)}{dt} = \gamma I(t)$$



- E is latent, makes estimation harder.
- α – diagnosis rate.
- Not Infectious before I, the same as SIR.

Bayesian or the EM algorithm Inference

Time-varying SIR (vSIR)

$\beta(t)$ and $\gamma(t)$ change with time

$$\frac{dS(t)}{dt} = -\beta(t)I(t)s(t),$$
$$\frac{dI(t)}{dt} = \beta(t)I(t)s(t) - \gamma(t)I(t),$$
$$\frac{dR(t)}{dt} = \gamma(t)I(t),$$

Statistical Models: the ODEs specify the conditional means of indpt Poisson increments at t, leading to likelihood.

We propose a local least square regression estimation (Kernel Smoothing).

Why Time-varying Coefficients ?

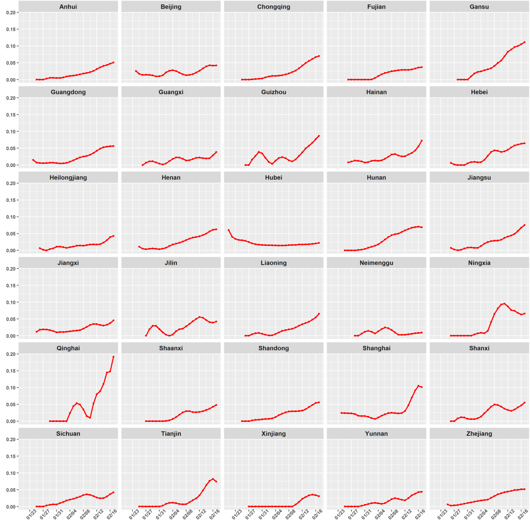
- $\beta(t)$ – the average rate of contact $\times$ probability of disease transmission per contact.

- An increasing public awareness plus control measures reduce the contact rate. And infectiousness may decay over time.

- Removal rate $\gamma(t)$ and the diagnostic rate $\alpha(t)$ were initially low and then increased as better cures and quicker diagnosis were available.

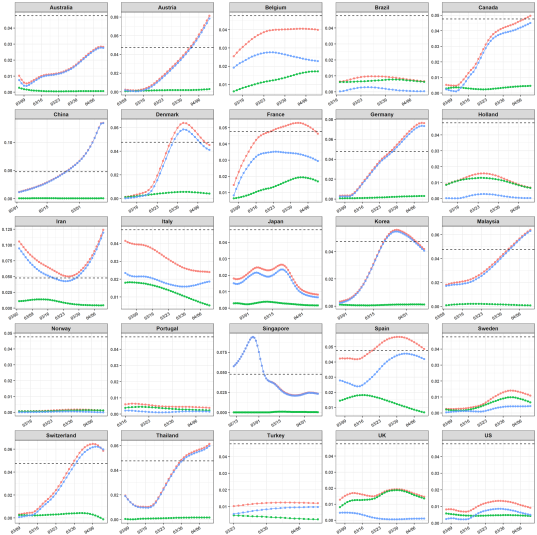
Removal Rates in China: Late Jan. to Mid-Feb.

- Jan 27^{th}, 0.0043 (0.007) for 27 provinces in China, and 15 of them is 0.
- Feb 3^{rd}, 0.0095 (0.006);
- Feb 10^{th}, 0.030 (0.017);
- Feb 17^{th}, 0.061 (0.032).



Removal (Death, Recover) Rates of 25 Countries.

- Estimated total removal γ_t (red), Death $\gamma_{d,t}$(green) and recovery $\gamma_{r,t}$(blue) for 24 countries and non-Hubei China.
- The grey horizontal dashed line marks 1/21.



Estimation for vSIR

Since $S(t)/N \approx 1$, $I(t) \approx I(t_1)\exp\{(\beta(t)s(t)-\gamma)(t-t_1)\}$. For each $t \geq w$, we estimate $\beta(t)-\gamma$ by local log-linear regression

$$\log I(t_1) \approx \alpha(t) + (\beta(t)s(t) - \gamma(t))t_1,$$

where $t_1 = t-w+1, \ldots, t$.

Can also do the kernel estimation based on

$$\begin{aligned} \frac{dN(t)}{dt} &= \beta(t) I(t) s(t) \\ \frac{dR(t)}{dt} &= \gamma(t) I(t) \end{aligned}$$

where $N(t) = I(t) + R(t)$.

$$\begin{aligned} \widehat{\beta(t)s(t)} &= \frac{\sum K(\frac{t-t_i}{h}) dN(t_i) I(t_i)}{\sum K(\frac{t-t_i}{h}) I^2(t_i)} \\ \hat{\gamma}(t) &= \frac{\sum K(\frac{t-t_i}{h}) dR(t_i) I(t_i)}{\sum K(\frac{t-t_i}{h}) I^2(t_i)} \end{aligned}$$

Inference for vSIR

- $\hat{\beta}(t) = \widehat{\beta(t) - \gamma}(t) + \hat{\gamma}(t)$
- $\mathrm{SE}_{\beta}(t) = \{\widehat{\mathrm{Var}}(\widehat{\beta(t) - \gamma}(t)) + \widehat{\mathrm{Var}}(\hat{\gamma}(t))\}^{1/2} + \widehat{\mathrm{Cov}}(\widehat{\beta(t), \hat{\gamma}}(t))$
- 95% CI for $\beta(t)$: $(\hat{\beta}(t) - 1.96\mathrm{SE}_{\beta}(t), \hat{\beta}(t) + 1.96\mathrm{SE}_{\beta}(t))$

Reproduction Numbers (RN): R_0 and R_t

- Basic RN R_0 and Effective R_t for $t > 0$
- For SIR and SEIR:
  $R_0 = \beta/\gamma = \beta D$, $D = 1/\gamma$ is infectious duration.
- For vSIR and vSEIR: $R_0 = \beta(0)/\gamma(0)$, $R_t = \beta(t)s(t)/\gamma(t)$.
- If $R_t > 1 (< 1)$, the epidemic grows (shrinks).
- R_t – **the driving force of the dynamic !**

vSIR Epidemic Progression and R_t

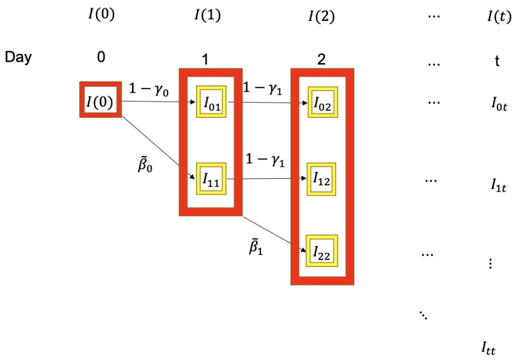
$I(t)$ – Infection loading at t.

$$\tilde{\beta}_t = \tilde{\beta}(t) = \beta(t)s(t)$$

- In expectation, $I(1) = (1 - \gamma_0 + \tilde{\beta}_0)I(0) > I(0)$ iff $1 - \gamma_0 + \tilde{\beta}_0 > 1$ iff $R_0 = \tilde{\beta}_0/\gamma_0 > 1$.

- Similarly, $I(2) > I(1)$ iff $R_1 = \tilde{\beta}_1/\gamma_1 > 1$.

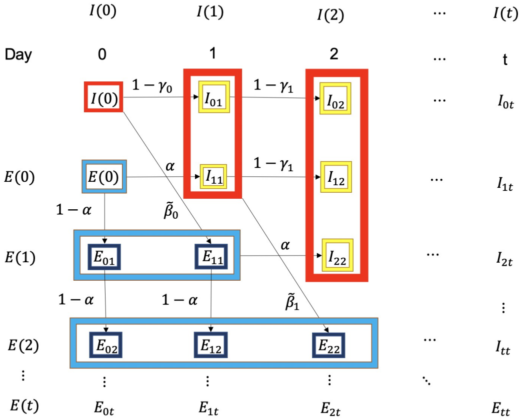
- $\{R_t\}$ track an epidemic being expanding or shrinking.



vSEIR Epidemic Progression and Determining Role of R_t

$E(t) + I(t)$ – Disease loading at t.

- In expectation,
  $E(1) = (1-\alpha_0)E(0) + \beta_0 I(0)$,
  $I(1) = (1-\gamma_0)I(0) + \alpha_0 E(0)$
- $E(1) + I(1) = E(0) + I(0) + (\beta_0 - \gamma_0)I(0) > E(0) + I(0)$ iff $R(0) = \frac{\beta_0}{\gamma_0} > 1$.
- Similarly,
  $E(2) + I(2) > E(1) + I(1)$ iff $R(1) = \frac{\beta_1}{\gamma_1} > 1$.
- Valid for any t !!



Estimation of R_t

- For SIR: $\hat{R} = \hat{\beta}/\hat{\gamma}$
- For vSIR: $\hat{R}_t = \hat{\hat{\beta}}(t)/\hat{\gamma}(t)$.
- However, $\hat{R}_t$ is erratic at early stage due to $\gamma(t)$ being small.
- We use $R_t^D = \hat{\beta}(t)D$ for $D = 7, 10.5$ and 14 days.
- D–the AVE duration of infectiousness under three scenarios.
- A smaller (larger) D for better (less) medical facilities and quicker (slower) response and treatments.

Two Parts of Infectious Duration D

- D_1: duration before diagnosed; D_2: duration after diagnosed and immediate hospitalization and thus quarantined.
- $D = D_1 + D_2$
- D_1 accounts for infection before I to cover up a limitation of vSIR and vSEIR models.
- D_2 should be short after being hospitalized, except in medically overwhelmed locations.

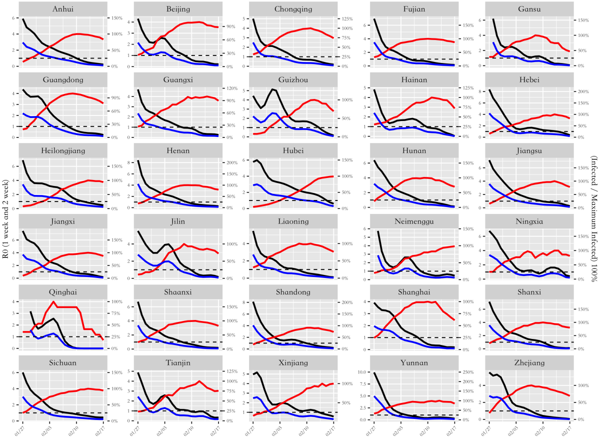
Empirical Information on D_1 and D_2

- 381 cases from *Shenzhen Online*, $D_2 = 14.85$ (3.33) days.
- 100 cases from Shaoyang, $D_1 = 5.67$ (3.86) and $D_2 = 10.12$ (2.74).
- The average incubation period from three studies ranged from 3.0 to 5.2 days; the median duration from onset to diagnosis was 4 days (Li et al, 2020 and Guan et al, 2020).
- The mean duration from onset to first medical visit and then to hospitalization were 4.6 and 9.1 days, respectively (Li et al, 2020).

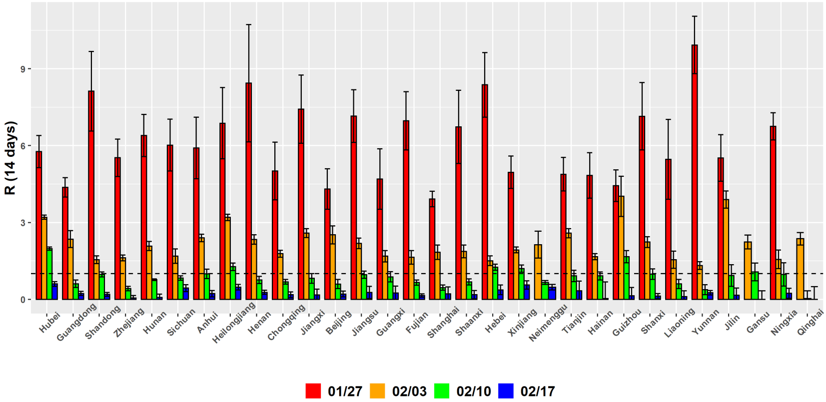
Tracking R_t^D for 30 Provinces in China

$D = 10.5$ (blue) and 14 (black). Red Lines $I(t)$

- Jan 27^{th}, AVE R^{14} was 6.14(1.49).
- Feb 3^{rd}, AVE R^{14} 2.18(0.67), a 64.5% reduction over the 7 days since Jan 27.
- Feb 10^{th}, AVE R^{14} dropped to 0.86(0.38), reflecting that the measures, including home quarantine and travel ban between different regions, have taken effect.
- Feb 17^{th}, the mean R^{14} reached 0.23 (0.15).
- The epidemic Lost POWER

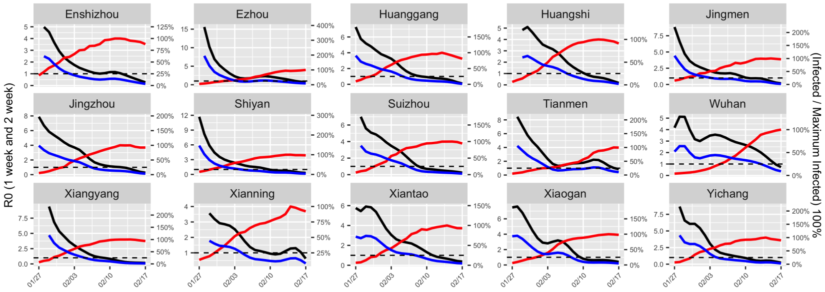


Three Weeks of COVID-19 Reproduction Numbers in China



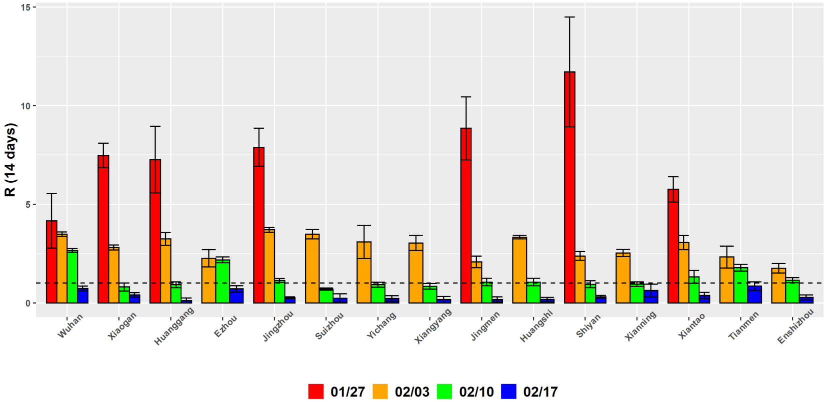
- On Feb 10^{th}, 5 provinces' R were significantly above 1 , and 14 provinces were significantly below 1 (at 5%).
- On Feb 17^{th}, all provinces' R were significantly below 1 (at 5% significance level).

Tracking R^D in 15 Hubei Cities



- On Jan 27, the 14-days R was 7.59($\pm$2.38) on average for Hubei cities, indicating a severe situation.
- On Feb 3, the mean R^{14} dropped to 2.84($\pm$0.59), a 62.6% reduction in the reproduction.
- On Feb 10, the mean R^{14} declined to 1.23 ($\pm$0.55), reflecting that the measures, including home quarantine and travel ban between different regions, have all taken effect.
- On Feb 17, the mean R^{14} reached 0.37 ($\pm$0.24). The turning point for Hubei was established.

The Three Weeks in 15 Hubei Cities



- On Feb 10^{th}, 5 Hubei cities' R^{14} were significantly above 1 (at 5% significance level), and 2 cities' R were significantly below 1.
- On Feb 17^{th}, all cities' R^{14} were significantly below 1 (at 5% significance level).

How to define the Turning point of an Epidemic ?

Mathematically, the first t that $R_t < 1$. Due to random fluctuations and errors in the epidemic data, the arrival of the turning point can be confirmed if

R_t is less than 1 at 5% significance level for $D/2$ days

If $D = 14$, R_t^{14} significantly below 1 for 7 consecutive days.

Time: 3 p.m. (Beijing Time), April 3, 2020

Five-Day Report on International Epidemic Situation of COVID-19

Pandemic continues: US persists as Italy levels off

Data: Based on the outbreak data up to 8 p.m. (Beijing Time), April 2, 2020

24 Countries concerned: (1) Asia: Iran, South Korea, Japan (excluding Diamond Princess), Malaysia, Singapore and Thailand; (2) Europe: Italy, Spain, France, Germany, UK, Holland, Switzerland, Belgium, Austria, Denmark, Norway, Sweden, Turkey (newly added), and Portugal (newly added); (3) North America: US and Canada; (4)Other: Brazil (newly added), and Australia (newly added).

Abstract: The epidemic situation in the United States has continually deteriorated, exhibiting a trend of exponential growth. While Italy's trend levels off, remaining European countries continue to show exponential growth and high mortality rates. The Korean epidemic has improved overall, but Japan had experienced a rebound in its epidemic situation. As the mandatory abilities of European and American governments are more limited than that of the Chinese government, the pandemic situation is at high risk of further worsening. If countries do not adopt harsh measures on blocking pathways of infection, 95% prediction interval for the average final number of total infections is between 5.5 millions-11.78 millions in these 24 countries. The lower limit decreases by 4.5 millions comparing to the previous report on March 29th. The upper limit is calculated excluding the Brazil's upper limit of 119 millions (Brazil epidemic has just started, exhibiting great uncertainty). We predict that the pandemic in the 24 countries will continue to late 2020 or even early 2021 (similar to the previous report, usually with about a week advance). The overall infection rate in the 24 countries will increase from 0.053% on April 2 to 0.38%-0.77%. The epidemic situations are in particularly concerning in developing nations with high percentage of low-income population and high density housing, such as Brazil. The long duration of overseas

1

Apr 3rd International Report

Daily Brief Reports

Domestic from Feb 3rd, and International from Feb 25th.

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北京大学 PEKING UNIVERSITY

2020 年 2 月 29 日 21 时

2 月 29 日疫情分析和全国 31 省市疫情等级

北京大学 PEKING UNIVERSITY

2020 年 3 月 2 日 21 时

3 月 2 日全国 31 省市疫情等级和结束时间预测

北京大学 PEKING UNIVERSITY

2020 年 3 月 9 日 21 时

3 月 9 日全国 31 省市疫情等级和结束时间预测

我们基于 3 月 9 日发布的截止于 3 月 8 日的疫情数据，使用我们研发的动态流行病模型，给出 30 省级行政区的传染再生系数 R。**我们结合 R 和过去 7 天的新增病例数，给出各省市目前疫情状况的评级，和各省市连续 14 天新增病例为零的时间预测和全部感染病例为零（疫情结束）的预测。**

传染再生系数 R 代表疫情传播的再生力，即每个患者在传染期内平均传染他人的数量。只有 **R 小于 1 时疫情才会出现下降，疫情会最终结束。**

疫情下降拐点的判定。由于疫情数据的随机波动和统计误差，我们认为只有一个省市的 **R 显著小于 1 的时间达到从染病到确诊的平均时间（可以用 7 天）后，才能确认拐点的到来；即如果 14 天 R 连续 7 天显著低于 1，就可以确定其拐点的到来。**具体结果见表 1 和图 1、2。

主要结果

1. **全国除宁夏外所有省市 14 天 R 全部显著低于 1，全国疫情的拐点在 2 月 11 号出现，2 月 18 号得到确立。**2 月 11 号后**全国疫情迅速改善，疫情已经进入结束倒计时阶段。**
2. **3 月 8 日湖北过去 7 天确诊病例首次低于 700 人，疫情已经全面好转。**湖北 R 最高的市仙桃也只有 0.2。
3. 中国疫情的迅速改善是由于从 1 月 23 号开始的大规模人口自我隔离和对人口流动控制的结果，中国的管控措施的效果非常显著，对目前其它国家的疫情很有借鉴。
4. 目前中国出现了多例境外疫情输入，需要引起重视。**甘肃已累计共 33 例来自境外的疫情输入，需要防范境外输入风险。**
5. **针对下一步的疫情管理，我们将全国 31 省市划分为七类。湖北为 F 类，疫情风险等级最高，疫情最严重。A++类表示现存感染病例为 0。A+类表示过去 14 天新增病例数为 0，疫情风险较低。红色省市为经济总量前 10 名的省加京、津、沪、渝。今日首次出现除青海、西藏外现存病例为 0 的省市福建。疫情结束表明所有患病人员出院，现存感染病例清零。连续 14 天当地无新增预测时间不讨论境外输入病例情况。**

A++类（共 5 省、市、自治区，今日新增安徽，新疆）：西藏，青海，安徽，新疆，福建：过去 14 天无新增病例，并无现存病例。福建，安徽，新疆现存感染病例清零。

1

(a) Domestic Reports from Feb 3rd

北京大学 PEKING UNIVERSITY

Time: 21:00 p.m. (Beijing Time), March 4, 2020

Daily Brief on International Epidemic Situation of COVID-19

北京大学 PEKING UNIVERSITY

Time: 15 p.m. (Beijing Time), March 29, 2020

Daily Brief on International Epidemic Situation of COVID-19

Pandemic is happening. Countries need to take more drastic measures.

北京大学 PEKING UNIVERSITY

Time: 3 p.m. (Beijing Time), April 3, 2020

Five-Day Report on International Epidemic Situation of COVID-19

Pandemic continues: US persists as Italy levels off

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1

(b) Intl. Reports from Feb 26th

Prediction

- The overall trends of $\beta(t)$ is decreasing, while the rate of deceasing gets smaller as time travels. To model such trend, we consider to fit a parametric regression

$$\beta(t) = \beta_\theta(t) = \frac{b}{t^\eta - a}.$$

- With the fitted $\tilde{\beta}(t)$ and the observed $\{S(T), I(T), R(T)\}$ at the current time T as the initial values, numerical solutions of the ODE system could be obtained.
- We then generate Poisson increments conditionally to progress ...

Bootstrap inference for prediction

- The increments of $S(t)$ and $R(t)$ are regarded to follow Poisson processes

$$-\Delta S(t) \sim \text{Poisson}\left\{\beta(t)s(t)I(t)\right\} \text{ and } \Delta R(t) \sim \text{Poisson}\left\{\gamma I(t)\right\}$$

- Generate Parametric bootstrap samples $\{(S^b(t), I^b(t), R^b(t))\}_{t=1}^T$ of the original process for $b = 1, 2, \ldots, B$ such that

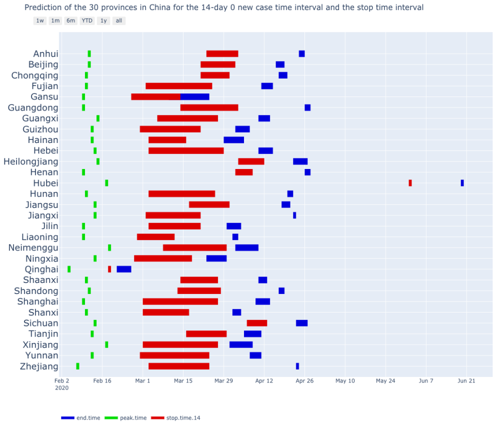
$$\begin{aligned}
&S^b(1) = S(1),\ I^b(1) = I(1),\ R^b(1) = R(1),\\
&\Delta S^b(t) \sim \text{Poisson}\left\{\hat{\beta}(t)S^b(t)I^b(t)/N\right\},\\
&\Delta R^b(t) \sim \text{Poisson}\left\{\hat{\gamma}I^b(t)\right\}\\
&S^b(t+1) = S^b(t) - \Delta S^b(t),\\
&R^b(t+1) = R^b(t) + \Delta R^b(t),\\
&I^b(t+1) = N - S^b(t+1) - R^b(t+1)
\end{aligned}$$

- Use the bias corrected bootstrap estimates for $\beta(t)$ and $\hat{\gamma}(t)$

The 95% Predicted Intervals for Peak, 14-day No New Cases and Ending Time

Based on Feb 10th and Feb 27th data.

The average prediction error for peaks were 2.1 days, 4.4 days for 14 days no new cases, and 11 days for the ending date, respectively.



The peak time (green region), first date of no new cases for 14 consecutive days (red region) and the ending date (blue region).

vSEIdR Model: Allow Infection in Exposed State

Our current international assessment uses this model.

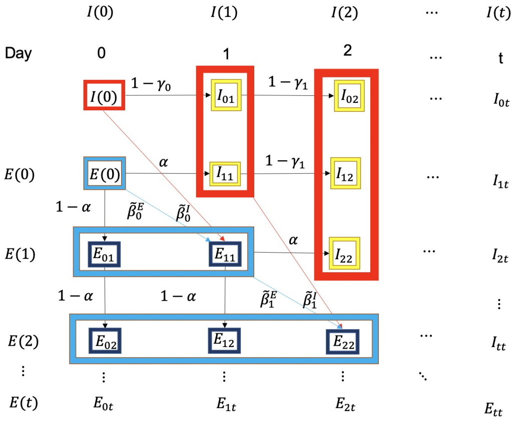
$$\begin{aligned}
\frac{dS(t)}{dt} &= -\{\beta_t^{\mathrm{E}} E(t) + \beta_t^{\mathrm{I}} I(t)\}\frac{S(t)}{M}, \\
\frac{dE(t)}{dt} &= \{\beta_t^{\mathrm{E}} E(t) + \beta_t^{\mathrm{I}} I(t)\}\frac{S(t)}{M} - \alpha E(t), \\
\frac{dI(t)}{dt} &= \alpha E(t) - \gamma_t I(t), \\
\frac{dR_r(t)}{dt} &= \gamma_{r,t} I(t) \text{ and } \frac{dR_d(t)}{dt} = \gamma_{d,t} I(t)
\end{aligned}$$

$\tilde{\beta}_t^{\mathrm{E}} = \beta^{\mathrm{E}} S(t)/M$ and $\tilde{\beta}_t^{\mathrm{I}} = \beta^{\mathrm{I}} S(t)/M$ be the effective disease transmission rates at time t.

$\gamma_t = \gamma_{d,t} + \gamma_{r,t}$ is the total removal rate.

vSEIdR Epidemic Progression and Role of R_t

- $E(t) + I(t)$ – Disease loading at t.
- $R_t = \frac{\beta_t^I s(t)}{\gamma_t} + \frac{\beta_t^E s(t)}{\alpha_t}$



Two-Stage *vSEIdR* estimation

- When $I(t)$ is small, the infection is mainly caused by $E(t)$. We can estimate $\beta(t) - \alpha(t)$.
- When $I(t)$ is large and $\Delta I(t)/I(t)$ is small, the ratio $k(t)$ between $E(t)$ and $I(t)$ is relatively a constant function.
  - Regressing $log\{I(t)\}$ on t, estimate $\alpha(t)\widehat{k(t) -} \gamma(t)$ for $\alpha(t)k(t) - \gamma(t)$.
  - Assuming $\alpha(t)$is known,

    $$\hat{k}(t) = \{\alpha(t)\widehat{k(t) -} \gamma(t) + \hat{\gamma}(t)\}/\alpha(t)$$

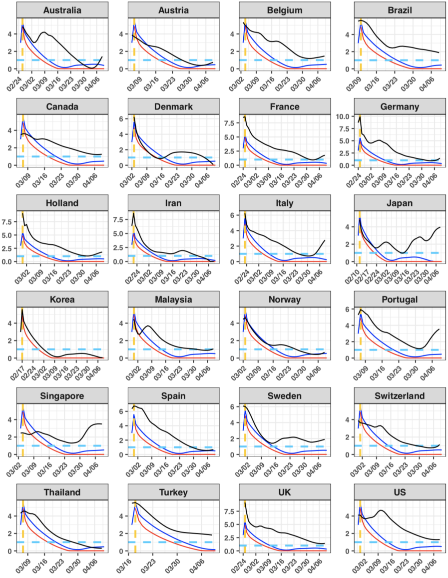
    is an estimate for $k(t)$
  - $E(t)$ can be estimated as $\hat{E}(t) = \hat{k}(t)I(t)$.
  - Applying local regression of $\log\{\hat{E}(t)\}$ on t to estimate the slope $\hat{\theta}(t)$.

$$\hat{\beta}(t) = \{\hat{\theta}(t) + \alpha(t)\}\frac{r\hat{k}(t)}{r\hat{k}(t) + 1}.$$

Effective Reproduction Numbers R_t for 24 Countries

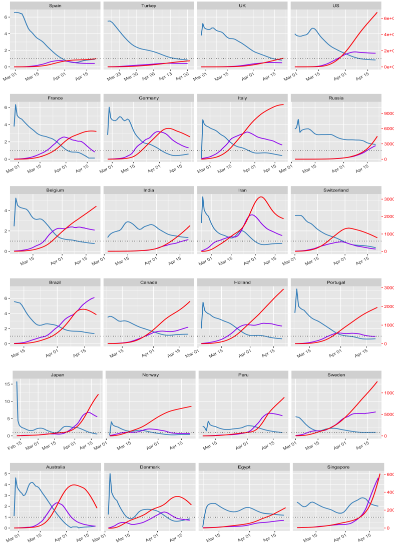
- The estimated effective reproduction number R_t curves (black) of the countries since their start dates of community transmission (yellow dashed vertical lines) versus those of China (red) and Korea (blue).

- The blue dashed line represents the critical threshold level 1.

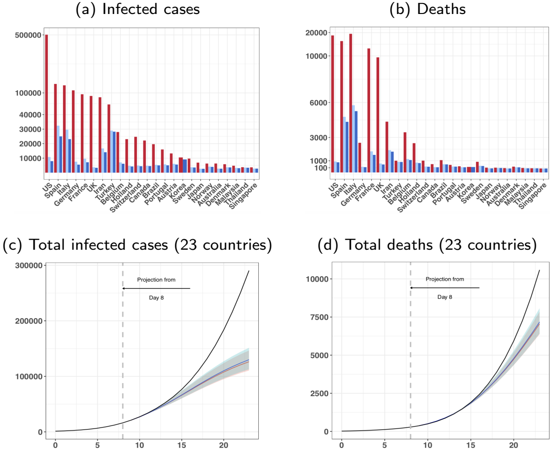


Effective Reproduction Numbers R_t for 24 Countries

- Blue lines – R_t
- Red lines – $I(t)$.
- Purple line– $\hat{E}(t)$.



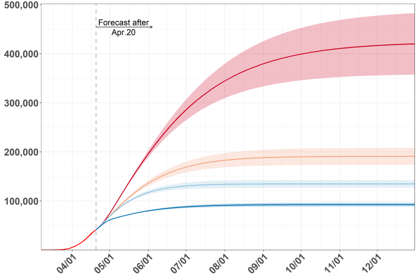
Scenario Analysis



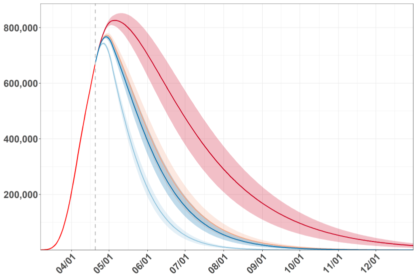
The observed numbers (red bar) of infected cases (a) and deaths (b) of the countries and the would-be ones under China (blue bar) and Korea (light blue bar)'s scenarios implemented from Day 8 to April 10; and the observed (black) total numbers of infected cases (c) and deaths (d) of the 23 countries excluding Korea and China and the would-be totals from Day 8 to Day 23 under China (red) and Korea (blue)'s scenarios. Day 23 is the shortest time range of the 23 countries from the start date to April 10.

Projected Death Tolls and Existing Infected Cases for US

Projected death tolls for US



Projected existing infected cases for US



Projected death tolls and existing infected cases under the two Natural Designs of respective countries, and Korea (blue) and Italy (red)'s recovery and death rates. Natural Designs 1 and 2 impose a minimum level of 1/17.5 (light blue) and 1/28 (orange) on the recovery rate, respectively. The data used for the forecasting are up to Apr. 20th.

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