TITLE

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Abstract

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Introduction

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Models and Methods

Data. We use daily confirmed case data $\mathbf{X} = (X_1, \ldots, X_T)$ from several different countries. These incidence data summarize the number of individuals X_t tested positive for SARS-CoV-2 RNA (using RT-qPCR) at each day t. Data was retrieved for X regions, see Table 1 for details and references. In regions in which there were multiple sequences of days with zero confirmed cases (e.g. France), we cropped the data to begin with the last sequence so that our analysis focuses on the first community-transmitted outbreak rather then isolated imported cases.

Region	Start date	End date	Reference
Austria	X Feb		Flaxman et al. (2020)
Wuhan, China	10 Jan	8 Feb	Pei & Shaman (2020)

Table 1: Reference for confirmed cases incidence data. All dates in 2020.

SEIR model. We model SARS-CoV-2 infection dynamics by following the number of susceptible S, exposed E, reported infected I_r, and unreported infected I_u individuals in a population of size N. This model distinguishes between reported and unreported infected individuals: the reported infected are those that have enough symptoms to eventually be tested and thus appear in daily case reports, to which we fit the model.

Susceptible (S) individuals become exposed due to contact with reported or unreported infected individuals (I_r or I_u) at a rate β_t or $\mu\beta_t$. The parameter $0 < \mu < 1$ represents the decreased transmission rate from unreported infected individuals, who are often subclinical or even asymptomatic. The transmission rate $\beta_t \geq 0$ may change over time t due to behavioral changes of both susceptible and infected individuals. Exposed individuals, after an average incubation period of Z days, become reported infected with probability α_t or unreported infected with probability $(1 - \alpha_t)$. The reporting rate $0 < \alpha_t < 1$ may also change over time due to changes in human behavior. Infected individuals remain infectious for an average period of D days, after which they either recover, or becomes ill enough to be quarantined. They therefore no longer infect other individuals, and the model does not track their frequency. The model is described by the following equations:

$$
\begin{aligned}
\frac{dS}{dt} &= -\beta_t S \frac{I_p}{N} - \mu\beta_t S \frac{I_s}{N} \\
\frac{dE}{dt} &= \beta_t S \frac{I_p}{N} + \mu\beta_t S \frac{I_s}{N} - \frac{E}{Z} \\
\frac{dI_r}{dt} &= \alpha_t \frac{E}{Z} - \frac{I_r}{D} \\
\frac{dI_u}{dt} &= (1 - \alpha_t)\frac{E}{Z} - \frac{I_r}{D}.
\end{aligned}
\tag{1}
$$

The initial numbers of exposed $E(0)$ and unreported infected $I_u(0)$ are considered model parameters, whereas the initial number of reported infected is assumed to be zero $I_r(0) = 0$, and the number of susceptible is $S(0) = N - E(0) - I_u(0)$. The vector θ of model parameters is

$$
\theta = \Big(Z, D, \mu, \{\beta_t\}, \{\alpha_t\}, \{p_t\}, E(0), I_u(0)\Big). \tag{2}
$$

This model is inspired by Li et al. (2020) and Pei & Shaman (2020), who used a similar model with multiple regions and constant transmission β and reporting rate α to infer COVID-19 dynamics in China and the continental US, respectively.

Likelihood function. The *expected* cumulative number of reported infected individuals until day t is

$$Y_t = \int_0^t \alpha_s \frac{E(s)}{Z}\, ds, \quad Y_0 = 0. \tag{3}$$

We assume that reported infected individuals are confirmed and therefore observed in the daily case report of day t with probability p_t (note that an individual can only be observed once, and that p_t may change over time, but t is a specific date rather than the time elapsed since the individual was infected). Hence, we assume that the number of confirmed cases in day t is binomially distributed,

$$X_t \sim Bin\big(n_t, p_t\big),$$

where n_t is the *realized* (rather than expected) number of reported infected individuals yet to appear in daily reports by day t. The cumulative number of confirmed cases until day t is

$$\tilde{X}_t = \sum_{i=1}^{t} X_i, \quad X_0 = 0.$$

Given $\tilde{X}_{t-1}$, we assume n_t is Poisson distributed,

$$\big(n_t \mid \tilde{X}_{t-1}\big) \sim Poi\Big(Y_t - \tilde{X}_{t-1}\Big), \quad n_1 \sim Poi(Y_1).$$

Therefore, $\big(X_t \mid \tilde{X}_{t-1}\big)$ is a binomial conditioned on a Poisson, which reduces to a Poisson with

$$\big(X_t \mid \tilde{X}_{t-1}\big) \sim Poi\Big(\big(Y_t - \tilde{X}_{t-1}\big) \cdot p_t\Big), \quad X_1 \sim Poi(Y_1 \cdot p_1). \tag{4}$$

For given vector θ of model parameters (Eq. (2)), we compute the expected cumulative number of reported infected individuals $\{Y_t\}_{t=1}^{T}$ for each day (Eq. (3)). Then, since $\tilde{X}_{t-1}$ is a function of $X_1, \ldots, X_{t-1}$, we can use Eq. (4) to write the probability to observe the confirmed case data $\mathbf{X} = (X_1, \ldots, X_T)$ as

$$\mathbb{L}(\theta \mid \mathbf{X}) = P(\mathbf{X} \mid \theta) = P(X_1 \mid \theta) P(X_2 \mid \tilde{X}_1, \theta) \cdots P(X_T \mid \tilde{X}_{T-1}, \theta). \tag{5}$$

This defines a *likelihood function* $\mathbb{L}(\theta \mid \mathbf{X})$ for the parameter vector θ given the data $\mathbf{X}$.

NPI model. To model non-pharmaceutical interventions (NPIs), we set the beginning of the NPIs to day τ and define

$$\beta_t = \begin{cases} \beta, & t < \tau \\ \beta\lambda, & t \geq \tau \end{cases}, \quad \alpha_t = \begin{cases} \alpha_1, & t < \tau \\ \alpha_2, & t \geq \tau \end{cases}, \quad p_t = \begin{cases} 1/9, & t < \tau \\ 1/6, & t \geq \tau \end{cases}, \tag{6}$$

where $0 < \lambda < 1$. The values for p_t follow Li et al. (2020), who estimated the average time between infection and reporting in Wuhan, China, at 9 days before the start of NPIs (Jan 23, 2020) and 6 days after start of NPIs. The parameter τ is then added to the parameter vector θ (Eq. (2)).

Model fitting. To fit our model (Eq. (1)) to the data $\mathbf{X}$ and estimate the model parameters θ, we apply a Bayesian inference approach. We define the following flat priors on the model parameters $P(\theta)$:

$$\begin{aligned} Z &\sim \mathit{Uniform}(2, 5) \\ D &\sim \mathit{Uniform}(2, 5) \\ \mu &\sim \mathit{Uniform}(0.2, 1) \\ \beta &\sim \mathit{Uniform}(0.8, 1.5) \\ \lambda &\sim \mathit{Uniform}(0, 1) \\ \alpha_1, \alpha_2 &\sim \mathit{Uniform}(0.02, 1) \\ E(0) &\sim \mathit{Uniform}(0, 3000) \\ I_u(0) &\sim \mathit{Uniform}(0, 3000) \\ \tau &\sim \mathit{Uniform}(1, T-1), \end{aligned} \tag{7}$$

where T is the number of days in the data $\mathbf{X}$. Most priors follow Li et al. (2020), except λ, which is used to enforce that the transmission rates are lower after the start of the NPIs ($\lambda < 1$). The likelihood function is defined in Eq. (5). The posterior distribution on the model parameters $P(\theta \mid \mathbf{X})$ is then estimated using an affine-invariant ensemble sampler for Markov chain Monte Carlo (MCMC) implemented in the `emcee` Python package (Foreman-Mackey et al. 2013).

Results

Several studies have described the effects of non-pharmaceutical interventions in several countries (Flaxman et al. 2020, Gatto et al. 2020). These studies have assumed that that the epidemiological dynamics change at a specific date, as in Eq. (6), set the change date τ to the official NPI date tau^*, and fit the model once for $t < \tau^*$ and once for $t \geq \tau^*$ (see TABLE2 for a summary of official NPI dates.) For example, Li et al. (2020) estimate the dynamics in China before and after τ^* at Jan 23. Thereby, they effectively estimate (β, α_1) and (λ, α_2) separately.

Here we estimate the posterior distribution of *effective* start date of the NPI, $P(\tau \mid \mathbf{X}$, as well as maximum a priori (MAP) estimates, $\hat{\tau}$, by jointly estimating $\tau, \beta, \lambda, \alpha_1, \alpha_2$ on the entire time series per region (e.g. Italy, Austria), rather than splitting the region time series at τ^*. FIGURE shows a comparison the official dates τ^* and our MAP estimates $\hat{\tau}$, with confidence intervals. In most cases analyses, we find that $\hat{\tau}$ and τ^* differ significantly: that is, the effective start of NPI was either advanced or delayed compared to the official date. In the following, we describe our findings on delayed and advanced start of NPI.

Delayed effective start of NPI. We find that our MAP estimates $\hat{\tau}$ often differ significantly from the official dates tau^*. For example, in Italy, the first case officially confirmed on Feb 21, a lockdown was delayed in Northern Italy on Mar 8, with social distancing implemented in the rest of the country, and the lockdown was extended to the entire nation on Mar 11 (Gatto et al. 2020). That is, the official date τ^* is either Mar 8 or 11. However, we estimate the effective date $\hat{\tau}$ at Mar 16 (the posterior probability that τ is later than Mar 11 is $(P(\tau > \tau^*) =???)$. Similarly, in Wuhan, China, lockdown was declared on Jan 23 (Li et al. 2020), but we estimate that the effective start of NPIs to be 3-4 days layer $(P(\tau > \tau^*) =???)$.

Advanced effective start of NPIs. In contrast, in some regions we estimate an effective start of NPIs $\hat{\tau}$ that is *earlier* then the official date τ^*. For example, social distancing was encouraged starting on Mar 8 (Flaxman et al. 2020), but mass gatherings still occurred on Mar 8, including a march of 120,000 people for the International Women's Day, and a football match between Real Betis and Real Madrid (2-1) with a crowd of 50,965 in Seville. A national lockdown was only announced on Mar 14

(τ^*) (Flaxman et al. 2020). Nevertheless, we estimate the effective start of NPI $\hat{\tau}$ at Mar 8 or 9, rather than Mar 14 ($P(\tau < \tau^*) =$???).

Match between effective and official start of NPI. We have also found a single case in which the official and effective dates match: Switzerland ordered a national lockdown on Mar 20 (τ^*), after banning public evens and closing schools on Mar 13 and 14 (Flaxman et al. 2020). Indeed, our MAP estimate $\hat{\tau}$ is Mar 20, and the posterior distribution shows two density peaks: a smaller one between Mar 10 and Mar 14, and a taller one between Mar 17 and Mar 22. It's also worth mentioning that Switzerland was the first to mandate self isolation of confirmed cases (Flaxman et al. 2020).

Discussion

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As several countries (e.g. Austria, Israel) begin to relieve lockdowns and ease restrictions, we expect similar delays and advances to occur: in some countries people will begin to behave as if restrictions were eased before the official date, and in some countries people will continue to self-restrict even after restrictions are officially removed. Such delays and advances could confuse analyses and lead to wrong conclusions about the effects of NPI removals.

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References

Flaxman, S., Mishra, S., Gandy, A., Unwin, J. T., Coupland, H., Mellan, T. A., Zhu, H., Berah, T., Eaton, J. W., Guzman, P. N. P., Schmit, N., Cilloni, L., Ainslie, K. E. C., Baguelin, M., Blake, I., Boonyasiri, A., Boyd, O., Cattarino, L., Ciavarella, C., Cooper, L., Cucunubá, Z., Cuomo-Dannenburg, G., Dighe, A., Djaafara, B., Dorigatti, I., Van Elsland, S., Fitzjohn, R., Fu, H., Gaythorpe, K., Geidelberg, L., Grassly, N., Green, W., Hallett, T., Hamlet, A., Hinsley, W., Jeffrey, B., Jorgensen, D., Knock, E., Laydon, D., Nedjati-Gilani, G., Nouvellet, P., Parag, K., Siveroni, I., Thompson, H., Verity, R., Volz, E., Gt Walker, P., Walters, C., Wang, H., Wang, Y., Watson, O., Xi, X., Winskill, P., Whittaker, C., Ghani, A., Donnelly, C. A., Riley, S., Okell, L. C., Vollmer, M. A. C., Ferguson, N. M. & Bhatt, S. (2020), 'Estimating the number of infections and the impact of non-pharmaceutical interventions on COVID-19 in 11 European countries', *Imp. Coll. London* (March), 1–35.
URL: *https://doi.org/10.25561/77731*

Foreman-Mackey, D., Hogg, D. W., Lang, D. & Goodman, J. (2013), 'emcee : The MCMC Hammer ', *Publ. Astron. Soc. Pacific* **125**(925), 306–312.

Gatto, M., Bertuzzo, E., Mari, L., Miccoli, S., Carraro, L., Casagrandi, R. & Rinaldo, A. (2020), 'Spread and dynamics of the COVID-19 epidemic in Italy: Effects of emergency containment measures', *Proc. Natl. Acad. Sci.* p. 202004978.
URL: *http://www.pnas.org/lookup/doi/10.1073/pnas.200497811*

Li, R., Pei, S., Chen, B., Song, Y., Zhang, T., Yang, W. & Shaman, J. (2020), 'Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2)', *Science (80-.).* p. eabb3221.
URL: *https://www.sciencemag.org/lookup/doi/10.1126/science.a*

Pei, S. & Shaman, J. (2020), 'Initial Simulation of SARS-CoV2 Spread and Intervention Effects in the Continental US', *medRxiv* p. 2020.03.21.20040303.
URL: *http://medrxiv.org/content/early/2020/03/23/2020.03.21.2*