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Discussion on "The timing and effectiveness of implementing mild interventions of COVID-19 in large industrial regions via a synthetic control method" by Tian et al.

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DISCUSSION

We congratulate Tian et al. for their great work on assessing the effectiveness and timing of Coronavirus Disease 2019 (COVID-19) interventions during early 2020 in Shenzhen, one of the largest industrial regions in China. In response to the pandemic, many recent research works are dedicated to predicting new or cumulative infections during the early phase of COVID-19 outbreaks. Among them, most rely on using epidemic models to estimate the infection trajectories. See for example, [3] and [2], among others. Not many focus on the statistical inference for the differences between the actual and hypothetical scenarios, the insight of which is helpful in determining the timeliness of interventions and the impact of such interventions. Tian et al. provide an elegant answer to such problems by adopting a synthetic control method (SCM) under the potential outcome framework.

The daily cumulative count of confirmed cases is the outcome of interest in consideration. Typically, the trajectory of the number of cumulative confirmed cases is modeled through epidemiological models, such as a Susceptible-Exposed-Infectious-Removed (SEIR) compartment model. Population-wise epidemiological models usually assume knowledge about the disease dynamic. See [1] and references therein for a comprehensive review of the commonly adopted epidemic models and their assumptions. For COVID-19, some of these assumptions would not hold. First and most notably, the homogeneous mixing assumption assumes an individual will meet any other individual in the population with the same probability regardless of demographical differences; but in reality such interactions are clustered. For example, individuals in the same age range (spouses, friends or peers) or with a 20–35 year gap (parents and children) tend to mix with a higher probability. Second, many existing epidemic models fail to account for a latency period where an individual may be infectious before symptom onset. It is important to note that the Exposed compartment in a standard SEIR model does not account for such symptom onset latency, but rather a latency in becoming infectious after being exposed.

Here, the novel SCM proposed by Tian et al. avoids making typical epidemiological modeling assumptions. By creating a synthetic control of Shenzhen, the method implicitly assumes that the disease dynamic should be the same between Shenzhen and its control, no matter how complicated such a dynamic is. Using the same example given above, the SCM allows both Shenzhen and its control to have non-homogeneous mixing among populations, but as long as the mixing pattern remains the same, their results are comparable and the difference reflects the true intervention effect under such mixing pattern. In other words, their proposed method for assessing the effectiveness of the mild intervention in Shenzhen does not necessarily make any explicit assumptions on the disease dynamic. This is a notable advantage of the SCM over most existing methods, provided that such control can be easily identified. The paper provides and describes in details a systematic procedure in identifying such synthetic control for Shenzhen from counties in the US based on their respective population density, latitude, and observed incidence trajectories. A convenient permutation test is also proposed to test the significance of the estimated intervention effect under this framework.

In addition to the SCM approach, Tian et al. also proposes a new epidemiological model to assess the timing effect of Shenzhen's mild intervention, defined as the effect due to delaying the start of intervention. Approaching from a slightly different angle than the SCM, the delayed intervention is modeled through a compartment model referred to as the Susceptible-Infectious-Hospitalized-Removed (SIHR) model. The SIHR model actively incorporates the incubation period of COVID-19 into the Infectious compartment in the sense that infection occurs only during the incubation period; when a patient shows any symptoms (i.e., reaching the end of the incubation period), this individual will be hospitalized, which is also a valid assumption given hospital resources are abundant and there is no delay in hospitalization. Mainly, by separately considering Infectious and Hospitalized compartments, the model actively assesses the pre-symptomatic transmission rate. This is an important feature of COVID-19 that could potentially bias the estimation of existing epidemic models if

such an incubation period is not appropriately accounted for.

The choice of using the logistic function for the time-varying β also reflects the reality. This function considers the transmission rate β to be approximately constant before and after the intervention, while the adaptation to the intervention is relatively quick. Then, a delayed intervention can be assessed by shifting the β function rightward over time by h amount of days. For example, the potential scenario if the start of such intervention was delayed from Jan 23 to Jan 26, i.e., by letting $h = 3$ days. Along this line, it is tempting to use the SIHR model to assess the treatment effect due to delaying the intervention by even further, say, let $h > 12$, which yields results that may be used to provide a second answer to the question addressed by the SCM model. It would be interesting to know how the disease dynamic-free SCM model and the dynamic-based SIHR model differ or coincide in this case.

In summary, the work proposes two elegant solutions to assess the effectiveness of the mild interventions of COVID-19 implemented in Shenzhen, China. The first being a synthetic control method to estimate the counterfactual of Shenzhen for intervention effect assessment. The second being a modified epidemic compartment model to account for an incubation period, used for assessing effects due to delayed delivery of interventions. Both methods are novel and effective in conducting estimation and inference for the timing of interventions, and are valuable to other cities and countries with a similar need.

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