INTRODUCTION

As of March 27, 2020, there were 504,806 confirmed cases of a coronavirus disease 2019 (COVID-19) reported worldwide and 134 countries were reporting community transmission [1]. In Korea, a total of 9,332 confirmed cases were reported from January 20, 2020, when the first case was confirmed, to March 27, 2020. The daily number of confirmed cases in Korea increased rapidly after a large-scale cluster of COVID-19 cases occurred in mid-February at the Sincheonji Church in Daegu, reaching 909 newly confirmed cases per day on February 29, 2020. After February 29, 2020 the number of new cases has decreased, but small and large outbreaks are still being reported nationwide, and the total number of new cases outside of Daegu has increased as the immigration of COVID-19 from foreign countries increases [1].

The reproduction number (R) is defined as the average number of infected people generated during the infectious period of an infected patient. It is an index to quantify the transmissibility of infectious disease. The R value varies over time during epidemic periods owing to various factors such as infection control strategies, pathogen characteristics, population immunity, and changes...
in contact behaviors between infectious and susceptible individuals. This time-varying $R$ value is known as an instantaneous reproduction number or time-variant reproductive number ($R_t$). Therefore, observing changes in $R$ is an important indicator for evaluating the effectiveness of infection control strategies and monitoring the spread of infection [2]. This study estimated $R_t$ of COVID-19 using the information on confirmed cases in Seoul, Korea. It also summarized the results using the existing $R_t$ statistical software package, EpiEstim.

**METHODS**

Daily numbers of confirmed cases were obtained from COVID-19 status reports provided by the official website of Seoul city [3]. Moreover, information such as the presence or absence of symptoms and time of symptom onsets in the confirmed cases was collected from the official websites of Seoul district offices. A total of 329 cases were confirmed as infected from January 23, 2020, when the first case was confirmed in Seoul, to March 22, 2020. Table 1 shows the basic characteristics of these confirmed cases.

Software packages such as $R_0$ and EpiEstim that are optimized for estimating $R_t$ have been developed [4,5]. In this study, EpiEstim was used because it was developed recently and it requires less computing time than the other [5]. Generation time, which is required to calculate $R_t$, is a time interval between infector’s infected date and its consecutive infectee’s infected date. However, generation time is usually estimated based on the difference between the time of symptom onset of the infector and the infectee, which is called serial interval, as it is often difficult to know the exact time of infection [6]. This study assumed the serial interval as gamma distributed with a mean of 3.96 days and a standard deviation of 4.75 days, which was reported in China [7].

$R_t$ was estimated based on the daily number of confirmed cases ($R_{t,c}$) and symptom onset ($R_{t,s}$) because it is difficult to identify the exact time of infection. Twelve confirmed cases before February 16, 2020 were excluded from the analysis because from January 23, 2020 to February 16, 2020, there was no $R_{t,c}$ for a considerable period, thus we could not assume that they were infected from previous case within Seoul. Four more confirmed cases were excluded with symptoms but their onset dates of symptoms were missing. Finally, 313 confirmed cases were included in the analysis. In asymptomatic cases, the time of symptom onset was assumed to be the same as the time of diagnosis ($n=70$). In sensitivity analysis, $R_t$ was calculated by assuming the times of symptom onset in asymptomatic cases as confirmed date ($T_D$), $T_D$-1 day, $T_D$+1 day, and $T_D$+2 days. Then, those calculated $R_t$ were compared to the calculated $R_t$ with assumption of asymptomatic cases’ symptom onset date as $T_D$. The data analysis was performed using the R version 3.6.3 (https://cran.r-project.org/bin/windows/base/old/3.6.3/) and EpiEstim, and the median $R_t$ and 95% confidence intervals (CIs) were obtained.

**Ethics statement**

This study uses data from official websites which are opened to public. So, this study is subject to institutional review board exception in accordance with article 13 of the enforcement ordinance (study using existing data or documents on subjects, etc.).

**RESULTS**

Figure 1 shows the distribution of the $R_{t,c}$ and $R_{t,s}$ in 313 confirmed cases included in the analysis. Figure 2A presents the median and 95% CI of $R_t$ estimated using $T_D$ information. Assuming this $R_t$ as $R_{t,c}$, $R_{t,s}$ exhibited a decreasing trend from February 25, 2020 to March 6, 2020, which fell below 1 and then increased. It decreased again on March 10, 2020 and has shown a value of < 1 after March 16, 2020. The median value and 95% CI of $R_t$ which was estimated using the $R_{t,s}$, are shown in Figure 2B. Assuming this $R_t$ as $R_{t,c}$, $R_{t,s}$, decreased to < 1 from February 20, 2020 to March 4, 2020, it increased shortly, and then decreased again from March 10, 2020 remaining below 1 after March 14, 2020.

Figure 3 compares the mean $R_t$ calculated based on the $R_{t,c}$ and $R_{t,s}$. Overall, $R_{t,c}$ and $R_{t,s}$ showed similar changes in pattern; however, $R_{t,c}$ showed more abrupt changes than $R_{t,s}$, and its highest and lowest values were estimated to be higher or lower than $R_{t,s}$, respectively. Moreover, the points in time when the uptrend or downtrend changes occurred were approximately 1 day after $R_{t,s}$ reflecting the lag time for testing and to confirm the diagnosis af-
In the primary analysis, the symptom onsets of asymptomatic patients (n = 70) were assumed to be the same as $T_D$. To perform sensitivity analysis, $R_t$ were calculated and compared, assuming the times of symptom onset were the same as $T_D - 2$ days, $T_D - 1$ day, $T_D + 1$ day, and $T_D + 2$ days, relative to $T_D$. Under each assumption, the 95% CI of the $R_t$ values overlapped considerably, and the changes over time showed a similar pattern, as shown in the Supplementary Material 1.

**DISCUSSION**

In this study, the daily $R_t$ of COVID-19 in Seoul from February 23, 2020 to March 22, 2020, was estimated using the data on the $R_{t_c}$ and $R_{t_s}$. Daily $R_t$ refers to the infectivity of newly confirmed cases on day $t$. In other words, an increase in $R_t$ indicates that infected individuals are likely to transmit the disease more actively than previously, and this requires more intensive interventions for infection control. In contrast, current strategies to control infection are effective when $R_t$ decreases. If the $R_t$ constantly remains below 1, the epidemic will be disappeared [3].

When the $R_t$ was estimated using the $R_{t_c}$ and $R_{t_s}$ in Seoul, $R_t$ values decreased from late February to early March and remained below 1 with some variations. This is possibly owing to the raised awareness of the public, enhanced infection control strategies, and social distancing, following a cluster outbreak that occurred at the Shincheonji Church in Daegu, Korea. The number of confirmed cases increased rapidly after another cluster outbreak was reported on March 10, 2020 at a call center in Guro-gu, Seoul. The $R_t$ values remained higher than 1, reflecting the high transmission of the disease. However, the $R_t$ decreased without further increase and has remained below 1 since March 10, 2020, after implementing infection control guidelines in high-risk workplaces, recommending the prohibition of mass gatherings, and limiting religious and public facility use as well as enhanced social distancing.

The $R_t$ values obtained using the $R_{t_c}$ and $R_{t_s}$ were comparable, despite of slight differences. When the $R_{t_c}$ was used in the calculation, variations in the $R_t$ were greater as the total number of confirmed cases increased rapidly. This was due to an increase in diagnostic testing after more investigations were completed following outbreaks or policy implementations. However, the variations in $R_t$ declined when the values were calculated using the daily number of symptom onsets because symptom onsets are...
distributed widely before and after \(T_p\). Nevertheless, trends in \(R_t\) value changes were similar in both cases. In COVID-19, most patients developed mild initial symptoms, which made it difficult to determine the exact time of symptom onset. Therefore, the similar pattern of the estimated \(R_t\) indicate that the \(R_t\) using the \(R_t_c\) may be useful to estimate the pattern of infection transmission and to evaluate the effectiveness of the infection control strategies in the early stages.

In the sensitivity analysis conducted in the asymptomatic cases with an assumption that the time of symptom onset was the same as \(T_{1_0}\), the trend in estimated \(R_t\) showed similar changes in original data. The original data assumed that asymptomatic cases’ symptom onset dates were same as \(T_{1_0}\). Accordingly, the estimated \(R_t\) falls within the 95% CI of the original data. This indicates that assuming the time of symptom onset in asymptomatic cases is the same as the date of confirmation is not significantly different from other assumptions in asymptomatic cases.

There are several points to consider when interpreting \(R_t\) obtained in our study. First, the \(R_t\) may be underestimated as it gets closer to the latest date. The reason is that fewer values of symptom onset are used for the \(R_t\) value estimation than the actual number of confirmed cases due to lag time between symptom onset and confirmed date. Second, our study used Chinese serial interval as the generation time to estimate \(R_t\). Since the generation time may be different from China, it is necessary to estimate \(R_t\) based on the estimated generation time in Korea, especially in Seoul. Third, the foreign immigration of confirmed cases was not considered. More accurate \(R_t\) prediction is possible if the infection transmission is traced accurately and confirmed whether there was an immigration of confirmed cases form outside of Seoul.

In conclusion, the \(R_t\) estimated from using the \(R_t_c\) and \(R_t_s\) in Seoul were both useful in evaluating effectiveness of the infection control strategies. The values have remained below 1 since March 15, 2020, indicating a decreased rate of infection transmission from confirmed cases in the community. However, further studies should be conducted as the influx of confirmed cases from abroad and from other regions in Korea are increasing. Furthermore, the effectiveness of the infection control strategies should be monitored constantly at local and national levels, using \(R_t\) estimated with the \(R_t_c\) and \(R_t_s\).

**SUPPLEMENTARY MATERIALS**


**CONFLICT OF INTEREST**

The authors have no conflicts of interest to declare for this study.

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**AUTHOR CONTRIBUTIONS**

Conceptualization: BP, SGM. Data curation: YKK, SGM, BJN. Funding acquisition: BYC. Methodology: BP, JC, WSS, JHK. Writing – original draft: SGM, YKK, WSS, JHK, JC, BJN, BP, BYC. Writing – review & editing: SGM, YKK, WSS, JHK, JC, BJN, BP, BYC.

**ORCID**

Seong-Geun Moon: http://orcid.org/0000-0002-5019-3483; Yeon-Kyung Kim: http://orcid.org/0000-0002-8417-0730; Woo-Sik Son: http://orcid.org/0000-0002-4211-4546; Jong-Hoon Kim: http://orcid.org/0000-0002-9717-4044; Jungsoon Choi: http://orcid.org/0000-0001-6815-1006; Baeg-Ju Na: http://orcid.org/0000-0002-3742-6035; Boyoung Park: http://orcid.org/0000-0003-1902-3184; Bo Youl Choi: https://orcid.org/0000-0003-0115-5736

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