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

OBJECTIVES: To estimate time-variant reproductive number ($R_t$) of coronavirus disease 19 based on either number of daily confirmed cases or their onset date to monitor effectiveness of quarantine policies.

METHODS: Using number of daily confirmed cases from January 23, 2020 to March 22, 2020 and their symptom onset date from the official website of the Seoul Metropolitan Government and the district office, we calculated $R_t$ using program R's package "EpiEstim". For asymptomatic cases, their symptom onset date was considered as -2, -1, 0, +1, and +2 days of confirmed date.

RESULTS: Based on the information of 313 confirmed cases, the epidemic curve was shaped like 'propagated epidemic curve'. The daily $R_t$ based on $R_t$ peaked to 2.6 on February 20, 2020, then showed decreased trend and became <1.0 from March 3, 2020. Comparing both $R_t$ from $R_t$ and from the number of daily onset cases, we found that the pattern of changes was similar, although the variation of $R_t$ was greater when using $R_t$. When we changed assumed onset date for asymptotic cases (-2 days to +2 days of the confirmed date), the results were comparable.

CONCLUSIONS: $R_t$ can be estimated based on $R_t$ which is available from daily report of the Korea Centers for Disease Control and Prevention. Estimation of $R_t$ would be useful to continuously monitor the effectiveness of the quarantine policy at the city and province levels.

KEY WORDS: COVID-19, Communicable disease, Epidemics, Seoul
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_t 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_t 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 (Rt_c) and symptom onset (Rt_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 Rt_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_t)−2 days, T_t+1 day, T_t+1 day, and T_t+2 days. Then, those calculated R_t were compared to the calculated R_t with assumption of asymptomatic cases’ symptom onset date as T_t. 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 Rt_c and Rt_s in 313 confirmed cases included in the analysis. Figure 2A presents the median and 95% CI of R_t estimated using T_t information. Assuming this R_t as R_t, R_t, 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 Rt_s are shown in Figure 2B. Assuming this R_t as R_t, R_t, 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 and R_t. Overall, R_t and R_t showed similar changes in pattern; however, R_t showed more abrupt changes than R_t, and its highest and lowest values were estimated to be higher or lower than R_t, respectively. Moreover, the points in time when the uptrend or downtrend changes occurred were approximately 1 day after R_t, reflecting the lag time for testing and to confirm the diagnosis af-

Table 1. Baseline characteristics of 329 confirmed coronavirus disease 2019 (COVID-19) case in Seoul from January 23, 2020 to March 22, 2020

| Characteristics                  | n (%)       |
|----------------------------------|-------------|
| Sex                              |             |
| Male                             | 161 (48.9)  |
| Female                           | 168 (51.1)  |
| Age (yr)                         |             |
| <10                              | 5 (1.5)     |
| 10-19                            | 11 (3.3)    |
| 20-29                            | 83 (25.2)   |
| 30-39                            | 51 (15.5)   |
| 40-49                            | 55 (16.7)   |
| 50-59                            | 70 (21.3)   |
| 60-69                            | 31 (9.4)    |
| 70-79                            | 15 (4.6)    |
| 80-89                            | 6 (1.8)     |
| ≥90                              | 2 (0.6)     |
| Days since symptoms to diagnosis (d) |             |
| Asymptomatic                     | 70 (21.5)   |
| ≤3                               | 113 (34.8)  |
| 4-7                              | 85 (26.1)   |
| >7                               | 57 (17.5)   |

1Those who do not have symptom onset information (n=4) are not calculated.
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 $Rt_c$ 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 $T_p$, 2 days to $T_p + 2$ days, the trend in estimated $R_t$ showed similar changes in original data. The original data assumed that asymptomatic cases’ symptom onset date were same as $T_p$. Accordingly, the estimated $R_t$ fell within the 95% CI of the original data. This indicates that assuming the time of symptom onset in asymptomatic cases as 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 $Rt_c$ and $Rt_s$ 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 $Rt_c$ and $Rt_s$.

**SUPPLEMENTARY MATERIALS**

Supplementary materials is available at http://www.e-epih.org/. Korean version is available at http://www.e-epih.org/.

**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/0000-0002-0421-4546; Jong-Hoon Kim: http://orcid.org/0000-0002-9717-4044; Junsoo 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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