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MAJOR ARTICLE

# Impact of Nonpharmaceutical Interventions on the Incidence of Respiratory Infections During the Coronavirus Disease 2019 (COVID-19) Outbreak in Korea: A Nationwide Surveillance Study

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***Background.*** Many countries have implemented nonpharmaceutical interventions (NPIs) to slow the spread of coronavirus disease 2019 (COVID-19). We aimed to determine whether NPIs led to the decline in the incidences of respiratory infections.

***Methods.*** We conducted a retrospective, ecological study using a nationwide notifiable diseases database and a respiratory virus sample surveillance collected from January 2016 through July 2020 in the Republic of Korea. Intervention period was defined as February–July 2020, when the government implemented NPIs nationwide. Observed incidences in the intervention period were compared with the predicted incidences by an autoregressive integrated moving average model and the 4-year mean cumulative incidences (CuIs) in the same months of the preintervention period.

***Results.*** Five infectious diseases met the inclusion criteria: chickenpox, mumps, invasive pneumococcal disease, scarlet fever, and pertussis. The incidences of chickenpox and mumps during the intervention period were significantly lower than the prediction model. The CuIs (95% confidence interval) of chickenpox and mumps were 36.4% (23.9–76.3%) and 63.4% (48.0–93.3%) of the predicted values. Subgroup analysis showed that the decrease in the incidence was universal for chickenpox, while mumps showed a marginal reduction among those aged <18 years, but not in adults. The incidence of respiratory viruses was significantly lower than both the predicted incidence (19.5%; 95% confidence interval, 11.8–55.4%) and the 4-year mean CuIs in the preintervention period (24.5%; $P < .001$).

***Conclusions.*** The implementation of NPIs was associated with a significant reduction in the incidences of several respiratory infections in Korea.

**Keywords.** nonpharmaceutical intervention; social distancing; COVID-19; respiratory infection; South Korea.

Nonpharmaceutical interventions (NPIs) have been implemented widely to control the global spread of coronavirus disease 2019 (COVID-19) since February 2020 [1]. While specific practices vary across individual countries and settings, most public health strategies share the core elements of NPIs: social distancing, "test and isolate" symptomatic people, hand hygiene, respiratory etiquette, and environmental cleaning [2]. Social-distancing measures aim to reduce the transmission of disease by decreasing the frequency and duration of social contact. They include avoiding physical contact and mass gatherings, school and workplace closures, and travel restrictions. The universal use of facemasks was added to mandates later during the epidemic, as more evidence of their benefit emerged [3]. These elements of NPIs are not novel; they have been studied and prepared for decades as an important strategy to slow the spread of novel respiratory virus infections, such as a novel influenza A [4–6]. However, they have never been applied so broadly in modern times before this pandemic, thus providing the opportunity to examine the effects at a societal level.

The Republic of Korea has been able to flatten the curve so far, in stark contrast to other countries with a comparable population and economy. The first case of COVID-19 in South Korea was confirmed on 20 January 2020; 1 month later, a regional outbreak originated from a church gathering, which led to an explosive increase in the number of cases over the next 2 months. In response, the health authorities of South Korea implemented nationwide NPIs to slow down the spread of the epidemic (Figure 1). High compliance with NPIs, combined with widespread testing and effective contact tracing, led to a decline in the number of daily new cases since late April [7]. Considering that these interventions were successful in

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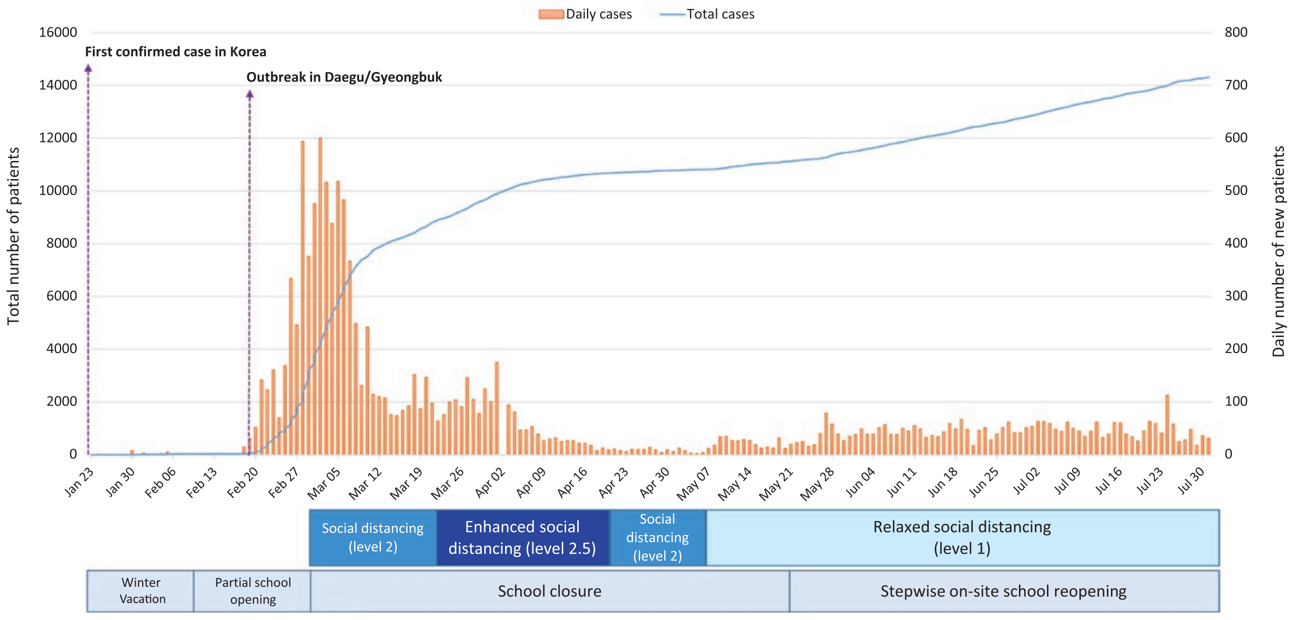


**Figure 1.** Daily number of confirmed cases of COVID-19 and nonpharmaceutical interventions. Abbreviation: COVID-19, coronavirus disease 2019.

containing the spread of COVID-19, this provided a unique opportunity for us to investigate the effect of NPIs on the incidence of other respiratory infections.

We compared the incidence of other infectious diseases that are transmitted via respiratory secretions before and after the implementation of NPIs in South Korea to examine their effect on these diseases.

## METHODS

### Data Source

The monthly numbers of reported cases were obtained from the notifiable diseases database curated by the Korea Center for Disease Control and Prevention (KCDC). Physicians who diagnosed diseases designated as notifiable are required by law to report them without delay. The number of cases was divided by the annual midyear population obtained from the Korean Statistical Information Service (http://kosis.kr) to calculate the monthly incidence per 1 000 000 population. The numbers of respiratory viruses and enteroviruses identified from respiratory specimens by polymerase chain reaction (PCR) were collected weekly through the national sample surveillance for acute respiratory infections, which is managed by the Korea Influenza and Respiratory Viruses Surveillance System (KINRESS) operated by the KCDC. Participating institutions reported the number of positive results from patients with acute respiratory illnesses on a weekly basis. As the sample surveillance was not based on population-based data, crude numbers of positive cases were analyzed. All surveillance data are accessible to the public through the KCDC website (http://cdc.go.kr/npt).

### Study Design

This study was a retrospective, ecological study examining the change in the incidence of various respiratory infections after the implementation of NPIs against COVID-19. Target infectious diseases were selected from among notifiable diseases using the following criteria: (1) principal mode of transmission is respiratory (droplet or airborne), (2) clinical course is acute or subacute, and (3) annual incidence exceeds 100 cases. The preintervention period was designated as January 2016–January 2020 and the intervention period was February–July 2020.

We constructed models to predict incidences in the intervention period from the trends of incidences in the preintervention period using an autoregressive integrated moving average (ARIMA) model. The actual incidences and model predictions were visually examined to determine whether the observed incidences during the intervention period lay within the 95% confidence intervals (CIs) of the predicted values. Furthermore, the observed cumulative incidence (CuI) during the intervention period was compared against the expected CuI in the prediction models and the mean CuI during the same period (February–July) in the preintervention period. Subgroup analyses were performed for 3 age groups (0–6, 7–17, ≥18 years) for notifiable diseases, which was planned a priori.

To exclude the possibility of underreporting or a lapse of surveillance during the COVID-19 epidemic, the incidences of notifiable nonrespiratory infections were examined using the same methods stated above. Notifiable diseases with 1000 or more cases per year were included; however, zoonotic diseases were excluded as they occur predominantly in summer and fall in South Korea.

There have been 2 distinct regional clusters of COVID-19 cases in South Korea: one in the Daegu/Gyeongbuk area, which experienced a regional outbreak from February through early April, and one in the Seoul/Gyeonggi/Incheon metropolitan area, the most densely populated area in South Korea, which saw a steady increase in confirmed cases with multiple small clusters since May. Difference-in-difference analysis was conducted to evaluate the difference in the effect of NPI among these regions. This research was conducted ethically in accordance with the World Medical Association's Declaration of Helsinki, and the study protocol was approved by the institutional review board of the Severance Children's Hospital, Yonsei University College of Medicine, Republic of Korea (no. 4-2020-0820).

#### Statistical Analysis

Seasonal ARIMA models were constructed to forecast incidences during the intervention period. Parameters were determined by comparing multiple candidate models in terms of residuals, autocorrelation coefficients, and Akaike information criterion. Mean absolute percentage error was calculated to examine the predictive accuracy of the ARIMA models. The difference between CuIs was tested using Student's $t$ test. Difference-in-difference was estimated as previously described; detailed statistical methods are described in the Supplementary Methods [8]. All tests were 2-tailed, and $P$ values less than .05 were considered statistically significant. Statistical analyses were performed using R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria) and SAS software version 9.4 (SAS Institute, Inc, Cary, NC, USA).

## RESULTS

#### Incidences of Notifiable Diseases

Five infectious diseases that met the inclusion criteria were included in our analysis: chickenpox, mumps, invasive pneumococcal disease (IPD), scarlet fever, and pertussis. Seasonal ARIMA models were constructed, and the parameters and model characteristics are shown in Supplementary Table 1. Compared with predicted incidences, the actual incidences of chickenpox and mumps during the intervention period were significantly lower (Figure 2). The incidences of IPD, scarlet fever, and pertussis were also lower than predicted values, but lay within 95% CIs of the predicted values. Actual CuIs during the intervention period of chickenpox and mumps were 278.01 and 111.01, respectively, which were 36.4% (95% CI, 23.9–76.3%) and 63.4% (95% CI, 48.0–93.3%) of the predicted incidences (Table 1A). Cumulative incidences of study diseases during the intervention period were universally lower than the mean CuIs during the same months of the preintervention period. Scarlet fever (15.8% of the mean preintervention CuI), pertussis (34.2%), and chickenpox (38.4%) showed a larger reduction in CuIs, while those of mumps (58.7%) and IPD

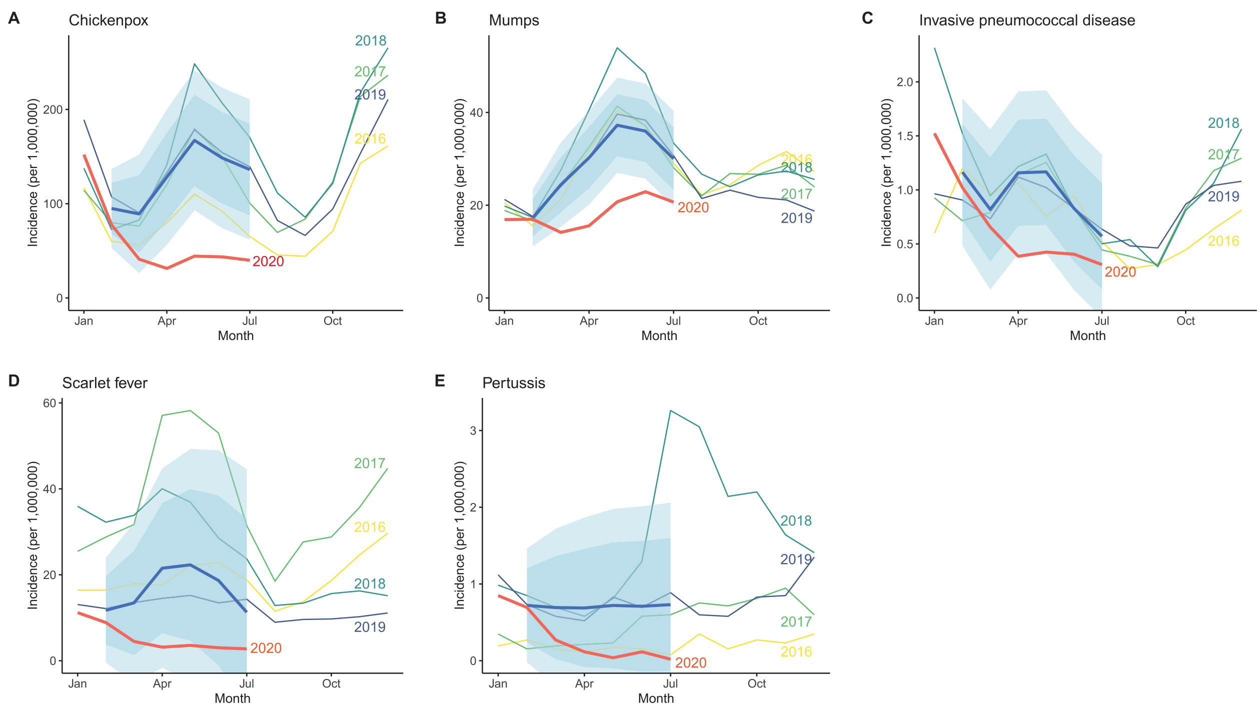


**Figure 2.** *A–E*, Monthly incidence of notifiable respiratory infections and predicted incidence by ARIMA model. Thick red lines denote the observed incidence in the intervention period; thick blue line, the predicted incidence; blue shading, 80% and 95% confidence intervals of the predicted incidence. Abbreviation: ARIMA, autoregressive integrated moving average.

**Table 1. Cumulative Incidences of Respiratory Infections From February Through July of Each Year**

| Disease | February–July 2020, n | Cumulative Incidence, February–July (per 1 000 000) | | | % Predicted (95% CI) | % Mean (2016–2019)[a] | *P* |
|---|---|---|---|---|---|---|---|
| | | Observed (2020) | Predicted[a] | Mean (2016–2019)[b] | | | |
| (A) Respiratory infections from the national notifiable diseases database | | | | | | | |
| Overall | | | | | | | |
| Chickenpox | 14 412 | 278.01 | 764.38 | 723.47 | 36.37 (23.88–76.30) | 38.43 | <.001 |
| Mumps | 5755 | 111.01 | 175.15 | 189.22 | 63.38 (47.98–93.34) | 58.67 | <.001 |
| Invasive pneumococcal disease | 166 | 3.20 | 5.71 | 5.56 | 56.09 (31.55–220.50) | 57.63 | .013 |
| Scarlet fever | 1341 | 25.87 | 98.94 | 163.57 | 26.14 (10.62–∞) | 15.81 | <.001 |
| Pertussis | 65 | 1.25 | 4.26 | 3.66 | 29.43 (11.30–∞) | 34.24 | .026 |
| Age 0–6 years | | | | | | | |
| Chickenpox | 7170 | 2727.18 | 6218.14 | 6491.43 | 43.86 (26.90–118.64) | 42.01 | <.001 |
| Mumps | 2142 | 814.73 | 1358.76 | 1468.13 | 59.96 (42.10–104.15) | 55.49 | <.001 |
| Invasive pneumococcal disease | 11 | 4.18 | 7.40 | 8.67 | 56.52 (26.78–902.18) | 48.25 | .016 |
| Scarlet fever | 1016 | 386.45 | 1409.76 | 2267.63 | 27.41 (11.59–1263.35) | 17.04 | <.001 |
| Pertussis | 15 | 5.71 | 10.31 | 15.98 | 55.31 (10.31–∞) | 35.71 | .012 |
| Age 7–17 years | | | | | | | |
| Chickenpox | 5688 | 129.13 | 453.29 | 376.19 | 28.49 (19.23–54.90) | 34.33 | <.001 |
| Mumps | 2451 | 55.65 | 82.41 | 92.50 | 67.52 (48.07–113.42) | 60.16 | <.001 |
| Invasive pneumococcal disease | 1 | 0.02 | 0.11 | 0.08 | 19.98 (5.91–∞) | 28.19 | .078 |
| Scarlet fever | 268 | 6.08 | 14.78 | 37.21 | 41.17 (11.91–∞) | 16.35 | <.001 |
| Pertussis | 19 | 0.43 | 2.37 | 2.07 | 18.22 (4.88–∞) | 20.80 | .029 |
| Age ≥18 years | | | | | | | |
| Chickenpox | 1554 | 35.28 | 61.54 | 47.79 | 57.33 (45.55–77.35) | 73.83 | .013 |
| Mumps | 1162 | 26.38 | 32.29 | 33.85 | 81.71 (62.69–117.30) | 77.93 | .005 |
| Invasive pneumococcal disease | 154 | 3.50 | 6.49 | 5.95 | 53.85 (30.36–238.09) | 58.79 | 0.021 |
| Scarlet fever | 57 | 1.29 | 2.07 | 2.35 | 62.40 (38.23–169.60) | 55.13 | .003 |
| Pertussis | 31 | 0.70 | 2.10 | 1.21 | 33.51 (18.75–153.20) | 57.95 | .242 |
| (B) Respiratory virus infections reported from the national sample surveillance network | | | | | | | |
| Enterovirus | | 39 | 1146.82 | 1229.25 | 3.40 (0.54–∞) | 3.17 | <.001 |
| Respiratory viruses (except enterovirus) | | 8409 | 43 074.79 | 34 354.00 | 19.52 (11.77–55.38) | 24.48 | <.001 |
| Adenovirus | | 914 | 4704.96 | 4827.50 | 19.43 (8.81–685.04) | 18.93 | <.001 |
| Bocavirus | | 336 | 4102.29 | 3587.00 | 8.19 (5.10–16.45) | 9.37 | <.001 |
| Parainfluenzavirus | | 316 | 7952.53 | 5482.75 | 3.97 (2.83–6.67) | 5.76 | <.001 |
| Respiratory syncytial virus | | 1718 | 2773.57 | 2232.75 | 61.94 (11.94–377.64) | 76.95 | .451 |
| Rhinovirus | | 2989 | 15 265.41 | 11 299.25 | 19.58 (14.99–28.22) | 26.45 | <.001 |
| Metapneumovirus | | 470 | 6965.98 | 5014.75 | 6.75 (4.34–13.85) | 9.37 | <.001 |
| Coronavirus | | 1666 | 1786.83 | 1910.00 | 93.24 (28.49–351.24) | 87.23 | .667 |
| (C) Nonrespiratory infections from the national notifiable diseases database | | | | | | | |
| Hepatitis A | 1890 | 36.46 | 25.70 | 114.35 | 141.87 (20.86–∞) | 31.88 | .031 |
| Hepatitis C | 5896 | 113.73 | 101.76 | 101.31 | 111.77 (88.44–151.82) | 112.27 | .021 |
| Carbapenem-resistant Enterobacterales | 7719 | 148.90 | 162.95 | 119.25 | 91.38 (80.61–105.46) | 124.86 | .006 |

Observed CuI in 2020, CuI predicted by autoregressive integrated moving average model, and mean CuI in the past 4 years (2016–2019) are shown.

[a]Values for "(B)" reflect numbers of positive cases, February–July.

[b]Values for "( C)" reflect means (2018–2019).

Abbreviations: CI, confidence interval; CuI, cumulative incidence.

(57.6%) were smaller. However, they all showed a statistically significant reduction in CuIs.

Subgroup analysis showed an age-specific effect of NPIs on the incidences of respiratory infections (Supplementary Figures 1–3 and Table 1). The incidence of chickenpox was substantially lower during the intervention period for all age groups. Mumps showed a marginal reduction in incidence among those aged 0–6 and 7–17 years, but not in adults. Invasive pneumococcal disease, scarlet fever, and pertussis also showed decreased incidence, but the difference was small and not statistically significant. The incidence of chickenpox declined to the largest extent among persons in the age group of 7–17 years (28.5% of the predicted CuI; 95% CI, 19.2–54.9%), followed by that in the 0–6-year age group (43.9%; 95% CI, 26.9–118.6%) and then among those aged 18 years and older (57.3%; 95% CI, 45.6–77.4%). The CuIs of all diseases were significantly lower than the mean preintervention CuIs, except that of IPD among those aged 7–17 years (Table 1A).

We examined whether there exists a difference in the degree of decreasing trends in the incidences of respiratory infections by region (Supplementary Table 2). However, the difference-in-difference regression indicated no significant difference between the Daegu/Gyeongbuk area and the remaining regions, despite more stringent NPIs used during a large regional outbreak in the area. Similarly, there was no difference in the degree of decreasing incidences between the Seoul/Gyeonggi/Incheon metropolitan area, which is the most populous region with the largest number of cases of COVID-19, and elsewhere.

#### Sample Surveillance for Respiratory Viruses

The weekly incidence of respiratory viral infections was significantly lower than both the predicted incidence (19.5%; 95% CI, 11.8–55.4%) and the 4-year mean incidence in the preintervention period (24.5%; $P < .001$) (Figure 3 and Table 1B). When examined separately by species, the number of specimens that tested positive for bocavirus, parainfluenza virus, rhinovirus, and metapneumovirus were significantly lower during the intervention period, while those of respiratory syncytial virus (RSV) and coronavirus were comparable to both the predicted incidence and 4-year mean incidence. The relative CuIs were smaller (4.0–19.6% of the mean preintervention CuIs) compared with those of notifiable diseases (29.4–63.4%).

#### Incidences of Notifiable Nonrespiratory Infections

Hepatitis A, hepatitis C, and carbapenem-resistant Enterobacterales (CRE) infections met the inclusion criteria for notifiable nonrespiratory infections. The observed incidences of all 3 diseases during the intervention period remained within the 95% CIs of model predictions (Figure 4). Hepatitis C and CRE were newly designated as notifiable diseases in July 2017; thus, the observed CuIs were compared against the mean CuIs in 2018–2019 (Table 1C). The CuIs of hepatitis C and CRE during the intervention period were 112.3% and 124.9% of the preintervention mean CuIs, respectively. A large surge in hepatitis A was observed in 2019, which led to a relatively smaller CuI in the intervention period (31.9% of the preintervention mean). However, the observed CuI of hepatitis A lay within the 95% CI of the predicted value.

## DISCUSSION

This nationwide study demonstrates a remarkable reduction in the incidence of highly transmissible infections following the implementation of NPIs that were enforced to control COVID-19. This trend may vary by age, suggesting that these transmissible diseases may be affected differently depending on the degree of NPI implementation and age-specific factors. Even as the COVID-19 pandemic continues, the reduction in the incidence of other respiratory infections may provide secondary benefits, as this can decrease the efforts put into screening and isolation and reduce medical expenses related to COVID-19, especially since it is difficult to distinguish this disease from other respiratory infections [9].

The monthly incidence rates of notifiable diseases decreased remarkably to 26–63% of the predicted values, regardless of their high infectivity (eg, chicken pox $R_0 = 6.3–13.8$, pertussis $R_0 = 7.3–18.5$, mumps $R_0 = 4.3–11.2$, scarlet fever $R_0 = 3.7–8.0$) [10]. In particular, chickenpox and mumps showed a significant reduction in both the prediction models and the CuIs compared with that in the past 4 years. Meanwhile, the incidences of pertussis and IPD were not high enough to detect any difference and that of scarlet fever has shown a downward trend in recent years. These are limitations in analyzing the effects of NPIs.

Interestingly, the incidence of notifiable diseases began to decline even before late February, which was when NPIs were officially recommended by health authorities. This finding suggests that voluntary social distancing and behavior changes by individuals had begun before the government-led mandates in Korea. Based on mobile big data, the daily movement of people in February 2020 was seen to decrease by up to 38% compared with that during 2–20 January 2020 (before the first Korean COVID-19 confirmed case) [11]. The authors of the study also reported that the daily number of passengers at major subway stations in Seoul was also significantly lower. Similar study results were recently published in the United States [12, 13]. Nolen et al [12] reported that hospitalization rates for non–COVID-19 respiratory illnesses had begun to decline before mandatory social distancing in Alaska. Another study comparing the diagnosis rates of common infectious diseases in children (aged 0–17 years), before and after imposing strong social-distancing measures, including movement restrictions in Massachusetts, reported a significant reduction in several respiratory illnesses by 10–101% [13]. Unlike the above 2 studies in the United States, our data show that less-stringent

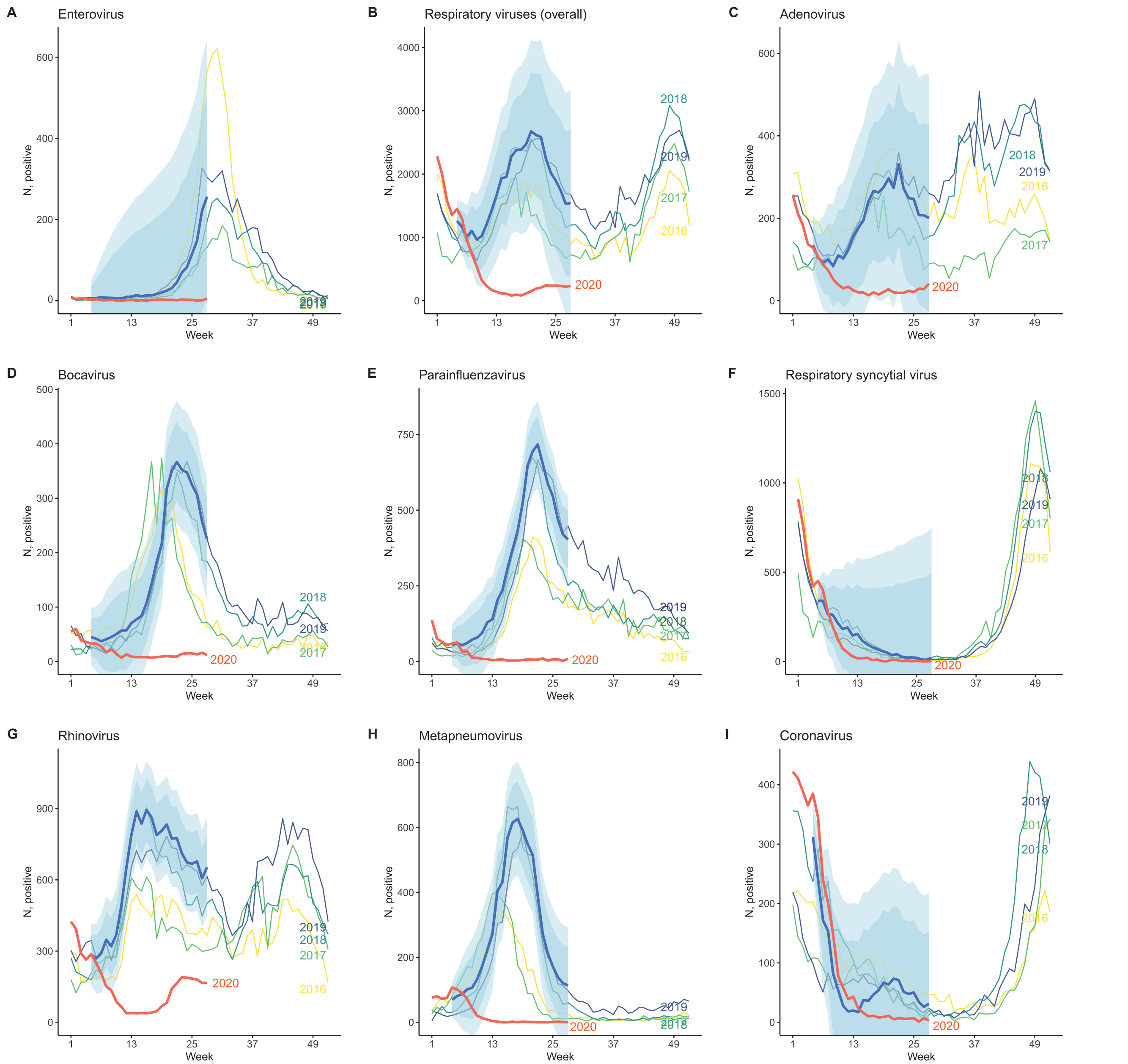


**Figure 3.** *A–I*, Weekly reported cases of respiratory virus infections from a nationwide sample surveillance network. Thick red lines denote the observed incidence in the intervention period; thick blue lines, the predicted incidence; blue shading, 80% and 95% confidence intervals of the predicted incidence. Abbreviation: N, number.

means of social distancing without movement restrictions or remote working (commonly called "lockdown") can also reduce the spread of highly transmissible infections.

Decreased incidence of infectious diseases by enforcing NPIs is not characteristic of some respiratory infections but appears to be a common phenomenon in transmissible pathogens, mainly represented by respiratory viruses, which are transmitted by droplets or direct contact. Previous studies evaluating the effects of social distancing have reported a reduction in nonspecific acute respiratory illnesses, including influenza-like illness and pneumonia [12–15]. However, respiratory viruses included in our study were identified through a PCR-based test, and we demonstrated numbers showing that all the respiratory viruses recorded by the KINRESS had a decreasing trend. In particular, enterovirus infections, which are most prevalent during the summer in temperate climates, were remarkably reduced to 3% of the last 4-year mean. A recent Taiwanese study reported a reduction in enterovirus infections along with influenza during the 2019–2020 winter season after wearing masks and social distancing during the COVID-19 outbreak [16].

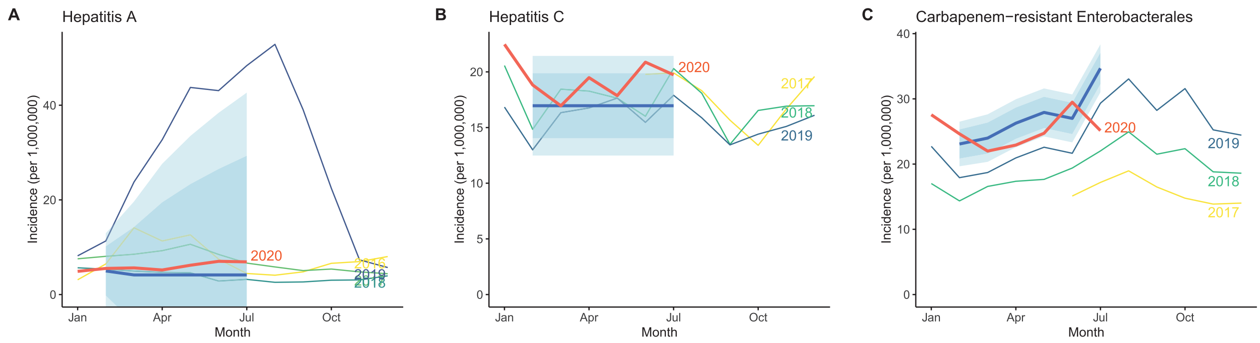


**Figure 4.** *A–C*, Monthly incidence of notifiable nonrespiratory infections and predicted incidence by ARIMA model. Thick red lines denote the observed incidence in the intervention period; thick blue lines, the predicted incidence; blue shading, 80% and 95% confidence intervals of the predicted incidence. Abbreviation: ARIMA, autoregressive integrated moving average.

However, this study did not include similar data for the summer season. Our study included data for the summer season (June to July) as well, which allowed us to distinctly observe the continued decline in enterovirus infections [16]. Meanwhile, in countries in the Southern Hemisphere, influenza activity was very low during the typical influenza season, June–August 2020 [17]. Since the NPIs against COVID-19 have stayed in place in South Korea, we would be able to observe whether the decline in infections caused by respiratory viruses such as RSV and influenza (which are prevalent in the winter season) continues in the coming winter months in the Northern Hemisphere.

Mumps and rhinovirus infections tended to increase after May 2020 when social-distancing measures were relaxed, while the incidence of other transmissible diseases remained at low levels during the whole period. One of the reasons for this could be increased exposure among vulnerable children of that age as schools or daycare centers opened, but it is unclear why only infections due to these 2 respiratory viruses increased. In addition, a low cross-immunity to heterogeneous subtypes of rhinovirus and waning herd immunity against mumps could be potential causes, but more long-term surveillance data are required to clarify the certainty and persistence of these results [18–21].

The degree of reduction in notifiable diseases after NPIs were enforced differed by age group. In general, the decrease in all notifiable diseases in children was greater than that in adults; in particular, chickenpox and mumps decreased by 40–66% compared with the last 4-year mean in children, but only by 22–26% in adults. One of the possible explanations is that NPI was enforced more strongly among children than adults. While adults were not forced to work from home, on-site school reopening had been delayed until 20 May. After that, schools were opened as follows: high school (ages 16–18 years) first, then kindergarten (ages 3–6 years), middle school (ages 13–15 years), and elementary school (ages 7–12 years). This judgment was made considering the need for child care, the possibility of poor compliance with infection-control policies among young children, the high-density facilities, and the possibility of transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to grandparents who are at higher risk for severe illness from COVID-19 [22, 23]. Along with the delay in reopening schools, multifaceted interventions such as restrictions on the use of indoor play facilities and large academies may have also contributed to reducing the likelihood of transmission.

This study nevertheless has some limitations. First, although physicians are obliged to report notifiable diseases to the health authorities, there is the possibility of over- or underreporting as well as misdiagnosis. However, we also examined the incidences of 3 common nonrespiratory infections. Their incidences during the COVID-19 pandemic were similar or larger compared with baseline or model predictions, suggesting the absence of underreporting. Second, even though only notifiable diseases with more than 100 cases per year were included, these numbers may be insufficient to detect differences to a statistically significant degree, particularly in subgroups. Third, we could not exclude imported cases due to limitations of the database. However, the number of imported cases included in the study was very small (<20 cases per year), so it would not exert a meaningful effect on the results. Finally, factors indirectly related to NPIs (eg, healthcare-seeking behaviors) could not be accounted for in the analysis.

We demonstrated that the implementation of NPIs was associated with a significant reduction in the incidences of several respiratory infections in South Korea. As NPI measures continue to be in place during the COVID-19 pandemic, further research is needed to determine if this associated decreased trend is sustained in the coming winter months.

## Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

## Notes

***Author contributions.*** K. H. and J.-M. K. had full access to the study data and take responsibility for their integrity and accuracy of analysis. Concept and design: K. H. and J. J., and J.-M. K. Acquisition, analysis, or interpretation of data: K. H., M. K., J. H., J. J., J. G. A., J.-H. K., and J.-M. K. Drafting of the manuscript: K. H. and J.-M. K. Statistical analysis: K. H., J. H., and J. J.

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