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Reply to Park et al

TO THE EDITOR—I read with great interest the recent data provided by Dr Park et al regarding on the impact of nonpharmaceutical interventions (NPIs) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on incidence of gastrointestinal illness in South Korea [1]. The authors note that the

incidence of norovirus and rotavirus was lower in 2020 compared with 2015–2019, whereas the incidence of *Salmonella* spp., *Campylobacter* spp., and *Clostridium perfringens* was similar or higher than prior years.

Although the qualitative findings are interesting, it is important to note that firm statistical conclusions cannot be drawn because statistical significance and confidence intervals are not reported, which makes it difficult to determine if the reported association is within the bounds of what might be expected based on natural year-to-year variation and secular trends in incidence. For example, despite the positive point estimate (suggestive of increased risk under social distancing), incidence for *Campylobacter* spp. has been gradually increasing over time in many countries [2], and the authors' results suggest this may also be the case in South Korea, with 2020 incidence being similar to that observed in 2019. Qualitatively, incidence of *C. perfringens* also appears to be increasing over time in South Korea. Thus, the positive point estimate for these pathogens might be more reflective of secular trends than being causally related to NPIs implemented in response to SARS-CoV-2. In contrast, after March 2020, the incidence of rotavirus appears to be far below the reported incidence for any previously reported year. Norovirus incidence appears to be lower than prior years, but there is 1 year that is similar to the patterns observed in 2020.

Additionally, the authors appear to average their reported effect estimates of the entire 2020 calendar year, even though widespread NPIs did not begin until March. This approach could have biased the overall effect estimates towards the null. This potential bias is particularly pertinent for winter-time pathogens like norovirus and rotavirus, for which annual incidence is usually highest early in the calendar year in temperate climates like South Korea [3, 4]. Including these months in the overall estimate for 2020 would tend to dilute the true impact of NPIs, biasing the overall effect

estimate toward the null. I note that 2020 appeared to be an initially severe norovirus year, with incidence not beginning to drop until around the time that social distancing began around week 9. In contrast, rotavirus activity appeared to be lower than usual, even in January and February.

Despite these challenges, the reported data provide interesting insight into descriptive differences in incidence between pathogens that may relate to their transmission dynamics. Generally, social distancing would be expected to have the greatest impact on direct transmission pathways. The authors acknowledge that all 3 foodborne pathogens exhibit similar or higher risk compared with prior years, whereas norovirus and rotavirus, which are efficiently transmitted from person to person, exhibited the opposite pattern. Among the 3 foodborne pathogens, it is interesting to note that *Campylobacter* and *C. perfringens* do not commonly spread from person to person and require ingestion of contaminated food to spread [2, 5], and would therefore be less likely to exhibit a decline in incidence. In contrast, *Salmonella* can be transmitted both person to person and through contaminated food [6], which may explain the smaller point estimate for this pathogen.

We are only just beginning to understand the impact of the coronavirus disease 2019 (COVID-19) pandemic on infectious disease transmission. Future data from various settings regarding the impact of NPIs on incidence, including for nonrespiratory pathogens, are important as we seek to understand the far-reaching impact of these interventions. As NPIs begin to relax, it will also be instructive to see how reduced circulation interplays with declining population immunity to shape outbreak dynamics going forward [7].

Notes

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An Opportunity to Better Understand the Impact of Coronaviruses on Immunocompromised Patients

LETTER TO THE EDITOR—In my time as an epidemiology student, I have examined health outcomes and the overall impact of influenza on public health. This is why I read the recent article by Li et al [1] with great interest. The authors examined the outcomes of inpatients and outpatients with confirmed reverse transcription polymerase chain reaction (RT-PCR)-positive tests for influenza A or B or at least 1 of 4 common coronaviruses (229E, HKU1, NL63, and OC43) between June 2016 and February 2019, before the coronavirus disease 2019 (COVID-19) pandemic began to impact the United States. They found that patients with these common coronavirus infections had a higher risk of death and pneumonia than those with influenza, although there was no difference in intensive care unit admission rates. The authors examined the effects and distribution of covariates including comorbid conditions that have established associations with poor influenza and coronavirus outcomes, such as hypertension, type 2 diabetes, obesity, chronic ischemic heart disease, chronic kidney disease, and chronic lung disease. However, the authors did not examine another prominent condition that is related to severe influenza outcomes and could have an important association with coronavirus infections: immunocompromise.

A 2016 study found that the prevalence of immunocompromise in the United States is around 3%, making it fairly common [2]. Immunocompromise can result from a variety of causes including

autoimmune disorders, human immunodeficiency virus (HIV), and treatments for conditions like cancer or solid organ transplant. While patients who are immunocompromised have significantly worse influenza outcomes [3, 4], the effect of immunocompromise on coronavirus outcomes is less clear. The authors chose the comorbid conditions they would include in this study based on a recent article that did not find cancer to be significantly associated with COVID-19 outcomes [5]. However, the Centers for Disease Control and Prevention still consider immunocompromised patients to be at increased risk for severe negative outcomes due to COVID-19 infection [6]. There is mixed evidence that both supports and refutes this association [7, 8]. The effect of immunocompromise on common coronavirus outcomes is also not well understood, although it seems that patients who are immunocompromised experience more severe outcomes [9]. Data on who is experiencing immunocompromise or who has an immunocompromised condition are available in ICD-10 codes and in electronic health records, which were the data sources in this study, so even if the available evidence was mixed, it seems that not including immunocompromised patients in this study was a missed opportunity to contribute to our understanding of the impact of immunocompromise on common coronavirus outcomes.

Coronaviruses were circulating in the population before COVID-19, and they will likely continue to circulate long after we have overcome the pandemic. Understanding the enhanced risks that immunocompromised people have regarding common coronavirus infections can serve to better protect this population from severe outcomes in the future, and contribute to the way we treat and assess risk for immunocompromised patients during this pandemic.

Notes

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