A Retrospective Database Analysis of Before and After Social Distancing in Relation to Pediatric Infection Rate and Healthcare Services Usage During the COVID-19 Pandemic

Ran Levy, MD¹, Regev Cohen, MD²,³,⁴, Liat Lev-Shalem, PhD⁵, Arik Eisenkraft, MD⁶, Tehila Fisher Yosef, MD¹

¹Maccabi Healthcare Services, Israel; ²Ruth and Bruce Rappaport Faculty of Medicine, Technion University, Haifa, Israel; ³Infectious Diseases Unit, Laniado Medical Center, Netanya, Israel; ⁴Infectious Diseases Unit, Hillel-Yaffe Medical Center, Hadera, Israel; ⁵Maccabitech Institute of Research and Innovation, Maccabi Healthcare Services, Israel; ⁶The Institute for Research in Military Medicine, The Hebrew University Faculty of Medicine and the IDF Medical Corps, Jerusalem, Israel.

†Corresponding Author: Prof. Arik Eisenkraft, MD, MHA; Institute for Research in Military Medicine, Faculty of Medicine, The Hebrew University of Jerusalem and the IDF Medical Corps, POB 12272, Jerusalem 91120, Israel. Tel: +972-52-9210896, +972-2-6757657, Fax: +972-2-6757660, email: aizenkra@gmail.com.

Running title: COVID Social Distance and Infection Rate.
Abstract

Background
Social distancing policy was introduced in Israel in 2020 to reduce the spread of COVID-19. The aim of this study was to analyze the effect of social distancing on other infections in children, by comparing disease rate and healthcare utilization before and after social distancing.

Methods
This was a before-and-after study. Within this retrospective database analysis of parallel periods in 2019 (Period 1 and 2) and 2020 (period 3 - pre-lockdown period, and Period 4 - lockdown period) we included all pediatric population registered in the electronic medical records of the Maccabi Healthcare Services, Israel, looking at the occurrence of non-COVID infections, antibiotic purchasing, doctor visits, Ambulatory Emergency Care Centers visits, Emergency Departments’ visits, and hospitalizations.

Results
776,828 and 777,729 children from 2019 and 2020, respectively, were included. We found a lower infection rate in 2020 vs 2019. We did not find a difference in infection rate between Periods 1-2, while a significant difference was found between Periods 3-4. We found a significant difference between Periods 2-4, with a higher RR than in Periods 1-3. A modest decrease in Ambulatory Emergency Care Center visits, and lower increase in emergency department visits and hospital admissions was found in 2020.

We found decreases in antibiotic purchasing between Periods 1-3 and Periods 2-4, more pronounced in 2020 than in 2019.

Conclusions and Relevance:
Analysis of before and after social distancing and masking showed reduced prevalence of non-COVID pediatric infections, consumption of health care services, and antibiotics consumption.

Keywords: COVID-19; social distancing; infection rates; big data analysis; pediatrics
Introduction

Following the spread of the COVID-19 pandemic in Israel, a national social distancing policy including lockdown was adopted as part of efforts to control the spread of the first wave of the disease. This policy included the closing of schools, kindergartens, nurseries, informal youth organizations, and most working places unless defined as crucial to battle the pandemic and sustain the economy, lasting between 03/17/2020-04/19/2020. Simultaneously, telemedicine solutions were rapidly implemented, like in other countries [1-5]. Extensive guidance was given through traditional and social media platforms regarding distancing, hand washing, and using facemasks; and severe constraints were imposed on transportation and ambulation. People were not allowed to host anyone outside of their nuclear family, and distance confinement was limited to 100 meters from residence [6]. Several studies were conducted to test whether implementing these measures helped in reducing the COVID-19 transmission. A European study compared the transmission and COVID-19 incidence curves in Europe using the data of the European Centre for Disease Prevention and Control, correlating it with the level of mobility, presence, and crowdedness of the population in public spaces based on cellular communication and GPS data [7]. The researchers found that social distancing directly and strongly delayed the viral spread. Another study analyzed the effects of the general lockdown in 12 countries on the community spread and mortality and found that general lockdown was associated with a significant decrease in both [8]. Recently, a drastic decrease of registries for most infections was found, suggesting effects of non-pharmaceutical interventions, such as social distancing, on overall disease transmission [9]. While these studies focused on SARS-COV-2, studies, investigating effects of social distancing on the potential decrease in the occurrence of other infectious diseases are scarce, and usually focused on respiratory infections and did not cover all non-COVID
infections. For instance, Noh et al. have shown that during the COVID-19 pandemic and social
distancing imposed in South Korea, the infection rate of influenza has decreased compared to
previous years [10]. Other studies conducted before the pandemic have shown that social
distancing and school closing are effective measures in reducing rates of influenza [11-13]. To
date, there are only few publications from Israel on the impact of social distancing during the
COVID-19 pandemic on the general morbidity caused by infections in the country [14].
Previously, it was shown that closing schools during the winter due to strikes led to a significant
decrease in rates of upper respiratory tract diseases among school children [15].
In Israel, all residents are entitled to basic health care as a fundamental right, health care
is universal, and participation in a medical insurance plan is compulsory. As such, it can serve as
an important source of data in testing the impact of social distancing.
This study compares the occurrence of non-COVID infections among the pediatric population
registered in the Maccabi Healthcare Services (MHS) before and after the implementation of the
COVID-19 social distancing policy, and with the occurrence in the preceding year.

Methods
Study Design
The study is a before and after retrospective database analysis of a cohort of pediatric patients at
MHS. The total MHS database includes data on 2 million members and represents a sample
comprising 25% of the Israeli population. The study population is composed of all children who
were up to eighteen years of age at each of the two research periods in 2019 and 2020. The
lockdown period in Israel started on March 17th, 2020, and ended on April 19th, 2020. For the
data analysis, we defined the pre-lockdown period as the time between January 1st-March 22nd,
2020, regarded as part of the winter season in Israel, and assuming that the effect of the
lockdown on infections will be apparent a week after its initiation. Lockdown as well as the
immediate post-lockdown period was defined as the time between March 23rd-July 31st, 2020,
regarded as the spring/early summer seasons in Israel. Equivalent periods in 2019 were
compared. We named the periods Period 1 (January 1st-March 22nd, 2019), Period 2 (March 23rd-
July 31st, 2019), Period 3 (January 1st-March 22nd, 2020), and Period 4 (March 23rd-July 31st,
2020). Also, beyond comparing the before and after periods with relation to the lockdown
(Periods 1-3 and 2-4), we compared the differences between Periods 1-2 and 3-4 in order to
analyze any potential natural seasonal influence (winter vs spring and early summer in Israel)
and put these differences in a better context.

The study was approved by the MHS ethics committee. Because there was no identification of
the subjects for whom data were retrieved, informed consent was waived.

Data
The database integrated information from the patients’ electronic medical records including
diagnoses made by the physician, medication prescriptions and purchases, consultations,
hospitalizations, procedures, and sociodemographic data [16]. It was collected over two
consecutive years - 2020 (study group), and 2019 (control group), from doctor visits,
Ambulatory Emergency Care Centers, Emergency Departments and hospitalizations, and
socioeconomic data (SES) of the MHS. In terms of diagnosis, once COVID-19 infection was
ruled-out, the diagnosis of a specific non-COVID infection was based on the discretion of the
pediatrician based on findings during the visit, as always practiced.
Statistical Analysis

Descriptive statistics were presented as n and percentages. Differences between groups were tested using independent sample t-tests and Chi-Square tests, results are shown as risk ratios. P values <.05 were considered statistically significant. All analyses were performed using IBM SPSS v.28® (IBM, NY, US).

Results

781,939 children aged 0-18 years were included in the study group (data collected from 2020), 4,210 were excluded after they were found to be positive to COVID-19, with 777,729 included in the final analysis. The control group included 776,828 children aged 0-18 (data collected from 2019) (Table 1). 51.2% of the participants in 2019 and 2020 were males (396,352 and 408,741, respectively). It is important to state that the two groups overlapped by a large part.

We have analyzed the effect of social distancing and masking on infection rate beyond the natural difference between the winter and the spring/early summer, by comparing between the four defined Periods (Table 2). We found a higher infection rate in 2019 than in 2020. We did not find a difference in the total number of children with an infection between Period 1 and Period 2 (RR 1.00, 95% CI 0.99-1.00, p<.001) in 2019, while a significant difference was found between Period 3 and 4 in 2020 (RR 0.62, 95% CI 0.61-0.62, p<.001). When stratified by age groups, we found that at the age range of 0-1 year, there was a higher increase in infection rate between Periods 1-2 compared with Periods 3-4 (RR 1.56, 95% CI 1.54-1.59, p<.001 vs RR 1.08, 95% CI 1.07-1.1, p<.001, respectively, Supplemental Table 1). In all other age groups, in Period 2 we found fewer infections compared with Period 1, and a greater decrease between Periods 3-4 (p<.001 in all, Supplemental Table 1). This was true for all infections included in
the dataset, with decreased infectious rates between 2019 (Periods 1-2) and 2020 (Periods 3-4) for acute upper respiratory tract infection and common cold, influenza, sore throat, tonsillitis, pharyngitis and nasopharyngitis, herpangina and herpetic gingivostomatitis, acute otitis media, bronchiolitis, pneumonia and bronchopneumonia, gastroenteritis, diarrhea, and dysentery, oxyuriasis, urinary tract infection and pyelonephritis, impetigo, conjunctivitis, hand-foot-and-mouth disease, cellulitis, and fever as a general diagnosis. In all, we found p<.001. Due to low rates of meningitis, we did not include this diagnosis in the final analysis (36 cases in 2019 and 20 cases in 2020).

Next, we analyzed the difference between Periods 1-3, and between Periods 2-4 (the lockdown period) (Table 3). The RR between Periods 1-3 was 0.95 (95% CI 0.94-0.96, P<.001), while between Periods 2-4 it was 0.59 (95%CI 0.58-0.59, P<.001). As shown in the Supplemental Table 2, this pattern was present in all age groups, and in all infections included in the data set, with a higher RR between Periods 2-4 than between Periods 1-3, and a p<.001 in all infection rates between Periods 2-4.

When analyzing visits to the emergency department, hospital admissions, and ambulatory emergency care centers in Periods 1-2 and Periods 3-4, we found a modest decrease in Ambulatory Emergency Care Center visits in 2020 (RR 1.64, 95% CI 1.58-1.69, P<.001 versus an increase in 2019 (RR 0.84, 95% CI 0.81-0.88, P<.001) (Supplemental Table 3). In both years (Periods 1-2 and Periods 3-4) there was an increase in emergency department visits and hospital admissions, but this was milder in 2020 (RR 1.60, 95% CI 1.57-1.63, P<.001 vs RR 1.20, 95% CI 1.17-1.22, P<.001 for emergency department visits, and RR 1.53, 95% CI 1.49-1.58, P<.001 vs RR 1.11, 95% CI 1.08-1.15, P<.001 for hospital admissions, Supplemental Table 3). When comparing Periods 2-4 to Periods 1-3 we found higher RR in admission rates to
the Ambulatory Emergency Care Centers (1-3 - RR 0.82, 95% CI 0.79-0.85, P<.001 vs 2-4 - RR 0.42, 95% CI 0.41-0.44, P<.001, respectively), and lower RR in visits to emergency departments (RR 0.94, 95% CI 0.92-0.96, P<.001 vs RR 0.70, 95% CI 0.69-0.72, P<.001, respectively) and hospital wards (RR 0.98, 95% CI 0.95-1.01, P<.001 vs RR 0.71, 95% CI 0.69-0.73, P=NS) (Table 4).

When comparing Periods 1 and 2 we found a significant increase in antibiotic purchasing among all of the pediatric population, but when comparing Periods 3 and 4 we found a significant decrease (1-2 - RR 1.12, 95% CI 1.11-1.13, <.001 vs 3-4 - RR 0.79, 95% CI 0.78-0.79, P<.001). When further stratifying the pediatric population, this was true in all age groups (p<.001 in all, (Supplemental Table 4). Lastly, when comparing antibiotic purchasing between Periods 1-3 and Periods 2-4 we found a decrease in both comparisons, more pronounced in 2020 than in 2019 (1-3 - RR 0.82, 95% CI 0.81-0.83, p<0.001 vs 2-4 - RR 0.58, 95% CI 0.57-0.58, p<0.001, respectively) (Table 5 and Supplemental Table 5).

Discussion

In this study, we analyzed data of a large pediatric population comparing non-COVID infection rates, antibiotic purchasing, and doctor visits between 2019 and 2020, focusing on before and after the COVID-19 lockdown and social distancing period. Importantly, this policy was a dramatic step never implemented in Israel until that point. Within this population, we found a significant decrease in all infections within the registry in the study group (2020) when compared to the control group (2019), and in all age groups.

Moreover, infections that typically increase in the second period of the year showed lower rates in Period 4. This included acute gastroenteritis, acute otitis media, ocular infections, tonsillitis,
and herpangina. When looking at hand, foot, and mouth disease, we usually see the appearance of outbreaks during the spring and early summer, a pattern that was found in 2019. However, in 2020 we found a dramatic decrease in Period 4, further emphasizing the effect of social distancing on its spread.

Similarly, in 2019 we see an increase in gastroenteritis cases between Periods 1-2. Yet, in 2020, there were no changes in the rate of gastroenteritis between Periods 3-4. Children in childcare centers tend to get more infections, and young children are the most likely to catch infections.

There are several reasons for the spread of infections among children in everyday life. Contact transmission is the principal mode of transmission for most childhood infections, typically via the hands of the infected children or caregivers [17, 18]. Fecal-oral transmission of enteric pathogens or the transmission of respiratory pathogens through hands that have been contaminated by the secretions of infected children is such an example. Children in group settings such as schools and kindergartens encounter many other children, so they have a much greater chance of getting an infection from others, while sharing toys and touching each other during play. Also, many children have not yet learned how to use the toilet properly or the importance of proper hand hygiene. In many places the playground and toilet infrastructure are not kept properly clean, leading to contact with fomites. Another route for disease transmission is through droplet contact since children do not always cover their coughs and sneezes. Adding to the above is understaffing and high rates of staff turnover in many child-care centers [18].

Our findings could indeed represent lower rates of infection transmission during the lockdown and social distancing. Still, other explanations should also be considered, including lower rates of diagnosis resulting from patients not arriving at the clinics due to fear of being infected with COVID-19, and physicians tending to diagnose patients using telehealth platforms, which have
grown substantially during the pandemic and might lead to misinterpretation in some of the cases. However, we regard these as contributing factors to our findings. We found a significant decrease in visits to the emergency departments, hospitalization rates, and visits at the ambulatory emergency care centers during the lockdown period and after, suggesting reduced numbers of severe infections. This is probably also related to the population's fear of getting infected while visiting a clinic or a hospital during the pandemic. However, for the sake of being cautious, and as there is still a level of uncertainty regarding this component of the study, we cannot be sure there were no confounding factors not related to the lockdown.

We also found a significant decrease in antibiotic purchasing in the study group compared with the control group and in all ages. This is in accord with the scope of decrease we found in the infectious disease registry, in all ages. Several studies discuss the increase in prevalence of infections following removal of the lockdown [19, 20]. This phenomenon contributes to the notion that the reduction was connected with the lockdown rather than with other reasons such as immunologic development of children. There are several limitations to this study. A before-after study might be confounded by other factors and secular trends during the lockdown period. Many viral and bacterial infections appear in seasonal cycles – a phenomenon that is often not fully-explained, and sometimes there are deviations in this seasonal pattern [21]. In the past year, there were several reports of a significant decline in influenza cases around the world. There were also reports of other infections who markedly declined during the lockdown period, and resurged, sometimes outside of the normal seasonality, following the uplifting of the non-pharmacological restrictions [19]. In Israel, the Israel Center for Disease Control has shown that the lockdown changed the seasonal pattern of several respiratory infections and the number of infections has dramatically decreased.
during the lockdown period, differing significantly from previous years, with data from 2010 and until now [22]. Moreover, the very fact that we found a decrease in all infections in the lockdown period, suggests that our findings are not accidental, as it is unlikely that a significant deviation in the seasonality of multiple infections will appear simultaneously in all. The same applies to the decrease in consumption of all components of healthcare services. When looking at other factors, no changes were made to the vaccination policy or to the costs of treatment within the MHS. As previously noted, the availability of treatment has changed in light of the lockdown. Still, we looked at all of the components of medical care, including clinics, call centers, and hospitals, and they all remained available to the public as they were before lockdown. However, we found a decline in all, which is better-explained by reduced rate of infections than by any other explanation. All of this reinforces the assessment that the reduction in non-COVID infections has a direct connection with the policy of lockdown and social distancing. As this study focuses on rates of infections, we have included all aspects of medical care related to that, and we did not look at other non-COVID conditions. However, various studies have shown a decline of about 30% in non-infectious or non-communicable diagnoses such as the diagnosis of malignancy during the lockdown [23]. Though it is difficult to make an accurate separation of the direct effect of the lockdown on healthcare-seeking-behavior of people, at least in relation to infectious diseases of the airways, people actually did come and seek healthcare services in order to rule-out or confirm a diagnosis of COVID-19, and once ruled out, the working diagnosis of another viral disease has been recorded. The abnormal increase in incidence of infections with the removal of the lockdown also indicates a real and non-artificial decline of infections during the lockdown, especially in infections of short duration [19]. In these cases, such as RSV bronchiolitis, one cannot blame the lockdown for leading to a late diagnosis. In addition, while it
can be argued that people in general have consumed fewer healthcare services in the community, it is not expected that children with a serious infection that requires hospitalization will not be hospitalized for sociological or psychological reasons. If the explanation for the change we saw was sociologic (e.g., fear of getting infected with COVID-19 in the clinic) we would not see a gap in children's hospitalizations due to respiratory illness. A recent study has found that during the lockdown period there was a decrease not only in the diagnosis of acquired pneumonia in the community but also in invasive pneumococcal disease [24]. This further strengthens our observation. There are cases in which drugs were prescribed without mentioning a specific infectious agent. Though this could result in a reporting bias, this has not changed in recent years as this is an inherent bias in the reporting system and we do not think it influenced the results. We looked at the antibiotic purchasing rate, but we do not have data on their actual consumption. Several components might have influenced our results, such as purchasing yet not consuming the antibiotics, lack of physicians' availability, and incomplete registries. However, these complex components were always present, leading us to claim that the changes we found are related to the strict social distancing imposed on all - healthcare providers as well as patients - as the single most important factor that changed between the periods. This study focused on infectious diseases only. It is important to conduct similar analyses of other clinical conditions, to allow a better and a comprehensive understanding of the full effects of social distancing on the health of children during the COVID-19 pandemic.

**Conclusions**

When analyzing the registry, non-COVID pediatric infections, antibiotic purchasing, and consumption of MHS services, we found lower rates of infections during and after social distancing in the first wave of COVID-19 when compared to the preceding year and in all age
groups. Future studies should examine the impact of reduced antibiotic consumption on antibiotic resistance.

Notes

Author contributions. R. L. and A. E. conceived of and designed the analyses. R. L. and L. L. S. collected the data. R. L., R. C., L. L. S., A.E., and T. F. Y. performed the data analyses. R. L., R. C., A.E., and T. F. Y. interpreted the data results. R. L., and A. E. wrote the first draft of the work. All authors revised the work critically for intellectual content, approved the final version of the work to be published, and are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Table 1. Number of children included in the study, divided into age groups.

| Age Groups (years) | 2019      | 2020      |
|--------------------|-----------|-----------|
| Total              | 776,828   | 777,729   |
| 0-1                | 70,942 (9.2%) | 69,812 (8.8%) |
| 1-6                | 225,435 (28.7%) | 224,724 (28.2%) |
| 6-12               | 256,865 (33.2%) | 258,210 (32.4%) |
| 12-18              | 223,586 (28.9%) | 224,983 (30.7%) |
Table 2. Infection rate in the two study groups. Comparing Period 1 (January 1st-March 22nd, 2019) with Period 2 (March 23rd-July 31st, 2019) and Period 3 (January 1st-March 22nd, 2020) with Period 4 (March 23rd-July 31st, 2020, the lockdown period).

| Disease                                      | Period 1 ref. | Period 2 | RR (95% CI) | p-value | Period 3 ref. | Period 4 | RR (95% CI) | p-value |
|----------------------------------------------|---------------|----------|-------------|---------|---------------|----------|-------------|---------|
| Total Number of Children with Infection     | 152,359       | 19.7     | 151,892     | 19.6    | 148,370       | 18.7    | 91,781      | 11.6    | 0.62 (0.61-0.62) | <.001 |
| Acute Upper Respiratory Tract Infection, Common Cold | 20739         | 2.7      | 13981       | 1.8     | 18274         | 2.3     | 9059        | 1.1     | 0.5 (0.48-0.51) | <.001 |
| Influenza                                   | 11121         | 1.4      | 250         | 0.03    | 11174         | 1.4     | 80          | 0       | 0.01 (0.01-0.01) | <.001 |
| Sore Throat, Tonsillitis Pharyngitis, Nasopharyngitis | 22055         | 2.8      | 25305       | 3.3     | 24741         | 3.1     | 13563       | 1.7     | 0.55 (0.54-0.56) | <.001 |
| Herpangina, Herpetic Gingivostomatitis       | 3310          | 0.4      | 5499        | 0.7     | 2703          | 0.3     | 2434        | 0.3     | 0.9 (0.85-0.95) | <.001 |
| Acute Otitis Media                          | 26983         | 3.5      | 22992       | 3       | 25331         | 3.2     | 9593        | 1.2     | 0.38 (0.37-0.39) | <.001 |
| Bronchiolitis                                | 4062          | 0.5      | 451         | 0.1     | 3059          | 0.4     | 237         | 0       | 0.08 (0.07-0.09) | <.001 |
| Pneumonia, Bronchopneumonia                 | 9540          | 1.2      | 5827        | 0.8     | 7192          | 0.9     | 887         | 0.1     | 0.12 (0.12-0.13) | <.001 |
| Gastroenteritis, Diarrhea, Dysentery         | 16061         | 2.1      | 33752       | 4.4     | 14666         | 1.8     | 14354       | 1.8     | 0.98 (0.96-1) | <.001 |
| Oxyuriasis                                   | 5389          | 0.7      | 7836        | 1       | 5212          | 0.7     | 6442        | 0.8     | 1.24 (1.19-1.28) | <.001 |
| Urinary Tract Infection and Pyelonephritis   | 3060          | 0.4      | 4166        | 0.5     | 2878          | 0.4     | 3411        | 0.4     | 1.19 (1.13-1.25) | <.001 |
| Impetigo                                     | 1517          | 0.2      | 3986        | 0.5     | 1922          | 0.2     | 2988        | 0.4     | 1.55 (1.47-1.65) | <.001 |
| Conjunctivitis                               | 19512         | 2.5      | 24591       | 3.2     | 18980         | 2.4     | 11628       | 1.5     | 0.61 (0.6-0.63) | <.001 |
| Hand-Foot-and-Mouth Disease                 | 770           | 0.1      | 1052        | 0.1     | 2275          | 0.3     | 342         | 0       | 0.15 (0.13-0.17) | <.001 |
| Cellulitis                                   | 1690          | 0.2      | 3603        | 0.5     | 1666          | 0.2     | 2800        | 0.4     | 1.68 (1.58-1.79) | <.001 |
| Fever                                       | 54562         | 7        | 53346       | 6.9     | 58086         | 7.3     | 35428       | 4.5     | 0.61 (0.6-0.62) | <.001 |
Table 3. Infection rate in the two study groups. Comparing Period 1 (January 1st-March 22nd, 2019) with Period 3 (January 1st-March 22nd, 2020) and Period 2 (March 23rd-July 31st, 2019) with Period 4 (March 23rd-July 31st, 2020, the lockdown period). NS – not significant.

| Disease                                | Period 1 | Period 3 | RR (95% CI) | p-value | Period 2 | Period 4 | RR (95% CI) | p-value |
|-----------------------------------------|----------|----------|-------------|---------|----------|----------|-------------|---------|
| Total Number of Children with Infection| 152,359  | 148,370  | 0.95 (0.94-0.96) | <.001   | 151,892  | 91,781   | 0.59 (0.58-0.59) | <.001   |
| Acute Upper Respiratory Tract Infection, Common Cold | 20739    | 18174    | 0.85 (0.84-0.87) | <.001   | 13981    | 9009     | 0.63 (0.61-0.65) | <.001   |
| Influenza                              | 11121    | 11115    | 0.97 (0.95-1)   | NS      | 250      | 77       | 0.3 (0.23-0.39) | <.001   |
| Sore Throat, Tonsillitis, Pharyngitis, Nasopharyngitis | 22055    | 24586    | 1.09 (1.07-1.11) | <.001   | 25305    | 13417    | 0.52 (0.51-0.53) | <.001   |
| Herpangina, Herpetic Gingivostomatitis | 3310     | 2690     | 0.79 (0.75-0.83) | <.001   | 5499     | 2426     | 0.43 (0.41-0.45) | <.001   |
| Acute Otitis Media                     | 26983    | 25238    | 0.91 (0.97-1.03) | <.001   | 22992    | 9549     | 0.41 (0.4-0.41)  | <.001   |
| Bronchiolitis                          | 4062     | 3046     | 0.73 (0.7-0.77) | <.001   | 451      | 236      | 0.51 (0.44-0.56) | <.001   |
| Pneumonia, Bronchopneumonia            | 9540     | 7156     | 0.73 (0.71-0.75) | <.001   | 5827     | 886      | 0.15 (0.14-0.16) | <.001   |
| Gastroenteritis, Diarrhea, Dysentery    | 16061    | 14599    | 0.89 (0.87-0.91) | <.001   | 33752    | 14259    | 0.41 (0.4-0.42)  | <.001   |
| Oxyuriasis                             | 5389     | 5177     | 0.97 (0.97-0.97) | <.01    | 7836     | 6411     | 0.8 (0.77-0.82)  | <.001   |
| Urinary Tract Infection and Pyelonephritis | 3060    | 2862     | 0.91 (0.87-0.96) | <.001   | 4166     | 3394     | 0.79 (0.76-0.83) | <.001   |
| Impetigo                               | 1517     | 1910     | 1.23 (1.15-1.31) | <.001   | 3986     | 2988     | 0.7 (0.7-0.77)   | <.001   |
| Conjunctivitis                         | 19512    | 18885    | 1.23 (1.15-1.31) | <.001   | 24591    | 11559    | 0.46 (0.45-0.47) | <.001   |
| Hand-Foot-Mouth Disease                | 770      | 2264     | 2.87 (2.64-3.11) | <.001   | 1052     | 342      | 0.32 (0.28-0.36) | <.001   |
| Cellulitis                             | 1690     | 1662     | 0.96 (0.9-1.03)  | NS      | 3603     | 2786     | 0.75 (0.72-0.79) | <.001   |
| Fever                                  | 54562    | 57803    | 1.03 (1.02-1.04) | <.001   | 53346    | 35023    | 0.64 (0.63-0.65) | <.001   |
Table 4. The number of children admitted to emergency centers, emergency rooms, and hospital wards in 2019 and in 2020. Comparing Period 1 (January 1st-March 22nd, 2019) with Period 3 (January 1st-March 22nd, 2020) and Period 2 (March 23rd-July 31st, 2019) with Period 4 (March 23rd-July 31st, 2020, the lockdown period). NS – not significant.

| Clinical setting                      | Period 1 | Period 3 | RR (95% CI) | P    | Period 2 | Period 4 | RR (95% CI) | P    |
|---------------------------------------|----------|----------|-------------|------|----------|----------|-------------|------|
|                                       | N        | %        |             |      | N        | %        |             |      |
| Ambulatory Emergency Care Center visits | 5532     | 0.7      | 4645        | 0.6  | 9061     | 1.2      | 3910        | 0.5  |
|                                       |          |          | 0.82 (0.79-0.85) | <.001 |          |          | 0.42 (0.41-0.44) | <.001 |
| Emergency room visits                 | 18155    | 2.3      | 17488       | 2.2  | 29005    | 3.7      | 20908       | 2.6  |
|                                       |          |          | 0.94 (0.92-0.96) | <.001 |          |          | 0.70 (0.69-0.72) | <.001 |
| Hospital admissions                   | 7788     | 1        | 7801        | 1    | 11954    | 1.5      | 8691        | 1.1  |
|                                       |          |          | 0.98 (0.95-1.01) | NS   |          |          | 0.71 (0.69-0.73) | <.001 |

Table 5. Comparing purchase of antibiotics at the same time periods in 2019 and 2020. Comparing Period 1 (January 1st-March 22nd, 2019) with Period 3 (January 1st-March 22nd, 2020) and Period 2 (March 23rd-July 31st, 2019) with Period 4 (March 23rd-July 31st, 2020, the lockdown period).

| Period 1 | Period 3 | RR (95% CI) | p-value | Period 2 | Period 4 | RR (95% CI) | p-value |
|----------|----------|-------------|---------|----------|----------|-------------|---------|
|          | N        | %           |         |          | N        | %           |         |
| Purchase of Antibiotics               | 83869    | 10.8        |         | 70469    | 8.9      | 0.82 (0.81-0.83) | <.001  |
|                                      | 93684    | 12.1        |         | 55325    | 7        | 0.58 (0.57-0.58) | <.001  |