

Trends in Pediatric Ambulatory Practice during COVID-19 Lockdown

Herman Avner Cohen MD^{1,5}, Maya Gerstein MD^{1,5}, Vered Shkalim Zemer MD^{2,5}, Sophia Heiman MD^{1,5}, Yael Richenberg MD³, Eyal Jacobson MD³, and Oren Berkowitz PhD PA-C⁴

¹Pediatric Ambulatory Community Clinic, Petah Tikva, Israel

²Clalit Health Services, Petah Tikva, Israel

³Dan-Petah Tikva District, Clalit Health Services, Israel

⁴Department of Health Systems Management, Ariel University, Ariel, Israel

⁵Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

ABSTRACT **Background:** On 18 March 2020, the Israeli Health Ministry issued lockdown orders to mitigate the spread of coronavirus disease 2019 (COVID-19).

Objectives: To assess the association of lockdown orders on telemedicine practice and the effect of social distancing on infectious diseases in a primary care community pediatric clinic as well as the rate of referrals to emergency departments (ED) and trends of hospitalization.

Methods: Investigators performed a retrospective secondary data analysis that screened for visits in a large pediatric center from 1 January to 31 May 2020. Total visits were compared from January to December 2020 during the same period in 2019. Visits were coded during the first lockdown as being via telemedicine or in-person, and whether they resulted in ED referral or hospitalization. Month-to-month comparisons were performed as well as percent change from the previous year.

Results: There was a sharp decline of in-person visits (24%) and an increase in telemedicine consultations (76%) during the first lockdown ($P < 0.001$). When the lockdown restrictions were eased, there was a rebound of 50% in-person visits ($P < 0.05$). There was a profound decrease of visits for common infectious diseases during the lockdown period. Substantial decreases were noted for overall visits, ED referrals, and hospitalizations in 2020 compared to 2019.

Conclusions: COVID-19 had a major impact on primary care clinics, resulting in fewer patient-doctor encounters, fewer overall visits, fewer ED referrals, and fewer hospitalizations.

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KEY WORDS: community healthcare center, infectious diseases, pediatrics, telemedicine, telehealth

On 30 January 2020, the World Health Organization (WHO) declared the coronavirus disease 2019 (COVID-19) outbreak to be a public health emergency of international concern. On 11 March 2020, the outbreak was declared to be a pandemic [1,2]. On 18 March 2020, the Israeli Health Ministry issued statewide executive lockdown orders to help mitigate the risk that COVID-19 hospitalizations would overwhelm the health-care infrastructure. Other factors that potentially decreased the rate of virus spread and subsequent hospitalizations included kindergarten and school closures, social distancing guidelines, the wearing of facemasks, and general pandemic awareness. Medically necessary travel was permitted during the first lockdown period and people had the option to visit their medical providers in-person, even for routine care, but they also had the option to utilize existing telemedicine alternatives.

We aimed to assess the association of these lockdown orders and the trend of telemedicine vs. in-person visits and to determine the effect of the social distancing on commonly diagnosed infectious diseases in a pediatric community healthcare center (PCHC). We also explored the rate of referrals to the emergency department (ED) and the trends of hospitalization in a tertiary children's hospital.

PATIENTS AND METHODS

SETTING AND DATA SOURCE

Clalit Health Services (CHS) is Israel's largest health fund and serves as both insurer and healthcare provider, insuring 54% of Israel's population and supplying most of the healthcare services within its system. These services include primary, secondary, and tertiary care (including a third of the acute care beds in Israel), as well as pharmacies and paramedical services. In CHS, children are predominantly treated at communi-

ty-based primary care clinics by board-certified pediatricians, non-board-certified pediatricians and general practitioners. Primary care is provided in 1400 community-based clinics, where PCHCs coexist with traditional single and group clinics. All of CHS's primary and secondary care physicians use an advanced electronic medical records system, which feeds data into the central database of the organization and contains more than a decade of stored data. The population registered and treated at our PCHC is 9000 children and adolescents, aged from one day to 25 years of age. All the patients belong to the PCHC as a group. Physician reimbursement is based on the total number of patients registered to the PCHC and not as a fee-for-service model.

The PCHC is open 12 hours a day from Sunday through Thursday and 4 hours on Fridays. Our PCHC staff comprises eight board-certified pediatricians, four nurses, four front desk staff, and one pharmacist. Three of the physicians were over 67 years of age at the time of the COVID-19 pandemic. Our PCHC staff also provided physician and nurse encounters as a backup for children belonging to other clinics (in solo or group practices) in our area, when necessary.

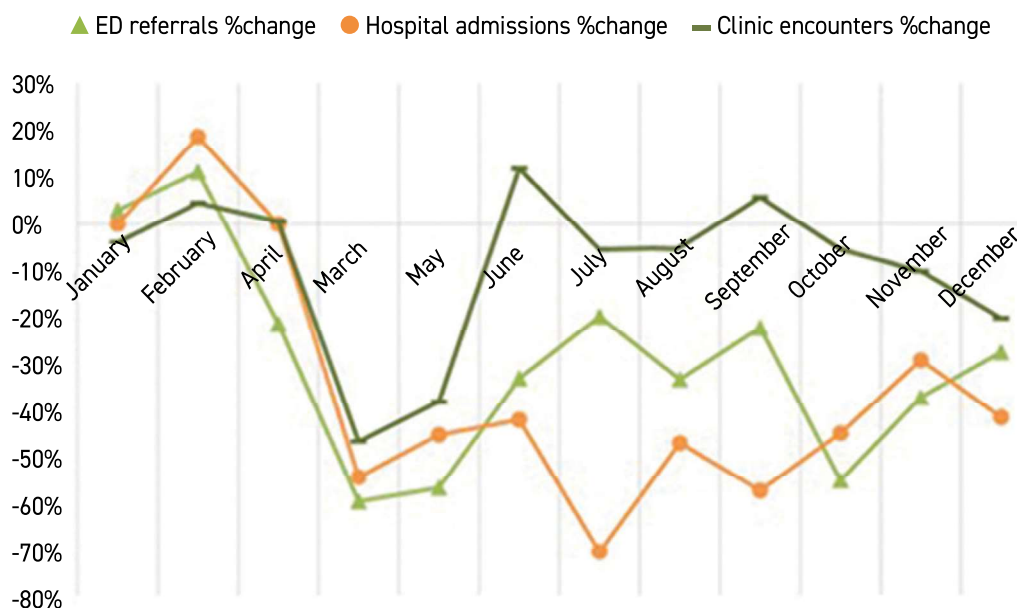
During the beginning of the COVID-19 pandemic, our staff worked in two shifts. During every shift there were at least three or four physicians one of whom worked with extensive personal protective equipment (PPE) and examined any child who attended with fever and/or respiratory complaints. The other physicians assessed patients with any other complaints (either

at an in-person visit or via telemedicine consultation). These physicians wore facemasks and gloves. The physicians over 67 years of age did not examine any patient with a high suspicion of Covid-19.

During the pandemic, we also served as a city sentinel clinic for the children with COVID-19 who were registered at the PCHC. We screened the number of patient encounters at the PCHC from January 2019 through 31 December 2019 according to visit type and referral (clinic, ED, hospital admission) and compared them to the number of visits during the same period of 2020. The clinic visits included in-person visits and telemedicine consultations. Data for telemedicine consultation were only available up to 31 May 2020. All types of visits were documented in the medical record file of the CHS. In-person visits were defined as a visit where the patient physically showed up at the PCHC. A telemedicine visit was defined as a scheduled or impromptu phone/video call with the pediatrician without the patient physically attending the clinic. The study assessed the pattern of using telemedicine technologies before and during the COVID-19 pandemic.

We sought to determine the effect of social distancing on a few common infectious diseases commonly diagnosed in pediatric primary care that are contagious to various extents: viral infection, pneumonia, acute otitis media, streptococcal and non-streptococcal pharyngitis, upper respiratory infection (including stridor), impetigo, conjunctivitis, gastrointestinal infection, and urinary tract infection. Data for infectious diseases

Figure 1. Percent change of ED referrals, hospital admissions, and clinic encounters by month from 2019 to 2020
ED = emergency department



were only available from 1 January 2020 through 31 May 2020.

We randomly chose a week before the effects of the pandemic, in January 2020, and one week in each month during the lockdown orders in March to April, and immediately following the first lockdown in May 2020. We also looked for the differences in the number of children who attended the ED or were hospitalized.

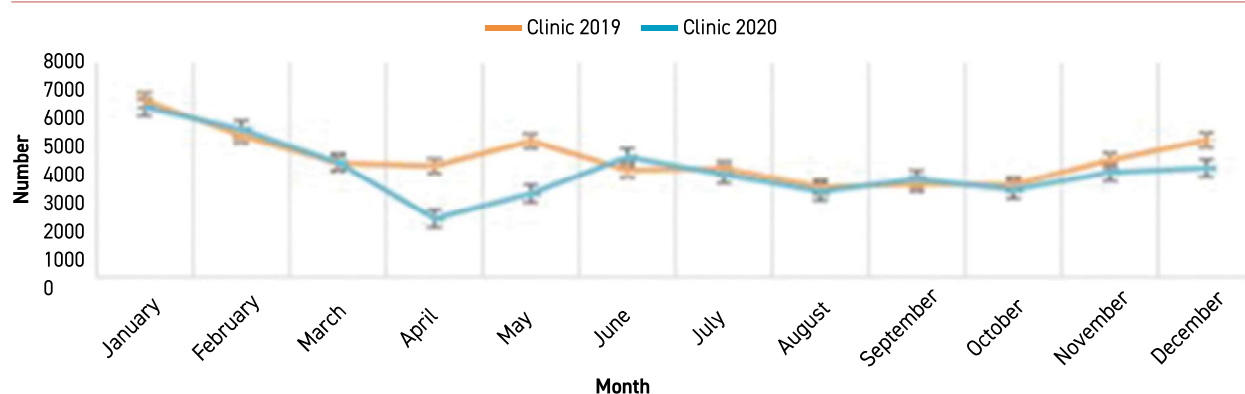
The study was approved by the local institutional review board.

STATISTICAL ANALYSIS

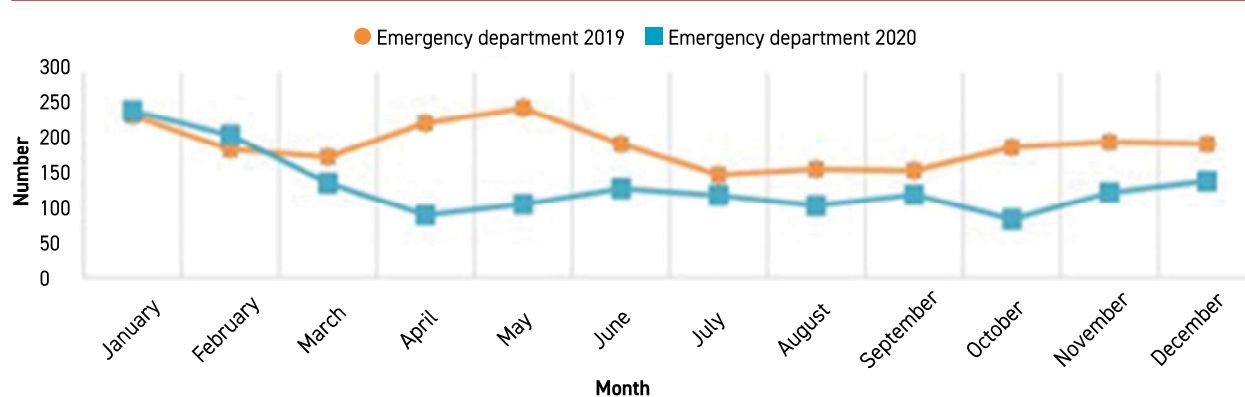
Descriptive statistics included frequencies and proportions. Percent change over time was displayed with a 95% confidence interval (95%CI). Pearson's chi-square test compared categorical variable rates. Changes from month to month were compared

Figure 2. Number of total monthly visits in a tertiary pediatric community healthcare center in 2019 vs. 2020 by visit type

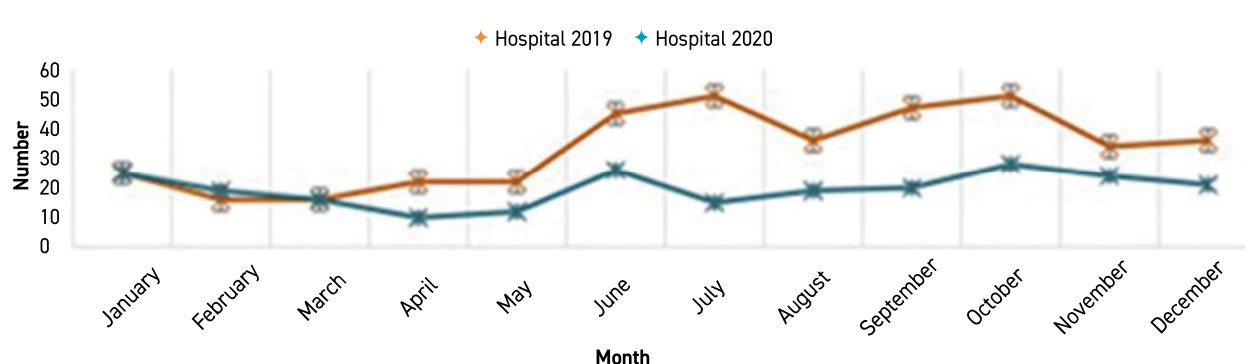
[A] Clinic encounters



[B] emergency department (ED) referrals



[C] Hospital admissions



with a two-sided test for equality of column proportions using a Bonferroni correction for multiple comparisons. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 25.0 (SPSS, IBM Corp, Armonk, NY, USA).

RESULTS

CLINIC ENCOUNTERS AND REFERRALS

During the year 2020, a total of 48,002 patient encounters at the PCHC were documented compared with 53,290 in the year 2019. There was a notable decrease in April 2020 of -47% (95%CI -57%, -37%) and May 2000 of -38% (95%CI -48%, -28%) compared with the same months in 2019. These results correlated with the tail end of the first lockdown. The visits increased significantly for June, up 12% (95%CI 2%, 22%). A second 3-week lockdown occurred from 17 September until 11 October and then a third lockdown began incrementally in December, where we saw a decrease again in clinical encounters compared to the previous year of -20% (95%CI -30%, -10%) [Figure 1]. The number of ED referrals diverged from March 2020 and never returned to previous levels for the remainder of the year 2020 [Figure 2]. ED referrals had a -22% reduction (95%CI -34%, -9%) in March. The number of hospital admissions diverged from April 2020 and never returned to previous levels for the remainder of the year 2020 [Figure 2]. Hospital ad-

missions had a -55% reduction (95%CI -83%, -27%) in April [Figure 1].

TELEMEDICINE

There were 2772 (17.4%) clinical encounters randomly sampled from the PCHC between 1 January 2020 and 30 May 2020. A total of 2650 pediatric cases between the ages of 0–19 years were included in the analysis. Sex was almost evenly distributed, and 42% of the cases were in the age group of 0–3 years [Table 1].

Over the entire period, 45% of encounters were via telemedicine and the remaining 55% were in-person. However, the fluctuations over the months varied significantly, with 76% of visits being in-person before the lockdown during January 2020 and a complete reversal to 76% of visits being telemedicine at the height of the lockdown, during April 2020.

Statistically significant changes in the number of telemedicine encounters occurred between each individual month, with a significant increase over the lockdown period (March–April) and then a reduction after the lockdown period [Table 1]. Telemedicine increased from 24% in January to 67% in March ($P < 0.05$) and peaked in April at 76% ($P < 0.05$) before coming back down in May to 50% ($P < 0.05$, chi-square test for overall period changes: $P < 0.001$) [noted in Table 1 with individual subscripts].

INFECTIOUS DISEASES

All the studied infectious diseases decreased from the period between January to May 2020, as presented in Table 2. The most dramatic changes between January and March/April (lockdown

Table 1. Visit type and demographics by month during 2020

	Total	January, n=1176	March, n=507	April, n=364	May, n=603	P value
Visit type						
Telemedicine	1203 (45%)	283 (24%)	341 (67%)	276 (76%)	303 (50%)	< 0.001*
In-person	1447 (55%)	893 (76%)	166 (33%)	88 (24%)	300 (50%)	
Age groups, years						
0–3	1124 (42%)	521 (44%)	233 (46%)	161 (44%)	209 (35%)	< 0.001*
4–9	806 (30%)	378 (32%)	125 (25%)	98(27%)	205 (34%)	
10–19	721 (27%)	278 (24%)	149 (29%)	105 (29%)	189 (31%)	
Sex						
Male	1413 (53%)	633 (54%)	284 (56%)	182 (50%)	314 (52%)	0.31*
Female	1238 (47%)	544 (46%)	223 (44%)	182 (50%)	289 (48%)	

All values are by n (%)

Values in the same row are significantly different at $P < 0.05$ in the two-sided test of equality for column proportions. Tests assume equal variances and are adjusted for all pairwise comparisons within a row of each innermost subtable using the Bonferroni correction

*Pearson chi-square test for groupwise comparison

Table 2. Representative common weekly diagnoses documented in our patients in January 2020 and percent change during the lockdown [March-May 2020]

Diagnosis	January 2020, N	March 2020, N (% change from previous month)	April 2020, N (% change from previous month)	May 2020, N (% change from previous month)
Cough	195	45 (-77%)	30 (-33%)	17 (-43%)
Fever	172	39 (-77%)	16 (-59%)	31 (94%)
Otitis media	78	13 (-83%)	7 (-46%)	9 (29%)
Pharyngitis/tonsillitis	35	8 (-77%)	5 (-38%)	7 (40%)
Conjunctivitis	32	8 (-75%)	9 (13%)	3 (-67%)
Pneumonia	27	3 (-89%)	0 (-100%)	1 (NA)
Viral infection	23	0 (-100%)	1 n/a	1 (0%)
Gastrointestinal infection	17	7 (-59%)	6 (-14%)	10 (67%)
Urinary tract infection	5	3 (-40%)	3 (0%)	6 (100%)
Impetigo	4	1 (-75%)	1 (0%)	3 (200%)

months) occurred in the categories of viral infection: from 23 cases in January to none in March (-100%); pneumonia: from 27 cases in January to 3 in March (-89%); and otitis media: from 78 cases in January to 13 in March (-83%). When the lockdown was relaxed in May, the prevalence of most infectious diseases increased, the largest increases occurring for impetigo: from one case in April to three in May (200%); urinary tract infection: from three cases in April to six in May (100%); and fever: from 16 cases in April to 31 in May (94%). Fever was mostly related to any kind of infectious disease without a specific site or organ, mostly, but not all, as part of a viral infection. However, due to the retrospective nature of this study, we were unable to determine the final diagnosis for each episode of fever. Nevertheless, we noted a profound reduction in this diagnosis also between January and the months of lockdown.

DISCUSSION

This study highlights the rise in the use of telemedicine and the decrease of in-person visits during the first COVID-19 lockdown in Israel. The level of referrals, from PCHC to ED and hospital admission, decreased in March/April and never returned to the previous year's rate for the remainder of 2020. Public health measures to counter the COVID-19 pandemic, such as stay-at-home lockdown orders, mask-wearing, and social distancing probably reduced the need for medical care at the PCHC in part by curtailing the spread of other infections and altering the epidemiology of injuries. Interventions such as closures, physical distancing, use of facemasks, and hand-washing can be expected to reduce the transmission of many infectious diseases, especially in children [3,4].

Our results are in line with reports of similar decreases in clinical services from around the world. Thornton et al. [5] reported a 25% countrywide drop in ED visits in the United Kingdom within one week of their national lockdown. In the United States, the lay press described decreases in ED visits by as much as half the normal volume [6] and the CDC reported

a decline of 42% in ED visits during the early COVID-19 pandemic, with the steepest decreases in persons aged < 14 years [7]. The proportion of infectious disease-related visits was four times higher during the early pandemic period [7]. Wong et al. [8] reported an ED volume decrease of nearly 50% and suggested that there was increasing evidence that patients with emergencies were avoiding the ED due to fear of contracting COVID-19. On 23 April 2020, the commonwealth fund reported that the number of visits to ambulatory care practices declined by nearly 60% [9].

Telemedicine (or telehealth) is defined by the U.S. National Institutes of Health (NIH) as the use of technology to provide and support healthcare at a distance [10]. The technology used can be phone calls, emails, text messages, picture/video-clips, or videoconferencing. In Israel [11,12], COVID-19 guidelines encouraged the use of telemedicine in ambulatory settings for children and adults during the pandemic. Telemedicine visits were intended to better support patients at home and divert them from the PCHC, thus reducing potential infectious exposures.

Our data show that in May 2020 (after the end of the first lockdown), in-person visits returned to 50% of the total visits and telemedicine visits fell to 50% of the total visits. This finding is also in accordance with the report of Grossman et al. [13] who demonstrated that by the end of the first lockdown, most of the Israeli pediatricians preferred to revert to in-person visits after the pandemic subsided, and preferred to base their clinical decisions on in-person visits rather telemedicine encounters. The inability to perform a virtual physical examination and the lack of visual clues, which aid physicians in identifying patients in acute conditions, are some of the reasons why pediatricians preferred to return to traditional in-person visits as soon as possible [14]. Pediatricians who use telemedicine must maintain a high level of suspicion for severe illnesses.

As the first lockdown restrictions were lifted in Israel, the face-to-face pediatric visits increased rapidly, suggesting that parents

may also have preferred in-person visits since they were usually the ones who made the visit choice. Our data from a large PCHC support this preference and suggest that the large increase in the use of telemedicine was preferred only as a temporary solution during the lockdown period. The sustained increase in phone visits after lockdown relaxation compared to pre-lockdown levels probably reflects the continuing policy of social distancing even after lockdown relaxation. Grossman et al. [13] reported that the main early adopters of telemedicine technology were the physicians who will likely preferred the frequent use of telemedicine services even after the pandemic has resolved [14]. Gamus and colleagues [15] concluded that the greater management acceptance of telemedicine by decision makers and greater willingness to fund its deployment may lead to accelerated dissemination of the technology to cope with the ever-growing needs of the Israeli healthcare system, and hence allow quick response in times where face-to-face visits are not accessible.

Potential limitations of telemedicine include situations in which in-person visits are more appropriate due to urgency, underlying health conditions, or the necessity to perform an adequate physical examination. There are also logistical limitations due to limited access of some patients to technological devices (e.g., smartphone, tablet, computer), which are needed for a telemedicine visit or connectivity issues. Other patients or providers may not be comfortable with the technology needed for telemedicine or may not agree to the impersonality of a telemedicine consultation.

Social distancing policies enacted in Israel during the COVID-19 pandemic largely removed children from school, daycare facilities, and other contact with peers, which resulted in a significant decrease in the diagnosis of common infectious diseases among children. The prevalence of each condition was significantly lower during the social distancing period. The smaller decrease in diagnosis for urinary tract infection, an infectious but generally not contagious disease, suggests that changes in care-seeking behavior had a relatively modest effect on the other observed declines.

Hatoun and co-authors [16] also reported a profound decrease in the occurrence of common pediatric infectious diseases in Massachusetts due to social distancing policies. They also reported that 3 of the studied diseases, namely, influenza, croup, and bronchiolitis, essentially disappeared with social distancing [16]. The transmission of common infectious diseases decreased with social distancing and these data demonstrate the extent to which transmission of common pediatric infections can be altered when close contact with other children is eliminated. This reduction can be attributed to a decline in the prevalence of the conditions, or a choice not to seek care when the conditions occurred [17].

Gavish and colleagues [18] reported a decrease in the number of hospitalization due to bacterial infection, especially regarding skin and osteoarticular infections. A general decrease in the number of ED referrals and number of hospitalizations was

also reported during the 2019 COVID-19 pandemic [19,20].

Our study was limited, first because we only included information from a single representative week of each month to analyze telemedicine utilization and infectious diseases during the beginning of the outbreak and first lockdown. We only had general visit numbers for the remainder of the year. Nevertheless, we were still able to capture statistically significant differences. Second, this study represented findings from a large PCHC that had enough pediatricians to perform work in two shifts during the lockdown period and these results might not be generalizable to smaller primary care community-based clinics with fewer resources.

CONCLUSIONS

There was a rise in the use of telemedicine technologies during the first COVID-19 lockdown in Israel. We noted that the transmission of common infectious diseases decreased with social distancing. As office visits, ED referrals, and hospital admissions declined, telemedicine proved to be the tool of choice for maintaining continuity of care during stay-at-home orders. After the end of the first lockdown, there was a rebound in the in-person visits and a decline in the telemedicine consultations. The ED referrals and hospital admissions never returned to previous year levels after the first lockdown, and the number of clinical encounters continued to fluctuate for the rest of the year during the second and third lockdowns.

Correspondence

Dr. V. Shkalim Zemer

Clalit Health Services, Petah Tikva 4972339, Israel

Phone: (972-3) 910-1200

Fax: (972-3) 910-1201

email: shine6@walla.co.il

References

1. Rasmussen SA, Thompson LA. Coronavirus disease 2019 and children: what pediatric health care clinicians need to know. *JAMA Pediatr* 2020; 174: 743-4.
2. Appel S, Kaidar-Person O, Lawrence YR, et al. The coronavirus pandemic in Israel: implications for radiation oncology departments. *IMAJ* 2020; 22: 211-3.
3. Hatoun J, Correa ET, Donahue SMA, Vernacchio L. Social distancing for COVID-19 and diagnoses of other infectious diseases in children. *Pediatrics* 2020; 146: e202006460.
4. Kanu FA, Smith EE, Offutt-Powell T, Hong R; Delaware Case Investigation and Contact Tracing Teams, Dinh TH, Pevzner E. Declines in SARS-CoV-2 transmission, hospitalizations, and mortality after implementation of mitigation measures- Delaware, March-June 2020. *MMWR Morb Mortal Wkly Rep* 2020; 69: 1691-4.
5. Thornton J. Covid-19: A&E visits in England fall by 25% in week after lockdown. *BMJ* 2020; 369: m1401.
6. Kocher KE, Macy ML. Emergency department patients in the early months of the coronavirus disease 2019 (COVID-19) pandemic-What have we learned? *JAMA Health Forum* 2020; 1: e200705.
7. Hartnett KP, Kite-Powell A, DeVies J, et al; National Syndromic Surveillance Program Community of Practice. Impact of the COVID-19 pandemic on emergency department visits - United States, January 1, 2019-May 30, 2020.

- MMWR Morb Mortal Wkly Rep 2020; 69: 699-704.
8. Wong LE, Hawkins JE, Langness S, Murrell KL, Iris P, Sammann A. Where are all the patients? Addressing Covid-19 fear to encourage sick patients to seek emergency care. *NEJM Catalyst*. Published online 14 May 2020. [Available from <https://catalyst.nejm.org/doi/full/10.1056/CAT.20.0193>]. [Accessed 12 May 2020].
 9. Mehrotra A, Chernew M, Linetsky D, Hatch H, Cutler DA. The impact of the COVID-19 pandemic on outpatient visits: a rebound emerges. The Commonwealth Fund. Published online 19 May 2020. [Available from <https://www.commonwealthfund.org/publications/2020/apr/impact-covid-19-outpatient-visits>]. [Accessed 12 May 2020].
 10. American Telemedicine Association. What is telemedicine? [Available from <https://www.americantelemed.org/ata-news/what-is-telemedicine-exactly>]. [Accessed 12 May 2020].
 11. Grossman Z, Barak S, Tzimmerman D, et al; Israeli Pediatric Association. [Guidance for community pediatricians, March 20, 2020]. [Available from <https://www.pediatrics.org.il/images/covid-19-ped.pdf>]. [Accessed 4 June 2020]. [Hebrew].
 12. Czerninski R. COVID-19 crisis and the opportunities to advance telemedicine. *IMAJ* 2020; 22: 527-8.
 13. Grossman Z, Chodick G, Reingold SM, Chapnick G, Ashkenazi S. The future of telemedicine visits after COVID-19: perceptions of primary care pediatricians. *Isr J Health Policy Res* 2020; 9: 53.
 14. Salk ED, Schriger DL, Hubbell KA, Schwartz BL. Effect of visual cues, vital signs, and protocols on triage: a prospective randomized crossover trial. *Ann Emerg Med* 1998; 32: 655-64.
 15. Gamus A, Chodick G. Telemedicine after COVID-19: the Israeli perspective. *IMAJ* 2020; 22: 467-9.
 16. Hatoun J, Correa EM, Donahue SMA, Vernacchio L. Social distancing for COVID-19 and diagnosis of other infectious diseases in children. *Pediatrics* 2020; 146: e2020006460.
 17. Isba R, Edge R, Jenner R, Broughton E, Francis N, Butler J. Where have all the children gone? Decreases in pediatric emergency department attendances at the start of the COVID-19 pandemic of 2020. *Arch Dis Child* 2020; 105: 704.
 18. Gavish R, Krause I, Goldberg L, et al. A drop in number of hospitalizations among children with bacterial infections during the COVID-19 pandemic. *Pediatr Infect Dis J* 2021; 40: e39-41.
 19. Barten DG, Latten GHP. Re: 'Non-Covid-19 visits to emergency departments during the pandemic: the impact of fear'. *Public Health* 2020; 185: 47.
 20. Kadambari S, Abo YN, Phuong LK, Osowicki J, Bryant PA. Decrease in Infection-related hospital admissions during COVID-19: why are parents avoiding the doctor? *Pediatr Infect Dis J* 2020; 39: e385-6.

Capsule

Antibody evasion properties of SARS-CoV-2 Omicron sublineages

Continuing surveillance of the evolution of Omicron has since revealed the rise in prevalence of two sublineages, BA.1 with an R346K alteration (BA.1+R346K, also known as BA.1.1) and B.1.1.529.2 (BA.2), with the latter containing 8 unique spike alterations and lacking 13 spike alterations found in BA.1. Iketani and colleagues to included antigenic characterization of these new sublineages. Polyclonal sera from patients infected by wild-type SARS-CoV-2 or recipients of current mRNA vaccines showed a substantial loss in neutralizing activity against both BA.1+R346K and BA.2, with drops comparable to that already reported for BA.1. These

findings indicate that these three sublineages of Omicron are antigenically equidistant from the wild-type SARS-CoV-2 and thus similarly threaten the efficacies of current vaccines. BA.2 also exhibited marked resistance to 17 of 19 neutralizing monoclonal antibodies tested, including S309 (sotrovimab), which had retained appreciable activity against BA.1 and BA.1+R346K. This finding shows that no authorized monoclonal antibody therapy could adequately cover all sublineages of the Omicron variant, except for the recently authorized LY-CoV1404 (bebtelovimab).

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Eitan Israeli

Capsule

SARS-CoV-2 is associated with changes in brain structure in UK Biobank

Douaud et al. investigated brain changes in 785 participants of UK Biobank (aged 51–81 years) who were imaged twice using magnetic resonance imaging, including 401 cases who tested positive for infection with SARS-CoV-2 between their two scans, with 141 days on average separating their diagnosis and the second scan, as well as 384 controls. The availability of pre-infection imaging data reduces the likelihood of pre-existing risk factors being misinterpreted as disease effects. The authors identified significant longitudinal effects when comparing the two groups, including a greater reduction in grey matter thickness and tissue contrast in the orbitofrontal cortex and parahippocampal gyrus; greater changes in markers of tissue damage in regions that are

functionally connected to the primary olfactory cortex; and a greater reduction in global brain size in the SARS-CoV-2 cases. The participants who were infected with SARS-CoV-2 also showed on average a greater cognitive decline between the two time points. Importantly, these imaging and cognitive longitudinal effects were still observed after excluding the 15 patients who had been hospitalised. These mainly limbic brain imaging results may be the in vivo hallmarks of a degenerative spread of the disease through olfactory pathways, of neuroinflammatory events, or of the loss of sensory input due to anosmia.

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Eitan Israeli