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ORIGINAL RESEARCH

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Modified body mass index *z*-scores in children in New York City during the COVID-19 pandemic

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Objectives: Determine whether the negative impact of the COVID-19 pandemic on weight gain trajectories among children attending well-child visits in New York City persisted after the public health restrictions were reduced.

Study Design: Multicenter retrospective chart review study of 7150 children aged 3–19 years seen for well-child care between 1 January 2018 and 4 December 2021 in the NYC Health and Hospitals system. Primary outcome was the difference in annual change of modified body mass index *z*-score (mBMIz) between the pre-pandemic and early- and late-pandemic periods. The mBMIz allows for tracking of a greater range of BMI values than the traditional BMI *z*-score. The secondary outcome was odds of overweight, obesity, or severe obesity. Multivariable analyses were conducted with each outcome as the dependent variable, and year, age category, sex, race/ethnicity, insurance status, NYC borough, and baseline weight category as independent variables.

Results: The difference in annual mBMIz change for pre-pandemic to early-pandemic = 0.18 (95% confidence interval [CI]: 0.15, 0.20) and for pre-pandemic to late-pandemic = 0.04 (95% CI: 0.01, 0.06). There was a statistically significant interaction between period and baseline weight category. Those with severe obesity at baseline had the greatest mBMIz increase during both pandemic periods and those with underweight at baseline had the lowest mBMIz increase during both pandemic periods.

Conclusion: In NYC, the worsening mBMIz trajectories for children associated with COVID-19 restrictions did not reverse by 2021. Decisions about continuing restrictions, such as school closures, should carefully weigh the negative health impact of these policies.

KEYWORDS
BMI, modified BMI *z* score, obesity, pandemic NYC, restrictions

Abbreviations: BMI, body mass index; CDC, Centers for Disease Control and Prevention; CI, confidence interval; COVID-19, coronavirus disease 2019; EHR, electronic health records; ICD-10, International Classification of Diseases, tenth revision; mBMIz, modified body mass index z-score; NYC, New York City; NYCHHC, New York City Health and Hospitals; ZIP, zone improvement plan.

Risa Bochner and Renee Bargman are senior co-authors.

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1 | INTRODUCTION

New York City (NYC) was an early epicentre of coronavirus disease 2019 (COVID-19) and closures of schools,[1] non-essential businesses, playgrounds, and other recreational facilities were implemented in March 2020.[2] After 3 months, partial reopening began,[3] but public schools relied on remote or hybrid learning platforms with extracurricular activities suspended through the summer of 2020 and the entire 2020–2021 school year.[4] Although schools reopened for the 2021–2022 school year, ongoing waves of new cases raise concerns about whether or not to consider closing schools again.

Understanding the full health impact of the restrictions during the COVID-19 pandemic is critical for policy makers.[5,6] Studies suggest that health behaviours are poorer in children during times when they are not in school because they have fewer opportunities for healthy eating and physical activities.[7–9] Research on the impact of pandemic closures shows students had reduced physical activity[10,11] and increased consumption of unhealthy foods,[12–15] raising concerns about the childhood obesity epidemic.[10]

Several studies examined pandemic-related changes in body mass index (BMI) trajectories for children and adolescents,[16–18] and three patterns are emerging.[19] First, these studies consistently show that American children tended to gain excessive weight during the pandemic.[16–19] Second, the impact of the pandemic on weight gain differed by sociodemographic characteristics, especially race/ethnicity, age, and gender.[16] Finally, pandemic BMI trajectories may differ by pre-pandemic weight category, with those who were in the highest weight categories experiencing the greatest BMI acceleration during the pandemic.[16,17,19] However, it was anticipated that, as schools and other facilities reopened, these patterns would be reversed.

The current study explored the impact of early (2020) and late (2021) COVID-19 pandemic-related activity restrictions on modified BMI *z*-score (mBMIz) trajectories of patients aged 3–19 years, who received healthcare from a NYC public safety-net hospital system through December 2021. We also examined whether the odds of having overweight, obesity, or severe obesity were increased during the early-pandemic and late-pandemic relative to the pre-pandemic period (2018–2019). Finally, we explored whether sociodemographic factors including baseline weight category, age category, sex, race/ethnicity, and insurance status modified the effect of the early- and late-pandemic periods on these outcomes.

2 | METHODS

2.1 | Study design and sample

This is a multicenter, retrospective chart review study of children and adolescents aged 3–19 years who received well-child care at NYC Health and Hospitals (NYCHHC) between 1 January 2018 and 4 December 2021. NYCHHC is a public safety-net hospital system serving over 1 million New Yorkers yearly in over 70 locations across the city's five boroughs. The Biomedical Research Alliance of New York Institutional Review Board approved the study.

We identified patients using electronic health records (EHR) from 32 NYCHHC paediatric ambulatory care facilities. The study sample included all paediatric patients who attended an annual well-child visit with height and weight data recorded at a NYCHHC ambulatory care facility 13 June to 31 December 2020, and who had attended similar well-child visits in each of the previous 2 years. We also followed-up patients who had a well-child visit in 2021.

Well-child visits were identified using the International Classification of Diseases, tenth revision (ICD-10) diagnoses (ICD-10 codes Z00.121 and Z00.129). In some cases, more than one visit in a year was coded as a well-child visit. The last well-child visit in any calendar year was used in the current analysis.

A total of 10 702 children had eligible visits in 2018, 2019, and 2020. We excluded 2383 children with chronic health conditions that affect baseline adiposity (Cushing's Syndrome, ICD-10 E24.0 to E24.9; hypothyroidism, ICD-10 E03.0 to E03.9; hyperthyroidism, ICD-10 E05.0 to E05.9; cancer, ICD-10, C80.1; inflammatory bowel disease, ICD-10 K51. 90; celiac disease ICD-10 K90.0; eating disorders ICD-10 F50.0 to F50.9; and psychiatric disorders ICD-10 F01 to F99).[20] We also excluded 65 children whose BMIs were extremely high or extremely low, likely indicating errors in recording either height or weight, and 1119 children whose height measures decrease from 1 year to the next (15 fit both those criteria). Since we could not validate height and weight records in EHR database with any external source, we conservatively report on the analyses that excluded all 1169 children with non-physiologic height or weight data. The final analysis sample comprised 7150 patients. Of these patients, 4554 (63.6%) had a well-child visit in 2021.

2.2 | Study measures

Data were extracted from each well-child visit including: date of visit, age in months, height in cm, weight in kg, sex (male and female), insurance status, borough of residence, and, when available, zone improvement plan (ZIP) code of residence. BMI was calculated using recorded height and weight (weight in kg/height in m^2), age and sex using a SAS program and 2000 Centers for Disease Control and Prevention (CDC) growth charts for the United States,[21,22] as well as BMI percentile, BMI *z*-score, and mBMIz. The main outcome for the current study was based on mBMIz. The BMI *z*-score is a measure of relative weight, adjusted for age and sex, using the U.S. population as the standard reference group.[23] The mBMIz is similar to the BMI *z*-score, except it is calculated based on a fixed standard deviation, which makes it more useful in populations that include people with extreme BMIs for age.[24–28] The BMI is expressed relative to the median BMI in units of ½ the distance between −2 and +2 *z* scores.[22] This measure is commonly used for comparisons of weight across group and monitoring trajectories over time.[24–26,28,29] The mBMIz scores were calculated using the SAS program for the CDC growth charts.[22]

The main outcome measure was annual change in mBMIz, which we calculated for three time periods: change during the pre-pandemic (2018–2019), early-pandemic (2019–2020), and late-pandemic (2020–2021) periods. To calculate this measure, we calculated mBMIz for each of the four visits (2018, 2019, 2020, and 2021) and then calculated the difference for the visits associated with each of the three periods. Because the time period between visits for each child differed, we followed the procedure described by Cheng et al.[29] and divided the difference in mBMIz scores by the number of months between visits, then multiplied this by 12 to obtain an average annual change in mBMIz for each period.

The secondary outcome measure was a binary measure calculated for each of the 4 years: having overweight, obesity, or severe obesity versus having underweight or normal weight as defined by Barlow et al.[30] and derived from BMI percentiles. Overweight was defined as having a BMI percentile between 85% and 94.9%; obesity was between 95% and 98.9%; and severe obesity was greater than 99%, while underweight was defined as having a BMI percentile less than 5% and normal weight was between 5% and 84.9%.

2.3 | Covariates

Sociodemographic variables used in these analyses included continuous age in years, age group (under 5 years, 5 to less than 8 years, 8 to less than 15 years, and 15 years or older), sex (male or female), race/ethnicity (Hispanic, non-Hispanic Black, non-Hispanic White, non-Hispanic Asian, non-Hispanic Native Hawaiian/Pacific Islander), insurance (governmental, commercial, other, and no insurance/no data), and residential NYC borough. ZIP code data were matched with 2019 American Community Survey data to obtain ZIP code level median household income.[31] ZIP code data were also matched with an online NYC Department of Health and Mental Hygiene COVID database[32] to obtain ZIP code level COVID-19 death rates through August 2020. Residential ZIP codes were categorized as having a high COVID-19 death rate if the rate was greater than the NYC ZIP code median.

2.4 | Data analyses

We first describe the sociodemographic and clinical data using frequencies and percentages calculated for categorical data, and means and standard deviations or medians and interquartile range calculated for continuous data. We then report on weight, BMI, BMI percentile, BMI *z*-score, and mBMIz for each year, as well as annual change in mBMIz in the pre-pandemic (2018–2019), the early-pandemic (2019–2020), and the late-pandemic periods (2020–2021). We conducted linear regression analyses using generalized estimating equations to tests for the statistical significance of annual change in mBMIz differences for each of the two pandemic periods compared with the pre-pandemic period. In these analyses, annual change in the mBMIz associated with each period was the dependent variable and independent variables included period (pre-pandemic, early-pandemic, late-pandemic), age category, sex, race/ethnicity, insurance status, and baseline (2018) weight category. The coefficients associated with each period can be interpreted as the difference in the period-level increase or decrease in mBMIz between the pre-pandemic period and that period, adjusting for other characteristics. Subsequent analyses tested for the statistical significance of the differences in the observed change by baseline (2018) weight category by including an interaction term for period by baseline weight category.

Analyses were first conducted in the full sample ($N = 7150$), examining the difference in mBMIz for the early-pandemic period, and then repeated in the subsample that had 2021 data ($N = 4554$) to include examination of the differences in mBMIz for both early- and late-pandemic periods. The coefficients associated with the early-pandemic period and each demographic characteristic for the full sample ($N = 7150$) and subsample ($N = 4554$) were essentially the same, so we present data for the full model except when reporting on the late-pandemic period. Finally, the above analyses were repeated with having overweight, obesity, or severe obesity versus having underweight or normal weight for each year as the dependent variable. Logistic regression analyses using generalized estimating equations were conducted, and the resulting exponentiated coefficients associated with 2019, 2020, and 2021 can be interpreted as odds ratios (ORs) of odds of being in the overweight, obesity, or severe obesity weight category in that year relative to 2018.

3 | RESULTS

The mean age of the 7150 children in our sample was 8.3 years (standard deviation = 3.3). About half (47.7%) of the children were female, and most were Hispanic (37.9%) or non-Hispanic Black (36.6%). Most children in our sample had government insurance (83.8%). All five boroughs were represented. Only 65 children (0.9%) resided outside of the NYC area, which included Westchester, Pennsylvania, and New Jersey (data not included). The median household income was $40 449. Of those living in NYC, 76% resided in a ZIP code with a COVID-19 death rate higher than the NYC mean rate. At baseline (2018), the majority were in the normal weight category (53.2%), 288 (4.0%) were in the underweight category, and the rest were in overweight ($N = 1227$, 17.2%), obesity ($N = 1323$, 18.5%), or severe obesity ($N = 505$, 7.1%) categories (Table 1).

Table 2 shows the mean weight, BMI, BMI percentile, mBMIz, months of observation, and the proportion of the sample with overweight, obesity or severe obesity in each year. Weight, BMI, BMI percentile, mBMIz and the proportion of the sample with overweight, obesity, and severe obesity weight status all increased over time, with the greatest increase occurring during in the early-pandemic period (Table 2).

The mean annual changes in mBMIz in the pre-pandemic, early-pandemic, and late-pandemic periods were 0.02 (standard deviation = 0.7776), 0.19 (standard deviation = 0.50), and 0.06 (standard deviation = 0.57), respectively. This pattern differed by baseline (2018) weight category. During the pre-pandemic period (2018–2019), the

TABLE 1 Demographic and clinical characteristics of 7150 children and adolescents who had well-child visits each year between 2018 and 2021 in New York City

Characteristic	*N* (percent of 7150)
Age group	
Less than 5 years	1308 (18.3)
5 to less than 8 years	2104 (29.4)
8 to less than 15 years	3537 (49.3)
15–18 years	211 (3.0)
Age in years at baseline (mean, standard deviation)	8.3 (3.3)
Female sex	3409 (47.7)
Race/ethnicity	
Hispanic	2713 (37.9)
Non-Hispanic Black	2615 (36.6)
Non-Hispanic Asian	300 (4.2)
Non-Hispanic white	66 (0.9)
Non-Hispanic Native Hawaiian/Pacific Islander	26 (0.4)
Missing	1430 (20.0)
Insurance	
Government	5989 (83.8)
Commercial	869 (12.2)
Other	99 (1.4)
Missing/none	193 (2.7)
New York City borough	
Bronx	2953 (41.3)
Brooklyn	2071 (29.0)
Manhattan	1177 (16.5)
Queens	860 (12.0)
Staten Island	24 (0.3)
Not residing in New York City	65 (0.9)
Median household income for ZIP code (25th, 75th percentile)[a]	40 449 (28 760, 52 409)
Number of children residing in a ZIP code with high COVID death rate[b]	5468 (76.5)
BMI category in 2018	
Underweight	288 (4.0)
Normal	3807 (53.2)
Overweight	1227 (17.2)
Obesity	1323 (18.5)
Severe obesity	505 (7.1)

Abbreviations: BMI, body mass index (calculated as weight in kg divided by height in m^2).
[a]$N = 7122$.
[b]ZIP code confirmed death rate greater than NYC median 372.4 ($N = 7073$).

TABLE 2 Weight, BMI, BMI percentile and modified BMI *z*-score between 2018 and 2021 in New York City

Characteristic	Mean (standard deviation)	Percent increase from previous year (%)
Weight (kg)		
2018	34.67 (17.44)	
2019	38.95 (18.8)	12.3
2020	45.86 (20.87)	17.7
2021	48.85 (21.05)	6.5
BMI		
2018	19.16 (4.63)	
2019	19.80 (4.96)	3.3
2020	21.36 (5.60)	7.9
2021	21.90 (5.74)	2.5
BMI percentile		
2018	67.61 (30.87)	
2019	68.72 (30.52)	1.6
2020	73.42 (29.01)	6.8
2021	74.26 (28.95)	1.1
BMI *z*-score (modified)		
2018	0.65 (1.42)	
2019	0.67 (1.39)	3.1
2020	0.90 (1.42)	34.3
2021	0.94 (1.43)	4.4
Months of observation		
Pre-pandemic (2018–2019)	11.33 (3.70)	
Pandemic (2019–2020)	14.27 (3.24)	
Recent (2020–2021) ($N = 4554$)	10.46 (2.54)	
Overweight, obesity, or severe obesity	*N* (percent of total)	
2018	3055 (42.7)	
2019	3226 (45.1)	
2020	3729 (52.2)	
2021	2460 (54.0)	

Abbreviations: BMI, body mass index (calculated as weight in kg divided by height in m^2). $N = 7150$ for 2018, 2019, 2020; $N = 4554$ for 2021.

mean annual mBMIz change showed improvement for all categories, except those in the normal weight category. Those in the underweight category gained weight on average (mean annual mBMIz change = 0.37, SD = 1.02). Those in the overweight, obese, and extremely obese categories remained stable or lost weight on average (overweight mean change = −0.00, SD = 0.56; obese mean change = −0.08, SD = 0.62; extremely obese change = −0.36, SD = 1.29). Those in the normal weight category also gained weight on average (mean change = 0.08, SD = 0.75).

During the early-pandemic period (2019–2020), the mean annual mBMIz change showed deterioration for all baseline (2018) weight categories. The mean annual mBMIz for the underweight category indicated a smaller weight gain than in the pre-pandemic period (mean

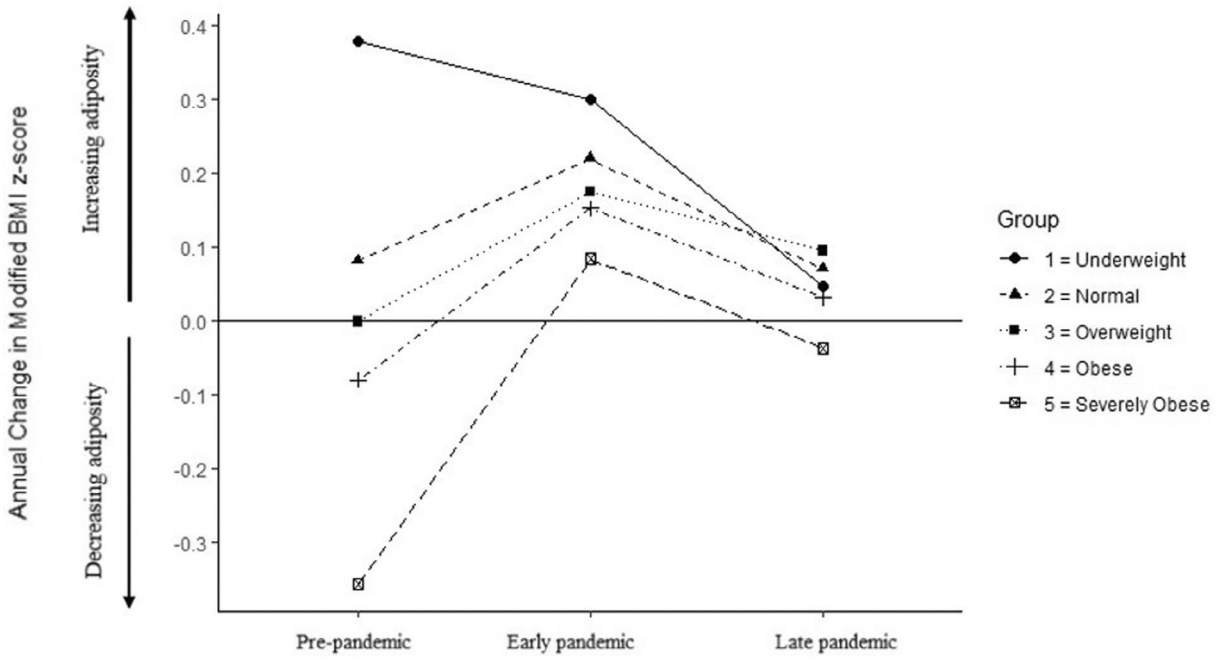

FIGURE 1 Change in annual mBMIz during the pre-pandemic, early-pandemic and late-pandemic periods by 2018 BMI category. Change in annual mBMIz during the pre-pandemic, early-pandemic and late-pandemic periods by 2018 BMI category. The 0 on the *Y*-axis represents no change in annual mBMIz, positive numbers represent increasing adiposity, and negative numbers represent decreasing adiposity

change = 0.30, SD = 0.72). All of the other categories had weight gain (normal weight mean change = 0.22, SD = 0.50); overweight mean change = 0.17, SD = 0.44; obese mean change = 0.15, SD = 0.46; extremely obese change = 0.08, SD = 0.57). The increase in the normal weight category during the early-pandemic period exceeded the observed increase during the pre-pandemic period.

During the late-pandemic period (2020–2021), the mean annual mBMIz change for all categories except the underweight category, showed improvement relative to the early-pandemic period. However, for overweight, obese and extremely obese categories, the observed change during this period did not return to the observed change during the pre-pandemic period (overweight mean change = 0.09, SD = 0.53; obese mean change = 0.03, SD = 0.53; extremely obese change = −0.04, SD = 0.71). The normal weight category showed improvement in mBMIz relative to both the early-pandemic period and the pre-pandemic period (mean change = 0.07, SD = 0.57). The underweight category had a smaller weight gain than in both the early-pandemic and pre-pandemic periods (underweight mean change = 0.05, SD = 0.72). Figure 1 illustrates these patterns.

Multivariable analyses that adjusted for age category, sex, race/ethnicity, insurance status, and baseline (2018) weight category showed that the mean difference between early-pandemic period change and the pre-pandemic change was 0.18 (95% confidence interval [CI]: 0.15, 0.20). The mean difference between the late-pandemic period change versus pre-pandemic change was 0.04 (95% CI: 0.01, 0.06). There was a significant interaction effect of period by baseline weight category ($p < 0.05$).

Finally, multivariable analyses with odds of having overweight, obesity, or severe obesity as the dependent variable, confirmed the above patterns. The OR for the baseline period (2019 relative to 2018) was 1.11 (95% CI: 1.07, 1.14), 1.48 (95% CI: 1.42, 1.54) for the early-pandemic period (2020 relative to 2018), and 1.58 (95% CI: 1.49, 1.67) for the late-pandemic period (2021 relative to 2018).

4 | DISCUSSION

The findings from this large sample of children and adolescents from a NYC public hospital system, the epicentre of the first wave of COVID-19 in the United States, demonstrated an accelerated rate of excess weight gain during the early-pandemic (through 2020) compared with baseline and, for the first time, persistence of these unhealthy trends into the late-pandemic (through 2021), although of a smaller magnitude. The mean annual mBMIz in the sample was relatively unchanged in the pre-pandemic years (mBMIz = 0.65 in 2018 and mBMIz = 0.67 in 2019), increased to 0.90 in 2020 and to 0.94 in 2021. This corresponds to an increase in the mean BMI percentile of the sample from 69th to 73rd percentile in just 1 year and a subsequent increase to the 74th percentile in the last year. Furthermore, during the early-pandemic, children and adolescents were 1.48 times more likely to have overweight, obesity or severe obesity compared with their pre-pandemic (2018) weight, and in late-pandemic this rose to 1.58 times more likely compared to baseline.

These findings reinforce and expand on published studies of children and adolescents during the first year of the COVID-19

pandemic that found increased weight gain associated with the pandemic.[16–19,33] Accelerated weight gain during the early-pandemic period was present for children and adolescents with normal weight, overweight, and obesity at baseline but was greatest for those with severe obesity. No studies to date have followed weight trajectories into the late-pandemic through 2021, and our study showed that while weight gain persisted at a lower magnitude, the odds of having overweight, obesity, and severe obesity weight status continued to increase.

This study adds to the growing evidence of an alarming and sustained worsening of childhood obesity secondary to the COVID-19 pandemic that has public health implications. Policies to close the schools were made for safety reasons (to prevent the ongoing spread of the illness), but are likely to be associated with unintended consequences including worsening weight changes. It is increasingly clear that children who were at most risk prior to the pandemic have suffered the worst consequences of the shutdowns in regards to their cardiometabolic health in addition to learning loss and psychological distress.[34,35] Since improvement in weight in children and adolescents has historically proven to be difficult, this trend is alarming. The findings from 2021 show that a partial "return to normal" might not quickly ameliorate the problem. Partial return to normal in late-pandemic NYC meant that while most businesses have been allowed to reopen, most public and charter school children continued to attend school remotely without the benefit of organized afterschool and other activities. Targeted interventions may be necessary to fully address the consequences of decreased access to healthy food and increased sedentary time during the pandemic. Specifically, it stands to reason that in order to reverse the trends post-pandemic, public health needs to focus on doing exactly the reverse of a lockdown—increasing availability of healthy food, increasing in-school and afterschool activities and exercise and minimizing screen time. Perhaps after the pandemic schools may consider adding more recess and physical activity time in the day. Furthermore, decisions to close schools again in the future should both balance these negative health consequences for children and adolescents and perhaps policy makers might consider implementing prevention strategies in the event future closures are needed.

Our study additionally showed that there was a relatively smaller weight gain during the early- and late-pandemic periods for children and adolescents who had underweight at baseline, indicating a decrease in catch-up growth in this sub-group compared to the 2018–2019 years. A possible explanation for this is increased food insecurity during the COVID-19 pandemic. Feeding America projected an increase of 17 million Americans becoming food insecure in 2020[36] and Niles et al.[37] found a 32.3% increase in household food insecurity with 35.5% of households classified as newly food insecure. Pre-pandemic, nearly, 35 million children received free meals in schools daily, and despite the attempts to still provide meals, many families ended up forgoing this vital assistance.[38] An additional factor may be that the underweight group may include many children with medical and developmental disabilities such as cerebral palsy or autism who normally receive school based services,[39] which they had to forgo during school closures. It is possible that their weight gain suffered because they were missing a large component of their care. The association between food insecurity with undernutrition and stunting in children and adolescents is well-established.[40] In this study, the underweight category was the only one to experience further deterioration in 2021, raising the spectre that more children are food insecure in late-pandemic as family's resources become exhausted. Paradoxically, food insecurity has also been associated with paediatric obesity and may play a role in this study's findings of worsening obesity among those already suffering from overweight.[41] Food insecurity was not measured in this study and further research is required to understand the relationship between the observed trends and food insecurity.

A limitation of this study is that children who did not have data for at least 3 years of the study period were excluded, and 2021 data were only available for about two-thirds of participants. It is possible that these children not included in the analysis exhibit a different pattern of weight gain and deserve further study. Another limitation is that our retrospective study was based solely on EHR data and 1169 children were excluded likely due to measurement or input errors in the EHR. The reasons for accelerating mBMIz trajectories during lockdown could not be identified and developing strategies to reverse these trends may require a deeper understanding of the underlying etiologies. There may be value in examining whether comorbidities affect these finding and whether we see a change in clinical and laboratory abnormalities such as prediabetes, transaminitis, and hypertension.

The major strength of this study is its large sample size. The data are based on objectively measured and recorded anthropometric measures. In addition, the study outcomes were tracked from 2018 to 2021 and is the first study to date to include 2021 data. This study, while having a smaller population than some of the others,[16,19] followed a population of children and adolescents that experienced the pandemic under similar circumstances—living in small, urban apartments without private outdoor space,[42] attending schools in a district that had the same policies for all students,[43] living in a city that had strong mitigation policies and mandates.[44]

5 | CONCLUSION

Among a cohort of children and adolescents attending well-child visits within a public hospital system in NYC, social distancing measures implemented during the COVID-19 pandemic were associated with worsening mBMIz trajectories. Although the rate of unhealthy weight gain slowed in the late-pandemic period, excessive weight gain persisted for children and adolescents with overweight, obesity, and severe obesity while catch-up weight gain decreased further in children in the underweight category. We have to grapple with and reverse the unintended consequences of public health measures that inflicted harm on children by developing interventions that will arrest and reverse these trends.

AUTHOR CONTRIBUTIONS

Assia Miller, Risa Bochner and Renee Bargman conceptualized the study, designed the data collection tools, collected data, drafted the

initial manuscript, reviewed, and revised the manuscript. Nancy Sohler and Rose Calixte contributed to study design, performed the data analysis, reviewed and revised the manuscript. Vivian Chin, Vatcharapan Umpaichitra, Warren Seigel, Lee Waldman, Sundari Periasamy, Mahrukh Bamji, Nikita Nagpal, Carol Duh-Leong, Makhmood Reznik, Mary Messito, and Ninad Desai, Cameron Chan, Elman Shalmiyev and Natalia Novikova contributed to study design, reviewed, and revised the manuscript. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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