ORIGINAL ARTICLE

Consequences of Undervaccination — Measles Outbreak, New York City, 2018–2019

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ABSTRACT

BACKGROUND

Measles was declared eliminated in the United States in 2000, but the risk of outbreaks owing to international importations remains. An outbreak of measles in New York City began when one unvaccinated child returned home from Israel with measles; onset of rash occurred on September 30, 2018, 9 days after the child returned home.

METHODS

We investigated suspected cases of measles by conducting interviews, reviewing medical and immunization records, identifying exposed persons, and performing diagnostic testing. Measles–mumps–rubella (MMR) vaccine (given as either MMR or measles–mumps–rubella–varicella vaccine and collectively referred to as MMR vaccine) uptake was monitored with the use of the Citywide Immunization Registry. The total direct cost to the New York City Department of Health and Mental Hygiene was calculated.

RESULTS

A total of 649 cases of measles were confirmed, with onsets of rash occurring between September 30, 2018, and July 15, 2019. A majority of the patients (93.4%) were part of the Orthodox Jewish community, and 473 of the patients (72.9%) resided in the Williamsburg area of Brooklyn, New York. The median age was 3 years; 81.2% of the patients were 18 years of age or younger, and 85.8% of the patients with a known vaccination history were unvaccinated. Serious complications included pneumonia (in 37 patients [5.7%]) and hospitalization (in 49 patients [7.6%]); among the patients who were hospitalized, 20 (40.8%) were admitted to an intensive care unit. As a result of efforts to promote vaccination, the percentage of children in Williamsburg who received at least one dose of MMR vaccine increased from 79.5% to 91.1% among children 12 to 59 months of age. As of September 9, 2019, a total of 559 staff members at the Department of Health and Mental Hygiene (7% of the agency) had been involved in the measles response. The cost of the Department of Health and Mental Hygiene response was $8.4 million.

CONCLUSIONS

Importation of measles and vaccination delays among young children led to an outbreak of measles in New York City. The outbreak response was resource intensive and caused serious illness, particularly among unvaccinated children.

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A list of investigators is provided in the Supplementary Appendix, available at NEJM.org.

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Before licensure of the first measles vaccine in 1963, approximately 500,000 cases of measles and 500 measles-related deaths were reported annually in the United States.[1] Measles was declared eliminated in the United States in 2000.[2] However, the risk of reintroduction and transmission is a constant threat because of continued measles activity in much of the world.[3-5] Periodic measles outbreaks reported in the United States show the consequences of this ongoing risk.[1,4]

In New York City, an international gateway for travel, imported cases of measles are identified on a regular basis, and several measles outbreaks have been reported since 2000. The last two outbreaks occurred in 2013 and 2014, with 58 and 25 cases, respectively.[6,7] The most recent outbreak began when one unvaccinated child returned home from Israel with measles; onset of rash occurred on September 30, 2018, 9 days after the child returned home. At that time, a large measles outbreak had been occurring in Israel.[8] Additional measles importations from Israel and from parts of Europe to New York City ignited what has become the largest measles outbreak in the United States since 1992. We describe the epidemiologic features of this outbreak; the control measures that were taken, including use of the public health authority; and the importance of the existing public health infrastructure in mounting an effective response.

METHODS

IDENTIFICATION OF MEASLES CASES

All cases of suspected measles that occur in the five boroughs of New York City are required to be reported immediately to the New York City Department of Health and Mental Hygiene.[9] All reports are investigated by interviewing the patient or the patient's parent or guardian, reviewing medical and immunization records, and identifying the probable source of infection. Persons born before 1957 are considered to be immune.[10] Persons (contacts) are identified as having been potentially exposed to measles if they had been in the same place at the same time (or within 2 hours) as a person contagious with measles (e.g., at an outpatient medical facility, apartment building, or school).

The New York City Public Health Laboratory performed most of the diagnostic testing for measles. Serum specimens were tested for measles-specific IgM with the use of a qualitative enzyme-linked immunosorbent assay (ELISA) and for measles-specific IgG with the use of a qualitative chemiluminescent immunoassay (the DiaSorin Liaison Measles IgG assay). Measles virus RNA was detected with the use of a real-time reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay (TaqMan RT PCR, Applied Biosystems) targeting the measles nucleoprotein gene.[11] Genotyping of the measles nucleoprotein gene in measles-positive specimens was performed at the Wadsworth Center Laboratory of Viral Diseases.[12]

An outbreak case was defined as a patient who had a rash and either laboratory evidence of infection (i.e., detection of measles virus RNA or measles-specific IgM) or an epidemiologic link to a laboratory-confirmed case and in whom the onset of symptoms occurred on or after September 30, 2018. Patients with measles considered to be part of the outbreak included New York City residents and international visitors to New York City who were either part of the Orthodox Jewish community or resided in, or were traceable to, a neighborhood with community transmission; domestic visitors to New York City were not included in the count. Certain patients for whom clinical information was not available were included in the case count if the diagnostic tests (RT-PCR assay or assay to detect IgM) were positive and if they otherwise met the criteria described above. Because of the potential for a false positive IgM assay, patients who lacked clinical information and had only a positive IgM assay were included only if they were confirmed to be unvaccinated, since the likelihood of a true infection would increase in the absence of vaccination.

No financial or in-kind funding was provided to conduct this evaluation beyond regular city tax levy funds and routine funding from the Centers for Disease Control and Prevention for surveillance activities and emergency preparedness.

MEASLES–MUMPS–RUBELLA AND MEASLES–MUMPS–RUBELLA–VARICELLA VACCINATION

In New York City, all vaccine doses administered to persons 18 years of age or younger are required to be reported to the Citywide Immunization Registry — a database of birth and im-

munization records — within 14 days after administration.[13,14] The Citywide Immunization Registry was used to obtain the immunization status of cases and contacts.

For population-level analyses, the percentage of children 12 to 59 months of age in New York City who had received one or more doses of measles-containing vaccine (given as either measles–mumps–rubella [MMR] or measles–mumps–rubella–varicella [MMRV] vaccine and collectively referred to as MMR vaccine; 1% of measles-containing vaccines reported to the Citywide Immunization Registry were not MMR or MMRV vaccine) was calculated on the basis of doses reported to the Citywide Immunization Registry. The percentage of children who had received MMR vaccine was calculated for each New York City ZIP Code. For this calculation, the numerator was the number of children 12 to 59 months of age who had received at least one valid dose of MMR vaccine, had a current address in a New York City ZIP Code, and were not reported by their caregiver as having moved out of New York City — information we obtained from the Citywide Immunization Registry — and the denominator was the 2018 New York City population estimates, which were modified to create subborough–level estimates based on the county-level interpolated intercensal population estimates from the U.S. Census Bureau.[15] MMR vaccinations in ZIP Code areas where measles had been detected were aggregated to determine neighborhood-level coverage. Coverage was mapped with ArcMap software, version 10.5.1 (Esri). Separately, the number of doses of MMR vaccine administered to children 12 to 59 months of age (on the basis of the criteria described above) was tracked; data were analyzed on a weekly basis, and the numbers of doses were compared with those from the same period in the previous year. Analyses were performed with the use of SAS software, version 9.4 (SAS Institute).

RESOURCE MOBILIZATION

To ensure a robust public health response, the Department of Health and Mental Hygiene expanded its outbreak response on the basis of the epidemiologic features of the outbreak. These efforts culminated in the full agency-wide emergency activation of its Incident Command System on March 27, 2019.[16]

COST EVALUATION

The total direct cost to the Department of Health and Mental Hygiene was calculated as the sum of inputs (i.e., supplies, materials, equipment, and services) and personnel (i.e., salary). The personnel cost included overtime pay as well as the salaries of temporary-agency personnel and staff members of the Department of Health and Mental Hygiene for time devoted to the outbreak response during regular business hours.

RESULTS

DETAILS OF THE OUTBREAK

As of September 3, 2019, when the outbreak was declared to be over (two incubation periods [42 days] after the infectious period of the last case ended), 649 cases of measles were confirmed, with onsets of rash occurring between September 30, 2018, and July 15, 2019 (Fig. 1). The median age of the patients was 3 years (range, 1 month to 70 years), and 60.1% were male. A total of 81.2% of the patients were 18 years of age or younger, and 85.8% of the patients with a known vaccination history were unvaccinated (Table 1).

A majority of the patients (93.4%) were part of the Orthodox Jewish community and resided in the Williamsburg (473 patients [72.9%]) or Borough Park (121 patients [18.6%]) neighborhood of Brooklyn. Most of the patients in both neighborhoods were children, but in Borough Park, the median age shifted from 1 year (during the period from October 2018 through January 2019) to 13.5 years (during the period from February 2019 through July 2019). The median age of the patients in Williamsburg was 3 years. In April 2019, the outbreak spread from Borough Park to neighboring Sunset Park, Brooklyn, where limited measles transmission occurred. Limited transmission also occurred in Crown Heights, Brooklyn (8 patients [1.2%]), where half the cases were in persons 18 years of age or older. Additional affected patients resided in other New York City neighborhoods but generally were associated with exposure that linked back to Williamsburg, Borough Park, or other areas outside New York City where measles was present. Among the 43 patients (6.6%) who were not part of the Orthodox Jewish community, a majority (38 patients) were Latino.

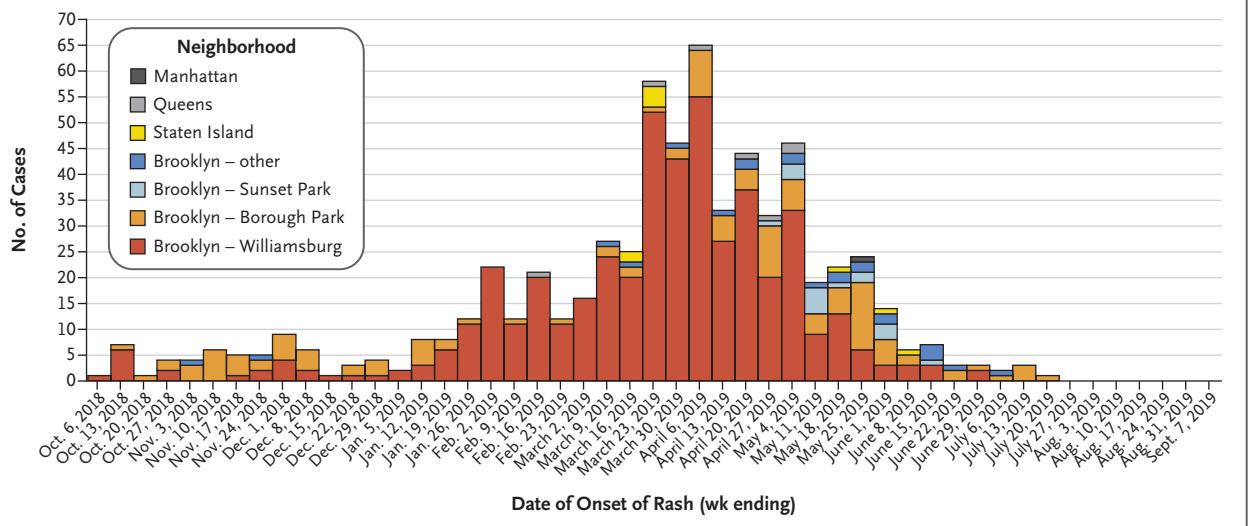

Figure 1. Numbers of Outbreak-Associated Cases of Measles.

Shown are the numbers of cases of measles according to the date of onset of rash and the neighborhood of residence in New York City. Dates are based on the following hierarchy, according to available data: date of onset of rash, date of laboratory report, and date of provider report.

Table 1. Age Group and Vaccination Status of Patients with Measles Infection.*

Age Group	Unvaccinated	One Previous Dose of MMR Vaccine†	Two Previous Doses of MMR Vaccine†	Unknown Vaccination Status	Total
			number of patients (percent)		
<6 mo	26 (4.0)	0	0	0	26 (4.0)
6 to <12 mo	74 (11.4)	2 (0.3)	0	0	76 (11.7)
1 to <5 yr	244 (37.6)	32 (4.9)	1 (0.2)	0	277 (42.7)
5 to 18 yr	129 (19.9)	6 (0.9)	10 (1.5)	3 (0.5)	148 (22.8)
>18 yr	3 (0.5)	6 (0.9)	22 (3.4)	91 (14.0)	122 (18.8)
Total	476 (73.3)	46 (7.1)	33 (5.1)	94 (14.5)	649 (100.0)

* All percentages reflect the percentage of total cases (649 patients). The measles–mumps–rubella (MMR) vaccine was given as either MMR or measles–mumps–rubella–varicella (MMRV) vaccine and collectively referred to as MMR vaccine.
† Patients were included in this category if they received MMR vaccine 21 days or more before the onset of rash or 21 days or more before diagnostic testing was performed if the onset of rash was unknown.

Complications among the 649 patients included diarrhea (14.2%), otitis media (9.7%), and pneumonia (5.7%). No deaths were reported (Table 2). Among 49 patients (7.6%) who were hospitalized, 20 (40.8%) were admitted to an intensive unit care, 10 (20.4%) underwent noninvasive mechanical ventilation, and 40 (81.6%) had more than one complication (Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). Among 37 children who were hospitalized with measles, 35 (94.6%) were confirmed to be unvaccinated; of the remaining children, neither of whom had an underlying medical condition, 1 child had received one dose of MMRV vaccine and the other child had an unknown vaccination status. The

vaccination status was unknown for all 12 hospitalized adults. Measles was reported in 3 pregnant persons at 14 weeks, 33 weeks, and 34 weeks of gestation; no complications associated with measles occurred, and all the infants were born healthy and tested negative for measles. One hospitalized child was immunocompromised. Three of 5 patients born before 1957 were hospitalized.

Among the 649 cases of measles, 564 (86.9%) were confirmed on the basis of laboratory testing, including 20 in persons for whom there was no clinical information, and 85 (13.1%) were confirmed on the basis of epidemiologic linkage to another laboratory-confirmed case. Genotype D8, one of the most common genotypes circulating worldwide,[4] was identified in all 355 outbreak-related patients in whom genotyping of the measles virus strain was performed. Ten confirmed cases of measles identified during the outbreak period were not considered to be part of the outbreak, because they occurred in persons who were not part of the Orthodox Jewish community and they were not traceable to a neighborhood with community transmission: 6 cases were internationally imported or had links to international importations (1 of which was genotype B3 [distinct from that of the outbreak]), 1 case not internationally imported was genotype B3 and 1 case was epidemiologically linked to this case, and 2 cases had no geographic or epidemiologic association with the outbreak. An additional 33 patients were investigated for measles but were not counted as having confirmed cases because they had previously received MMR vaccine and the measles vaccine strain (genotype A) was detected.

Transmission commonly occurred in settings including the home (through contact with immediate and extended family members, friends, and neighbors), schools, and childcare programs. Measles was acquired from outside New York City in 11 patients; these locations included Israel (4 patients), the United Kingdom (2 patients), Ukraine (1 patient), New York outside New York City (3 patients), and New Jersey (1 patient). A total of 40.8% of the patients were thought to have acquired the disease through community-wide transmission, with no single point source reported; the transmission setting could not be identified for 4.8% of the patients (Table 3).

Table 2. Complications in Patients with Measles Infection.*

Complication	Patients (N=649)
	no. (%)
Hospitalization	49 (7.6)†
Admission to intensive care unit	20 (3.1)
Diarrhea	92 (14.2)
Otitis media	63 (9.7)
Pneumonia	37 (5.7)
Encephalitis	0
Death	0

* All percentages reflect the percentage of total cases (649 patients). Complications are not mutually exclusive (see Table S1).
† The number of patients who were hospitalized includes 35 patients who were unvaccinated, 1 patient who received one dose of MMRV vaccine, and 13 patients whose vaccination status was unknown.

Table 3. Transmission Settings of Patients with Measles Infection.*

Source of Infection	Patients (N=649)
	no. (%)
Household member or extended family member	157 (24.2)
Neighbor in the same building or an adjacent building	92 (14.2)
School or center-based childcare program	63 (9.7)
Health care facility†	21 (3.2)
Importation	11 (1.7)
Social gathering	5 (0.8)
Home-based childcare	3 (0.5)
Work	1 (0.2)
Community‡	265 (40.8)
Unknown	31 (4.8)
Total	649 (100.0)

* All percentages reflect the percentage of total cases (649 patients). Each patient was included in only one category. Data are preliminary as of December 20, 2019.
† All cases acquired through nosocomial transmission occurred in outpatient medical facilities.
‡ Patients in this category were thought to have acquired the disease through community-wide transmission, with no single point source reported.

CONTROL MEASURES

More than 20,000 named contacts were identified, including an estimated 1000 exposures among infants younger than 1 year of age, 400 exposures among pregnant persons, and 100 exposures among potentially immunocompromised persons. Effort was made to inform contacts about the exposure either by personnel at the location of exposure (e.g., a school or medical facility) or by the Department of Health and Mental Hygiene, and the contacts were referred for postexposure prophylaxis with MMR vaccine, immune globulin, or home quarantine, as indicated.[10]

Unvaccinated children were identified with the use of the Citywide Immunization Registry; the Department of Health and Mental Hygiene and medical facility personnel then used this information to contact patients or their parents about making an appointment for MMR vaccination and to estimate MMR vaccination coverage at the health care facility level. Recommendations for MMR vaccination were revised for persons residing in, or regularly spending time in, neighborhoods of New York City in which ongoing measles transmission was present. The recommendations included an early, additional dose of MMR vaccine for infants 6 to 11 months of age (which did not count toward the routine two-dose series), an early second routine dose of MMR vaccine for children 1 to 4 years of age, and two doses of MMR vaccine for adults born in 1957 or later who did not have documentation of previous vaccination with two doses of a measles-containing vaccine or whose vaccination status was unknown.

On December 6, 2018, schools and childcare programs in Williamsburg and Borough Park were notified that all children without age-appropriate MMR vaccination or proof of measles immunity,[10] including those with medical or religious exemptions, were to be prohibited from attending school and childcare programs. Weekly audits of 101 facilities were conducted to ensure adherence to the required exclusions. Under an order of the commissioner of the Department of Health and Mental Hygiene, programs that did not adhere to the requirements were subject to fines, closure, or both. Twelve programs, including three schools and nine childcare programs, were closed temporarily during the response. An emergency order, which required MMR vaccination or proof of measles immunity for all persons living, working, or going to school in the four affected Williamsburg ZIP Code areas, was issued on April 9, 2019.[17] A total of 232 summonses were issued by the Department of Health and Mental Hygiene to individual persons for not adhering to the emergency order. Additional control measures are described in the Supplementary Appendix.

VACCINATION COVERAGE

From October 1, 2018, through September 1, 2019, a total of 188,635 doses of MMR vaccine were administered to children 12 to 59 months of age by medical providers citywide in New York City, and 11,964 doses were administered in Williamsburg; there were 23,320 more doses citywide and 4216 more doses in Williamsburg than the respective doses administered in the same time period during the previous year. The percentage of children 12 to 59 months of age in Williamsburg who received at least one dose of MMR vaccine increased from 79.5% to 91.1% between October 1, 2018, and September 1, 2019. In addition to expected peaks in MMR vaccinations associated with adherence to vaccination requirements for the start of school, several outbreak-related interventions were associated with an increase in MMR vaccinations (Fig. 2).

COST EVALUATION

As of September 9, 2019, a total of 559 staff members at the Department of Health and Mental Hygiene (7% of the staff members in the agency) had worked on the measles response in time-limited waves. At the peak of the agency's participation in late May 2019, a total of 261 staff members were supporting the measles response. As of August 31, 2019, $8.4 million had been spent on the response: $1.5 million in inputs and $6.9 million in personnel.

DISCUSSION

This measles outbreak is the largest reported in the United States since 1992.[18] The outbreak occurred because of multiple importations of measles into a community that had been targeted by antivaccination groups, resulting in a large undervaccinated and susceptible population of young children, primarily between 1 and 4 years of age.[19] We and others have observed

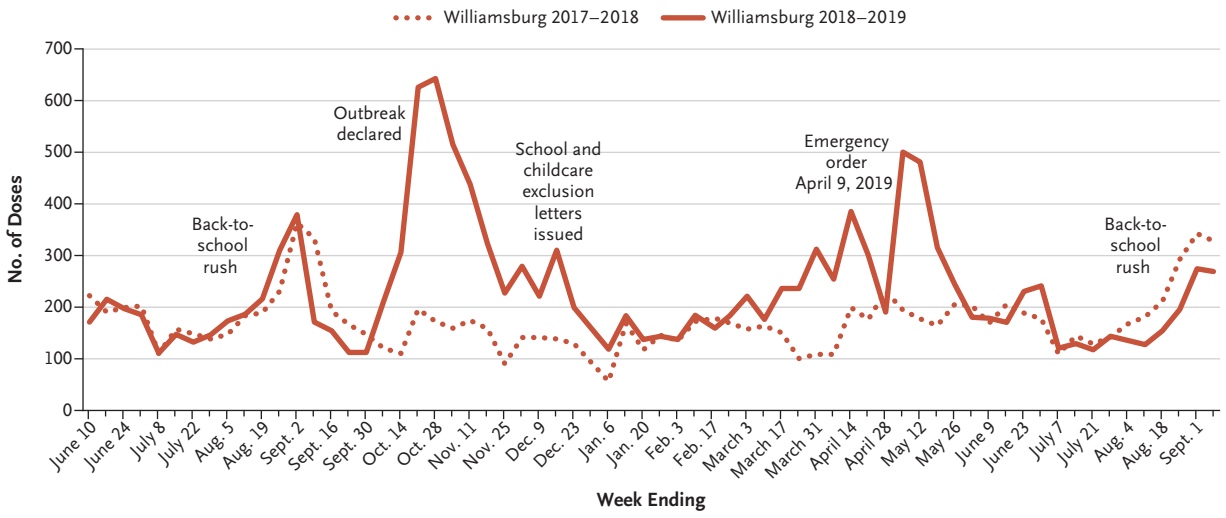

Figure 2. Numbers of Doses of MMR Vaccine Administered to Children 12 to 59 Months of Age in Williamsburg, Brooklyn.

School and childcare exclusion letters were issued on December 6, 2018, on December 21, 2018, and on January 9, 2019. Updated exclusion guidance was issued on February 13, 2019, to allow some students in kindergarten through 12th grade to attend school. Schools and childcare facilities were notified of updated exclusion requirements on April 2, 2019. Adapted from the New York City Department of Health and Mental Hygiene Citywide Immunization Registry; data are as of September 1, 2019. The measles–mumps–rubella (MMR) vaccine was given as either MMR or measles–mumps–rubella–varicella vaccine and collectively referred to as MMR vaccine.

previous outbreaks of vaccine-preventable diseases among persons with low vaccination coverage.[7,20-22]

During focus groups conducted by the Department of Health and Mental Hygiene after a mumps outbreak in 2009–2010[23] in this same community, mothers expressed concern about vaccines and autism, vaccine safety, and whether children are receiving too many vaccines too early in life. Antivaccination sentiments were deepened when an organization targeted this community with misleading materials regarding the risk of vaccination.[19] To address these concerns, the Department of Health and Mental Hygiene reprinted and mailed two booklets that provided accurate information about vaccines to 29,000 households in Borough Park and Williamsburg, and a campaign was launched to combat vaccine myths in affected communities.[24,25]

Interrupting measles transmission was challenging because of the complexity of the outbreak, including numerous chains of transmission fueled by importation, nonadherence to the school and childcare center exclusions mandated by the Department of Health and Mental Hygiene, and transmission in schools and childcare centers with high numbers of religious exemptions to vaccination. Anecdotal reports suggested that parents were holding "measles parties" to deliberately expose their unimmunized children to measles. In addition, in some cases, the diagnosis of measles was made several weeks to months after illness had begun, when the children's parents brought them to a medical provider for serologic testing so they could return to school. Delayed identification of measles in these situations hindered the ability of the Department of Health and Mental Hygiene to implement real-time control measures.

The complications reported during this outbreak are a reminder of the seriousness of measles. The observed percentage of patients with complications is consistent with that seen historically. From 1985 to 1992, diarrhea was reported in 8% of patients, otitis media in 7%, pneumonia in 6%, and death in less than 1%.[1] In contrast, adverse events after measles vaccination are estimated to occur at a rate of 30.5 adverse events per million doses distributed (<0.001%).[26]

To control this outbreak, the Department of Health and Mental Hygiene implemented several unique policy decisions. The exclusions of all unvaccinated children in schools and childcare programs affected by the outbreak in Williams-

burg and Borough Park were justified, given the importance of these settings for transmission. In one school, 1 contagious student led to more than 25 infections in other students and to further spread to multiple other persons outside the school. Overall, in addition to the 9.7% of persons who acquired measles in a school or childcare facility, an additional 48 persons acquired measles from school or childcare attendees. The Department of Health and Mental Hygiene required vaccination among persons living in a specific geographic area. The Board of Health of New York City agreed with this approach and voted to support the agency's strategy.[27] Furthermore, the Supreme Court of Kings County upheld the authority of the Department of Health and Mental Hygiene to require vaccination.[28,29] Although some people had questioned whether requiring vaccination would be effective,[30] the success of these two approaches is evidenced by the increase in MMR vaccination and the decrease in measles cases seen after the implementation of these strategies.

The importance of existing infrastructure in implementing an effective measles outbreak response cannot be overstated. The Citywide Immunization Registry was established in 1996, and decades of investment have produced an immunization information system with high provider participation and quality data.[31,32] After September 11, 2001, the Department of Health and Mental Hygiene leveraged federal public health and health care system preparedness funds to invest in staff, create and exercise response plans, and develop a strong incident command structure, all of which provided a mechanism to rapidly mobilize resources. The cost of $8.4 million underestimates the total cost of the outbreak and is limited to the public health response of the Department of Health and Mental Hygiene; it does not account for costs to medical facilities, other agencies, patients, and the affected communities and does not include the in-kind costs of staff members at the Department of Health and Mental Hygiene who are funded by outside agencies or the indirect costs of taking staff away from routine duties. The calculation of costs incurred for staff working on the measles response during regular business hours was dependent on staff remembering to document time designated for the measles outbreak.

Measles is one of the most contagious infectious diseases.[33] Even a single person with measles can lead to a large outbreak when the virus is introduced into an area with vaccination coverage below that which would be needed to maintain herd immunity. In a globally mobile world, an index of suspicion for measles should be maintained when a person presents with a clinically compatible illness so that the implementation of immediate control measures and diagnostic testing can begin if needed. Global efforts to control or eliminate measles may reduce the burden of measles both abroad and in the United States.[3] Combatting antivaccination misinformation at the local, national, and global level must remain a priority.[34] In New York City, the limited transmission of this outbreak beyond the Orthodox Jewish community highlights the effectiveness of a high-quality, national two-dose MMR vaccination program in maintaining high population-level immunity.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the New York City Department of Health and Mental Hygiene or the Centers for Disease Control and Prevention.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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APPENDIX

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