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The Effects of Vaccination Status and Age on Clinical Characteristics and Severity of Measles Cases in the United States in the Postelimination Era, 2001–2022

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Abstract

Background.—Despite high vaccine effectiveness, wild-type measles can occur in previously vaccinated persons. We compared the clinical presentation and disease severity of measles by vaccination status and age in the postelimination era in the United States.

Methods.—We included U.S. measles cases reported from 2001 to 2022. Breakthrough measles was defined as cases with ≥ 1 documented dose of measles-containing vaccine, classic measles as the presence of rash, fever, and ≥ 1 symptoms (cough, coryza, or conjunctivitis), and severe disease as the presence of pneumonia, encephalitis, hospitalization, or death. Vaccinated cases with low- and high-avidity immunoglobulin G were classified as primary (PVF) and secondary (SVF) vaccine failures, respectively.

Results.—Among 4056 confirmed measles cases, 2799 (69%) were unvaccinated, 475 (12%) were breakthrough infections, and 782 (19%) had unknown vaccination; 1526 (38%), 1174 (29%), and 1355 (33%) were aged <5 , 5–19, and ≥ 20 years, respectively. We observed a general decline in classic presentation and severe disease with an increase in the number of doses and

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Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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fewer complications among children aged 5–19 years compared to other age groups. Among 93 breakthrough cases with avidity results, 11 (12%) and 76 (82%) were classified as PVF and SVF, respectively, with a higher proportion of PVFs having a classic measles presentation and severe disease than SVFs.

Discussion.—Breakthrough measles cases tended to have milder disease with less complications. A small proportion of breakthrough infections were due to PVF than SVF. It is critical to maintain high measles-mumps-rubella vaccination coverage in the United States to prevent serious measles illnesses.

Keywords

measles; United States; vaccination; age; postelimination

The implementation of a routine 2-dose measles-mumps-rubella (MMR) vaccination program in the United States in 1989 led to sustained declines in measles disease burden in the country and culminated in measles being declared eliminated in the United States in 2000 [1]. However, measles introductions still occur through international importations that may result in transmission locally, primarily in under-/unvaccinated subpopulations.

A single dose of MMR vaccine is approximately 93% effective, and 2 doses are approximately 97% effective at preventing measles [2]. According to the U.S. measles vaccination schedule, a first dose is recommended from 12–15 months of age and a second dose from 4–6 years of age. Despite the high effectiveness of MMR vaccines, measles can occur in previously vaccinated persons, and the expected proportion of measles cases among previously vaccinated persons increases with higher vaccination coverage [3, 4]. In the United States, $\geq 90\%$ of children born between 2011–2019 received ≥ 1 doses of MMR vaccine by 24 months of age [5], and $\sim 13\%$ of all measles cases reported between 2001–2015 occurred in previously vaccinated persons [6]. Breakthrough measles is the occurrence of wild-type measles in persons with documented measles vaccination and can occur from primary or secondary vaccine failure [7, 8]. Primary vaccine failure (PVF) occurs when the immune system fails to mount an appropriate immunologic response following vaccination, and can be related to vaccine administration error, improper vaccine storage, or biological factors [9]. Secondary vaccine failure (SVF) refers to insufficient response to vaccine or waning of vaccine-induced immunity after an appropriate immunologic response to vaccination [8, 10, 11]. Evaluation of prior immunity at the time of presentation using immunoglobulin G (IgG) avidity testing, either alone or in combination with plaque reduction neutralization (PRN) testing, can help distinguish between PVF and SVF.

A milder, modified clinical presentation of measles in previously vaccinated persons was first described in the early 1970s [12, 13]. Since then, several studies have identified milder/modified measles symptoms in vaccinated persons after known exposure to wild-type virus [10, 14–17]. These cases have been reported to have lower rates of hospitalizations and complications, nonspecific respiratory symptoms with no fever, the absence of classic measles symptoms (cough, coryza, conjunctivitis), and lower likelihood of transmission of measles to others [18].

Identification of measles in previously vaccinated persons is important for controlling measles transmission because these cases are potentially infectious, although they may be challenging to recognize and diagnose clinically. Surveillance of measles cases among vaccinated persons is also critical for monitoring changes in the epidemiology of measles after elimination. We used national U.S. postelimination surveillance data to compare the clinical characteristics and disease severity among confirmed measles cases by vaccination status, age, and PVF or SVF.

METHODS

Data Sources

Measles is a nationally notifiable condition in the United States and local and state health departments investigate and classify cases per standard case definitions published by the Council of State and Territorial Epidemiologists and link cases epidemiologically. Measles cases that are confirmed are reported to the Centers for Disease Control and Prevention (CDC) directly to the National Center for Immunization and Respiratory Diseases, and through the Nationally Notifiable Diseases Surveillance System [19]. We analyzed available information on the demographics, vaccination status (0, 1, ≥ 2 , unknown doses of a measles-containing vaccine), measles presentation (fever, rash, cough, coryza, and/or conjunctivitis), complications (diarrhea, otitis media, pneumonia, encephalitis), outcomes (hospitalization, death), and laboratory testing results of all confirmed cases of measles reported in the United States from 1 January 2001 to 31 December 2022.

Study Definitions

Confirmed measles cases are defined as patients with an acute febrile rash illness and either laboratory evidence of measles infection or direct epidemiologic linkage to a laboratory-confirmed case [20]. We defined breakthrough measles cases as confirmed measles cases who had received at least 1 documented dose of a measles-containing vaccine based on information reported to the CDC. Classic measles presentation was defined as the presence of rash, fever, and at least 1 of the following symptoms (cough, coryza and/or conjunctivitis), and severe disease as the presence of pneumonia, encephalitis, hospitalization, or death. We categorized cases that were epidemiologically linked to at least 1 other case as epidemiologically linked cases and those without epidemiologic linkage as sporadic cases.

Laboratory Testing

Upon request from jurisdictions, the CDC tested serum samples from breakthrough cases for IgG avidity level and measles neutralizing antibody titers. The avidity of measles-specific IgG antibodies was tested by modification of a commercial measles IgG enzyme immunoassay (Captia Measles IgG, Trinity Biotech, Jamestown, NY), as previously described [21]. Measles-neutralizing antibody titers were measured by PRN tests, as previously described [21]. For PRN testing, serum specimens were tested in parallel with World Health Organization Second International Standard Anti-Measles serum (IS, coded 66/202, supplied by National Institute for Biological Standards and Control, South Mimms, UK). Serum specimens from breakthrough cases were collected within 3–10 days after rash

onset, during the acute phase of infection. Cases with low avidity IgG were classified as PVF and cases with high avidity IgG were classified as SVF. We also evaluated a subset of breakthrough cases with SVF and high PRN titers ($\geq 40\,000$ mIU/mL). Vaccine failure classifications are similar to previous studies [10, 22].

Statistical Analysis

Descriptive analyses were performed to compare the demographic and clinical characteristics of all confirmed measles cases according to vaccination status.

We then compared the clinical presentation and severity of measles cases by vaccination status and age among cases with nonmissing data on vaccination status and age. We constructed multivariate binomial logistic regression models to examine the association between clinical presentation/disease severity (classic measles presentation, presence of fever and rash, presence of cough, coryza, and/or conjunctivitis, complications, hospitalization, death, and severe disease) as the outcome variables and vaccination (1 or ≥ 2 doses vs no vaccination) as the predictor variable. Because age is known to influence both disease severity and vaccination status, age in years was included in these models a priori. We similarly assessed the association between clinical presentation/disease severity as the outcome variables and age group (<12 months, 12 months–4 years, and ≥ 20 years vs 5–19 years) as the predictor variable, adjusting for vaccination status. The associations were reported as odds ratios (ORs) with associated 95% confidence intervals (CIs).

In the subset of breakthrough cases with available avidity and PRN testing results, we describe differences in demographic and clinical characteristics among cases with PVF or SVF.

Data were analyzed using SAS, version 9.4 (SAS Institute, Cary, North Carolina). Statistical significance was defined as a 2-sided $P < .05$. The CDC reviewed this investigation for human subjects protection and determined it to be nonresearch.

RESULTS

A total of 4056 confirmed measles cases were reported in the United States during 2001–2022, among whom 2799 (69%) were unvaccinated, 258 (6%) had received 1 dose of a measles-containing vaccine, 217 (5%) had received ≥ 2 doses, and 782 (19%) had unknown vaccination status; the median age for these 4 groups was 5 (interquartile range [IQR]: 1–14), 11 (IQR: 2–34), 23 (IQR: 18–30), and 34 (IQR: 24–45) years, respectively (Table 1). Among case patients aged ≤ 15 months, 16 months–19 years, and ≥ 20 years, 2%, 11%, and 18% had received ≥ 1 doses of a measles-containing vaccine, respectively. Rash was reported in 86% cases (median rash duration, 5 days), fever in 84% cases, and cough, coryza, and/or conjunctivitis in 77% cases. Thirty-seven percent of cases had at least 1 complication, with diarrhea (20%) and otitis media (11%) being the most frequently reported. Eighteen percent of cases were hospitalized (median hospital stay, 4 days), and 3 deaths were reported (1 unvaccinated, one 1-dose vaccinated, and 1 with unknown vaccination status) (Table 1).

Among 3274 (81% of 4056) with available information on both vaccination status and age, we observed a general decline in full measles symptomatology and in severe outcomes with an increase in the number of doses received (Table 2, Supplementary Figure 1). Adjusting for age, we found a significantly lower odds of a classic measles presentation (OR 0.35, 95% CI, .25–.50), rash and fever (OR, 0.22; 0.12–0.41), cough, coryza, and/or conjunctivitis (OR, 0.17; 0.11–0.26), complications (OR, 0.39; 0.26–0.57), hospitalization (OR, 0.33; 0.20–0.53), and severe disease (OR, 0.52; 0.33–0.80) among case patients with ≥ 2 doses of a measles-containing vaccine compared to case patients with 0 doses. Classic measles presentation and having complications were significantly associated with receipt of 1 dose of a measles-containing vaccine (Figure 1). We also observed a general trend of fewer complications, hospitalizations, and severe disease among children and adults aged 5–19 years compared to younger and older age groups (Table 3). Adjusting for vaccination status, case patients aged <12 months, 12 months–4 years, and ≥ 20 years had significantly higher odds of complications, hospitalization, and severe disease compared to case patients aged 5–19 years (Figure 1). Similar trends in disease symptomatology and severity based on vaccination status and age were observed when restricting the analyses to those with real-time polymerase chain reaction (RT-PCR)–confirmed measles, epidemiologic-linkage, age ≥ 12 months, 0 doses, and within age-groups (Supplementary Tables 1–4).

Of the 475 measles cases who were reported to have received at least one dose of a measles containing-vaccine, 93 had avidity testing results available: 11 (12%) were classified as PVF and 76 (82%) as SVF (Figure 2). Individuals with SVF were older than those with PVF; median age of 29 years (IQR: 22–35 years) and 21 years (IQR: 2–29 years), respectively. The proportion of measles cases with a classic measles presentation, complications, hospitalization, and severe disease were generally higher among those with PVF compared to SVF (Table 4).

Among the 76 measles cases with SVF, 67 had PRN results available: 24 (36%) had a PRN <40 000 mIU/mL and 43 (64%) had a PRN ≥ 40 000 mIU/mL (Figure 2). Overall, the clinical presentation and severity of measles was similar between measles cases with SVF and a high PRN compared to those with SVF regardless of PRN results.

DISCUSSION

Measles vaccines are highly effective at preventing measles and are generally thought to provide lifelong protection to almost all vaccinees [2, 23]. Yet, vaccine failures occasionally occur, particularly with intense exposure, with breakthrough cases primarily reported in households, hospitals, and other congregate settings [24–29]. In elimination settings, decreases in the proportion of measles cases who are vaccinated has been suggested as a marker for lower vaccination rates and declining measles control, since the proportion of vaccinated cases is expected to rise with increasing coverage [3, 30]. We show that during the postelimination period in the United States, 11% of confirmed cases were reported among vaccinated persons, similar to findings from earlier postelimination years (12.8%) [6].

One third of breakthrough measles cases among persons with 2 MMR doses were reported to lack classic measles symptoms, with breakthrough cases most often missing coryza, cough, or conjunctivitis. These findings highlight the importance of keeping a high suspicion for measles among all febrile patients with rash, including vaccinated persons with a known exposure to measles. Differences in the presence of fever and rash between vaccinated and unvaccinated cases were less pronounced, and only statistically different when comparing twice-vaccinated versus unvaccinated cases; such differences are difficult to assess with this surveillance dataset because the clinical criteria used in the Council of State and Territorial Epidemiologists measles case definition requires the presence of at least fever and rash. Because of the potential for a modified clinical presentation, the clinical diagnosis of breakthrough measles cases is challenging, and studies that capture the full spectrum of symptoms associated with these infections are needed to inform recommendations for appropriate laboratory testing when measles is suspected in previously vaccinated persons. Although the current clinical criteria (at a minimum fever and rash) might not be capturing all measles infections in previously vaccinated persons, the U.S. experience of short chains of transmission despite continued importations [1] indicates that the most epidemiologically relevant infections are being identified, and that in a context of high population immunity, elimination can be sustained with current case definitions.

Breakthrough measles cases tended to have lower rates of complications, with the least severe disease among twice-vaccinated persons, underscoring the value of receipt of a full series of MMR in preventing severe illness. Prior studies have also noted breakthrough infections to have milder presentations [15, 22, 29, 31]. We thought it would be important to also account for age, which affects both vaccination status and disease severity. Confirming prior observations of higher disease severity at the extremes of age [17, 23], we show disease severity to be lowest in the 5- to 19-year-old group, with higher rates of complications and hospitalization among infants, young children, and adults. Importantly, we found that the effect of the vaccine on the presence of classic measles symptoms and disease severity persisted when controlling for age, as did the effect of age on disease severity when controlling for vaccination. In addition, similar trends in symptomatology and disease severity were observed when infants, who are more likely to be unvaccinated and to have more severe disease, were excluded from the analyses, and when the analyses of age was restricted to only those who were unvaccinated.

Although not examined in these analyses, measles transmission has been reported from breakthrough measles cases. Both direct observations [15, 29, 31, 32] and modeling studies [18] suggest that the risk of transmission from breakthrough cases is much lower compared to that from unvaccinated cases. This lower risk of transmission from vaccinated persons might be related to milder disease and lower levels of virus shedding [29, 33]. A higher likelihood of vaccinated persons to have contacts who are vaccinated (ie, clustering) might also play a role in certain settings [18]. Because of the potential for onward transmission, breakthrough measles cases in the United States are reported and managed in the same manner as unvaccinated cases including standard laboratory confirmation [34]. Stringent case management is important because there might be delays in confirming the vaccination status of cases, or the vaccination status might remain unknown. In addition, IgG avidity and PRN testing are only available at specialized laboratories, which increases the turnaround

time of these tests. Therefore, rapid classification of a vaccinated case as PVF or SVF is often not possible.

Among a subset of 93 breakthrough cases with avidity testing, the majority were categorized as having SVF (82%) as opposed to PVF (12%), which was not unexpected. In settings with high 2-dose measles vaccine coverage, only a small proportion (<10%) of children will not develop protective immunity after the first dose, and 95% of these children will respond to the second dose, so at baseline, the majority of vaccinated persons would have developed antibodies against measles. Distinguishing between PVF and SVF was useful in further confirming that vaccinated cases with laboratory evidence of a prior immune response to measles had a milder presentation compared to vaccinated cases in whom laboratory evidence indicated they were naïve to measles. Although the number of PVF cases in this study was small, our results suggest that their clinical presentation might be closer to that of unvaccinated cases, implying their transmission potential might also be similar, but this needs to be investigated further.

Several limitations should be considered. Complete clinical information and vaccination status was unavailable for 19% of cases, so we limited our assessment of the effect of vaccination status on the clinical presentation and severity of measles to cases with nonmissing data. If underreporting of classic symptoms and of severe outcomes were more common with vaccinated compared to unvaccinated cases, this could have biased our analyses. However, our evaluation of PVF versus SVF (excluding unvaccinated cases) also showed more incomplete symptomatology and declining severity in persons with prior immunity versus those without prior immunity, and our results are consistent with prior studies evaluating vaccine failures. Approximately 19% of measles cases were reported to have no or unknown rash or fever, and technically would not meet the case definition for measles. These patients were classified as confirmed cases by local and state health departments, and missing information on fever or rash could be related to incomplete data transmission to CDC, or incomplete ascertainment during case investigations. Occasionally, cases lacking fever or rash are reported as confirmed when testing results are positive. Ninety-five percent of cases with no rash or fever and 68% of cases with unknown rash or fever had laboratory confirmation of measles infection in our dataset. Hospitalization may not always be an indicator of disease severity because cases may be admitted for diverse reasons (observation, diagnostic workup, isolation, underlying medical condition), and based on the provider's level of comfort managing measles. Because the measles vaccine is highly effective at preventing measles, it is possible that some vaccinated persons might have been misdiagnosed as having measles. However, confirmation of measles in the United States requires either an epidemiological link to an infectious case, or laboratory confirmation of disease. Restricting our analyses to epidemiologically linked cases and to cases confirmed by measles RT-PCR showed similar results (Supplementary Table 1). Unvaccinated persons might have been given post-exposure prophylaxis (vaccine or immunoglobulin), which we did not account for, but this would have lessened their disease severity, and we still saw differences in disease severity by vaccination status.

Based on data from more than 4000 measles cases reported in the United States in the past 22 years, we found that both receipt of MMR vaccine and age were independently

associated with the severity of measles; measles was generally more severe among unvaccinated persons (compared to vaccinated cases) and at the extremes of age. We also demonstrate the scarcity of PVFs in a setting with high 2-dose measles vaccine coverage. These findings highlight that in the rare instance in which the vaccine does not prevent measles, measles vaccine receipt can prevent severe clinical outcomes associated with measles. Because measles antibodies have been shown to wane slowly over time [35], questions remain about whether this could lead to increases in measles susceptibility and measles transmission from vaccinees in the future. Thus, as vaccinated cohorts continue to age in elimination settings, continued monitoring of vaccine failures and of possible sustained transmission among vaccinated populations is warranted. This is of relevance as long as global measles elimination targets remain unmet and measles importation risk persists.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability.

Data are not publicly available.

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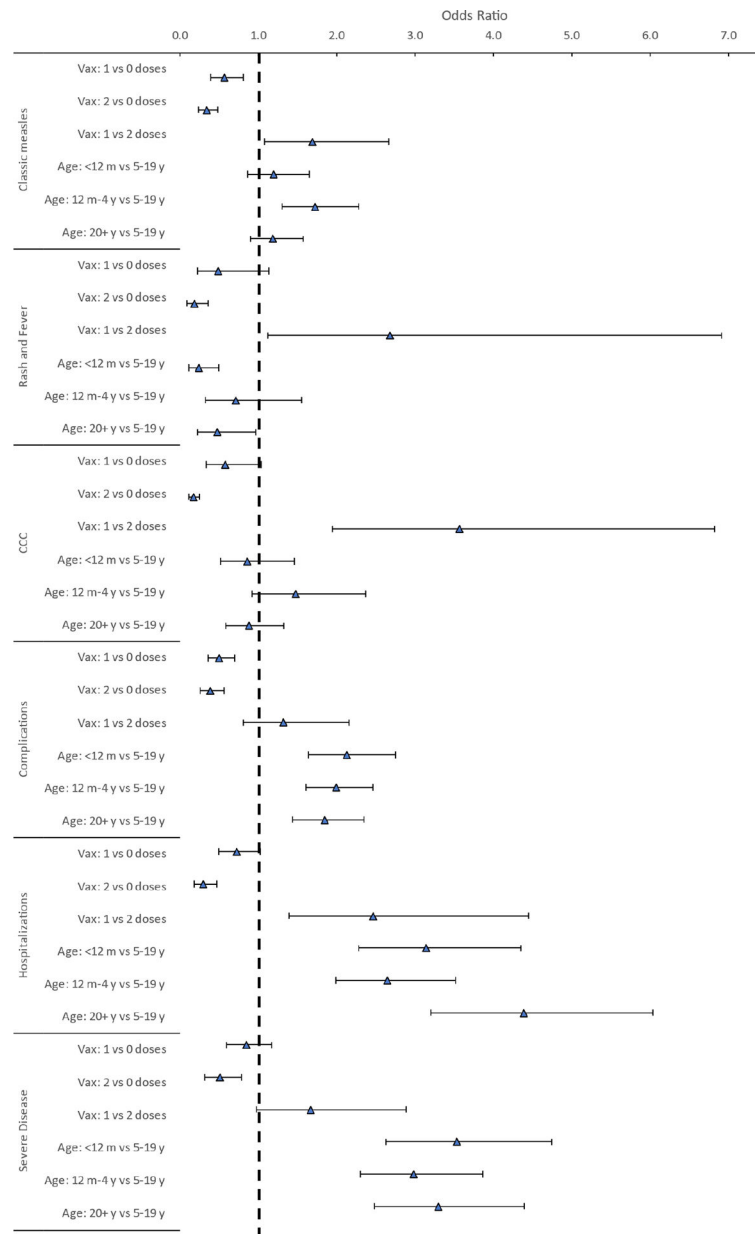
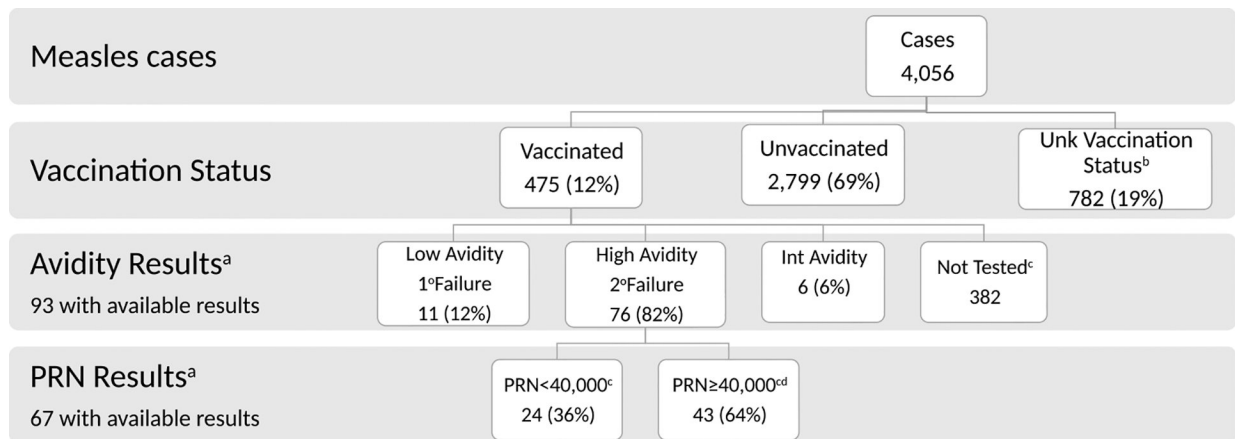


Figure 1. Odds ratios of vaccination and age group by measles clinical presentation and severity, United States, 2001–2022. Abbreviation: CCC, cough, coryza, and/or conjunctivitis.

**Figure 2.**

Classification scheme of vaccine failure cases using avidity and plaque reduction neutralizing (PRN) assays, United States, 2001–2022. Vaccinated case patient had received 1 or more doses of a measles-containing vaccine. Primary vaccine failure is defined as low avidity and secondary vaccine failure is defined as high avidity. ^aPercentages among cases with available results. ^bAmong 782 with unknown vaccination status, 66 had avidity results (13 primary vaccine failure, 50 secondary vaccine failure, 3 intermediate avidity); among 50 with secondary vaccine failure, 30 had low PRN and 16 had high PRN. ^cAmong 67 with available PRN results, the proportion with a positive measles RT-PCR were as follows: 17/24 (71%) with PRN < 40 000 mIU/mL, 14/34 (41%) with PRN ≥ 40 000 mIU/mL, and 6/9 (67%) with PRN results both < 40 000 mIU/mL and ≥ 40 000 mIU/mL. ^d9 cases had 1 specimen with a PRN < 4000 mIU/mL and another specimen with a PRN ≥ 40 000 mIU/mL. Abbreviations: Int, intermediate; PRN, plaque reduction neutralizing assay; RT-PCR, real-time polymerase chain reaction; Unk, unknown.

Table 1.

Demographic and Clinical Characteristics of Measles Case Patients According to Vaccination Status, United States, 2001–2022 (N = 4056)

Characteristics ^a	Vaccination Status					Total 4056				
	Unvaccinated 2799	1-dose Vaccinated 258	≥2-dose Vaccinated 217	Unknown 782						
Age group ^b										
0–5 mo	97	3%	0	0%	0	0%	97	2%		
6–11 mo	373	13%	7	3%	0	0%	13	2%	393	10%
12–15 mo	224	8%	8	3%	2	1%	13	2%	247	6%
16 mo–4 y	651	23%	99	38%	7	3%	32	4%	789	19%
5–19 y	988	35%	37	14%	67	31%	82	10%	1174	29%
20–29 y	248	9%	27	10%	84	39%	167	21%	526	13%
30–49 y	167	6%	70	27%	57	26%	359	46%	653	16%
≥50 y	51	2%	10	4%	0	0%	115	15%	176	4%
Unknown	0	0%	0	0%	0	0%	1	0%	1	0%
Median age (IQR), y	5 (1–14)	11 (2–34)	23 (18–30)	34 (24–45)	10 (2–26)					
Sex										
Male	1300	46%	128	50%	92	42%	315	40%	1835	45%
Female	1495	53%	129	50%	125	58%	465	59%	2214	55%
Unknown	4	0%	1	0%	0	0%	2	0%	7	0%
Rash										
Any	2411	86%	218	84%	187	86%	663	85%	3479	86%
Generalized ^c	1593	66%	160	73%	141	75%	461	70%	2355	68%
None	13	0%	4	2%	2	1%	5	1%	24	1%
Unknown	375	13%	36	14%	28	13%	114	15%	553	14%
Median duration (IQR), d ^d	5 (4–6)	5 (3–6)	4 (3–6)	5 (3–7)	5 (4–6)					
Fever										
Any	2368	85%	213	83%	174	80%	633	81%	3388	84%
None	43	2%	5	2%	16	7%	25	3%	89	2%
Unknown	388	14%	40	16%	27	12%	124	16%	579	14%
Median temperature (IQR), °C	39.4 (38.9–39.7)	38.9 (38.5–39.7)	38.9 (38.3–39.4)	38.9 (38.3–39.4)	39.3 (38.7–39.6)					

Characteristics ^a	Vaccination Status						Total 4056			
	Unvaccinated 2799	1-dose Vaccinated 258	≥2-dose Vaccinated 217	Unknown 782						
Temperature ≥39.4 °C ^e	630	23%	50	19%	24	11%	109	14%	813	20%
Cough, coryza, or conjunctivitis										
Any	2240	80%	199	77%	142	65%	553	71%	3134	77%
None	105	4%	16	6%	48	22%	89	11%	258	6%
Unknown	454	16%	43	17%	27	12%	140	18%	664	16%
Cough										
Yes	2070	74%	172	67%	119	55%	495	63%	2856	70%
No	213	8%	41	16%	69	32%	131	17%	454	11%
Unknown	516	18%	45	17%	29	13%	156	20%	746	18%
Coryza										
Yes	1756	63%	142	55%	83	38%	364	47%	2345	58%
No	468	17%	62	24%	97	45%	254	32%	881	22%
Unknown	575	21%	54	21%	37	17%	164	21%	830	20%
Conjunctivitis										
Yes	1485	53%	116	45%	66	30%	324	41%	1991	49%
No	663	24%	83	32%	112	52%	275	35%	1133	28%
Unknown	651	23%	59	23%	39	18%	183	23%	932	23%
Complications										
Any ^f	1127	40%	79	31%	57	26%	247	32%	1510	37%
None	1672	60%	179	69%	160	74%	535	68%	2546	63%
Unknown	738	26%	76	29%	48	22%	202	26%	1064	26%
Diarrhea										
Yes	584	21%	37	14%	25	12%	158	20%	804	20%
No	1288	46%	129	50%	131	60%	375	48%	1923	47%
Unknown	927	33%	92	36%	61	28%	249	32%	1329	33%
Otitis media										
Yes	378	14%	18	7%	11	5%	21	3%	428	11%
No	1476	53%	143	55%	139	64%	485	62%	2243	55%
Unknown	945	34%	97	38%	67	31%	276	35%	1385	34%

Characteristics ^a	Vaccination Status					Total 4056	
	Unvaccinated 2799	1-dose Vaccinated 258	≥2-dose Vaccinated 217	Unknown 782			
Pneumonia							
Yes	154	9	5	38	5%	206	5%
No	1683	159	157	496	63%	2495	62%
Unknown	962	90	55	248	32%	1355	33%
Encephalitis							
Yes	7	1	2	1	0%	11	0%
No	1821	172	160	532	68%	2685	66%
Unknown	971	85	55	249	32%	1360	34%
Outcomes							
Hospitalization							
Yes	473	46	21	187	24%	727	18%
No	1444	151	160	407	52%	2162	53%
Unknown	882	61	36	188	24%	1167	29%
Median hospital duration (IQR), d	4 (2–5)	5 (4–6)	5 (4–6)	5 (4–5)		4 (3–5)	
Death							
Yes	1	1	0	1	0%	3	0%
No	2798	257	217	781	100%	4053	100%
Severe disease ^g							
Yes	519	48	24	200	26%	791	20%
No	2280	210	193	582	74%	3265	80%

Abbreviation: IQR, interquartile range.

^a Data are presented as No. (%), or no./No. (%), unless otherwise indicated.

^b One person had missing age.

^c Percentage with generalized rash calculated among those with rash; information on whether rash was generalized was available for 2474 (71%) with rash.

^d Duration of rash was available for 1503 (43%) with rash.

^e Temperature was available for 1721 (51%) with fever.

^f Any complication includes having diarrhea, otitis media, pneumonia, or encephalitis. Some case patients had more than 1 complication.

Severe disease was defined as the presence of pneumonia, encephalitis, hospitalization, or death.

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Table 2.

Clinical Presentation and Diseases Severity of Measles According to Vaccination Status, Among Cases With Non-missing Data on Vaccination Status and Age, United States, 2001–2022 (N = 3274)

	Vaccination Status							
	Unvaccinated		1-dose Vaccinated		≥2-dose Vaccinated		Total	
	No.	%	No.	%	No.	%	No.	%
No. cases	2799		258		217		3274	
Clinical presentation ^a								
Classic measles presentation ^b								
Yes	2162	87%	184	80%	130	67%	2476	85%
No	320	13%	45	20%	63	33%	428	15%
Rash and fever								
Yes	2307	98%	204	96%	169	90%	2680	97%
No	47	2%	8	4%	18	10%	73	3%
Cough, coryza, and/or conjunctivitis								
Yes	2240	96%	199	93%	142	75%	2581	94%
No	105	4%	16	7%	48	25%	169	6%
Disease severity ^a								
Complications ^c								
Yes	889	43%	54	30%	37	22%	980	41%
No	1172	57%	128	70%	132	78%	1432	59%
Hospitalization								
Yes	473	25%	46	23%	21	12%	540	24%
No	1444	75%	151	77%	160	88%	1755	76%
Death								
Yes	1	0%	1	0%	0	0%	2	0%
No	2798	100%	257	100%	217	100%	3272	100%
Severe disease ^d								
Yes	519	19%	48	19%	24	11%	591	18%
No	2280	81%	210	81%	193	89%	2683	82%

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^a The number of cases included in each clinical presentation or disease severity category might not sum to the total number of cases because of missing or unknown values.

^b Classic measles presentation defined as presence of rash, fever, and at least 1 of the following symptoms (cough, coryza, and/or conjunctivitis).

^c Complications defined as presence of, diarrhea, otitis media, pneumonia, or encephalitis.

^d Severe disease defined as the presence of pneumonia, encephalitis, hospitalization, or death.

Table 3.

Clinical Characteristics of Measles Case Patients According to Age Group, Among Cases With Nonmissing Data on Vaccination Status and Age, United States, 2001–2022 (N = 3274)

	Age Group							
	<12 mo		12 mo–4 y		5–19 y		≥20 y	
	No.	%	No.	%	No.	%	No.	%
No. cases	477		991		1092		714	3274
Clinical presentation ^a								
Classic measles presentation ^b								
Yes	378	86%	806	90%	774	83%	518	82%
No	59	14%	94	10%	158	17%	117	18%
Rash and fever								
Yes	403	95%	851	98%	850	99%	576	96%
No	19	5%	15	2%	12	1%	27	4%
Cough, coryza, and/or conjunctivitis								
Yes	393	94%	825	96%	811	94%	552	90%
No	23	6%	31	4%	52	6%	63	10%
Disease severity ^a								
Complications ^c								
Yes	185	50%	358	46%	223	31%	214	40%
No	186	50%	414	54%	506	69%	326	60%
Hospitalization								
Yes	112	31%	198	26%	80	12%	150	31%
No	255	69%	557	74%	612	88%	331	69%
Death								
Yes	0	0%	0	0%	1	0%	1	0%
No	477	100%	991	100%	1091	100%	713	100%
Severe disease ^d								
Yes	122	26%	219	22%	94	9%	156	22%
No	355	74%	772	78%	998	91%	558	78%

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^a The number of cases included in each clinical presentation or disease severity category might not sum to the total number of cases because of missing or unknown values.

^b Classic measles presentation defined as presence of rash, fever, and at least 1 of the following symptoms (cough, coryza, and/or conjunctivitis).

^c Complications defined as presence of, diarrhea, otitis media, pneumonia, or encephalitis.

^d Severe disease defined as the presence of pneumonia, encephalitis, hospitalization, or death.

Table 4.

Demographic and Clinical Characteristics of Measles Case Patients According to Avidity and PRN Results, United States, 2001–2022 (N = 93)

	Low Avidity/Primary Vaccine Failure ^a	High Avidity/Secondary Vaccine Failure ^a	High Avidity and PRN ≥40 K/Secondary Vaccine Failure ^a
	11	76	43
Age group			
<12 mo	0	0	0
			0%
12 mo–4 y	3	1	0
			0%
5–19 y	2	14	5
			12%
≥20 y	6	61	38
			88%
Median age (IQR), y	21 (2–29)	29 (22–35)	30 (23–34)
Clinical presentation			
Classic measles presentation ^b			
Yes	6	37	20
			57%
No	1	29	15
			43%
Rash and fever			
Yes	7	56	29
			88%
No	0	7	4
			12%
Cough, coryza, and/or conjunctivitis			
Yes	6	41	22
			63%
No	1	24	13
			37%
Complications ^c			
Yes	2	11	5
			15%
No	5	49	29
			85%
Hospitalization			
Yes	2	7	5
			17%
No	4	51	24
			83%
Death			
Yes	0	0	0
			0%
No	11	76	43
			100%
Severe disease ^d			
Yes	2	7	5
			12%

	Low Avidity/Primary Vaccine Failure ^a	High Avidity/Secondary Vaccine Failure ^a	High Avidity and PRN ≥40 K/Secondary Vaccine Failure ^d
No	9	69	38
		82%	91%
			88%

Abbreviations: IQR, interquartile range; PRN, plaque reduction neutralization.

^a Among 11 with primary vaccine failure, 5 (45%) were vaccinated with 1 dose and 6 (55%) with 2 doses. Among 76 with secondary vaccine failure, 19 (25%) were vaccinated with 1 dose and 57 (75%) were vaccinated with 2 doses. When comparing cases with primary and secondary vaccine failure, only age group and median age were significantly different between the 11 cases with primary and 76 with secondary vaccine failure using the Fisher exact test and the Wilcoxon rank-sum test, respectively; clinical presentation and disease severity were not significantly different between these 2 groups. Results were the same when comparing 11 cases with primary vaccine failure and 43 cases with secondary vaccine failure and a PRN of ≥40 K.

^b Classic measles presentation defined as presence of rash, fever, and at least 1 of the following symptoms (cough, coryza, and/or conjunctivitis).

^c Complications defined as presence of, diarrhea, otitis media, pneumonia, or encephalitis. Among 15 with complications, 10 only had diarrhea, 2 had otitis media only, 1 had encephalitis alone, 1 had both diarrhea and otitis media, and 1 had diarrhea, otitis media, pneumonia, and encephalitis.

^d Severe disease defined as the presence of pneumonia, encephalitis, hospitalization, or death.