

Effect of Measles Vaccination on Disease Severity and Complications: A Systematic Review and Meta-Analysis

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Abstract

Background: Measles remains a highly contagious vaccine-preventable disease-causing substantial morbidity and mortality, particularly among unvaccinated and under-vaccinated populations. Declining immunization coverage, vaccine hesitancy, and post-pandemic disruptions highlight the need to assess the association between vaccination status and measles severity, complications, and clinical outcomes.

Objectives: To evaluate the effects of measles vaccination on disease severity and complications among infected individuals.

Methods: This systematic review and meta-analysis adhered to PRISMA guidelines. The study included patients diagnosed with measles and compared clinical severity and complications between vaccinated and unvaccinated individuals. A comprehensive search of PubMed, Scopus, EBSCO Host, and Cochrane Library was conducted to identify observational studies comparing clinical outcomes between the two groups. Pooled odds ratios (ORs) with 95% confidence intervals were calculated using a random-effects model, and heterogeneity was assessed using the I^2 statistic.

Results: Of 2,661 identified records, after removing duplicates (n=765) and screening (n=1860), 14 out of 36 studies met eligibility criteria for final analysis. Measles vaccination was linked to reduced odds of hospitalization (OR 0.58, 95% CI 0.42–0.81), severe disease (OR 0.53, 95% CI 0.33–0.85), complications (OR 0.62, 95% CI 0.51–0.75), and pneumonia (OR 0.63, 95% CI 0.50–0.80), but not encephalitis (OR 1.95, 95% CI 0.67–5.66) nor mortality (OR 0.50, 95% CI 0.13–1.82). Heterogeneity ranged from low to substantial, especially for hospitalization and severe disease.

Conclusion: Measles vaccination significantly reduces severe outcomes and complications, underscoring its important role in disease prevention and severity reduction while reinforcing the need for stronger global immunization efforts.

Keywords: Complications, measles, severity, vaccination

Introduction

Measles is an extremely contagious airborne disease caused by a single-stranded RNA virus

of the Morbillivirus genus, with a primary reproduction number (R_0) of 12–18.¹ It remains a major cause of vaccine-preventable morbidity and mortality worldwide, affecting

both children and adults through acute illness and potential long-term complications.¹ In 2023, approximately 10.3 million measles cases occurred globally, representing a 20% increase from 2022, with an estimated 107,500 deaths, mainly among children under five.² The WHO European Region reported 127,350 cases in 2024, the highest incidence in 25 years.³ Preliminary CDC data from February 2026 also reported 8,892 measles cases in Indonesia between August 2025 and January 2026, ranking third worldwide after Angola and India.⁴ Although immunization has reduced annual measles deaths from around 780,000 in 2000 to about 95,000 in 2024, most fatalities still occur among unvaccinated or under vaccinated children.⁵

Vaccine hesitancy substantially contributes to declining herd immunity. Parental reluctance to vaccinate has increased since the COVID-19 pandemic, worsening pre-existing gaps in immunization coverage observed during outbreaks such as the 2018 European measles outbreak. Studies have identified misinformation, particularly through social media, lower educational attainment, and reduced trust in healthcare systems as key factors associated with vaccine refusal. Socioeconomic influences are complex: hesitancy may occur among college-educated mothers in middle- to high-income settings influenced by social media, while in low-income and minority populations, barriers more often involve access and cost.^{6,7} Due to funding cuts, more than 20 million children face disruptions in immunization.⁸

Vaccination remains the cornerstone of measles prevention. The two-dose MMR vaccine provides strong protection and is recommended during infancy and early childhood to maintain herd immunity.^{9,10} However, global coverage remains below the 95% target. In 2023, only 74% of children received both doses, and more than 22 million missed their first dose, contributing to outbreaks in 57 countries.^{2,11} Between 2010 and 2019, coverage stagnated, and the COVID-19 pandemic increased zero-dose children to 18.6 million in 2021, with Indonesia, Nigeria, India, and Brazil accounting for more than half of these cases.¹²

Despite high vaccine efficacy, inadequate coverage leaves many individuals susceptible. Vaccine hesitancy occurs across socioeconomic groups, while concerns regarding waning vaccine-induced immunity and viral genetic variation remain incompletely understood.¹³⁻¹⁵ Evidence suggests that

unvaccinated or partially vaccinated individuals may experience more severe disease and complications, but findings vary by country, age group, and outbreak context.^{16,17} Therefore, a rigorous quantitative assessment is needed to determine how previous measles vaccination status influences disease severity and clinical outcomes. This systematic review and meta-analysis aim to evaluate the impact of measles vaccination on disease severity, complications, and critical outcomes across diverse settings.

Methods

This study presents a systematic review and meta-analysis, employing rigorous methods to compile, identify, evaluate, and synthesize data from pertinent primary studies. The selected study design enables both narrative and quantitative assessment of the effects of vaccination on the severity and outcomes among patients with measles infection. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Studies were included in this systematic review according to the following criteria: (1) participation of patients with laboratory-confirmed or clinically diagnosed measles infection; (2) reporting of vaccination status, encompassing both unvaccinated individuals and those vaccinated fully (more than two doses) or partially (one dose) using measles-containing vaccines such as the measles vaccine or MMR vaccine; (3) documentation of severity and outcomes related to measles infection, including hospitalization, mortality, pneumonia, and encephalitis incidence; (4) observational study design, including cohort and case-control studies; and (5) publication in English with full-text availability. Studies were excluded if they were reviews, case reports, case series, cross-sectional studies, animal or in vitro studies, books, book chapters, editorials, or conference abstracts.

A comprehensive literature search was carried out utilizing four electronic databases: PubMed, Scopus, EBSCOHost, and Cochrane Library, on 19 March 2026, with the search limited to studies published within the past 10 years. The search strategy incorporated a combination of Medical Subject Headings (MeSH) and free-text terms relevant to the population ("measles", "rubeola"), intervention ("vaccination", "vaccinated", "immunization", "vaccine status"), and outcomes ("severity",

"complications", "hospitalization", "pneumonia", "encephalitis", "mortality"), combined with Boolean operators AND and OR. Supplementary Table 1 & 2. All records retrieved from the databases were imported into a screening tool, with duplicate entries systematically removed. Study selection occurred in two phases: (1) title and abstract screening, and (2) full-text review. Both stages were conducted independently by two reviewers, who assessed studies for eligibility based on predefined inclusion and exclusion criteria. Discrepancies were addressed through discussion and consultation with a third reviewer. The screening and selection process was documented using a PRISMA flow diagram, with all procedures recorded in Google Sheets and further supported by Rayyan software (www.rayyan.ai).

Data collected from the studies that met the screening criteria encompassed author names, publication year, country, study setting, population characteristics (including sample size and age group), vaccination status (number of vaccine doses received and type of vaccine), outcomes, as well as the number of partial and total events related to measles severity and complications. Information on hospitalization, severe disease, any complications, including pneumonia and encephalitis were systematically extracted from each study. Severe disease was defined as cases presenting with significant complications such as systemic symptoms, respiratory distress, or the requirement for intensive care.

The category "any complications" included participants experiencing at least one of the following: pneumonia, diarrhea, encephalitis, otitis media, or other reported measles-related complications. The assessment process involves documenting all relevant information from the included studies; however, no specific measurement or scoring system has been implemented to determine this. All extracted data were summarized in the study characteristics table.

The methodological quality of each included study was evaluated using the Newcastle-Ottawa Scale (NOS), an established instrument for assessing the risk of bias of non-randomized observational studies. Cohort or case-control studies were assessed across three domains: selection (4 items), comparability (1 item), and either outcome/follow-up (cohort) or exposure ascertainment (case-control) (3 items), with a maximum attainable score of 9 stars per study. Studies receiving 7–9 stars

were classified as high quality, those scoring 4–6 stars as moderate quality, and scores between 0–3 stars as indicative of low quality, with higher scores reflecting a lower overall risk of bias.

Statistical analyses were conducted utilizing Review Manager 5.4. When available, raw data were extracted from each included study to serve as the primary effect measures. Pooled odds ratios (ORs) with corresponding 95% confidence intervals (CIs) were calculated using a random-effects model with the Mantel-Haenszel method based on the expectation of substantial clinical and methodological heterogeneity across included studies. Heterogeneity was evaluated via the I^2 statistic using Dersimonian-Laird as the variance estimator, with values interpreted as follows: <25% indicating low, 25–50% moderate, and ≥50% high heterogeneity. Statistical significance was established at a p-value threshold of <0.05 for all analyses. Sensitivity analyses were conducted using leave-one-out analysis. Given the limited number of included studies, publication bias was not assessed through funnel plot asymmetry or Egger's test.

Results

The primary search was conducted across PubMed, Scopus, EBSCO Host, and Cochrane Library, and yielded a total of 2,661 records. After removing 765 duplicates, 1,896 records were screened based on title and abstract, during which 1,860 records were excluded due not represent about measles, vaccination and disease severity. Based on the predefined inclusion and exclusion criteria, 36 articles were selected for full-text retrieval and were successfully assessed for eligibility using the PICO framework. Finally, 14 studies met the criteria and were included in this systematic review Fig. 1.

In this systematic review, 14 studies were evaluated, involving a total of 5,866 (14.7%) vaccinated and 39,825 (85.3%) unvaccinated participants. Eight studies focused on pediatric population, while six studies examined mixed-age groups. The overall age span of participants ranged from less than one year to over sixty years. Most studies originated from high-income countries (France, United States, Netherlands, and Romania), while other studies were conducted from upper-middle-income (Iraq and Türkiye), lower-middle-income (Kyrgyzstan and Tunisia), and low-income countries (Somalia and Uganda).

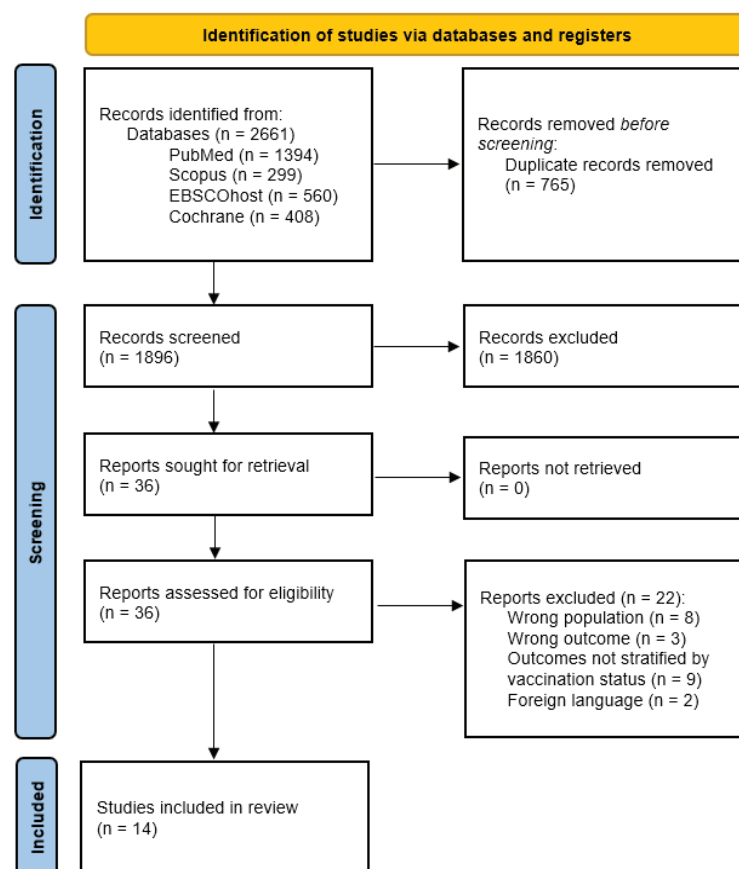


Fig. 1 PRISMA Flowchart

Based on study environments, five studies were community-based, five hospital-based, and four were conducted in outbreak settings. Table 1.

Among the studies assessed in this review, eight were judged as high quality (NOS ≥ 7), mainly because they used extensive population-based data and properly accounted for confounding factors. Some hospital-based studies received moderate quality ratings (NOS = 6), mostly due to insufficient multivariable adjustments and possible selection bias. In general, the quality of the studies included ranged from moderate to high Table 2.

A total of six studies comprising 4,492 vaccinated and 29,328 unvaccinated measles patients were included in the analysis of hospitalization risk. The pooled results indicated a statistically significant association between vaccination and reduced odds of hospitalization (OR = 0.58, 95% CI: 0.42–0.81, $p = 0.001$), suggesting that vaccinated individuals had a 42% lower likelihood of hospitalization compared to their unvaccinated counterparts.

Study heterogeneity was high ($I^2 = 77\%$, $\text{Tau}^2 = 0.10$, $\text{Chi}^2 = 21.66$, $p = 0.0006$). Fig. 2. Removal of Bennasrallah *et al.* decreased heterogeneity to 42%, suggesting that this study was a potential source of variability across studies. Supplementary Table 3.

Subgroup analysis based on study setting indicated variability in effect estimates. In community-based studies (3 studies; $n = 4,195$ vaccinated, 26,453 unvaccinated), vaccination was significantly associated with reduced odds of hospitalization (OR 0.65, 95% CI 0.51–0.83, $p = 0.0006$), with moderate heterogeneity observed ($I^2 = 56\%$). Conversely, no significant association was identified in the outbreak setting subgroup (2 studies; $n = 195$ vaccinated, 2,688 unvaccinated; OR 0.42, 95% CI 0.08–2.28, $p = 0.31$), however, this subgroup demonstrated extremely high heterogeneity ($I^2 = 92\%$, $\text{Tau}^2 = 1.39$), driven by markedly divergent individual estimates. The single hospital-based study by Mawlood *et al.* also reported a non-significant association (OR 0.74, 95% CI 0.45–1.22, $p = 0.23$).

Table 1 Study Characteristics

Author, Year	Country	Study Design	Setting	Number of populations	Age Group	Vaccination Status	Outcome	Vaccine Type	Case Definition
Bennasrallah, <i>et al.</i> , 2026	Tunisia	Case-control	Outbreak setting	396	All ages	1 dose (n=38), 2 doses (n=22), unvaccinated (n=260)	Hospitalization, mortality	MCV	Laboratory-confirmed
Bonetton, <i>et al.</i> , 2020	France	Retrospective cohort	Community-based	10,399	All ages	1 dose (n = 568), 2 doses (n=478), unvaccinated (n=9,353)	Severe disease	MCV	Surveillance-reported
Bursal, <i>et al.</i> , 2025	Turkey	Retrospective cohort	Hospital-based	367	Pediatric	1 dose (n = 85), 2 doses (n=18), unvaccinated (n=264)	Pneumonia, mortality	MCV	Laboratory-confirmed
Chery, <i>et al.</i> , 2018	United States	Retrospective cohort	Community-based	232	All ages	1 dose (n=20), ≥2 doses (n=26), unvaccinated (n=186)	Hospitalization	MCV	Laboratory-confirmed
Dam, <i>et al.</i> , 2020	Netherlands	Retrospective cohort	Outbreak setting	2,676	All ages	1 dose (n=121), 2 doses (n=15), 3 doses (n=1), unvaccinated (n=2,428)	Hospitalization, any complications, pneumonia, encephalitis	MMR	Laboratory-confirmed
Dobrin, <i>et al.</i> , 2025	Romania	Retrospective cohort	Hospital-based	455	Pediatric	≥1 dose (n=83), unvaccinated (n=373)	Severe disease, pneumonia	MMR	Laboratory-confirmed
Donadel, <i>et al.</i> , 2021	Romania	Case-control	Outbreak setting	300	Pediatric	≥1 dose (n=49), unvaccinated (n=251)	Mortality	MCV	Laboratory-confirmed & epidemiological Surveillance-reported
Geier, <i>et al.</i> , 2019	United States	Retrospective cohort	Community-based	85	Pediatric	≥1 dose (n=9), unvaccinated (n=76)	Any complications	MMR	Laboratory-confirmed
Khalupko, <i>et al.</i> , 2025	Kyrgyzstan	Retrospective cohort	Hospital-based	105	Pediatric	≥1 dose (n=50), unvaccinated (n=55)	Severe disease, any complications, pneumonia	MCV	Laboratory-confirmed
Leung, <i>et al.</i> , 2025	United States	Retrospective cohort	Community-based	4,056	All ages	1 dose (n=258), ≥2 doses (n=217), unvaccinated (n=2,799)	Hospitalization, severe disease, any complications, pneumonia, encephalitis, mortality	MCV	Clinical, laboratory-confirmed, epidemiological

Table 1 Continued

Author, Year	Country	Study Design	Setting	Number of populations	Age Group	Vaccination Status	Outcome	Vaccine Type	Case Definition
Mafigiri, <i>et al.</i> , 2017	Uganda	Case-control	Outbreak setting	64	Pediatric	≥1 dose (n=23), unvaccinated (n=41)	Mortality	MCV	Clinical & laboratory-confirmed
Mawlood, <i>et al.</i> , 2025	Iraq	Prospective cohort	Hospital-based	289	Pediatric	≥1 dose (n=102), unvaccinated (n=187)	Pneumonia, Hospitalization	MCV	Clinical & laboratory-confirmed
Mohamud, <i>et al.</i> , 2023	Somalia	Retrospective cohort	Hospital-based	93	Pediatric	≥1 dose (n=9), unvaccinated (n=84)	Any complications#	MCV	Clinical, medical records, exposure history, laboratory-confirmed
Stoian, <i>et al.</i> , 2025	Romania	Retrospective cohort	Community-based	29,148	All ages	1 dose (n=2,404), 2 doses (n= 1,219), 3 doses (n=51), unvaccinated (n=23,468)	Hospitalization, pneumonia, encephalitis	MMR	Confirmed: laboratory, Probable: clinical and epidemiological

MCV = Measles-Containing Vaccine; MMR = Measles-Mumps-Rubella; *1-18 y.; #including pneumonia, diarrhea, encephalitis, otitis media, or other reported measles-related complication

Table 2 NOS Quality Assessment of Included Studies

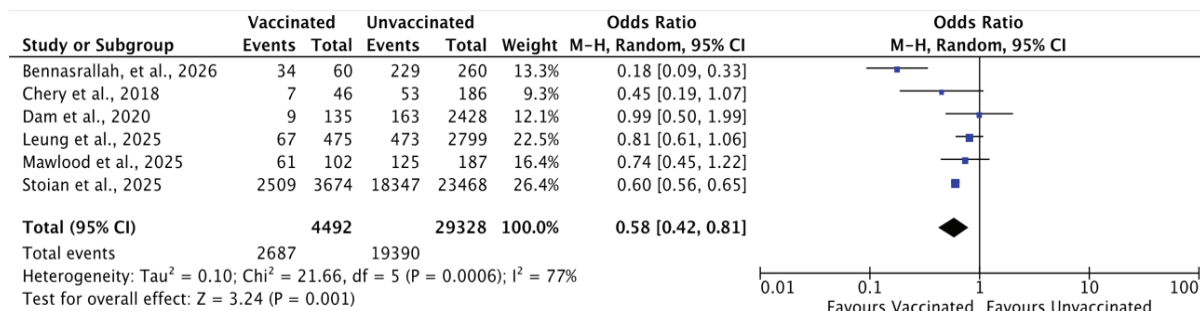
Study	Selection	Comparability	Outcome / Exposure	NOS Score	Risk of Bias
Cohort studies					
Bonetton, <i>et al.</i> , 2020	****	**	**	8	Low
Bursal, <i>et al.</i> , 2025	****		***	7	Low
Chery, <i>et al.</i> , 2018	****		***	7	Low
Dam, <i>et al.</i> , 2020	****	**	***	9	Low
Dobrin, <i>et al.</i> , 2025	****		***	7	Low
Geier, <i>et al.</i> , 2019	***		***	6	Moderate
Khalupko, <i>et al.</i> , 2025	***	*	***	7	Low
Leung, <i>et al.</i> , 2025	****	**	***	9	Low
Mawlood, <i>et al.</i> , 2025	***		***	6	Moderate
Mohamud, <i>et al.</i> , 2023	***		***	6	Moderate
Stoian, <i>et al.</i> , 2025	****		***	7	Low
Case-control studies					
Bennasrallah, <i>et al.</i> , 2026	****	*	**	7	Low
Donadel, <i>et al.</i> , 2021	****	*	**	7	Low
Mafigiri, <i>et al.</i> , 2017	***	*	**	6	Moderate

NOS = Newcastle-Ottawa Scale. Selection max: cohort/case-control = 4 stars. Comparability max: 2 stars. Outcome/Exposure max: cohort/case-control = 3 stars. Overall max: cohort/case-control = 9 stars. Risk of bias classification: cohort/case-control: ≥ 7 = low, 5–6 = moderate, ≤ 4 = high

Analysis revealed no significant differences between setting subgroups ($\text{Chi}^2=0.48$, $p=0.79$, $I^2=0\%$) Supplementary Fig. 1. Analysis by age groups showed similar patterns in both categories. In the mixed or all-ages subgroup (5 studies; 4,390 vaccinated, 29,141 unvaccinated), vaccination was linked to a significant reduction in hospitalizations (OR 0.55, 95% CI 0.42–0.81, $p=0.0003$), although there was high variability between studies ($I^2=81\%$). For the pediatric-only subgroup (1 study; 102 vaccinated, 187

unvaccinated), the trend was comparable but not statistically significant (OR 0.74, 95% CI 0.45–1.22, $p=0.23$), likely due to the smaller sample size and reduced statistical power. No significant difference was observed between the age subgroups ($\text{Chi}^2=0.81$, $p=0.37$, $I^2=0\%$) Supplementary Fig. 2.

Dose-stratified analysis for hospitalization revealed a clear dose-response relationship between the number of vaccine doses received and the degree of protection against hospitalization. Full vaccination (≥ 2 doses)

**Fig. 2 Forest Plot of Pooled Odds Ratios for Reduced Hospitalization Events**

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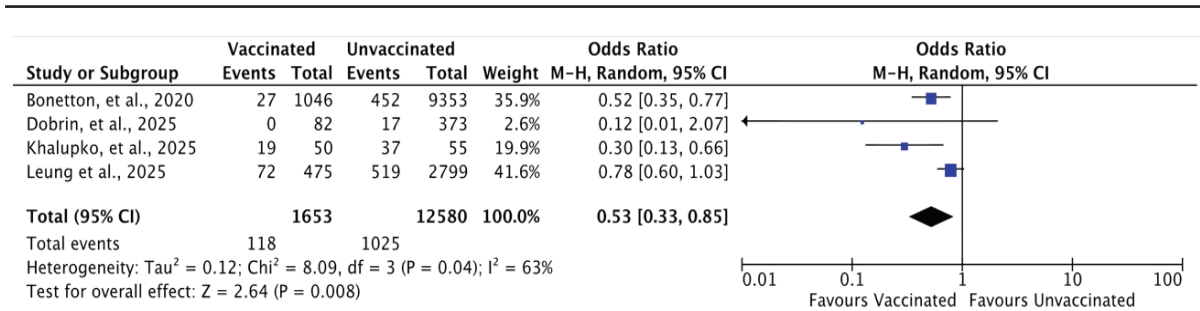


Fig. 3 Forest Plot of Pooled Odds Ratios for Reduced Severe Disease Events

was associated with significantly lower odds of hospitalization compared with unvaccinated individuals (OR 0.30, 95% CI 0.16–0.55; $p<0.0001$; $I^2=79\%$) across four studies, with consistent protective effects. Supplementary Fig. 3. Partial vaccination (1 dose) showed a non-significant reduction in hospitalization risk (OR 0.73, 95% CI 0.49–1.06; $p=0.10$; $I^2=71\%$) with greater variability between studies. Supplementary Fig. 4. Overall, the findings indicate a dose-response pattern, with full vaccination providing stronger protection against hospitalization, although substantial heterogeneity remained due to differences in study characteristics and clinical settings.

A total of four studies comprising 1,653 vaccinated and 12,580 unvaccinated measles patients were included for the analysis of severe disease. The pooled results indicated that vaccination was significantly correlated with lower odds of severe measles (OR 0.53, 95% CI 0.33–0.85, $p=0.008$), implying that vaccinated individuals had a 47% reduced likelihood of developing severe illness compared to those who were unvaccinated. However, substantial heterogeneity was observed across studies, and the pooled estimate should be interpreted with caution ($I^2 = 63\%$, $\text{Tau}^2 = 0.12$, $\text{Chi}^2=8.09$, $p=0.04$).

Fig. 3. Sensitivity analysis demonstrated that excluding Leung *et al.* substantially reduced heterogeneity ($I^2=15\%$). Conversely, removal of Bonnetton *et al.* resulted in a notable change in the pooled effect estimate (OR 0.46, 95% CI 0.19–1.14) which may have had a considerable influence on the overall effect.

Five studies involving 678 vaccinated and 5,442 unvaccinated patients found that vaccination significantly reduced the odds of measles-related complications by 38% (OR 0.62, 95% CI 0.51–0.75, $p<0.00001$). Study heterogeneity was low ($I^2=1\%$), and all individual estimates favored vaccination, except Geier *et al.* and a non-significant trend in Dam *et al.* and Mohamud *et al.* Fig. 4. Sensitivity analysis showed removal of Leung *et al.* altered the pooled estimate (OR 0.69, 95% CI 0.43–1.11, $p=0.13$), indicating that the overall effect may be influenced by this study.

Seven studies comprising 4,621 vaccinated and 28,574 unvaccinated participants were included in the pneumonia analysis, rendering it the outcome with the greatest number of contributing studies. Vaccination was significantly associated with a decreased likelihood of developing pneumonia (OR 0.63, 95% CI 0.50–0.80, $p=0.0001$), indicating a 37% reduction in odds compared to unvaccinated

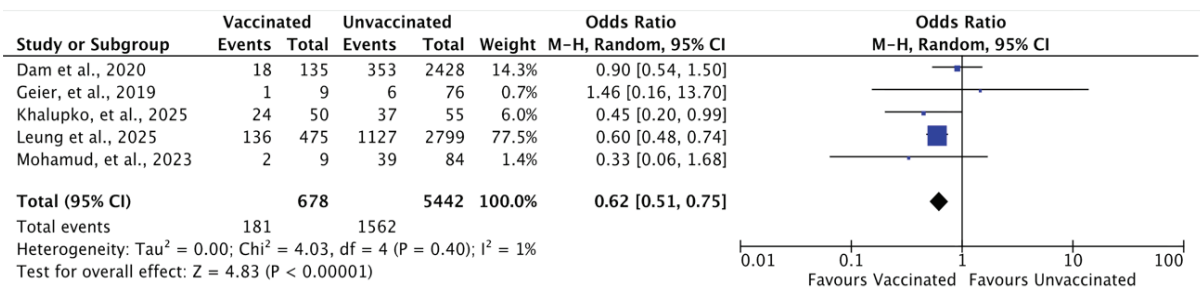


Fig. 4 Forest Plot of Pooled Odds Ratios for Reduced Any Complications Events

individuals. Importantly, heterogeneity was moderate among the studies ($I^2 = 44\%$, $\text{Tau}^2 = 0.04$, $\text{Chi}^2 = 10.76$, $p = 0.10$). Supplementary Fig. 5. Sensitivity analysis confirmed the stability of the pooled estimate for the pneumonia outcome (OR range: 0.61–0.67). Supplementary Table 3. Three studies comprising 4,284 vaccinated and 28,695 unvaccinated patients were incorporated into the encephalitis analysis. In contrast to other complication outcomes, the pooled results did not reveal a statistically significant relationship between vaccination status and encephalitis risk (OR 1.95, 95% CI 0.67–5.66, $p = 0.22$). Heterogeneity was minimal ($I^2 = 0\%$, $\text{Tau}^2 = 0.00$, $\text{Chi}^2 = 1.05$, $p = 0.59$). Supplementary Fig. 6.

Mortality was assessed among five studies involving 703 vaccinated and 3,572 unvaccinated measles patients. The pooled analysis showed no statistically significant association between vaccination status and mortality (OR 0.50, 95% CI 0.13–1.82; $p = 0.29$), although the estimate suggested a potential protective effect. Moderate heterogeneity was observed ($I^2 = 46\%$) and the limited number of mortality events (8 vs. 72 deaths) reduced statistical power. Supplementary Fig. 7.

Discussion

Despite the availability of an effective vaccine, measles outbreaks persist in settings with inadequate immunization coverage. This systematic review and meta-analysis demonstrate that measles vaccination is consistently associated with reduced hospitalization, lower disease severity, and fewer complications in both adults and children. Vaccinated individuals showed decreased odds of severe outcomes, such as hospitalization with full doses, and the risk of complications, particularly pneumonia, was consistently lower among vaccinated groups. No significant association was observed for encephalitis, likely reflecting its low incidence and limited statistical power. Subgroup analyses indicated stronger protective effects in community-based settings and mixed-age populations.

These findings are biologically plausible. Measles virus enters via respiratory droplets, attaching to CD150 (SLAMF) and nectin-4 receptors through its hemagglutinin (H) protein, with the fusion (F) protein enabling viral entry into host cells.^{10,18} Subsequent viral dissemination via infected lymphocytes induces lymphopenia and profound immune suppression, characterized by reduced IL-12,

impaired interferon signaling through its P, V, and C proteins, and apoptotic depletion of T cells, B cells, and MALT cells, resulting in long-lasting immunosuppression and increased susceptibility to secondary infections well beyond the acute illness. Acute complications include pneumonia (the leading cause of measles-related hospitalization and death among unvaccinated children), otitis media, keratoconjunctivitis, and diarrhea, while virus-induced immunosuppression further aggravates respiratory complications including pleural effusion, pneumothorax, and ARDS. In pregnant women, measles is associated with increased risks of miscarriage, preterm birth, low birth weight, and maternal death.¹⁰ Rare neurological sequelae such as ADEM, MIBE, and SSPE may also occur, potentially causing severe disability or fatality.¹⁹ Measles symptoms generally appear 10–14 days post-exposure, with rash emerging 7–18 days after exposure.⁵

The live-attenuated measles vaccine counters these mechanisms by inducing robust humoral and cellular immunity. Limited viral replication triggers antigen presentation via MHC molecules, activating CD4⁺ and CD8⁺ T cells and stimulating high-affinity neutralizing antibodies targeting the H protein, while memory B and T cells enable rapid viral control upon re-exposure.^{20,21} This limits viral replication and systemic dissemination, providing a coherent immunological basis for the attenuated disease course observed in vaccinated individuals and the reduced odds of hospitalization, severe disease, and pneumonia.²⁰

Variability in the magnitude of protection may reflect differences in vaccination schedules, cold chain integrity, and coverage rates, all of which influence immunogenicity.²⁰ The absence of a significant effect following single-dose vaccination may indicate that one dose provides insufficient immune protection, potentially due to primary vaccine failure or incomplete vaccine-induced immunity. Viral genotypic variation, while limited given measles' antigenic stability relative to other RNA viruses, may also modestly affect T-cell recognition and contribute to partial immune escape.²² Host factors, including age, nutritional status, and immune competence, further modify vaccine effectiveness, providing a plausible explanation for why protection, though consistent, does not reach completeness across all outcomes.^{5,20}

Disparities between LMICs and high-income countries further contribute to this

variation. Approximately 95% of measles-related deaths occur in LMICs, where vaccine coverage and healthcare access are frequently suboptimal.⁵ Malnutrition, prevalent in these settings, may impair vaccine-induced immunity by reducing antibody production and T-cell function, leading to higher risks of severe outcomes even among vaccinated individuals as illustrated by Mohamud *et al.*, who demonstrated the greatest benefit of vaccination for reducing complications in a pediatric population in Somalia.

This review has several strengths. The large aggregate sample size supports statistical reliability, and protective effects were consistently observed across hospitalization, severe disease, and complication outcomes. Subgroup analyses by setting, age group, and number of doses added analytical depth, and the overall methodological quality of included studies was moderate to high. Heterogeneity was present, particularly in the hospitalization and severe disease analysis, likely driven by differences in study designs, settings, population characteristics, and inconsistent outcome definitions. In the pneumonia analysis, a single high-weight study may have disproportionately influenced pooled estimates. The predominance of observational studies limits causal inference, and hospital-based recruitment introduces potential selection bias. Variations in vaccine type and schedule were not formally analyzed, and subgroup analyses for rare outcomes such as encephalitis and mortality were constrained by small sample sizes and low event rates. Dose-stratified comparisons between partial and full vaccination were only possible for the hospitalization outcome due to insufficient dose-level data across studies for other outcomes. Publication bias cannot be excluded.

Clinically, these findings suggest that vaccination status should inform risk stratification, with unvaccinated individuals warranting closer monitoring and earlier intervention.⁵ At the public health level, maintaining high coverage through routine measles-containing vaccine programs such

as MMR remains essential, particularly given recent resurgences in regions with immunization gaps. Beyond direct protection, measles vaccination reduces immune suppression and secondary infections, potentially limiting unnecessary antibiotic use and contributing to antimicrobial resistance mitigation.²³ Notably, current evidence indicates that measles virus evolution is constrained by multiple co-dominant neutralizing epitopes, making new serotype emergence highly unlikely and supporting the continued effectiveness of existing vaccines against circulating genotypes.²⁴ Future research should prioritize prospective study designs, standardized outcome definitions, evaluation of optimal dosing schedules across diverse epidemiological contexts, and assessment of the broader economic impact of vaccination programs including healthcare cost reduction and long-term disease burden.²⁵

Measles vaccination is associated with improved clinical outcomes, including reduced hospitalization, disease severity, and complications. A dose-response effect was observed, as full vaccination provided significant protection against hospitalization, whereas partial vaccination showed no significant benefit. Notably, the protective benefit against hospitalization and pneumonia as the most prevalent and clinically relevant complication of measles was both robust and consistent. However, no significant link was found between vaccination status and the risks of encephalitis or mortality, likely because of the low number of cases and limited statistical power. Despite some variability in severe disease outcomes, studies consistently showed a protective effect. Measles vaccination is important for preventing infection, reducing severity, and minimizing complications. Increasing coverage is crucial to lower measles-related risks, especially in under-immunized populations.

Acknowledgment

Search strategy data and supplementary files is available on request.

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