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Acute management of measles: A systematic review of therapeutic strategies

Amandeep Kaur [a], Ugo Alaribe [a], Joseph Varon [a,b], Sidra Hassaan [c,d], Matthew Halma [b,d,*]

[a] Dorrington Medical Associates, 2219 Dorrington Street, Houston, TX, 77030, USA
[b] Independent Medical Alliance, 2001 L St. NW Suite 500, Washington, DC, 20036, USA
[c] Department of Pharmacy, Jinnah University for Women, 5-C Nazimabad, Karachi, 74600, Pakistan
[d] Open Source Medicine Foundation, Open Source Medicine OÜ, Pärnu mnt. 139c, Tallinn, 11317, Estonia

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ABSTRACT

Measles remains one of the most contagious viral infections, and its resurgence due to declining global vaccination coverage has renewed interest in therapeutic and preventive strategies. This systematic review analyzes current and emerging acute therapies and their relationship to measles virology and clinical outcomes. A systematic search of PubMed, Scopus, Web of Science, China National Knowledge Infrastructure and Google Scholar (1990–2025) was conducted using predefined inclusion and exclusion criteria to identify clinical studies on acute measles treatment. Despite being used off-label, ribavirin and interferon-α have demonstrated reductions in severity and complications in small clinical trials and case reports. Vitamin A supplementation remains the only widely recommended therapy with strong evidence for reducing morbidity and mortality, particularly in children with deficiency. Traditional Chinese medications such as Tanreqing and Xiyanping show symptomatic improvement but require mechanistic validation. Investigational therapeutics, including polymerase inhibitors such as ERDRP-0519, monoclonal antibodies targeting the fusion protein, and antiviral candidates such as remdesivir, offer promising future options. While vaccination remains essential, adjunctive therapies provide additional tools to reduce complications in under-vaccinated populations.

1. Introduction

Measles is one of the world's most contagious viral diseases, with an estimated basic reproduction number (R_0) of 12–18, the highest among human pathogens (Guerra et al., 2017). Despite the availability of a safe and effective vaccine for decades (Van Boven et al., 2010), measles cases have surged in recent years (Bednarczyk and Sundaram, 2025). In 2023 alone, over 10.3 million cases and 107,000 deaths were reported worldwide, representing a 21% increase over the previous year and reversing years of progress toward measles elimination (WHOa), (WHOb). Multiple factors are contributing to this resurgence, including vaccine hesitancy, healthcare system disruptions caused by the COVID-19 pandemic, and disparities in vaccine access across regions (The State of the World, 2023). The World Health Organization and UNICEF reported that 22 million children missed their first measles-containing vaccine dose in 2022, the highest number since 2008, leaving millions susceptible to outbreaks (The State of the World, 2023). In the United States, the CDC recorded 285 confirmed cases in the first half of 2024, nearly five times the 58 cases reported in all of 2023, with 40% requiring hospitalization, often in unvaccinated children under five years of age (Measles Cases and Outbreaks). As of November 26, 2025, the US has reported 1798 confirmed cases in 2025 across 43 jurisdictions, with 46 outbreaks and 3 deaths, marking the highest annual total since the elimination status in 2000 (Measles Cases and Outbreaks). Preliminary global data for 2025 indicate continued surges, with over 196,270 suspected and confirmed cases reported as of May 2025 (WHOa). These trends underscore the urgency of strengthening immunization programs and improving vaccine equity. They also highlight the need for additional strategies, including research into acute therapeutics, to protect under-vaccinated populations during outbreaks and reduce measles-related complications and deaths.

* Corresponding author. Independent Medical Alliance, 2001 L St. NW Suite 500, Washington, DC, 20036, USA.
E-mail addresses: amanksarai@gmail.com (A. Kaur), drualaribe11@gmail.com (U. Alaribe), jvaron@imahealth.org (J. Varon), sidmashahid@gmail.com, shassaan@opensourcemed.info (S. Hassaan), mhalma@imahealth.org (M. Halma).

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2. Systematic review methods

A systematic search was performed across PubMed, Scopus, Web of Science, China National Knowledge Infrastructure (CNKI), and Google Scholar for studies published between 1990 and 2025. Clinical trials, observational studies, case series and preclinical studies related to the acute treatment of measles infection were eligible for inclusion. Studies were excluded if they lacked therapeutic outcome data, did not pertain to acute measles infection, or were not peer-reviewed. Only literature with extractable clinical or mechanistic outcomes was included to ensure transparency and reproducibility.

Detailed inclusion and exclusion criteria are summarized in Table 1. The study selection process followed PRISMA 2020 guidelines, as illustrated in Fig. 1.

The search revealed ten articles on treatments for acute measles (Supplementary Table 1), six of these being clinical trials (Table 2), and four being preclinical studies (Supplementary Table 1).

3. Epidemiology of measles

Measles, once an endemic disease in the USA, was considered eliminated in 2000, owing to wide vaccination coverage (Mathis et al., 2022). The decade prior to the introduction of the initial inoculation in 1963 was marked by approximately 500 deaths attributed to the disease per year, mostly in children (Hinman et al., 1983). Before mass immunization efforts, infection was ubiquitous, affecting 95% of the population under 15 years of age (Hinman et al., 1983). Following the introduction of the measles vaccine, infection rates dropped precipitously, with less than 10% of counties in the USA reporting any cases.

Despite the historical success of immunization, protective coverage has declined significantly. In Canada, the rate of Measles, Mumps, and Rubella (MMR) vaccine uptake has decreased from 89.5% in 2019 to 82.5% in 2023 (Public Health Agency of Canada). Declining trust in medical authorities since the COVID-19 pandemic has negatively impacted childhood immunization rates (Halma and Guetzkow, 2023). Additionally, this distrust may be manifesting in other domains, as climate change skepticism is highly correlated with being unvaccinated for COVID-19 (Gounaridis and Newell, 2024), and such skepticism appears to have risen since the pandemic (Ipsos).

Measles is transmitted through airborne respiratory droplets and can remain infectious on surfaces or in the air for up to 2 h, allowing rapid spread among susceptible individuals (Clinical Overview of Measles). Transmission begins several days before the onset of the characteristic rash and continues for several days afterward, contributing to explosive outbreaks in populations with low immunization rates (Clinical Overview of Measles. The extremely high R_0 of 12–18 explains why at least 95% coverage with two doses of a measles-containing vaccine is required to maintain herd immunity and prevent outbreaks (Guerra et al., 2017).

Global surveillance shows significant setbacks: in 2023, only one-third of countries achieved recommended measles surveillance targets, and global MMR vaccine coverage declined from 86% in 2019 to 83% in 2023 (WHOa). These declining trends have led to rising outbreaks even in countries with previously strong immunization programs, often affecting communities with persistent gaps in protective coverage (Measles Cases and Outbreaks). High-risk populations include infants too young for inoculation, malnourished or immunocompromised children, pregnant women, and displaced or marginalized groups (Clinical Overview of Measles). While case fatality rates average 0.1–0.3% in high-income settings, they can reach 3–6% or higher in low-resource environments, underscoring the stark inequities in clinical outcomes (Moss, 2017). Addressing these challenges requires both sustained protective efforts and the development of adjunctive therapies that could help reduce severe disease and mortality during outbreaks (Laksono et al., 2016).

Table 1
Inclusion and exclusion criteria.

Criterion Type	Description
Inclusion Criteria	- Publication date: 1990–2025. - Study type: Clinical trials (RCT, observational), case series, mechanistic studies. - Focus: Acute treatment of measles infection - Data: Extractable clinical (e.g., morbidity, mortality, symptom duration) or mechanistic outcomes (e.g., viral replication inhibition). - Peer-reviewed: Yes.
Exclusion Criteria	- No therapeutic outcome data (e.g., purely epidemiological). - Not pertaining to acute measles (e.g., SSPE-only, chronic). - Non-peer-reviewed (e.g., preprints, abstracts). - Duplicate or irrelevant (e.g., general viral infections, non-human only). - Insufficient detail (e.g., outcomes not quantifiable).

Description: Eligibility criteria applied during study screening and selection for this systematic review.
Abbreviations: RCT, Randomized Controlled Trial; SSPE, subacute sclerosing panencephalitis.

4. Virology & pathogenesis

Measles virus (MeV) is an enveloped, negative-sense, single-stranded RNA virus in the genus Morbillivirus of the family Paramyxoviridae (Laksono et al., 2016). The virus encodes six structural proteins, including the hemagglutinin (H) and fusion (F) glycoproteins, which mediate attachment to host cells and membrane fusion, respectively. MeV primarily infects immune and respiratory epithelial cells by binding to CD150/SLAM receptors on lymphocytes and nectin-4 on epithelial cells, initiating replication in the respiratory tract before systemic dissemination (Rota et al., 2011). The systemic spread of MeV leads to viremia, infecting multiple organs and causing a range of clinical manifestations.

A critical element of MeV pathogenesis is its long incubation period of 9–19 days (Clinical Overview of Measles. Peak viral replication and systemic dissemination occur during this time, preceding the onset of the characteristic maculopapular rash (Laksono et al., 2016). The clinical signs, including the rash, often coincide with the robust, adaptive virus-specific immune response, which begins to clear the infection (de Swart, 2009). Because MeV is typically diagnosed clinically upon the appearance of the rash (Clinical Overview of Measles), direct antivirals are often introduced at a time when the patient is already on the path toward viral clearance (Laksono et al., 2016). This fundamental timeline underscores why measles prevention through vaccination is overwhelmingly the strongest recommended public health strategy over reactive treatment.

One hallmark of measles infection is profound immune suppression, characterized by the depletion of preexisting B and T cell memory, a process known as “immune amnesia,” which results in increased susceptibility to secondary infections for months or even years after recovery (Mina et al., 2015). Recent studies have demonstrated that incomplete regeneration of B cell populations after measles infection contributes to this prolonged vulnerability, further increasing risks of severe illness (Petrova et al., 2019). The characteristic descending maculopapular rash of measles results from a cell-mediated immune response targeting virus-infected endothelial cells in the skin (de Swart, 2009). Severe complications, including pneumonia, diarrhea, encephalitis, and otitis media, remain the leading causes of measles-associated deaths, particularly in malnourished children in low-resource settings (Laksono et al., 2016). A rare but fatal complication, subacute sclerosing panencephalitis (SSPE), can develop years after initial infection, resulting in progressive neurological deterioration due to persistent MeV infection in the central nervous system. Understanding the detailed virology and immunopathogenesis of measles is critical to guiding vaccine strategies and informing research on potential antiviral

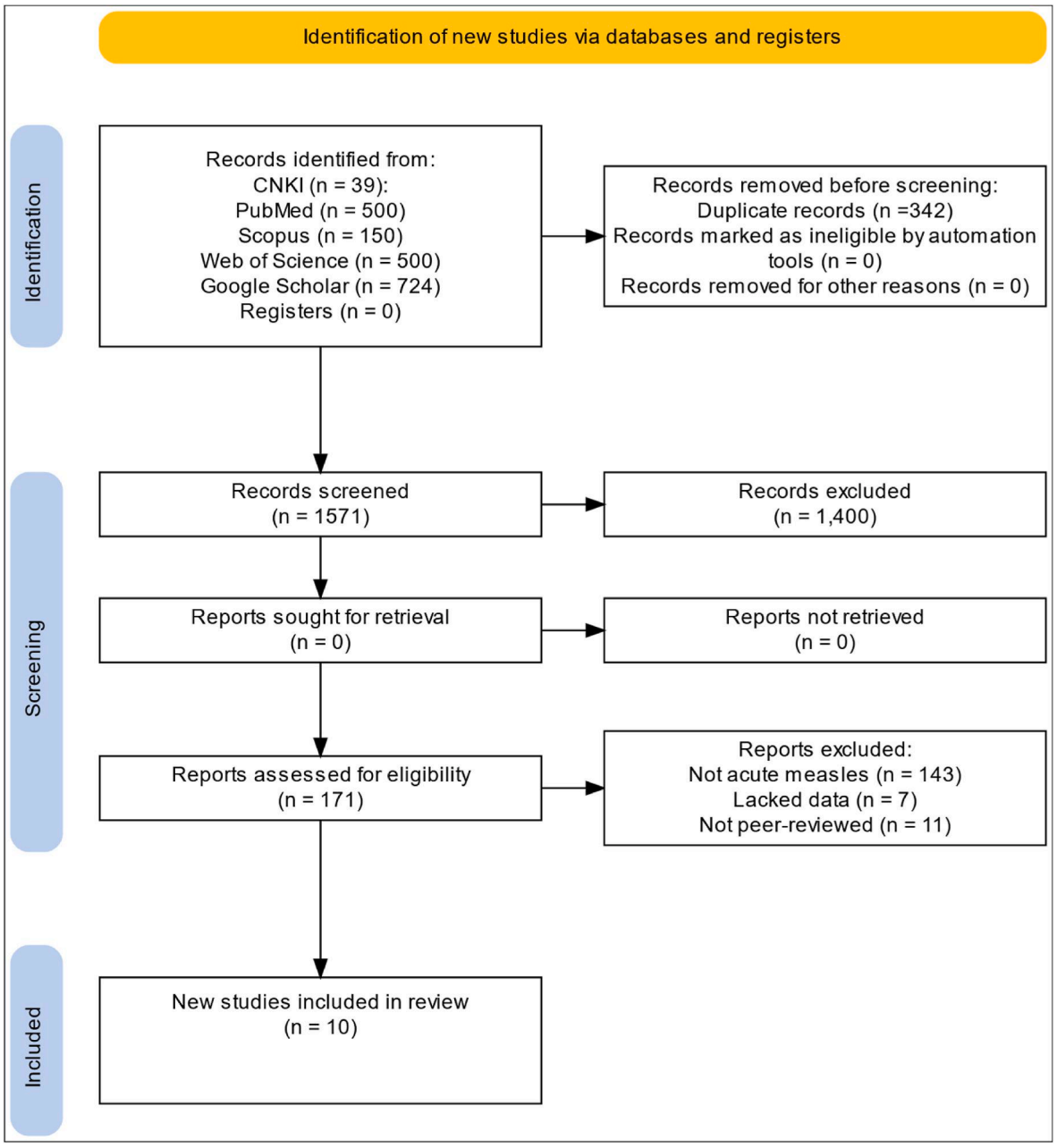

Fig. 1. PRISMA 2020 Flow Diagram. Created using an online tool (Haddaway et al., 2022).

therapies.

5. Treatment of acute measles

While prevention remains the most effective strategy against measles, cases do occur in unvaccinated individuals or through breakthrough infections. In such scenarios, acute treatment strategies are essential not only for managing the infection itself but also for mitigating potential long-term sequelae of measles, such as immune amnesia and increased susceptibility to secondary infections (Mina et al., 2015), (Petrova et al., 2019). Currently, no antivirals are approved specifically for measles virus infection; management remains largely supportive (Measles Cases and Outbreaks), (Clinical Overview of Measles). However, several pharmacologic, immunomodulatory, and experimental approaches have emerged, each supported by varying degrees of clinical and preclinical evidence.

5.1. Patient categories and therapeutic rationale

When considering acute measles treatment, it is important to categorize patients by the severity and nature of their disease:

- **Uncomplicated Acute Measles:** Managed primarily with supportive care (hydration, antipyretics). Direct antiviral use is typically not indicated due to the late timing of diagnosis relative to peak viral replication.
- **Complicated Acute Measles (e.g., Pneumonia, Severe Diarrhea):** Requires aggressive supportive care, treatment of secondary bacterial infections (e.g., antibiotics), and high-dose Vitamin A supplementation, particularly in children (Shann et al., 2000).
- **Measles in Immunocompromised Patients:** These patients often have difficulty clearing the virus, leading to prolonged, severe infection. This category is where off-label use of antivirals like

Table 2
Clinical trials on measles treatments.

Study	Population	Intervention	Comparator	Key Outcomes	Effect Estimate/ Outcome Magnitude	Statistical Significance	Study Design	ROB2 Risk	References
Yao et al. – Vitamin A	98 children (6 mo–12 yrs)	Vit A (2.5 M IU PO) + routine care	Routine care	↓ Fever 2.1 days avg; ↓ hospitalization 3.4 days	RR 0.58 (95% CI 0.40–0.85)	p = 0.006	RCT (unblinded)	Moderate	Yao et al. (2017)
Zhu et al. – Tanreqing	76 adults (18–27 yrs)	Tanreqing IV + standard care	Ribavirin + vitamins	↓ Fever 1.8 days avg; ↓ complications 30%	RR 0.65 (95% CI 0.45–0.92)	p = 0.01	RCT (unblinded)	Moderate	Zhu (2024)
Jian et al. – Glycyrrhizin + Ribavirin	103 patients (5–38 yrs)	Combo IV × 7–10 days	Ribavirin only	↓ Fever 2.4 days; ↓ hospital stay 2.7 days	RR 0.63 (95% CI 0.42–0.88)	p = 0.005	RCT (2-center unblinded)	Moderate	Jian et al. (2012)
Wang et al. – Interferon α-2a vs Ribavirin	81 patients (3–26 yrs)	IFN α-2a IM × 3 days	Ribavirin IV × 5 days	↓ Fever 1.9 days; ↓ rash duration 2.6 days	RR 0.66 (95% CI 0.44–0.90)	p = 0.008	RCT (quasi-randomized)	Moderate–High	Wang and Yang (2004)
Zhang et al. – Measles Enema	108 children (5 mo–6 yrs)	TCM enema + Standard meds	Western meds only	↓ Symptom resolution time 3 days	RR 0.70 (95% CI 0.52–0.94)	p = 0.03	RCT (unblinded)	Moderate	Zhang (2013)
Zhao et al. – Acyclovir + Xiyanping	76 patients (5–25 yrs)	Combo IV	Acyclovir only	↑ QoL score +15%; ↓ rash duration 2 days	RR 0.72 (95% CI 0.50–0.94)	p = 0.02	RCT (unblinded)	Moderate	Zhao (2023)

Note: Summary of included clinical trials evaluating acute pharmacologic therapies for measles. Effect estimates are reported as risk ratios (RR) with 95% confidence intervals (CI) where available, and p-values as reported by the original authors. Reference numbers correspond to the numbered reference list.
Abbreviations: CI, confidence interval; IFN, interferon; RCT, randomized controlled trial; RR, risk ratio; Vit A, vitamin A.

ribavirin and interferon-α is most commonly considered for potential benefit (Mina et al., 2015), (Bichon et al., 2017).

- **Measles with Neurological Complications (including SSPE):** Treatment is largely supportive for acute encephalitis. SSPE is a fatal long-term consequence with no effective cure, though research into antivirals and immunomodulators continues.

5.2. *Mechanistic discussion of antivirals and adjunctive therapies*

To strengthen the utility and clinical relevance of this systematic review, we connect the identified therapies to their mechanisms of action and to the pathophysiology of measles. This section integrates therapeutic mechanisms with current outbreak dynamics, making the review directly relevant to both clinical decision making and public health policy in the U.S. and beyond (Measles Cases and Outbreaks).

5.2.1. *Antiviral therapies (Ribavirin and interferon-α)*

Ribavirin, a broad-spectrum nucleoside analog, is used compassionately in severe or immunocompromised measles cases, with reports of reduced illness duration and fewer complications (Mina et al., 2015), (Bichon et al., 2017). Mechanistically, it acts via direct antiviral activity and innate immune modulation to curb replication (Sengupta and Chattopadhyay, 2024), (Morgenstern et al., 2005). A double-blind, randomized, placebo-controlled trial demonstrated that ribavirin-treated children experienced milder disease and fewer complications compared to controls (Uylangco et al., 1981).

Interferon-α (IFN-α-n1) has also been evaluated in pediatric measles (Lecciones et al., 1998). Similar to ribavirin, it leverages antiviral properties and innate immune modulation (Sengupta and Chattopadhyay, 2024), (Morgenstern et al., 2005). In a randomized study, orally administered IFN-α significantly reduced the duration of fever, malaise, and rash, while demonstrating a favorable safety profile (Lecciones et al., 1998).

Despite these promising results, both ribavirin and interferon remain off-label for measles and are generally reserved for severe or life-threatening cases, particularly in immunocompromised patients (Mina et al., 2015).

5.2.2. *Traditional Chinese Medicine (TCM) and herbal compounds*

Traditional Chinese medications such as Tanreqing and Xiyanping have been included in clinical trials summarized in Table 1. These formulations are considered for their possible antiviral and anti-inflammatory effects (Bai et al., 2025), though further mechanistic studies are warranted (Bai et al., 2025).

- Xiyanping (studied with Acyclovir in Table 1) is hypothesized to act as an anti-inflammatory/antiviral agent.
- Tanreqing (studied in Table 1) is considered for its possible antiviral and anti-inflammatory effects (Bai et al., 2025).
- Glycyrrhizin (studied with Ribavirin in Table 1) is hypothesized to act as an anti-inflammatory or immunomodulatory agent.
- The “Measles Enema” formulation (studied in Table 1) provided symptomatic improvement.

5.2.3. *Vitamin A upplementation*

Vitamin A supplementation remains the most consistently validated adjunct therapy. Its benefit is attributed to its immunomodulatory effects and ability to restore epithelial integrity, which is critical in preventing secondary infections (Vitamin A), (Alfred and KeithP, 1996). Randomized controlled trials and meta-analyses show that high-dose vitamin A (200,000 IU for children and 100,000 IU for infants, administered on two consecutive days) significantly reduces measles-related mortality, particularly in children under two years of age (Hussey and Klein, 1990), (Coutsoudis et al., 1991), (D'Souza and D'Souza, 2002).

The World Health Organization recommends supplemental vitamin A in all children with severe measles infection, though this is often ignored in high-resource settings (D'Souza and D'Souza, 2002). The effect may be less pronounced in older children (Cleary and Hallak, 2023) and in children in high-resource settings who are less likely to be vitamin A deficient (Lo Vecchio et al., 2021).

5.3. *Investigational antivirals*

Novel small-molecule inhibitors targeting the measles virus RNA-dependent RNA polymerase (RdRp) have demonstrated substantial preclinical promise (Krumm et al., 2014), (Wittwer et al., 2021). ERDRP-0519 showed potent antiviral activity by locking the polymerase

in an inactive conformation, halting viral RNA synthesis (Krumm et al., 2014), (Wittwer et al., 2021). In non-human primates, prophylactic and therapeutic administration of ERDRP-0519 prevented clinical disease and improved survival (Wittwer et al., 2021). Additional structural studies confirmed the molecular mechanism, showing that ERDRP-0519 inhibits all RNA synthesis through direct interaction with the L protein of the viral polymerase (Wittwer et al., 2021). The broad-spectrum antiviral remdesivir has also been described as a potential antiviral therapy for measles through its action as a nucleoside analog polymerase inhibitor (Schmitz et al., 2024).

In parallel, monoclonal antibodies against the measles virus fusion (F) protein have been developed. Cryo-electron microscopy revealed that mAb 77 stabilizes the prefusion state of the F protein, effectively blocking its transition to the postfusion state required for viral entry (Zyla et al., 2024). Together, ERDRP-0519 and fusion protein–targeting antibodies represent the most advanced candidates for future therapeutic development.

5.4. *Supportive and passive immunotherapies*

Although not antiviral, antibiotics such as co-trimoxazole play an important role in reducing secondary bacterial complications, particularly pneumonia, which remains a leading cause of measles-related deaths in resource-limited settings (Shann et al., 2000). Intravenous immunoglobulin (IVIG) may be given post-exposure to high-risk individuals, providing temporary passive immunity and reducing the risk of developing severe measles. However, IVIG is not effective as therapeutic if a patient already has measles.

5.5. *Summary of clinical trials*

Table 2 provides a concise summary of key clinical trials evaluating acute treatments for measles, including pharmacological agents like Vitamin A, Ribavirin, and Interferon, as well as Traditional Chinese Medicine (TCM) formulations. The outcomes generally show symptomatic improvement and reduction in complications, though the studies are frequently limited by non-blinded randomized controlled trial (RCT) designs and moderate to high risk of bias (ROB2). The variety of compounds studied, including those aimed at direct antiviral action (Ribavirin, Interferon) and those offering supportive or anti-inflammatory effects (Vitamin A, TCMs), highlights the diverse, mostly experimental approaches taken in the absence of an approved antiviral therapy (Clinical Overview of Measles).

6. Conclusion

Strengthening measles immunization programs must remain the primary global priority. Vaccination prevents disease, decreases viral transmission, and eliminates the need for antiviral intervention. Nevertheless, adjunctive therapies, including Vitamin A, Ribavirin, and Interferon-α, and emerging antiviral candidates, play an important role in reducing complications and protecting susceptible or under-vaccinated populations during outbreaks. Continued research is urgently needed to validate novel antivirals and immunomodulatory treatments while global efforts prioritize robust vaccination coverage.

CRediT authorship contribution statement

Amandeep Kaur: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Ugo Alaribe:** Writing – review & editing, Writing – original draft, Investigation. **Joseph Varon:** Writing – review & editing, Writing – original draft, Conceptualization. **Sidra Hassaan:** Writing – review & editing, Writing – original draft, Investigation. **Matthew Halma:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.antiviral.2026.106361.

Data availability

No data was used for the research described in the article.

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