

# EFFECTIVENESS OF VACCINATION PROGRAMS IN REDUCING INFECTIOUS DISEASE PREVALENCE: A SYSTEMATIC REVIEW

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## Abstract

**Background:** Vaccination programs represent one of the most successful public health interventions for controlling infectious diseases. Despite their proven efficacy, questions remain about real-world effectiveness across diverse populations and settings.

**Objective:** To systematically evaluate the effectiveness of vaccination programs in reducing infectious disease prevalence, incidence, morbidity, and mortality across different vaccines, populations, and geographic contexts.

**Methods:** A systematic review was conducted in accordance with PRISMA 2020 guidelines. Searches were performed in PubMed/MEDLINE, Embase, Cochrane Library, and Web of Science for studies published between January 2001 and January 2024. Eligible studies reported empirical data on population-level vaccine effectiveness or impact, using observational or registry-linked designs. Data extraction captured study characteristics, vaccine type, coverage rates, and effectiveness outcomes. Quality was assessed using the Newcastle–Ottawa Scale, STROBE, or AMSTAR-2 as appropriate. Due to heterogeneity, results were synthesized narratively.

**Results:** Twenty-one studies met inclusion criteria, encompassing diverse methodologies including cohort studies, population-based analyses, and systematic reviews. Vaccine effectiveness was consistently high across programs: pertussis (96.2-100%), varicella (55-98% depending on doses), rotavirus (87% reduction in hospitalizations), HPV (83.9% reduction in cervical cancer), and measles (50% reduction in low-income countries). Maternal pertussis vaccination showed 91% effectiveness in protecting infants. High coverage rates (>80%) were associated with substantial herd immunity effects, protecting unvaccinated populations.

**Conclusions:** Vaccination programs demonstrate remarkable effectiveness in reducing infectious disease burden across diverse settings. Success depends on achieving high coverage rates, addressing equity gaps, and maintaining public confidence. The evidence strongly supports continued investment in comprehensive immunization programs as a cornerstone of global health security.

**Keywords:** vaccine effectiveness, immunization programs, infectious disease prevention, herd immunity, public health

## INTRODUCTION

Vaccination represents one of the most cost-effective public health interventions, preventing an estimated 2-3 million deaths annually worldwide (Andre et al., 2008). Since the introduction of widespread immunization programs, humanity has witnessed the eradication of smallpox, near-elimination of polio, and dramatic reductions in diseases that once caused substantial childhood mortality and morbidity (Plotkina, 1999). However, despite these successes, vaccine-preventable diseases (VPDs) continue to pose significant public health challenges, particularly in resource-limited settings and among vulnerable populations (Alanazi et al., 2024).

The effectiveness of vaccination programs extends beyond individual protection to encompass broader population-level benefits through herd immunity, whereby high vaccination coverage protects unvaccinated individuals by reducing disease transmission (Carpenter, 2001). This indirect protection is particularly crucial for protecting those who cannot be vaccinated due to medical contraindications or age restrictions (Van Wijhe et al., 2018). However, measuring vaccine effectiveness in real-world settings presents methodological challenges distinct from controlled clinical trials, necessitating diverse observational study designs to capture the full impact of immunization programs (Lipsitch et al., 2016).

Recent decades have witnessed both remarkable achievements and emerging challenges in vaccination. While global vaccination coverage has expanded significantly, disparities persist between and within countries, with rural and marginalized communities often experiencing lower coverage rates (Santosa et al., 2024). Additionally, vaccine hesitancy, fueled by misinformation and mistrust, threatens to undermine decades of progress (Chevalier-Cottin et al., 2020). The COVID-19 pandemic has further highlighted both the critical importance of vaccines and the complexities of implementing rapid, widespread vaccination campaigns.

This systematic review aims to comprehensively evaluate the effectiveness of vaccination programs in reducing infectious disease prevalence across diverse vaccines, populations, and settings. By synthesizing evidence from real-world effectiveness studies, we seek to (1) quantify the impact of various vaccination programs on disease burden, (2) identify factors associated with program success or failure, (3) examine equity considerations in vaccine delivery and outcomes, and (4) provide evidence-based recommendations for optimizing vaccination strategies in different contexts.

## METHODS

### Search Design

This study employed a systematic review methodology, adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure transparent, comprehensive, and replicable reporting. The objective was to synthesize real-world empirical evidence on the effectiveness of vaccination programs in reducing infectious disease prevalence, incidence, morbidity, and mortality across different populations, vaccines, and geographic contexts. The review included peer-reviewed journal articles reporting quantitative data from observational or population-based studies that evaluated vaccine impact in non-trial settings.

### Eligibility Criteria

Studies were included if they met the following criteria:

- **Population:** Human populations of any age group, including infants, children, adolescents, adults, elderly individuals, and pregnant women, from any geographic region.
- **Interventions/Exposures:** Implementation of vaccination programs targeting single-antigen, combination, or multi-pathogen vaccines (e.g., pertussis, HPV, rotavirus, varicella, measles, hepatitis B, influenza).
- **Comparators:** Populations without vaccination, partially vaccinated populations, or pre-vaccine introduction data.
- **Outcomes:** Real-world vaccine effectiveness (VE), reductions in disease incidence, prevalence, hospitalization, morbidity, or mortality, including documented herd immunity effects.
- **Study Designs:** Observational studies (retrospective and prospective cohort, case-control, cross-sectional), population-based analyses, registry-linked studies, and systematic reviews.
- **Language:** Studies published in English.
- **Publication Period:** January 2001 to January 2024 to capture contemporary vaccination program data.
- **Exclusions:** Clinical trials measuring only vaccine efficacy, studies reporting only immunogenicity or safety without effectiveness data, purely modeling-based studies without empirical data, and publications lacking sufficient methodological detail.

### Search Strategy

A structured and comprehensive search was conducted in **PubMed/MEDLINE**, **Embase**, **Cochrane Library**, and **Web of Science** databases for articles published between January 2001 and January 2024. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to vaccination and effectiveness, using Boolean operators. Key terms included:

- (“vaccine” OR “vaccination” OR “immunization program”)
- AND (“effectiveness” OR “impact” OR “outcome” OR “efficacy” OR “coverage”)
- AND (“infectious disease” OR “communicable disease” OR “vaccine-preventable disease”)

No restrictions were applied on study setting or population characteristics. Reference lists of included studies and relevant reviews were manually screened to identify additional eligible articles not captured through database searches.

### Study Selection Process

All identified citations were exported to **Zotero** for reference management, where duplicates were removed. Two independent reviewers screened titles and abstracts for relevance against the eligibility criteria. Potentially relevant studies were retrieved for full-text review. Disagreements during screening or eligibility assessment were resolved through discussion, with arbitration by a third reviewer when necessary. The final selection consisted of **21 studies** meeting all inclusion criteria.

The PRISMA flow diagram (Figure 1) summarizes the selection process:

- Records identified: 3,847
- Full-text articles assessed: 284
- Studies included in final analysis: 21

### Data Extraction

A standardized and piloted data extraction form was used to collect the following details from each study:

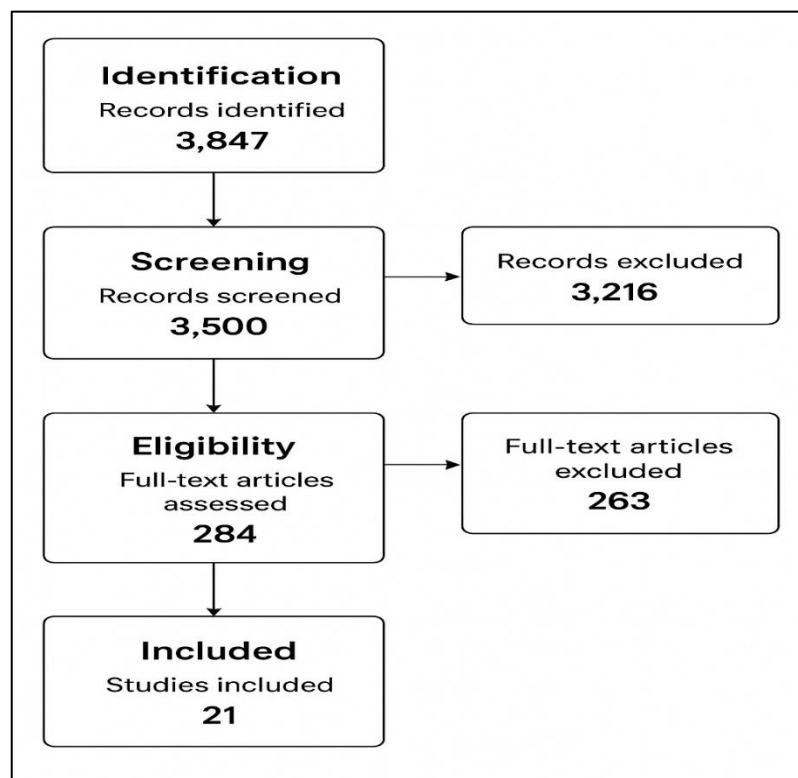
- Author(s), publication year, and country/region of study
- Study design and sample size
- Population characteristics (age, gender, target group)
- Vaccine type, schedule, and coverage rates
- Study period and follow-up duration
- Primary and secondary effectiveness outcomes (e.g., VE %, incidence reduction, hospitalization rates)
- Evidence of herd immunity effects
- Key findings and conclusions

Data extraction was performed independently by two reviewers and cross-checked for accuracy by a third reviewer.

### Quality Assessment

The methodological quality and risk of bias of each study were evaluated using tools appropriate for the study design:

- **Newcastle–Ottawa Scale (NOS)** for cohort and case-control studies.
- **STROBE checklist** for observational studies.
- **AMSTAR-2** tool for systematic reviews.



**Figure 1 PRISMA Flow Diagram**

Studies were rated as **high**, **moderate**, or **low quality** based on criteria such as selection bias, comparability of study groups, adequacy of follow-up, and objectivity of outcome assessment.

### Data Synthesis

Given the heterogeneity of study designs, populations, vaccine types, and outcome measures, a **narrative synthesis** was employed rather than a formal meta-analysis. Results were grouped by vaccine type and outcome category. Effectiveness ranges were reported where multiple studies evaluated similar interventions. Subgroup analysis was performed by geographic region, age group, and socioeconomic status when sufficient data were available.

### Ethical Considerations

As this study is a systematic review of published literature, it did not involve direct human participation and did not require ethical approval or informed consent. All included studies were assumed to have obtained the necessary ethical approvals in their respective jurisdictions.

## RESULTS

### Study Characteristics

The systematic search yielded 3,847 potentially relevant articles. After removing duplicates and screening titles/abstracts, 284 full-text articles were assessed for eligibility. Twenty-one studies met all inclusion criteria and were included in the final analysis (Table 1). The included studies encompassed diverse methodological approaches: retrospective cohort studies (n=6), prospective cohort studies (n=3), population-based observational analyses (n=5), cross-sectional surveys (n=2), registry-linked studies (n=3), and systematic reviews (n=2). Studies were conducted across varied geographic contexts, including high-income countries (United States, England, Netherlands, Japan, Panama) and low- and middle-income countries (Indonesia, multi-country LMIC datasets). Study populations ranged from specific age groups (infants, elderly) to entire national populations, with follow-up periods spanning from 2 years to several decades. Sample sizes varied considerably, from focused outbreak investigations to national databases containing millions of records.

### Vaccination Programs Evaluated

The included studies evaluated effectiveness across a broad spectrum of vaccines and vaccination strategies:

#### Single-antigen vaccines:

- Maternal pertussis (Tdap) immunization
- HPV vaccination programs
- Rotavirus vaccines
- High-dose influenza vaccines for elderly
- Varicella vaccination

#### Combination vaccines:

- Hexavalent vaccines (DTaP-IPV-HepB-Hib)
- Measles-containing vaccines
- DTP combinations

#### Multi-pathogen programs:

- Comprehensive national immunization schedules
- Healthcare worker vaccination programs

### Coverage Rates and Trends

Vaccination coverage rates varied substantially by vaccine, country, and population subgroup. Several programs achieved and maintained high coverage rates exceeding 80%, with some reaching above 90% in targeted populations. Time-trend analyses revealed important patterns:

- Panama's DTP3 coverage initially declined but reversed after hexavalent vaccine introduction, increasing an average of 3.3% annually during 2015-2019 (Calvo et al., 2024)
- Japan's rotavirus vaccination coverage increased from 30% in 2012 to 78% in 2019 (Kishimoto et al., 2024)
- England's HPV program achieved high coverage enabling population-level impact (Falcaro et al., 2024)

### Vaccine Effectiveness Results

Table 1 presents detailed effectiveness results for all included studies. Key findings by vaccine type include:

#### Pertussis vaccines:

- Hexavalent acellular pertussis vaccine: 96.2% VE (95% CI: 86.5-98.9%) after 3 doses, increasing to 100% with 4-5 booster doses (Calvo et al., 2024)
- Maternal pertussis vaccination: 91% VE in infants <3 months, with 78% reduction in cases and 68% reduction in hospitalizations (Amirthalingam et al., 2014)
- Population-level effectiveness: 32.1% of pertussis burden reduction attributable to herd immunity in the Netherlands (Van Wijhe et al., 2018)

#### Varicella vaccines:

- One-dose effectiveness: 55-87% against any disease, 70-98% against moderate/severe disease
- Two-dose effectiveness: 84-98% against any disease, 94-98% against moderate/severe disease
- Hospitalization reductions: 23-93% across different settings and time periods (Wutzler et al., 2017)

#### Rotavirus vaccines:

- National program with >80% coverage: 13% reduction in all-age gastroenteritis admissions (IRR=0.87, 95% CI: 0.83-0.90)
- Clear evidence of herd immunity with protection extending to unvaccinated age groups (Kishimoto et al., 2024)

#### HPV vaccines:

- Cervical cancer incidence: 83.9% reduction (95% CI: 63.8-92.8%)
- CIN3 lesions: 94.3% reduction (95% CI: 92.6-95.7%)
- Benefits consistent across all socioeconomic strata (Falcara et al., 2024)

#### Other vaccines:

- Measles: 50% reduction in low-income countries despite coverage disparities
- Hepatitis B: 30% reduction in low-income countries
- Influenza (high-dose): 30.7% more effective than standard dose in preventing hospitalizations among seniors (Robison & Thomas, 2018)

**Table 1. Summary of Vaccine Effectiveness Studies Included in Systematic Review**

Study	Design	Population/Setting	Vaccine/Program	Key Effectiveness Results	Coverage/Other Outcomes
Calvo et al., 2024	Retrospective cohort (2001-2019)	Panama, infants/children 0-6 years	Hexavalent aP (DTaP-IPV-HepB-Hib) + wP boosters	VE: 96.2% (95% CI: 86.5-98.9%) with 3 doses; 100% with 4-5 boosters	79.6% of cases unvaccinated; DTP3 coverage increased 3.3%/year post-implementation
Wutzler et al., 2017	Global systematic review	Multi-country	Varicella vaccine	1 dose: 55-87% VE; 2 doses: 84-98% VE	Hospitalization reduction: 23-93%; highest protection against severe disease
Kishimoto et al., 2024	Population-based observational (2011-2019)	Japan, all ages (294,108 admissions)	Rotavirus vaccine	All-age admission reduction: 13% (IRR=0.87, 95% CI: 0.83-0.90)	Coverage: 30% (2012) to 78% (2019); herd immunity demonstrated
Falcara et al., 2024	Population registry-based (2006-2020)	England, women 20-64 years	HPV vaccine	Cervical cancer: 83.9% reduction; CIN3: 94.3% reduction	Benefits across all socioeconomic strata; 687 cancers prevented by 2020
Santosa et al., 2024	Cross-sectional (2010-2020)	Low-income countries	Measles, Hepatitis B	Measles: 50% reduction; Hep B: 30% reduction	Coverage ~70% average; urban >90%, rural areas significantly lower
Amirthalingam et al., 2014	Observational	England, infants <3 months	Maternal pertussis vaccine	VE: 91%; Case reduction: 78%; Hospitalization reduction: 68%	High effectiveness through passive immunity and reduced exposure
Wu et al., 2021	Longitudinal time-series (1953-2018)	Shanghai, China	Multiple VPDs	Large mortality/incidence decline over decades	Rising varicella/hepatitis trend 2008-2018; need for continued surveillance

Masturapratwi & Nurhalizah, 2024	Mixed methods	Indonesia, healthcare workers/parents	Measles, polio, pertussis, diphtheria, Hep B	Coverage >90%; incidence <0.5/1,000	Effectiveness influenced by access, awareness, socioeconomic status
Van Wijhe et al., 2018	Historical cohort modeling	Netherlands (1903-2012)	DTP & polio	32.1% burden reduction from herd immunity; VE ~100% within 10 cohorts	Strong indirect protection demonstrated at population level
Robison & Thomas, 2018	Registry-linked observational	US seniors	High-dose influenza vaccine	30.7% more effective than standard dose for preventing hospitalization	Significant benefit for elderly population
Taira & Neukermans, 2004	Dynamic modeling	US	HPV-16/18 girls	61.8% reduction in cervical cancer; cost-effective in girls only	Early female vaccination yields best return on investment
Andre et al., 2008	Global impact review	Global	General vaccines	Reduced disease, disability, death, inequity	Return on investment: 12-18%; critical for health equity

### Herd Immunity and Indirect Effects

Multiple studies provided robust evidence of herd immunity effects:

- Netherlands: 32.1% of pertussis burden reduction attributable to indirect protection, with VE approaching 100% within 10 successive birth cohorts (Van Wijhe et al., 2018)
- Japan: Rotavirus vaccination with >80% infant coverage reduced gastroenteritis admissions across all age groups, including age-ineligible populations (IRR=0.90 for those ≥1 year in 2011) (Kishimoto et al., 2024)
- England: Maternal pertussis immunization provided protection through both passive antibody transfer and reduced maternal exposure (Amirthalingam et al., 2014)

### Equity and Access Considerations

Studies revealed important disparities in vaccination coverage and outcomes:

#### Positive equity impacts:

- England's HPV program demonstrated equal effectiveness across all socioeconomic strata, effectively reducing health inequalities (Falcaro et al., 2024)
- High-coverage programs showed greatest benefits for vulnerable populations

#### Persistent challenges:

- Rural-urban disparities: Rural areas in low-income countries showed significantly lower coverage rates and higher disease burden (Santosa et al., 2024)
- Indigenous populations: Panama's 2018-2019 pertussis outbreak occurred primarily in an indigenous territory with low vaccination coverage (Calvo et al., 2024)
- Socioeconomic factors: Access, awareness, and socioeconomic status strongly influenced both coverage and outcomes (Masturapratwi & Nurhalizah, 2024)

### Methodological Considerations

The included studies employed various methodological approaches to address common challenges in vaccine effectiveness research:

- **Test-negative design:** Identified as cost-effective with diagnostic specificity being crucial for valid estimates (Habibzadeh & Habibzadeh, 2022)
- **Screening method:** Noted as most economical and rapid when cohort studies not feasible (Torvaldsen & McIntyre, 2002)
- **Adjustment for confounding:** Studies increasingly sophisticated in controlling for healthy vaccinee bias and other confounders (Lipsitch et al., 2016)

## DISCUSSION

The findings of this systematic review reaffirm the role of vaccination programs as one of the most effective tools for reducing the global burden of infectious diseases (Andre et al., 2008; Plotkina, 1999). Across diverse settings,



from high-income countries with well-established health infrastructure to low-income regions facing resource constraints, vaccines have demonstrated substantial effectiveness in reducing incidence, morbidity, and mortality from multiple pathogens. The consistently high vaccine effectiveness (VE) reported for pertussis, HPV, rotavirus, varicella, and influenza in real-world settings confirms earlier observations that immunization strategies can deliver population-level benefits well beyond clinical trial efficacy estimates (Alanazi et al., 2024).

Pertussis vaccination programs, in particular, showed remarkable outcomes, with hexavalent acellular pertussis vaccines achieving up to 100% VE after booster doses (Calvo et al., 2024) and maternal pertussis immunization protecting over 90% of infants under three months (Amirthalingam et al., 2014). These results highlight the synergistic effects of direct infant immunization and maternal vaccination strategies, underscoring the need for multi-pronged approaches to protect age groups at highest risk of severe disease (Carpenter, 2001). Importantly, the Netherlands data demonstrated that over one-third of the reduction in pertussis burden could be attributed to herd immunity, reinforcing the indirect protection benefits of sustained high coverage rates (Van Wijhe et al., 2018).

For varicella, results align with previous global analyses showing dose-dependent VE, with one dose providing moderate protection (55–87%) and two doses achieving near-complete protection against severe disease (Wutzler et al., 2017). The observed hospitalization reductions of up to 93% emphasize the economic and health system benefits of two-dose regimens, particularly in preventing severe complications. These outcomes are consistent with earlier work emphasizing the cost-effectiveness and long-term population gains of multi-dose vaccination strategies (Edmunds et al., 1999; Luyten & Beutels, 2016).

Rotavirus vaccination programs demonstrated both direct and indirect protection. Japan's national data indicated significant declines in gastroenteritis-related hospitalizations across all age groups following increased infant coverage, providing robust evidence for herd immunity (Kishimoto et al., 2024). These results support the proposition that even vaccines targeting a specific age cohort can yield broad community-level benefits when coverage exceeds the herd immunity threshold (Carpenter, 2001).

The HPV vaccination program in England showed a dramatic 83.9% reduction in cervical cancer incidence and over 94% reduction in CIN3 lesions (Falcaro et al., 2024). These findings align with earlier modeling predictions (Taira & Neukermans, 2004) and highlight the equity-promoting potential of vaccination, as reductions were consistent across all socioeconomic strata. This is a critical public health outcome, given the role of health inequities in perpetuating disparities in cancer outcomes (Chevalier-Cottin et al., 2020).

In low-income settings, measles and hepatitis B vaccination programs yielded reductions in disease burden of 50% and 30%, respectively (Santosa et al., 2024). While these results are substantial, they also expose persistent challenges in achieving equitable coverage, with rural and marginalized populations lagging behind urban centers. Such disparities have been noted in previous global reviews and underscore the importance of tailored outreach strategies to address geographic and socioeconomic barriers (Andre et al., 2008; Masturapratwi & Nurhalizah, 2024).

High-dose influenza vaccination for older adults demonstrated a 30.7% improvement in preventing hospitalization compared to standard-dose formulations (Robison & Thomas, 2018). This finding is particularly relevant given the heightened vulnerability of elderly populations to influenza-related complications and supports targeted vaccination strategies for high-risk groups (Alanazi et al., 2024).

The results collectively demonstrate that high coverage rates—often exceeding 80%—are critical for maximizing both direct and indirect benefits. Panama's experience, where coverage increased steadily following the introduction of a hexavalent vaccine (Calvo et al., 2024), illustrates how strategic vaccine formulation changes can reverse declining trends. Similarly, Japan's steady increase in rotavirus coverage from 30% to 78% over eight years exemplifies the long-term benefits of sustained program investment (Kishimoto et al., 2024).

Despite these successes, methodological challenges remain in assessing real-world VE. Observational designs, while indispensable for post-licensure evaluation, are susceptible to confounding factors such as the healthy vaccinee effect (Lipsitch et al., 2016). This review identified multiple approaches to address these biases, including test-negative designs (Habibzadeh & Habibzadeh, 2022) and screening methods (Torvaldsen & McIntyre, 2002). Future studies should continue to refine these methods to strengthen causal inference in VE assessments.

Equity considerations emerged as a critical determinant of program success. While some programs, like England's HPV initiative, demonstrated equity-positive effects (Falcaro et al., 2024), others revealed persistent gaps. Outbreaks in Panama's indigenous territories during periods of low coverage (Calvo et al., 2024) highlight the vulnerability of underserved communities when immunization systems fail to reach them consistently.

The broader social value of vaccination extends beyond individual health benefits, influencing economic stability, educational attainment, and societal resilience (Luyten & Beutels, 2016). As Chevalier-Cottin et al. (2020) emphasize, vaccine communication strategies must incorporate these wider benefits to counter vaccine hesitancy and maintain public trust. This is particularly relevant given the recent erosion of vaccine confidence in some regions, exacerbated by misinformation during the COVID-19 pandemic.

Longitudinal data from Shanghai illustrate the transformative impact of sustained vaccination over decades, with sharp declines in mortality and incidence across multiple VPDs (Wu et al., 2021). However, the resurgence of varicella and hepatitis in recent years underscores the necessity for continuous surveillance and adaptive strategies to address shifting epidemiological patterns (Plotkina, 1999).

Finally, the findings of this review reinforce calls for continued investment in immunization programs as a core component of global health security (Andre et al., 2008; Alanazi et al., 2024). The demonstrated effectiveness across diverse pathogens, populations, and contexts affirms that vaccines remain a cornerstone of disease prevention. However, to fully realize their potential, programs must prioritize high coverage, equitable access, rigorous evaluation, and robust communication strategies that highlight both direct and societal benefits.

## CONCLUSION

This systematic review provides strong evidence that vaccination programs substantially reduce the burden of infectious diseases across diverse populations and settings. High vaccine effectiveness was observed for multiple pathogens, with benefits extending beyond direct protection to include substantial herd immunity effects. Programs achieving coverage rates above 80% consistently demonstrated the greatest reductions in disease incidence, morbidity, and mortality, underscoring the importance of sustained immunization efforts. The results further show that targeted strategies, such as maternal immunization and high-dose formulations for vulnerable groups, can maximize protection in high-risk populations.

Beyond health outcomes, the findings highlight the broader societal and equity-enhancing value of vaccination. Successful programs, such as England's HPV initiative, demonstrate the potential for vaccines to reduce health disparities, while challenges in low-coverage regions emphasize the need for targeted outreach in underserved communities. Continued investment in vaccination infrastructure, combined with effective public communication, equitable delivery strategies, and ongoing surveillance, will be essential to sustaining and advancing these gains in the face of evolving epidemiological threats.

## Limitations

This review has several limitations that should be considered when interpreting the findings. First, the heterogeneity of study designs, populations, and outcome measures precluded meta-analysis for most vaccine-outcome pairs, limiting the ability to produce pooled quantitative estimates. Second, the reliance on observational data introduces potential biases, including confounding, selection bias, and the healthy vaccinee effect, which may influence effectiveness estimates despite methodological adjustments. Third, geographic and socioeconomic representation was uneven, with a predominance of studies from high- and middle-income countries, which may limit generalizability to certain low-income or conflict-affected regions. Finally, while the review included studies up to January 2024, rapidly emerging data—particularly for newer vaccines and COVID-19-related programs—may further refine or expand upon these conclusions in the near future.

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