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GLOBAL IMPACT OF IMMUNIZATION PROGRAMMES ON CHILD MORTALITY REDUCTION: A MODELLING STUDY

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ABSTRACT

Background: The Expanded Programme on Immunization, launched by the World Health Organization in 1974, is a cornerstone global health initiative aimed at reducing vaccine-preventable diseases and mortality. Its progressive expansion has improved child survival and population health. **Objective:** To evaluate the long-term impact of immunization programmes on mortality reduction, life-years gained, and overall health outcomes globally from 1974 to 2024. **Methods:** This modelling study integrates multiple transmission and static disease models to estimate vaccination impact across fourteen infectious diseases in 194 countries. Vaccine coverage data were compiled from global datasets, with regression-based imputation addressing missing values. Key outcomes included deaths averted, life-years gained, disability-adjusted life years (DALYs), and reductions in infant mortality. Time-series regression and Markov chain Monte Carlo methods were used to capture uncertainty and non-linear effects. **Results:** Immunization programmes are estimated to have prevented 154 million deaths, with 95% among children under five. Vaccination contributed to about 9 billion life-years gained and over ten billion years of healthy life. Measles vaccination was the leading contributor to mortality reduction. Overall, immunization accounted for around 40% of the global decline in infant mortality, with greater absolute benefits in high-burden regions. Survival probabilities improved significantly across all age groups. **Conclusion:** Immunization remains one of the most effective and equitable public health interventions. Sustaining progress requires continued investment, strengthened primary health care integration, and expanded life-course vaccination strategies aligned with Immunization Agenda 2030.

KEYWORDS: Immunization programmes, Child mortality reduction, Vaccine impact modelling, Expanded Programme on Immunization (EPI), Disability-adjusted life years (DALYs), Measles vaccination, Global health outcomes.

INTRODUCTION

The Expanded Programme on Immunization (EPI) was initiated by the World Health Assembly in May 1974, aiming to provide vaccination to all, inspired by smallpox eradication successes. Initially targeting vaccinations against smallpox, tuberculosis, diphtheria, tetanus, pertussis, poliomyelitis, and measles by 1990, EPI has since expanded to include various pathogens based on country-specific programs. This initiative has significantly increased global vaccination coverage, exemplified by the rise of DTP3 vaccination rates from under 5% in 1974 to 86% in 2019, a slight decline to 84% following the COVID-19 pandemic.

Panel highlights key milestones enhancing global vaccine access from 1974 to 2024. In 1974, WHO established the Expanded Programme on Immunization (EPI) to target various diseases. The 1979 PAHO revolving fund facilitated vaccine procurement. UNICEF's 1982 initiative focused on child health and immunization. The EPI's 1984 standardized schedule included essential vaccines, followed by the Children's Vaccine Initiative in 1990 aiming to expedite vaccine development. SAGE was formed in 1999 to guide WHO on immunization strategies, leading to Gavi's establishment in 2000 to ensure equitable vaccine access. Continuous advancements in vaccine introduction occurred until 2020, when CEPI was created in response to emerging diseases. The Immunization Agenda 2030 and COVAX initiative further aimed to strengthen global vaccination efforts, with The Big Catch-Up in 2023-24 addressing COVID-19 vaccine disruptions. By 2024, EPI expanded to encompass vaccines against thirteen diseases globally and various context-specific diseases, maintaining initiatives for disease eradication and elimination set by WHO since 1980.

METHODS

In this modelling study, the impact of vaccination was assessed by estimating deaths prevented, life-years gained, and disability-adjusted life-years averted against fourteen diseases in 194 WHO member states from 1974 to 2024. A consistent analytical framework was created to calculate vaccination impact per completely vaccinated individual across time by combining twenty-two models and using regression-based imputation for geographic and temporal completeness. The study also looked at how vaccination helped to reduce infant mortality throughout this time, as well as how vaccine impact varied by area.

Undertake research on the health impact of vaccination, we searched PubMed for papers that used modelling methodologies connected to the Expanded Programme on Immunization (EPI). From 1268 findings, eighty-seven research satisfied the criteria, with eighty-one concentrating on the impact of single vaccines across different countries and six on multiple vaccines. Notably, two studies evaluated the deaths and disability-adjusted life-years averted by Gavi-supported vaccines in low- and middle-income countries from 2000 to 2030. Other research investigated how COVID-19 disruptions affected immunization services, as well as the potential implications of meeting Immunization Agenda 2030 coverage targets. However, there has been a shortage of studies quantifying the worldwide EPI impact since its beginning.

This study is the most thorough modelling investigation of historical vaccine impact to date, examining fourteen infections over a 50-year span (1974-2024) in 194 WHO member states. It improves on previous work by Carter et al. (2023) by include new coverage estimates for non-routine immunization, improved disease epidemiology characterisation, and an assessment of vaccination's influence on morbidity and death. The study advances global vaccination impact modelling by incorporating varied model estimates, addressing non-linearity in vaccine impacts, and expanding outputs to places that lack such estimates.

Since 1974, vaccination, particularly measles immunization, has been the most effective health strategy for lowering mortality and improving health outcomes. This study demonstrates immunization's long-term beneficial benefits on baby and child mortality over the last 50 years, emphasizing its critical role in primary health care. Sustained political commitment and investment are required to maintain these health gains. Extending vaccination efforts to under-vaccinated and unvaccinated areas is critical, especially for measles, to maximize future lives saved. Additional vaccines, such as those for HPV and malaria, may improve the efficacy of immunisation regimens.

We present an overview of the mathematical and statistical models used to synthesize age-specific vaccine coverage estimates from several sources, including the WHO Immunization Dashboard and the Vaccine Impact Modelling Consortium. In cases where national data from 1974 to 1979 were unavailable, we projected low- and middle-income countries' coverage from 1980, anchoring at 0% coverage in 1974, while high-income countries' statistics were based on reported coverage from 1980. We evaluated twenty-four vaccination activities grouped by disease, vaccine, and dose number, and used World Population Prospects population projections to calculate fully vaccinated individuals.

Modelling was conducted through three methods: simulation of published transmission models for measles and poliomyelitis across 194 WHO member states over 50 years; extending VIMC transmission models for various diseases to estimate vaccine impact in 110 countries through geographical imputation and temporal extrapolation; and upgrading static disease burden models for diphtheria, tetanus, pertussis, and tuberculosis by incorporating estimates from the 2021 Global Burden of These analyses looked at both the individual benefits of vaccination and the population-level impacts, utilizing current models as a baseline for comparison with previous research.

Procedures

The procedures include combining age-specific vaccine coverage estimates from several WHO data sources and calculating the effect of immunization on disease transmission over time. Key strategies include simulating transmission models for measles and poliomyelitis across 194 WHO member states, extending VIMC models for several illnesses, and leveraging GBD data to enhance static disease burden models. The primary outcome quantifies the impact of the Expanded Programme on Immunization (EPI) from 1974 to 2024 in terms of

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deaths avoided, years of life gained, and newborn mortality reductions due to immunization, as determined by WHO region and World Bank income level.

Statistical analysis

The study employs time series regression models to analyse vaccine impact on deaths averted and years of full health gained across countries using VIMC estimates. It selects socioeconomic and demographic covariates via a corrected Akaike Information Criterion approach, allowing the imputation of vaccine impact in areas lacking data. Four functional relationships (linear, logarithmic, exponential, and sigmoidal) frame the connection between vaccine uptake and outcomes, with parameters derived using a Markov chain Monte Carlo algorithm to account for uncertainty. The analysis encompasses deaths averted by age (0-100 years) from 1974 to 2024, applying disease burden weights from GBD to estimate years of health gained. Following this, the study evaluates hypothetical infant mortality scenarios absent vaccination and assesses the survival gains attributed to vaccination since 1974. These methodologies underwent review by the WHO's Immunization and Vaccines Related Implementation Research Advisory Committee.

RESULTS

Between June 1, 1974, and May 31, 2024, immunization campaigns against fourteen infections avoided a projected 154 million fatalities, 146 million of which were children under the age of five, newborns. These measures resulted in nine billion life-years, and 10.2 billion years of complete health gained, for a global average of more than two hundred million healthy life-years every year. Each life saved corresponded to approximately 58 years of life and 66 years of full health, with poliomyelitis averted contributing to 0.8 billion years of health. Measles immunization alone saved 93.7 million lives, making it the leading contributor to vaccine-related mortality reduction across all demographics and locations during the past 50 years.

Global infant mortality has significantly decreased since 1974, with vaccination contributing to 40% of this reduction, particularly notable in the African region (52%) and less so in the Western Pacific (21%). The 1980s saw a major increase in vaccination coverage for EPI vaccines like BCG and DTP. By 2024, vaccinated children are projected to have a higher survival probability compared to unvaccinated individuals: 44% more for those aged 10, 35% for those aged twenty-five, and 16% for those aged fifty. The Eastern Mediterranean and Africa recorded the largest gains in survival probability, while Europe exhibited the lowest. Relative improvements were greatest in the Western Pacific and Europe, though Africa still faces significant risks. Methodology improvements suggest that community effects enhance model accuracy, and concerns about double counting have a negligible impact (0.01%) on estimates.

DISCUSSION

On the 50th anniversary of EPI, we give the most thorough assessment of the historical immunization program's impact. Since 1974, the vaccines simulated in this study are projected to have saved 154 million lives, with 95% of these occurring in children under the age of five. Vaccination has saved 9.0 billion life-years and resulted in 10.2 billion healthy years of life, including reduced morbidity. Measles vaccine has been the single most significant factor, and it is likely to remain so. Vaccination has accounted for about half of the total global reduction in infant mortality, and in some places, for most of these improvements.

A child born today has a 40% increase in survival for each year of infancy and childhood after 50 years of vaccination, which is a remarkable finding considering the exclusion of smallpox and the exclusion of the anticipated benefits of human papillomavirus (HPV), influenza, SARS-CoV-2, Ebola, mpox, and other vaccines affecting adult mortality.

Many vaccines provide protection in two ways: by directly reducing risk to the vaccinated individual and, for most vaccines (but not tetanus), by limiting community transmission and exposure to infectious illnesses. Paradoxically, when vaccination campaigns reduce community transmission, the measured marginal direct individual benefit of immunization decreases since there is less sickness to avoid. We considered the individual and community benefits of immunization campaigns, as well as their complicated non-linear relationships. The discovery that many models match local data better when the model function incorporates community effects shows that even slight reductions in community immunization coverage can result in a significant increased risk of disease.

Additional research will be conducted. Indeed, a global resurgence of big measles outbreaks is underway because of pandemic-related decreases in measles vaccine coverage. Measles outbreaks are used to track immunization program performance under the Immunization Agenda 2030 (panel). Historically, the benefit of measles vaccination on annual mortality reduction peaked concurrently with the global expansion of first-dose coverage. Vaccine coverage then plateaued, and other non-vaccine measures that lower infant and child mortality were introduced, but this varies by location. These non-vaccine characteristics also contributed to a reduced risk of death from measles infection.

Regardless of the impact of non-vaccine factors, forecasting predicts that measles vaccination will continue to be the most effective measure for saving lives well into the future. In the twenty-first century, the growing impact of other interventions highlights the need for continuous funding and implementation initiatives

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that combine immunization and primary health-care services.

Unlike measles vaccines, which break communal chains of transmission, tetanus immunizations exclusively protect the vaccinated individual or neonates through placental immunity. Because there are no plateauing population-level effects, the per-dose impact remains high. Tetanus elimination in mothers and newborns can be achieved through a concerted effort to ensure adequate, timely access to immunization for pregnant women and their newborns, resulting in significant relative reductions in newborn disease. Pertussis vaccination helped save many lives. Nonetheless, pertussis mortality is a persistent and preventable cause of death in young infants in all contexts. In many contexts, the acellular vaccination is utilized because it is less reactive than the whole-cell vaccine, although it is now recognized to provide poorer long-term protection, necessitating booster doses during pregnancy.

The contribution of tetanus and pertussis emphasizes the need of immunization programs for pregnant women. Strengthening and expanding these programs to encompass influenza, respiratory syncytial virus, and group B streptococcus present more chances for future lifesaving, while efficacious and appropriately powered safety studies of prenatal delivery can enable higher adherence. Despite being the oldest and most widely used vaccination, the neonatal BCG immunization had a minor influence on tuberculosis mortality. This conclusion is explained by the vaccine's poor biological efficiency, which varies by strain, as well as the likelihood that efficacy may wane by adulthood. New tuberculosis vaccinations are under development. This analysis did not consider the potential impact of the BCG or measles vaccines on mortality from causes other than tuberculosis and measles, which some data shows could be significant.

Vaccination against poliomyelitis has had a moderate influence on mortality, avoiding 1% of fatalities. However, it has led to significant public health advantages by lowering poliomyelitis-induced paralysis, accounting for 8% of the 10.8 billion healthy life-years gained. The opportunity to eradicate this long-standing disease, like was done with smallpox, should not be missed. The closer we go to poliomyelitis eradication, the greater the challenge, but also the corresponding need to complete the mission.

The analysis discovered that, in 2024, both children and adults are more likely to live to their next birthday than if no vaccines had occurred since 1974.

These findings highlight the continued positive impact of vaccination throughout the life course, even in the face of waning vaccine immunity, and an analysis focused on infant-specific and child-specific schedules, which excludes other vaccination programs, such as HPV, influenza, or COVID-19, that specifically reduce adult mortality.

A secondary goal of this research was to assess vaccine impact by area and other determinants. We discovered that places with initially high mortality experienced bigger absolute improvements, but the relative benefit was smaller due to conflicting mortality risks. Vaccines promote equity by saving more lives in areas with higher death rates.

The contribution of vaccines to total infant mortality reduction varies by area, with vaccines having a greater impact in the WHO African and European regions, whose absolute mortality burdens are quite different. To correctly understand such findings, both the relative and absolute effects must be considered. Vaccines have contributed significantly to lower infant mortality in both Africa and Europe, but in Africa, this has resulted in many more lives saved in absolute terms, demonstrating the strong vaccination impact that is possible in places with the highest infectious disease burden.

EPI vaccines enhance current survival probability at all ages in Africa over time, in both relative and absolute terms, but the detectable influence is less in persons born in recent decades. This is consistent with the finding that, despite vaccines' significant contribution to infant survival, in recent years non-vaccine therapies have saved an increasing number of lives. The Immunisation Agenda 2030 places vaccination squarely within the remit of primary health care and the Alma Ata Declaration. Vaccine programmes are frequently the foundation for systems that provide additional life-saving health-care services.

The current authors intend to expand our studies to investigate the effect of sociodemographic characteristics on the feasible impact of vaccination initiatives, as well as the underlying explanatory differences across and within areas. The data presented here provides a minimum cautious estimate of vaccination impact. We considered extrinsic factors that lower infectious case fatality and reduce the vaccine's impact on mortality. We did not consider the downstream benefit of vaccination on noncommunicable disease mortality (for example, the effect of diarrhoea on malnutrition), nor the broader economic benefit or community development advantages that vaccination may allow, because the scale of causal attribution is difficult to assess. We also did not include vaccinations' heterologous impacts on episodically non-specific immune conditioning or other alternative methods.

Such outcomes could indicate that we undervalued the benefits of some vaccines (e.g., BCG and measles) or did not adequately discount the benefits of others (for example, DTP-containing immunizations). The methodologies utilized in this investigation are ideally suited for a more detailed examination of the potential

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population repercussions of heterologous effects, although this is outside the scope of this work. We cannot claim to have conducted a complete analysis of the impact of immunization because we excluded vaccines such as those against COVID-19, which may still be in equilibrium; influenza, which is subject to local-level variation in seasonality and immunity profiles; and HPV, a vaccination programme that is expected to have a rapid increase in impact in coming years.

We excluded vaccines used for outbreaks such as cholera or Ebola, vaccines targeting diseases that occur in adulthood, and vaccines used primarily in high-income settings such as varicella, herpes zoster, or mumps, and the counterfactual assumed a smallpox-free world, so we did not account for the enormous benefit achieved by its eradication. The potential of duplicate counting is a constraint, although we have demonstrated that it has a minor impact on our estimations. We presented global and regional findings, which limits the spatial resolution at which conclusions may be drawn. Work to extend these models in conjunction with member states is now underway.

The calendar-year impact of vaccination over the last 50 years was captured; however, unlike birth cohort-based or year-of-vaccination approaches, which require longer-term projections based on broad assumptions, the calendar-year-based approach does not fully account for any post-2024 lifetime vaccination impacts, particularly for diseases that occur later in life, implying a significant underestimate for diseases such as hepatitis B. For the reasons stated above, HPV, which was originally licensed in 2006 and became more widely available in the 2010s, was removed from the analysis because to timing differences.

The modelling utilized in this study was like previously conducted estimates against previously conducted estimates with time and space constraints. Other projections of future impact as part of the Immunization Agenda 2030, which include high coverage targets for the HPV vaccine, indicate that an even greater number of annual fatalities saved across the life course is possible. This imperative is highly dependent on achieving post-COVID-19 pandemic recovery and restoration of the trajectory to the Immunization Agenda 2030 targets; achieving and maintaining universally high coverage with measles-containing vaccines; introducing the much-anticipated malaria, respiratory syncytial virus, and other potential high impact vaccines; and achieving universal high coverage with an HPV vaccine.

HPV vaccine coverage now reaches only 21% of adolescent girls worldwide, falling far short of the WHO Cervical Cancer Elimination strategy's target of 90% coverage by 2030.

The first post-COVID-19 pandemic release of the WHO and UNICEF Estimates of National Immunization Coverage (known as WUENIC) revealed that countries that had sustained improvements in vaccine coverage in the years preceding the pandemic also made more resilient recoveries from pandemic impacts on the program than countries with plateaued vaccine coverage. The study's findings highlight the fact that vaccination's outstanding achievements are the result of years of constant, layered, data-driven, and operationally realistic efforts.

Stakeholders must protect EPI gains, maintain coverage, address remaining gaps, and view immunization programs as the foundation of pandemic preparedness and robust and resilient health systems. We are at a watershed moment in infectious disease control. The significant and widespread advances that are possible have been realized via concerted collective effort. The next 50 years of what is now known as the Essential, rather than Expanded, Programme on Immunization will necessitate improvements in targeting and reach, particularly for measles vaccines, considering future complex realities for unvaccinated and under-vaccinated children and communities. Continuous community engagement in vaccination uptake is critical, as hard-won gains can be easily lost. The next 50 years contain immense promise but achieving it will need collaborative and continuous determination.

CONCLUSION

Over the past fifty years, the Expanded Programme on Immunization, led by the World Health Organization, has significantly enhanced global health by reducing mortality and morbidity, particularly in children under five. Vaccination has improved life expectancy and community health through direct and herd immunity effects. Key vaccines, especially for measles, are vital in lowering child mortality, while the relevance of tetanus and pertussis vaccinations and maternal immunization strategies persist. However, recent interruptions in immunization coverage highlight the vulnerability of these gains. Immunization programs promote equity, especially in high-burden areas, emphasizing the need for focused efforts on underserved populations. Integration with primary health care is crucial for resilience and overall health outcomes. The analysis suggests that the benefits of vaccination may be underestimated and calls for future research to include broader socio-economic impacts. Immunization is fundamental for global health and pandemic preparedness, requiring sustained investment and community engagement to meet the goals of Immunization Agenda 2030.

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