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EPI@50 impact modeling analysis

"Contribution of vaccination to improved child survival: modelling 50 years of the Expanded Programme on Immunization"

Frequently Asked Questions (FAQs)

1. What is EPI?

2024 marks the 50th anniversary of the Expanded Programme on Immunization (EPI), an initiative launched by member states at the World Health Assembly in 1974 with the goal of providing universal access to life-saving vaccines for children worldwide. Building on the success of smallpox eradication, at its inception EPI expanded from smallpox to include vaccines against diphtheria, measles, pertussis, polio, tetanus and tuberculosis. It now covers vaccines against 13 vaccine preventable diseases across the life course and over 17 context-specific vaccine preventable diseases. EPI is now commonly referred to as the Essential Programme of Immunization.

For more information, please see 50th anniversary of the Expanded Programme on Immunization (EPI) (who.int)

2.Why this analysis?

To evaluate the impact of EPI, WHO together with leading infectious disease modelling groups has estimated the impact of vaccination against 14 diseases in 194 Member States over the last 50 years. Both routine immunization and supplementary immunization activities have been incorporated. Impact is measured as the number of deaths averted, life years gained, years of full health gained (disability-adjusted life years averted), and contribution of vaccination to improved infant (i.e. a child in their first year of life) survival. The results are intended to be released on 24 April at 15:00 CEST during the World Immunization Week.

3. Which pathogens are included in this analysis?

The analysis quantifies the impact of vaccination against 14 diseases including diphtheria, *Haemophilus influenzae* type B, hepatitis B, Japanese encephalitis, measles, meningitis A,

pertussis, invasive pneumococcal disease, poliomyelitis, rotavirus, rubella, tetanus, tuberculosis, and yellow fever.

These diseases represent the majority of EPI's 13 vaccine-preventable diseases, except HPV and COVID-19.[1]

Of over 17 context-specific vaccine-preventable diseases, Japanese encephalitis, meningitis A, and yellow fever are included.[2]

4.Why were HPV and COVID-19 not included?

HPV was excluded due to incomparability of timeframe to capture expected outcomes. There is a long time lag between vaccination and related key health gains (such as averting cervical cancer). First licensed in 2006, HPV vaccines started being introduced more widely from 2010 onwards. Therefore, full impact is not captured by a retrospective analysis. However, other studies that look at potential future impact suggest that even a greater number of deaths could be averted over the life course.

COVID-19 was excluded due to challenges in even short-term estimates of global public health gains through vaccination in a highly dynamic epidemiological context. There is large uncertainty around disability weights for mild infections. Disability weights are used to calculate years of full health gained (disability-adjusted life years averted).

The Vaccine Impact Modeling Consortium (VIMC) is currently working on generating COVID-19 vaccine impact estimates for a subset of countries. We are collaborating with VIMC to cover all 194 Member States as part of our future work on IA2030 impact goal indicator 1.1. ("number of future deaths averted through immunization").

5. Why were JE, MenA and Yellow Fever included?

Three diseases from 17 context-specific VPDs are included in this analysis. JE, MenA, and Yellow Fever vaccines and related immunization activities are supported by Gavi, the Vaccine Alliance. Mathematical models for these three diseases are part of the VIMC portfolio.

[1] 13 global VPDs: **BCG,** COVID-19, **Diphtheria, HepB, Hib,** HPV, **Measles. PCV, Pertussis, Polio, Rotavirus, Rubella, Tetanus**

[2] 17 context-specific VPDs: Cholera, HepA, Influenza, **Japanese Encephalitis,** RSV, Malaria, **Meningitis,** Mpox, Mumps, Rabies, RSV, TCV, Tick-Borne Encephalitis, Varicella, Dengue, **Yellow Fever,** Zoster

6. What did we do to estimate the impact of vaccination over the last 50 years?

We used a suite of mathematical and statistical models to estimate the global and regional public health impact of vaccination against 14 diseases. Estimates of deaths averted and years of full health gained (DALYs averted) come from the Vaccine Impact Modeling Consortium,[3] static models developed by WHO,[4] and other dynamic transmission modeling groups.[5]

To estimate the historical impact, we need a counterfactual (i.e. what has not happened but could, would, or might under different conditions). In this analysis, we compared two scenarios: 1) mortality and morbidity with the coverage of all routine and supplementary activities that took place from 1974- 2024 and 2) mortality and morbidity under a hypothetical scenario of *no vaccination* in the same period. Modeled outcomes were used to estimate the contribution of vaccination to globally declining infant mortality rates.

We used estimates from these models where possible. In case of missing years and countries, we used temporal extrapolation and geographical imputation.

7. Were you able to generate modeling estimates for all countries? And for all years?

Temporal extrapolation

To estimate impact in periods not covered, we first fit a relationship between vaccine impact and vaccine coverage for each country and disease. This relationship can take one of four forms that represent individual and population level benefits of vaccination. Using this fitted relationship, we inferred vaccine impact either back or forward in time according to observed coverage.

Geographical imputation

We fitted time series regression models with vaccine impact for each vaccine and each country where model estimates are already available. The time series regression models include a wide variety of predictor variables that give rise to differences across countries (e.g. malnutrition, access to clean water and sanitation, Gini coefficient/inequality, health

[3] models from VIMC (8 diseases: Hib, hepB, JE, IPD, rotavirus, rubella, mening A and YF); VIMC modelling is available for 2000-2024 for 110 countries (where appropriate)
[4] Static models by WHO (4 diseases: diphtheria, tetanus, pertussis, and tuberculosis); WHO static modelling is based upon GBD estimates that is available for 1980-2021 for all 194 countries
[5] Other dynamic transmission models (2 diseases: measles, polio)

spending, etc). We then used these models to impute impact in countries for which we had no modeling estimates.

8. What assumptions did you make for years without coverage estimates?

Vaccination coverage estimates are available from 1980 to 2022. We made broad assumptions for the following years.

1974-1980
- Vaccination coverage was constant over the 1974-1980 period for countries with high-income World Bank status in 1980.
- Vaccination coverage linearly increased from zero over 1974-1980 period for countries with middle- or low-income World Bank status in 1980.

2022-2024
- We used 2022 estimates for 2023 and 2024.

9. What did we find?

- Since 1974, vaccination has averted over 154 million deaths (6 deaths every minute), including 146 million among children under 5 years, of whom 101 million infants.
- Measles vaccination accounted for 60% of the total benefit of vaccination over this 50-year period. Of the nearly 154 million lives saved since 1974, nearly 94 million were a result of the measles vaccine.
- For every life saved, 66 years of full health were gained (disability-adjusted life years averted) on average, translating to 10.2 billion years of DALYs averted in total.
- Global infant mortality has declined substantially since 1974, and vaccination has accounted for 40% of that decline, and over 50% in the African region.
- In 2024, a child at any age under-10 is 40% more likely to survive to their next birthday compared to a hypothetical scenario of no historical vaccination.
- Increased survival probability is observed even well into late adulthood.

10. Why does it matter?

Vaccination in the last half century has made the greatest contribution of any health intervention to mortality reduction and years of full health gained.

The results demonstrate the monumental achievement of the Expanded Programme on Immunization in reducing child mortality over the past 50 years. Millions of lives have been saved, and billions of years of full health have been gained thanks to vaccination.

Vaccines account for over 40% of the decline in global infant mortality since 1974. The relative contribution of vaccines was especially high during the 1980s during the intense scale-up of the original EPI vaccines. Increasing importance of non-vaccine factors highlights the need for strengthening primary health care and addressing social determinants of health to further improve child survival.

Substantial gains in childhood survival highlight the importance of sustained efforts to protect gains from the past decades and extend further benefits to un- and under-vaccinated children and missed communities. The results from this study demonstrate that the impact of vaccination programmes on survival persist throughout the life-course.

Continuing the success of EPI will require ongoing catch-up and future strengthening of immunization programmes through the Immunization Agenda 2030.

For more information, please see https://www.immunizationagenda2030.org/

11. What vaccines have produced the biggest health benefits?

Looking at the last 50 years we see the primary importance of measles vaccine. Measles vaccination accounted for 60% of the total benefit of vaccination over this 50-year period. Of the nearly 154 million lives saved since 1974, nearly 94 million were a result of the measles vaccine.

Yet we are losing ground against measles with pandemic associated disruptions in immunization. There were still 33 million children who missed a measles vaccine dose in 2022: nearly 22 million missed their first dose and an additional 11 million missed their second dose. Coverage of 95% or greater with 2 doses of measles-containing vaccine is needed to protect communities from outbreaks.

Forward projections show that measles will remain the most important preventable cause of ongoing mortality. By reaching aspirational IA2030 coverage targets, an estimated 50 million deaths are expected to be averted due to vaccinations administered between the years 2021 and 2030, of which measles account for the largest proportion (37%). Please see **Question 12** for more information on IA2030 vaccine impact estimates.

12.How does it compare to other estimates?

This study is the most comprehensive modeling analysis of historical vaccine impact to date. It covers 14 pathogens with a 50-year timeframe (1974-2024) at the global level (194 countries).

Two studies conducted by the Vaccine Impact Modelling Consortium (VIMC) estimated the number of deaths and DALYs averted due to vaccines supported by Gavi, the Vaccine Alliance in low- and middle-income countries from 2000-2030.

- Li et al (2021) estimated the calendar year impact of 37 million (30–48) deaths averted between 2000 and 2019 and 32 million (17-41) deaths averted between 2020 and 2030 due to vaccination against 10 pathogens in 98 LMICs.
- Using an alternative method which attributes long term impact of vaccination to the year in which the vaccination activity took place ("year-of-vaccination" method), Toor et al (2021) estimated that 50 million (41-62) deaths were averted by vaccination activities against 10 pathogens in 112 LMICs that took place between 2000 and 2019 and 47 million (39-56), between 2020-2030.

Using the same "year-of-vaccination" method, WHO and its partners projected that 51.5 million (44.0–63.2) deaths will be averted due to vaccination activities between 2021 and 2030 against 14 pathogens in 194 countries (Carter et al 2023). The results from this work have been used as the global target number ("50 million deaths averted") for the Impact Goal Indicator 1.1. "Number of further deaths averted through immunization" as part of the Immunization Agenda 2030 Monitoring & Evaluation framework. The same study estimated that the historical number of deaths averted is 29.7 million (26.6–33.8) from 2001 to 2010 and 40.2 million (36.0–45.2) from 2011-2020.

13.Why is this a conservative estimate?

The analysis presented is a conservative estimate, because:

(1) We estimated the averted deaths that would have occurred in the past 50 years. **This does not include deaths that will yet be averted by vaccines given in the last 50 years**, for example the benefits of hepatitis B vaccine are seen years later, and we did not capture those benefits. We have also not included vaccines such as HPV that children receive in adolescence but that prevents cancers in adult life. Please see **Question 11** for other estimates that use alternative approach.

We also did not include recently introduced vaccines like COVID-19 or the new malaria vaccines.

(2) **We did not include flow-on effects of vaccines on non-communicable disease**. For example, preventing infectious diarrhoeal disease through vaccination may have benefits for preventing subsequent malnutrition. Such benefits are more difficult to quantify and were not included. There is evidence that some vaccines have effects on diseases other than those they are designed to prevent, and these also were not included. We also did not account for the community and economic benefits of better overall health and the positive feedback this has on reducing mortality.

(3) **Quantification of vaccine impact is limited to 14 diseases only,** not including other vaccines such as Ebola, HPV, influenza, MPox, mumps, SARS-CoV-2, smallpox, varicella, etc. That also impact preventable adult mortality. We also did not include important regional vaccines like the new vaccines against malaria, a major killer in Africa.

Please see **Question 3** for the scope of diseases.

14. How did you take into consideration other confounding factors for child mortality reduction from the last 50 years? (E.g. reduction in poverty and malnutrition or improvements in water and sanitation)

We used UN World Population Prospects 2022 data for historical infant and child mortality values and rates. The factors mentioned above are implicit in this observed data.[6]

In addition, such factors may also be reflected in model parameters (e.g. change in CFR over time) for certain dynamic transmission models and are indirectly captured during model alignment processes that match model outcomes to country-specific epidemiological data.

For countries without existing modeling estimates, we imputed estimates by using time series regression models with a wide variety of predictors related to malnutrition, inequality, and the other sociodemographic variables.

[6] To estimate attributability of vaccination to declining infant mortality rates, we compared this observed data to two hypothetical historical scenarios: 1) where no vaccination was implemented over the past 50 years (using deaths averted estimates from our modeling estimates), and 2) where no factors – including those mentioned above- improved infant survival probabilities.

15. For the relative decrease in infant mortality and contribution of vaccination, what drives differences across regions?

The magnitude of vaccines' contribution to infant mortality is variable across regions, ranging from 21% in the Western Pacific Region to 52% in the African region.

Contribution of vaccination to decrease in infant mortality rate (1974-2024)

Region	Proportion
Global	40%
AFR	52%
AMR	41%
EMR	33%
EUR	43%
SEAR	22%
WPR	21%

While vaccines have played an important role for infant survival, contribution of non-vaccine factors has increased over time and is becoming more important. Immunization programmes often serve as the backbone for health systems that provide other life-saving interventions, and the IA2030 places vaccination squarely within the remit of primary health care and the Alma Ata Declaration.

While examination of non-vaccine factors is not the main focus of this analysis, our future work will explore underlying factors (including sociodemographic factors) that drive differences within and across regions.

16. How can we best interpret the results on marginal increase in survival probability?

The results are a snapshot of the 2024 context, showing differences in survival rates between two scenarios: 1) a scenario where all routine and supplementary activities took place as observed in the last 50 years and 2) a hypothetical scenario of no vaccination since 1974.

The x-axis shows age groups for the 2024 population. The y-axis shows the relative difference (proportional change) and absolute difference (percentage point reduction) in survival probability between two scenarios for the corresponding age group in the x-axis. Plot lines are shown for the world and by WHO region.

Giving two examples to aid the reader:

In 2024, a child at any age under 10 years is at least 40 percent more likely to survive to their next birthday compared with the hypothetical scenario of no vaccination over the last 50 years (see the "World" plot line for relative change).

The results highlight the continued positive effect of vaccination for other age groups. In 2024, 50-year olds are 16 percent less likely to survive than if there had there been no vaccination in the last 50 years (also see the "World" plot line for relative change).

17. Why are country estimates not available?

Our estimates are aggregated at regional and global level. Modeled estimates at the country level present substantial uncertainty as they did not go through a standardized fitting process and are not necessarily calibrated for all countries. Ongoing work to extend our models with the engagement and consultation with Member States is underway.

18.Where can I find more details about methods and results?

The open source code library for this analysis is publicly available from the GitHub repository: https://github.com/WorldHealthOrganization/epi50-vaccine-impact

The manuscript was accepted for publication in T*he Lancet* on 22 April 2024.
The repository contains the latest version of the manuscript:
https://github.com/WorldHealthOrganization/epi50-vaccine-impact/tree/master/manuscript