# Articles

# Health impact and economic evaluation of the Expanded Program on Immunization in China from 1974 to 2024: a modelling study

Chaofan Wang\*, Xiaozhen Lai\*, Kaja Abbas, Koen B Pouwels, Haijun Zhang, Mark Jit, Hai Fang

## **Summary**

**Background** The Expanded Program on Immunization (EPI), initiated by WHO in 1974, is a cornerstone of public health. China's EPI covers more than a sixth of the world's population and includes eight routine vaccines with high coverage rates. This study aimed to estimate health and economic impacts of China's EPI over the past 50 years (1974–2024).

Methods This study mathematically modelled the impact of all eight routine vaccines in China's EPI against eight pathogens (measles, pertussis, hepatitis B, tuberculosis, hepatitis A, Japanese encephalitis, meningitis A, and poliomyelitis) based on data availability and their substantial disease burden, particularly accounting for non-linearities in vaccine impact. Health and economic outcomes were determined using mathematical models between a counterfactual scenario without vaccination (vaccine coverage set to zero) and the current vaccination scenario (routine vaccination scheduled at age 0–6 years), based on calendar year and birth cohort approaches. The health impact of China's EPI from 1974 to 2024 was measured in the number of cases, deaths, and disability-adjusted life-years (DALYs) averted.

**Findings** We estimated that China's EPI averted 703.02 million cases (95% credible interval 699.51–722.80) and 2.48 million deaths (2.14-2.97) in 1974–2024 based on the calendar year approach, equivalent to averting an estimated 160.22 million DALYs (145.05-196.99). Using the birth cohort approach, we predicted 707.41 million cases (703.93-727.03) and 7.01 million deaths (6.95-7.87) averted over the lifetime, corresponding to 279.02 million DALYs (265.78-316.12). From a societal perspective, the aggregated cost of vaccination was estimated to be US\$124.06 billion (120.49-127.49), although the benefits amounted to \$2417.85 billion (2359.38-2710.35). China's EPI yielded an aggregate benefit–cost ratio of 19.48 (18.82-22.08) from the societal perspective and 8.02 (7.64-8.80) from the provider's perspective.

Interpretation China's EPI has shown remarkable health and economic achievements, contributing to worldwide EPI success in the past 50 years. Further investment in EPI is warranted to sustain coverage and expand vaccine inclusion in China and globally.

Funding Beijing Natural Science Foundation.

Copyright © 2025 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

## Introduction

The year 2024 marked the 50th anniversary of the global Expanded Program on Immunization (EPI).<sup>1</sup> In 1974, WHO launched the EPI in an effort to combat global infectious diseases by ensuring coverage of essential vaccines worldwide, which initially encompassed four routine vaccines: measles, diphtheria-tetanuspertussis (DTP), BCG, and poliomyelitis. From 1974 to 2024, the WHO estimated that the global EPI has prevented a total of 154 million deaths.<sup>2</sup>

China, the most populous country in the world until 2023,<sup>3</sup> historically had a high burden of infectious disease morbidity and mortality<sup>4</sup> and formally launched the EPI in 1978. Before this event, China started using BCG and pertussis vaccines in 1960, then the poliomyelitis vaccine in 1962, measles vaccine in 1965, and Japanese encephalitis vaccine in 1967.<sup>5</sup> In 2002, China fully

integrated hepatitis B vaccine into the EPI and renamed the programme to the National Immunization Program.<sup>6</sup> In 2008, China expanded the EPI by replacing the measles vaccine with the measles-mumps-rubella vaccine and adding vaccines for hepatitis A, Japanese encephalitis, and *Neisseria meningitidis* serogroups A and C. Since 2016, China has reached national coverage of more than 95% for each of the eight EPI vaccines (measles-mumps-rubella, DTP, BCG, poliomyelitis, hepatitis A, hepatitis B, Japanese encephalitis, and *Neisseria meningitidis* serogroups A and C).<sup>7</sup>

In the past five decades, declines in reported disease burden associated with EPI vaccines in China have been well documented.<sup>8,9</sup> However, comprehensive health impact and economic evaluation of China's EPI in the past 50 years remain unclear.<sup>10</sup> The Vaccine Impact Modelling Consortium (VIMC) modelled the health impact of





# Lancet Public Health 2025

Published Online April 23, 2025 https://doi.org/10.1016/ S2468-2667(25)00039-8

For the Chinese translation of the abstract see **Online** for appendix 1

\*Contributed equally

School of Public Health (C Wang BS, X Lai PhD, H Zhang MS), Peking University **Health Science Center-Chinese** Center for Disease Control and **Prevention Joint Center for** Vaccine Economics (C Wang, X Lai, H Zhang, Prof H Fang PhD), and China Center for Health Development Studies (C Wang, X Lai, H Zhang, Prof H Fang), Peking University, Beijing, China: Nuffield Department of Population Health (X Lai) and Nuffield Department of Primary Care Health Sciences (K B Pouwels PhD), University of Oxford, Oxford, UK; Department of Infectious Disease Epidemiology, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK (K Abbas PhD, Prof M Jit PhD); School of Tropical Medicine and Global Health, Nagasaki University, Nagasaki, Japan (K Abbas); International Vaccine Access Center, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA (H Zhang); Centre for Mathematical Modelling of Infectious Diseases, London School of Hygiene and Tropical Medicine, London, UK (Prof M Jit)

Correspondence to: Prof Hai Fang, China Center for Health Development Studies, Peking University, Beijing 100191, China hfan@hsc.pku.edu.cn

#### Research in context

#### Evidence before this study

In 1974, the WHO launched the Expanded Program on Immunization (EPI) to combat global infectious diseases, and 2024 marked the 50th anniversary of this global initiative. We searched PubMed, Web of Science, and Google Scholar in English and China National Knowledge Infrastructure and Wanfang in Chinese for studies published from database inception to Aug 31, 2024, on the health impact and economic evaluation of immunisation programmes in China. The search terms included combinations of "immunization/vaccination", "health impact/disease burden", and "cost-effectiveness/ economic evaluation" in both languages. Our search identified 104 studies, 21 of which were conducted on China's immunisation programmes. However, most of these studies focused on specific pathogens and shorter timeframes. The Vaccine Impact Modelling Consortium assessed the health impact of vaccination in 112 low-income and middle-income countries (LMICs), including only three EPI vaccines in China (measles, hepatitis B, and Japanese encephalitis). Some studies have conducted economic evaluations of multiple vaccine programmes but focusing on LMICs as a whole or on specific countries. No study has comprehensively assessed the health impact and cost-effectiveness or benefit of all eight vaccines included in China's EPI.

#### Added value of this study

This study provides the first comprehensive evaluation of the public health impact, cost-effectiveness, and cost-benefit of

vaccination against ten pathogens in 112 low-income and middle-income countries (LMICs) from 2000 to 2030, covering three EPI vaccines in China (measles, hepatitis B, and Japanese encephalitis).11 The health impact of all eight EPI vaccines used in China since 1974 has yet to be assessed within the country-specific context. The WHO has also evaluated the 50-year contribution of global EPI, and reported aggregated results at regional and global levels, but modelled estimates for China and all other WHO member states were not included given the uncertainties in country-level estimates.<sup>2</sup>

There is an evidence gap on the health and economic impacts of EPI in China. This evidence is essential not only to show the remarkable achievements of China's EPI but also to advocate for the expansion of the programme to include vaccines recommended by the WHO that are currently not covered by government funding in China.12 Economic evaluations are important given that the perceived high budget impact of non-EPI vaccines constitutes a primary barrier preventing their inclusion in China's EPI, despite their recognised efficacy.13 Furthermore, China's EPI is a major component of global EPI, since China accounts for more than a sixth of the global population.

This study aimed to estimate the health and economic See Online for appendix 2 impacts of China's EPI in 1974–2024. The analysis spans

China's EPI spanning a 50-year period (1974–2024). Using mathematical models, we quantified the substantial reductions in cases, deaths, and disability-adjusted life years (DALYs) across eight vaccine-preventable pathogens, highlighting the substantial health gains attributable to vaccination. Our estimates indicated that China's EPI in 1974–2024 prevents 707.41 million cases and 7.01 million deaths, resulting in a reduction of 279.02 million DALYs based on the birth cohort approach. The economic analysis showed that the aggregated benefits of the EPI, amounting to US\$2417.85 billion, far exceeded the aggregated costs of \$124.06 billion, with a benefit-cost ratio of 19.48 from the societal perspective and 8.02 from the provider's perspective.

#### Implications of all the available evidence

China's EPI has delivered substantial long-term health and economic benefits. In the past 50 years, the programme has substantially reduced disease burden and showed a high benefit-cost ratio, highlighting its crucial role in improving public health outcomes and providing substantial economic value. These achievements underscore the importance of further prioritising and investing in vaccination programmes, in China but also globally as similar vaccination initiatives could yield similar health and economic benefits.

calendar years and annual birth cohorts, alongside economic evaluation results for each vaccine, to support advocacy efforts and inform economic health and policy decisions in China.

## Methods

# Study design

This study mathematically modelled the impact of all eight routine vaccines in China's EPI against eight pathogens (measles, pertussis, hepatitis B, tuberculosis, hepatitis A, Japanese encephalitis, meningitis A, and poliomyelitis). The selection of these pathogens was based on data availability and their substantial disease burden in China, particularly accounting for non-linearities in vaccine impact.14 These eight pathogens collectively represented the majority of disease burden prevented by EPI in China and the broader Western Pacific region.<sup>2</sup> We focused on estimates from 1974 onwards, to account for the historical development of vaccination before EPI was formally launched. We designed two scenarios: a vaccination scenario with reported and projected coverage, and a counterfactual no vaccination scenario with zero vaccine coverage. In the vaccination scenario, we focused only on routine vaccination scheduled at age 0-6 years (appendix 2 p 13), given the infrequency and scarce

documentation surrounding EPI vaccination campaigns in China. In the counterfactual no vaccination scenario, we set vaccine coverage to zero due to the impracticality of simulating coverage metrics without government funding. This approach aligned with established practices in previous literature from the WHO and the VIMC,<sup>2,11</sup> ensuring a consistent baseline for comparison and isolating the impact of vaccination. We also conducted sensitivity analyses using varied levels of vaccine coverage. The health impact of China's EPI from 1974 to 2024 was measured in the number of cases, deaths, and disability-adjusted life years (DALYs) averted. Deaths averted specifically refer to the number of individuals expected to survive until they reach their respective life expectancies as a result of vaccination. The incremental cost-effectiveness ratios and benefit-cost ratios were used to evaluate the economic feasibility of China's EPI.

Annual demographic data and projections in China, including birth rates, age-stratified death rates, and population statistics, were obtained from the UN World Population Prospects.<sup>15</sup> Vaccine coverage rates from 1983 to 2022 in China were aggregated from various sources, including the WHO and UNICEF Estimates of National Immunization Coverage, surveillance data from the Chinese Center for Disease Control and Prevention, and published literature.<sup>9,16,17</sup> The coverage data were fitted to generalised additive models with restricted maximum likelihood to estimate vaccine coverage before 1983, which is important for modelling early disease burden, with an anchored 0.01% coverage in the year when a specific vaccine was initially introduced in China (appendix 2 pp 9–11). We projected that vaccine coverage rates after 2022 would remain the same as in 2022, given the minimal variations observed in the past 5 years, including during the COVID-19 pandemic.18 A similar approach has been used by the WHO and VIMC to estimate vaccine coverage rates.<sup>2,11</sup>

### Health impact modelling

We developed an age-structured stochastic dynamic compartment model for each of the seven pathogens, except for Japanese encephalitis, to elucidate the combined effects of the natural course of infection, demographic changes, and herd immunity. For Japanese encephalitis, a static model was used based on a preestablished catalytic model assuming a constant force of infection.<sup>19</sup> Dynamic models simulate the transmission dynamics of infectious diseases and account for the direct effects of vaccination on the vaccinated population and the indirect effects of vaccination on the vaccinated (but not protected) and unvaccinated populations. On the contrary, static models solely evaluate the direct effects of vaccination, presuming that vaccination coverage does not alter the intensity of pathogen transmission in an unvaccinated population. The synthesised health impact reported by these eight models in 1974-2024

represented the aggregate outcomes of China's EPI. We have briefly summarised our modelling process (appendix 2 pp 4–16), and provided detailed descriptions for each pathogen (appendix 2 pp 17–42).

To accurately capture the dynamics of eight pathogens, we calibrated each of the eight models using the Markov Chain Monte Carlo algorithm with external datasets. To address concerns about the quality of death reports and accurately reflect the impact of vaccination on treatment costs, we chose incidence or prevalence as our calibration targets. Specifically, for measles, pertussis, hepatitis A, Japanese encephalitis, meningitis A, and poliomyelitis, we used annual incidence data reported by the National Notifiable Infectious Disease Reporting System of China.48 For hepatitis B, we calibrated the model with annual HBsAg+ prevalence reported in a meta-analysis.20 For tuberculosis, we used annual incident cases in China sourced from the WHO.21 Trajectory matching between model predictions and observed data, spanning from 1974 to 2022, was conducted using the Markov Chain Monte Carlo (appendix 2 pp 5-8).

Age-stratified, pathogen-specific cases, deaths, and DALYs from 1974 to 2024 were estimated. DALYs serve as a metric for quantifying the years of healthy life lost due to disability and premature death. Following previous literature, time discounting was not applied in the calculation of DALYs.<sup>2,11,22</sup> This approach could possibly overestimate the present value of mortality-related productivity losses, which in turn might lead to overestimated economic impact. Sensitivity analyses of 3% and 5% discounting rates were applied to check the robustness of economic evaluation. We used two approaches of aggregation to present the results: calendar year and birth cohort. The calendar year approach facilitated the evaluation of averted disease burden by vaccination for specific years, thus providing a cross-sectional view of the impact. The birth cohort approach allowed for the summation of disease burden throughout the lifespan of each annual birth cohort born in 1974-2024, enabling an assessment of averted disease burden by vaccination over the entire lifetime.

To estimate the health impact of vaccination, we integrated vaccine effectiveness and coverage to derive effective vaccine coverage. This composite measure was then used to back calculate disease burden under a hypothetical scenario in which historical vaccination for the eight EPI vaccines did not occur. The population attributable impact of vaccination for each pathogen was estimated as the proportion of annual cases, deaths, and DALYs attributable to each pathogen that have been averted through vaccination. Life expectancy values specific to China, stratified by year, were sourced from the World Population Prospects.<sup>15</sup> Potential double counting of deaths averted by multiple vaccines was also done by the VIMC (appendix 2 p 16).<sup>2</sup> External validation was conducted by comparing the averted deaths per

1000 individual vaccines in this study with those provided by the VIMC to support model reliability (appendix 2 pp 12–13).

### **Economic evaluation**

Based on the health impact derived from disease transmission models, we estimated the associated costs and benefits using a decision tree model or a Markov progression model, depending on the disease's natural history and data availability. A societal perspective was adopted to capture the comprehensive costs and benefits of vaccination, with a health-care provider's perspective used as an alternative perspective. All costs and benefits were inflated to 2022 monetary values based on China's consumer prices from the World Bank.<sup>23</sup> The currency conversion from Chinese renminbi to US dollar was conducted using the exchange rate of US\$1 equal to ¥6.73.



Figure 1: Vaccine coverage and doses against eight pathogens from 1974 to 2024 in China (A) The reported and projected coverage rates for eight vaccines. (B) The cumulative number of doses distributed annually for eight vaccines.

The benefit–cost ratio is defined as the ratio of total benefits to the total costs associated with vaccination. Total costs include expenses related to vaccine procurement, vaccination administrative services, transportation, and time incurred by children's guardians. Total benefits include the averted vaccine-preventable disease treatment costs and labour productivity gains, calculated using the cost-of-illness approach. The incremental costs to incremental DALYs averted between scenarios with and without vaccination, indicating the additional costs required to avert one DALY. To assess the robustness of our findings, probabilistic sensitivity analysis using Monte Carlo simulations was conducted.

Demographic data were reported in their original form, since the underlying data sources do not provide uncertainty bounds. The reported uncertainty estimates reflect a combination of uncertainty in epidemiological inputs and model specification, quantified using the posterior distribution of calibrated parameters, and uncertainty in cost inputs, quantified with probabilistic sensitivity analysis in the economic evaluation. For each pathogen, medians (along with the 2.5% and 97.5% quantiles) were calculated to derive central estimates and 95% credible intervals (CrIs). To aggregate estimates across various pathogens, a Monte Carlo sampling technique was used, under the assumption that the uncertainty distribution of outcomes for each model was independent of those in the others.

#### Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

## Results

From 1974 to 2024, the projected coverage rates for eight EPI vaccines in China have shown an upward trend. In 1974, the vaccine coverage rates were 2% for BCG, 21% for DTP, 6% for poliomyelitis, 53% for measles, and 9% for Japanese encephalitis vaccines (figure 1A). By 2011, all eight EPI vaccines had reached at least 95% coverage. Subsequently, they have maintained high levels with minor fluctuations. The total number of administered vaccine doses also showed an overall increasing trend in coverage, albeit with fluctuations (figure 1B). The peak in vaccine doses occurred in 2012 at 427 · 19 million (95% CrI 411 · 66–442 · 46). Subsequent trends in vaccine doses have predominantly mirrored fluctuations in the birth rates, rather than variations in vaccine coverage.

Vaccines showed a pronounced effect in averting disease burden across all eight pathogens based on the calendar year approach (figure 2; appendix 2 pp 43–47). Between 1974 and 2024, 703  $\cdot$  02 million cases (95% CrI 699 $\cdot$ 51–722 $\cdot$ 80) and 2 $\cdot$ 48 million deaths (2 $\cdot$ 14–2 $\cdot$ 97) were prevented (figure 3A; table). These estimates correspond to averting an estimated 160 $\cdot$ 22 million



Figure 2: Estimates of annual pathogen-specific deaths from 1974 to 2024 in China

Estimates of all-age deaths for each of the eight pathogens under two scenarios: vaccination (blue) and no vaccination (red) based on the calendar year approach. The corresponding shaded areas represent 95% creditable intervals (2.5% and 97.5% quantiles), whereas grey shaded areas indicate where the 95% creditable intervals for the two scenarios overlap.

DALYs (145.05–196.99; table). Among these vaccines, measles vaccine had the largest impact on disease burden, averting a total of 442.86 million cases (436.97–448.76) and 1.01 million deaths (0.92–1.12), which translated to 49.48 million DALYs (45.60–59.43). This led to a decrease of 95.59% (95.35–95.95) in measles cases, 90.18% (88.24–92.38) in measles deaths, and 90.05% (86.90–92.56) in measles-related DALYs. In terms of deaths averted per 1000 vaccinated individuals based on the calendar year approach, the measles vaccine also had the highest rate at 1.45 (1.31–1.58), followed by the hepatitis B vaccine (1.22 [0.57–1.88]), and Japanese encephalitis vaccine (0.87 [0.72–1.00]; figure 3B; appendix 2 p 48).

Based on the birth cohort approach, a collective 707·41 million cases (95% CrI 703·93–727·03) and 7·01 million deaths (6·95–7·87) were averted over the lifetime, corresponding to 279·02 million DALYs (265·78–316·12; figure 3; table). Hepatitis B vaccination was estimated to have averted 12·69 deaths (11·79–13·60)

per 1000 vaccinated individuals (figure 3; appendix 2 p 48) or a total of  $5 \cdot 26$  million ( $5 \cdot 20-6 \cdot 02$ ) deaths by birth cohort, the largest among the eight vaccines. The majority of hepatitis B-related deaths occurred in individuals aged older than 40 years, primarily due to decompensated cirrhosis and hepatocellular carcinoma in later life. Although the hepatitis B vaccine was introduced in China in 1990, its impact was not apparent between 1990 and 2004 but became evident from 2005 onwards.

In comparison, the health impact of vaccination on deaths and DALYs on birth cohorts born in 1974–2024 was larger than those occurring in calendar years 1974–2024 (appendix 2 pp 49–51). This difference is mainly attributed to the ages at which deaths from hepatitis B, hepatitis A, and tuberculosis occur. The impact of double counting on deaths averted was low (<0.02%; appendix 2 p 16).

The benefit–cost and cost-effectiveness of China's EPI are shown in figure 4 and appendix 2 (pp 52–57). From the



Figure 3: Cases, deaths, and DALYs averted by eight vaccines from 1974 to 2024 in China

(A) Cases, deaths, and DALYs averted based on the calendar year and birth cohort approaches. (B) Average number of deaths averted per 1000 vaccinated individuals based on the calendar year and birth cohort approaches. The error bars indicate 95% credible intervals. DALY=disability-adjusted life year.

societal perspective, the aggregated cost of vaccination from 1974 to 2024 was estimated to be US\$124.06 billion (95% CrI 120.49-127.49), including \$69.91 billion (67.86-71.81) for vaccine procurement and administrative services, and \$54.15 billion (52.63-56.89) for transportation and time costs incurred by caregivers (appendix 2 p 52). The aggregated benefit of vaccination over the lifetime of the vaccinated birth cohorts totalled \$2417.85 billion (2359.38-2710.35), including \$560.38 billion (539.54-611.92) for reduction in disease treatment costs and \$1857.46 billion (1819.84-2098.43) for decrease in direct non-medical expenses and increase in labour productivity (appendix 2 p 52). The benefit-cost ratio of each vaccine based on the birth cohort approach exceeded 1, with the aggregated benefit-cost ratio of EPI against eight pathogens calculated at 19.48 (18.82-22.08) from the societal perspective (figure 4; appendix 2 p 54). Among the eight vaccines, hepatitis B reached the highest benefit of \$1499.31 billion (1459.12-1740.87), coupled with the highest benefit–cost ratio of 148.01 (128.80-178.90). Based on the calendar year approach, the benefit–cost ratio of each vaccine (except for hepatitis A) also surpassed 1, and the aggregated benefit–cost ratio of EPI against eight pathogens was 10.13 (8.87-12.01; figure 4; appendix 2 p 53). From the health-care provider's perspective, the benefit–cost ratios remained above 1, at 8.02 (7.64-8.80) based on the birth cohort approach and 3.98 (3.47-4.72) based on the calendar year approach (figure 4; appendix 2 p 55–56).

In terms of cost-effectiveness (appendix 2 p 57), all eight vaccines were cost-saving from the societal perspective, irrespective of whether data were analysed

									:  ;			
	Cases in millions				Deaths in millic	SUC						
	No vaccination	Vaccination	Averted	Reduction	No vaccination	Vaccination	Averted	Reduction	No vaccination	Vaccination	Averted	Reduction
Calendar year.	approach											
Measles	463·29	20·43	442.86	95-59%	1·12	0.11	1.01	90.18%	54·95	5.47	49-48	90-05%
	(431·08-495·10)	(17·04–23·08)	(436·97-448·76)	(95-35-95-95)	(0·70–1·55)	(0.07-0.15)	(0.92-1.12)	(88.24–92.38)	(29·70–90·05)	(2.92–9.14)	(45-60-59-43)	(86-90–92-56)
Pertussis	181·73	19·10	162-63	89.49%	0·16	0.02	0.14	87.50%	12·54	1.23	11·31	90·19%
	(141·76–250·00)	(14·28–27·06)	(160-46-179-80)	(88.22–90.69)	(0·11-0·25)	(0.01–0.02)	(0.13-0.17)	(86.72–91.70)	(8·37–18·63)	(0.80–1.83)	(11·01–12·81)	(88·71-91·60)
Hepatitis B	119·37	39·11	80.26	67·24%	4·01	3.48	0-53	13·22%	110-84	89·53	21·31	19-23%
	(109·79–128·00)	(36·84-41·66)	(77.76–82.06)	(66·33–67·81)	(2·99–5·06)	(2.70–4.24)	(0-25-0-85)	(6·67–20·05)	(70-08-164-02)	(53·13-129·22)	(10·17–38·70)	(9-72-31-77)
Active	88·49	78·97	9.52	10.76%	4·42	4·17	0.25	5.66%	321·15	296·39	24·76	7·71%
tuberculosis	(83·78–93·35)	(72·37–85·59)	(8.11-11.12)	(9.19-12.49)	(3·31–5·55)	(3·08–5·28)	(0.00-0.53)	(0.00-11.64)	(245·67–401·30)	(225·41–375·00)	(5·01-43·54)	(1·60–13·10)
Hepatitis A	10.46	8.07	2·39	22.85%	0·16	0.13	0.03	18·75%	4:75	3·78	0.97	20.42%
	(8.24–12.26)	(6.51–9.42)	(1·71–2·96)	(17.16–27.81)	(0·09–0·23)	(0.08–0.19)	(0.01–0.05)	(4·47–29·37)	(2·57-7·79)	(2·07–6·21)	(0.15–1.85)	(3.30–33.84)
Japanese	3.09	0.99	2·10	67-96%	0.48	0.16	0-32	66·67%	44·15	14·26	29.89	67.70%
encephalitis	(1.93–5.12)	(0.64-1.78)	(1·92–2·55)	(61-05-71-02)	(0.27–0.86)	(0.09–0.30)	(0-30-0-42)	(59·75-71·53)	(21·62-86·35)	(7·15–29·56)	(27.40–38.40)	(59.16-72.63)
Meningitis A	3·76	1.08	2.68	71·28%	0.22	0.06	0.16	72·73%	14·55	4·15	10.40	71.48%
	(3·43-4·00)	(1.00–1.16)	(2.58-2.71)	(70·06–71·94)	(0.13-0.34)	(0.04–0.10)	(0.14-0.19)	(65·95–77·00)	(7·68–25·11)	(2·33-7·20)	(9.20–13.22)	(63.93-77.39)
Poliomyelitis	0.70	0·12	0.58	82·86%	0.05	0.01	0.04	83·20%	14·57	2·47	12·10	83.05%
	(0.69–0.71)	(0·11–0·12)	(0.57–0.58)	(82·36–83·24)	(0.04–0.07)	(0.01-0.01)	(0.04-0.05)	(81·61–84·67)	(10·02–19·09)	(1·61–3·22)	(11·30–12·99)	(81.17-85.33)
Aggregate	870-89	167.87	703·02	80.72%	10·62	8.14	2.48	23·35%	577·50	417·28	160.22	27·74%
	(868-83-891-10)	(165.99–171.70)	(699·51–722·80)	(80.39–81.22)	(10·41–11·07)	(7.90–8.45)	(2.14–2.97)	(20·39–27·17)	(574·53–615·90)	(407·99-441·10)	(145.05–196.99)	(24·95–32·27)
Birth cohort a	pproach											
Measles	437.83	1.05	436.78	99.76%	0.60	0.01	0-59	99.20%	29.82	0.27	29-55	99-09%
	(400.87-474.80)	(0.87–1.23)	(430.25-442.97)	(99.74–99.78)	(0.37–0.83)	(0.00-0.01)	(0-55-0-64)	(99.04-99.42)	(16-07-48-76)	(0·13-0·45)	(28-06–34-78)	(98-77–99-38)
Pertussis	180-48	12.68	167.80	92·97%	0.16	0.01	0.15	93·75%	12·51	1.07	11·44	91.45%
	(141-58–246-60)	(9.78–16.99)	(165.98-182.05)	(92·30–93·75)	(0.11-0.24)	(0.01-0.02)	(0.14-0.17)	(91·95–94·55)	(8·37–18·55)	(0.70–1.57)	(11·15-12·89)	(90.23–92.79)
Hepatitis B	105·77	24·42	81·35	76-91%	6·54	1·28	5.26	80-43%	188.67	40·97	147·70	78.28%
	(95·46–115·11)	(22·79–26·27)	(78·63-83·21)	(76-13-77-38)	(5·34-8·76)	(1·03-1·45)	(5.20–6.02)	(79-55–82-93)	(112.02–285.60)	(25·86–60·78)	(134·22–172·96)	(75.13-80.86)
Active	81·15	68.48	12.67	15·61%	3·13	2.71	0.42	13.42%	235·24	200.92	34·32	14·59%
tuberculosis	(76·26–86·17)	(61.57–75.59)	(11:19-14:09)	(13·86–17·24)	(2·21-4·09)	(1.86-3.61)	(0.18-0.67)	(5.94–20.43)	(174·84–298·30)	(146.78-260.90)	(17·57-49·93)	(7·60-20·42)
Hepatitis A	5.01	1.70	3·31	66.07%	0.05	0.01	0.04	87.51%	2.00	0.59	1.41	70-50%
	(3·46–6·05)	(1.47–1.92)	(2·85–3·43)	(62.29–67.36)	(0.02–0.08)	(0.00–0.01)	(0.04-0.05)	(84.94–89.58)	(1.01–3.34)	(0.34–0.91)	(1.24–1.78)	(65-04-76-36)
Japanese	3.03	0·90	2·13	70·30%	0·47	0.14	0-33	70·21%	43·32	12·86	30.46	70·31%
encephalitis	(1.89–4.98)	(0·57–1·53)	(1·99–2·62)	(64·98–74·02)	(0·26–0·84)	(0.08–0.26)	(0-31-0-42)	(63·99–74·72)	(21·14-84·19)	(6·34–25·65)	(28.63-40.73)	(73·51-80·07)
Meningitis A	3·44 (3·16–3·62)	0.73 (0.69-0.76)	2.71 (2.64–2.73)	78.78% (78.22-79.07)	0.20 (0.12–0.31)	0.04 (0.03-0.06)	0.16 (0.15-0.19)	80-00% (75-24-82-78)	13·45 (7·08–23·22)	2.87 (1.65–5.02)	10.58 (9.72-13.20)	78.66% (72.81–82.86)
Poliomyelitis	0.73	0.07	0.66	90-41%	0.05	0.00	0.05	90.79%	15·05	1.49	13·56	90.10%
	(0.71–0.74)	(0.06–0.07)	(0.65–0.66)	(90-25–90-83)	(0.04–0.07)	(0.00-0.01)	(0.05-0.05)	(89.85-91.74)	(10·36–19·74)	(0.98–1.95)	(12·74-14·42)	(88.90–91.50)
Aggregate	817-44	110-03	707-41	86·54%	11.20	4·19	7.01	62·59%	540.06	261.04	279-02	51.66%
	(814-86-837-60)	(108-93-112-40)	(703-93-727-03)	(86·30–86·90)	(10·95-12·07)	(4·04-4·39)	(6.95-7.87)	(61·77–65·71)	(536.09–580.60)	(255·23-279·20)	(265·78–316·12)	(49.17–55.00)
Data are median	(95% credible interval	s). DALYs=disability-	adjusted life years.									
Table: Cases, de	aths, and DALYs av	erted from 1974 to	o 2024 in China									



Figure 4: Benefit-cost ratios for eight vaccines from 1974 to 2024 in China from societal and health-care provider's perspectives

Benefit-cost ratio and 95% credible intervals based on the calendar year (A) and birth cohort (B) approaches, calculated by dividing total benefits by total costs. A benefit-cost ratio higher than 1 indicates that benefits outweigh costs and lower than 1 suggests the intervention might not be economically viable. The societal perspective adopts total costs, which encompass a broader range of expenses. The health-care provider's perspective considers direct disease cost and vaccination cost.

bases on the calendar year (except for hepatitis A vaccine with an incremental cost-effectiveness ratio of \$600 per DALY averted) or the birth cohort approaches. The incremental cost-effectiveness ratio plot in appendix 2 (p 59) clearly shows that most points fell within the costsaving quadrant. Consistent results from additional scenarios with varying vaccine coverage rates, discounting rates, and benefit measurements are presented in appendix 2 (pp 61–65).

# Discussion

From 1974 to 2024, the health impact of China's EPI has been substantial, yielding notable reductions in the number of cases, deaths, and DALYs of eight vaccinepreventable infectious diseases. Our modelling study uniquely assessed the direct benefits to vaccinated individuals and the broad societal benefits stemming from herd protection among the unvaccinated population in China. To our knowledge, this study is the first to present an economic evaluation of China's EPI spanning the period from 1974 to 2024. From a societal perspective, the total benefits of China's EPI far exceeded the total costs of investing in EPI, with aggregate benefit–cost ratios surpassing 1 and aggregate incremental cost-effectiveness ratios showing costsaving. This study also highlights the benefits of high coverage rates of EPI vaccines to public health in China. Moreover, the benefits of childhood vaccination extend beyond immediate health outcomes, with observable reductions in adult mortality across birth cohorts.

Measles vaccination was estimated to have averted a substantial number of cases, deaths, and DALYs in China based on calendar year and birth cohort approaches and showed high benefit–cost ratios. Hepatitis B vaccination emerged as a pivotal contributor to mortality reduction, although China officially introduced hepatitis B into the EPI later in 2002. China, with the world's largest population of patients with hepatitis B,<sup>24</sup> has reached remarkable coverage rates for the birth dose of hepatitis B vaccination since 2016. Additionally, hepatitis B modelling in our study considered the prevention of mother-to-child transmission, which has been widely implemented in China.

No previous study has explored the health impact and economics of all routine vaccines in China's EPI since 1974. However, studies have looked at a few pathogens over shorter timespans. The VIMC has estimated the health impact of vaccination programmes against ten pathogens (Haemophilus influenzae type B, hepatitis B, human papillomavirus, Japanese encephalitis, measles, Neisseria meningitidis serogroup A, rotavirus, rubella, Streptococcus pneumoniae, and yellow fever) in LMICs from 2000 to 2030.<sup>11,18</sup> Among the ten pathogens analysed in the VIMC study, three—measles, hepatitis B, and Japanese encephalitis-were covered by vaccines included in China's EPI. The VIMC reported 0.9 deaths averted per 1000 individuals vaccinated against measles, 12.0 deaths averted per 1000 individuals vaccinated against hepatitis B, and 0.5 deaths averted per 1000 individuals vaccinated against Japanese encephalitis in 2000–30 in China based on the birth cohort approach,<sup>11</sup> whereas our study estimated 0.44 deaths averted per 1000 individuals vaccinated against measles, 12.69 deaths averted per 1000 individuals vaccinated against hepatitis B, and 1.06 deaths averted per 1000 individuals vaccinated against Japanese encephalitis during the same time period. Research has mainly focused on the burden of single pathogens. One study reported the health impact of diphtheria-tetanus-polio vaccination in China for 40 birth cohorts from 1978 to 2017, finding a reduction of pertussis cases similar to our estimates based on the birth cohort approach.25 Another study on hepatitis B found that, over 18 years (1992-2009), hepatitis B vaccination in China prevented 24.0 million chronic infections and 4.3 million future deaths, which is similar to the results reported in our study;<sup>26</sup> therefore, our estimates are generally consistent with previous ones, with differences possibly driven by variations in model types and data sources (appendix 2 pp 12–13).

The findings of the economic analyses, whether calculated from a societal or provider's perspective, align with other assessments of immunisation programmes in different national contexts. A 2020 study, using data from VIMC, reported a return on investment ratio of 19.8 for immunisation initiatives targeting ten pathogens across 94 LMICs from 2021 to 2030.27 In parallel, a US based study estimated a societal benefit-cost ratio of 10.9 for routine childhood immunisation spanning the 1994-2023 birth cohorts.<sup>28</sup> A study from Colombia further suggested a return on investment ratio of 3.9 for a single cohort using a static model.<sup>29</sup> The observed variations are likely due to differences in pre-vaccination disease burden and the specific vaccines included in immunisation programmes. Nevertheless, all studies consistently show that the financial benefits of vaccination substantially outweigh the costs, underscoring the exceptional costbenefit and effectiveness. Our economic results are also broadly consistent with previous large-scale domestic interventions with lifelong impacts,<sup>30</sup> remaining a highly valuable investment for governments seeking to maximise population health benefits.

This study has some limitations. First, the study did not estimate the health impact of China's EPI on the burden of mumps, rubella, diphtheria, and tetanus. Although previous WHO literature reported low health impact of rubella, diphtheria, and tetanus vaccinations in the Western Pacific region and China,<sup>2</sup> the aggregate health impact and economic evaluation in China's EPI might be slightly underestimated. Second, for some diseases (such as pertussis), under-reporting might have occurred in earlier years. Due to an absence of reliable parameters, we calibrated the reported incidence based on authoritative data sources, resulting in more conservative estimates that might underestimate the health and economic impacts of China's EPI. Third, although the study assumes uniform vaccination coverage across regions based on the consistent and high vaccination rates within China, regional variations could influence the effectiveness of vaccination programmes. Future research could explore how these regional differences affect vaccine uptake and subsequent health outcomes. Finally, the model did not account for other external interventions implemented during this period that have also reduced infections. These factors might influence the estimates, possibly leading to an overestimation of the effect.

Our analysis highlights the substantial gains from China's investments in EPI. These achievements provide impetus to enhance immunisation coverage and include additional vaccines recommended by WHO into the programme with further investment.

#### Contributors

HF conceived this study and led the analysis. CW and XL prepared and analysed the data and have directly assessed and verified all the underlying data in the study. XL, CW, and HF wrote the first draft of the manuscript. KA, KBP, HZ, and MJ provided feedback during the design and interpretation of the project and contributed to revisions of the manuscript. All coauthors contributed to reviewing and editing the manuscript and approved the final text. CW and XL contributed equally as co-first authors. HF made the final decision to submit for publication.

## Declaration of interests

HF received funding from the Bill & Melinda Gates Foundation, National Natural Science Foundation of China, Beijing Natural Science Foundation, and Sanofi. XL received funding from Beijing Natural Science Foundation and China Postdoctoral Science Foundation. KA received funding from Vaccine Impact Modelling Consortium, Japan Agency for Medical Research and Development, International Vaccine Institute, Save the Children, WHO, Gavi (the Vaccine Alliance), and the Gates Foundation. MJ received funding from the Gates Foundation and Wellcome Trust. All other authors declare no competing interests.

## Data sharing

The primary data sources used in this study are available in the appendix 2 (pp 4–42). Readers who wish to access data can contact the corresponding author, for additional information or specific datasets.

#### Acknowledgments

This study was funded by Beijing Natural Science Foundation (funding number 9222013).

#### References

- World Health Assembly (27th: 1974). The Expanded Programme on Immunization: the 1974 Resolution by the World Health Assembly. Assignment Child 1985; 69–72: 87–88.
- 2 Shattock AJ, Johnson HC, Sim SY, et al. Contribution of vaccination to improved survival and health: modelling 50 years of the Expanded Programme on Immunization. *Lancet* 2024; 403: 2307–16.
- 3 UN. Global issues: population. https://www.un.org/en/globalissues/population (accessed June 2, 2024).
- 4 Wang H, An J, Yin Z. Achievements in prevention and control of seven infectious diseases targeted by the National Immunization Program in China across 70 years.
- Chinese Journal of Vaccines and Immunization 2019; 25: 359–67.
  Yu W, Lee LA, Liu Y, et al. Vaccine-preventable disease control in the People's Republic of China: 1949-2016. Vaccine 2018; 36: 8131–37.
- 6 Liu J, Liang W, Jing W, Liu M. Countdown to 2030: eliminating hepatitis B disease, China. Bull World Health Organ 2019; 97: 230–38.
- 7 Zhang H, Lai X, Mak J, et al. Coverage and equity of childhood vaccines in China. JAMA Netw Open 2022; 5: e2246005.
- 8 Dong Y, Wang L, Burgner DP, et al. Infectious diseases in children and adolescents in China: analysis of national surveillance data from 2008 to 2017. *BMJ* 2020; 369: m1043.
- 9 Pan J, Wang Y, Cao L, et al. Impact of immunization programs on 11 childhood vaccine-preventable diseases in China: 1950–2018. *Innovation (Camb)* 2021; 2: 100113.
- 10 Chen S, Yao L, Wang W, Tang S. Developing an effective and sustainable national immunisation programme in China: issues and challenges. *Lancet Public Health* 2022; 7: e1064–72.
- 11 Li X, Mukandavire C, Cucunubá ZM, et al. Estimating the health impact of vaccination against ten pathogens in 98 low-income and middle-income countries from 2000 to 2030: a modelling study. *Lancet* 2021; 397: 398–408.
- 12 Zhang H, Lai X, Patenaude BN, Jit M, Fang H. Adding new childhood vaccines to China's National Immunization Program: evidence, benefits, and priorities. *Lancet Public Health* 2023; 8: e1016–24.
- 13 Zhang H, Patenaude B, Ma C, Fang H. Vaccine pricing strategies in China. BMJ Glob Health 2023; 8: e011405.
- 14 Chinese Center for Disease Control and Prevention. Childhood immunization schedule for national immunization program vaccines—China (version 2021). 2021. https://weekly.chinacdc.cn/ fileCCDCW/journal/article/ccdcw/2021/52/PDF/210299.pdf (accessed May 12, 2023).
- 15 UN. World population prospects 2022. https://population.un.org/ wpp/ (accessed May 11, 2023).
- 16 WHO. WHO/UNICEF estimates of national immunization coverage. 2023. https://www.who.int/teams/immunizationvaccines-and-biologicals/immunization-analysis-and-insights/ global-monitoring/immunization-coverage/who-unicef-estimatesof-national-immunization-coverage (accessed May 12, 2023).

- 17 Wang F, Sun X, Wang F, et al. Changing epidemiology of hepatitis A in China: evidence from three national serological surveys and the national notifiable disease reporting system. *Hepatology* 2021; 73: 1251–60.
- 18 Hartner AM, Li X, Echeverria-Londono S, et al. Estimating the health effects of COVID-19-related immunisation disruptions in 112 countries during 2020–30: a modelling study. *Lancet Glob Health* 2024; 12: e563–71.
- 19 Quan TM, Thao TTN, Duy NM, Nhat TM, Clapham H. Estimates of the global burden of Japanese encephalitis and the impact of vaccination from 2000–2015. *eLife* 2020; 9: 9.
- 20 Liu Z, Lin C, Mao X, et al. Changing prevalence of chronic hepatitis B virus infection in China between 1973 and 2021: a systematic literature review and meta-analysis of 3740 studies and 231 million people. *Gut* 2023; 72: 2354–63.
- 21 Bagcchi S. WHO's global tuberculosis report 2022. *Lancet Microbe* 2023; 4: e20.
- 22 WHO. WHO methods and data sources for global burden of disease estimates 2000–2019. https://www.who.int/data/globalhealth-estimates (accessed June 1, 2024).
- 23 World Bank. Inflation, consumer prices (annual %)—China. 2022. https://data.worldbank.org/indicator/FP.CPI.TOTL. ZG?locations=CN (accessed April 8, 2024).
- 24 WHO. Up to 10 million people in China could die from chronic hepatitis by 2030—urgent action needed to bring an end to the silent epidemic. 2016. https://www.who.int/hongkongchina/news/ detail/26-07-2016-up-to-10-million-people-in-china-could-die-fromchronic-hepatitis-by-2030-urgent-action-needed-to-bring-an-end-tothe-silent-epidemic (accessed June 21, 2023).
- 25 Wu D, Jing R, Zheng H, et al. Health and economic evaluation of vaccination against pertussis in China: a 40-year analysis. *Value Health* 2023; 26: 666–75.
- 26 Hadler SC, Fuqiang C, Averhoff F, et al. The impact of hepatitis B vaccine in China and in the China GAVI project. *Vaccine* 2013; 31 (suppl 9): J66–72.
- 27 Sim SY, Watts E, Constenla D, Brenzel L, Patenaude BN. Return on investment from immunization against 10 pathogens in 94 low- and middle-income countries, 2011–30. *Health Aff (Millwood)* 2020; 39: 1343–53.
- Zhou F, Jatlaoui TC, Leidner AJ, et al. Health and economic benefits of routine childhood immunizations in the era of the vaccines for children program—United States, 1994–2023. MMWR Morb Mortal Wkly Rep 2024; 73: 682–85.
- 29 Soto-Moreno JA, Coe M, Parellada C, Tantri A, Angarita-Contreras MC, Acosta P. Socioeconomic and fiscal returns of expanded investment in immunization: a case for life-course vaccination in Colombia. *Health Aff Sch* 2024; 2: qxae042.
- 30 Ma G, Meyer CL, Jackson-Morris A, et al. The return on investment for the prevention and treatment of childhood and adolescent overweight and obesity in China: a modelling study. *Lancet Reg Health West Pac* 2023; 43: 100977.