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RESEARCH ARTICLE

Cost–benefit analysis of the National Immunization Program in Spain

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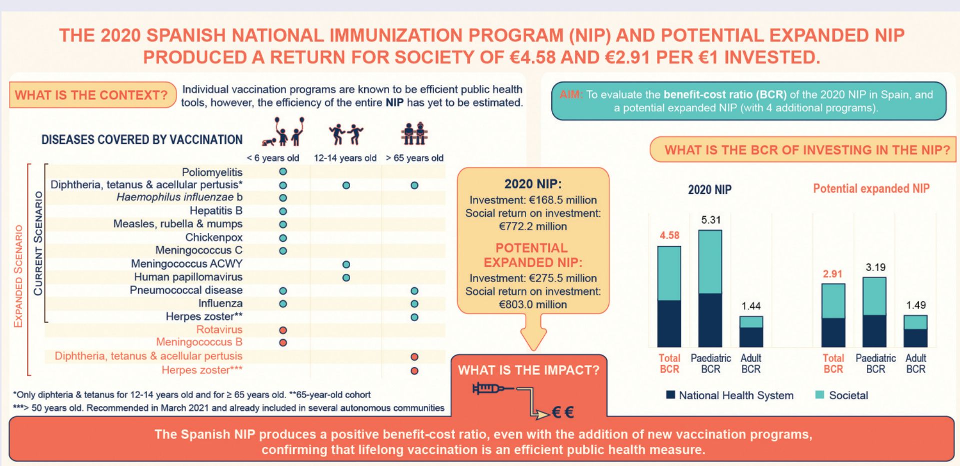
ABSTRACT

Broad benefits of vaccination programs are well acknowledged but difficult to measure, especially when considering all vaccines included in a National Immunization Program (NIP). The aim was to conduct a cost–benefit analysis of the entire NIP in Spain, and an expanded NIP including four potential additional programs. A cost–benefit analysis was performed in Excel to assess the economic and health benefits (€) of vaccinating a single cohort of newborns over a lifetime horizon compared to no vaccination, from a societal perspective: firstly, according to the 2020 NIP in Spain (including 2021 recommendation for herpes zoster in 65-year-olds); and secondly, with an expanded NIP (adding rotavirus and meningococcal B in infants, and pertussis booster in adults aged >65 years and herpes zoster in all adults >50 years). The main inputs were taken from published literature and Spanish databases. Results were presented as a benefit–cost ratio (economic benefit per €1 invested). A cohort of 343,126 newborns were included in the analysis. The total investment needed to vaccinate the cohort throughout their lifetime, according to the 2020 NIP and the expanded NIP, was estimated at €168.5 million and €275.5 million, respectively. Potential economic benefits were €772.2 million and €803.0 million, respectively. The societal benefit–cost ratio was €4.58 and €2.91 per €1 invested, respectively. Even with the addition of new vaccination programs, the Spanish NIP yielded positive benefit–cost ratios from the societal perspective, demonstrating that NIPs spanning the full life course are an efficient public health measure.



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Cost–benefit analysis; vaccination; National Immunization Program; public health; Spain

Introduction

Immunization is a crucial part of primary health care, preventing life-threatening diseases and supporting longer, healthier lives.[1] High immunization rates have helped reduce many infectious diseases, including diphtheria, poliomyelitis, and rubella. According to the World Health Organization, immunization is "one of the best health investments money can buy."[1]

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The recent coronavirus disease 2019 (COVID-19) pandemic highlighted the importance of vaccines beyond protecting vaccinated people. Vaccination protected the most vulnerable groups with reduced immunity, e.g., newborns, older adults, and high-risk populations, and helped social and economic activity to resume normally. This increased awareness of broad health and economic vaccination benefits can lead to new vaccines being introduced in National Immunization Programs (NIPs), especially if the burden of disease and indirect costs averted for society are considered.

The costs and health benefits of specific vaccination programs have previously been assessed in Spain.[2–5] Only one study analyzed the costs of all vaccines included in the Spanish NIP, based on a cohort born in 2019.[6] The NIP was found to be highly efficient, due to its relatively low costs (i.e., lifetime costs of €626 and €726 per healthy man and woman, respectively), but the study only assumed the important health benefits, rather than valuing them.[6]

The efficiency of vaccination programs is widely accepted, but the precise value is not easy to measure, due to difficulties in capturing long term and indirect benefits of vaccines. Assessing the efficiency of all vaccination programs included in the entire NIP of a country is an even greater challenge, given the many vaccines used that affect different diseases and may be given at different periods over the recipient's lifetime. One way to measure the efficiency of health technology investments is to estimate the cost–benefit analysis (CBA), which provides the economic return per euro invested in health technology. There are no studies to date, in Spain or elsewhere, calculating the benefit–cost ratio (BCR) of all vaccination strategies included in an NIP, and covering the societal perspective. This can be a useful measure to inform decision-makers about vaccine efficiency from a broader perspective, and about the value of future investments in vaccines.

In this context, the aim of this analysis was to assess the BCR, considering both economic and health benefits, of administering the vaccines recommended in the Spanish NIP used in 2020[7] (and including the herpes zoster (HZ) vaccine recommended in March 2021 for 65-year-olds[8]), throughout life, to the entire Spanish population born in 2020. In addition, the BCR of an expanded NIP was assessed; with four additional vaccination programs that could potentially be added in the near future (i.e., adding rotavirus and meningococcal B vaccination in infants, a pertussis booster in adults aged >65 years and those in close contact with infants, and the HZ vaccination for all adults aged >50 years).

Materials and methods

A model developed in Microsoft Excel simulated a hypothetical cohort over lifetime, to compare the costs and benefits of vaccination according to 1) the 2020 NIP, and 2) the expanded NIP, versus no vaccination.

The cohort consisted of 343,126 people born in Spain in 2020 (176,249 males and 166,877 females).[8] Age- and sex-specific mortality rates were applied from 2019 data[8,9] as 2020 rates were heavily influenced by COVID-19. One-year cycles and half-cycle correction were used. A time horizon of 100 years covered life-expectancy of the cohort (i.e., 80.86 years in men; 86.22 years in women).[10]

The '2020 NIP' considered for the analysis included the mandatory minimum vaccinations that the Autonomous Communities must comply with in 2020,[11] as well as HZ vaccination for 65-year-olds which was recommended in March 2021[7] as several Autonomous Communities already implemented its following recommendations (Figure 1).[12,13] The 2020 NIP remained unchanged until the end of 2022,[14] and was recently updated in 2023.[15] In the 'expanded NIP' two infants and two adult vaccination programs were added to the 2020 NIP, based on scientific societies' recommendations or available evidence (Figure 1). These programs were

	Diseases covered by vaccination	Prenatal	2m	4m	6m	11m	12m	15m	3y	6y	12y	14y	50y	65y
2020 NIP	Poliomyelitis		DTaP/ IPV/ Hib/ HB	DTaP/ IPV/ Hib/ HB		DTaP/ IPV/ Hib/ HB				DTaP/ IPV				
	Diphtheria, tetanus, acellular pertussis	dTap										Td		Td
	Haemophilus influenzae b													
	Hepatitis B													
	Measles, rubella, mumps						MMR		MMR + VZV					
	Chickenpox							VZV						
	Meningococcal C			MenC			MenC							
	Meningococcal ACWY										Men ACWY			
	Human papillomavirus (girls)										HPV girls*			
	Pneumococcal disease		PCV	PCV		PCV								PPSV23
	Influenza	Flu												Flu
	Herpes zoster (=65y)													HZ
Expanded NIP	Meningococcal B		MenB	MenB			MenB							
	Rotavirus		Rota	Rota	Rota									
	Diphtheria, tetanus and pertussis												dTap	
	Herpes zoster (≥50y)												HZ	

Figure 1. Vaccines included in the 2020 NIP and expanded NIP. HPV 2-dose vaccination for girls aged 12 years; dTap/DTaP: diphtheria, tetanus, and acellular pertussis (upper or lower case depending on the viral load of each vaccine); **Flu**: influenza; **HB**: hepatitis B; **Hib**: *Haemophilus influenzae* b; **HPV**: human papillomavirus; **HZ**: herpes zoster; **IPV**: inactivated polio vaccine; **m**: months; **MenACWY**: meningococcal ACWY disease; **MenB**: meningococcal B disease; **MenC**: meningococcal C disease; **MMR**: measles, mumps, and rubella; **NIP**: National Immunization Program; **PCV**: pneumococcal conjugate vaccine; **PPSV23**: 23-valent pneumococcal polysaccharide vaccine; **Rota**: rotavirus; **Td**: tetanus and diphtheria; **VZV**: varicella-zoster virus; **y**: years.

not included as part of the 2022 NIP. For infants, routine rotavirus and meningococcal B (MenB) vaccination was recommended[16] and implemented in some regions (MenB was eventually included in the 2023 NIP[15]).[17–21] A pertussis booster was recommended (with the diphtheria, tetanus, and acellular pertussis [dTap] vaccine instead of the tetanus and diphtheria [Td] vaccine) for adults aged >65 years[22] and for adults in close contact with infants, to prevent transmission.[23] Also for adults, the extended NIP included HZ vaccination for all adults from the age of 50 years, instead of just adults aged 65 years old[8] as HZ incidence increases considerably from the age of 50 years.[24]

A CBA, commonly used for investment projects, was conducted to compare the benefits of the NIP, expressed in monetary units, with its costs. The BCR indicates how much benefit would be obtained for each additional €1 invested (Equation S1). A BCR greater than 1.0 indicates that every €1 invested in vaccination results in more than €1 in savings.[25]

The methodology of the economic analysis performed in this study is shown in Figure S1. Briefly, the analysis consisted of three steps: 1) calculation of vaccine investment (including all direct health costs); 2) literature search for selection of the most complete cost–benefit analyses (in the diseases included in step 1 above) that could best be adapted to Spain (see Table S2); 3) the selected cost–benefit ratios were multiplied by the investment made in Spain. A 3% discount rate was applied to costs and benefits (if necessary), following Spanish recommendations[26–29] and in order to have a present day value by discounting future health benefits and costs. Costs were updated to 2020 euros (€) using the consumer price index for healthcare.[30]

The BCR for each vaccine-preventable disease in the NIP was sourced from publications most appropriate to the Spanish setting (i.e., in Spain or with similar schedule, coverage, recent and complete data, and societal perspective). Spanish data were identified for varicella, pneumococcal disease (children and adults), rotavirus, and influenza (adults). All studies, except one,[31] included a societal perspective, allowing the total BCR to be separated into the National Health Service (NHS) perspective (only including direct healthcare costs) versus societal perspective (including direct non-health costs, direct costs for the patient, and indirect costs) BCRs in most cases (Table S1). For diseases with no BCR found for the required age group, a conservative approach was applied, including the costs without assuming any vaccine benefit. This was the case for influenza (prenatal), diphtheria, tetanus and pertussis (prenatal and adults), meningococcal C disease, meningococcal B disease, and diphtheria–tetanus (adults). To calculate the BCR per disease, the BCRs obtained from the primary studies were applied to the cost of the investment calculated for Spain. Taking a conservative approach, the BCR was only considered over the time horizon included in the primary study (e.g., varicella vaccination provides life-long immunity, but the vaccine benefit was assumed to be 15 years, in line with the primary study time horizon; and for influenza, studies apply a time horizon of 1 year as it is an annual vaccine, so the model assumed adults receive the vaccine annually from the age of vaccination until death) (see Table S2 for study details).

Costs for the NIP were calculated, considering population data, vaccine and administration costs, and vaccination coverage (Equation S2).

In the base case, the unit cost of vaccines was conservatively based on the list price per dose,[32] and the potential impact of public purchase prices was investigated in sensitivity analyses. The vaccine administration cost was € 6.11 per nurse visit.[6] Co-administration of vaccines (Table S3) was considered throughout the NIP and costed as a single visit.

Vaccination coverage rates (Figure S2) were used to calculate the acquisition cost of vaccines for the general population. For the 2020 NIP, published official vaccination coverage rates were used.[33–40] For adult vaccinations in the 2020 NIP with no coverage data in Spain (e.g., pneumococcal disease) and for the expanded NIP for adult vaccines administered from age 50 years, the coverage rate for influenza in people aged ≥65 years was assumed (expert group consensus). For infant rotavirus and meningococcal B vaccination, coverage was based on meningococcal B coverage in Castilla y León,[41] as it is the region with the longest experience of implementing this vaccine as part of its regional immunization program.

As a complementary study, cases and deaths prevented were extracted from the published studies presenting BCR data, and annualized rates were calculated to allow for counting of cases. The cases and deaths prevented (Table S4) were included using the time horizon of the reference study. For diseases and vaccines where herd immunity applies (Table S5), the additional cases and deaths prevented were included. If the coverage needed to achieve herd immunity was not reported, the target coverage recommended by health authorities was used (Table S5). When Spanish coverage was lower than herd immunity/recommended coverage, only cases and deaths prevented in the vaccinated population were calculated. When Spanish coverage was higher than herd immunity/recommended coverage, cases and deaths avoided were calculated for the entire vaccinated and unvaccinated population (in the age groups with higher coverage) (see Appendix).

Sensitivity analysis

A one-way deterministic sensitivity analysis (DSA) was performed to assess uncertainty around base case inputs and its impact on results. Vaccine list prices were discounted by 36%, reflecting the median discount from public tenders.[42] Administration costs were varied by 20%. Discount rates of 0% and 5% were assessed. Finally, two scenarios with BCRs were tested: first, BCRs were adjusted in direct proportion to Spanish coverage levels for diseases where Spanish coverage did not reach herd immunity/recommended coverage; second, a more accurate approximation of total BCR was made, by excluding vaccination programs with no published BCR.

Results

The distribution of men and women by age for the Spanish cohort born in 2020 is shown in Figure S3.

Table 1. Lifetime investment in the 2020 and expanded NIP (€, 2020).

Antigen	2020 NIP	% of total investment	Expanded NIP	% of total investment
Prenatal vaccination	**11,199,556**	**6.6%**	**11,199,556**	**4.1%**
Diphtheria, tetanus, pertussis	7,246,774	4.3%	7,246,774	2.6%
Influenza	3,952,781	2.3%	3,952,781	1.4%
Paediatric vaccination	**141,143,531**	**83.8%**	**240,897,368**	**87.4%**
Pneumococcal disease	51,166,067	30.4%	50,381,039	18.3%
Human papillomavirus	20,703,222	12.3%	20,703,222	7.5%
Meningococcal C	18,371,796	10.9%	17,787,735	6.5%
Varicella	15,986,172	9.5%	15,986,172	5.8%
Measles, rubella, mumps	9,322,486	5.5%	8,996,943	3.3%
Diphtheria, tetanus, pertussis	7,634,456	4.5%	7,585,342	2.8%
Meningococcal ACWY	6,166,178	3.7%	6,166,178	2.2%
Poliomyelitis	5,150,340	3.1%	5,101,226	1.9%
Haemophilus influenzae b	3,321,407	2.0%	3,272,292	1.2%
Hepatitis B	3,321,407	2.0%	3,272,292	1.2%
Rotavirus	-	-	34,964,426	12.7%
Meningococcal B	-	-	66,680,500	24.2%
Adult vaccination	**16,128,965**	**9.6%**	**23,378,637**	**8.5%**
Herpes zoster	9,069,882	5.4%	15,468,377	5.6%
Influenza	6,162,588	3.7%	6,204,057	2.3%
Pneumococcal disease	665,821	0.4%	707,289	0.3%
Diphtheria and tetanus*	230,674	0.1%	998,914	0.4%
Total	**168,472,052**	**100%**	**275,475,560**	**100%**

*With pertussis vaccination in the expanded NIP; **NIP**: National Immunization Program.

Investment in vaccines

The investment needed to vaccinate the cohort born in Spain in 2020 throughout life was estimated at €168.5 million with the 2020 NIP (Table 1). Most of this investment (83.8%) was for pediatric vaccinations, followed by adult (9.6%) and prenatal (6.6%) vaccinations. Pediatric vaccines for pneumococcal disease represented the largest share of investment (30.4%). Vaccine administration costs were €18.3 million (10.9%) of the total investment (Table S6).

Investment in the expanded NIP amounted to €275.5 million, of which vaccine administration costs were €19.3 million (7.0%) (Table S6). The proportion of investment allocated to each age group remained similar (i.e., 87.4% pediatric, 8.5% adult, and 4.1% prenatal) with the highest investment in pediatric vaccinations (e.g., MenB 24.2%), despite expanding adult vaccinations (Table 1).

Economic and health benefits

The potential economic benefit of vaccination was €772.2 million with the 2020 NIP, of which €748.9 million (97%) came from pediatric vaccination and €23.3 million from adult vaccination. No BCR was available for prenatal vaccination programs. Economic benefits increased by 4.0% in the expanded NIP, to €803.0 million (Table 2).

Regarding the health benefits of pediatric vaccination, the 2020 NIP prevented, in the short term, 52,054 cases of pneumococcal disease over 2 years, 847 cases of *Haemophilus*

Table 2. Lifetime benefits of the 2020 and expanded NIP (€, 2020).

Antigen	2020 NIP	Time horizon	Expanded NIP	Time horizon
Prenatal vaccination	**NR**	**NR**	**NR**	**NR**
Diphtheria, tetanus, pertussis	NR	NR	NR	NR
Influenza	NR	NR	NR	NR
Paediatric vaccination				
Pneumococcal disease	29,676,319	2 years	29,221,003	2 years
Human papillomavirus	101,611,414	Lifetime	101,611,414	Lifetime
Meningococcal C	NR	NR	NR	NR
Varicella	19,732,465	15 years	19,732,465	15 years
Measles, rubella, mumps	242,384,640	40 years	233,920,511	40 years
Diphtheria, tetanus, pertussis	206,130,321	15 years	204,804,232	15 Years
Meningococcal ACWY	6,382,131	5 years	6,382,131	5 years
Poliomyelitis	113,194,290	60 years	112,114,852	60 years
Haemophilus influenzae b	17,935,597	5 years	17,670,379	5 years
Hepatitis B	11,857,422	70 years	11,682,084	70 years
Rotavirus	-	-	31,097,673	5 years
Meningococcal B	-	-	NR	NR
Adult vaccination				
Herpes zoster	14,239,715	30 years	24,285,353	30 years
Influenza	7,518,358	1 year	7,568,949	1 year
Pneumococcal disease	1,533,234	5 years	1,628,727	5 years
Diphtheria and tetanus*	NR	NR	1,288,598	30 years
Total	**772,195,905**		**803,008,370**	

*With pertussis vaccination in the expanded NIP; **NIP**: National Immunization Program; **NR**: not reported. Influenza vaccine is administered to adults annually until death; thus costs and health benefits were considered annually from the age of influenza vaccination onwards.

influenzae b (88.6%), meningococcal ACWY (8.9%), and meningococcal C (2.6%) over 5 years, and 269,167 cases of pertussis (90.9%), diphtheria (9.1%), and tetanus (0.005%) over 15 years. Over 40 years to a full lifetime, it would prevent 1,215,742 cases of varicella (30.8%), measles (27.1%), mumps (16.6%), rubella (13.3%), and different cancers related to the human papillomavirus (12.2%) (Figure 2). Adult vaccination prevented up to 24,262 cases of HZ (52.0%), pneumococcal disease (24.3%), and influenza (23.7%) over the remaining lifetime (Figure 2).

Deaths averted with the 2020 pediatric NIP amounted to 9 over 5 years, 2,557 over 15 years, and more than 6,277 over 30 years. Among adults, 455 deaths due to pneumococcal disease were averted over 5 years (Figure S4).

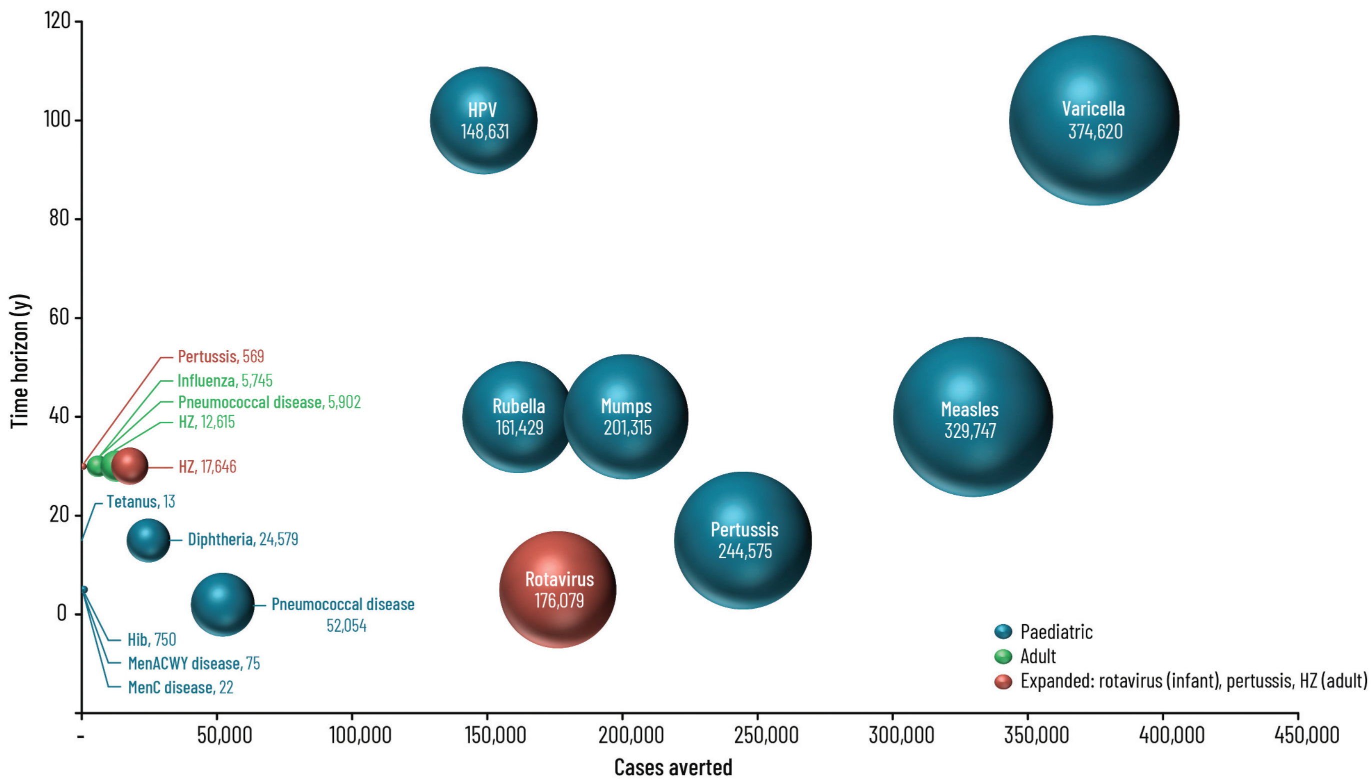

Figure 2. Number of cases averted (over time horizons) with the 2020 NIP and expanded NIP. **Hib**: *Haemophilus influenzae* b; **HPV**: human papillomavirus; **HZ**: herpes zoster

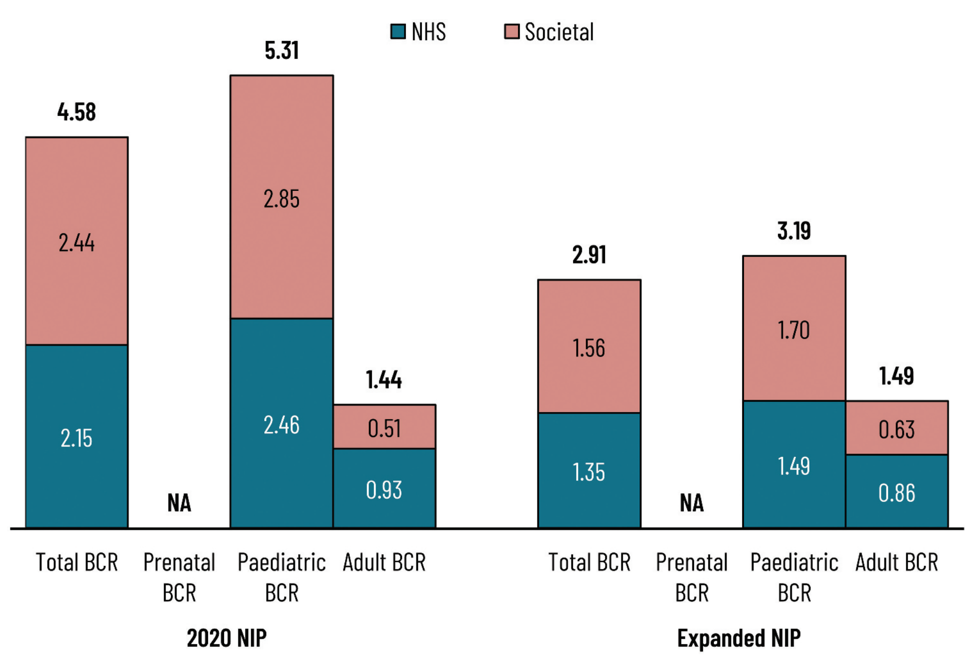

Figure 3. Benefit–cost ratio of the 2020 NIP and expanded NIP. **NA**: Not available due to the lack of published data on prenatal BCR; **BCR**: benefit–cost ratio; **NHS**: National Health Service; **NIP**: National Immunization Program

Additionally, with the expanded NIP, 176,079 rotavirus cases would be prevented over 5 years, and 182 deaths over 30 years. Finally, reducing the vaccination age of HZ cohort vaccination prevented 5,031 additional cases over 30 years and two deaths over lifetime, and 569 pertussis cases were prevented over 30 years (Figure 2 and Figure S4).

Benefit–cost ratio

The BCR of the 2020 NIP was 4.58 overall, of which the BCR was 5.31 for pediatric vaccination, and 1.44 for adult vaccination (Figure 3). The BCR was higher from a societal perspective than the NHS perspective, reflecting the impact of immunization programs beyond the patient. In the 2020 NIP, the societal BCR was 2.44 (53%) per €1 invested versus 2.15 for the NHS BCR. In the expanded NIP, the BCR was 2.91 overall, of which 54% of the BCR was due to societal benefits (Figure 3).

Sensitivity analyses

In sensitivity analyses, excluding vaccines from the analysis without a published BCR had the largest impact on results (in the base case, only costs and no health benefits of these vaccines were included). This resulted in an increase in the BCR to 5.57 (2020 NIP) and to 4.47 (expanded NIP) (Figure 4).

Benefits were obtained from available literature; thus, the DSA only varied discount rates for studies where it was not previously applied, and with a time horizon over 1 year. Increasing the discount rate to 5% decreased the BCR to 3.49 (2020 NIP) and 2.65 (expanded NIP), while not discounting increased the BCR to 4.68 (2020 NIP) but also decreased the BCR in the expanded NIP to 2.86. This discrepancy is probably driven by the addition of the meningococcal B vaccine, since the investment in this vaccine was included in the first year of the analysis (without discount); however, no health benefit data were available to be used for the BCR of this vaccine, thus almost certainly underestimating the full BCR.

With a hypothetical discount to vaccine prices (to reflect lower public contract prices versus list prices in Spain), the investment needed decreased to €113,771,349, resulting in a BCR of 4.67 (current NIP) per €1 invested.

Discussion

This is the first study to estimate the BCR of a complete NIP, providing a comprehensive exploratory estimate of the BCR for the NIP in Spain. The investment needed to immunize the cohort of newborns in Spain throughout life was €168.5 million with the 2020 NIP, and the estimated benefit obtained from this investment was €772.2 million. Thus, the BCR was 4.58, which means that, for every €1 invested in the

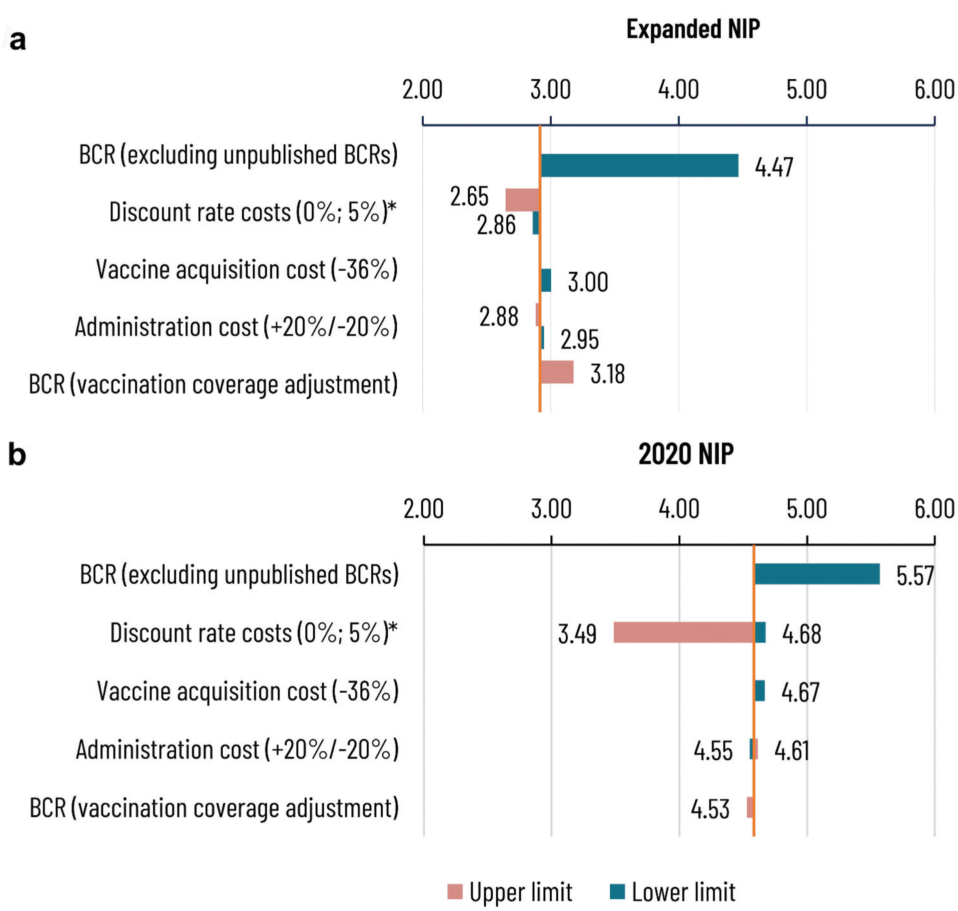

Figure 4. Deterministic sensitivity analysis results (changes to BCR with varying inputs). The deterministic sensitivity analysis results show how the BCR changes when varying input parameters. No change to discounting of benefits was possible in the DSA, as data on economic benefits from all studies included discounting. **BCR**: benefit–cost ratio; **DSA**: deterministic sensitivity analysis; **NIP**: National Immunization Program

current NIP, there is a potential societal gain of €4.58. With an expanded NIP including vaccination programs based on scientific and medical society recommendations, the BCR was 2.91, also resulting in positive societal gains.

The results highlight the remarkable societal BCR obtained from pediatric vaccination, due to the wider development of childhood versus adult vaccination programs, as well as the long-life expectancy over which infants and children can capture the economic and health benefits of vaccination. In Spain, and other European countries, protecting the aging population, who are at higher risk from infectious diseases due to age-related immunity decline, is becoming a priority.[43] Although the COVID-19 pandemic helped raise awareness about the importance of vaccination to protect adults and reduce the healthcare system burden,[44,45] there are still fewer adult vaccination programs, with lower levels of implementation and coverage.[43] In Spain, the direct medical costs of four vaccine-preventable diseases among adults (HZ, pneumococcal disease, influenza, and pertussis) was estimated to be €134.1 million in 2015 (nearly 60% were hospital costs).[46] Improving vaccination coverage in adults supports a life-course vaccination approach, which can help reduce disease burden and healthcare costs, given the increased socioeconomic impact of the aging population that is expected in Europe in the next decade.[43,47–49] In addition, promoting health and prevention strategies, including vaccination, will help reduce intergenerational inequities by including adults into healthy aging strategies.[47,50]

The current analysis estimated that an investment of €168 million (€304 million undiscounted) in lifetime vaccines is needed to protect a cohort of newborns in Spain in 2020. This investment represents a small proportion of public health investments, i.e., 0.22% of the total public healthcare expenditure and 21.01% of public health service expenditure in 2019.[51] Values from 2019 were used in this comparison to avoid a potential bias due to expenditure on COVID-19 vaccines in 2020. A similar figure of 0.25% of total public healthcare expenditure was reported as the annual level of investment needed to fund vaccination programs in Spain (considering all cohorts vaccinated in a year versus this analysis which considered vaccination of a single cohort over lifetime).[6]

Soler Soneira et al. (2020)[6] estimated the lifetime costs of the NIP in Spain (i.e., €726 and €626 per healthy woman and man, respectively) using public contract prices for vaccines. By replicating their cost estimations in this analysis (2020 NIP), the lifetime costs of vaccination (until 83 years) amounted to €1,248 and €1,047 per healthy woman and man, respectively, with discrepancies mainly due to vaccine price differences (public contract prices versus list prices).

A study in the United States estimated the lifetime social value of the childhood vaccination program (i.e., diphtheria, tetanus, acellular pertussis, hepatitis A, hepatitis B, *Haemophilus influenzae* type b, inactivated polio vaccine, measles, mumps, rubella, pneumococcal conjugate vaccine, rotavirus, and varicella) in the 2017 birth cohort. For every $1 invested in childhood vaccination, a total of $7.50 would be saved from the societal perspective, of which $2.80 would be healthcare system cost savings.[52]

Following NIP changes in 2023 (e.g., inclusion of MenB vaccination), the Spanish NIP in use today has evolved into a mix of the current and extended NIPs from the analysis. Thus, the inclusion of new antigens in the expanded NIP could be applicable to the 2023 situation, showing that investment in the Spanish NIP remains an efficient use of resources.

Future research is needed to better capture the real costs and benefits of all vaccines in the NIP, and to raise awareness with decision-makers of the lifetime benefits of vaccination to society and healthcare systems. Some studies[53,54] have shown that as vaccination programs successfully control diseases, a new infection equilibrium can be achieved over time, with an evolving BCR as a result. Future studies may investigate whether the BCR value over time can help to inform changes to vaccination policies, such as moving from routine vaccination to outbreak control.

Limitations

The present analysis adopted a conservative approach in the absence of more accurate data, therefore there are some limitations to the interpretation of results. A novel methodological approach was implemented, in which health and economic benefits were derived from previous CBAs identified from the literature and adapted to the Spanish context. The use of the most applicable published data, rather than data derived from context-specific cost–benefit models, from meta-analyses or other quantitative synthesis methods, was justified as there are no currently agreed methods for pooling cost-effectiveness estimates from multiple economic evaluations, to extrapolate and predict outcomes across countries.[55] The economic CBA approach was the most suitable, as a cost-effectiveness model including all the strategies in the NIP is not feasible, as it would require an individual model for each infectious disease, and thus adding enormous complexity to the analysis. The objective of the approach used was to provide a starting point for discussions about the efficiency of NIPs and their social BCR. Other limitations related to the lack of up-to-date values on BCR for some vaccines (e.g., hepatitis B in children and pneumococcal disease in adults) dating back from 2000s[56,57] and for the estimated economic impact of some strategies, especially in prenatal and childhood programs. As it was not possible to apply a specific BCR for all vaccination programs in the NIP, the results are highly likely to underestimate the value of the NIP. Studies included in the analysis had major methodological differences, e.g., regarding time horizon, target population, burden of disease, and health benefits. Data for Spain were not always available, so studies from other countries, as similar as possible to the Spanish setting, were considered. The effectiveness of vaccination in reducing healthcare resource use, however, may differ according to utilization patterns in different countries. Similarly, in some studies, CBAs converted health benefits into costs using willingness-to-pay thresholds, which may vary by country. In some cases, the benefit of a vaccination program was derived from a country using a different vaccine to the one marketed in Spain in the NIP. Due to the lack of data, some assumptions had to be made regarding coverage and herd immunity.

Conclusions

This analysis using a novel methodological approach has shown that lifelong vaccination is an efficient preventive measure providing public health benefits, for which the investments are outweighed by the health and economic benefits. Efficiency is maintained when more vaccines are included in the NIP, by preventing disease, long-term disability and death and offsetting healthcare costs and productivity losses.

Regardless of the economic impact of individual vaccination programs, when considered within the framework of a NIP, vaccination produces a positive return on investment with health and economic benefits for society. This analysis can be useful to healthcare payers and providers, in highlighting the benefits of pediatric and adult vaccination for society.

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Disclosure statement

Andrea Garcia and Laura Vallejo are employees of GSK. Laura Vallejo holds financial equities in GSK. Ekkehard Beck was employed by GSK at the time the study was carried out, he is currently employed by Moderna, and he declares holding stock in this company. Alvaro Hidalgo, president of Foundation Weber, declares that this entity received fees from GSK for conducting this study. Almudena Gonzalez-Dominguez, Mathilde Daheron, Néboa Zozaya González, Irene Fernández Meco and Ana Durán are employees of Vivactis Weber, that received fees from GSK for conducting this study. Antonio J Garcia Ruiz participated as a Weber consultant. Maria Fernandez Prada, Alberto Pérez Rubio and Natalia Cassinello received fees from GSK for their expert advice during study conduction. All authors declare no other financial or non-financial relationships and activities and no other conflicts of interest.

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Author's contributions

All authors participated in the conception and design, data acquisition, and results interpretation of the analysis performed; they also contributed to the drafting of the paper, critical revision of the content. and the final approval of the version to be published. All authors agree to be accountable for all aspects of the work.

Ethical approval

Ethics approval was not required as this study was based on published data and. therefore. did not involve human participants.

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