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Trends in governmental expenditure on vaccination programmes in the Netherlands, a historical analysis

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ABSTRACT

Background: Health economic evaluations are often required before implementing a vaccination programme. Such evaluations rarely consider the historical context of a vaccination programme. We review the financial history of vaccination programmes in the Netherlands, and compare these to demographic and macroeconomic developments as well as avoided mortality burden.
Methods: Previously uncatalogued historical expenditures on the Dutch National Immunisation Programme (NIP) and influenza vaccination were obtained from official reports. Costs were adjusted for inflation using Consumer Price Indices and expressed in Euro of 2016. Estimates on mortality burden averted were obtained from previous research and used to calculate the ratio of expenses to averted mortality burden for vaccinations against diphtheria, tetanus, pertussis, polio, measles, mumps and rubella for birth cohorts 1953–1992.
Results: Developments towards a uniform government funded NIP started early 1950s with vaccinations against diphtheria, pertussis and tetanus, culminating in its official launch in 1957 together with polio vaccinations. Since the 1980s, expenditure increased nearly five-fold mostly due to the addition of new vaccines, while spending on already implemented vaccinations tended to decline. Overall, expenditure increased from € 5 million in 1957 to € 93 million in 2014. Relative to total healthcare expenditure, the NIP contributed little, ranging between 0.05% and 0.14%. Spending on influenza vaccination increased from € 37 million in 1996 to € 52 million in 2014, while relative to total healthcare expenditure it decreased from 0.069% to 0.055%. In 2014, 0.15% of healthcare expenditure and € 533 per birth was spent on vaccination programmes. Overall, for birth cohorts 1953–1992, € 5.4 thousand (95% confidence interval: 4.0–7.3) was expended per year-of-life-lost averted.
Conclusion: The actual costs per year-of-life gained are more favorable than estimated here since averted medical costs were not included. Although expenditure on vaccination programmes increased substantially, the contribution to overall healthcare expenditure remained small.

1. Introduction

Currently, health economic evaluations of vaccines are a common part of vaccine research. In the Netherlands, the introductions of new vaccines are generally discussed by a special committee of the Health Council of the Netherlands on several criteria before they are considered for inclusion in the National Immunization Programme (NIP). These criteria include the severity of the disease, effectiveness and safety of the vaccine, its acceptability, whether the public health issue is urgent enough, and the cost-effectiveness of the vaccine [1].

Cost-effectiveness analyses were not always part of the decision making process surrounding vaccines. The merits of Edward Jenner's vaccine against smallpox were measured on its safety and efficacy, not its costs. Similarly, the inclusion of diphtheria, pertussis, tetanus, polio, measles, mumps, and rubella, were not evaluated on their cost-effectiveness or cost-saving potential

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before they were introduced [2]. In general, considerations on healthcare costs were by far not as prominent as they are nowadays. Also, the first vaccination programmes were introduced in a time with higher infectious disease morbidity and mortality as compared to today, which may have led to an easier decision on implementation of preventive measures without a strong need for economic arguments since the public health benefits were more clear.

The economic aspects of vaccinations have only begun to play an important role in decision making over the past several decades, partially due to the substantial increase in healthcare expenditure in most high income countries [3]. In addition, recently introduced vaccines such as the pneumococcal vaccines and the vaccines against human papillomavirus are much more complicated to produce, have a higher price, and their benefits are sometimes less visible than the older vaccines [4,5]. For a government with restricted budgets, these developments have led policy makers to focus on cost-effectiveness analyses of medical and preventive interventions including vaccines [6].

The benefits, and indeed the cost-effectiveness, of many vaccination programmes are well understood. However, these often pertain to current and potential future vaccines, with less of a focus on the history of vaccination programmes. For the Netherlands, the historical mortality and morbidity benefits of vaccinations programmes have previously been explored, but historical expenditure analyses have not been done [7,8]. Evaluations of costs, and especially those for new and generally more expensive vaccines, should be viewed in the context of vaccination programmes as a whole and their history. Understanding their history may help to better evaluate the benefits and costs of old and new vaccines and furthermore will provide valuable insight into the developments of expenses over time for purposes of health care budgeting and assessing the affordability of vaccination programmes.

To provide such an understanding, we review the historical costs of vaccination programmes in the Netherlands up to 2014, with a focus on childhood and influenza vaccinations. We discuss the historical costs of the Dutch vaccination programmes and analyse the developments in government expenditure on these programmes since implementation. In particular, we examine whether the expenditure on vaccination programmes has increased relative to other measures such as total healthcare expenditure and Gross Domestic Product (GDP). Lastly, we utilize results from previous studies on the impact of vaccination programmes on mortality burden averted in the Netherlands to give a ballpark estimate of the combined costs and effects of vaccination programmes against diphtheria, tetanus, pertussis, polio, measles, mumps, and rubella.

2. Organisation and funding of vaccination programmes

2.1. Childhood vaccination programmes

Table 1 provides a brief overview of the developments around vaccination programmes in the Netherlands. Officially, the Dutch NIP was launched in 1957 with the start of mass vaccinations against polio, but already in 1953 mass vaccinations against diphtheria were implemented. Although a toxoid-vaccine against diphtheria was available since the mid-1920s, diphtheria vaccinations in the Netherlands were not widespread before 1953, with only 4–13% of the population being vaccinated in the early 1940s [9]. Vaccinations were generally provided by local private healthcare providers or government bodies and administered by general practitioners to children aged between 4 and 9 years, while most cases of diphtheria occurred in younger children, thus limiting the potential impact of these vaccinations. The vaccines were paid for by parents, private or social health insurances, charities, or other local funding organisations, but there was no coherence between regions or a central coordination of vaccination efforts [10].

In the early 1950s the Healthcare Inspectorate increased their efforts to get more children vaccinated and at a lower age. To do so, financial support was offered to Child Welfare Centers by providing a reimbursement of 1 Dutch Guilder for each registered vaccination starting in 1951 (1 Dutch Guilder in 1951 was equivalent to a purchasing power of € 3.7 in 2016). This was done through a local and government financed fund called the 'Praeventiefonds', which was tasked to provide financial support to organisations and groups to improve public health and combat disease. In 1953, the government extended its support by providing the vaccines free of charge. Vaccines were produced or bought by the National Institute for Public Health and provided through the Healthcare Inspectorate. During this time, vaccines against pertussis and tetanus became available and were provided for free through the same structure. This marks the start of the developments that would eventually lead to the organized vaccination programme we know today.

Providing financial support and consolidating the organisation of vaccination efforts increased vaccination coverage (coverage of the diphtheria vaccine for infants increased from 20% in 1953 to over 50% in 1955 [7]), but it became clear that in order to reach more children, closer collaboration between municipalities and healthcare workers was required. To unite the organisations involved in vaccinations, the first so-called 'entgemeenschap' was launched in 1955. Within this collaborative framework, Child Welfare Centers, local general practitioners, cross-organisations, municipal health services, and local governments worked together to coordinate vaccination efforts [11].

At the same time, it was recognized that a uniform registration system of vaccination was needed to monitor the progress and success of the vaccination campaigns. Since the 19th century a register of smallpox vaccinations was already kept by municipalities and was now extended with the new vaccines. At birth, children received a card on which all vaccinations were to be registered. With each vaccination, healthcare workers would send a note to the local municipality where the vaccination was recorded.

All efforts of the preceding years came together with the mass vaccination against poliomyelitis in 1957 which sparked an increased public interest in vaccination. A major nationally coordinated vaccination campaign, staged over multiple years, was organised in which all children born since 1945 were invited to be vaccinated against poliomyelitis. This catch-up vaccination programme was executed from 1957 until 1962 and reached more than 2.6 million children. It also marked the launch of the new registration system as well as the start of the expansion of the collaborative framework of 'entgemeenschappen' to the rest of the Netherlands. The mass vaccination campaign against poliomyelitis is therefore seen as the official start of the Dutch NIP [11]. Children were generally vaccinated at Child Welfare Centers and at schools, and since the official launch of the NIP practically all vaccinations are administered through governmental channels without substantial private vaccination. Due to the new more uniform approach, the coverage increased dramatically and by 1964 childhood vaccination coverage was over 90% [7]. Historically the coverage remained very high for all vaccines, with only the HPV vaccine, introduced in 2010, lagging behind at an uptake of 45.5% for girls born in 2003 [12].

The Praeventiefonds continued to financially support the NIP until 1963, when the Ministry of Social Affairs and Public Health took over the complete funding of the vaccination programme, now containing the vaccines against smallpox and the combined DTP-IPV-vaccine (diphtheria-pertussis-tetanus-inactivated poliomyelitis).

Table 1
Short history of the Dutch National Immunization Programmes.

Year	Vaccine	Target group	Modifications and other remarks	Remarks on funding and organisation
1799	Smallpox	School-going children and infants. Under 1 year of age.		
1951				Start financial support of Child Welfare Centers by the Praeventiefonds.
1953	Diphtheria	Infants under 1 year of age.		Government starts providing vaccines free of charge.
1954	DTP	Infants under 1 year of age.	Diphtheria combined with tetanus and pertussis in DTP.	
1955				Start first 'entgemeenschap'
1957	Poliomyelitis	Catch-up campaign: everyone born since 1945 (3 doses). Routine vaccination: 3-, 4-, 5-, and 11- month-olds (4 doses).		Official start of Dutch NIP.
	DTP	3-, 4-, 5-, 11-month-olds (4 doses)	Catch-up vaccinations were offered at 4 and 9 years.	
1959				'Entgemeenschappen' extended over the rest of the Netherlands.
1962	DTP-IPV	3-, 4-, 5-, 11-month-olds (4 doses).	DTP combined with inactivated poliomyelitis vaccine in DTP-IPV.	
1963				Complete funding of the NIP provided by the government.
1965	DT-IPV	4- and 9-year-olds.		
1974	Rubella	11-year-old girls.	Smallpox vaccination discontinued.	Funding provided through social health insurance.
1976	Measles	14-month-olds.		
1987	MMR	14-month-old and 9-year-old boys and girls.	Measles combined with mumps and rubella in MMR	
1993	*Haemophilus influenza* serotype b (Hib)	3-, 4-, 5-. 11-month-olds (4 doses).	As a separate vaccination.	Government and other organisations funded a national campaign to inform risk-groups of influenza vaccination.
1995	Influenza	Risk groups[1]	Start of nationally organised influenza vaccination for risk-groups.	
1996	Influenza	65-year-olds and over.	Influenza vaccination extended to 65-year-olds and over.	Influenza vaccination financed through social health insurance.
1999			Starting age for DTP-IPV and Hib one month earlier, at 2, 3, 4, and 11 months-of-age.	
2001	Acellular pertussis (aP)	4-year-olds.	As a separate vaccine.	
2002	Meningococcal serotype C (MenC)	Catch-up campaign: everyone 18 years of age and younger. Routine vaccination:14-month-olds		
2003	Hepatitis B (HepB)	2-, 3-, 4-, and 11-month-old children with parents from high risk countries and children from mothers who carry hepatitis B-virus (4 doses).		
	DTP-IPV-Hib		Hib combined with DTP-IPV in DTP-IPV-Hib.	
2005			Pertussis component in DTP-IPV-Hib for infants replaced with acellular pertussis.	
2006	7-valent pneumococcal conjugate vaccine (PCV-7)	2-, 3-, 4-, and 11-month-olds (4 doses).		Coordination of influenza vaccination handed to the National Institute for Public Health and the Environment (RIVM).
	HepB0	Directly after birth for children from mothers who carry hepatitis B-virus.	HepB combined with DTP-IPV-Hib for risk groups	
	DTaP-IPV		Acellular pertussis for 4-year-olds now combined in DTaP-IPV.	
2007				'Entgemeenschappen' integrated in RIVM.
2008	DTaP-IPV-Hib-HepB	Children with down syndrome.		
	Influenza	60-year-olds and over.	Target age for influenza vaccination lowered to 60 years from 65.	
2010	Human papilloma virus (HPV)	12-year-old girls (3 doses).		
2011	PCV-10		PCV-10 replaces PCV-7.	
	DTaP-IPV-Hib-HepB	2-, 3-, 4-, and 11-month olds.	Now as a combination vaccine for all children.	
2013	PCV-10	2-, 4-, and 11-month olds.	Change from four to three doses of PCV-10.	

Table 1 (*continued*)

Year	Vaccine	Target group	Modifications and other remarks	Remarks on funding and organisation
2014	HPV		Change from three to two doses of HPV.	
2018	MenACWY		MenACWY replaces MenC.	Dutch NIP incorporated in the Public Health Act.

RIVM: National Institute for Public Health and the Environment. NIP: National Immunisation Programme.
Vaccines key: aP, acellular-pertussis; DTP, diphtheria-tetanus-pertussis; IPV, inactivated polio vaccine; Hib, *Haemophilus influenza* serotype b; HepB, hepatitis B; MenC, meningococcal serotype C; MenACWY, meningococcal serotype A, C, W, and Y; MMR, measles-mumps-rubella; PCV, pneumococcal conjugate vaccine; HPV, human papillomavirus.
[1] Risk groups for influenza vaccinations were defined by the Health Council of the Netherlands.

Since 1974, funding was provided through the collective and government funded social health insurance (the 'Algemene Wet Bijzondere Ziektekosten'; AWBZ) which covers every Dutch citizen. All subsequent vaccines that were added to the NIP were financed in this way until 2015 when the AWBZ was abolished. In 2018, the childhood vaccination programmes were incorporated in the Public Health Act, and in the mean time it was covered directly by the budget of the Ministry of Health, Welfare and Sports. Currently, the NIP is coordinated by the National Institute for Public Health and the Environment which is also responsible for communication on the NIP, and the registration, purchase, storage, and distribution of vaccines.

2.2. Influenza vaccination programme

The first successful influenza vaccine was developed in the early 1940s and used by the US military in 1944 and 1945. In the following two decades it became clear that the influenza virus mutates rapidly and that the vaccine needs to be reformulated regularly to match it with the expected strain of influenza, although an occasional mismatch does occur [13].

Like the NIP, initially there was no national programme for influenza vaccination in the Netherlands. Vaccinations were distributed by pharmacies and administered by and at general practitioners and targeted towards risk groups. The Health Council of the Netherlands reported each year on which risk groups should be vaccinated. These groups included patients with respiratory or heart problems, patients with diabetes mellitus, patients with HIV, and other groups with medical conditions that impair an adequate immune response. Individuals belonging to the risk groups were invited each year by the general practitioner to receive the influenza vaccine.

In 1991 the vaccination coverage among high risk groups in the general population was estimated at around 28%, while coverage among the risk groups may have been as high as 56% [14,15]. Vaccination was ongoing in earlier years and coverage was likely around 5%, but little to no data are available [16]. Reasons for this low vaccination coverage were that part of the target group refused vaccination because of doubts about efficacy, fear of side-effects, and because they thought it was not necessary. In addition, physicians also had doubt about the efficacy of the vaccine, side effects, the target groups to be vaccinated and how to reach them, and the need to vaccinate. Finally, practical reasons about access and availability may have resulted in lower uptake, as patients were requested to get the vaccine at the general practitioner [17].

In the early 1990s, the government and other organisations decided to actively intervene and increase the coverage of influenza vaccination. This was initially attempted by reaching out to the risk groups through media campaigns. In 1992 and 1993 the Ministry of Public Health, Welfare, and Sports, as well as other organisations including pharmaceutical companies and the National Organisation of General Practitioners, financed a national campaign, including television commercials, to inform risk-groups on the annual influenza vaccination [18]. The next step was achieved in 1995 when a national vaccination campaign was organised by the National Organisation of General Practitioners. This programme was extended in 1996 to also include everyone over 65 years of age, a strategy which was shown to be favourable in cost-effectiveness research [19]. Similar to the NIP, it was to be financed by public funds through government funded social health insurance. Although funded similarly, influenza vaccinations are not part of the NIP but organised as a separate programme. Reason for this separation is that the vaccination needs to be repeated each year and target specific risk groups and the elderly rather than focussing on children in general.

In 1997 the programme became officially known as the National Programme Influenza Prevention and in 2008 the target age was further extended to everyone over 60 years of age in addition to risk-groups. Currently, the programme is coordinated by the National Institute for Public Health and the Environment (RIVM) that also purchases and distributes the vaccines. In recent years the vaccination coverage has been declining steadily from 71.5% in 2008 to 53.5% in 2016 [20,21]. This is possibly due to an increase in healthy elderly within the target population who perceive lower risks of influenza and are less willing to vaccinate.

3. Price development of vaccines and vaccination programmes

3.1. Data and methods

We obtained previously uncatalogued historical expenditure data on the NIP from 1951 up to 2014, from various official reports ranging from annual reports of the Praeventiefonds, the Ministry of Public Health, Welfare, and Sports and her predecessors, and other official publications. For the periods 1973–1976 and 1978–1981 no data was available. We also obtained the expenditure on influenza vaccinations from 1996 up to 2014. These expenses reflect the government expenditure on the NIP and influenza vaccination, and include vaccine costs, costs of administration, personnel costs, and overhead costs, but may not contain all costs associated with vaccination programmes, such as implementation costs or catch-up campaigns. These costs are however minor compared to the costs of vaccines and overhead costs themselves. For most periods these costs were not separately specified. Expenditure on specific vaccinations in the NIP from 1995 to 2013 (no data for 2014 were available) were obtained from databases of the Dutch Health Authority. For influenza vaccination, no specific expenditures were available for the period 2004–2008 and cost for this period were based on available subsidies as reported in the 'Staatscourant' (the official Dutch Government Gazette).

We obtained the number of births, population size, as well as overall healthcare expenditure from Statistics Netherlands [22,23]. For the overall healthcare expenditure, no data was available prior to 1972. Gross Domestic Product was obtained from the Netherlands Bureau for Economic Policy Analysis [24]. We used population and birth statistics to calculate the cost per capita

(expenditure per year divided by the total population of that year) and the cost per birth (expenditure per year divided by the total number of live births of that year).

We adjusted the development of expenditures of the Dutch NIP, GPD, and overall healthcare costs for inflation using the Consumer Price Index (CPI) published by Statistics Netherlands [25]. By adjusting for the general price development of a basket of consumer goods and services, the movements in the expenditures on the NIP are the combined result of changes in the volumes and the specific price movements of vaccinations only. The expenditures were expressed in prices of 2016 (in Euro) and data prior to 2002 was first converted to Euro from Dutch guilders where € 1 = 2.20371 Dutch Guilder.

We expressed the expenditure on the NIP and influenza vaccination programme relative to demographic changes (population and births) and macroeconomic changes (total healthcare expenditure and GDP).

Previously we have analysed the childhood mortality benefits of vaccinations programmes against diphtheria, tetanus, pertussis, polio, measles, mumps, and rubella [7]. In short, we estimated the years-of-life-lost among children and young adolescents (up to 20 years-of-age; YLL20) born between 1953 and 1992, that are prevented by vaccination programmes in the Netherlands. We showed that the mortality burden for these diseases already declined before the start of vaccination due to various other reasons (like improvements in nutrition, welfare, housing conditions, and so on), but that vaccines still contributed substantially in further lowering mortality burden, for more details see [7]. Here, we assess the ratio of the government expenditure on vaccination programmes for a certain year and the (previously) estimated YLL20 prevented for everyone born in that year. Because expenditure was not reported separately during the period, it was not possible to provide estimates separately for each vaccine. For years with missing expenditure data, we assumed the costs would be the

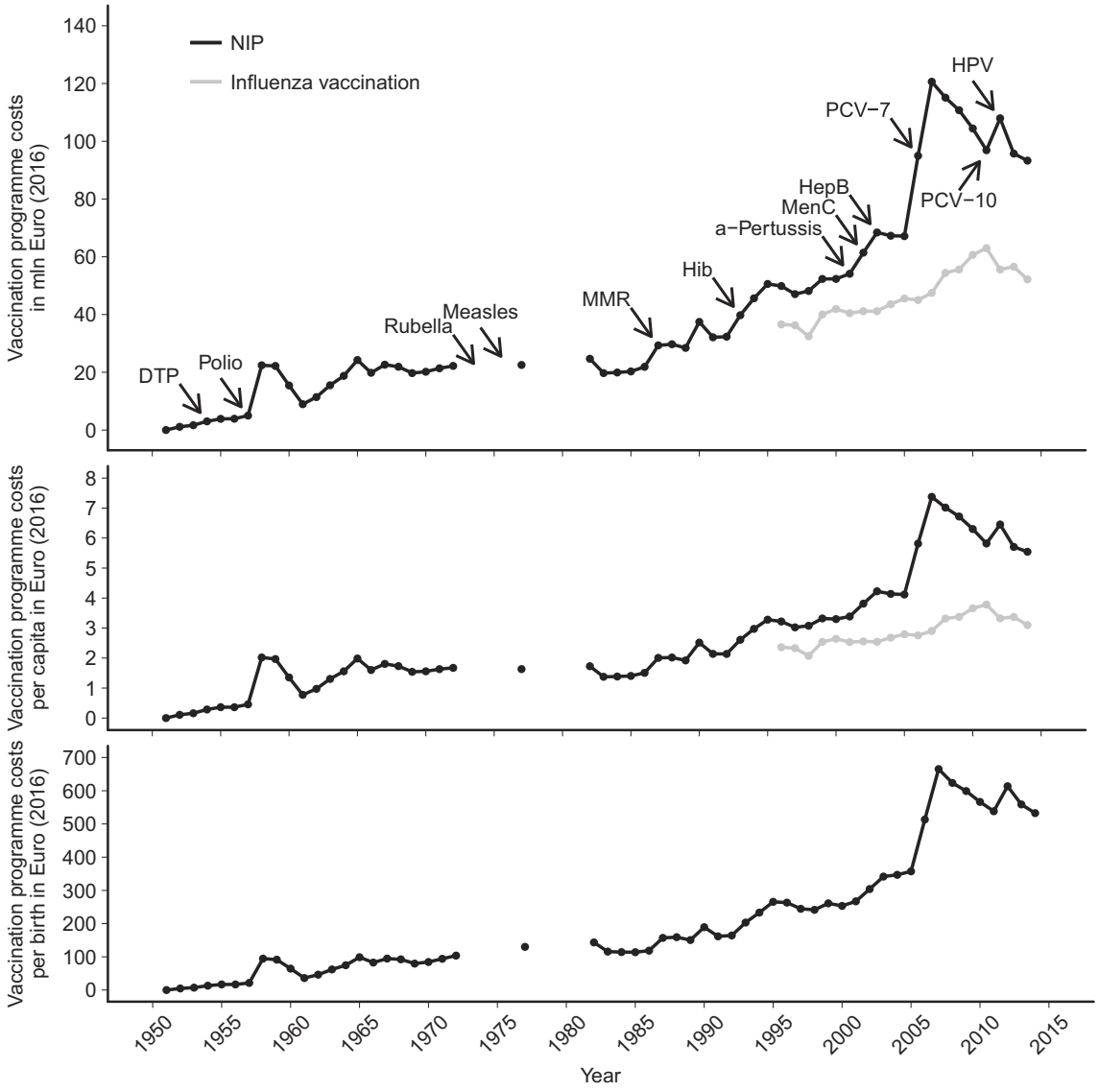

Fig. 1. Government expenditure on the Dutch National Immunisation Programme (NIP), 1951–2014 and influenza vaccination programme 1996–2014. Black line indicates expenditure on the NIP, grey line indicates the expenditure on the influenza vaccination programme. Arrows indicate when new vaccines are included in the Dutch NIP. All costs are expressed in Euro of 2016 adjusted for inflation using Consumer Price Indexes. All prices express government expenditure according to various official reports. Data for the periods 1973–1976 and 1978–1981 were unavailable. Vaccines key: DTP-IPV, diphtheria-tetanus-pertussis-inactivated poliomyelitis; rubella in 1974, only for 11-year old girls; MMR, measles-mumps-rubella, for both boys and girls of 14 months of age; Hib, *Haemophilus influenza* serotype b; a-Pertussis, acellular-pertussis; MenC, meningococcal C; HepB, hepatitis B; PCV-7, 7-valent pneumococcal conjugate vaccine; HPV, human papillomavirus.

same as the last known costs. Note that this analysis excludes morbidity and only focusses on the mortality due to a select number of diseases and only up to 20 years of age. Our purpose here is not a formal cost-effectiveness analysis, which would go well beyond the scope of this manuscript, but an indication of the costs per year-of-life-lost prevented. As such, costs and YLL20 are also not discounted.

4. Results

Fig. 1 shows the total expenditure, expenditure per birth, and expenditure per capita on the Dutch NIP and influenza vaccination programme. In general, the expenditure on the NIP increased gradually over time from € 5 million (mln) in 1957 to € 93 mln in 2014. Government expenditure increased in particular since the end of the 1980s. The increase in costs is mainly due to the addition of new vaccines such as the MMR-vaccine in 1987, the vaccine against *Haemophilus influenza* in 1993, acellular pertussis in 2001, meningococcal C in 2002, and hepatitis B for risk groups in 2003. The expenditure on the NIP increased again in 2006 with the inclusion of PCV-7; from € 67 mln in 2005 to € 120 mln in 2007. The per capita and per birth expenditure on the NIP followed a similar trend, increasing from € 0.46 to € 5.54 per capita and € 21 to € 533 per birth between 1957 and 2014. At its peak in 2007 the NIP cost € 7.37 per capita and € 665 per birth. Since 2007, the costs of the vaccination programme have been declining. Similar to the NIP, the expenditure on the influenza vaccination programme increased, from € 37 mln in 1996 to € 52 mln in 2014. In total, the government spent € 145 mln (€ 8.65 per capita) on the NIP and influenza vaccination programme in 2014.

A breakdown of the costs of the NIP by vaccine is shown in Fig. 2. While the total expenditure on vaccinations increased substantially when a new vaccine was introduced, the costs of a specific vaccine seemed to decline over time, possibly due to better price tendering and international developments on the vaccine market (when more competitors join the market). For example, expenditure on the MMR-vaccine declined from € 6.9 mln in 1987 to € 2.6 mln in 2013. Reformulations of vaccines (such as combining DTP-IPV-Hib with HepB) did not substantially impact total expenditure. The main cause of the increase in costs in 2007 was the inclusion of the PCV-7 vaccine. In 2012, the expenditure on PCV declined dramatically due to better pricing for the PCV-10 vaccine.

Fig. 3 shows the expenditure on the NIP and influenza vaccinations as proportions of the GDP and healthcare expenditure. Overall, expenditure relative to GDP and healthcare expenditure increased as more mass vaccination programmes were implemented in the Netherlands. The proportion of healthcare expenditure spent on the NIP ranged between 0.05% and 0.14%. Similar to the overal developments in vaccination expenditure, the proportionate expenditure on the NIP increased up to 2007, after which a steady decline was observed. Interestingly, relative healthcare expenditure on influenza vaccination showed a decrease from 0.069% in 1996 to 0.055% in 2014. In total, 0.022% of GDP and 0.15% of healthcare expenditure was spent on vaccination programmes in 2014.

The ratio of expenditure to averted mortality burden among children and young adults (expressed as costs per YLL20) born between 1953 and 1992, for vaccinations against diphtheria, tetanus, pertussis, polio, measles, mumps, and rubella is presented in Fig. 4. The costs per YLL20 averted changes over time for these vaccines. As the mortality burden averted declined the cost per YLL averted increases from € 1.2 thousand (95% confidence interval: € 0.8 – € 1.9) in birth cohort 1953 to € 20.3 thousand (95% confidence interval: € 15.1 – € 27.5) in birth cohort 1992. In total over this period € 5.4 thousand (95% confidence interval: € 4.0 – € 7.3) was spend per YLL20 averted.

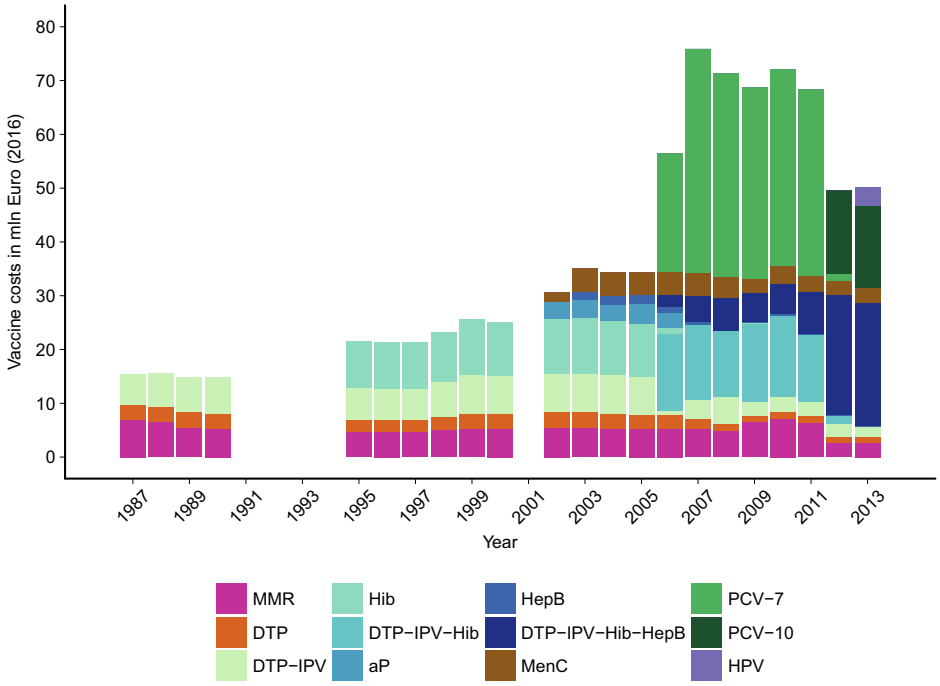

Fig. 2. Breakdown of costs by vaccine from 1987 to 2013. All costs are expressed in Euro of 2016 adjusted for inflation using Consumer Price Indexes. Data prior to 1987, from 1991 to 1994, and for 2001 are missing. Vaccines key: aP, acellular-pertussis; DTP, diphtheria-tetanus-pertussis; IPV, inactivated poliomyelitis; Hib, *Haemophilus influenza* serotype b; HepB, hepatitis B; MenC, meningococcal C; MMR, measles-mumps-rubella; PCV, pneumococcal conjugate vaccine; HPV, human papillomavirus. Due to differences in data sources, the timing of costs specified here may not correspond exactly to those in Fig. 1 or changes in the programme listed in Table 1. HPV vaccination was officially launched in 2010 for 12-year old girls but until 2012 the HPV programme was funded directly by VWS and expenditures were confidential.

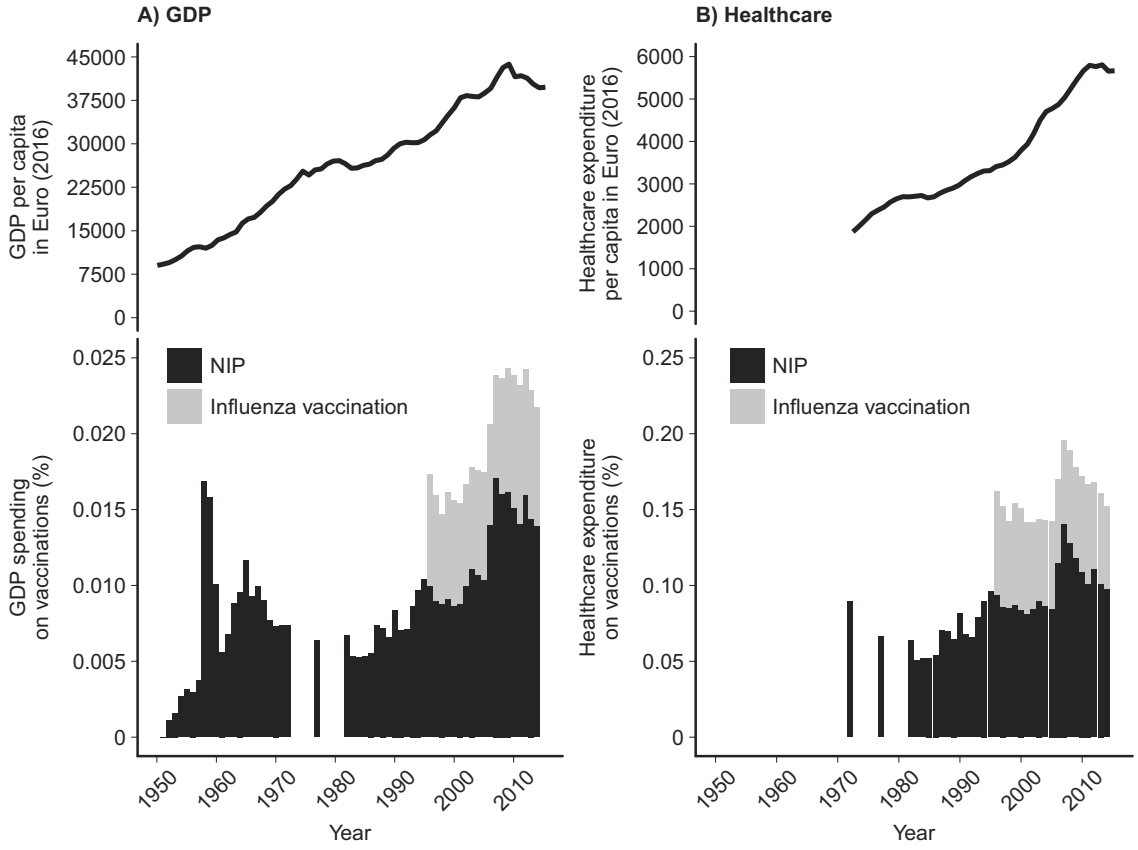

Fig. 3. Government expenditure on vaccination programmes relative to macroeconomic developments. (A) Government expenditure relative to Gross Domestic Product (GDP) 1951–2014 and (B) government expenditure relative to total healthcare expenditure 1972–2014. Top panels show the per capita GDP and total healthcare expenditure, bottom panels show percentages expended on the National Immunisation Programme (NIP) and the influenza vaccination programme. All costs are expressed in prices of 2016 adjusted for inflation using Consumer Price Indexes. Data on cost of the NIP for the periods 1973–1976 and 1978–1981 are missing; no data is available on healthcare expenditure from 1951 to 1971.

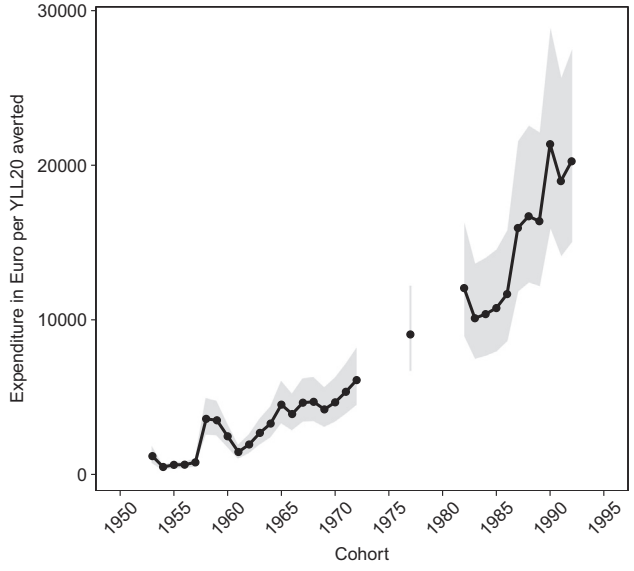

Fig. 4. Government expenditure on the Dutch National Immunisation Programme per year of life lost up to age 20 years (YLL20) averted for birth cohorts 1953–1992. Estimates on mortality burden averted among children and young adolescents up to the age of 20 were obtained from [7]. The black line indicates expenditure on the NIP per YLL20 averted by vaccination programmes and the grey area indicates the 95% confidence interval. All costs are expressed in Euro of 2016 adjusted for inflation using Consumer Price Indexes. All prices express government expenditure according to various official reports. Data for the periods 1973–1976 and 1978–1981 were unavailable.

5. Discussion

Vaccines are often hailed as one of the most effective public health methods in preventing infectious diseases. As the cost of new vaccines increase and in time where policy makers are confronted with limited resources and budget constraints, a historical perspective and good understanding of the evolution of the expenditure on vaccination programmes may help give context to today's decision making problems and provide insight into the affordability of these programmes. Here we explored the organizational and historical costs of vaccination programmes in the Netherlands.

The expenditure on the Dutch National Immunisation Programme has increased substantially over time, with a near five-fold increase since the mid-1980s and a near doubling since the early 2000s. We found that, both absolute and relative expenditure spiked whenever a new vaccine was introduced, and that expenditures tend to stabilise or decline when a vaccination programme covered the same vaccines. In addition, while our approach is not—and was not intended as—a full cost-effectiveness analysis, our estimates indicate that vaccinations against diphtheria, tetanus, pertussis, polio, measles, mumps, and rubella have a very favourable expenditure to averted mortality ratio.

There are two main reasons for the increase in vaccination expenditure on the long term. First, the number of included vaccines has increased. Nowadays, the Dutch NIP includes vaccines against 12 infectious diseases. Second, new vaccines are introduced at progressively higher prices. The current low costs

of vaccines included in the early days of the Dutch NIP sharply contrast the new generation of vaccines which have much higher price tags. These next-generation vaccines are more complex to manufacture and thus cost more in the early years of implementation.

Over time the costs of each specific vaccination, including the more recent vaccinations, declined. The expenditure on the MMR-vaccination for example declined by more than 60% between 1987 and 2014. This was partially due to tendering for better prices and a decline in the number of births. That expenditure on specific vaccinations declines over time is likely to be true for the newer vaccines as well as evidenced by the decline in expenditure on PCV after 2011. Vaccination against PCV-7 started in 2006 and dramatically increased the expenditure on the NIP. However, with the shift to PCV-10 in 2011 and the change to a 3-dose schedule in 2013, prices dropped considerably.

Pneumococcal vaccination thus has had a sizable impact on the overall expenditure on vaccination programmes in the Netherlands. While a formal cost-effectiveness analysis was beyond the scope of this study, previous studies on the cost-effectiveness of pneumococcal vaccines vary greatly, ranging from cost saving, to borderline or unfavorable depending on the assumptions in the models used [26–32]. For the Netherlands, cost-effectiveness studies show a similar picture with generally borderline to unfavourable cost-effectiveness ratios [28,33]. Mainly the steep price coupled with serotype replacement resulted in relatively poor cost-effectiveness ratios. These have improved however with the change to a 3-dose PCV-10 schedule. Recent years has also seen an increasing interest and implementation of vaccination of elderly against pneumococcal disease [34,35]. In 2018, the Health Council of the Netherlands advised in favour of vaccination with pneumococcal polysaccharide vaccine (PPV-23) for the elderly in the Netherlands [36].

Contrary to the childhood vaccination programmes, the expenditure on the national influenza vaccinations has not seen a drastic increase since 1996. However, as the elderly population is expected to increase in the coming decades due to the aging population, an increase in the expenditure on influenza vaccinations is to be expected.

Although the total government expenditure on vaccination programmes has increased substantially, overall the impact on total healthcare expenditure is very small. An earlier analysis showed that spending on vaccinations in 2003 was € 8.96 per capita (1.17% of total spending on prevention in the Netherlands); compared to € 6.77 in our study [37]. Although the approaches differ and included expenditure on screening, they broadly corroborate our results. Compared to other European countries, the Netherlands spends relatively little of its healthcare budget on vaccination programmes, accounting for only 0.15% in 2014, and this has been decreasing since 2007. In part this decline is due to the slow implementation of new vaccines in the Netherlands. In an analysis of seven other European countries spending on vaccine procurement ranged from 0.25% (Spain, 2012) of healthcare budget to 0.47% (Germany, 2014) [38]. This may in part be due to differences in the vaccines included and in financing of healthcare between European countries and thus differences in total healthcare spending. An update to their analysis showed a similar picture for more recent years [39]. In 2014, the Netherlands ranked 15th in the world rankings of highest expenditure on healthcare as percentage of GDP (9th on rankings per capita), spending 10.9% of its GDP on healthcare; Germany ranked 10th with 11.3% while Spain ranked 40th [40].

The costs reported here may not include all costs that are related to vaccination. It is often unclear what is actually included in the reported government expenditure on vaccination programmes. For example the reported numbers may not include expenses related to catch-up campaigns. For example, the catch-up campaign with meningococcal serogroup C vaccine in 2002, is estimated to have cost at least € 76 mln [41]. Although substantial, these are one-time expenses. In addition, while vaccines are generally considered as safe, they might cause adverse reactions, such as swellings at the injection site. These side-effects may result in healthcare utilization and thus vaccine-related healthcare costs. These costs were not taken into account here. Nevertheless, the government expenditure on vaccination programmes we reported here gives an indication of the order of magnitude on how much these programmes have cost and how the expenditures have developed over time.

Vaccination programmes are often considered amongst one of the most cost-effective public health interventions and highly effective in preventing infectious disease morbidity and mortality [7,42–44]. Here we add to previous work by estimating the ratio of expenditure to averted mortality burden for a selected number of vaccinations [7]. Although the ratio increased over time, due to declines in mortality burden, overall these ratios suggest that vaccination programmes have been highly cost-effective. The ratios presented here are similar but not identical to incremental cost-effectiveness ratios. We only accounted for mortality burden for a select number of diseases, and lacked the information required for more specific calculation of morbidity for this period. In addition, by preventing disease and mortality, vaccines also avert medical cost incurred due to treatment of those diseases, costs associated with productivity loss by parents tending to stricken children, as well as other costs due to long-term sequelae. These cost savings were not taken into account. As these costs associated with disease can be substantially higher than the costs of vaccination, many vaccines will be cost saving [45]. Some studies have suggested that the benefits of vaccination programmes also extend to other areas such as lifetime income, increasing overall well-being, better school attendance of children due to increased health, and as a consequence of these other benefits gains in productivity and longevity [46,47]. Evidence for such broader impacts remains limited [48].

For the near future, vaccination costs will increase further due to the implementation of next-generation vaccines or extending the target group of implemented vaccines. In 2018 meningococcal vaccination against serotype C was replaced with the vaccine against serotypes A, C, W, and Y. Moreover, the Health Council of the Netherlands recommended vaccination against rotavirus for infants with high-risk conditions (mainly preterm infants, infants with a low birthweight, or infants with birth defects). Interestingly, they also stated that vaccination of all children against rotavirus would only be recommended when the cost-effectiveness would be beneficial, i.e. the vaccine price would be low enough [49]. In the near future, the Health Council of the Netherlands will advise on a new vaccine against herpes zoster for the elderly. In addition, new target-groups of existing vaccine are under consideration, such as maternal pertussis vaccination (positive recommendation by the Health Council of the Netherlands in 2015), pneumococcal vaccination for elderly, HPV vaccination for boys, combined hepatitis A and B vaccination for children, and influenza vaccination for children.

The success of a vaccination programmes is inherently tied to the willingness of policy makers to finance the purchase and delivery of vaccines, the monitoring of their effects in terms of coverage, adverse events, and the occurrence of the target diseases [4,50]. Because vaccination programmes are implemented on a large scale, targeting entire birth cohorts, it is easy to perceive them as costly endeavours. Using a historical perspective, we have shown that vaccination programmes only constitute a small portion of the government spending on healthcare and their total costs, although increasing, are relatively low. We have also shown that vaccination-programmes against diphtheria, tetanus, pertussis,

polio, measles, mumps and rubella provided a large mortality burden averted at relatively modest costs. Inclusion of a new vaccine might result in an increase in expenditure. Such jumps in expenditure should always be substantiated by additional health gains. Moreover, the expenditure on these vaccines should always be viewed in context with the history of vaccination programmes as a whole; evaluations of the costs and effects of old and new vaccines should not be done in isolation. Understanding the evolution of vaccination programmes both in an organization and financial perspective may help put context to the budgetary impact of future vaccines.

6. Conclusion

Our historical perspective on the financial developments of vaccination programmes shows that while vaccination programmes have become more expensive, they have a relatively low impact on overall healthcare expenditure, and have been highly cost-effective in reducing mortality burden. While recent vaccines are progressively more expensive, over time, the costs of implemented vaccinations tend to decline. It is important to understand the financial evolution of vaccination programmes as it provides the context for today's decision-making.

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Declaration of Competing Interest

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