Summary
Infectious diseases impose a considerable mortality and morbidity burden to susceptible adult populations and high economic costs to patients and government-funded health care systems. Effective population-based immunization programs may prevent life-threatening diseases [diphtheria, tetanus, seasonal influenza, pneumococcal diseases] as well as diseases which adversely impact patients' quality of life [pertussis and herpes zoster]. Governmental investments in immunization may offer a range of broader immediate, short and long-term benefits that conventional economic evaluations dismiss. This study employed a “government perspective” analytic framework to estimate the governmental return on investment for immunizing adults in the Netherlands. A cohort model was developed simulating the epidemiology, health and social insurance costs and the lifetime tax of immunized and non-immunized individuals aged 50. Immunization was estimated to result in discounted lifetime health and social insurance cost-savings of €6.6 million and €4.2 million, respectively. Moreover, immunization was linked to a discounted gross tax revenue gain of €537 million over the remaining lifetime of the cohort. Based on the investment costs of vaccinating those aged 50, immunization yielded a benefit-cost ratio of 4.02, suggesting a 4-fold rate of return for the government.

Introduction
Infectious diseases impose a considerable mortality, morbidity and economic burden to susceptible populations and health care systems. A considerable part of this burden could be prevented through universal immunization programs. Although much attention has been paid to childhood immunisation, many vaccinations are available for adults to prevent life-threatening diseases [diphtheria, tetanus, seasonal influenza, pneumococcal diseases] as well as for diseases which adversely impact patients' quality of life [pertussis and herpes zoster]. For example, infections of the lower respiratory track (pneumonia and influenza) are a leading cause of death in adulthood. By contrast, due to universal childhood vaccination and boosters, diphtheria and tetanus have
become very rare infections in Europe. This illustrates that maintaining high vaccination throughout all age groups, including adults, especially aged above 50, is essential to protect the population and avoid the risks of outbreaks.

It is increasingly recognized that diseases resulting in individuals withdrawing from the work force, absenteeism and working inefficiently (i.e. presenteeism), retiring or dying prematurely have economic and therefore, fiscal consequences for governments. Moreover, in light of an ageing population, and consequently a shrinking labor force, Governments are under pressure to maintain sustainable health care systems. Considering the strength of evidence in relation to the economic benefit of healthy working-age adults, it is likely that adult immunization programs can contribute to both public health and economic goals. Indeed, governmental investments in immunization programs may offer a range of immediate, short-term and long-term economic benefits. Foremost, immunization has been frequently reported to result in efficient use of health care expenditures. Furthermore, several economic analyses suggest that immunizations are likely to be cost-effective strategies for those aged 50 years. Hence, adopting a life-course approach to immunization as part of healthy ageing policies and implementing immunization programs for adults aged above 50 may tackle the clinical and economic burden of infectious diseases.

In working-aged adults, recent investigations highlight how poor health can influence governments, both in terms of increased spending on transfer programs from the government to the citizens (i.e. disability costs and social insurance costs for increased absenteeism) and lost tax revenues attributed to premature mortality. While many think of older generations as being net users of government financed programs, the study of Health, Ageing and Retirement in Europe demonstrated that elderly populations, despite diminishing earnings, have a significant residual societal and fiscal value in terms of disposable income and consumption which translates into tax revenue for the government.

To better understand the economic benefits for government attributed to adult immunization, we estimated the gross tax receipts to the government for immunizations against communicable diseases (diphtheria, tetanus, pertussis, seasonal influenza, pneumococcal diseases, and herpes zoster) commonly administered to adults in The Netherlands based on changes in morbidity and mortality attributed to each immunization. To assess the fiscal impact of adult immunisation, this study followed a lifetime modelling approach which considered how investments in immunisation influence ongoing tax revenues to government (e.g. income tax, value added tax, social insurance contributions).
Methods and data

A “government perspective” assessment framework was used to compare the economic benefits associated with immunizing a cohort of adults aged 50 to the costs of immunizations. A cost-benefit analysis was conducted comparing the costs of immunizations with the short and long-term benefits resulting from immunizations for the government. The fiscal analysis framework described here is based on a methodology previously applied to childhood immunization. This framework has been adopted because a conventional economic framework for evaluating health conditions predominantly focuses on direct costs of health care, and dismisses the wider costs and benefits of changes in population health on the public sector. Adopting a “government perspective” approach to evaluate investments in health and resulting changes in morbidity and mortality provides a framework to estimate how governments benefit from adopting adult immunization programs. Specifically, assessing the impact that communicable conditions can have on productive capacity and consequently influencing future tax revenue for government. Similarly, costs that arise from severe morbidities linked to communicable conditions such as pneumococcal infection can give rise to additional costs to government (e.g., disability payments, social services and social insurances) for government, in addition to the traditional direct health costs.

To assess the fiscal impact of adult immunization a cohort model was developed in order to simulate the lifetime of an immunized and a non-immunized cohort of 50-year-old Dutch individuals. The age specific incidence of the scope infectious diseases and the corresponding mortality were multiplied with the number of survivors at each year t. Incident cases and deaths were reduced by the disease specific risk reduction attributed to immunizations. The non-immunized cohort was considered representative of the current situation in the Netherlands because current age-cohorts of 50 year old adults are not typically immunized against the under study diseases.

An illustration of the economic assessment methods used and the costs and benefits considered in the economic analysis is presented in Table 1. The discounted total lifetime direct and indirect tax (e.g., value added taxes) for a single cohort (N = 233,170) of immunized and non-immunized working-age adults aged 50 was projected. The increment of the total discounted lifetime direct and indirect tax between immunized and non-immunized cohorts was quantified. In addition, the study projected the incremental discounted direct medical cost-saving resulting from the reduction of morbidity and the prevented discounted disability costs. The indirect benefit of reducing the sick-days cost burden for the national insurance was also estimated as a benefit resulting from immunization for the working-aged adults.
The aforementioned discounted economic benefits were compared to the discounted total cost of immunization. Vaccination costs were deducted from the total benefits of vaccinations to calculate the Net Benefit of investing in an adult vaccination program. Moreover, the Benefit-Cost ratio was applied to reflect the rate of return from investing in vaccinations from the perspective of the Dutch government (Table 1).

Table 1 Model’s analytic framework

<table>
<thead>
<tr>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immunization benefits</strong> = \sum_{t=1}^{L_e} \frac{(Incremental Gross Tax + Health cost savings + NI burden reduction)}{(1 + r)^t}</td>
</tr>
</tbody>
</table>

- For **non-retired** individuals **gross tax** is the sum of **labour income tax** paid by individuals and **indirect or consumption tax**. A proxy of consumption tax was estimated by multiplying the VAT rate by the disposable income of individuals.
- For **retired** individuals, **indirect or consumption tax was considered as the benefit for the government**. Indirect tax was considered as the proportion of disposable income that goes to VAT.
- **Health costs and NI burden** were estimated as the sum of health – care costs, social services and disability costs resulting from the scope diseases.

<table>
<thead>
<tr>
<th>Costs</th>
</tr>
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<tbody>
<tr>
<td><strong>Immunization costs</strong> = \sum_{t=1}^{L_e} \frac{\text{Cov}<em>{t} \times \text{Cost}</em>{t} \times S_t}{(1 + r)^t}</td>
</tr>
</tbody>
</table>

Influenza immunization was considered to take place every year.

Increments refer to the difference between the immunized and non-immunized cohorts of working-age adults, aged 50. Where: r: discount rate; t: year; j: Vaccine type; Cov: Vaccination coverage rate; Cost: Vaccine cost; S_t: Number of survivors in year t; NI: National insurance.

**Economic assessments**
- **Net benefit** = Immunization benefits – Immunization costs
- **Benefit/Cost ratio** (considered as ROI) = Immunization benefit/Immunization cost

Table 2 illustrates the various epidemiological sources and economic data used in this research. Epidemiological data were obtained from the published literature and statistical databases. Specifically, age-specific incidence and mortality data were obtained for the infectious diseases under study\textsuperscript{17-20}. The current life expectancies were obtained from life tables\textsuperscript{18}. For consistency with other published economic analyses, cost-effectiveness analyses in The Netherlands were used to identify the direct medical cost per infection case, the number of sick-days lost per infection case and the percentage of infected persons that became disabled as a result of infections. The effectiveness of immunizations, in terms of reduction of incidence and mortality, was also
obtained from cost-effectiveness analyses for The Netherlands (Table 2). Costs per immunization consisted of the cost per total vaccination course needed plus the institutional cost per vaccine course in The Netherlands. In this research, the historical coverage immunization rate of 77% for Influenza vaccination was modelled and compared to a non-immunization scenario (Table 2). Disability annual costs per disability case were estimated based on the national aggregate statistics.

Table 2 Health economics and vaccination inputs

<table>
<thead>
<tr>
<th>Variables</th>
<th>Influenza</th>
<th>Pneumonia</th>
<th>IPD</th>
<th>Pertussis</th>
<th>Diphtheria</th>
<th>Tetanus</th>
<th>Herpes zoster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct per case medical cost</td>
<td>87</td>
<td>1,462</td>
<td>1,541</td>
<td>1,031</td>
<td>0</td>
<td>0</td>
<td>179</td>
</tr>
<tr>
<td>Absentism (sickdays) per case</td>
<td>3.25</td>
<td>5</td>
<td>5</td>
<td>5.98</td>
<td>0</td>
<td>0</td>
<td>10.1</td>
</tr>
<tr>
<td>Disability cases</td>
<td>0%</td>
<td>1.5%</td>
<td>1.5%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Reduction incidence</td>
<td>27%</td>
<td>11%</td>
<td>97%</td>
<td>89%</td>
<td>0%</td>
<td>0%</td>
<td>67%</td>
</tr>
<tr>
<td>Reduction mortality</td>
<td>42%</td>
<td>11%</td>
<td>97%</td>
<td>89%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Immunization coverage</td>
<td>77%</td>
<td>77%</td>
<td>77%</td>
<td>77%</td>
<td>77%</td>
<td>77%</td>
<td>77%</td>
</tr>
<tr>
<td>Vaccination cost per immunization</td>
<td>12.35</td>
<td>137.12</td>
<td>18.30</td>
<td>77.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Institutional costs per immunization administered</td>
<td>5.95</td>
<td>11.90</td>
<td>5.95</td>
<td>5.95</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sources: 36, 37, 38, 39, 20, 40, 21, 41

Booster doses were not considered for any of the assessed immunizations.

The national statistics were researched to identify age-specific earnings which were, in turn, adjusted for labor force participation by age. Age-specific annual earnings and disposable income were obtained from published sources. Specifically, the household surveys were used to quantify the age-specific level of earnings, disposable income and direct tax paid by an average individual over his or her lifetime. Moreover, the progressive tax system that applies to The Netherlands was modelled. Costs and benefits were discounted at the long-term (10-year) bond rate of the European Central Bank (1.8%). The latter rate was used to inflate costs and earnings to reflect future cost-inflation and wage productivity changes.

Results

The universal adult immunization program for the vaccine-preventable diseases in the Netherlands was projected to prevent 34,528 infectious disease cases over the remaining life span of the cohort, and roughly 5,782 premature deaths from...
infections. It was estimated that immunizations may reduce the number of lost work-days by 127,480 days with an estimate of 29 fewer disability cases over the remaining working years for those vaccinated at 50-years of age. The majority of infection cases prevented was attributed to immunization against herpes zoster which is associated with a frequent and high morbidity burden, followed by the prevention of seasonal influenza. The cumulative preventable mortality burden, over the life span of the cohort, was estimated at 736 deaths related to invasive pneumococcal diseases and 3,126 and 1,921 related to pneumonia and influenza-attributable deaths, respectively (Figure 1).

The health cost savings was projected to reach €6.6 million (Table 3). Immunization resulted in €4.2 million social insurance savings paid towards disability and sick day payments to workers and prevented the cost of €502,426 in disability benefits resulting from the infectious diseases under study (Table 3). The most significant economic benefit was linked to future lifetime tax contributions from implementing adult vaccination. Immunization would result in a gross tax revenue gain of €537 million over the remaining life years of the cohort (Table 3). As this benefit reflects the discounted gross tax revenue for the government due to the prevention of premature mortality, the distribution of this benefit across the preventable diseases was proportional to the distribution of preventable deaths.

The budgetary estimates for vaccinating a cohort of individuals aged 50 was estimated to be €136 million, which includes annual costs for influenza vaccination for the remainder of life. Based on the investment costs of vaccinating those age 50 in the year 2012, the project revenue gains yielded a net benefit (discounted benefits minus discounted costs) of roughly €426 million and benefit-cost ratio of 4.02 (Table 3).

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Break-down of discounted lifetime total costs and total benefits of immunization for the Dutch government</th>
</tr>
</thead>
<tbody>
<tr>
<td>Government budget item</td>
<td>Value</td>
</tr>
<tr>
<td>Medical cost-savings</td>
<td>Savings</td>
</tr>
<tr>
<td>Productivity loss (social insurance)</td>
<td>Savings</td>
</tr>
<tr>
<td>Prevented disability costs</td>
<td>Savings</td>
</tr>
<tr>
<td>Gross discounted tax</td>
<td>Revenue</td>
</tr>
<tr>
<td>Total discounted economic benefits of immunization (1)</td>
<td></td>
</tr>
<tr>
<td>Total discounted cost of immunization (2)</td>
<td></td>
</tr>
<tr>
<td>Net benefit [Discounted Benefits – Discounted Costs] (1)–(2)</td>
<td></td>
</tr>
<tr>
<td>Benefit: cost ratio [Discounted Benefits: Discounted Costs] (1) : (2)</td>
<td></td>
</tr>
</tbody>
</table>
Figure 1  Age-specific, infection-attributable deaths for immunized and non-immunized cohorts of working-age adults aged 50
**Discussion**

Over the past century, dramatic reductions in morbidity and mortality in developed economies have provided considerable economic benefits to nations as people have lived longer, more productive lives. To a large extent, vaccination has contributed to these economic benefits. In coming generations, the opportunities for economic growth are under threat due to fewer numbers of working-age adults supporting tax-financed public programs. Europe's population is ageing rapidly and by 2025, nearly 50% of Europeans will be 50 years or older. By 2050, it is estimated that two people of working age will support one "retiree", as opposed to 4 at present. The European Commission estimates that, in most EU Member States, health care spending will increase by approximately 25% (gross domestic product) due to the growing numbers of older citizens alone.

As many Member States seek opportunities to improve productive capacity, and reduce unemployment, adult immunization policies could be one of the contributors to achieve these goals. In recent years many OECD countries have started to increase the legal age of retirement to alleviate strains on pension budgets. For pension reforms to succeed requires not only public acceptance, but also provision of appropriate health care and preventative services to ensure workers are healthy enough to remain in the workforce. If one considers that health status is one of the main determinants of retirement, then investing in health and preventative measures is a sensible solution to prolonging productive working years. Furthermore, when these policies are viewed in light of studies showing that higher proportions of older workers may contribute to reduced youth unemployment rates, the potential economic benefits of a healthy cohort of older workers could be amplified.

Increasingly disease prevention is at the top of the policy agenda in Europe as a means to reduce patient burden and demand for health care. This is particularly relevant for older persons that often have chronic conditions making them susceptible to infectious diseases. It is likely that cost savings can also be achieved through improved prevention as noted in previous investigations indicating for every $1 invested in childhood vaccines, $5 in direct health costs can be avoided, and $11 in societal value can be obtained. However, current spending patterns continue to focus on inpatient and outpatient services with prevention budgets representing less than 3% of annual health budget in most EU countries, with declines in vaccination coverage observed in several countries.

As the number of working-age adults is starting to shrink, the importance of a healthy workforce for maintaining economic growth is one of the
opportunities where health policy and vaccination programs can influence population health and in-turn economic outcomes\textsuperscript{15, 24, 32}. The risks associated with an ageing society are not only economic. Considering the increased demands of an ageing population on public finances and the necessity to increase taxes on those working to fund commitments to social programs, commentators have suggested that age-related expenditure patterns could lead to intergenerational conflict between generations\textsuperscript{33, 34}. Indeed, research into intergenerational inequity has noted a steady deterioration in intergenerational fairness over the past two decades, with increasing burden being placed on younger generations\textsuperscript{35}.

To put into context the fiscal analysis described here, it is important to understand the magnitude that ill-health can have on governments. In 2008, a report commissioned by the UK government, describing the impact of ill health in working-age adults, suggesting that health care costs of illness represented only 8-15\% of total government costs. The findings of the report suggest that applying a health service or societal perspective analytic framework to evaluate health, in working-age adults, would not take into account approximately 90\% of costs that fall on the UK government attributed to lost taxes and increased public transfers\textsuperscript{11}. With regard to the economics of vaccines it has also been argued that neither cost-effectiveness nor cost-benefit analysis has taken full account of the broader economic impacts of immunization\textsuperscript{14}. In the light of this, our analysis attempted to quantify the fiscal benefit in terms of gross tax revenue, health service and social insurance savings that an adult immunization program against seven preventable infections may yield.

Our results suggest that every €1 invested in adult vaccination commencing at the age of 50 would yield €4.02 over the lifetime of the cohort. The economic consequences of reducing the number of infectious cases in adults was projected to yield a range of benefits for government including medical cost-savings reduced disability costs and increased tax revenue linked to labour force activity. To estimate this entails accounting for future income tax payments based on retirement at the age of 67, lifetime value added tax contributions, and social insurance contributions, based on changes in morbidity and mortality linked to immunization. These three transfers from citizen to state over their remaining lifetime reflect the financial value of changes in tax revenue linked to infection rates from the perspective of the Dutch government.

There are several limitations that need to be taken into consideration when considering the analysis described here. Firstly, the fiscal modelling
framework, like other government cost-benefit analyses, is based on assumptions regarding future economic conditions which can influence productivity, growth and wages. Due to uncertainty about the future these assumptions are held constant in the analysis. Although it is recognized that changes in macroeconomic parameters in the future could seriously influence the conclusions drawn here. Secondly, the current analysis is based on the hypothesis that the elderly have a substantial residual economic value for the society and the government and on the hypothesis that societies prefer more survival for the elderly compared to less survival. Thus, pensions were considered a source of income which is, in turn, partly transferred back to the government in the form of indirect or consumption tax. In fiscal accounting terms, pensions represent a cost for the government. An economic analysis for the elderly though, taking into account the excessive costs of pension resulting from increased mortality due to immunizations would implicitly suggest that less survival is cost-beneficial thus, preferred over a higher quantity of survival. In addition, consumption or indirect tax may have multiplicative effects through consumption multipliers which were not included in the present research.

The analysis described here demonstrates that investments in adult immunization yield positive benefits for government in terms of cost savings and increased tax revenue. Although this analysis is specific for the Netherlands, the results are relevant for countries across Europe, because they share many features in terms of tax burden and social transfer costs. Whilst there could be some variation across Europe one would expect to find consistency in terms of the productivity gains and associated gross tax revenue linked with adult immunization.

Past analyses of vaccines have focused on the economic burden associated with ageing populations, often alluding to the residual economic value of older persons. Our findings are consistent with a study of Health, Ageing and Retirement in Europe (2005) which demonstrated that elderly populations, despite diminishing earnings have a significant residual societal and fiscal value in terms of disposable income and consumption which translates into tax revenue for the government. Considering the impending fiscal challenges associated with an ageing population, the findings described here could be an important consideration in future health policies.

Maintaining people in the workforce, healthy and productive are a key priority for public debt sustainability and economic growth. Health may positively impact the economy through several channels which influence productive output and creativity. In turn, this growth can lead to improved tax revenue for the government that can be channelled to public investments
and to stimulate the economy with multiplicative economic effects. This
cyclical nature of health, investments in health, and fiscal benefits has been
highlighted by the WHO and can contribute to sustainable public finances².

Our analysis is pertinent not only to countries with tax-funded health systems
but also to countries with high rates of private health care. Nevertheless, in the
former systems increasing tax revenues is core to sustaining an effective health
care system. European policy-makers may wish consider comprehensive
adult vaccination programs as one of the policy options for improving
the welfare of society that will also influence a broad range of economic
outcomes, and enable people to extend their working years. Indeed, public
investments in adult vaccination are shown to provide significant return on
investment attributed to reduced government expenditure and increased tax
revenues (approximately 4-fold in the prototype study of the Netherlands).
Furthermore, intergenerational fairness is an important policy consideration
with respect to how resources are allocated throughout members of society
and those that are required to pay for public programs.

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PART III

PAEDIATRIC CHRONIC DISEASES