Novel economic perspectives on prevention and treatment: case studies for paediatric, adolescent and adult infectious and chronic diseases

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THE NEED FOR NOVEL ANALYTIC ECONOMIC EVALUATION METHODS

In light of austerity measures, policy appraisals should go further than the cost-effectiveness and assess the cross-sectorial impact not only of treatments but also of preventive health interventions. Investments in health may have economic benefits that go far beyond the health sector. Understanding and integrating into the economic analyses, the complex relationships among health interventions, health outcomes, education, labor productivity and several other externalities has implications for all types of health care interventions.

Broader evaluation perspectives require more extensive data collection. However, evidence on the “broad” benefits of many health interventions is largely lacking. In paediatric infectious and chronic diseases there is relatively little longitudinal research documenting the long-term effects of health status in early life. The scarcity of data is despite the growing body of evidence demonstrating the detrimental impact to an individual's lifetime prospects. The demanding nature of data and analytical requirements should not distract from the fact that broad-perspective evaluations of health care interventions will provide with useful information to inform resource allocation decision making.

The economic theory provides analysts with a range of microeconomic and macroeconomic analytical tools for assessing the broader consequences of diseases and subsequently the benefits of therapeutic and preventive health interventions. Ideally, a full economic package, encompassing microeconomic and macroeconomic analyses is warranted to inform resource allocation decisions. In a critical appraisal of the existing methods, presented earlier in this thesis, it was shown that each type of analysis may not come to precisely the same end-result compared to when done separately.

**Practical applications of a government perspective quantitative analytic framework**

In this thesis a novel quantitative analytic “government perspective” or fiscal framework is proposed and applied, to show how the prevention and treatment of infectious and chronic paediatric and adult diseases and conditions can impact government fiscal accounts. A comparative analysis of the case studies, the evidence used and the economic assessments conducted is presented in Table 1. The proposed framework was deemed as particularly relevant for immunizations which represent a high-cost investment which pays-off years or even decades after the actual immunization takes place.
Furthermore, because immunization programs are often funded directly from finance departments, describing health gains in terms of net tax revenue for government maybe language more familiar to finance departments which are the final payers of health care interventions in many countries.

The first case study presented in this Thesis evaluated investments in rotavirus immunization in two developing countries, Ghana and Vietnam. These two analyses were based on the observation that in these countries the mortality and morbidity burden of rotavirus are substantial. Moreover, previous studies had suggested that indirect costs represented a significant proportion of costs, implying that the fiscal effects will also be significant. This case study quantified the productivity and therefore, tax loss as a result of premature mortality and the direct and indirect costs resulting from the disease. By projecting the net discounted tax for single and multiple cohorts of immunized and non-immunized against rotavirus cohorts, the studies suggested that despite the low incomes in the two scope countries, investing in immunization may result in substantial long-term net fiscal benefits for the government.

The second case study assessed a novel immunization in a developed country i.e Germany. The study assessed a relatively high cost immunization namely, that of adolescent males and females against HPV. The study estimated both the broader economic consequences associated with HPV immunization and conducted a CBA of investing in immunization from a societal and government’s or fiscal perspective. The emphasis was put on the immediate economic benefits that the government derives from decreased mortality and morbidity i.e tax revenue from the higher quantity of survival and reduced health care costs stemming from decreased morbidity. The study modelled and projected the epidemiology of HPV-related cancers and pre-cancer stages in males and females. The lifetime age and gender specific earnings and tax of average German citizens were quantified. Economic benefits quantified in terms of medical cost-savings, increased productivity, increased earnings and increased tax revenue for the governments. The study showed that immunization against HPV results in a positive incremental net discounted tax when comparing a cohort of immunized to a cohort of non-immunized males and females. The societal and government perspective or fiscal CBAs showed that the benefit-cost ratio of immunization was greater than 1 (>1) thus, positive returns on investment.

Vaccinations are not only beneficial to governments when implemented to paediatric populations. Based on the hypothesis that working-aged adults have a considerable “residual value”, in terms of earnings and tax, we employed a “government perspective” assessment framework to estimate the governmental return on investment for immunizing adults against seven
Table 1  Comparative analysis of case studies

<table>
<thead>
<tr>
<th>Item</th>
<th>Rotavirus immunization</th>
<th>HPV immunization</th>
<th>Adult immunizations</th>
<th>ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
<td>Ghana, Vietnam</td>
<td>Germany</td>
<td>Netherlands</td>
<td>Germany</td>
</tr>
<tr>
<td>Comparators</td>
<td>Immunized vs.</td>
<td>Immunized vs.</td>
<td>Immunized vs.</td>
<td>Treated vs.</td>
</tr>
<tr>
<td></td>
<td>non-immunised</td>
<td>non-immunised</td>
<td>non-immunised</td>
<td>untreated ADHD</td>
</tr>
<tr>
<td></td>
<td>multiple birth cohorts</td>
<td>cohort</td>
<td>cohort</td>
<td>cohort</td>
</tr>
<tr>
<td>Direct medical cost</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Caregivers burden</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Sickleave/ Sickdays</td>
<td>Yes for parents</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Age specific earnings</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Gender specific earnings</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Educational specific-earnings</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Unemployment</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Disability rates</td>
<td>Yes</td>
<td>Yes</td>
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</tr>
<tr>
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</tr>
<tr>
<td>Educational costs</td>
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</tr>
<tr>
<td>Direct tax</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</tr>
<tr>
<td>Indirect tax</td>
<td>Yes</td>
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<td>Yes</td>
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<td>Gross discounted tax analysis</td>
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<td>Yes</td>
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<td>Yes</td>
</tr>
<tr>
<td>Net discounted tax analysis</td>
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<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Societal CBA</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Fiscal or Gov. perspective CBA</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

infectious diseases in The Netherlands. Immunization was estimated to result in discounted lifetime health and social insurance cost-savings due to decreased morbidity and to lifetime discounted gross tax revenue gain due to increased survival quantity.
Another two case studies, presented in this Thesis, applied the proposed quantitative analytic framework in the chronic paediatric condition of ADHD. These two studies were based on a well-established causal relationship between educational attainment and earnings\(^5\). In economic theory, higher educational attainment implies a higher potential for increased lifetime earnings which, in turn, provides the basis for higher tax revenue. When considering the long-term economic prospects of a society, the populations’ level of education is deemed as an important determinant of economic growth\(^6\). An analysis of cross-country data estimated that an additional year of schooling roughly raises the growth rate by 0.44% per year\(^6\).

The main hypothesis of these studies was that health care technologies aiming at reducing the effect of ADHD on school achievement may have a considerable and quantifiable value for the governments. Evidence from observational studies evaluating the educational attainment of individuals with and without ADHD, the age specific and education specific lifetime earnings and taxes were projected and compared. The medical costs of ADHD treatment were also quantified. Moreover, based on evidence regarding the resource intense health-seeking behavioural patterns of individuals with ADHD the longer-term health care care costs were projected. The first study assessed and confirmed using the lifetime net discounted tax the fiscal sustainability of treating ADHD individuals in Germany whereas the second study conducted a societal CBA.

**Decision making and novel economic evaluations frameworks**

The genesis of the quantitative analytic framework proposed here lies on the generational accounting methodology. The generational accounting theory was developed by Auerbach, Gokhale, and Kotlikoff as an intergenerational framework to evaluate the fiscal consequences of government policy decisions\(^7\). The generational accounting approach is commonly followed by Treasury departments and international organizations such as the World Bank and IMF which often apply a generational accounting framework to analyse policy decisions\(^7\). Inherent in these methodologies is the value of translating health capital into productive output and future tax revenue for government. Applying this methodology to health care appears to address contemporary concerns about the sustainability of health care systems and social insurance in Europe and elsewhere.

The underlying hypothesis of this methodology is that finance sustainability is influenced by two opposing population forces that influence government expenditure and tax revenues. As populations age, the opposing forces include economic growth influenced by labour market participation, and age-related expenditure. Thus, at each point in time it is possible to quantify the fiscal value of human life. This is particularly relevant for the prevention
and treatment of paediatric diseases. Assessing the fiscal value of protecting human life by deriving net tax revenues from health gains is an unconventional approach seldom considered in the health economics literature.

Of the first applications of this method in health was the work produced by Connolly et al., in assisted reproduction\textsuperscript{8-11}. Identifying the urgent need for increasing births, in view of declining birth rates, increasing numbers of aging and retired, and the predicted insolvency of social security Connolly et al., quantified the fiscal value of assisted reproduction for several countries\textsuperscript{8-11}. Using a similar framework the fiscal value of eliminating rotavirus infection in Egypt was quantified\textsuperscript{12}.

The proposed framework is also relevant for adult working-aged populations. Demographic projections suggest that the composition of European populations will change in the next few decades. Logically, a change in the population pyramid is expected to add budget pressures to the scarce governmental budgets. Despite the widespread belief that ageing leads to the escalation of cost a growing body of literature has shown that ageing per se is not the key cost driver\textsuperscript{13}. Evidence suggests that proximity to death is a key cost driver per person. Moreover, these studies suggest that the cost of dying declines with age and is higher for those who die prematurely. Furthermore, longevity is thought to result in lower average costs of dying whilst health care utilization rates do not increase continuously with age; rather they peak at around 80–85 years and then start to fall\textsuperscript{13}. In the light of this evidence an intergenerational tool for assessing health care interventions may be useful to policy-makers because it provides with quantification of the intertemporal relationship between health care decisions and healthy ageing.

**Decision making and economic evaluations**

Economic evaluations aim at informing decision making. Conventional economic evaluations address the issue of efficient use of health care resources mainly from the perspective of the health service. In more seldom cases the broader societal impact of diseases is assessed. According to Brouwer and Koopmanschap\textsuperscript{14} (2000) the results of economic evaluations should be pragmatically considered as an imperfect aid to decisions which aims at informing decision making by being factored into a multi-criteria decision making process rather than ‘prescribing’ to the budget holder an optimal allocation of resources.

In 2009 the World Health Organisation (WHO) acknowledged that injury and illness can impact government fiscal accounts both in terms of lost tax revenue and increased transfers costs\textsuperscript{15}. The implications of this report suggest that preventing illness would likely have a positive impact for government as more
people would be working and paying taxes. Moreover, a report commissioned by the UK government, describing the impact of ill health in working aged adults, suggested 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. Hence, economic assessments focusing solely on the health service cost may underestimate the economic impact of disease to governments. The proposed, in this Thesis, framework may capture a considerable proportion of the dismissed costs of diseases.

The framework described here may constitute a useful tool for evaluating the long-term intergenerational fiscal consequences of policy decisions. This framework has similarities with the traditional CBA and the broader economic benefits assessments. The hypothesis of this framework is that prevalence of diseases in the current and future generations that result in mortality and productivity losses, through morbidity and indirect consequences may be critical determinants of long-term public finance sustainability. In developing countries, health care investments may increase economic growth and therefore the income base which governments can tax. In turn, increased government revenues may result in more public investments which may trigger fiscal multiplier’s effects and improve development. In developed countries, maintaining ageing populations healthy will contribute to the sustainability of social and health protection systems.

Notwithstanding the economic notion of efficiency given the scarcity of resources, policy-makers increasingly face short-term budget constraints. In a CBA, social well-being will be maximized if interventions are ranked in decreasing order of cost: benefit-ratios and the interventions with the highest ratios would be implemented until the budget is exhausted. A similar decision making process could be followed from a fiscal or government perspective. Broadening the benefits that are taken into account in a CBA will make it more likely that health interventions with wider benefits and/or externalities will be selected for implementation under such a decision rule.

Making decision on the basis of CBA, regardless of the analytical perspective, is very often controversial especially when CBA is seen as a mechanism of monetarisation of health outcomes. In a review of the shortcomings of CBA as a decision making tool, ethical methodological and political caveats were identified. Methodological shortcomings mainly refer to the way that CBAs and other economic evaluations deal with uncertain parameters and risk. In the past few decades though, several stochastic methods have been developed which may eliminate the effects of uncertainty.
More importantly, ethical considerations arise when CBA is used in real-life. Ethical considerations stem mainly from the fact that CBA implicitly weights-up human life. Moreover, CBA may make inter-generational assessments and may omit equity considerations and favour efficiency. To the contrary, the advocates of CBA in healthcare view it as a means of weighting risks, costs and benefits. This weighting is deemed by economists as an inherent decision process that transcends every aspect of human economic behaviour. From an economic theory standpoint, attaining efficiency is the cornerstone of economic behaviour.

Ideally, an economic analysis should be able to capture both economical and ethical and equity considerations. The trade-off between equity and efficiency and the bioethics of economic evaluations and CBA are beyond the scope of this Thesis. Herein, we present the case in favour of quantifying the broader consequences of diseases and therefore, the broader economic benefits of therapeutic and preventive interventions. It is advocated that the economic theory provides with a plethora of macro and microeconomic methods for assessing the burden of disease and the costs and benefits of health interventions. A government perspective quantitative analytic framework, or in another words a fiscal approach to conducting a CBA is presented. This framework may prove useful and inform the allocation of scarce governmental budgets within the health care setting and at a wider, cross-sectorial level.

Developing and implementing novel methods which factor in a variety of economic considerations is important as current economic evaluations may underestimate, in many cases, the true benefits of health interventions. Novel economic evaluations should have a broader scope than conventional cost-effectiveness analyses and integrate several different perspectives including that of the government which is, in a considerable number of countries, the key payer of health care services. Integrating these evaluations into a multi-criteria decision analysis is a systematic way of counting costs and benefits for a variety of perspectives and may lead to efficient and equitable allocation decisions of scarce resources.

References
SUMMARY

In the literature of economics, “good health” has been found to be linked with economic growth. Health is an important component of human capital. “Good health” results in higher productivity, educational attainment, employment rates and income. Historically, economic growth has allowed public investments in health care infrastructure that, in turn, have led to the improvement of health status. Economic growth and demographic changes have also resulted in escalating health care costs which add pressures to public finances. Given the scarcity of resources, cost pressures mandate rationalization and attainment of economic efficiency.

Economic evaluations in health care have been a valuable tool for identifying efficient allocations of resources and have informed resource allocation decision making. Conventional economic evaluations mainly address the issue of health care service budget efficiency and they seldom quantify wider consequences. The latter include a variety of externalities, the impact of diseases on cognition and school performance as well as behavioural effects that may alter economic decisions. Approaching economic evaluations in health care from a broad perspective that accounts for a considerable proportion of the broader health benefits and externalities, requires a new conceptualization and new methods for the quantification of benefits.

In Part I of this Thesis a quantitative analytic methodological framework for assessing the government perspective or fiscal impact of health conditions and the fiscal benefits of therapeutic interventions and immunizations, is presented. Part II of this Thesis applies the method to paediatric, adolescent and adult vaccinations. Part III aims to quantify the broader benefits of treating ADHD in Germany.

Traditional approaches for evaluating health programs focus on health service and societal perspectives and may fail to consider broader impacts on productivity and future government tax revenue tied to productive labour output. In Part I a methodological framework for assessing the impact of health conditions on government tax revenue is presented and tested in paediatric conditions which may impact educational attainment. The framework links differences in educational attainment to education specific wages. It combines methods from human capital economics, health economics, cohort epidemiological modelling and generational accounting. This framework integrates program analysis with fiscal accounting to estimate how investments in health care influence future government tax
revenue and thus, it is relevant to tax-financed health systems concerned about their sustainability. The presented framework may inform policy analysis with respect to resource allocation and funding and provides a tool for cross-sectorial comparisons.

The government perspective fiscal framework described in Part I was implemented to show how governments may benefit from investments in immunisation as a supplementary approach to conventional cost-effectiveness approaches. The fiscal impact of changes in morbidity and mortality attributed to rotavirus immunisation was quantified in Ghana and Vietnam. The research derived the impact of rotavirus morbidity and mortality on lifetime productive capacity and related tax transfers, and the demand for government transfers in relation to education and health care in immunized and non-immunized cohorts.

The discounted age-specific net tax revenue was derived by deducting transfers from gross taxes and discounting for time preference. In Ghana, taking into account immunisation costs, tax and transfers, the estimated net discounted tax for the immunized cohort was estimated to generate $2.6 billion in net taxes up to age 65. In Vietnam, the net revenue attributed to the immunised cohort reached $55.17 billion suggesting an incremental benefit of approximately $29 million.

An application of the framework to HPV adolescent immunization was subsequently produced. HPV infections are known to cause a substantial burden in females and males as they associate with several genital cancers and a subset of head and neck cancers as well as with genital warts. The research estimated the fiscal consequences associated with HPV immunization in males and females. Moreover, the research produced a CBA of investing in universal immunization in Germany.

To estimate the economic benefits attributed to immunization-related changes in morbidity and mortality, direct and indirect tax rates were linked to differences in age and gender specific earnings. Over the lifetime of the combined male/female cohorts, the analysis demonstrated that universal immunization against HPV yields a benefit-cost ratio greater than 1 in terms of additional gross tax revenues for the German government. Moreover, universal HPV immunization may result in positive incremental net tax (i.e. tax revenue-transfers) for the German government.

The last application of the method in infectious diseases assessed the costs and benefits associated with immunizing susceptible adult populations through
population-based immunization programs against diphtheria, tetanus, seasonal influenza, pneumococcal diseases, pertussis and herpes zoster.

The research estimated the benefits linked to governmental investments in immunization in the short and long-term. This study employed a "government perspective" analytic framework to estimate the governmental return on investment for immunizing adults in the Netherlands. Immunization was linked to a discounted gross tax revenue gain of €537 million over the remaining lifetime of a single birth cohort. Based on the investment costs of vaccinating those aged 50, immunization yielded a considerably favourable benefit-cost ratio of 4.02.

In Part III of this Thesis, we applied the proposed framework in the chronic paediatric condition of ADHD. Two studies were conducted based on a well-established causal relationship between educational attainment and earnings. The main hypothesis of these studies was that health care technologies aiming at reducing the effect of ADHD on school achievement may have a considerable and quantifiable value for the governments.

In the first study, evidence from observational studies evaluating the educational attainment of individuals with and without ADHD, the age specific and education specific lifetime earnings and taxes were projected and compared. The medical costs of ADHD treatment were also quantified. Moreover, based on evidence regarding the resource intense health-seeking behavioural patterns of individuals with ADHD the longer-term health care costs were projected. The first study assessed and confirmed using the lifetime net discounted tax the fiscal sustainability of treating ADHD individuals in Germany. The second study conducted a societal CBA for the theoretical benefits of treatments.

The first study showed that investments in ADHD interventions allowing more children to achieve their educational potential may offer fiscal benefits generating a positive rate of return. The lifetime net tax revenue for a non-ADHD individual was approximately €80,000 higher compared to an untreated ADHD individual. The fiscal burden of untreated ADHD, based on a cohort of n=31,844 born in 2010, was estimated at €2.5 billion in net tax revenue losses compared with an equally-sized non-ADHD cohort. ADHD interventions providing a small improvement in educational attainment resulted in fiscal benefits from increases in lifetime tax gains. The projected rate of return suggests that for each Euro spent on a new ADHD intervention the government and social insurance system may gain €1.39 in lifetime discounted net tax revenue and €3.02 in discounted gross tax revenue.
The second study collated observational ADHD evidence with demographic and human capital economics methods to quantify ADHD's impact on educational attainment and long-term labour outcome in Germany. Moreover, the theoretical benefits deriving from effective interventions targeting ADHD were quantified. It was estimated that the average per capita lifetime earning loss associated with ADHD was €92,000 suggesting a societal loss of €2.93 billion from a single cohort (n = 31,864). The CBA suggested that reasonably effective interventions may justify considerable investment in ADHD targeted intervention.

Originating from the observed gap between micro and macro estimates attributed to health and the subsequent challenges this gap presents to our understanding of health-related productivity changes and consequently economic benefits, a critique of the existing methodologies was conducted. Subsequently, it is proposed that there is a transitional domain that links the microeconomic and macroeconomic improvement attributed to health status changes. Currently available economic evaluation methods typically omit these consequences however; they may be adjusted to integrate these transitional consequences.

Notwithstanding the caveats and practical challenges of conducting a broader economic analysis, it is suggested that broadening the benefits that are taken into account in an economic evaluation, will make it more likely that health interventions with wider benefits and/or externalities will be selected for implementation.
SAMENVATTING

In de economische literatuur wordt een “goede gezondheid” veelal gelinkt met economische groei. Welzijn is een belangrijk onderdeel van het menselijk kapitaal. “Gezondheid” resulteert in een hogere productiviteit, een hoger opleidingsniveau, hogere werkgelegenheid en een hoger inkomen. Historisch gezien heeft economische groei de ruimte gegeven aan publieke investeringen in de infrastructuur van de gezondheidszorg. Die op hun beurt, voor verbeteringen hebben gezorgd van het maatschappelijk welzijnspeil. Economische groei en demografische veranderingen zijn uitgelopen in een zeer sterke groei in de kosten van de gezondheidszorg, welke druk leggen op de publieke financiering. Gezien de schaarste van de middelen vereist de kostendruk een verstandelijke benadering en economische krachtigheid.

Economische schattingen zijn een waardevol instrument gebleken in de gezondheidszorg voor het identificeren en het informeren bij de besluitvorming van het efficiënt toewijzen van middelen. Conventionele economische gezondheidsvaluaties richten zich voornamelijk op het rendement van de gezondheidszorg-service-begroting en richten zich zelden op de bredere gevolgen. Het laatste betreft een variatie aan externe, de impact van ziektes op kennis en prestaties op school en ook gedragseffecten die economische beslissingen kunnen veranderen. Het benaderen van economische evaluaties in de gezondheidszorg in een breed perspectief, welke rekening houdt met een aanzienlijk deel van de bredere voordelen voor welzijn en externe, vereist een nieuwe beeldvorming en nieuwe methoden voor de meting van de voordelen.

In Part I van dit proefschrift wordt een kwantitatief analytisch methodologisch kader voor het beoordelen van het perspectief van de fiscale invloed van gezondheidsproblemen en de fiscale voordelen van preventieve en therapeutische ingrepen (interventies) en immunisaties gepresenteerd. Part II van dit proefschrift betreft de methode op pediatrische, jongeren en volwassenen immunisering. Part III richt zich op het meten van de bredere voordelen van het behandelen van ADHD in Duitsland.

Traditionele benaderingen voor het evalueren van welzijnsprogramma’s leggen hun focus op gezondheidszorg en maatschappelijke perspectieven. Daarbij kunnen ze falen in het rekening houden met de invloed op productiviteit en toekomstige belastinginkomsten in verhouding tot arbeidsproductiviteit. In Part I wordt een kwantitatief analytisch methodologisch kader voor het beoordelen van het effect van gezondheidsproblemen op belastinginkomsten gepresenteerd en getest in pediatrische condities welke impact kunnen heb-
ben op het opleidingsniveau. Het kader verbindt verschillen in opleidings-
niveau met onderwijs specifieke lonen. Het combineert methoden uit human
capital economics, health economics, cohort epidemiological modelling en
generational accounting. Dit kader integreert programma-analyse met fiscale
boekhouding om te kunnen bepalen hoe investeringen in de gezondheids-
zorg toekomstige belastinginkomsten kunnen beïnvloeden en daarom, het
is relevant voor gezondheidszorg systemen welke gefinancierd worden op
basis van belastinggeld, dat deze zorg dragen voor hun duurzaamheid. Het
gepresenteerde kader kan beleidsanalyse informeren met respect voor de
toezijding van middelen en financiering en zorgt voor een instrument voor
cross-sectorale vergelijkingen.

Het overheids gerichte fiscale begrotingskader uit Part I is geïmplementeerd
om te laten zien hoe overheden voordeel kunnen hebben van investeringen
in immunisering als een aanvullende benadering tot een conventionele kos-
ten-effectieve aanpak. Het fiscale effect bij veranderingen van ziekte- en sterf-
tecijfers toegeschreven aan rotavirus immunisering, is aangetoond in Ghana
en Vietnam. Het onderzoek heeft het effect afgeleid van rotavirus ziekte- en
sterftecijfers op levenslange productiecapaciteit en gerelateerde belasting over-
drachten en de vraag om overheids overdrachten, in relatie tot educatie en ge-
zondheidszorg in geïmmuniseerde en niet-geïmmuniseerde groepen.

De gereduceerde leeftijd-specifieke netto belastinginkomsten zijn afgeleid
door overdrachten van bruto belastingoverdrachten en discontering af te
trekken in een tijdsvoorkeur. In Ghana, rekening houdend met immunisering
costen, belasting en overdrachten, is de geschatte netto gereduceerde belas-
tingen voor de gevaccineerde groepen $2.6 miljard aan netto belastinginkom-
en, tot de leeftijd van 65. In Vietnam, de netto inkomsten toegeschreven aan
de gevaccineerde groepen bedraagt $55.17 miljard, daarmee een stapsgewijs
voordeel suggererend van ongeveer $29 miljoen.

Een toepassing van het kader HPV volwassen immunisering is eveneens ont-
wikkeld. HPV infecties staan er om bekend een zware last te zijn voor vrou-
wen en mannen omdat ze geassocieerd worden met genitale kanker en een
subgroep van hoofd- en nekkanker en ook genitale wratten. Het onderzoek
verwachtte fiscale consequenties in verband met HPV immuniseaties bij man-
nen en vrouwen. Het onderzoek geeft bovendien een kosten-baten analyse
van investeringen in universele immunisering in Duitsland.

Om de economische voordelen, toegeschreven aan immunisering gerelat-
eerde veranderingen in ziekte- en sterftecijfers, in te kunnen schatten, zijn
directe en indirecte belastingen tarieven gelinkt aan verschillen in leeftijd- en
Samenvatting

gender specifieke inkomsten. Gedurende de levensloop van de gecombineerde mannen/vrouwen groepen, heeft de analyse laten zien dat universele HPV vaccinatie een baten/kosten ratio groter dan 1 oplevert, op het gebied van additionele bruto belastinginkomsten voor de Duitse overheid. Bovendien, universele HPV immunisering kan resulteren in positieve stapsgewijze neto belastinginkomsten (i.e. belastinginkomsten overdrachten) voor de Duitse overheid.

De laatste toepassing van de methode bij infectie ziektes heeft de kosten en baten geassocieerd met immunisering van vatbare volwassen populaties onderzocht doormiddel van bevolkingsgebaseerde immunisatie programma’s tegen difterie, tetanus, jaarlijkse griep, pneumokokkeninfeccties, kinkhoest en herpes zoster.

Het onderzoek schat de voordelen gelinkt met overheidsinvesteringen in immunisering op korte en lange termijn. Deze studie heeft gebruik gemaakt van een “overheids perspectief” analytisch kader om de overheids teruggave bij investeringen van het immuniseren van volwassenen in Nederland. Immunisering is gelinkt aan een gereduceerde bruto belastingwinst van €537 miljoen voor de resterende levensloop van een enkele geboorte groep. Op basis van de investeringskosten van het vaccineren van mensen van 50 jaar, heeft immunisering een aanzienlijk gunstiger baten/kosten ratio van 4.02 opgeleverd.

In Part III van dit proefschrift hebben we het voorgestelde kader toegepast bij de chronische pediatrische aandoening ADHD. Twee studies zijn verricht, gebaseerd op een reeds bevestigd causaal verband tussen opleidingsniveau en inkomen. De hoofdhypothese van deze studies was dat gezondheidszorg technologieën die zich richten op het verminderen van het effect van ADHD op schoolprestaties een aanzienlijk en meetbare waarde heeft voor overheden.

In de eerste studie zijn bewijzen uit observationele studies, welke het opleidingsniveau van individuen met en zonder ADHD, de leeftijd- en opleidingspecifieke levenslange belastbare inkomsten evalueren, geprojecteerd en vergeleken. De medische kosten van ADHD behandelingen zijn ook becijferd. Bovendien, gebaseerd op bewijzen aangaande intense welzijnsbevorderende gedragspatronen van individuen met ADHD, zijn de lange termijn gezondheidskosten geprojecteerd. De eerste studie, gebruik makend van de levenslange neto gereduceerde belastingen, toetst en bevestigt de fiscale duurzaamheid van de behandeling van ADHD individuen in Duitsland. De tweede studie heeft een maatschappelijke kosten/batenanalyse voor de theoretische behandelvoordelen uitgevoerd.
De eerste studie laat zien dat investeringen in ADHD interventies die meer kinderen hun opleidingspotentieel laat bereiken, fiscale voordelen kunnen bieden welke een positief rendement genereren. De levenslange netto belastinginkomsten voor een non-ADHD individu is ongeveer €80,000 hoger in vergelijking tot een onbehandeld ADHD individu. De fiscale last van een onbehandeld ADHD individu, gebaseerd op een groep van $n=31,844$ geboren in 2010, is geschat op €2.5 miljard in netto belastinginkomstverliezen, in vergelijking tot een vergelijkbare non-ADHD groep. ADHD interventies bieden een kleine verbetering in opleidingsniveau, welke resulteren in fiscale voor- delen door levenslange belasting winsten. Het geprojecteerde rendement suggereert dat voor elke Euro besteed aan een nieuwe ADHD interventie, de overheid en het sociale verzekeringssysteem €1.39 winst ontvangt aan levenslange netto gereduceerde belastinginkomsten en €3.02 in gereduceerde brutobelastinginkomsten.

De tweede studie bundelt observationeel ADHD bewijs met demografische en human capital economics methoden, om ADHD invloed op opleidingsniveau en lange termijn arbeidsuitkomst in Duitsland af te bakenen. Bovendien worden de theoretische voordelen, afgeleid van effectieve interventies gericht op ADHD, gekwantificeerd. Bepaald is dat het gemiddelde inkomstenverlies geassocieerd met ADHD per hoofd van de bevolking €92,000 bedraagt, wat een maatschappelijk verlies van €2.93 miljard suggereert van een enkele groep ($n=31,864$). De kosten/baten analyse suggereert dat redelijkwijzi effectieve interventie, aanzienlijke investeringen gericht op de interventie van ADHD rechtvaardigen.

Voortkomend uit de waargenomen kloof tussen micro- en macroschattingen, toegeschreven aan welzijn en de daaropvolgende uitdagingen die deze kloof biedt aan ons begrip van welzijn-gerelateerde productiviteitsveranderingen en bijkomende economische voordelen, is er kritiek op de bestaande methodieken verricht. Aanvullend is voorgesteld dat er een overgangsdomein is, welke de micro- en macro-economische verbetering toegeschreven aan welzijnsveranderingen verbindt. De tegenwoordig beschikbare economische evaluatie methoden laten doorgaans deze gevolgen achterwege, echter; zij kunnen worden aangepast om deze overgangsgevolgen te integreren.

Ondanks de kanttekeningen en de praktische uitdagingen voor het uitvoe- ren van een bredere economische analyse, wordt gesuggereerd dat het ver- ruiming van de voordelen, waar rekening mee wordt gehouden in een econ- omische evaluatie, het waarschijnlijker maakt dat welzijnsmaatregelen met bredere voordelen en/of externe effecten, de voorkeur hebben.
LIST OF PUBLICATIONS BY NIKOLAOS KOTSOPoulos

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This thesis is published within the Research Institute SHARE (Science in Healthy Ageing and healthcaRE) of the University Medical Center Groningen / University of Groningen.

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In the pharmaceutical industry Nikos has held various roles. In his last industry role he was responsible for market access, pricing and reimbursement at GlaxoSmithKline in Greece. Nikos has also worked at the GlaxoSmithKline headquarters in the UK. He has developed global health outcomes strategies for several therapeutics and vaccines. Moreover, he has designed and developed health economic models and willingness to pay (WTP) studies for several infectious diseases. Furthermore, he has been involved in the implementation of patient reported outcome (PRO) studies and multinational Phase II and III clinical trials for Sepsis. As a consultant, Nikos has significant experience in the development of health economic models, in qualitative and quantitative pricing research, in policy research and analysis. He has worked on a broad range of therapeutic areas and pharmaceutical technologies. Moreover, he has extensive experience in the economic analysis of vaccines.

Nikos holds a degree in economics from the University of Athens, Greece and a master’s degree in health economics from The City University, London (UK). In 2012 Nikos started his research to support his doctoral Thesis at the University of Groningen, The Netherlands with Professor Maarten Postma. Nikos’ research focused on methods for assessing the broader economic consequences of therapies and preventive strategies. In 2012 a grant from the WHO was received to research new methods for quantifying the broader economic impact of vaccines. In the past three years, Nikos conducted research on the economics of paediatric and adult vaccinations and on ADHD. In 2013 Nikos received an award for his research in the broader economic benefits of HPV vaccination, presented at the Annual European ISPOR conference in Dublin, Ireland.

Since 2011 Nikos works with Global Market Access Solutions, St-Prex, Switzerland as a health economist.