On the economics of malaria suppression

Emiel Sanders

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Supervisor:
Yvonne Adema

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Erasmus University Rotterdam

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Abstract

Using WHO-CHOICE methodology, we found several established malaria interventions and the introduction of a vaccine and combinations thereof to be highly cost-effective (8-127 int$/DALY) in sub-Saharan Africa, where the malaria disease burden is highest. By means of Solow modeling, we estimate that continuous malaria suppression increases per capita income up to 50% compared to a non-intervention scenario after a time span of 65 years.

1. Introduction

Approximately 1 million people die yearly of the consequences of malaria and more than 3 billion individuals, spread over 107 countries in which malaria is endemic, are at risk of contracting the parasitic disease (WHO (2005), Breman *et al.* (2004)). The total estimated incidence amounted to 402 million cases in 2004 (Korenromp, 2004). According to the WHO (2002), malaria is the eighth largest contributor to the global burden of disease and the second largest to the disease burden in Africa in terms of disability adjusted life years (DALY's). In this continent 60% of total malaria morbidity and over 90% of malaria related death occur. Malaria *P. falciparum*, one of the four species that cause malarial infections in humans, is largely responsible for this burden. 82% of total malaria related death comes about before the age of 5 and 5-8% of child mortality in Africa is ascribed to malaria (Bryce *et al.*, 2005). As effective and affordable malaria control interventions exist, this human tragedy and the large economic cost (Chima *et al.*, 2003) can be mitigated. Scaling up existing interventions and the introduction of new ones would reduce this toll and also contributes to achieving the Millennium development goals (MDG's), especially numbers 4 and 6, i.e. the reduction of child mortality and the combat against malaria and other diseases[1]. To do so, cost-effectiveness analysis is a tool to prioritize the gains and the costs of interventions. We conduct such a study and estimate the efficiency of existing methods and of the introduction of a malaria vaccine. In addition, we assess their impact on macroeconomic growth. We estimate the direct and indirect effects of malaria interventions on economic wellbeing.

The outline is as follows. We start our study with the review of literature that is followed by a description of the methods used in our analysis. The results are presented afterwards. At the end the discussion and the conclusion are found.

2. Review of literature

Below a short review of the literature on cost-effectiveness and macroeconomic studies related to malaria are shown. At the end the value added of this study is described.

[1] http://www.un.org/millenniumgoals/

2.1 Cost-effectiveness studies

Many cost-effectiveness studies follow the methodology set by the WHO-CHOICE project, an initiative installed by the WHO in 1998 to assist policy makers in their decisions on interventions and programmes that maximize health gains, in terms of disability adjusted life year (DALY), given budget constraints. An overview of several control interventions is found on the WHO-CHOICE website (http://www.who.int/choice/en/) and in a special issue of the *British Medical Journal*, November 2005. However, this methodology has not always been the norm. Considering malaria, Goodman *et al.* (2000) put forward an overview in which 15 other cost-effectiveness studies that use different methodologies are displayed. These studies express effectiveness either in terms of morbidity or mortality. Those analyses that use a combined measurement of effectiveness mortality and morbidity captured by DALY and follow WHO-CHOICE's guidelines are outnumbered.

Malaria interventions are classified in two groups. Those that reduce malaria incidence are considered to be of a preventative nature and those that negatively affect malaria mortality are the so-called curative interventions.

Using data on the burden of malaria (Najera *et al.*, 1996 and Murray *et al.,* 1996) and the methodology as used in the Global Burden of Disease (Murray *et al.*, 1996), Goodman, Coleman and Mills (2000) find malaria control interventions to be highly cost-effective. For insecticide treated bed nets (ITN) and indoor residual spraying (IRS) they find respective costs (1995 US$) per DALY to range between 19-85 and 16-29, respectively. Intermittent preventative treatment (IPT) for pregnant women is estimated between 4-29 US$ per DALY. Curative interventions were also analyzed and considered highly cost-effective. Chemoprophylaxis for children, and improvements in case management, such as improving compliance and availability of drugs, were estimated at a respective cost-effectiveness of 3-12 and 1-8 US$ per DALY. Although these results are encouraging several remarks have to be made. Firstly, the analysis is conducted for sub-Saharan Africa as a whole. Differences in costing structures or malaria epidemiology are accounted for in a rough manner. Secondly, it is unclear to what extent effectiveness of the malaria interventions, obtained from the literature and control-trials, is discounted for factors that obstruct them. Lastly, only individual interventions are compared. Intervention packages are not scrutinized.

By means of a 10 year implementation program, Morel *et al.* (2005) estimated the cost-effectiveness of seven malaria interventions and combination thereof for different coverage levels in two sub-Saharan African regions in terms of 2000 US $ per DALY. Epidemiological data came from the 2002 Global burden of disease (GBD) estimates. Data on efficacy and costs of the interventions were obtained from experts and literature. Morel *et al.* (2005) calculated the net effectiveness of the interventions given a baseline efficacy that is corrected for patients' behaviour (adherence to regimen), pharmacokinetics (success of intervention when regimen is not followed) and resistance to drugs (biogenetics), regardless of geography. Total costs are estimated by means of the CostIt model (Baltussen *et al.*, 2003) and cover unit costs, distribution costs, media costs and labour costs. The evaluated interventions are case management with chloroquine (CQ), sulfadoxine-pyrimethamine (SP), non-artemisinin based combination therapy (non-ACT) and artemisinin based combination (ACT). Also insecticide treated nets (ITN), indoor residual spraying (IRS), intermittent presumptive treatment (IPT) during pregnancy were evaluated. The authors found all interventions except that of IPT to be highly cost-effective (9-35 int$/DALY) at a 80% coverage level, however most rewarding are high-coverage levels of ACT.

In their cost-effectiveness study, Breman *et al.* (2006) examine the following interventions: ITN, IRS, IPT during pregnancy and a change of first line drugs. They focus on the area of sub-Saharan Africa where malaria is highly endemic but stable. Epidemiological data are obtained from Breman *et al.* (2004) and WHO (2002). Data on costs and effects of interventions are obtained from different sources. The methods used to perform the cost-effectiveness analysis are unclear. Again all interventions evaluated (ITN, IRS and IPT during pregnancy) are considered to be highly cost-effective as they range between 11-24 mean cost (in US$ 2001) per DALY.

2.2 Macroeconomic studies

Health has in general a positive and significant effect on economic growth. In terms of mortality, Bloom *et al.* (2004) show in their overview that in 12 out of 13 studies health has a positive and significant impact on economic growth. All studies use cross-country regression analysis and employ other explanatory variables to estimate the economic impact of health. In terms of morbidity, Mills and Shillcutt (2004) demonstrate that this dimension of health has a major impact on economic activity

through its adverse effects on productivity, investment and education. When considering poor health states, among that malaria, Cole and Neumayer (2006) argue that morbidity plays a more important role than mortality in relation to economic development.

Before turning to malaria, we highlight HIV/AIDS as the other communicable disease that has been scrutinized in an macroeconomic context. The literature on the economic modelling of HIV/AIDS can be sub-divided in three groups. The bulk of the literature estimates the macroeconomic cost of HIV/AIDS by means of (augmented) Solow models, using either a one-sector or two-sector neoclassical growth model, specified to individual countries or in a cross-country manner. Among these works are that of Over (1992), Cuddington (1993), Cuddington and Hancock (1992, 1994), MacFarlan and Sgherri (2001) and Haacker (2002a, 2002b). All estimate the endemic to have a negative effect on welfare, be it rather small as the full impact of the epidemic has not yet been recognized at that time of the early writings. Haacker puts forward frameworks for macroeconomic modelling of HIV/AIDS. These models are popular among macroeconomists studying HIV/AIDS as in hardest hit areas data are scarce and of poor quality. Moreover, the Solow model is considered the workhorse model health impacts. The second group of macroeconomists uses CGE-techniques for estimating the welfare impact of HIV/AIDS. Among those is Arndt and Lewis (2001), that estimate the South African economy to slow yearly by 2.6 percentage points over the 1997-2010 simulation period using a no-AIDS and an AIDS scenario. The last group uses different econometric techniques to model the macroeconomic impact of HIV/AIDS. Bloom and Mahal (1997) take into account effects of simultaneity and possible correlations of factors that influence growth to determine the effect of AIDS on economic well-being. Interestingly, their outcome estimates that the epidemic has an insignificant effect on the growth rate of per capita income. A study by Bonnel (2000) estimates that HIV/AIDS reduced economic growth over the 1990-1997 period by 0.7% per year using cross-country regressions in Southern Africa. The slowdown is exacerbated in the presence of malaria by 0.4% per year.

Many microeconomic studies on the impact of malaria on households and firms have been conducted which are nicely summed up by Chima *et al.* (2003). The amount of their macroeconomic counterpart is small. Those that have been performed can be divided in three categories. The first group encompasses those studies (Shephard *et al.*(1991), Ettling *et al.* (1991) and Leigthon *et al.*(1993)) that estimate

the economic burden of malaria on a macroeconomic level by summing up the direct and indirect costs of malaria. The direct costs are the sum of the household and government expenditures on malaria treatment and prevention. The indirect costs are the losses of economic output due to mortality, morbidity and debility. These are proxied by the adult output per day times the estimated productive time lost due to both adult and childhood malaria episodes. These authors estimate a negative impact of malaria on economic development of 0.6% and over of total GDP in several African countries. Goodman *et al.* (2000) argue that the methodology of summing up direct and indirect costs should be used with care as deviations in the base values have strong effects on aggregate values.

Among the second group are the studies of Gallup and Sachs (1998) and McCarthy *et al.* (2000) which estimated the impact of malaria on economic well-being by means of regression analysis similar to the methodology of Barro (1991). Gallup and Sachs (1998) conclude that for the 1965-1990 period, countries with severe malaria had much lower economic growth amounting to 1.3% per year in terms of GDP per capita. In their regression they include several factors likely to influence economic growth. These are initial income levels, initial human capital stock (measured by secondary school enrolment rates and life expectancy at birth), economic policy (measured by trade openness and an index of the quality of public institutions) and geographical variables (measured by an indicator for the geographical tropics and the fraction of the population within 100 km of the coast). In their study malaria is approximated by the malaria index. This is the product of the percentage of malaria endemic land area in 1965 and the percentage of malaria *P. falciparum* cases in 1990. In addition, they conclude that a 10% reduction in the malaria index would have resulted in a 0.3% increase in terms of GDP per capita per annum over the same period.

McCarthy *et al.* (2000) assess the economic impact of malaria in terms of average per capita GDP by using several explanatory variables. These are the investment ratio, primary and secondary school enrolment rates, initial income per capita, openness measured as total trade per total GDP, political freedom, the number of revolutions per year, an index of assassinations and a malaria morbidity variable. The latter is proxied by the incidence of malaria episodes over three five-year periods starting in 1983 complemented by data on sanitation, climate and location, health expenditures, among others. By including these variables the effectiveness of the use

of protective malaria measurements across regions is taken into account. Gallup and Sachs' (1998) malaria variable lacks such a dimension. An average over five years is taken to overcome misrepresentation as malaria incidence varies strongly over time. The authors find a strong and significant negative impact of malaria on economic development, however the impact differs sharply among countries. For the most countries annual per capita growth is reduced by a quarter percent while an average of -0.55% GDP growth is estimated for sub-Saharan countries.

The differences between the findings of Gallup and Sachs (1998) and McCarthy *et al.* (2000) are partly assigned to the different periods of analysis. The former authors analyze the economic impact of malaria for the 1965-1990 period, while the latter consider the 1983-1998 period. Mills and Shillcutt (2004) argue that most progress in reducing the adverse consequences of malaria has been accomplished prior to the timeframe used by McCarthy *et al.* (2000). In addition, the malaria variable used by McCarthy *et al.* takes into account several other explanatory variables which they think nuance the adverse economic effects of malaria. The malaria variable used by Gallup and Sachs is primarily focused on geography and prevalence. Also the use of a different set of control variables may contribute to the different outcomes of both studies.

The third group of macroeconomic studies on malaria encompasses the study of Barlow (1967). In his article Barlow uses a Cobb-Douglas production function with skilled and unskilled labour and capital as input factors to estimate the impact of malaria eradication on long-run GDP per capita in Sri Lanka (Ceylon). Labour is disaggregated into skilled and unskilled labour as it is assumed that malaria is a low income disease mainly because it is avoidable. To estimate this impact, two scenarios on the basis of demographic differentials of eradication and non-eradication are run and compared to each other. It is assumed that eradication has a direct effect on labour inputs through its effects on mortality and fertility and on morbidity and debility. Indirect effects on capital inputs occur through changing public and private saving rates. Barlow estimates that in the short run GDP per capita is positively affected up to 10% due to malaria eradication. In the long run, however, population growth diminishes this gain. Several authors questioned Barlow's study. With respect to our study, Frederiksen (1966), Borts (1967) and Brown (1986) are most important. They argue that Barlow failed to take into account the economic effect of malaria

eradication through increased agricultural productivity in areas that were previously impassable due to malaria endemicity.

In this study a similar model to that of Barlow (1967) is used, but it differs in several ways. Firstly, we do not disaggregate the labour population into skilled and non-skilled as according to Gallup and Sachs (1998) malaria does not differentiate between rich and poor people. Secondly, we take into account the indirect effects of (partial) malaria eradication through its effect on TFP. The elasticity of TFP to malaria incidence estimated by Cole and Neumayer (2006) is used for this purpose. By including the indirect effects, we take into account the argument made by Gallup and Sachs (1998) who state that these effects are substantial. Thirdly, contrary to Barlow who argues the malaria intervention costs are insignificant, we do include them to estimate the net effects of the proposed malaria interventions on economic well-being. Lastly, unlike Barlow's model that disaggregates savings into private, government and foreign savings, we consider the total savings rate.

Criticism made by Frederiksen (1966) and others on the positive effects of malaria eradication on land use is acknowledged in the literature study by Goodman *et al.* (2000). However, the relationship has not been academically validated and therefore not been quantified. Only one study by Wang'ombe and Mwabu (1993) is present that examines the relationship between malaria and land use. They find at the household level insignificant effects of malaria on the cassava production and cultivated land area, which they attribute to the coping strategies when households are affected by malaria. Goodman *et al.* (2000) point to methodological weaknesses in the Wang'ombe *et al.* (1993) study. They state that the impact of malaria on long-term land exploitation cannot be derived from household studies. So, the impact of malaria on land use is acknowledged by several authors, however the negative relationship has not been proved. Therefore, we abstain from including land as a distinctive production factor of GDP and focus solely on TFP, total labour and capital stock. Nevertheless, Frederiksen *et al.* point to an anomaly which has also been mentioned by Gallup and Sachs (1998). Due to malaria, investments in profitable sectors such as tourism (and agriculture) are abstained from. Eradication, therefore, would increase the return on investment in these sectors and attract investors. The Solow model does not allow for these behavioural changes. A change in the savings rate could circumvent this stringency of the Solow model, however we prefer maintaining a constant savings rate for two reasons. Firstly, few studies on the savings behaviour in

relation to malaria, both on a micro and a macro level, exist to fully capture this conduct (Chima *et al.*,2003). Secondly, based on Modigliani's life cycle theory, adjusting household saving rates upward would pose intergenerational consumption problems. We think the current generation is unwilling to increase savings as this sacrifice in lower current consumption is too large. Moreover, when increasing government savings it is likely that the government is unable to balance its budget as the sum of total government consumption and investments increase total taxes. By adjusting TFP (and therefore GDP) for malaria incidence, we sidestep the inability of the Solow model to anticipate on higher returns on investment when the malaria burden is brought down.

With our study we contribute to the overall literature in several ways. Firstly, the estimation of the cost-effectiveness of a malaria vaccine is a novelty. Secondly, the value added is to be found in introducing a model which directly links the effects of health interventions on economic growth through the stock of labour. Thirdly, to our knowledge, this study is the first in estimating the economic impact of malaria interventions for Africa on a macroeconomic level and in assessing which of these are most efficient.[2] Lastly, our model enables us to quantify the direct and indirect effects of malaria interventions separately in contrast to the studies using a Barro (1991) regression methodology.

3. Methods

Below the methodologies of the cost-effectiveness analysis of malaria interventions as well as the macroeconomic impact study are described. Both studies cover 4 regions located in sub-Saharan Africa (as defined by the MNP-institute) in which *P. falciparum* is highly endemic. Table 1 gives a list of countries by region.

[2] On a macroeconomic level Abegunde *et al.* (2007) estimated the cost of chronic diseases by means of a Solow model. Their methodology is different from ours as they only include the direct effects of reducing the prevalence of chronic diseases. Further studies on health interventions on macroeconomic level are to our knowledge non-existent.

Region 1	**Region 2**
Western Africa	*Central Africa*
Cape Verde	Cameroon
Chad	Central African Republic
Benin	Congo
Gambia	Congo, the Democratic Republic of the
Ghana	Equatorial Guinea
Guinea	Gabon
Côte d'Ivoire	
Liberia	
Mali	
Mauritania	
Niger	
Nigeria	
Guinea-Bissau	
Saint Helena	
Sao Tome and Principe	
Senegal	
Sierra Leone	
Togo	
Burkina Faso	
Region 3	**Region 4**
Eastern Africa	*Southern Africa*
Burundi	Angola
Comoros	Botswana
Ethiopia	Lesotho
Eritrea	Malawi
Djibouti	Mozambique
Kenya	Namibia
Madagascar	Zimbabwe
Mauritius	Swaziland
Réunion	Tanzania, United Republic Zambia
Rwanda	
Seychelles	
Somalia	
Sudan	
Uganda	

Table 1 Countries by region.

We focus on these regions due to its high malaria mortality (over 90% of world fatalities (WHO mortality database, 2005)) and malaria prevalence (61% of world total, (Korenromp, 2005)). C++ implementation in M programming language (http://www.my-m.eu/) is used to perform the analyses. All monetary values are expressed in international dollars, int$, i.e. US dollars for the year 2000. Data have been converted to region specific values, when necessary by means of a weighted average.

3.1 Cost-effectiveness analysis malaria interventions

We determine the cost-effectiveness of malaria control interventions by estimating their total costs and their influence on population health using a simple demographic model. In doing so, we follow the guidelines as formulated by the WHO-CHOICE project (http://www.who.int/choice/en/), which enables us to comprehensively assess the health impact of the interventions. A gradual approach of this methodology is shown in appendix A, which is derived from Niessen *et al.* (2009).

Demographics and malaria epidemiology

Based on the 2005 population stock across region, sex and 1-year age cohorts (aged between 0-100) obtained from the MNP-institute, we annually simulate population dynamics by means of fertility and mortality rates.

Constant total fertility rates (MNP, 2000) and a constant birth-ratio are used to estimate total birth across region and sex. We consider women of child bearing age (WCBA) to give birth when aged between 15 and 50 years old. The birth-ratio, ratio of newborn boys over girls, is estimated on the basis of the 2005 population stock. Total birth is kept constant during the cost-effectiveness analysis.

Total death across sex, age and region is composed of malaria and non-malaria related death. Total and malaria mortality rates over sex and age (0-1, 1-4, 5-year age cohorts between age 5 and 85 and 85+) are derived from the WHO 2005 mortality database. Background mortality is calculated as the differential of the two rates, which we keep constant over time.

Modelling is such that a time lag of one year is present before total birth enters population dynamics. Death is modelled instantaneously.

The malaria epidemiology is derived from the core demographic model as described above. Malaria prevalence rates are calculated as the product of incidence rates across region, sex and age (0-4, 5-14, 15+), a two-week average per malaria episode and the total population stock that is estimated by the demographic model. Incidence rates are obtained from Korenromp (2005). Malaria related death is calculated by the product of total malaria mortality rates and total population stock. Table 2 shows total population and an estimation of the burden of malaria across regions in 2005.

	Total population	Incidence	Gross incidence rate	Deaths	DALY's*[3]
Region 1	276,011,300	117,264,000	0.42	490,801	15,406,410
Region 2	83,785,560	34,275,940	0.41	154,549	4,555,666
Region 3	225,042,700	46,745,320	0.21	165,437	5,787,988
Region 4	120,388,300	43,949,840	0.37	106,961	3,417,455
Total	705,227,860	242,235,100	0.34	917,748	29,167,519

Table 2 Total population stock and burden of malaria across region, 2005.
* Disability adjusted life years.

Malaria interventions

Few means are available to combat malaria. To simplify our analysis we evaluate the cost-effectiveness of five malaria control interventions and combinations thereof instead of the seven interventions as put forward by Morel *et al.* (2005). We abstain from evaluating several curative methods, which are SP, non-ACT and IPT during pregnancy. However, we evaluate the introduction of a vaccine. So, we focus on three preventative interventions (ITN, IRS and a vaccine) and two curative interventions (case management with CQ and ACT) and combinations thereof. In total we analyze 19 intervention packages. Although SP is more effective than CQ and both have the same cost-basis (Morel *et al.*, 2005), we focus on the latter as it is used in all focus regions for combating severe malaria *P. falciparum* (World malaria report, 2008). We refrain from evaluating SP during pregnancy due its low effectiveness and high cost (Morel *et al.*, 2005). We choose ACT instead of non-ACT because the former is adopted as the first line treatment for severe *P. falciparum* in all focus regions. In addition, non-ACT is less effective than ACT and costs approximately the same as ACT (Morel *et al.*, 2005, World malaria report 2008).

We use the data of Morel *et al.* (2005) on the net effectiveness and the costs of all interventions, excluding the vaccine to determine their cost-effectiveness. Table 3 shows the net effectiveness of the individual malaria control interventions.

Intervention	Reduction in incidence (%)	Reduction in case fatality (%)
Insecticide treated bed nets (ITN)	50	20
Indoor residual spraying (IRS)	50	20
Vaccine	65.9	26.4*
Case management CQ		27
Case management ACT		63

Table 3 Net effectiveness individual malaria interventions.
* same proportional reduction in incidence and case fatality as used for ITN and IRS is applied.

We employ the conclusions of Aponte *et al.* (2007) on the net efficacy of a candidate malaria candidate vaccine, which they tested in a highly endemic area of

[3] The burden of malaria is estimated by means of the WHO-CHOICE methodology by eliminating malaria related morbidity and mortality.

Mozambique. The total costs of the vaccine is composed of two parts, the vaccine and the non-vaccine costs. The former we obtained from expert's opinion and the latter is a conservative approximation of pneumococcal non-vaccine costs estimated by Sinha *et al.* (2007). See appendix B for an overview of the evaluated interventions and their costs.

The effects of these interventions and their combinations on the region specific malaria incidence and mortality rates enable us to estimate the regional burden of disease. By doing so, we adjust regionally for the coverage level of established health care facilities that hamper malaria transmission and the number of malaria fatalities (World malaria report 2005, 2008). Table 4 displays the coverage levels of the selected malaria control interventions.

Intervention	**Region 1**	**Region 2**	**Region 3**	**Region 4**
Insecticide treated bed nets	2.6%	0.9%	3.0%	2.9%
Indoor residual spraying	0.3%	0%	4.4%	8.0%
Vaccine	0%	0%	0%	0%
Case management CQ	38.7%	44.4%	14.2%	36.6%
Case management ACT	5.6%	1.6%	18.8%	41.7%

Table 4 Coverage levels malaria control interventions across region.

In line with the WHO-CHOICE methodology, we assume the interventions to be effective for a period of 10 years after which malaria incidence and mortality rates return to pre-intervention levels. All interventions but the vaccine apply to the 80% of the full population, i.e. we increase coverage levels to 80%. A conservative approach for implementing a malaria vaccination programme is assumed: only newborns are vaccinated. Evaluation is performed 100 years after the intervention programme ends to include all healthy life years gained. We assume that resistance to the curative methodologies does not occur. Model uncertainties are accounted for by means of hazard equations which assume a normal distribution when calculating risks of contracting malaria and dying of the consequences of it.

Health gains are expressed as the average number of disability adjusted life years (DALY's) averted. These are calculated by applying region-specific disability weights for the general population by age and sex (http://www.who.int/choice/demography/health_valuations/en/index.html). When infected with malaria, a universal disability weight of 0.6 is assigned (GBD, 1990). Costs are calculated in yearly averages. Both health gains and costs are discounted

over time by a rate of 1.5% and 4.5%, respectively. Then, the division of costs over health gains gives us the desired cost-effectiveness ratio in terms of int$/DALY.

To determine to what extent the evaluated interventions contribute to the Millennium Development Goals (MDG's) we estimate their impact on under 5 mortality. We do so by taking a conservative approach and analyze the impact of the most cost-effective interventions as we believe policymakers will choose those interventions that are most efficient. Again during 10 years interventions are assumed to be effective after which malaria incidence and mortality return to pre-intervention levels. Once more, only newborns are vaccinated. The other interventions apply to the whole under 5 population. Then, the average proportional difference in malaria mortality summed over sex and under 5 population over 15 years is taken, which will be our impact measurement of the interventions on malaria mortality.

Lastly, we analyze if eradication of malaria mortality is feasible given the effectiveness of the malaria control interventions. We do so by scrutinizing their impact on malaria mortality rates.

3.2 Macroeconomic impact analysis malaria interventions

To determine the macroeconomic impact of the malaria packages as described in appendix B we link the demographics and epidemiology model applied in the cost-effectiveness analysis with the general Solow model for closed economies. We calculate the direct effects of the interventions and complement these results by accounting for the indirect effects of malaria suppression and compare both with a non-intervention scenario. When the labour force is fully covered by the interventions, in 2070, we evaluate the impact on economic well-being in terms of GDP per capita.

Four channels are present through which we project the effects of malaria interventions on economic well-being. Firstly, malaria mitigating policies negatively influence malaria incidence and mortality. Therefore, when intervening, total labour stock expands. By means of our demographics and epidemiology model we project these effects of interventions on total labour stock over time and across regions. Secondly, when infected with malaria one is confronted with a productivity loss. We

account for this loss through the disability weight of malaria. Successful interventions reduce this loss and therefore the labour force becomes more productive. Thus, when effectively intervening in malaria prevalence the labour stock increases in size and strength. These two dimensions are captured by the effective labour variable (discussed below) that is a production factor in the Solow model. Thirdly, if the intervention costs are borne by the economy under consideration, savings are diverted away from investments and total GDP is negatively influenced as capital accumulation is hampered. Through these three channels (size and vigour of the labour force and capital accumulation) economic well-being is directly influenced. Indirectly, malaria tends to affect economic growth through its undesirable effects on total factor productivity (TFP), as pointed upon by Gallup, Sachs and Mellinger (1998) and Cole and Neumayer (2006). Due to malaria endemicity, investments are refrained from and the transmission of ideas and knowledge is hindered through limitations of internal movement. By adjusting for these effects on TFP, we strive to take into account their arguments and estimate the indirect effects of malaria suppression.

3.2.1 Demographics and epidemiology model

We build upon the demographics and epidemiology model as described in the previous section. Total birth is estimated by constant fertility rates, that is the assumption of constant total birth is omitted. We start our analysis from steady state, i.e. the model is calibrated in a way that the malaria and non-malaria population grow at the same constant rate. The interventions are applied for an indefinite period of time, so the WHO-CHOICE methodology is abstained from. Costs are not discounted.

3.2.2 Solow model

Inspired by Solow (1956), Cuddington and Hancock (1994) and Haacker (2002a) estimated the economic impact of HIV/AIDS in Southern Africa using a modified Solow model from which we depart our analysis. We choose this model as it incorporates the desired channels mentioned earlier through which malaria-interventions affect economic well-being.

Using a Cobb-Douglas form, the Harrod-neutral[4] production function for closed economies in discrete time periods is the following:

$$Y_{it} = K_{it}^{\alpha}(A_{it}E_{it})^{1-\alpha} \quad \text{in which } 0 < \alpha < 1, \tag{1}$$

where Y_{it} represents income (GDP) and A_{it} is the total factor productivity variable. K_{it} is the stock of physical capital and E_{it} represents effective labour input. α is the elasticity of output with respect to physical capital which is kept constant over time. Subscripts *i* and *t* denote respectively region and time in years.

In the base-year, 2005, the TFP-variable, A_{i0} is fitted by means of equation (1). Data for GDP, measured in constant 2000 US$, are obtained from the United Nations Statistics division. The MNP-institute provided us with annual data on capital stock, expressed in constant 2000 USD, and elasticities to physical capital. Labour input for the base-year we obtained from our demographics and epidemiology model.

In our model, TFP evolves over time according to:

$$A_{i(t+1)} = (1 + g_i + \gamma(\Psi_{it} - \Psi_{it-1}))A_{it} \tag{2}$$

where γ represents a constant universal elasticity adjusting TFP for malaria incidence, i.e. γ is an estimation of the indirect effects of malaria on economic well-being. To this end, we use the calculations of Cole and Neumayer (2006). The authors argue that poor health negatively affects labour productivity and human capital accumulation and that labour and capital are not allocated efficiently. As data limitations deter exact examination of these linkages, poor health is best modelled when determining its impact on TFP. They estimate the impact of malaria on TFP using a production function composed of physical capital, human capital and total labour stock. As an indicator of malaria, the authors use the one provided by Gallup *et al.* (1999), which is the product of land area subject to malaria and the percentage of malaria *P. falciparum* cases. When estimating the impact of poor health on TFP by

[4] That is, technological progress is exogenous and labour augmenting.

means of a regression, trade openness, share of agricultural value added to GNP and the inflation rate are included as control variables. The analysis is applied to a panel of 6 regions using 5-yearly intervals between 1965-1995. Fixed effects are reported as a Hausman test suggests that country effects are correlated with the explanatory variables and therefore inconsistencies exist. Cole and Neumayer find that a 1% increase in malaria incidence will reduce TFP by 0.58-0.75%. As we believe that the countries used in their study are representative for our analysis, we use their calculations when determining the economic impact of malaria interventions indirectly, using the low impact scenario of 0.58%.

Ψ_{it} represents the proportional reduction in *total* malaria incidence summed over sex and age over time and across region. So, $\Psi_{it} - \Psi_{it-1}$ is the difference in proportional malaria incidence in two consecutive time periods. Our conservative implementation approach for the malaria vaccine program forces us to model the indirect effects of malaria suppression on TFP in this way.

In (2) g_i is the constant non-intervention TFP-growth rate that is estimated on basis of historical data over the period 1990-2005, by means of equations (1) and (2) with $\Psi_{it} - \Psi_{it-1} = 0$. We find TFP growth rates to range between -1.0% (Central Africa) and + 1.1% (Eastern Africa). As pointed upon by Sorensen *et al.* (2005), TFP growth rates have to be positive to reach a plausible steady state level and to accord with empirics in the long run. Therefore, we altered Central Africa's TFP growth rate to ensure all focus regions to experience positive TFP growth. We assigned the lowest TFP-growth rate across regions, i.e. that of region 1.

Next, the physical capital variable, K_{it} , evolves over time according to:

$$K_{i(t+1)} = \tau_i Y_{it} + (1-\delta)K_{it} - \varepsilon_{it}\Omega c_i N_{it}, \qquad (3)$$

where τ_i is the economy's savings rate (MNP, 2004), which is assumed to be constant over time[5] and δ is the constant universal depreciation rate, that is set at 8% (Haacker, 2002a)[6]. The last term of equation (3), $\varepsilon_{it}\Omega N_{it}c_i$, is the cost of malaria interventions that is carried by the economy under consideration and hampers capital accumulation. When omitting this term, one estimates the gross effects of malaria interventions. $c_i N_{it}$ is the product of the constant per capita cost of the intervention package (see appendix B) and total population. Ω is the constant universal fraction of savings that is diverted away from capital accumulation as a result of malaria intervention costs. We assume that two thirds of the total costs of malaria interventions are funded externally (based on the World Health Report 2008). Assuming that a quarter of these grants crowds out other investment projects, a decline of 17% (i.e. 67% * 25%) in savings is experienced. The one third of total malaria cost that is financed by the economy under consideration decreases disposable income, we assume to an extent of 80%. As we consider a closed economy, 20% of the total costs borne by the economy deplete capital accumulation. Then, in effect, a 6% (i.e. 33% * 20%) decline in savings occurs on the account of funding internally the intervention costs. Summing up, we arrive at a Ω of 23%. When the economy under consideration will bear these costs, we assume other things, such as current government spending, being equal. Then, $\Omega N_{it}c_i$, is the proportion of total costs of the intervention that impedes capital accumulation, $K_{i(t+1)}$. We include adjustment factor ε_{it} as the steady state growth rates of all variables, with exception of the last term, in equation (3) are equal to the sum of the population growth rate, n_i, and TFP growth, g_i. In steady state $\Omega N_{it}c_i$ grows at a lower rate, n_i. Then, steady state is not attained. To adjust for this anomaly, we include ε_{it} to ensure that all variables in (3)

[5] Although Nur (1993) states that households who are affected by malaria have to hire labour when incapable to work and therefore savings are decreased, in our analysis we keep saving rates constant in line with the assumptions of Solow (1956). This reasoning is ratified by Chima et al. (2002) who argue that too little studies are present to extrapolate field-studies on saving behaviour in relation to malaria to nation-wide estimates. The one that is present (Shephard, 1991) is entrenched with difficulties. Given our spectrum of countries we feel keeping saving rates constant gives a better reflection of reality. Therefore, we deviate from Haacker (2002a) who modelled total investments on the basis of household savings and HIV/AIDS prevalence.

[6] This is a substantial depreciation rate. However, we feel that using this rate is justified as we focus on African countries.

grow at the same rate. We normalize $\varepsilon_{i0} = 1$ and assume that it grows at the TFP growth rate.

Effective labour, E_{it}, as a production factor of gross domestic product, encompasses both a measurement of quantity and quality of the labour force. It is composed of the malaria- and non-malaria population, and is defined as following:

$$E_{it} = \sum_{m=1}^{2} \sum_{k=15}^{65} (HSV_{imk} - z\, b_{imk}) L_{itmk} \qquad (4)$$

Total labour force, which is estimated in the demographics and epidemiology model, across regions, *i*, over time, *t*, sex, *m*, and 1 year-age cohorts, *k*, is denoted by L_{itmk}. We consider the active labour force to be aged 15-65. No adjustments are made for unemployment due to poor data availability as done in similar studies, among that of Abegunde *et al.* (2007). We do correct for productivity differences across region, age and sex by means of health state valuations (HSV). The parameter *z*, constant over time and across regions, indicates the fraction of work lost per worker due to malaria incapacitation. It is equal to one minus the universal disability weight of malaria. Malaria prevalence across region, age and sex is captured by b_{imk}. We deviate from Cuddington and Hancock (1994) by disallowing work experience as a factor of labour efficiency. In contrast to HIV/AIDS, work experience is not relevant in case of malaria as adult malaria mortality is insignificant. Therefore, this variable, which in the literature is modelled to be only dependent on age (see e.g. Cuddington (1993, 1994), Haacker (2002a)), will not influence economic development in case of malaria.

Rearranging equation (4) gives the following:

$$E_{it} = \sum_{m=1}^{2} \sum_{k=15}^{65} (HSV_{imk} - zb_{imk}) L_{itmk} = \sum_{m=1}^{2} \sum_{k=15}^{65} (HSV_{imk} * L_{itmk} - z * L_{itmk}^{malpop}) =$$

$$\sum_{m=1}^{2} \sum_{k=15}^{65} (HSV_{imk} * (L_{itmk}^{non-malpop} + L_{itmk}^{malpop}) - z * L_{itmk}^{malpop}) =$$

$$\sum_{m=1}^{2} \sum_{k=15}^{65} (HSV_{imk} * L_{itmk}^{non-malpop} + disablity\_weight_{mal} * L_{itmk}^{malpop})$$

(5)

Equation (5) simply states that the labour population is divided into a non-malaria and into a malaria population in which we consider the latter be discounted by the malaria disability weight. The former is adjusted for the region-specific health state valuations for the general population.

3.2.3 Solow's steady state

When intervening in malaria for an indefinite period of time, the malaria and non-malaria population growth rates, and therefore total population growth, n_i, become constant over time. Therefore, the proportional difference in malaria incidence, $\Psi_{it} - \Psi_{it-1}$, gets equal to zero as the interventions are fully implemented over time. So, equation (2) is reduced to $A_{i(t+1)} = (1 + g_i)A_{it}$. With the other parameters constant as well, our model fulfils Solow's conditions to reach steady state in which all regions will experience balanced growth over time. The per worker GDP and capital steady state levels are derived below.

Given the constant total population growth rate in the long run and the fact that the effective labour population is derived from total population we use the following characterization of the evolution of effective labour:

$$E_{i(t+1)} = (1 + n_i)E_{it} \qquad (6)$$

Then the technology adjusted per capita production function, in which the lower-case symbols with a tilde represent the per effective worker technology adjusted variables in capital letters, $\tilde{k}_{it} = \frac{K_{it}}{A_{it}E_{it}}$ and $\tilde{y}_{it} = \frac{Y_{it}}{A_{it}E_{it}}$, is obtained by dividing (1) by the labour force as defined in (6) and adjusting for technology, A_{it}. This gives:

$$\tilde{y}_{it} = \tilde{k}_{it}^{\alpha} \qquad (7)$$

Given that $A_{i(t+1)} = (1+g_i)A_{it}$ and $E_{i(t+1)} = (1+n_i)E_{it}$, and replacing the steady state value of $\varepsilon_{it}\Omega N_{it}c$ over Y_{it} by Φ_i equation (3) can be rewritten as follows:

$$\tilde{k}_{i(t+1)} = \frac{1}{(1+n_i)(1+g_{it})}((\tau_i - \Phi_i)\tilde{y}_{it} + (1-\delta)\tilde{k}_{it}) \qquad \text{with } \Phi_i = \frac{\varepsilon_{it}\Omega N_{it}c}{Y_{it}} \quad (8)$$

Given that $\tilde{y}_{it} = \tilde{k}_{it}^{\alpha}$ and solving (8) for $\tilde{k}_{i(t+1)} = \tilde{k}_{it}$ we find the steady state level for technological adjusted capital per worker, $\tilde{k}_{it}^{*}$. This gives:

$$\tilde{k}_i^{*} = \left(\frac{(\tau_i - \Phi_i)}{n_i + g_i + \delta + n_i g_i}\right)^{1/(1-\alpha)} \quad (9)$$

By means of equations (7) and (9) we derive the technology adjusted output per capita:

$$\tilde{y}_{it}^{*} = \left(\frac{(\tau_i - \Phi_i)}{n_i + g_i + \delta + n_i g_i}\right)^{\alpha/(1-\alpha)} \quad (10)$$

In per capita effective terms, equations (10) and (11) become:

$$k_{it}^{*} = A_{it}\left(\frac{(\tau_i - \Phi_i)}{n_i + g_i + \delta + n_i g_i}\right)^{1/(1-\alpha)} \quad \text{and}$$

$$y_{it}^{*} = A_{it}\left(\frac{(\tau_i - \Phi_i)}{n_i + g_i + \delta + n_i g_i}\right)^{\alpha/(1-\alpha)} \quad (11)$$

From (11) we can derive some important statements. Per worker capital and output steady state levels decrease as the population growth, n_i, and the cost of malaria interventions, Φ_i, increase. If an intervention brings down malaria prevalence and productivity loss due to malaria (captured by *b* and *z* respectively), then the stock of effective labour, E_{it}, will increase and per capita steady state levels consequently

decrease. Higher saving rates, τ_i, and a lower depreciation rate, δ, have the opposite effect. Moreover, lower malaria prevalence rates increase A_{it} indirectly and therefore as well per capita capital and output steady state levels. So, malaria-interventions affect per capita output through their effect on A_{it}, n_i, Φ_i, b_i, and z in opposite ways. Moreover, from (11) we acknowledge that the steady state growth rates for per worker output and capital are equal to g_i. Redefining (11) in terms of total GDP and capital steady state levels, we see that both grow at rate $g_i + n_i$.

The model as defined in equation (1) to (11) is labelled as the "closed-economy model" and will be our model to analyze and project the economic impact of malaria-interventions. Our analysis covers a period of 45 years and starts from steady state: we calibrated the Solow model by means of the 2005 capital stock. Table 5 shows the input values of the Solow model across regions in 2005.

Input variable	**region *1***	**region *2***	**region *3***	**region *4***
elasticity to physical capital (α)	0.5	0.5	0.5	0.5
depreciation rate (δ)	8%	8%	8%	8%
savings rate (s)	29%	24%	12%	23%
TFP growth rate (g_i)	0.5%	0.5%*	1.1%	0.8%
Effective labour stock (millions)	149	45	121	67
initial GDP per effective worker (y)	670	711	480	836
initial capital per effective worker (k)	1812	1505	485	1792
initial population growth rate (n)	2.33%	2.38%	2.45%	1.27%

Table 5 Basic parameters Solow model across region.
* TFP growth rate is similar to that of region 1, the lowest rate across regions.

3.2.4 Growth accounting

In the following, we conduct GDP growth accounting by means of the production function as defined by (1). Not only is growth accounting of importance to identify the sources of economic growth, but also to point to the production factors through which malaria interventions affect economic well-being.

Taking logs and time differences from (1) we get:

$$\ln Y_{i(t+1)} - \ln Y_{it} = (1-\alpha)(\ln A_{i(t+1)} - \ln A_{it}) + \alpha(\ln K_{i(t+1)} - \ln K_{it}) + (1-\alpha)(\ln E_{i(t+1)} - \ln E_{it}) \quad (12)$$

which can be written in growth rates g_i as:

$$g_{it}^{Y} = (1-\alpha) g_{it}^{A} + \alpha g_{it}^{K} + (1-\alpha) g_{it}^{E} \quad (13)$$

We see from (13) that GDP grows at rate $(g_i + n_i)$ given that g_{it}^{K} grows at rate $(g_i + n_i)$ in its steady state.

3.2.5 Sensitivity analysis Solow model

By means of a Tornado analysis we tested the sensitivity of our model by varying the values of several parameters separately and projected their impact on GDP per capita. We used both positive and negative intervals of 5%, 10%, 15%, 20% and 25% of the depreciation rate, elasticity to physical capital, TFP-growth- and savings rate. Other variables were left out of the analysis as these were real observations or a fitted value of these observations (TFP in 2005). One must keep in mind that this sensitivity analysis scrutinizes parameters individually, not in unity. This is a weakness as parameters may reinforce each other. However, by taking large variances this limitation is to be compensated. We found no abnormalities when conducting the sensitivity analysis. That is, varying the variables mentioned above substantially did not alter model outcomes substantially.

4. Results

4.1 Cost-effectiveness study

Given our data and model assumptions, increasing coverage levels from current levels as exposed in table 4 to 80% shows that all evaluated malaria control interventions are highly cost-effective with averages of 8-126 int$/DALY across all regions. The results of all interventions across regions are shown in tabular and graphic form in appendix C.

The expansion paths indicated by the lines that connect the dots that lie closest to the south-east corner of figures 1-4 show the order of interventions in terms of health gains given certain budget constraints. From our analysis we conclude that this order is the same irrespective of region, i.e. the same intervention packages are most cost-effective in all regions. However, in general, the health impact of the interventions over their total costs as well as their incremental cost-effectiveness is more favorable in regions 1 and 2 than in the other regions.

When resources are limited, we conclude that intervening in malaria by means of ACT case management is most cost-effective, especially in regions 1 and 2 where cost-effectiveness ratios range between 9.22 and 7.55 int$/DALY, respectively. For regions 3 and 4 these ratios are 21.18 and 30.42 int$/DALY, respectively. Complementing this control intervention with a vaccination program would increase health gains most at lowest cost, at incremental cost-effectiveness ratios between 42-76 int$/DALY across regions. The last intervention package that lies on the expansion paths that achieves highest gains at lowest cost is adding to the previous package ITN and IRS. Then differential cost-effectiveness increases between 26-83 int$/DALY across regions.

We conclude that developing a malaria vaccine is only cost-effective when it is used in combination with at least ACT. Although a vaccine's effectiveness is not impeded by patient's behavior and pharmacokinetics and therefore this intervention has a substantial practical advantage over other malaria control interventions, the cost-effectiveness of a vaccine is high when used alone compared to other interventions. However, the assumption that the vaccine proportionally reduces incidence and case fatality to the same extent as ITN and IRS (see table 3) influences the statement made above strongly. Therefore, we believe that an analysis on the efficacy of a malaria vaccine on case fatality is of great importance.

Based on our analysis we strongly recommend that a swift change in curative intervention from CQ to ACT is made. When doing so, substantial higher health gains are achieved at approximately the same costs. Even for region 4, where current ACT coverage is relatively high, this gain is substantial. Fortunately, this policy change is endorsed by most countries in June 2008 (Malaria report, 2008).

When financial resources are substantial, but limited, we recommend to complement the intervention package composed of ACT and vaccine with either IRS or ITN as these two packages lie closely to the expansion paths displayed in figures 1-4. Then substantial gains are achieved at the expense of a small decrease in efficiency. We believe such a sacrifice is not justifiable in relation to other interventions packages.

Our results diverge from that of Morel *et al.* (2005), the only study we compare with as Breman's (2006) methodology is unclear and that of Goodman *et al.* (2000) comes

across with that of Morel *et al.* The differences in outcomes are ascribed to the differences in epidemiological data. Korenromp (2005) estimates total malaria incidence in 2005 to be equal to 233 million. The GBD approximates total incidence equal to 340 million (2002). Differences in the estimations of the WHO mortality database (2005) and GBD (2002) are smaller, the latter predicts 75.000 more malaria fatalities. So, our results on curative interventions are approximately the same and our cost-effectiveness results on preventative interventions are substantially lower. It should be noted that the GBD's age- and sex-distribution on malaria incidence and mortality is unclear.

In table 6 the average reductions in under 5 malaria mortality as a consequence of the three most cost-effective interventions are shown.

scenario no.	scenario	Region 1	Region 2	Region 3	Region 4
5	ACT	31%	33%	25%	16%
11	Vacc + ACT	39%	41%	34%	27%
19	ITN + IRS + Vacc + ACT	47%	49%	44%	38%

Table 6 Average reductions in under 5 mortality as a consequence of certain malaria interventions.

We see that substantial reductions in under 5 mortality are achieved when intervening by means of the most cost-effective interventions. Again the impact is larger across intervention packages for regions1 and 2 in which reductions of 31-49% are obtained. For regions 3 and 4 the mortality impact ranges between 16-44%. The intervention package composed of all three preventative interventions complemented with ACT yields the highest gain in terms of malaria mortality under 5's. Therefore we conclude that when intervening with this package, MDG's 4 and 6 are best served.

Eliminating under 5 and total malaria mortality by means of the interventions packages as defined in table 4 is unattainable. Even increasing coverage levels to 100% is insufficient to impede malaria mortality. Then, at most reductions in malaria mortality up to 85% are attainable. So, the net effectiveness of individual interventions have to increase to eradicate mortality as a consequence of malaria. Given the baseline efficacy of malaria interventions as shown by Morel *et al.* (2005) we believe substantial gains in effectiveness are attainable on the account of patient's behavior, pharmacokinetics and biogenetics.

4.2 Macroeconomic analysis

We conclude from our analysis that the total costs that refrain capital from accumulating fully are negligible in a macroeconomic context. This is understandable as the proportion of the costs of the most expensive intervention package discounted for the fraction of savings that is diverted away from capital accumulation over total GDP ranges between 0.01-0.03% across regions. So, contrary to a cost-effectiveness point of view, macroeconomists do not take into account interventions costs when deciding on intervening in malaria. This is in line with Barlow's (1967) conclusion.

After the intervention packages are installed, the new steady state is reached after approximately 120 years. This is understandable as is takes time before the impact of the control methodologies are seeped through the population and their children. Also, the Solow model has to adjust itself to these changes in effective labor. According to Solow's 1956 theory, in this new steady state, total capital stock and total GDP grow at a new rate, that is equal new population growth rates, $(g_i + n_i)_{post-\text{int}ervention}$. This is equal to the sum of the pre-intervention growth rates and the increase in population growth rates, which equals $(g_i + n_i)_{pre-\text{int}ervention} + \Delta n_i$.

It is important to understand the dynamics of the effective labour variable. Curative interventions reduce mortality and therefore fuel effective labour growth. In the unlikely event that only malaria incidence is reduced but mortality stays constant, an increase in the effective labour stock is experienced due to productivity gains: the more productive non-malaria population becomes larger and the less efficient malaria population stock decreases. Yet, in the end, effective labour growth stays the same as mortality stays constant. However, preventative interventions also negatively affect malaria mortality.

The dynamics described above are clearly shown in graphs 5 and 6 which show the influence of a preventative (ITN) and a curative (ACT) intervention on the effective labour growth rates, respectively. The slight increase in effective labour growth rate displayed in figure 5 is attributable to the decline in malaria mortality among adults. However, after a few years, the growth diminishes slightly as the labour force that survived malaria may die of other causes, i.e. total background mortality increases. The under 5's that that did not die of the consequences of malaria due to the ACT-intervention enter the labour force in 2015 onwards. This is seen in

the increase in the effective labour force growth rate. From 2030 forwards we see again decreased effective labour growth due to increased background mortality. This loss is recuperated in 2038 onwards as fertility has increased due to increased population stock.

The growth path of effective labour when intervening preventatively by means of ITN is displayed in graph 6. The sharp rise in effective labour growth rate in the year of intervention is attributed to the productivity gain that is attained as more people become healthy, i.e. the proportion of the malaria-population over the non-malaria population becomes smaller. This is confirmed by the fact that malaria population growth rates fall sharply after implementation, the non-malaria population grows harshly. However, this augment evaporates, be it partially as curative interventions also negatively affect malaria mortality. After this, the dynamics of the growth path are the same as when one intervenes curatively.

Combinations of curative and preventative interventions inhibit growth paths characteristics of both types.

The increases in total capital's and GDP's steady state growth rates are equal to the increases in effective labour growth rates. Therefore our results accord with Solow's theory. Table 10 in appendix D shows the results on GDP steady state growth rates across regions and interventions. Steady state GDP per capita growth across region is equal to g_i irrespective of the intervention.

We conclude from tables 8 and 10 that in general those interventions that have the highest gain in terms of DALY's averted, achieve the highest effective labour growth rates and therefore stimulate GDP steady state growth most. This makes sense. When calculating the gains in years lived with disability (YLD), a measurement of morbidity and therefore a measurement of productivity, over the gains in DALY's, we see that this proportion is large just after the interventions are implemented. After a short period of time, however, the importance of morbidity in total health gains decreases substantially implying that averted mortality plays a more important role over time. Subsequently, proportionally averted mortality contributes more to DALY's than morbidity does. Due to decreased mortality, effective labour growth increases. Then, the relationship between DALY's and steady state GDP growth is established and therefore effectiveness gains in terms of DALY's is what counts given

that mortality contributes more to overall health gains than morbidity does. So, intervening by means of ITN, IRS, ACT and a vaccination is not only cost-effective in terms of int$/DALY, but also stimulates GDP steady state growth most in all regions.

It is of importance to note that in the new steady state, the capital-output ratio, K_i / Y_i, has decreased. This implies that the importance of capital as a contributor of economic growth has diminished over time. This makes sense. When dividing the steady state levels of capital over output, we see that an increase in the population growth rate decreases the steady state capital-output ratio.

4.2.1 Direct effects of malaria interventions

The moment the interventions are implemented, the demographics and epidemiology and therefore the Solow model get out of balance. As theory predicts, during the transition to a new steady state, GDP growth accords to the growth accounting exercise given by equation (13).

As TFP-growth is constant, GDP growth is only influenced by the growth differentials of effective labour and total capital stock, that are multiplied by $(1-\alpha)$ and α, respectively. From the total capital accumulation function (3), we see that differences in total capital are influenced by total GDP and total capital in the previous year. However, their influences are discounted for by the savings and depreciation rate. So, when the malaria control interventions affect effective labour growth, GDP growth is positively influenced. Consequently, total capital accumulation and therefore capital growth is influenced, however to a lesser scale due to the damped influences of the depreciation and savings rate on GDP and total capital, respectively. These dynamics are clearly shown in graphs 5 and 6 where capital growth rates do not follow the same bumpy track as GDP growth rates. Instead over time capital growth increases more smoothly.

We evaluate the direct impact of the malaria interventions on GDP per capita in 2070 and express the results as a proportional difference compared with GDP per capita of the non-intervention scenario. See table 11, appendix D.

From the results in table 11 emerges the same picture as for total GDP growth rates, however in inverse: in general, those interventions that achieve the highest gain in terms of DALY's affect GDP per capita in 2070 worst. We find that the interventions directly decrease GDP per capita levels between 0.4-1.8% in 2070

across regions. This is understandable, the pie of GDP gets larger, however it has to be divided by more inhabitants. We see that population grows faster than GDP, so GDP per capita is smaller when intervening in malaria compared to a non-intervention scenario. So, where population has grown fastest, and therefore where the health gains in terms of DALY's are greatest, GDP per capita is worst affected.

4.2.2 Direct effects complemented with indirect effects

The indirect effects are modelled through the inverse relationship between malaria incidence and TFP growth. An instant increase in TFP occurs in all preventative interventions, with the exception of a malaria vaccine. As a conservative approach for implementing this medication is followed, malaria incidence decreases gradually over time. Figure 7 and 8 show the reduction in malaria incidence and growth paths of the TFP, total capital and GDP for ITN and the malaria vaccine respectively over time for region 1.

From both graphs we see that the mechanisms through which the malaria interventions directly affect GDP are overshadowed by TFP growth which is driven by the decrease of malaria incidence. From equation (13) we see that the impact of TFP growth on GDP growth is multiplied by $(1-\alpha)$. Again, from definition (3), we see the impact of TFP on total capital growth is mitigated and delayed. In steady state, TFP growth rate returns to its pre-intervention steady state level.

The main difference between intervening by means of ITN or a vaccine is the time-frame in which malaria incidence is decreased. The former achieves an instant decrease as we assume that coverage of the malaria interventions are directly implemented, see graph 7. Therefore a one-time peak in TFP growth is realised. As we assume a gradual implementation of the malaria vaccine, a more bumpy course of TFP growth arises, see figure 8.

We are aware that a large increase in TFP growth is unrealistic, however we assess the results in terms of GDP per capita after a time span of 65 years. So, whether interventions are gradually or instantly implemented, we argue that in the end our results are not altered by the course of TFP growth.

As TFP drives GDP growth to the largest extent and the fact that TFP is modelled by means of incidence reduction, it is no surprise that those interventions that yield the highest gain in proportional GDP per capita are the preventative interventions. The combination of ITN, IRS and a vaccine result in an increase in

GDP per capita between 43.5-49% in Africa in 2070. The least effective preventative intervention still yields a proportional increase in GDP per capita of 14.2% (see table 11 for an overview of all results).

The malaria control interventions should be scaled up as the economic gains as a consequence of malaria suppression are substantial. However, as malaria mortality and TFP are not related, our results show that solely intervening by means of ACT or CQ do not induce the complementary gains that preventative interventions do yield. Therefore, the most cost-effective interventions with the exception of ACT stimulate economic development in terms of GDP per capita. Though, intervening through ACT, ITN, IRS and a vaccine yield the highest gain in GDP per capita.

Overall, our analysis shows that the development of a vaccine is cost-effective when used in combination with other intervention methodologies, either ACT or ACT in combination with the other preventative interventions, IRS and ITN. More importantly, intervening by these means augments economic development substantially. Our study shows that intervening by means of ACT, ITN, IRS and a vaccine is cost-effective, but yields sub-optimal results in terms of macroeconomic gains.

5. Discussion

All studies have their assumptions that influence outcomes to a certain extent, this one included. Many debate the effectiveness of the malaria control interventions considered in this study. Morel *et al.* (2005) provide a nice overview of this discussion. Moreover, our assumption that a malaria vaccine reduces case fatality to the same extent as ITN and IRS is of importance when deciding on the implementation of a malaria vaccine. That is, the cost-effectiveness of the vaccine differs substantially if this medication reduces case fatality to a larger or smaller extent than assumed. Therefore, we believe more research on this topic should take place. However, one should take into account that, when immunized, behavioural characteristics of the patient and pharmacokinetics do not influence the effectiveness of the vaccine. We believe this to be a great advantage with respect to the other intervention methods. In addition, we feel that policy makers should take into account local influences when deciding on the malaria control interventions. The cost-

effectiveness study is not a blue-print for reducing the malaria burden given certain budget constraints.

When determining the macroeconomic impact of the malaria interventions several assumptions are debatable. Firstly, we implicitly assume that the effectiveness of the interventions remains constant during our period of analysis. Given that resistance to anti-malaria medication is likely to occur over time, this is a crude assumption. Secondly, Cole and Neumayer (2006) assume linearity in the relationship between TFP and malaria incidence. It is questionable to what extent such a relationship can be maintained. Moreover, when estimating the indirect effects of malaria on economic well-being, we ask ourselves whether this should be related to incidence.

The Solow model has some drawbacks. Mills and Shillcutt (2004) argue that capital accumulation in Solow models is overemphasized as a production factor of economic growth. Secondly, Sorensen *et al.* (2005) point to a limitation articulated in the assumption of the exogenous technological growth rate. Thirdly, Solow assumes the savings rate to be exogenous and constant over time. Ros (2003) reasons that this rate can rise as a consequence of increasing income levels or increasing marginal returns on capital. Considering the last two critiques, Solow models do not inhibit any feedback mechanisms and therefore we argue that these models are quite static.

Given these drawbacks and assumptions that strongly influence our study, we nevertheless believe that our methodology is suitable for simulating the economic impact of malaria interventions for several reasons. Firstly, the Solow model is the most commonly used workhorse model to discuss economic growth due to its simplicity. It estimates economic well-being in the long run by taking into account key macro-economic aggregates which are also commonly referred to in context of malaria. Secondly, considering the scarcity and the poor quality of data in countries where malaria is prevalent, the Solow model is still able to articulate on the course of an economy. Thirdly, the Solow model used in this study allows us to identify the direct and indirect effects of malaria interventions on economic growth through its impact on TFP. For these reasons, we consider the Solow model the tool of choice to organize thinking about the macro effects of malaria interventions.

6. Conclusion

Our study shows that in sub-Saharan Africa the development of a malaria vaccine is only cost-effective when this malaria control intervention is used either in combination with ACT or when it is complemented with ACT, ITN and IRS. The latter intervention package serves the Millennium Development Goals best. We found that intervening solely by means of ACT is also cost-effective. Moreover, this study concludes that elimination of malaria mortality is not feasible given the current effectiveness of the interventions and combinations thereof.

Intervening in malaria stimulates economic development substantially, given that curative interventions are not used solely but in combination with preventative interventions. Our cost-effectiveness and macroeconomic impact studies do not find a common intervention package that yield optimal results.

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Appendix A
Gradual approach cost-effectiveness assessment

1. Construction epidemiologic and demographic model
   Model describes interaction demographics and epidemiology
2. Data collection
   Collection of the data of relevance for the impact assessment
3. Construction of baseline scenario
   To calculate the cost-effectiveness of the interventions a benchmark of no intervention is established.
4. Estimation effectiveness interventions
   The effectiveness of the interventions that affect the epidemiological parameters will be estimated in terms of health gains, in our case DALY's averted.
5. Calculation of the total costs of the interventions
6. Overview cost-effectiveness interventions

Appendix B

		Region			
scenario no.	**scenario**	**Region 1**	**Region 2**	**Region 3**	**Region 4**
1	ITN	0.76	0.66	0.64	0.63
2	IRS	0.80	0.65	0.62	0.60
3	Vacc	10.97*	10.97*	10.97*	10.97*
4	CQ	0.24	0.21	0.20	0.20
5	ACT	0.25	0.21	0.21	0.20
6	ITN+CQ	0.99	0.86	0.84	0.82
7	ITN+ACT	0.99	0.86	0.84	0.82
8	IRS+CQ	0.93	0.79	0.76	0.74
9	IRS + ACT	0.93	0.79	0.77	0.75
10	Vacc + CQ	0.24	0.21	0.20	0.20
11	Vacc + ACT	0.25	0.21	0.21	0.20
12	ITN + IRS	1.29	1.11	1.08	1.05
13	ITN + Vacc	0.75	0.66	0.64	0.63
14	IRS + Vacc	0.80	0.65	0.62	0.60
15	ITN + IRS + Vacc	1.29	1.11	1.08	1.05
16	ITN + IRS + ACT	1.36	1.17	1.14	1.11
17	ITN + Vacc + ACT	0.99	0.86	0.84	0.82
18	IRS + Vacc + ACT	0.93	0.79	0.77	0.75
19	ITN + IRS + Vacc + ACT	1.36	1.17	1.14	1.11

Table 7 Analyzed interventions and their costs (int$ per capita) across region.
* per person vaccinated

Appendix C

		Average yearly cost (int$)				Average yearly effectiveness (DALY's averted)			
		Region				Region			
scenario no.	scenario	1	2	3	4	1	2	3	4
1	ITN	185	49	129	66	3	1	1	1
2	IRS	195	48	124	63	3	1	1	1
3	Vacc	95	29	77	39	3	1	1	1
4	CQ	58	16	40	21	2	0	1	0
5	ACT	61	16	42	21	6	2	2	1
6	ITN+CQ	241	64	169	86	4	1	2	1
7	ITN+ACT	242	64	169	86	8	3	3	1
8	IRS+CQ	227	58	153	78	4	1	2	1
9	IRS + ACT	227	59	155	79	8	3	3	1
10	Vacc + CQ	153	45	117	60	5	1	2	1
11	Vacc + ACT	156	45	119	60	9	3	3	1
12	ITN + IRS	314	82	217	110	5	1	2	1
13	ITN + Vacc	277	78	206	105	5	2	2	1
14	IRS + Vacc	290	77	202	102	6	2	2	1
15	ITN + IRS + Vacc	409	112	294	149	7	2	3	2
16	ITN + IRS + ACT	332	87	229	117	9	3	3	2
17	ITN + Vacc + ACT	337	93	246	125	10	3	4	2
18	IRS + Vacc + ACT	322	88	232	117	10	3	4	2
19	ITN + IRS + Vacc + ACT	427	116	306	155	11	3	4	2

Table 8 Average yearly cost and average yearly effectiveness across scenario and region (in millions).

		Region							
		1		2		3		4	
scenario no.	scenario	CE	ΔCE	CE	ΔCE	CE	ΔCE	CE	ΔCE
1	ITN	72.91	dominated	63.05	dominated	125.75	dominated	107.25	dominated
2	IRS	74.49	dominated	61.38	dominated	124.08	dominated	109.54	dominated
3	Vacc	28.82	dominated	29.62	dominated	56.93	dominated	48.26	dominated
4	CQ	38.16	dominated	39.64	dominated	43.82	dominated	62.69	dominated
5	ACT	9.42	9.42	7.55	7.55	21.18	21.18	30.42	30.42
6	ITN+CQ	62.87	dominated	57.61	dominated	93.79	dominated	95.62	dominated
7	ITN+ACT	30.08	dominated	25.35	dominated	62.27	dominated	71.65	dominated
8	IRS+CQ	59.06	dominated	52.92	dominated	84.86	dominated	86.29	dominated
9	IRS + ACT	28.09	dominated	23.24	dominated	57.36	dominated	67.48	dominated
10	Vacc + CQ	33.57	dominated	33.97	dominated	55.53	dominated	55.29	dominated
11	Vacc + ACT	17.95	42.92	16.45	43.90	39.75	76.54	43.43	56.56
12	ITN + IRS	66.59	dominated	57.76	dominated	119.14	dominated	102.05	dominated
13	ITN + Vacc	50.79	dominated	47.18	dominated	94.24	dominated	79.11	dominated
14	IRS + Vacc	52.39	dominated	46.52	dominated	93.04	dominated	78.82	dominated
15	ITN + IRS + Vacc	56.01	dominated	50.55	dominated	103.83	dominated	87.01	dominated
16	ITN + IRS + ACT	35.49	dominated	30.03	dominated	70.36	dominated	73.69	dominated
17	ITN + Vacc + ACT	33.52	dominated	29.80	dominated	68.75	dominated	68.94	dominated
18	IRS + Vacc + ACT	31.93	dominated	28.10	dominated	65.01	dominated	65.95	dominated
19	ITN + IRS + Vacc + ACT	38.25	26.23	33.74	21.28	76.23	54.84	72.98	62.88

Table 9 Average cost-effectiveness (CE) and incremental cost-effectiveness (ΔCE) (int$ per DALY averted) across scenario and region.

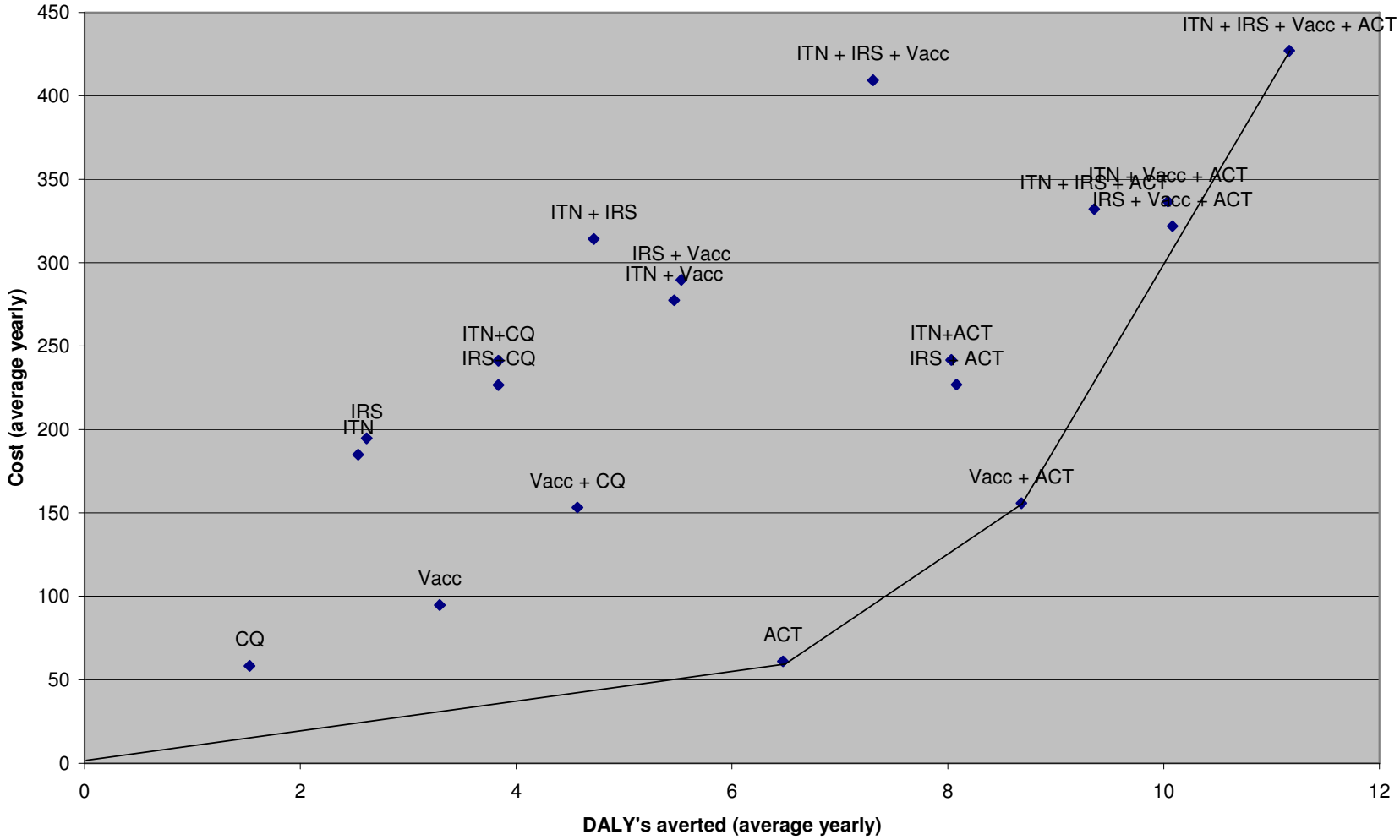

Figure 1 Cost-effectiveness pane region 1 (in millions).

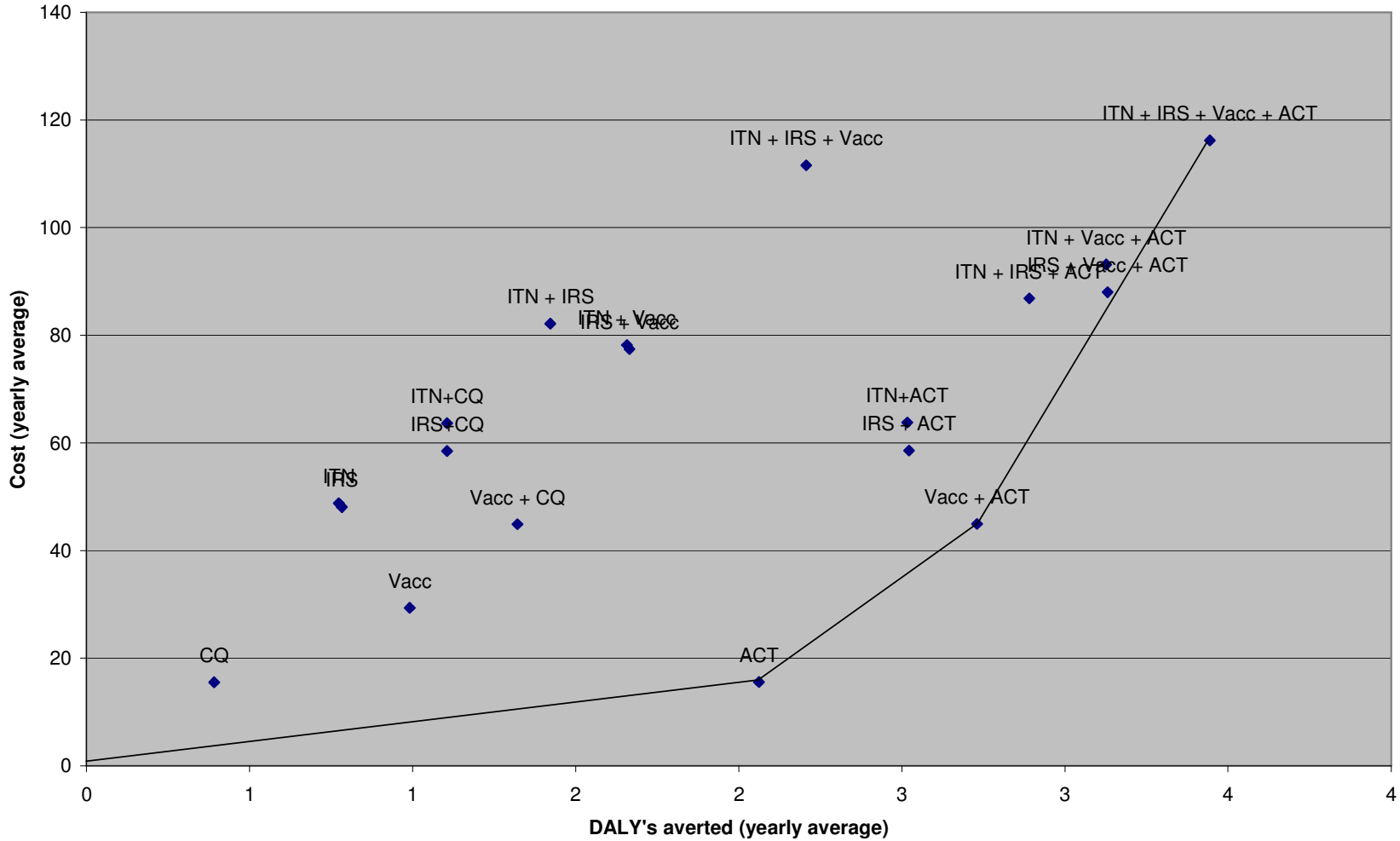

Figure 2 Cost-effectiveness pane region 2 (in millions).

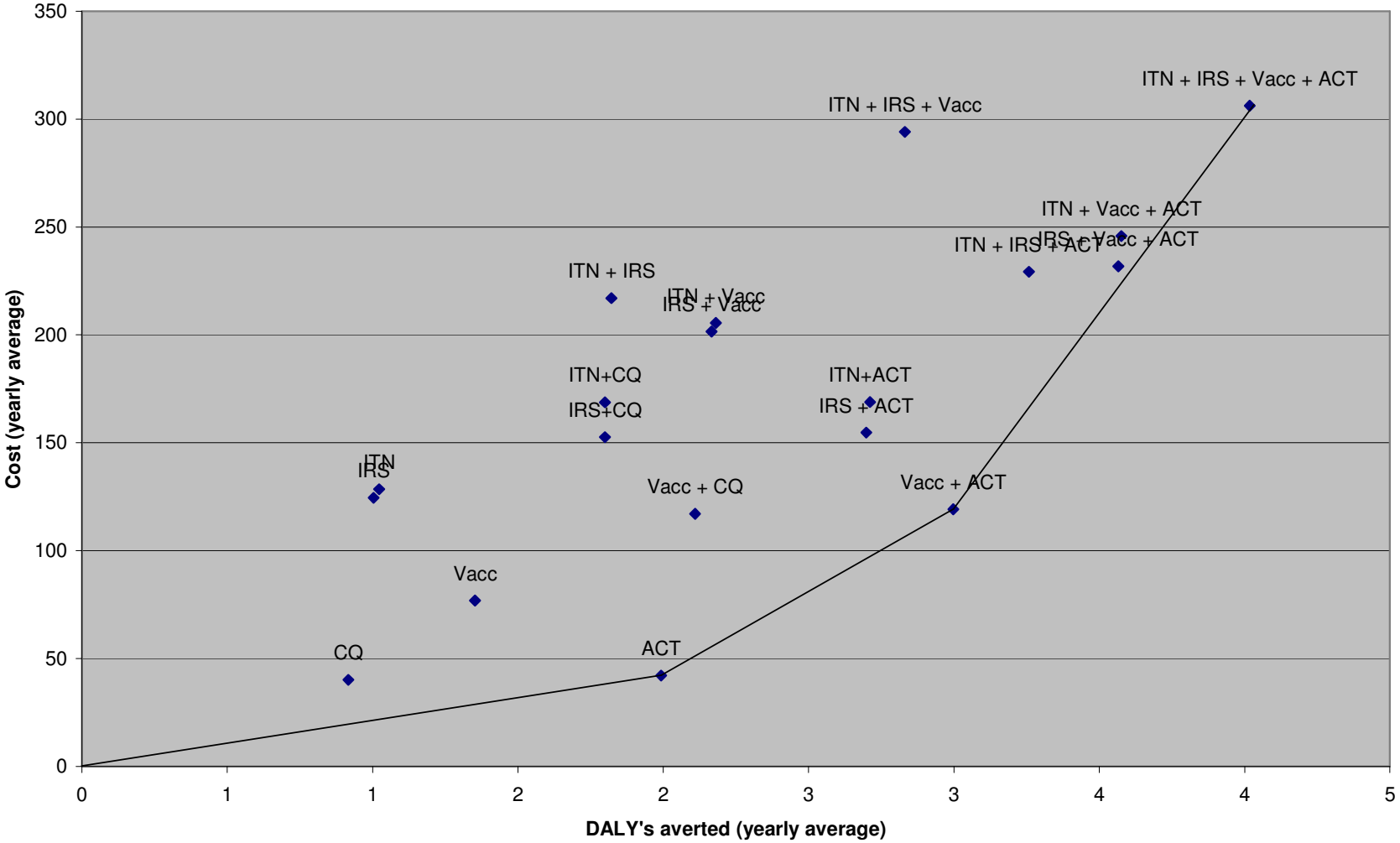

Figure 3 Cost-effectiveness pane region 3 (in millions).

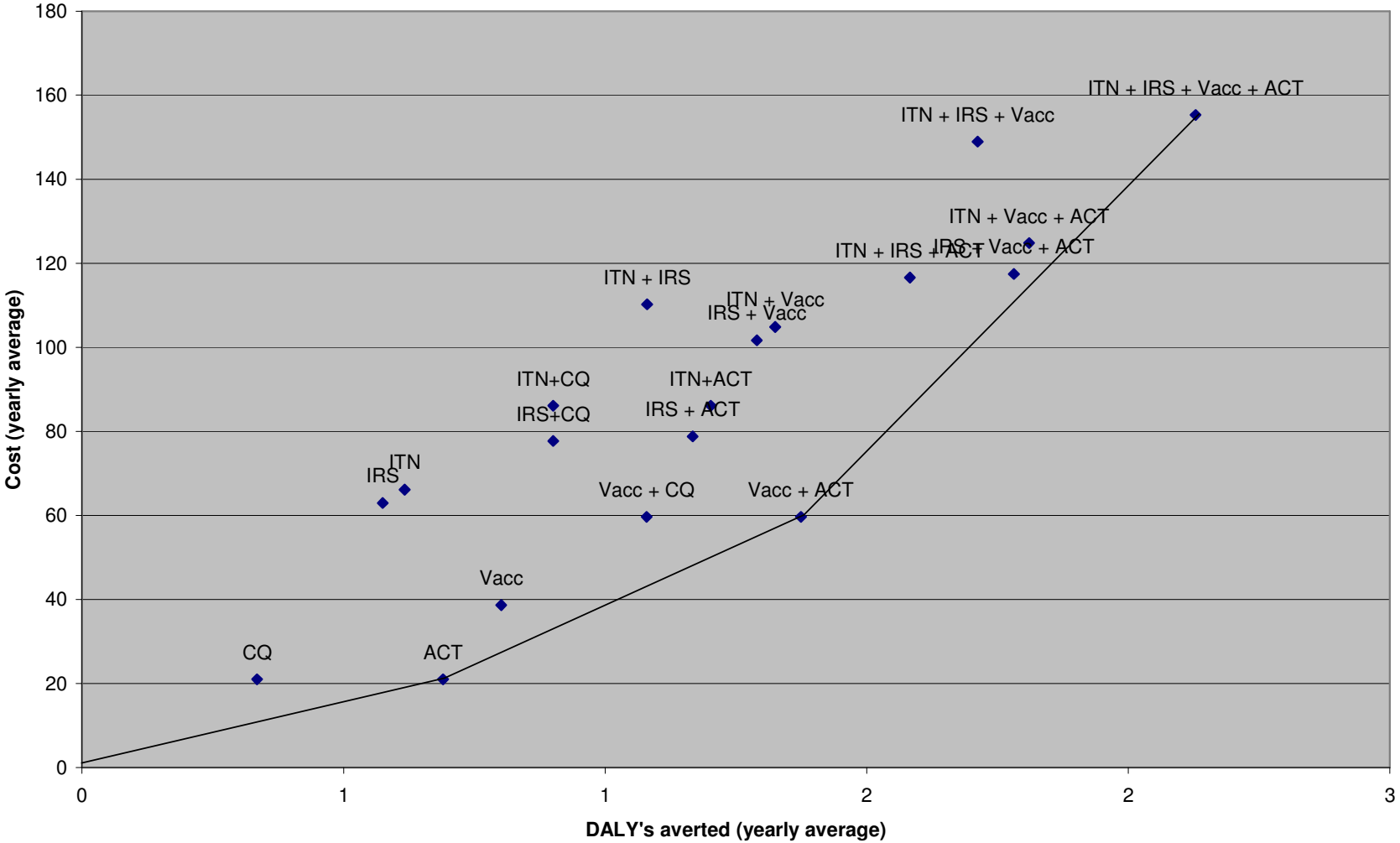

Figure 4 Cost-effectiveness pane region 4 (in millions).

Appendix D

		Region			
scenario no.	**scenario**	**1**	**2**	**3**	**4**
1	ITN	0.0275%	0.0262%	0.0115%	0.0151%
2	IRS	0.0283%	0.0265%	0.0113%	0.0141%
3	Vacc	0.0375%	0.0349%	0.0157%	0.0206%
4	CQ	0.0198%	0.0159%	0.0132%	0.0115%
5	ACT	0.0833%	0.0834%	0.0287%	0.0236%
6	ITN+CQ	0.0442%	0.0396%	0.0227%	0.0248%
7	ITN+ACT	0.0979%	0.0964%	0.0358%	0.0350%
8	IRS+CQ	0.0450%	0.0399%	0.0225%	0.0239%
9	IRS + ACT	0.0984%	0.0966%	0.0356%	0.0343%
10	Vacc + CQ	0.0531%	0.0475%	0.0261%	0.0297%
11	Vacc + ACT	0.1032%	0.1008%	0.0384%	0.0393%
12	ITN + IRS	0.0514%	0.0485%	0.0210%	0.0270%
13	ITN + Vacc	0.0592%	0.0556%	0.0248%	0.0325%
14	IRS + Vacc	0.0598%	0.0559%	0.0246%	0.0317%
15	ITN + IRS + Vacc	0.0781%	0.0733%	0.0323%	0.0419%
16	ITN + IRS + ACT	0.1107%	0.1076%	0.0416%	0.0441%
17	ITN + Vacc + ACT	0.1148%	0.1111%	0.0439%	0.0483%
18	IRS + Vacc + ACT	0.1151%	0.1112%	0.0438%	0.0477%
19	ITN + IRS + Vacc + ACT	0.1248%	0.1199%	0.0485%	0.0554%

Table 10 GDP's and total capital steady state growth differential accros region and intervention.

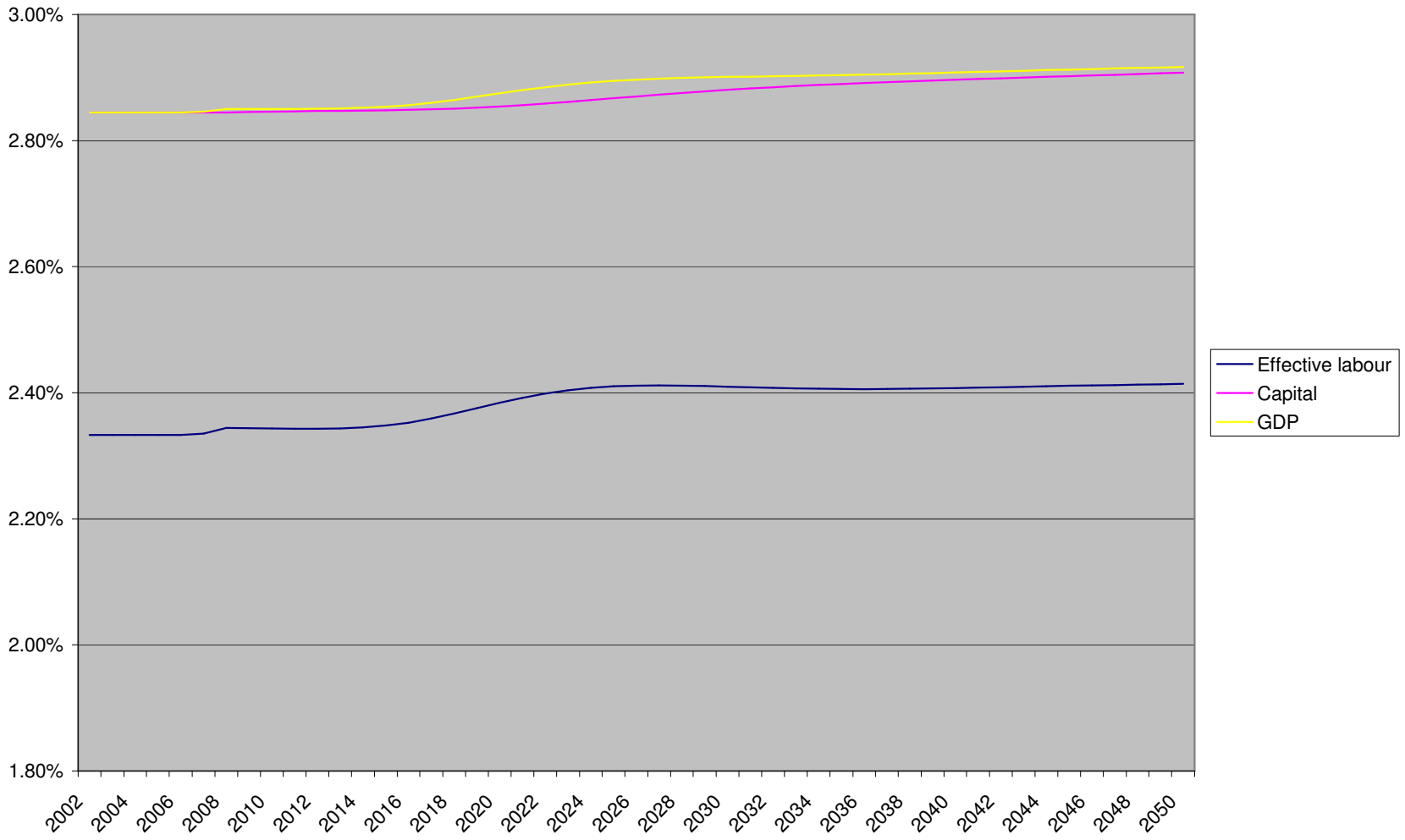

Figure 5 Transition paths of total GDP, capital and effective labour when intervening with ACT for region 1 over time.

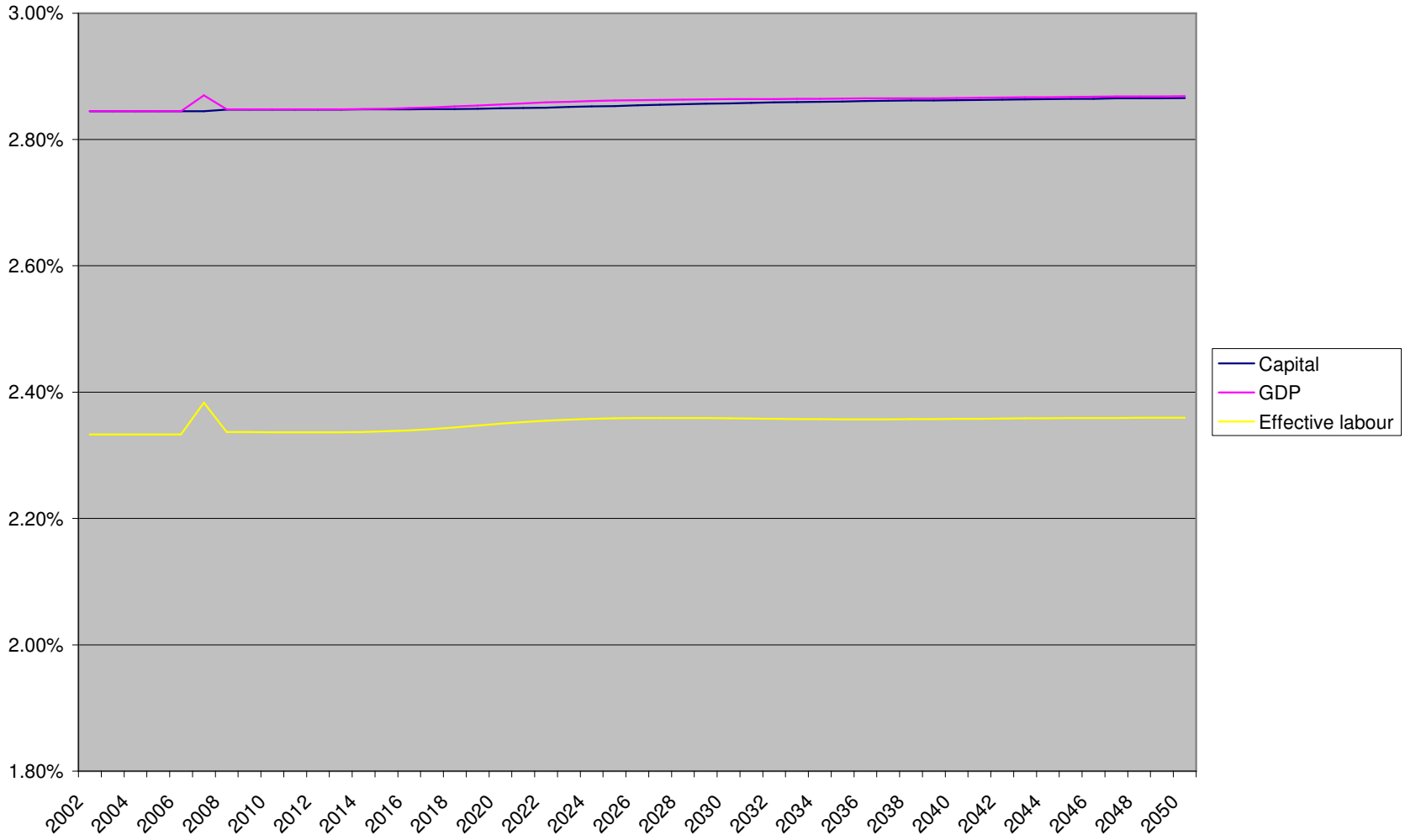

Figure 6 Transition paths of total GDP, capital and effective labour when directly intervening with ITN for region 1 over time.

		Direct effects				Direct and indirect effects			
		Region				Region			
scenario no.	scenario	1	2	3	4	1	2	3	4
1	ITN	-0.36%	-0.33%	-0.13%	-0.15%	15.4%	16.7%	21.6%	18.3%
2	IRS	-0.37%	-0.33%	-0.13%	-0.14%	15.9%	16.9%	21.2%	17.0%
3	Vacc	-0.49%	-0.43%	-0.18%	-0.21%	23.8%	25.3%	32.8%	28.2%
4	CQ	-0.30%	-0.23%	-0.20%	-0.18%	-0.30%	-0.23%	-0.20%	-0.18%
5	ACT	-1.26%	-1.22%	-0.43%	-0.36%	-1.26%	-1.22%	-0.43%	-0.36%
6	ITN+CQ	-0.61%	-0.52%	-0.30%	-0.30%	15.1%	16.4%	21.4%	18.2%
7	ITN+ACT	-1.42%	-1.35%	-0.49%	-0.46%	14.2%	15.5%	21.2%	18.0%
8	IRS+CQ	-0.62%	-0.53%	-0.29%	-0.29%	15.7%	16.7%	21.0%	16.9%
9	IRS + ACT	-1.43%	-1.35%	-0.49%	-0.45%	14.7%	15.7%	20.8%	16.7%
10	Vacc + CQ	-0.73%	-0.61%	-0.33%	-0.35%	23.5%	25.0%	32.6%	28.0%
11	Vacc + ACT	-1.49%	-1.39%	-0.52%	-0.49%	22.5%	24.0%	32.4%	27.8%
12	ITN + IRS	-0.68%	-0.62%	-0.24%	-0.29%	27.5%	29.2%	34.6%	30.3%
13	ITN + Vacc	-0.79%	-0.70%	-0.29%	-0.35%	35.6%	37.6%	44.3%	40.4%
14	IRS + Vacc	-0.79%	-0.70%	-0.29%	-0.34%	36.0%	37.8%	44.1%	39.6%
15	ITN + IRS + Vacc	-1.05%	-0.94%	-0.39%	-0.47%	43.5%	45.1%	49.5%	46.6%
16	ITN + IRS + ACT	-1.58%	-1.48%	-0.55%	-0.55%	26.4%	28.1%	34.2%	29.9%
17	ITN + Vacc + ACT	-1.63%	-1.51%	-0.58%	-0.59%	34.5%	36.5%	43.9%	40.1%
18	IRS + Vacc + ACT	-1.63%	-1.52%	-0.58%	-0.59%	34.9%	36.6%	43.7%	39.3%
19	ITN + IRS + Vacc + ACT	-1.76%	-1.62%	-0.63%	-0.68%	42.5%	44.1%	49.1%	46.3%

Table 11 Proportional differences in GDP per capita, direct effects and direct and indirect effects, across region and intervention.

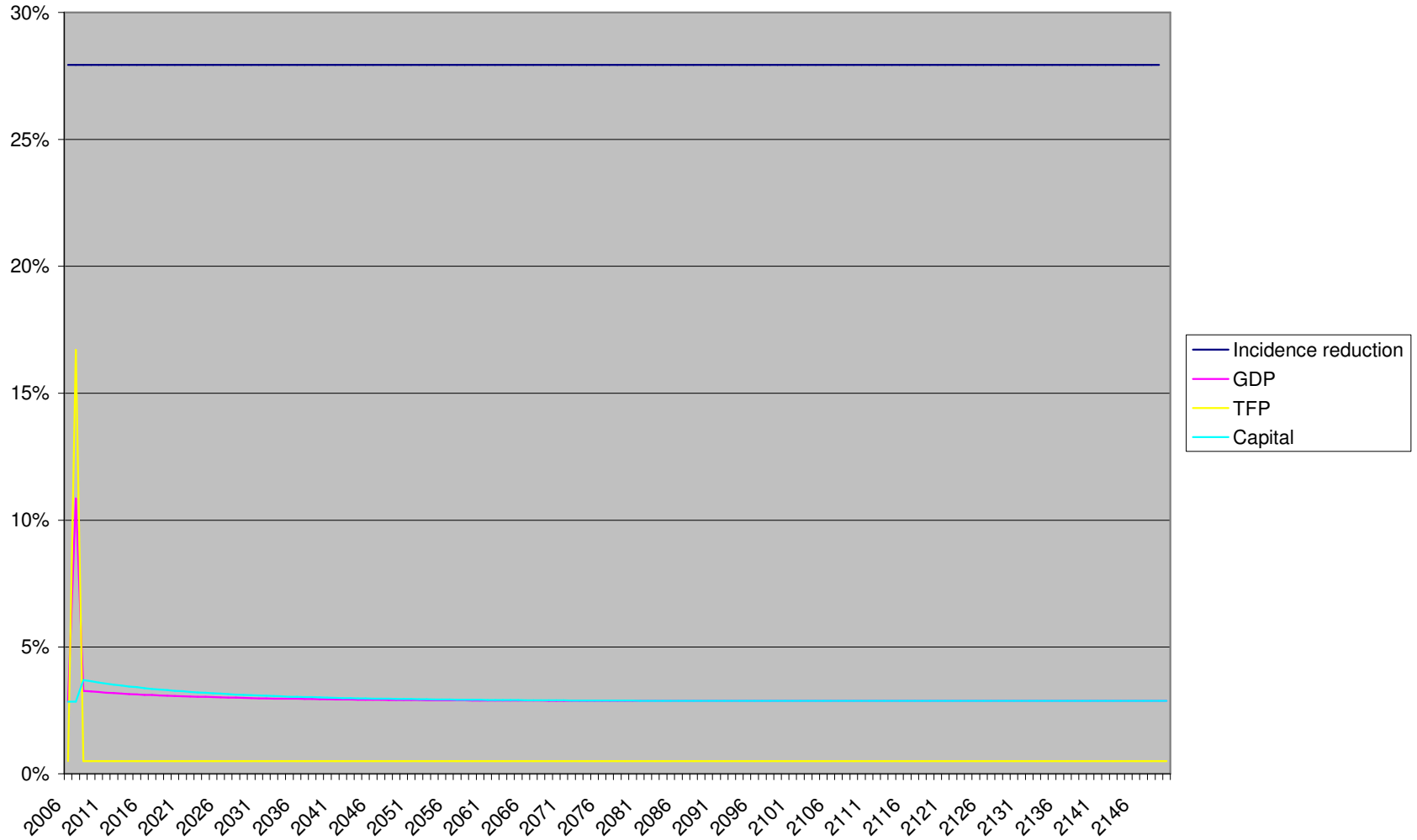

Figure 7 Transition paths of total GDP, capital and TFP when intervening with ITN for region 1 over time.

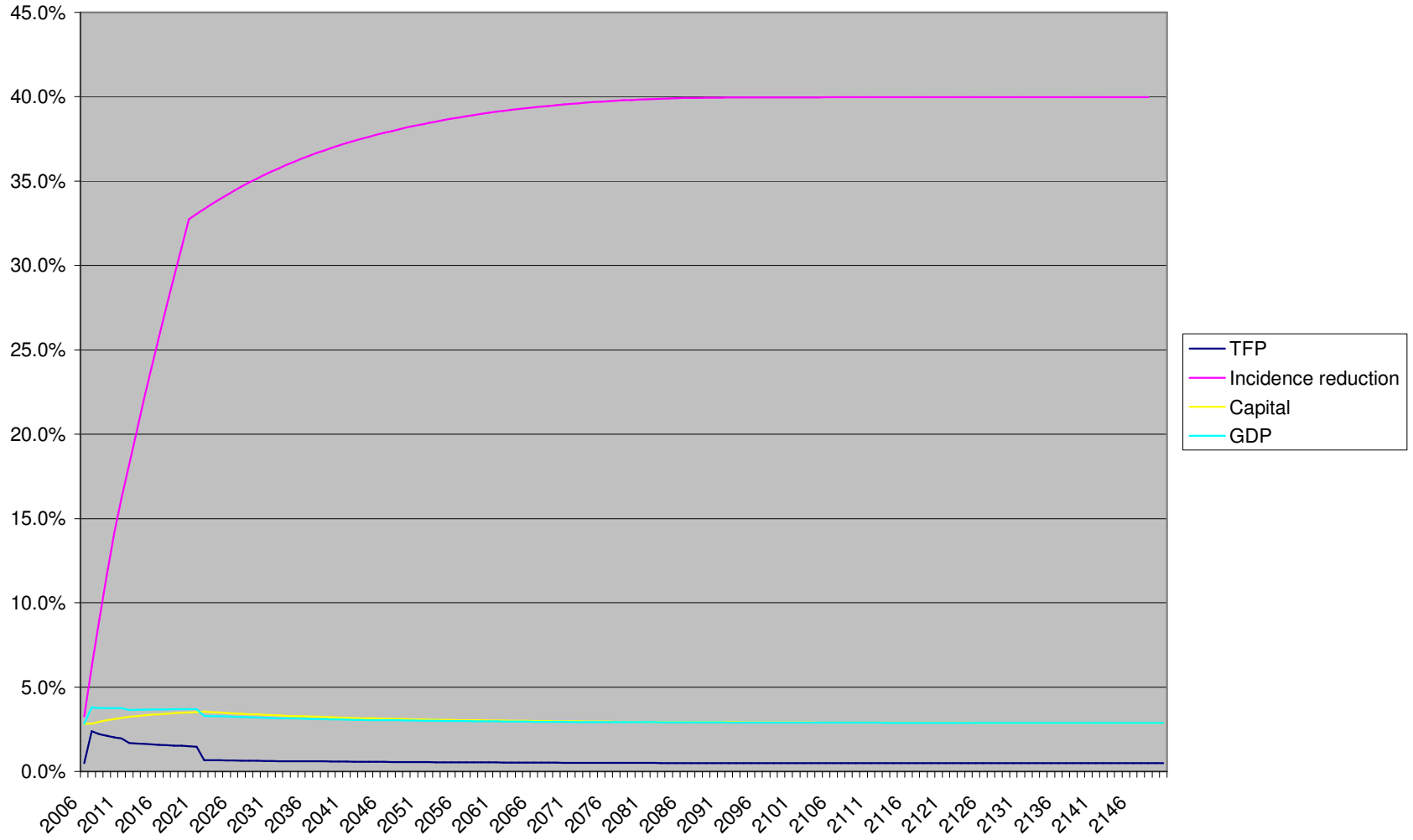

Figure 8 Transition paths of total GDP, capital and TFP when intervening with a vaccine for region 1 over time.