Copenhagen Consensus

Challenge Paper on Communicable Diseases

Anne Mills and Sam Shillcutt*
Health Economics and Financing Programme
London School of Hygiene & Tropical Medicine

February 2004

*Anne Mills is Professor of Health Economics and Policy and Head, Health Economics and Financing Programme, London School of Hygiene and Tropical Medicine, Keppel ST, London WC1E 7HT; tel +44 207 927 2354; email anne.millls@lshtm.ac.uk.

Sam Shillcutt is Research Fellow in the Health Economics and Financing Programme, London School of Hygiene and Tropical Medicine; tel +44 207 927 2090 email sam.shillcutt@lshtm.ac.uk

Acknowledgements
AM and SS are members of the Health Economics and Financing Programme (HEFP) which is funded by the Department for International Development of the United Kingdom. However the Department for International Development can accept no responsibility for any information provided or views expressed. We are very grateful to Catherine Goodman and Fern Terris-Prestholt for comments on the final draft, and more generally to our HEFP colleagues for support in tracing literature and discussion of drafts.

Table of Contents

Acknowledgements **1**
List of Figures **3**
List of Table **3**
Executive summary **4**

1 The challenge of communicable disease **8**

2 Assessing the opportunities **11**
2.1 The economic benefits of improved health and the availability of evidence 11
2.2 Methodological approach adopted 15

3 Control of malaria **18**
3.1 Identification and description 18
3.2 Alleviation of the challenge – interventions 23
3.3 Side effects 24
3.4 Economic evaluation 25
3.5 Feasibility 36

4 Control of HIV/AIDS **39**
4.1 Identification and description of opportunity 39
4.2 Alleviation of the challenge – interventions 45
4.3 Side effects 46
4.4 Economic evaluation 47
4.5 Feasibility 50

5 Strengthening basic health services **52**
5.1 Identification and description 52
5.2 Alleviation of the challenge 53
5.3 Side Effects 53
5.4 Economic Evaluation 54
5.5 Feasibility 56

6 Discussion and Conclusions **58**

Annex – Complete summary of results **62**

References **64**

Figures

1.1 Life expectancy at birth, 1955-2002 8
2.1 Channels through which illness reduces income 11
3.1 Effect of resistance on treatment failure 33
4.1 Long-run economic costs of AIDS in South Africa 43

Tables

1.1 Leading causes of death in children in developing countries, 2002 9
1.2 Risk of dying and avoidable mortality (%) in low- and middle-income countries 1998 9
2.1 Value of a DALY/YLL 16
3.1 Cost-Benefit Ratios in Malaria Control 26
3.2 Costs and benefits of malaria control estimated from macroeconomic models 27
3.3 Costs and benefits of ITNs 29
3.4 Costs and benefits of IPTp 31
3.5 Costs and benefits of changing from SP to ACT 34
3.6 Costs and benefits of scaling up ACT 34
3.7 Costs and benefits of a package of malaria control measures 35
4.1 Effects of HIV/AIDS on national GDP 2000-2025 44
4.2 Effect of HIV/AIDS on long-term GDP: No action taken 44
4.3 UNGASS HIV/AIDS recommendation 46
4.4 Net benefit in terms of 2000 national GDP by 2025 47
4.5 Costs and benefits of Thailand's 100% condom programme 1993-2000 48
4.6 Benefit cost ratios of interventions for SSA 49
4.7 Cost and benefits of the UNGASS package of interventions for middle and low- income countries 50
5.1 The WDR 93 minimum heath package 53
5.2 Costs and benefits of increased health expenditure 2002-2015 55
5.3 Costs and benefits of the 1993 World Development Report Package 55
5.4 Relaxing constraints: priority actions by type of country 56
6.1 Summary of key results 60

Executive summary

The challenge of communicable disease

Over the second half of the twentieth century, the world has seen enormous health improvements. However, developing countries have benefited unequally from health gains, with many, especially in sub-Saharan Africa (SSA), continuing to experience high mortality. Children bear a major burden of ill health, with infectious and parasitic diseases the main killers. Adults experience substantial premature mortality. Within countries, poorer groups have considerably worse health than the better off. Analysis of avoidable mortality highlights the importance of communicable disease, which represents around 90% of all avoidable mortality in almost all age/sex groups. The benefits of research mean that tools and approaches now exist to address the great majority of the burden of communicable disease, most notably malaria, TB, and HIV/AIDS, as well as vaccine preventable diseases. However, large numbers of people do not have effective access to prevention and treatment, and as a result die.

The paper focuses on three opportunities:

- Malaria control
- HIV/AIDS control
- Strengthening basic health services.

This categorisation has been chosen largely because malaria and HIV/AIDS are major causes of disease burden and economic losses; cost-effective interventions are known to exist for their control; there is recent literature which can be drawn on to estimate costs and benefits; and these diseases are currently the focus of world attention. Basic health services have been chosen as the third opportunity since they address a major part of the disease burden, and represent explicitly the infrastructure that needs to be in place for people's main health needs to be met.

The economic benefits of improved health

The relationship between illness and income is complex. Effects are felt both directly (through the immediate impact of ill health on productive activities) and indirectly, via the effects of illness on fertility, morbidity, mortality and intellectual capacity, and hence on the labour force size, composition and quality, and on the capacity of countries to engage in the global economy. Empirical studies of the relationship between disease and economic outcomes fall into two categories: microeconomic and macroeconomic. The former study the link between disease/ill health at household or individual level, usually documenting the costs imposed by disease on households but not explicitly the benefits of disease control, and categorising costs as direct and indirect. Such estimates are likely to underestimate the true economic impact of a disease, since they neglect the impact of coping strategies and the broader, dynamic consequences of disease for the economy as a whole. In contrast, macroeconomic studies assess the influence of a disease on national income in cross-country comparisons. In principle they are better able than microeconomic studies to reflect the wide-ranging and dynamic implications of ill health, but raise concerns as to the extent to which other influences on economic growth are adequately allowed for. Again such studies usually document the cost of disease, but only by implication the benefits of disease reduction.

The most abundant literature is that on the cost-effectiveness of interventions, comparing intervention cost with benefits expressed in terms of health outcomes. Systematic approaches have recently been applied to the synthesis of both epidemiological studies and economic studies, making judgements on the quality of evidence, and facilitating conclusions on both health outcomes of interventions and cost-effectiveness. However, using these studies to evaluate the efficiency of health interventions in units that are comparable across economic sectors requires placing a monetary value on human life.

Given the limitations of the literature in terms both of quantity and quality, and the need to be comprehensive and consistent, estimates of costs and benefits were where possible calculated by the authors based on the literature rather than limiting the paper only to costs and benefits actually provided in the literature. Several different approaches were adopted. For the two diseases (malaria and HIV), evidence was drawn from three different sources:

- Studies of the macroeconomic impact of the disease
- Studies of the cost-effectiveness of interventions
- Evidence of the costs and health benefits of large scale country programmes.

For basic health services, evidence was drawn from two different sources:

- Regression analyses that measured the efficiency of health expenditure in generating health outcomes
- The costs and health benefits of a package of interventions recommended in the 1993 World Development Report.

Where possible, costs and benefits were summarised as both annualised net benefits (ANB) adjusted for Purchasing Power Parity and benefit cost ratios (BCR). A year of life lost was valued at 2003 per capita Gross National Income (GNI) (the ceiling ratio), and a discount rate (DCR) of 3% applied. In sensitivity analyses, the DCR was set at 6% and the ceiling ratio at the mean GNI for low and middle income countries of Int$3,830.

Control of malaria

Major reductions in the malaria burden and its eradication from temperate parts of the world gave reason for optimism in the mid twentieth century. However, in the 1980's, commitment to programmes waned and resistance to medicines and insecticides increased. With the increased use of new combination drugs and a greater international commitment to financing malaria control, there is again reason to believe that the burden of malaria can be substantially reduced. SSA experiences over 90% of the global burden of malaria; malaria causes around 20% of the mortality of children under 5; and it is the most important single infectious agent causing death in young children. Cost-benefit estimates were therefore made for SSA, drawing on macroeconomic studies; on cost-effectiveness studies of insecticide-treated mosquito nets, intermittent presumptive treatment of pregnant women (IPTp), and combination therapy (ACT); and evidence from recent successful malaria control efforts in the KwaZulu Natal province of South Africa. Based on estimates from macroeconomic models, we predicted that the ANB of eliminating 50% of malaria between 2002-15 would be Int$11-43 bn, with BCRs of 1.9-4.7. For the package of malaria control measures these were Int$47.4 bn and 27. The ANB of the successful South African malaria control programme was Int$9m, and it was cost saving.

Control of HIV/AIDS

The HIV/AIDS pandemic is devastating the economies of many low- and middle-income countries. Current estimates are that more than 22m people have already died, 34-46m are currently living with HIV/AIDS, and 5.3m new infections occur each year. The scale of the problem is such that it is considered a development issue and global security threat. The costs and benefits of approaches to addressing the epidemic were estimated, drawing on four different sources of information: a macroeconomic model of the gains to prevention in several north African and Middle Eastern countries at the 'nascent' stage of the epidemic; the costs and benefits of successful control in Thailand, at the 'concentrated' stage of the epidemic; evidence on the cost-effectiveness of a number of specific interventions in Africa; and estimates of the cost and health impact of the UNGASS global programme. For the group of North African/Middle Eastern countries, intervening now was estimated to save 15-30% of 2000 GNP by 2005. In Thailand, the ANB of the AIDS control was Int$3.5 bn and BCR 15. BCRs of individual interventions were highly variable but generally exceeded 2, with condom distribution and blood safety having BCRs of 466. The UNGASS package had ANB of Int$359.4 bn and BCR of 50.

Basic health services

The great majority of health interventions depend for successful and sustained implementation on an infrastructure of basic health services, consisting of community based services, health centres, and local hospitals. These can address much of the burden of ill health including that from maternal and neonatal conditions, childhood illnesses such as diarrhoea, ARI and vaccine preventable diseases, and malaria, TB and HIV/AIDS. Over the last decade recommendations have been made on a package of priority interventions to be delivered at this level. We estimated the costs and benefits of scaling up basic health services drawing on firstly evidence for HIPC countries of the relationship between health expenditure and health gains and the necessary increase in public spending to reach the MDG child mortality target; and secondly estimates of the costs and health benefits of the package of interventions recommended in the 1993 World Development Report. The first approach gives ANB of Int$50.0 bn and BCR 3.9 (though benefits for children only are included). The 1993 WDR package gives ANB of Int$534.1 bn and BCR of 2.6.

Conclusions

All sources of data used have severe shortcomings, which must inform the interpretation of the costs and benefits. In particular:

- The macroeconomic literature is quite inadequate;
- The microeconomic literature comes mainly from interventions implemented individually in the context of epidemiological trials; evidence of costs and health effects of large scale programme implementation is very limited. Health effects were translated into a monetary value using a somewhat arbitrary ceiling ratio.
- For the basic health services opportunity, benefits for children only are valued although other population groups are likely to benefit.
- Evidence from successful programmes is hard to interpret, since external factors may also have affected changes in health effects.

In addition, our estimates suffer from other shortcomings:

- Available costs were usually costs to the provider, excluding costs to users
- Resource savings were rarely included in the estimates
- We were unable to be explicit on which groups would benefit most under each of the challenges, and in particular on the extent to which the poorest would benefit.

Finally, macroeconomic estimates of benefits and calculations made from cost-effectiveness evidence cannot of course be assumed to be reflecting the same dimensions of benefits.

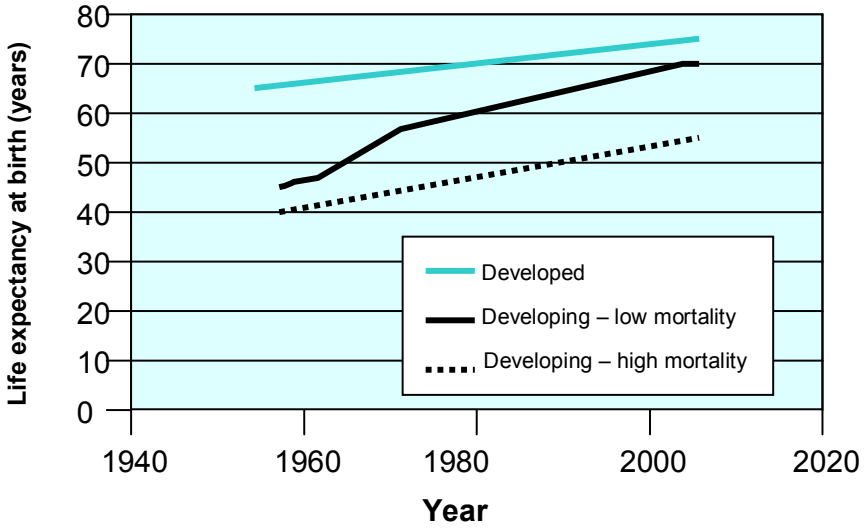
Given the weakness of the evidence base, it would be unwise to read too much into detailed differences between or within opportunities. However, a clear message from the calculations is that in general, the benefits from investing in communicable disease control greatly exceed the costs. It remains unclear whether greater priority should be given to controlling one specific disease, such as malaria or HIV/AIDS, or to a package of priority health services, and the decision will depend to a considerable degree on total funding available. However it cannot be emphasised enough that these three opportunities are not completely independent – both malaria and HIV/AIDS control must include a substantial component of strengthening health services if they are to be successful.

Finally, it should be noted that the productivity of health expenditure is likely to be greater both in a supportive policy environment, and where complementary investments take place, for example in female education.

1. The challenge of communicable disease

Over the second half of the twentieth century, the world has seen enormous improvement in health. Between 1960 and 1995, life expectancy in low income countries improved by 22 years, in contrast to 9 years in developed countries (*1*). However, developing countries have benefited unequally from health gains (*2*): the large life expectancy gap between developed and developing countries in the 1950s has changed to a large gap between developing countries with persisting high mortality (mainly in SSA), and those who have experienced rapidly falling mortality (Figure 1.1). For example, average adult life expectancy is below 40 years in several countries in the developing world, particularly in those severely affected by HIV such as Botswana. Sierra Leone has the highest mortality rates for infants and children under 5 years old in the world (*3*).

Figure 1.1: Life expectancy at birth, 1955-2002 (WHO 2003)



Of the 57m deaths in the world in 2002, nearly 20% were children under 5, and 98% of these were in developing countries (*4*). Communicable diseases represent 7 out of the top 10 causes of child deaths in developing countries, and account for around 60% of all such deaths (Table 1.1). Just over 30% of all deaths in developing countries are of adults aged 15-59, in contrast to 20% in developed countries, representing a substantial problem of premature adult mortality with strong economic implications. Within countries, the poorer groups have substantially poorer health than the better off: for example in Cambodia under five mortality in the poorest quintile, 147 per 1000, was three times that of the richest quintile, and in the Central African Republic, under five mortality of 189/1000 in the poorest quintile was double that of the richest quintile (*5*).

Table 1.1 Leading causes of death in children in developing countries, 2002 (*2*)

Rank	Cause	Numbers (000)	% of all deaths
1	Perinatal conditions	2 375	23.1
2	Lower respiratory infections	1 856	18.1
3	Diarrhoeal diseases	1 566	15.2
4	Malaria	1 098	10.7
5	Measles	551	5.4
6	Congenital anomalies	386	3.8
7	HIV/AIDS	370	3.6
8	Pertussis	301	2.9
9	Tetanus	185	1.8
10	Protein-energy malnutrition	138	1.3
	Other causes	1 437	14.0
	Total	**10 263**	**100**

The analysis of avoidable mortality undertaken by Working Group 5 of the Commission on Macroeconomics and Health (CMH) highlights the importance of focusing on communicable disease (*1*). Avoidable mortality is a population's excess risk of dying before age 70, as calculated by comparison with the death rates in another population: in this case non smokers in the richest countries. Table 1.2 shows that almost 90% of deaths in children under five are avoidable, and 84% of deaths in women aged 5-29. Avoidable mortality due largely to communicable disease represents around 90% of all avoidable mortality in all age/sex classes other than middle aged men, for whom it is 80%.

Table 1.2: Risk of dying and avoidable mortality (%) in low- and middle-income countries, 1998 (*1*)

	Males at ages			Females at ages		
Risk of dying	**0 to 4**	**5 to 29**	**30 to 69**	**0 to 4**	**5 to 29**	**30 to 69**
Low- and middle-income countries (a)	8.6	6.1	35.0	8.2	5.6	26.7
Nonsmoking, high-income population (b)	1.2	2.2	19.2	1.0	0.9	12.6
Excess risk of dying (avoidable mortality) in low- and middle-income countries (c = a – b)	7.3	3.9	15.7	7.2	4.7	14.2
Relative contribution of avoidable mortality to risk of dying in low- and middle-income countries (d = c/a)	86	63	45	88	84	53
Relative contribution of Group 1* causes to avoidable mortality	91	94	80	93	97	91

*Communicable diseases, maternal conditions, perinatal conditions, nutritional deficiencies

Historically, rapid declines in mortality have been the result of access to better housing, sanitation and education, growing incomes, and public health measures such as vaccination. The benefits of research mean that tools and approaches now exist to address the great majority of the burden of communicable disease, most notably malaria, TB, and HIV/AIDS, as well as vaccine preventable diseases. This helps to explain the current international focus on tackling these diseases. However, as Table 1.1 demonstrates, large numbers of people do not have effective access to prevention and treatment, and as a result die. For example, coverage of DPT3[1] is under 50% for children in households living below the poverty line of $1 per day (*5*); and only 2% of

[1] The third dose of the DPT vaccine, commonly used as a proxy for vaccination coverage

children are protected from malaria by sleeping under insecticide treated mosquito nets in Sub-Saharan Africa (*6*).

The control of communicable disease is achieved by some combination – depending on the disease – of action through a health service infrastructure and through specific targeted efforts which in some instances depend on the infrastructure and in others are independent of it. Hence the evaluation of the case for controlling specific communicable diseases cannot ignore its relationship with the health system. However, issues of whether successful health improvement can be achieved by general health system strengthening, or by targeted efforts focused on specific diseases, have been the subject of considerable controversy (*7*). The reality is that with the very unusual exception of diseases that can be eradicated (notably smallpox in the past and polio in the future), sustainable health improvement requires some combination of a strengthened and accessible health service plus focused efforts to strengthen the control of priority diseases. Nonetheless, given limited resources, there are choices to make, which this paper seeks to evaluate.

The paper has chosen to focus on three opportunities:

- Malaria control
- HIV/AIDS control
- Scaled up basic health services.

As emphasised above, this definition of the opportunities should not be taken to imply that these are completely distinct efforts. Expanded and improved basic health services are a precondition for malaria and HIV/AIDS control, though also address a much broader range of conditions including other communicable diseases such as acute respiratory infections, diarrhoeal diseases, TB, vaccine preventable diseases, and maternal/perinatal conditions. This categorisation of opportunities has been chosen largely because malaria and HIV/AIDS are major causes of disease burden and economic losses; cost-effective interventions are known to exist for their control; there is recent literature which can be drawn on to estimate costs and benefits; and these diseases are currently the focus of world attention. Basic health services have been chosen as the third opportunity since they address a major part of the disease burden affecting poor countries, and represent explicitly the infrastructure that needs to be in place for people's main health needs to be met.

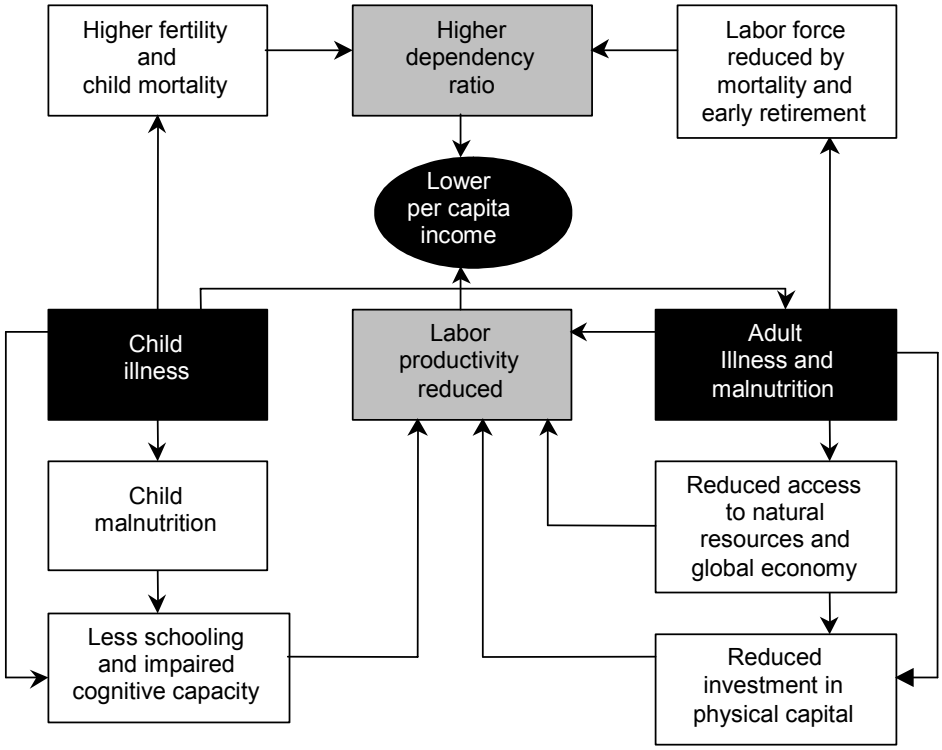
The following section provides an overview of the economic benefits of improved health, discusses the availability of evidence, and outlines the overall approach taken in the paper to estimating costs and benefits. Subsequent sections address each opportunity. A final section discusses methodological weaknesses and limitations, and draws conclusions.

2 Assessing the opportunities

2.1 The economic benefits of improved health and the availability of evidence

Health has both consumption and investment benefits. In other words, it is valued for its own sake, as well as a means to achieve other goals (such as a good income). The relationship between illness and income is complex, as illustrated in Figure 2.1 (*8*). Effects are felt both directly (through the immediate impact of ill health on productive activities) and indirectly, via the effects of illness on fertility, morbidity,

Figure 2.1: Channels through which illness reduces income (Ruger, et al 2001)



mortality and intellectual capacity, and hence on the labour force size, composition and quality, and on the capacity of countries to engage in the global economy.

Disease has been shown to have a major impact on the economy through these effects on productivity, education, and investment. As people fall ill, they are less likely to be able to work and less likely to be productive if they can. People have weaker incentives to invest in their education if it is uncertain that they will be alive to reap the benefits. There is also less incentive for people to save for their retirement, as shorter life spans reduce the value of saving and investment in productive assets. As foreign investors withdraw their money from these areas, the economic costs of disease are exacerbated (*9*). However, it has been argued that effective intervention can thrust the economy just as powerfully in a positive direction. Better health can lead to a demographic transition and economic growth in the long term. Initial reductions in child mortality are followed by a decline in fertility. As the flood of new children mature and reach working age, and a larger proportion of people are able to contribute to the economy, the wealth of the society rises substantially as is argued to have happened in East Asia between 1965-

2 (*9*). The massive improvements in public health that occurred in East Asia between 1965-1990 most powerfully show these effects, and may have accounted for as much as 1.68% of its economic growth during this period (*10*).

The CMH recently argued that the impact of health on economic development has been underestimated (*8, 11*), and that health improvements globally during the 20th century contributed as much, or more, to improvements in economic welfare as the innovations and expansion in material goods and services. Such conclusions have been drawn from studies which seek to explore the determinants of economic growth, and in particular the influence of improved health status. From the perspective of this paper, this literature presents two problems: it is not disease specific; and it does not address well what type of action might best improve health.

Empirical studies of the relationship between disease and economic outcomes fall into two categories: microeconomic and macroeconomic. The former study the link between disease/ill health at household or individual level. Usually they document the costs that disease imposes on the household, but not explicitly the benefits of disease control. Costs are commonly categorised as direct (household and government expenditure on prevention and treatment), and indirect (loss of productivity due to illness and death). There are strong reasons to believe that this simple methodology does not measure the true economic impact of a disease, not least because in response, households and firms adapt their productive activities, or 'cope'. Coping mechanisms are defined as strategies adopted by family members, friends and colleagues to minimise the effects of an illness on the welfare of all concerned (*12*). Sauerborn *et al.* identified 11 different kinds of household coping behaviours in response to illness episodes of all kinds in rural Burkina Faso (*13*). The most commonly used strategy was intra-household labour substitution in response to lost work time of household members. Direct costs were usually met by mobilising cash reserves and savings, selling livestock, or receiving gifts from other households.

Such strategies may have knock-on effects through depleted capital stock, lost savings and indebtedness. The sale of assets such as livestock potentially jeopardises the household asset base, with households emerging more vulnerable and less able to cope with further crises (*13*). A household without livestock, and unable to rely on gifts, may be forced to take out loans which could lead to serious debt and future impoverishment (*12*). These knock-on effects ultimately affect supply or production through low saving and investment. Furthermore, this means that the causal relationship by which disease affects the economy may not necessarily be through sick labour only, but also through lost capital and purchasing power.

The potential for labour substitution crucially affects the degree to which any loss of time is translated into a loss of output. Unemployment and underemployment are common features of underdeveloped economies, and farming is often undertaken communally, in households or extended families. In the event of temporary disability of a household member, the family workforce may provide a cushion, limiting the consequent loss of output. During some seasons, agricultural underemployment may be so prevalent that time lost by sick individuals can be fully compensated for. Similarly in the industrial and service sectors, other members of the workforce may cover to some extent for sick colleagues.

However, even if market output were maintained, there may be costs associated with labour substitution, depending on the value of the activities from which the substituting labour is withdrawn (*12*). Moreover, assessment of a single measure of household output, such as agricultural production, will not capture the total impact on household welfare as it ignores the quantity and quality of home production such as food preparation or child care, and participation in other activities, such as education or social organisations.

Coping strategies are likely to respond not only to actual illness, but also to the *risk* of disease. The risk of poor health status may have a pervasive effect on economic incentives, behaviour and strategies (*14*). Households and firms respond with anticipatory coping strategies, ranging from insurance mechanisms to changes in the organisation of productive activities (*12*). Although formal insurance is rare in developing countries, informal mechanisms are common, including social networks and community organisations, and incur administrative costs which produce efficiency losses in comparison with a risk-free setting. Precautionary measures affecting the organisation of economic activity are likely to have wide-reaching economic effects. High rates of absenteeism may engender labour supply responses such as limiting staff specialisation and maintaining labour reserves to reduce the risk of labour shortages at key times of the year, reducing the average labour productivity of all staff. Households may respond to the risk of high financial expenditure for serious illness by reducing their level of investment, or investing in assets which have higher liquidity but lower returns. Finally, the risk of disease may affect reproductive as well as productive strategies, for example increasing desired family size to insure against high rates of child mortality and increase the family's ability to cope when illness occurs (*12*).

The impact of these anticipatory coping strategies cannot be captured by comparing households or firms exposed to the same degree of risk because they reduce the average productivity of all households and firms, not just those experiencing illness during the study period. Thus microeconomic estimates are likely to be an underestimate.

In contrast, macroeconomic studies assess the influence of a disease on national income in cross-country comparisons, and methods and data permitting, are better able than microeconomic studies to reflect the wide-ranging and dynamic implications of ill health. Again such studies usually document the cost of disease, but only by implication the benefits of reduced disease. Compared to microeconomic studies, the volume of the macroeconomic literature is far more limited. Apart from the many econometric difficulties encountered such as omitted variable bias, there are problems in measures and data on disease prevalence, leading to some uncertainty on whether such studies really are picking up the impact of the disease in question.

There is some considerable overlap in the literature on the economic impact of malaria and that of HIV in terms of the mechanisms of influence. To a considerable extent ill health has common effects on households and the broader economy, though these can also differ depending on the nature of the disease. In particular, HIV/AIDS affects primarily adults, and malaria affects mainly children (in high burden settings), leading to some distinctly different effects (for example, malaria in children is unlikely to lead to the dissolution of a household, whereas HIV might well do so; severe malaria in children can have long term effects on intellectual development). For convenience in reflecting the body of evidence on each of the diseases, the detailed evidence on

economic impact is included in the disease specific sections, although this inevitably leads to some repetition of mechanisms between sections.

Studies – of which there are many – which evaluate actual interventions almost always have employed the analytical approach of cost-effectiveness analysis (CEA) rather than cost-benefit analysis (CBA), thus calculating cost per unit of health effect (such as a life saved, or a Disability Adjusted Life Year (DALY)[2] averted). Using these studies to evaluate the efficiency of health interventions in units that are comparable across economic sectors requires a monetary value to be placed on a human life. This value, the value of a statistical life (VSL), is intended to represent the marginal cost or benefit of saving a life to society (*15*). Two approaches may be taken to determine the VSL. The Human Capital approach assumes that productivity is a proxy for utility and estimates the VSL in terms of the present value of an individual's future earnings. It can be assumed to provide a lower bound on the value of life. Alternatively, a Willingness-to-Pay approach may be used, which assumes that an individual's preferences are reflected in his actual or hypothetical choices according to market prices. To translate cost-per-health effect into monetary metric, either of these approaches may be used. While research on the willingness-to-pay for a human life has been done in high-income countries (*16*), estimates for low income countries rely largely on expert opinion. For example the CMH argued that conventionally, each DALY can be valued at 'a multiple of annual income' (*17*). Lower cut-off points are more normally applied in low and middle income country settings: for example $25 per DALY as a criterion for a 'highly attractive' intervention, and $150 for an 'attractive' intervention (c1996 values) (*18*). In contrast, it has been argued that the UK cut off is around £30,000 (c$54,000), and possibly as high as £45,000 (c$80,000) (*19*), reflecting approximately two times per capita income.

Two other issues arise in drawing on this cost-effectiveness literature, which stem from its origin in clinical trials. Firstly, the evidence of efficacy produced by trials may provide a poor guide to the impact expected from routine service provision[3]. Secondly, such trials usually evaluate an intervention delivered on its own (eg insecticide treated nets (ITNs) for malaria control) whereas in reality packages of interventions are provided (eg ITNs plus treatment of child fevers). Interventions may be synergistic or competing, making it difficult to extrapolate the benefits of packages. Finally, the quantity of literature is very limited with respect to both geographical coverage and the range of interventions that require evaluation.
Nonetheless, these cost-effectiveness studies represent an important source of evidence. Moreover, systematic approaches have recently been applied to the synthesis of both epidemiological studies and economic studies[4], making judgements on the quality of the evidence, and drawing conclusions on both the health outcomes of interventions and cost-effectiveness. Given the existence of these syntheses for both malaria and HIV/AIDS interventions, this paper relies on these reviews rather than the original studies.

[2] DALYs are probably now the most commonly used unit of health outcome. They sum years of life gained and years lived with disability, weighted by the severity of the disability.
[3] Epidemiologists distinguish efficacy, that obtained under ideal conditions (usually a research study), with effectiveness, that obtained under more normal service conditions.
[4] The Cochrane library is one of the most up-to-date catalogue of reviews on the appropriateness and effectiveness of medical interventions, and can be accessed at http://www.cochrane.org/reviews/clibintro.htm

Benefits of disease control include not only health benefits, but also resource savings, as when preventive interventions reduce the need for treatment. While some cost-effectiveness studies take these into account, in general they are often neglected, in part because of equity concerns: resources are only saved if used in the first place, and those population groups which have worst access to care will spend less (and have less spent on them).

2.2 Methodological approach adopted

Given the limitations of the literature, the following approach was adopted. In general, conservative assumptions were made. For each opportunity, several different approaches were adopted to estimate costs and benefits. For the two diseases (malaria and HIV), evidence was drawn from three different sources:

- Studies of the macroeconomic impact of the disease
- Studies of the cost-effectiveness of interventions
- Evidence of the costs and health benefits of large scale programmes.

For basic health services, evidence was drawn from three different sources:

- Regression analyses that measured the effectiveness of health expenditure in generating health outcomes
- A major report to determine the cost of interventions that should take priority
- An analysis that determined the costs and benefits of a package of interventions that was recommended in the 1993 World Development Report.

Given the limitations of the literature in terms both of quantity and quality, and the need to try and be comprehensive in estimates of costs and benefits, these were where possible calculated by the authors based on the literature rather than limiting the paper only to costs and benefits actually provided in the literature. This also enables the paper to seek some degree of consistency in terms of years and scope of costs and benefits. Since the literature has very limited and patchy geographical coverage, rather than make heroic assumptions extrapolating country specific analyses to the whole developing world, costs and benefits were calculated for the geographical entity from where the evidence came. While this means that estimates cover very different areas, taken together the evidence gives a sense of the overall balance of costs and benefits.

Given the geographical focus of this paper, benefits accrue to the populations of low and middle income countries and if valued according to exchange rate conversions, would understate benefits when compared to another challenge where benefits to high income populations are included. Costs and benefits were therefore adjusted for Purchasing Power Parity (PPP), and expressed in 2003 international dollars (Int$). Each year of life lost (YLL), or DALY[5], was valued at per capita Gross National Income (GNI). Depending on the population served, the corresponding GNI was used to represent this value, or ceiling ratio (Table 2.1). While this choice of value is arbitrary, it is a conservative reflection of the level of its income the developed world is willing to spend on saving a year of life. To avoid disadvantaging low income countries (since the lower their income, the lower the value of benefits), results were recalculated in the

[5] both were used, depending on the original source. In general, for the conditions considered here which cause death, YLLs dominate in the DALY and so the values are very similar

sensitivity analysis using a standard value of Int$3,830/YLL or DALY averted, the mean GNI for low and middle income countries.

Table 2.1: Value of a DALY/YLL

Region	2001 PPP adjusted per-capita GNI (2003 Int$)	2001 per-capita GNI (2003 US$)
Low & middle income	$3,830	$1,160
East Asia & Pacific	$3,790	$900
Europe & Central Asia	$6,320	$1,970
Latin America & Caribbean	$6,900	$3,580
Middle East & North Africa	$5,430	$2,220
South Asia	$2,570	$450
Sub-Saharan Africa	$1,750	$460
Thailand	$6,230	$1,940
South Africa	$10,910	$2,820

Figures taken from (*3*).

Costs were calculated from a social perspective (ie including costs to both providers and users) where data permitted, though they often reflected provider costs only. Reductions in treatment expenditures arising from disease prevention were included where possible.

To make results comparable to those in other Challenge Papers, estimates were presented in terms of annualised net-benefit (ANB) and benefit-cost ratios (BCR). Where absolute levels of benefits and costs could not be estimated from information given in the literature, benefits were estimated from cost effectiveness ratios by dividing them by the ceiling ratio appropriate to the study. Where it was possible to estimate total costs and benefits, net-benefit was calculated with the equation (1):

$$NB_{Individual} = (R_C * Benefis) - Costs \qquad \text{(eq. 1)}$$

where Rc represents the ceiling ratio. Evidence of absolute costs and health benefits was given in two estimates from successful programmes (*20*) (*21*). Costs and benefits for individuals were calculated for other estimates, and scaled up to incremental target coverage levels for the population in need (PIN) (equation 2).

$$NB_{Total} = NB_{Individual} * Coverage * PIN \qquad \text{(eq. 2)}$$

Where possible, costs and benefits were estimated for the period 2002 to 2015 (to coincide with the Millennium Development Goals (MDGs)) and MDG targets were used, where relevant, to establish the desirable scale of interventions. Costs and benefits were adjusted by a discount rate (DCR) of 3%. Sensitivity analysis was used to explore the sensitivity of costs and benefits to changed assumptions, including a higher DCR (6%) and common ceiling ratio (Int$3,830).

For all models, it was assumed that scaled up coverage targets were achieved instantaneously. Where specific evidence was unavailable, parameter values were extrapolated assuming linear growth rates and relationships between data points calculated as incremental values: additional amounts relative to the costs and benefits of existing programmes.

3 Control of malaria

3.1 Identification and description

Introductory statistics

Malaria is the most important of the parasitic diseases of humans. Transmission occurs in 103 countries; more than 1bn people live in malarious areas; and between 1-3m people die from malaria each year. Malaria was eradicated from North America, Europe and Russia over the twentieth century, and for a period was substantially controlled in much of South Asia, but in recent decades has resurged. The increased threat from malaria is particularly a result of international neglect of the disease in the 1980s onwards following realisation that malaria eradication was not feasible; and major and increasing problems of resistance to the most commonly used drugs and insecticides.

Malaria is caused by four different species of the genus *Plasmodium*, of which the most dangerous is *P. falciparum*. Human infection occurs when the malaria vector, a female mosquito of the *Anopheles* genus, inoculates sporozoites from its salivary glands when it bites humans. The parasite reproduces within the human host, and the disease is transmitted by gametocytes in the blood meal when further female anophelene mosquitoes feed on the infected individual.

Epidemiological description

Malaria is primarily a tropical disease. *P. falciparum* predominates in SSA, which as a result bears over 85% of the disease burden and 90% of malarial deaths. *P. vivax* is more common in Central America and the Indian subcontinent. The epidemiology of malaria is complex, varying considerably from place to place. Transmission is termed stable when infection occurs all year round. In these settings small children are infected repeatedly early in life, and morbidity and mortality are considerable: (*22, 23*). Through repeated infection children develop immunity, meaning that as adults they may suffer febrile episodes but are very unlikely to die from malaria. Pregnant women are the other population group at high risk, since their immunity is impaired especially in the first pregnancy. In contrast, where transmission is low, unstable or very focal (termed unstable transmission), immunity is not acquired and symptomatic disease may occur at all ages. Areas with unstable malaria are prone to epidemics – for example northern India, Sri Lanka, Southeast Asia, southern Africa – which can cause many deaths.

The number of children dying of malaria rose substantially in eastern and southern Africa during the first half of the 1990s as compared to the 1980s, while in West Africa there was little change in the overall malaria mortality rate in children (*6*). The most likely explanation is the rapidly increasing levels of resistance to chloroquine (the most widely used treatment drug) in eastern and southern Africa.

Defining and measuring the malaria disease burden

Defining and measuring the health burden of malaria presents some major difficulties.

Mortality
Estimating the number of deaths due to malaria is notoriously problematic (*24*). Post-mortem questionnaires are relatively insensitive for detecting malaria deaths, because of the similarities between the symptoms of malaria and other severe diseases, such as pneumonia (*25*). Official reporting systems are often unreliable, as in many areas of Africa the majority of deaths occur at home and are not formally registered.

Malaria can contribute to death in young children in three main ways:

- an overwhelming acute infection can kill a child quickly
- repeated infections contribute to the development of severe anaemia, which substantially increases the risk of death
- low birthweight, a frequent consequence of malaria infection in pregnancy, is the major risk factor for death in the first month of life.

In addition, repeated infections make young children more susceptible to other common childhood diseases.

In SSA it is estimated that around 20% of mortality of children under 5 is due to malaria, and malaria is the most important single infectious agent causing death in young children. Around 1m deaths (range .744-1.3m) are estimated to occur in Africa, more than 75% of them in children (*26*).

Episodes of uncomplicated malaria
Uncomplicated malaria is typically treated on the basis of clinical symptoms alone. 400-900m acute febrile episodes are thought to occur yearly in African children under 5 living in endemic areas (*26*). If 30-60% of these children were parasitaemic, as reported in some studies, malaria cases in children would be 200-450m annually. Older age groups in Africa have around 0.4-1 episodes of malaria a year, and probably 2 or more febrile episodes. Worldwide there may be well over 2bn febrile episodes annually resembling malaria.

Severe disease
Severe malaria has two major clinical syndromes: malaria with respiratory distress; and malaria with neurological disturbance, or cerebral malaria (*27*). These occur primarily among children, but also affect adults in areas of low or unstable transmission. An estimated 3% of all attacks are severe, and in the absence of inpatient treatment around half of cases are likely to die (*28*). Even with optimal management of treatment, case fatality rates for cerebral malaria are around 19%, and would be much higher in many hospital settings in Africa given lack of resources and skilled staff.

Anaemia
Malaria is an important cause of anaemia in SSA (*24*). The severe form is a life-threatening condition in young children and often warrants blood transfusion, which increases the risk of HIV infection. In malaria-endemic areas, the incidence and age pattern of severe anaemia are strongly dependent on the intensity of *P. falciparum* transmission (*29*), and malaria control trials have been associated with significant reductions in the prevalence of anaemia in children and pregnant women (*30*).

Malaria in pregnancy
Anaemia is also a harmful manifestation of malaria in pregnancy. Pregnant women, as a result of malaria infection and especially in their first pregnancy, experience an

increased risk of maternal anaemia, abortion, still birth, and low birth weight, due to both prematurity and intra-uterine growth retardation (*31*). This is of particular concern because low birth weight is associated with increased neonatal mortality (*32*).

Interaction with other diseases

In addition to its direct role in morbidity and mortality, malaria is also thought to have a significant indirect effect in conjunction with other common diseases such as measles, respiratory infections, diarrhoeal disease and malnutrition, although the extent of the indirect impact is difficult to measure and not well understood. Evidence for a significant indirect effect is bolstered by malaria control trials which have found much larger reductions in all-cause mortality than would have been expected from data on malaria specific mortality alone (*30*). Moreover, the use of insecticide treated mosquito nets (ITNs) has led to reductions in deaths attributed to acute respiratory infections, acute gastro-enteritis and malnutrition as well as malaria (*33*). However, during the Garki project of residual spraying and mass drug administration, malaria control led to less than the expected impact on all-cause child mortality, which may be because children face "competing risks" from other potentially fatal diseases, so that a reduction in malaria risk increases their likelihood of falling victim to another cause (*34*).

Intellectual development

Although evidence is limited, it is likely that malaria significantly affects intellectual development and since variations in reasoning ability, cognitive skill, and years of schooling are considered to be important determinants of future variations in productivity and earnings of individuals (*35*), the economic impact is likely to be significant.

Survivors of cerebral malaria may be left with neurological sequelae including weakness in the limbs, speech disorders, behavioural disorders, blindness, hearing impairment, cerebral palsy and epilepsy. A review of comparable studies of African children found that 16% of cerebral malaria survivors had some kind of neurological sequelae at discharge, and for 6% of children these defects persisted for at least 6 months (*24*). No data were available on residual sequelae among adults.

There is good evidence on the association between iron deficiency anaemia (IDA) and poor performance in infant development scales, IQ and learning tasks in pre-school children and educational achievement among school-age children (*36*). Iron supplementation has been associated with improvement in mental development scale scores in infants (*37*) and significant increases in school achievement scores (*38*). However, it is not clear whether these findings for IDA apply equally to children with the type of anaemia associated with malaria.

Malaria may also affect intellectual development through the impact on school attendance. A study in the Gambia of the effects of insecticide-treated mosquito nets found that absenteeism because of fever was significantly higher in the control group (*39*).

Microeconomic Impact of Malaria

Microeconomic studies are concerned with impact at the level of a productive unit such as the household or firm. There is quite a voluminous literature, which we lack space to cover here but which is reviewed in (*40*).

Evidence on direct costs suggests that households can spend quite substantial sums on prevention and especially treatment, and also that direct costs to governments are substantial (for example an estimated 19% of the Rwandan Ministry of Health recurrent budget (*41*). In terms of indirect costs, the average time lost per episode for a sick adult ranges from 1 to 5 days, though these averages conceal considerable variation across individuals (*40*). In order to estimate total costs, Ettling *et al*. (*42*), using data from Malawi, multiplied the cost per episode by the predicted number of episodes per year and average household size to obtain a total annual cost per household of $40.02 or 7.2% of household income. For very low income households the total cost was $24.89, equivalent to 32% of income. Leighton and Foster (*43*) found that total household costs amounted to 9-18% of annual income for small farmers in Kenya, and 7-13% in Nigeria. Only one study, by Shepard *et al*. (*44*), has attempted to use such data to estimate the overall economic cost of malaria morbidity and mortality in Africa. Based on extrapolations from four country case studies in Burkina Faso (one district), Chad (one district), Congo (Brazzaville), and Rwanda, the total direct and indirect cost in 1987 was estimated to be $1,064m, $3.15 per capita, and 0.6% of the sub-Saharan Africa GDP (1999 prices). The authors predicted that the total cost would increase substantially over time based on projected increases in population, malaria incidence, the value of output, and the cost of antimalarials.

However this evidence on the microeconomic impact of malaria is in general partial and of questionable accuracy (*40, 45*), and there are many problems in using such data to reflect the burden to society or the potential benefits from control. Studies have generally focussed on febrile illness, overestimating the burden of uncomplicated malaria but underestimating the costs of severe illness, other debilitating manifestations (especially neurological sequelae, anaemia and cognitive development), and mortality. Many studies use inadequate data to calculate indirect costs, failing to account for seasonal variations, the difference between the average and marginal product of labour, and the ways households and firms "cope" in response to illness episodes. An alternative approach has been to estimate the net impact on output by looking directly at the statistical association between malaria and agricultural output through a production function (*46*). Findings have been contradictory, at least in part because of data and methodological weaknesses.

The evidence on the extent to which the burden falls more heavily on lower socio-economic groups is reasonably consistent (*47*). Studies examining socio-economic status using assets, education, and occupation all yield data that suggest an inverse relationship between the impact of malaria and socio-economic status.
Evidence on the impact of coping strategies in response to the *risk* of disease is fragmentary. Such strategies probably affect fertility decisions and crop choices, for example, but are difficult to identify since they reduce the average productivity of all households and firms, not just those experiencing illness during the study period. It is ironic that precautionary measures against the risk of malaria may lead analysts to conclude that the economic impact of malaria episodes is low, when the reverse is the

case. For example, maintaining a labour surplus, which is very costly to firms or households, would permit a high degree of labour substitution in response to a single episode.

Macroeconomic impact of malaria

Studies of the macroeconomic impact of malaria have produced conflicting results. Barlow (*48*) analysed the impact of near-eradication of malaria in Sri Lanka using a macro model which encompassed both demographic and economic variables, such as the labour force, savings and investment and public expenditure. He argued that, although there may have been a positive impact during the first decade, in the long-run the growth of output would have been outstripped by population growth, reducing real income per capita. These conclusions should be treated with caution for several reasons. The impact of malaria eradication on population growth in Sri Lanka has been a subject of great controversy, with some analysts arguing that its contribution was much lower than that assumed by Barlow. Borts argued that malaria control may change household savings behaviour if the productivity of capital is increased through, for example, the opening up of more productive land (*49*). More generally, models such as Barlow's have been criticised for over-emphasising the role of capital formation in economic growth. Finally, the relevance of Sri Lanka's experience to contemporary Africa is questionable, given that population density and demographic trends are very different, and malaria interventions focus on control rather than eradication.

A recently applied alternative approach has been to use malaria as an explanatory variable in economic growth models in the style of Barro (*50*). Gallup and Sachs (2001) used cross country regression analysis to relate the growth in GDP per capita between 1965 and 1990 to initial income levels, initial human capital stock, policy variables, geographical variables and a 'malaria index', calculated as the product of the fraction of land area with endemic malaria in 1965 and the fraction of malaria cases that were *P. falciparum* in 1990 (*51*). Their results suggested that countries with a substantial amount of malaria grew 1.3% per year less between 1965 and 1990 (controlling for other influences on growth), and that a 10% reduction in malaria was associated with 0.3% higher growth per year. McCarthy *et al*. employed a similar cross-sectional regression approach to explore the impact of malaria on average per capita growth rate in three five-year periods. They proxied the malaria burden with data on the incidence of malaria episodes, to account for the impact of differing use of protective measures on actual morbidity with given exposure (*52*). They also found a significant negative association between malaria and economic growth, although the estimated impact differed sharply across countries. The impact was smaller than that found by Gallup and Sachs, exceeding 0.25% per year in a quarter of the sample countries, and averaging 0.55% for those located in SSA[6].

[6] Reasons for the differences between the two models remain to be fully explored. A potential explanation lies in the time frame used in each evaluation; Gallup and Sachs (2001) use a dataset that spans 1965-1990 based on historical maps, while McCarthy and colleagues (2000) use WHO data between 1983-1997. A sizeable proportion of the advances in malaria control were lost during the 1980s, so the model by McCarthy *et al.* does not reflect many of the advances made previous to those years. Also, Gallup and Sachs use a malaria index, which ties the burden strongly to prevalence and geography. McCarthy et al consider that the distribution and amount of national income, along with access to health facilities, reduces the detrimental effects to the economy. The measure that McCarthy *et al*. use ties malaria prevalence less strongly to the detrimental effects of the disease.

These differences in growth rates translate into substantial differences in levels of income: for example countries with intensive malaria had income levels in 1995 only 33% that of countries without malaria, whether or not the countries were in Africa (*51*).

The contrasts between these results and those based on direct and indirect costs and production functions highlights the need to develop a much deeper understanding of the mechanisms by which malaria affects households and economies. Without this, it is difficult to evaluate existing estimates, both micro and macro.

3.2 Alleviation of the challenge – interventions against malaria

Compared to some tropical diseases, the epidemiological and cost-effectiveness literature on malaria is relatively strong for some key interventions (*28*), though **e**vidence of effectiveness is almost only available for individual interventions. In order to approximate a more realistic scenario, we identified a limited package of interventions whose total costs and benefits could be estimated[7]. Interventions were included that minimised overlap of target groups while maximising population coverage. Synergies in the costs and effects of different interventions was not considered due to lack of evidence. SSA was chosen as the geographical context, as 90% of the global burden of malaria falls on this region.

The package evaluated included two preventive interventions targeted to different population groups and one treatment intervention. An insecticide treated mosquito net (ITN) programme was included to reduce infections in children under 5 years in SSA as trials have shown they reduce overall child mortality by 19%[8] (*53*). However, only a small proportion of African children under 5 years old actually receive this protection (*6*). Residual spraying of homes with insecticide and chemoprophylaxis of children were excluded from the package as they target the same individuals.

Intermittent treatment of pregnant women (IPTp) in their first pregnancy (primigravidae) was included to protect children from dying from complications associated with low birth weight (*54*). In 1986, the WHO advocated that all pregnant women living in endemic areas be protected against malaria. Since concerns exist about the safety of prescribing new artemisinin-based combination therapies to pregnant women (*55*), and chloroquine (CQ) is associated with problems of resistance and compliance (*56, 57*), sulfadoxine pyramethamine (SP) is the recommended prophylactic therapy. IPTp consists of two curative doses given during the first and second trimesters of pregnancy during antenatal care visits. Antenatal care is common (around 65% coverage) in SSA; however, a considerable amount of scaling up of IPTp is needed as few of these women currently receive antimalarials.

A switch to artimisinin-based combination therapy (ACT) in SSA plus dipstick diagnosis was included as the treatment intervention as existing therapies, such as CQ and SP, are declining in efficacy. The WHO has argued that appropriate and timely case management should be seen as a key component of any malaria control programme (*58*). In reality, case management is often inadequate. The African Malaria Report 2003 reported that more than 80% of children treated for malaria received CQ, (*6*). A few

[7] This package should not be interpreted as a policy recommendation, but is selected purely for use here.
[8] Other age groups are likely to benefit from these nets, but to an unknown extent.

countries have switched to SP, but resistance is expected to increase rapidly to this drug: for example in Burundi, resistance to SP is already 50% (*59*).

Artemisinin derivatives provide an efficacious alternative to SP, and using them in combination with longer-acting drugs is likely to slow the growth of resistance (*56*). Artemisinins are eliminated from the body relatively quickly, reducing the time that they exist at sub-therapeutic concentrations which is when mutant parasites with small selective advantages proliferate relative to the rest of the parasite population, and drug resistance begins to develop. These parasites can be residual parasites not yet cleared from the initial infection, or those inoculated by a new infectious bite. In theory, the longer acting drug in the combination will protect the artemisinin derivative by maintaining therapeutic levels as the artemisinin is eliminated (*60*). South Africa has fully switched its first line drug policy to ACTs, and Tanzania, Zanzibar, and Burundi are all in the process of making the change (*6*). Although the technology has still to be fully developed for use in SSA, dipstick diagnosis was included with ACTs, in order to target treatment to those with malaria and avoid using expensive drugs for all fevers.

In addition to changing first line therapy, scaling up programmes to expand malaria treatment coverage is needed urgently. Approximately 42% of children with malaria receive antimalarials (*6*), and the majority of deaths in hospital occur within 24 hours of treatment, indicating that treatment was received too late (*61*). Prime reasons for low coverage include poor physical accessibility of health facilities and low levels of affordability of treatment (*62*).

3.3 Side effects

Positive side effects
Positive side effects in terms of economic development and improved individual welfare are taken into account as far as possible in the calculations below, so are not further discussed here.

Negative side effects
Medical interventions have both benefits and risks. In general, the licensing process for drugs, vaccines and chemicals used to improve human health requires good evidence on adverse effects. Beyond this, WHO, as the global normative authority, may choose not to recommend that countries use a particular product if it judges the evidence of benefit or adverse effects to be not sufficiently strong, and the balance of risks and benefits not sufficiently positive. That said, trials of new products can never be done in all relevant settings, and some adverse effects are rare given the sample size of studies, but nonetheless may be sufficiently serious to warrant withdrawal of a product. Monitoring systems exist in the more developed world to check for adverse reactions, though are rarely 100% effective given the difficulties of associating adverse effects with the product. For products used exclusively in the developing world, it is unlikely that adverse effects will be quickly detected unless they are very obvious.

With respect to the malaria interventions considered here, side effects are not of major concern. Insecticides recommended for use on nets are evaluated by WHOPES[9]. SP has been chosen as the WHO recommended drug for use in IPTp; adverse effects do

[9] http://www.who.int/ctd/whopes/

occur with SP, but are very rare. Artemisinin and ACTs have been used very widely in China and South East Asia, and appear to have few adverse effects (*63*). One specific concern is that given limited government controls on the use of drugs in low and middle income countries, it is very difficult to regulate the use of new drugs once available on the local market. This has implications for the development of resistance. Drugs taken in doses inadequate to cure the infection, or drugs taken by an uninfected person who subsequently becomes infected, can expose the malaria parasite to suboptimal drug levels, increasing the risk of resistance developing or being transmitted. Approaches to tackling this problem include international agreements with the pharmaceutical industry on marketing drugs; information campaigns to educate consumers on taking full courses of drugs; and drug retailer training programmes. However, since it is unlikely that such efforts will be fully effective, continued investment in the discovery of new drugs is also needed. This comes at a cost, which currently falls mainly on public and charitable funds (channelled though public private partnerships such as MMV[10]), given the limited incentives for the industry to invest in drugs whose market is severely limited by low purchasing power.

3.4 Economic evaluation

Despite the relatively large economic literature on the impact of malaria, especially at the microeconomic level, the volume of research has not produced many estimates of cost-benefit ratios. Recent economic analysis has focused almost exclusively on cost-effectiveness analysis (drawn on below) and cost benefit analyses date from the 1960s and 1970s. Table 3.1 below summarises their results based on a review quoted in Najera et al (*64*). These data are largely of historical interest, and are not used further here: no estimates relate to high transmission settings in SSA, and all rely on control methods (largely residual spraying) which are not favoured today in high transmission settings. However, the attractive benefit cost ratios should be noted.

Table 3.1: Cost-Benefit Ratios in Malaria Control

Source	Country	Method	Benefit Cost Ratio
Barlow 1968	Sri Lanka	Insecticide	146
Griffit, Rampana, and Mashaal 1971	Thailand	Chemoprophylaxis	6.5
Khan 1966	Pakistan	Eradication program	4.9
Livandas and Athanassatos 1963	Greece	Eradication program	17.3
Niazi 1969	Iraq	Eradication program	6.0
Ortiz 1968	Paraguay	Insecticides	3.6
San Pedro 1967	Philippines	Eradication program	2.4
Democratic Republic of Sudan 1975	Sudan	Control program	4.6

Source: Barlow and Grobar 1986.

BCRs and ANBs were estimated for SSA, drawing on recent evidence. Three approaches were taken:

1. macroeconomic evidence was used to estimate the economic costs associated with the burden of malaria and the benefits of malaria control, and related to recently estimated costs of control
2. the intervention package was evaluated based on microeconomic estimates of cost-effectiveness.
3. calculations of costs and benefits were made for Kwa-Zulu Natal in South Africa, which recently changed to an ACT.

[10] Medicines for Malaria Venture

Macroeconomic Approach

The Gallup and Sachs (*51*) and McCarthy *et al.* (*52*) models reviewed above predicted the additional amount that economies would have grown if malaria had been eradicated, the first predicting an additional 1.3% per person growth in annual GDP, and the second an additional 0.55%. While it is unreasonable to expect that current measures against malaria will be able to eradicate the global burden, the United Nations Millennium Project has set a goal to halve the malaria burden in sub-Saharan Africa by 2015 (*65*). Assuming that incremental reductions in malaria elicit economic payoffs at a constant rate, we extrapolated the economic benefits that would result if the Millennium Development Goal were reached. This extrapolation was determined according to a linear function between current and predicted malaria levels.

Working Group 5 (WG5) of the CMH estimated the annual per-capita cost of a package of interventions that would be necessary to achieve the MDG (*1*). For adults, it included recurrent and annual equivalent capital costs of measures to prevent and treat malaria. The costs of treating childhood malaria were aggregated with other medical costs for childhood illness in this report, and we used these costs in their entirety. Costs were averaged across high and low estimates, and discounted into the future. Overall, the cost of reaching the MDG would be Int$21 per person per year.

We calculated benefits by taking the difference between baseline and intervention scenarios of per-person GDP growth. A baseline scenario of economic growth with current levels of malaria was established based on the average annual GDP growth rate in SSA between 1990 and 2001 (2.15% per person per year) (*66*). From this baseline, we extrapolated the benefit of reducing the malaria burden by 50% for the 563 million people living at risk. Results are shown in table 3.2.

Table 3.2: Costs and benefits of malaria control estimated from macroeconomic models (2003 Int$)

Study used	Population benefiting	Total benefit (millions, 2002-15)	Total cost (millions, 2002-2015)	Net-benefit (millions, 2002-2015)	Annualised net-benefit (millions)	Benefit-cost ratio
Gallup and Sachs (2001)	563,282,922	$664,309	$142,473	$521,835	$43,486	4.7
McCarthy et al. (2000)	563,282,922	$275,948	$142,473	$133,475	$11,123	1.9

Population and GDP data taken from (*3*)

Assumptions used for cost and benefit calculations were varied in a rough sensitivity analysis. With a DCR of 6%, the ANB of the Gallup and Sachs (*51*) model decreased by 25%, and the ANB of the model by McCarthy and colleagues (*52*) decreased by 30%.

In their analysis, Gallup and Sachs (*51*) estimated further that a 10% reduction in malaria would allow economies to grow an additional 0.3% per person each year. Using this estimate as the lower limit of the function from which we extrapolated benefits, calculations showed that a 50% reduction in malaria would result in a 0.74% annual increase in per-capita GDP. Total net-benefit increased from $522 billion to $624 billion, and the BCR increased from 4.7 to 5.4.

If costs are decreased by 25% to allow for the costs of non-malaria interventions included in the full child treatment package, the total net-benefit in each scenario increases by $36 billion. The benefit cost ratio increases from 4.7 to 6.2 using Gallup and Sachs estimates, and from 1.9 to 2.6 using McCarthy *et al.*. If costs are increased by an arbitrary 25%, the BCR decreases to 3.7 for Gallup and Sachs and to 1.5 for McCarthy *et al*.

Microeconomic Approach

Microeconomic evidence on the three interventions applied to SSA (ITNs for children under 5 years, IPTp for first pregnancies, and ACTs to treat malaria) was taken from models constructed by teams at the LSHTM which used methods of probabilistic sensitivity analysis, thus allowing ranges of values to be used rather than single point estimates (*28, 67*). In these models, key determinants of cost-effectiveness were also included such as drug resistance, intensity of transmission season, behavioural factors, price of key commodities, and expected mortality. Costs were considered from a provider's perspective for all interventions except for ITNs, where the cost of community time was included. Benefits were measured in terms of DALYs calculated according to Mark II methods with no age weighting (*68*), except for IPTp which estimated YLLs. A standard West African life table was used for life expectancy (*69*).

The net-benefits of ITNs and IPTp were calculated according to income strata as used in the original models. Income strata were defined as having per-capita GNIs of less than Int$1300 for very low income countries, less than Int$3,000 for middle income countries, and above Int$3,000 for higher income countries. Variations in income strata affected staff salary and training costs in these models.

ITNs

The model drew evidence of effectiveness from a Cochrane meta-analysis of large scale trials (*53*). Deltamethrin rather than permethrin was assumed to be the insecticide since deltamethrin's unit cost is lower and it lasts twice as long. Costs in the model were drawn from the economic evaluations that accompanied the trials, published and unpublished literature, and expert consultation. Trials have not been conducted in areas of low-transmission intensity in sub-Saharan Africa, so results are relevant for areas of high and moderate transmission. The model measured effectiveness for children aged 1-59 months only.

Without any intervention, children aged 1-59 months in high transmission areas experience 1 to 2.9 clinical episodes of malaria (*70*). Although the ITN trials found a 19% reduction in all-cause mortality in children aged 1-59 months (*53*), effectiveness in practice can be expected to be lower than effectiveness in a trial. Households may not re-treat their nets, children may not sleep under them during periods of hot weather, other family members may use the nets, and nets may be taken away, destroyed or sold. The average compliance reported in the trials was 65%. Other studies have found that between 20% and 80% of nets are retreated (*71*) and that 57% to 97% of children use nets appropriately (*33, 72, 73*). The latter two estimates were averaged to estimate actual compliance. A linear relationship between compliance and effectiveness was assumed, such that zero compliance resulted in no effectiveness and 65% compliance resulted in the reduction in mortality found in the meta-analysis. Effectiveness results from the meta-analysis were multiplied by the ratio of actual compliance to trial

compliance to estimate effectiveness in a programme situation. Based on these assumptions, it can be expected that protected children will lose 0.19 fewer years due to malaria than unprotected children.

Costs included insecticide, staff, transport, other overheads, community time, a sensitisation and awareness campaign, and the cost of mosquito nets, and were updated to 2003 values from Goodman et al. (*28*). Although the programme was targeted at children aged 1-59 months, it was assumed that 2 - 3.9 nets would need to be supplied per household. The overall cost of the programme was Int$28.47, Int$29.02, and Int$33.50 per child with increasing income strata, with the cost of the net being the most important input.

We predicted the incremental economic returns of scaling up ITN coverage in SSA from 2% to 70% to protect an additional 61,143,375 children under five years old living in endemic areas. The ANB was Int$17 billion, with a BCR of 10. Table 3.3 shows the results by income strata.

Table 3.3: Costs and benefits of ITNs (2003 Int$)

Income strata (value of a DALY)	Additional children covered	Total benefit (millions, per year)	Total cost (millions, per year)	Annual net-benefit (millions)	BCR
Low income (Int$850)	41,445,555	$6,693	$1,179	$5,513	5.7
Middle income (Int$1,863)	14,995,918	$5,308	$435	$4,873	12.2
High income (Int$7,250)	4,701,375	$6,477	$158	$6,319	41.1

Calculated from (*3*), (*28*), (*1*)

The discount rate affects only the useful lifespan of the net, and has very little effect on ANB. Increasing the discount rate from 3% to 6% lowers ANB by less than 1%. Standardising the ceiling ratio to Int$3,830/DALY strongly affected the results, giving a ANB of Int$43 billion and a BCR of 25.1.

For several reasons, the calculation of ANB given by this model may be an overestimate. Families may wash nets more frequently, reducing effectiveness. Overall child mortality may be lower than the predicted baseline in higher income countries, and thus benefits may be exaggerated.

On the other hand, the calculation of ANB may be an underestimate:

- The model considers benefits only for children yet accounts for the cost of enough nets to protect entire families. If distribution were targeted so that only one net could be provided per child, the costs of the programme would be substantially reduced.
- The cost of nets was determined according to the price given for publicly administered programmes; privately-managed social marketing programmes may be able to provide nets at lower cost (*74*)
- A high community level of net use may protect families without nets living in the same area, through the ‘mass effect’ (*75*).

- Control households in epidemiological studies tend to have better outcomes than unobserved families due to the Hawthorne effect[11], thus producing a lower estimate of the difference between intervention and control.

The mechanism used to deliver an ITN programme is of vital importance to its cost-effectiveness. If the cost structure of net provision is shifted from the government to the consumer, overall costs to government would be lower than those found in the trials used in this analysis. However, evidence from the Gambia shows that effectiveness is likely to decrease substantially if this shift occurs, as demand for ITNs is price elastic (*62*). Given that willingness-to-pay (WTP) for nets appears to be greater than WTP for insecticide treatment (*62*), the imminent introduction of long lasting nets which do not require retreatment may increase the effectiveness of private purchases.

Prevention in pregnancy

We based our estimates on the model of Goodman et al that evaluated the cost-effectiveness of using SP to protect foetuses born to primigravidae (*76*). This study used evidence from a Cochrane review of strategies for preventing malaria during pregnancy, whose outcome measure was impact on low birth weight (*54*). In order to estimate impact in terms of deaths, Goodman et al modelled the impact of low birth weight on child survival using a Wilcox-Russell mortality curve and distributions of birth weight for both protected and unprotected foetuses.

Under ideal conditions, this model predicts that 0.011 fewer babies born to primigravidae will die with IPTp. However, treatment failure can occur for several reasons. Women may not begin prophylaxis early enough in their pregnancy, they may not fully comply with the drug regimen, and parasites may carry mutations that confer drug resistance. The model assumed that treatment was only successful if women made at least two visits per pregnancy before the end of their second trimester, took the correct doses at the appropriate times, and were not infected with resistant parasites. The effective reduction in neonatal mortality rate, D, was calculated as

$$D = d * (1-s) * (1-r) * (g + [1-g]z) * v_1 * v_2 \qquad \text{(eq. 3)}$$

where d is the maximum level of possible effectiveness, s is the still birth rate, r is parasite resistance, g is compliance to the correct drug regimen, z is the proportion of under-dosed cases where treatment was still effective, v_1 is the probability of attending the antenatal clinic during the first or second trimester, and v_2 is the probability of returning for a second visit.

It can be expected that drug resistance, r, will change through time. Based on methods used by Coleman et al. (*67*), we assumed that parasite resistance grows according to a sigmoidal trajectory using a logistic function. Longitudinal drug resistance studies in Eastern and Southern Africa suggest that the maximum rate at which resistance grows to SP, k_i, is between 30% and 50% per year (*77*). Current levels of resistance, $R_{i,0}$, were assumed to be 13% according to the mean of 39 sentinel sites in East Africa (*59*). The dynamic spread of drug resistance at time t was modelled using equation x.

[11] http://pespmc1.vub.ac.be/ASC/HAWTHO_EFFEC.html, and http://www.accel-team.com/motivation/hawthorne_02.html

$$R_{i,t} = k_i \left[\frac{R_{i,0}}{R_{i,0} + \left(k_i - R_{i,0}\right)\exp^{-r_i t}} \right] \quad \text{(eq. 4)}$$

A 13 year time frame was used to be consistent with other calculations in this paper. The model predicted that an average of 0.062 YLLs would be averted each year per child born to primigravidae.

Costs were determined according to income strata and updated from Goodman et al. (*76*). It was assumed that antenatal services already existed for women receiving this treatment, and that IPTp was added to the services currently provided. The mean incremental costs per primigravidae were Int$6.59 for very low income strata, Int$7.29 for middle income strata, and Int$12.47 for higher income strata.

This model predicts that the incremental net-benefit of scaling up IPTp from 0% to 90%, to cover an additional 4,860,000 primigravidae[12], will be Int$5,783 million between 2002 and 2015 (BCR of 12.1). Results according to income strata are given in table 3.4.

Table 3.4: Costs and benefits of IPTp (2003 Int$)

Income strata (value of a YLL)	Additional PG covered	Total benefit (millions, 2002-15)	Total cost (millions, 2002-15)	Net-benefit (millions, 2002-15)	Annualised net-benefit (millions)	Benefit-cost ratio
Low income (Int$850)	3,294,313	$2,260	$282	$1,978	$152	8
Middle income (Int$1,863)	1,191,955	$1,792	$112,899	$1,679	$129	16
High income (Int$7,250)	373,732	$2,187	$60,603	$2,126	$164	36.1

Calculated from (*3*), (*28*), (*1*) PG = primagravidae

The DCR has a substantial effect on net benefits because it influences the weight of future treatment failure due to increasing resistance. Changing the DCR from 3% to 6% increases net-benefit by 11%. Standardising the ceiling ratio to Int$3,830/YLL strongly affects results, giving a total net-benefit of Int$14,567 million for 2002-2015 and a BCR of 33.9.

Net-benefits may be underestimated if IPTp has an impact on child mortality beyond 28 days. In addition, the health benefit of IPTp for the mother in terms of reduced anaemia has not been included (*78*).

In other ways, the mortality associated with malaria may be overestimated. As in the ITN model, all cause mortality can be expected to be lower in wealthier counties, which would reduce the incremental mortality averted between the intervention and comparator. Malaria affects birth weight through both pre-term births and retarded interuterine growth during a full term. Mortality rates are higher for pre-term birth than retarded interuterine growth, but it is not clear which mechanism is influenced by SP. If IPTp affects only retarded interuterine growth, net-benefits would be lower.

[12] Based on estimates made by the U.S. Bureau of the Census that the number of births in SSA would increase from 25 million in 1996 to 33 million in 2020

Switching to ACTs

Based on a previous model (*67*), we evaluated the net-benefit of a change in policy from SP to ACT, including the use of dipsticks for diagnosis to ration drugs more efficiently and combat the spread of resistance. To account for resistance and to be consistent with other models, we evaluated this model over a 13 year time frame.

A simple decision tree of the diagnosis and treatment of malaria was used to follow the possible costs and outcomes of a patient presenting with malaria and receiving first line treatment. Costs were attached to the branches of the tree so that a cost would be estimated for each path that an outpatient could be expected to take. Cost per individual outpatient was calculated by multiplying the cost of each branch by the probability that it would be followed. The cost per adult treatment with ACT included an estimate of ACT drug costs (*60, 79*) and ranged between Int$3.57 and Int$8.57. The SP cost (which would be no longer incurred) was fixed at Int$0.50. We assumed that half of the patients presenting with malaria would be under five years old, and that they would receive a half-dose. As switching drug policy for people already receiving treatment is likely to use existing distribution and treatment systems, we assumed that no additional transport, administration, or overhead costs would be incurred.

The decision tree framework is useful because gross costs can be calculated for each strategy, as well as net costs between them. Net costs are particularly relevant for this analysis as ACTs are expected to improve health outcomes significantly. Reductions in the number of persistent cases of uncomplicated malaria and the number of cases developing to severe malaria would lead to lower follow-on treatment costs for providers. As severe malaria can lead to hospitalisation, these cost savings can be substantial, heavily influencing net-benefit. The annualised incremental cost of using ACTs instead of SP over a period of 13 years was calculated at Int$2.98 per malaria patient treated.

We evaluated outcomes according to treatment failure or cure, defined as adequate clinical response following WHO criteria (*80*). If treatment fails, the patient may develop severe malaria or continue to suffer from uncomplicated malaria. If severe malaria develops, they may seek inpatient care, where they will receive intravenous quinine. If they seek care with uncomplicated malaria, they may receive a second-line antimalarial[13]. The probabilities of full recovery or death were then estimated, as reported in Coleman et al. (*67*).

The probability of treatment failure, F, with a given first line drug, i, at time t was defined as being dependent on three main inputs. First, the proportion of malaria parasites, R, resistant to drug i at time t. Second, the probability, m, that a patient complies at the recommended dose with drug therapy i. Third the probability, p, that therapy i is effective despite the patient not complying fully with the treatment regimen.

As SP can be treated with a single dose, it can be expected that a high proportion of patients will fully comply. However, ACTs must be taken in several doses, and it is possible that patients will abandon treatment before finishing the full regimen. In a Zambian study, 21.2% of patients were non-compliant, with an additional 39.4% probably non-compliant (*81*). We assumed that 85%-95% of patients complied to SP,

[13] It was assumed that amodioquine was the second-line drug to SP, and that ACTs would be read ministered if ACT was used as first-line.

and 60%-80% of patients complied to ACT. In some cases of non-compliance with combination therapy, only minor underdosing may have occurred and some therapeutic effect may be experienced. In the absence of drug resistance, it was expected that ACTs would be effective in 10-30% of underdosed patients.

We assumed that all patients infected with resistant parasites experience treatment failure, regardless of whether or not they fully comply with the treatment regimen. Treatment with drug *i* at time *t* may be successful if the patient is not infected with resistant parasites and fully complies with the treatment regimen; the probability of this occurring is $(1\text{-}R_{i,t})m_I$. Alternatively, the patient may be infected with susceptible parasites but, despite not complying with the treatment regimen, is still cured; the probability of this occurring is $(1\text{-}R_{i,t})(1\text{-}m_i)p_i$. Thus

$$F_{i,t} = 1 - \left[\left(1 - R_{i,t}\right)m_i + \left(1 - R_{i,t}\right)\left(1 - m_i\right)p_i\right] \qquad \text{(eq. 5)}$$

defines treatment failure, which simplifies to

$$F_{i,t} = 1 - \left(1 - R_{i,t}\right)\left[m_i + p_i\left(1 - m_i\right)\right]. \qquad \text{(eq. 6)}$$

Levels of resistance were modelled using the same logistic function as in the IPTp model. The rate at which resistance will grow to ACTs has yet to be observed, and we assumed that it would grow at one-half the rate of SP based on the arguments outlined in section 3.2[14] (figure 3.1).

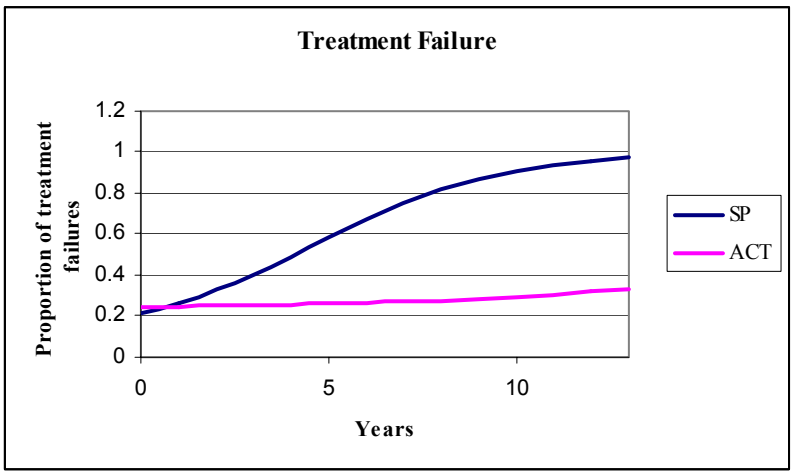


Figure 3.1 Effect of resistance on treatment failure (from (*67*))

The decision tree was used to calculate the probabilities of surviving or dying, which were converted to expected DALYs per patient. Estimates were made separately for patients over and under five years of age, and the total DALYs were calculated as a weighted average according to each group's share in the population. Overall, it can be expected that this policy change will avert 0.066 DALYs per case each year until 2015.

It has been estimated that children experience 200 million cases of malaria each year in SSA (*61*). If half of malaria cases affect adults in endemic areas, it can be assumed that

[14] The lower level of compliance to ACT makes treatment failure more likely at initial levels of resistance, despite its higher efficacy.

twice this number will occur in total (*67*). Currently, only about 42% of these cases receive an antimalarial, implying 168 million treatments needing a different drug. The incremental net-benefit of switching to ACT is given in Table 3.5.

Table 3.5: Costs and benefits of changing from SP to ACT (2003 Int$)

Intervention (value of DALY)	Malaria patients treated	Total benefit (millions, 2002-15)	Total cost (millions, 2002-15)	Net-benefit (millions, 2002-15)	Annualised net-benefit (millions)	Benefit-cost ratio
SP to ACT (Int$1,750)	168,000,000	$251,297	$6,510	$244,787	$18,830	38.6

Calculated from (*3*), (*67*), (*1*)

Increasing the DCR to 6% would decrease net-benefits by 23%. Standardizing the ceiling ratio to Int$3,830/DALY would increase net-benefits to Int$543 billion. Results are relevant also to countries still using CQ as unit costs for CQ and SP are very similar and patients are more likely to adhere to SP than CQ (*28*).

Scaling up ACT coverage

In order to halve the malaria burden by 2015 it will be necessary to scale up substantially the proportion of people who are treated for malaria (*1*). Adapting the decision tree used to evaluate a change in first-line therapy, we evaluated the net-benefit of extending ACT treatment to currently untreated malaria cases, to reach a treatment target of 70%, and including dipstick diagnosis in order to target treatment effectively.

Incremental costs of scaling up coverage can be expected to be much higher than for switching treatment policy since capacity expansion will be required. Costs include buildings and equipment, supervision and training, staff salaries, and costs incurred by individual patients. The incremental costs of scaling up ACT coverage were estimated at Int$20.21 per additional patient.

The health benefits of scaling up treatment will also be substantial. People with malaria that do not receive treatment can be expected to incur 0.310 DALYs, and patients treated with ACTs average 0.089 DALYs, over a 13 year time frame. An incremental 0.221 DALYs would be averted per patient.

Given that around 42% of cases in SSA are currently being treated with a malaria drug (*6*), if the proportion of cases treated for malaria is scaled up to 70%, it can be expected that an additional 112 million episodes will be treated each year. The incremental net-benefit of this policy change are shown in table 3.6.

Table 3.6: Costs and benefits of scaling up ACT (2003 Int$)

Intervention (value of a DALY)	Additional malaria patients covered	Total benefit (millions, 2002-15)	Total cost (millions, 2002-15)	Net-benefit (millions, 2002-15)	Annualised net-benefit (millions)	Benefit-cost ratio
SP to ACT (Int$1,750)	112,000,000	$157,683	$8,240	$149,443	$11,496	19.1

Calculated from (*3*), (*67*), (*1*)

Increasing the discount rate to 6% would decrease the net-benefit by 17%, and standardizing the ceiling ratio to Int$3,830/DALY would increase total net-benefits to Int$337 billion.

Package of interventions

Net-benefits and benefit-cost ratios for each of the three interventions are summarised in Table 3.7 in annual terms. In the absence of evidence on synergies between interventions, costs and benefits have been simply summed to illustrate the costs and benefits of the package.

Table 3.7: Costs and benefits of a package of malaria control measures (2003 Int$)

Intervention	Per-capita costs (annualised)	Total monetary benefit (annualised) (millions)	Total cost (annualised) (millions)	Net-benefit (annualised) (millions)	BCR
ITNs	$30.33 per child	$18,479	$1,773	$16,706	10.0
IPTp	$8.78 per PG	$480	$35	$445	12.1
Changing to ACT	$2.98 per malaria case	$19,331	$501	$18,830	38.6
Scaling up ACT	$20.21 per malaria case	$12,130	$634	$11,496	19.1
Total		$50,417	$2,942	$47,375	26.9

It should be noted that benefits in this table are valued using ceiling ratios specific to SSA. The value of benefits thus reflects the low incomes of SSA. We present results using a standardized ceiling ratio in the final section to adjust for this.

A notable feature of this analysis, largely neglected to date, has been the inclusion of considerations of drug resistance. Although this considerably complicates the analyses, not least because it requires analysis over time, it provides a more realistic estimate of costs and benefits. However, it should be noted that the costs of research into new drugs has not been included here as a cost.

Success story: KwaZulu Natal, South Africa

Evidence of the cost-effectiveness of different malaria treatment and control strategies was taken from the South East African Combination Antimalarial Therapy (SEACAT) study done in the Ingwavuma district in the KwaZulu Natal province of South Africa (*21*). This region is classified internationally as a low-transmission area and malaria is seasonal. In the year 2000, this region suffered a particularly severe outbreak of malaria, with nearly 6,000 cases per month at its peak. The national malaria programme was deemed ineffective and immediately changed.

The programme existing in 2000 consisted of insecticide residual spraying (IRS) with deltamethrin and malaria case management with SP. In 2002, IRS with a combination of deltamethrin (60%) and DDT (40%) was introduced, and first line drug treatment was changed to ACT. An economic evaluation was conducted to test the cost-effectiveness of this change in policy at one hospital and 9 clinics between 2000 and 2002. The authors separated the effects of ACTs from those of IRS using a Delphi survey of 10 international malaria experts.

The interventions were hugely successful as the facilities saw 21,874 fewer cases of malaria between 2000 and 2002. The Delphi survey suggested that ACT was responsible for averting 36% (range 25%-50%) of these cases. Assuming that people

with malaria would otherwise be treated with SP, 0.002 YLLs would be avoided for each case averted (*67*). Valuing each YLL according to the South African GNI (Int$10,910), the programme would have a monetary benefit of Int$202,798 (range $140,832 - $281,664). Int$774,630 were saved due to fewer treatments being necessary, and the net-benefit of the programme was Int$977,428 (range Int$915,463 - Int$1,056,294). Lowering the ceiling ratio to Int$3,830/YLL gives a net-benefit of Int$845,823.

In addition to being highly effective in averting malaria cases, this programme was cost saving: South Africa has a relatively well-developed primary care system, where 69% of people live within 5 km of a clinic. Publicly provided health care is widely used – over 93% of patients with malaria sought treatment from one of these clinics, which were backed by a well-regulated and reliable drug supply (*21*).

The findings of this study represent programme data, not a controlled trial. Cost-effectiveness may be overestimated if other factors, such as changes in climate and precipitation, contributed to the reduced prevalence of disease.

3.5 Feasibility

Feasibility can be examined according to a number of different dimensions, notably political, financial, and managerial. Many aspects of feasibility are common to all three opportunities, most notably because some of the malaria and HIV/AIDS interventions require a basic health service system. Hence the general discussion on feasibility is located in section 5.5, and the discussion here and in the subsequent HIV/AIDS feasibility section concentrates on issues specific to these two diseases, including the extent to which interventions can be successfully delivered where basic health services are weak.

Political feasibility has changed markedly in recent years with respect to malaria. A co-ordinated effort at international level, including the creation of Roll Back Malaria, culminated in the Abuja declaration. Malaria was included in the scope of the new Global Fund for AIDS, TB and Malaria. An external evaluation of RBM found it to have been highly successful in global advocacy, and in attracting attention to malaria control (*82*). The evaluation team estimated that international expenditures on malaria had doubled. However, there was lack of progress in demonstrating a significant reduction in the global burden of malaria. At country level, National Malaria Control Programmes and National Programme Officers were judged to be weak, and unable to advocate effectively. Hence political commitment remains an issue at the country level.

The Abuja Summit called for US$ 1bn a year to help Africa tackle malaria; however, this request may be an underestimate of the actual resources needed to address the epidemic effectively. CMHWG5 estimates, which sought to cost fully the provision of a package of malaria control measures at local level, estimated that to achieve high levels of coverage by 2015, $1.5-2.2 billion (US$2002) would be needed a year for prevention and treatment of adults in SSA, and a further $3.3-4.2 billion for a child treatment package which included malaria. Fighting malaria would be less costly than fighting HIV, which CMHWG5 estimated to cost between $10.1-12.1 billion a year in SSA by 2015.

Managerial feasibility can be examined with respect to the three interventions evaluated. With respect to ITNs, feasibility is dependent on the delivery strategy. At one extreme, a strategy of free public distribution is dependent on the existence of an effective basic heath service network, and a well managed supply pipeline from manufacturers to health centres. However, the Tanzanian experience demonstrates that in some settings, relying on private sector distribution channels and individual willingness to pay, stimulated by publicly funded social marketing campaigns and encouragement to manufacturers, can achieve a marked increase in net coverage. From a relatively small base of 200,000 nets per year in 1994, there has been a dramatic increase to domestic sales of around 1.5m nets in 2002[15]. Manufacturing capacity exceeds 4 million nets, and nets are being exported to other countries in Africa. The reasons for this expansion in net production include the positive impact of reductions in taxes and tariffs, and the effects of demand creation activities undertaken through a variety of small scale projects, and more recent large scale social marketing activities. Retail prices have fallen dramatically, to US$ 1.8 ex factory, presumably reflecting competition, and possibly also economies of scale operating at lower levels of the distribution system. There is anecdotal evidence that saturation of urban markets is leading to increased penetration into rural areas. The challenge currently faced is how to channel subsidies to those unable to pay the commercial price. While as in Tanzania, nets can be bundled with the initial insecticide treatment, encouraging re-treatment has proved a major problem in many countries. This problem will be solved in the foreseeable future by the introduction of long lasting nets.

IPTp delivery is dependent on an antenatal care (ANC) infrastructure. In most of SSA the percentage of primagravidae receiving antenatal care is high. Although historically the coverage of malaria prophylaxis of pregnant women in ANC has been very low, this has in part resulted from lack of attention to this intervention and low adherence to the previous drug, CQ. Intermittent treatment using SP improves adherence, which can also be improved by education of mothers. Thus except in countries with extremely weak ANC, this intervention is managerially feasible. In the future, development of resistance to SP will threaten this strategy, and research is urgently needed to identify anti-malaria drugs that are safe to give in pregnancy.

Malaria treatment for children and adults is accessed though both public and private sectors. In SSA, given the limited reach and often poor quality of government services, as much as 60% of treatments may be purchased from the private sector, often local drug shops and general stores (*62*). If the additional cost of ACT is to be matched by the benefits of reduction in the rate of growth of resistance, it is likely that coverage of ACTs must be high, and coverage of either of the component drugs given as monotherapy low[16]. This means that not only do public sector services need to be improved (considered below under section 5.5), but also private sector dispensing practices must be addressed. Experiences of how this can be done are accumulating, and include a combination of consumer education, improved drug packaging, and retailer training and support (*62*). Franchising and contracting approaches can be used to structure the implementation of these specific measures, and provide incentives for good practice.

[15] Kramer personnel communication

[16] Otherwise use of the monotherapy will increase the probability of resistance developing and spreading, and threaten the combination drug

4 Control of HIV/AIDS

4.1 Identification and description of opportunity

Introductory Statistics

HIV/AIDS affects nearly every country in the world, with more than 90% of infections occurring in developing countries (*83, 84*). Between 2.5 and 3.5 million people died from HIV/AIDS in 2003, accounting for over 5.1% of all deaths worldwide (*85, 86*). Current estimates are that more than 22 million people have died through the course of the epidemic (*11*), between 34 and 46 million people are currently living with HIV/AIDS, and 5.3 million new infections occur each year (*86*).[17] The problem has reached such a magnitude that it is considered not just a health issue, but a development issue (*87*), and most recently a global security threat (*88*). The Commission for Macroeconomics in Health argued that it is 'a distinct and unparalleled catastrophe' with the 'capacity to overturn economic development in Africa and in other regions for decades' (*51*). There have been recent suggestions that prevalence is lower than had been thought – for example 22m cases in SSA rather than 26.6m (*89*)– though still appallingly high.

Epidemiological Description

The distribution of HIV/AIDS is geographically diverse, and can be classified according to three stages of the epidemic; nascent, concentrated, and generalized (*84*). As large population studies are expensive and problematic, these definitions rely on prevalence levels among women attending ante-natal clinics and groups considered to be particularly at-risk. These high-risk groups include sex workers, injecting drug users (IDUs), the military, homosexual and bisexual men, and people already affected by another sexually transmitted infection (STI).

The HIV/AIDS epidemic can be categorised as nascent, concentrated, and generalised. The epidemic exists in its nascent stage where less than 5% of individuals in high risk groups are infected, and less than 1% of the overall population is affected (*86*). Over 2.3 billion people live in these areas, which include China, Indonesia, Papua New Guinea, several central Asian republics, the Baltic states, and parts of north Africa (*84*). The epidemic is in its concentrated stage where it has become established among high-risk groups (over 5%), but not amongst the general population. Concentrated epidemics exist in much of Latin America, several central Asian republics, SSA, and around heroin networks in Southeast Asia and Pakistan. The generalized form of the epidemic exists where over 5% of the overall population is affected (*84*). Southern and eastern Africa, along with a few countries in west Africa, are currently suffering this stage of the epidemic. In some areas the overall prevalence of infection may reach as high as 40%, as in Botswana (*86*).

While the HIV/AIDS epidemic has yet to be fully described, solutions lie in addressing the risk factors associated with its spread. A large proportion of HIV is transmitted through the sex industry, especially in areas where condom use is low. Without protection from condoms, individuals already infected by other sexually transmitted

[17] http://www.whitehouse.gov/onap/facts.html

infections (STIs) are particularly vulnerable to HIV infection. This risk factor is especially important in sub-Saharan Africa, where 90% of HIV infections are transmitted through heterosexual sex. Sex between men is another contributing factor to HIV spread, particularly in Latin America. Intravenous drug use (IDU) spreads the epidemic among users during nascent stages of the epidemic. These individuals then spread the virus further by infecting their sexual partners (*86*) (*84*).

Microeconomic impact

At the household level, HIV/AIDS can impose heavy cost burdens, undermine assets and livelihoods and be a cause of impoverishment. In many developing countries this is exacerbated by households' poor access to health services, and the high costs (both direct and indirect) of seeking treatment.

The costs of an adult death constitute the key microeconomic impact of the HIV/AIDS epidemic. Unlike malaria, HIV can affect poor and rich alike, though it might be expected that over time richer people would be more able and likely to adapt their behaviour. A number of household studies in subsistence economies have sought to measure the impact of an AIDS death, and to study how households cope (*90, 91*). The effects of HIV/AIDS are felt on two key farm parameters. First, household labour quality and quantity are reduced, initially as the infected person is less productive, and subsequently with their death. This is exacerbated when there is more than one infected person in a household, which is not unusual given the nature of transmission. In addition, household time is diverted to care for the sick person. For example, in the Thai study, 13% of school aged children in families with an AIDS sufferer were withdrawn from school to support the family (*90*); interruption of education, to care for parents, contribute to household income or food needs, or because of lack of money for school fees, was also found in the Ugandan study (*92*). Secondly, HIV/AIDS affects the availability of cash income. Financial resources have to be diverted to pay for medical treatment and funeral costs; since the disease is a chronic one, such costs can be very substantial and often will require sale of assets. In the Thai study, 60% spent all their savings as a result of the AIDS infection, and on average out of pocket medical expenditure from the beginning of the illness until death amounted to 6 months of average total household income (*90*). In the study in Tanzania, household medical expenses tended to be much higher for AIDS than for other causes of death (*91*). Funeral expenses are also a substantial expense, in the Tanzanian study amounting to about as much as medical care. Such diversion of expenditure can be at the expense of food consumption where resources are very limited.

Shortage of labour may lead households to change the mix of crops, shifting from cash to subsistence crops, or reduce the area under cultivation (*92*). In the longer term, households may dissolve or be reconstituted as children are fostered, orphaned or die, and spouses remarry or migrate.

However, households do not all respond in the same way, or suffer the same level of costs. Studies demonstrate that the impact of AIDS varies according to three sets of characteristics: those of the dead individuals, such as age, sex, and income; those of the household such as composition, assets, and source of livelihood; and those of the community, such as support systems and the availability of resources (*84*). In general, studies have suggested that households can be surprisingly resilient to the costs of

AIDS, precisely because of coping mechanisms: altering household composition (eg sending children to live elsewhere, or inviting adult relatives into the household); drawing down savings or assets (for example 41% of households with a death in the Thai survey reported selling land; and 60% of households in the Uganda study sold property to cover care costs); and drawing on assistance from other households (for example local associations may be set up specifically to assist community members with AIDS). In an African context, labour intensive farming systems with a low level of mechanization and agricultural inputs are said to be particularly vulnerable to the impact of AIDS (*92*).

As might be expected, the economic impact of AIDS is larger in poorer households. In the Thai study the lowest income and the least educated engaged in agricultural work were least able to cope (*90*). In the Tanzanian study, per capita food consumption dropped by 15% in the poorest 50% of households during the 6 months following the death, which would be likely to increase levels of malnutrition (*91*). Where the death was of a woman, children had lower school enrolment rates and were more likely to undertake activities normally done by women, such as cooking.

In addition to imposing costs on households, HIV/AIDS increases demands on government health care services since it increases demand for health care amongst adults, usually a section of the population where health care demands are relatively low. In addition, several studies suggest that adults with AIDS use more health care prior to death than those who die of other causes (*84*). Since HIV/AIDS also reduces the supply of health care, notably by reducing the supply of health care workers, the result is that health care facilities become swamped by chronic care patients. For example, the percentage of beds occupied by HIV-positive patients in 6 referral hospitals in developing countries with large epidemics was over 50% in 5 of the 6, and there was evidence that non-HIV positive patents were less likely to be admitted (*84*).

The consequences of HIV/AIDS for the business community have recently attracted increased attention (*93, 94*). AIDS not only increases absenteeism in people stricken by the virus, but also in those that must provide care for them. AIDS deaths increase staff turnover, and increase costs of re-assigning and training workers. Production processes become disrupted, and output of firms is decreased as a result. Firms are required to allocate more resources towards medical benefits for the sick and pensions for their dependents after they die. These effects are discussed further below.

Macroeconomic impact mechanisms

The mechanisms through which HIV/AIDS affects national economies are as yet poorly understood, and the variety of approaches and assumptions have lead to widely differing estimates of impact. Macroeconomic models, discussed later in this section, have sought to quantify the detrimental effect of the epidemic on productivity and economic growth, often summarised as the impact on total and per capita Gross Domestic Product (GDP). Making predictions about the effect of a hypothetical alternative to an existing scenario is a fundamental challenge of economic modelling. For areas where no intervention has been implemented, the impact of intervening must be estimated. Likewise, in areas where measures have been taken to combat HIV/AIDS, the disease burden in the absence of these measures must be approximated. Currently, no method for modelling

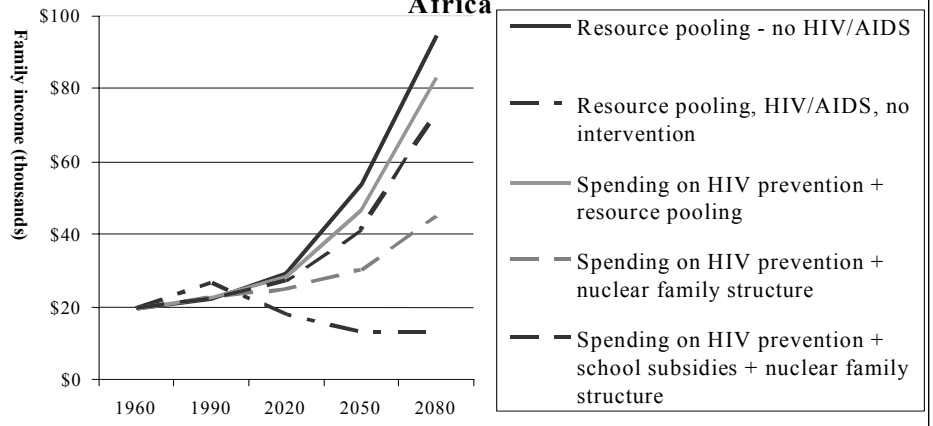
the macroeconomic effects of HIV/AIDS has been agreed upon; however, a review of existing work illustrates what progress has been made.
The question of how the costs and benefits of HIV/AIDS can be most appropriately quantified is fundamental in the macroeconomic modelling of the epidemic. The epidemic has a complex impact on economic growth since the majority of HIV related deaths are amongst people of working age. In the medium term, the size and composition of the labour force are affected mainly through increased mortality rates, whereas in the long term, declining birth rates also contribute to the loss of workers (*93*). Early models assumed that the economy would sustain these losses, as increased mortality would relieve pressure on existing land and physical capital. The argument supporting this assumption was that unemployment levels are currently very high in Africa, and immigrants often fill vacant positions. As a result, models created between 1980 and 1992 found that mortality would have little effect on output per head (*11, 95, 96*). However, more sophisticated approaches have recently been developed, and have found that reductions in the labour force have a powerful impact on GDP (*93, 97*).

The decimation of the labour force has economic costs in itself in terms of productivity and training in all areas of the public and private sectors. Aside from the impact of higher mortality rates, surviving workers are less productive as they spend more time away from work either caring for the sick or coping with their own infection. As experienced workers are eliminated from the labour force, new staff must be recruited and trained. These effects are likely to be especially important in the education sector as education is a strong determinant of the productivity of future generations. On the supply side, fewer teachers are available. For example, in Zambia the death rate of school teachers exceeds the annual capacity of teacher training colleges (*96*). Further, governmental funds allocated towards education are reduced. The demand for education is likely to become weaker, especially amongst vulnerable groups, as people become less certain about their future.

The structure of the household is another consideration that must be taken into account when measuring macroeconomic effects. The epidemic creates unprecedented numbers of full and partial orphans, disrupting traditional channels of community support and organization. Bell and colleagues (*95*) evaluated these effects by constructing a model that considered two family structures, nuclear and ‘pooling’. In a ‘pooling’ family structure, the extended family raises its children in a cooperative effort. Where this collective responsibility is not taken, transmission of knowledge vital for children to become productive members of society is weakened. When these children become adults, their capacity to raise their own children well is severely reduced.

Spending on HIV/AIDS prevention was found to be much more likely to reduce the impact of the epidemic on the South African economy if resources were pooled than if people were organized into nuclear families (*95*). If society is structured around nuclear families, these losses can be alleviated somewhat by educational subsidies. However, these subsidies are not as effective as family reorganization, as figure 4.1 shows.

Figure 4.1: Long-run economic costs of AIDS in South Africa



Calculated from (*95*)

From the perspective of government expenditure, fewer resources are available for investment in non-health related sectors as they are directed towards strategies that attempt to manage the epidemic. Governmental revenue declines as individual productivity decreases and levels of taxable income drop. As people change their spending patterns, and have less disposable income to save and spend, tax revenues decline further.

Haacker (*93*) demonstrated that the economic impact of HIV/AIDS is exacerbated when it is considered from the more realistic perspective of an open-economy, as compared to a closed-economy where the relationship to the rest of the world is ignored. In an open economy, the rate of return on domestic assets is linked to world interest rates, and foreign investors will be less inclined to risk ventures in that country as it becomes less productive. In addition, residents will have more incentive to invest abroad. Mortality is considered identically in each scenario, but reductions in the capital/labour ratio have greatest impact in the open economy. These assumptions have powerful effects on predictions about GDP. Depending on which perspective is taken, predictions about whether economic gains or losses can be expected are reversed. In Botswana, closed-economy assumptions predict that national GDP will rise by 9.6% in the long term; open-economy assumptions predict a 3.3% loss (*93*).

McPherson (*96*) has argued that the macroeconomic impact of HIV/AIDS predicted by current models is likely to be grossly understated. With the exception of Zerfu et al., no model has considered effects from disruption to agricultural production and food security (*98*), yet maize production in northern Zambia has decreased by 71% in the last decade, and 40% of positions in the Malawian Ministry of Agriculture are vacant, so these disruptions can be expected to be severe (*96*). Further, current models assume an early peak in the epidemic, which is unlikely to occur given the already devastated condition of many affected countries (*96*).

Regional impact estimates

Middle East and North Africa: For the Middle East and North Africa, a macroeconomic model was coupled with an HIV diffusion model that considered spread through both sexual transmission and intravenous drug use. Three types of labour were considered: skilled, unskilled, and unemployed. The model found that the most severe impact of the epidemic occurred on unskilled and unemployed groups. By 2025, it predicted that the epidemic would reduce the total GDP of North Africa by 35% of today's GDP, compared to projections of what would occur in the absence of HIV/AIDS (*97*). The expected losses borne by 9 countries in this region over this period are summarized in Table 4.1.

Table 4.1 Effects of HIV/AIDS on national GDP 2000-2025

	2000 GDP (in millions)	Percent loss No intervention	Monetary loss (in millions)
Algeria	$186,900	36.20%	$67,658
Egypt	$222,190	44.30%	$98,430
Iran	$364,400	33.60%	$122,438
Jordan	$18,684	27.90%	$5,213
Lebanon	$17,950	26.30%	$4,721
Morocco	$97,991	33.20%	$32,533
Tunisia	$58,574	45.50%	$26,651
Yemen	$13,954	31.40%	$4,382

Calculated from (*97*)

Sub-Saharan Africa: Haacker (*93*) devised a model for SSA that assumed HIV prevalence remains in a steady state, in order to examine its impacts on the macro economy. This assumption can also be justified on the basis that the prevalence of HIV in many countries may be approaching its natural limit. The model used evidence on the demographic impact of HIV from UNAIDS and the US Bureau of the Census to predict the effects of the epidemic at end-1999 levels on companies and disaggregated areas of the public sector. Effects on GDP were measured both from the perspective of an open economy and a closed economy. From the perspective of an open economy, the following losses to per-capita GDP can be expected in the long term (Table 4.2).

Table 4.2: Effect of HIV/AIDS on long-term GDP: No action taken

Country	Percent loss (per capita)
Botswana	3.2%
Lesotho	2.1%
Malawi	1.4%
Mozambique	1.2%
Namibia	1.8%
South Africa	1.8%
Swaziland	2.3%
Zambia	1.8%
Zimbabwe	2.3%

Calculated from (*93*)

4.2 Alleviation of the challenge - interventions

A complete package of services to alleviate the impact of the HIV/AIDS epidemic must include both treatment and preventive interventions (*1*). Whilst preventive measures are

crucial as AIDS is currently an incurable disease, a strong moral argument has been put forward to justify the inclusion of measures to treat the 34-46 million people currently infected by the virus (*86*). However, as ARV prices are changing rapidly and their effects in the developing world are highly uncertain, we have considered here primarily preventive interventions.

Nascent epidemic

In countries where the epidemic is nascent, treatment measures are expected to be a negligible component of overall costs and benefits as less than 5% of people in high-risk groups would be infected and condom distribution and expanding safe access to needles are considered the major preventive measures (*97*). However, the relative importance of intravenous drug use and sexual transmission as risk factors varies according to geography. Therefore, programmes need to be tailored to specific country needs.

Concentrated epidemics

Concentrated epidemics require both treatment and preventive interventions to address fully the health crisis, most notably a set of interventions specifically targeted to high-risk groups (such as IDUs, sex workers, and their clients). As an illustration, in 1989, the Ratchaburi province in Thailand introduced an initiative focused on prevention commonly known as the '100% condom programme', which expanded nationally by 1991 (*20*). In this programme, condoms were provided free of charge to brothel workers, who were required to refuse sex to anyone who refused to wear them. If an infection was detected in any of these workers, police had the right to close the brothel. Further, information was obtained from men who presented to governmental health clinics with STIs to trace their infection back to its source. Non-governmental organizations provided training and empowered experienced sex workers to train younger ones to negotiate condom use by their clients. Public health checks were also provided free of charge to these workers. The initiative directed at brothels was supplemented by a TV and radio campaign to warn men of the dangers of visiting brothels and not wearing a condom.

Generalised epidemics

A programme to address generalized epidemics would include many of the same interventions as in a concentrated epidemic, but they would be implemented on a wider scale. Creese et al (2002) provide a standardized review of the effectiveness and cost-effectiveness of HIV/AIDS interventions in sub-Saharan Africa (interventions are listed in section 4.4).

Stover and colleagues (*100*) designed a model to determine if the Declaration of Commitment, made by the United Nations General Assembly Special Session (UNGASS) in June 2001, to reduce the prevalence of HIV/AIDS by 25% by 2010 could be met. From a review of literature on effectiveness, they evaluated a general package of preventive interventions that should be implemented in low-and middle- income countries to combat the epidemic (table 4.3).

Table 4.3: UNGASS HIV/AIDS recommendation

Prevention Interventions
School-based AIDS education
Peer education for out-of-school youth
Outreach programmes for commercial sex workers and their clients
Condom social marketing
Treatment for STIs
Public sector condom promotion and distribution
Voluntary counselling and testing
Workplace prevention programmes
Prevention of mother-to-child transmission
Mass media campaigns
Harm reduction programmes
Outreach programmes for homosexual men

Source (*100*)

For some of these interventions (youth education programmes, social marketing schemes, workplace prevention programmes, harm reduction programmes, and outreach programmes for homosexual men) evidence on effectiveness is very limited.

4.3 Side effects

Positive side effects

HIV/AIDS interventions include both those focused on the sick individual, and those aimed at changing sexual practices and lifestyles within the household, amongst IDUs, within society more generally, and within the commercial sex trade. They are thus likely to have many beneficial side effects. Moreover, some of the interventions are not specific to HIV/AIDS, and provide protection against other diseases.

Examples of beneficial side effects include:

- Increased control of fertility through greater availability of condoms
- Reduced incidence of other STIs
- Better management of other STIs and TB
- Increased access to life saving blood transfusion
- Reduced transmission of disease through blood transfusions
- Reduced domestic violence as result of improved education on sexual health and support to women (*101*)
- Better educated youth as a result of school health education programmes
- Strengthened disease surveillance and epidemiological capacity at international and national levels.

Negative side effects

Comments above on the adverse effects of medicines and vaccines apply also here. However, there are some concerns specific to HIV, especially that of drug resistance, specifically in countries where controls are lax and affordability is low. Supply and resource constraints have encouraged practices such as the use of single-dose nevirapine to treat pregnant women, which has been shown to cause resistance in as many as 75% of women treated (*102*). The Global HIV/AIDS programme of the World Bank has

collaborated with other international bodies to make recommendations for how to rationally manage ARV programmes[18], and several initiatives are showing success in lowering the price of drugs (*103*).

4.4 Economic evaluation

Four approaches were taken to assess the costs and benefits associated with services proposed to address the HIV/AIDS epidemic:

1. Findings on the potential macro-economic impact of preventive measures in the Middle East and north Africa are reported, to exemplify benefits for countries in the nascent stage of the epidemic.
2. The costs and benefits from Thailand's response are estimated, to represent a successful programme implemented in a country in the concentrated stage of the epidemic.
3. Benefit cost ratios are calculated for the interventions in SSA.
4. The overall costs and benefits are estimated of the package of interventions advocated by UNGASS for low- and middle-income countries.

Nascent epidemic package

Robalino et al. (*97*) found that expanding condom use by 30% and access to safe needles for IDUs by 20% would prevent losses to the economy between 2000 and 2025 as high as 20% of 2000 GDP (Table 4.4).

Table 4.4: Net benefit in terms of 2000 national GDP by 2025 (2003 Int$)

	Implement immediately		Five year delay	
Country	**Percent loss averted**	**Monetary loss averted (in millions)**	**Percent loss averted**	**Monetary loss averted (in millions)**
Algeria	20.40%	$38,128	14.70%	$27,474
Egypt	27.50%	$61,102	19.20%	$42,660
Iran	20.60%	$75,066	14.40%	$52,474
Jordan	15.50%	$2,896	11.20%	$2,093
Lebanon	16.80%	$3,016	11.80%	$2,118
Morocco	20.10%	$19,696	14.00%	$13,719
Tunisia	30.40%	$17,806	22.30%	$13,062
Yemen	2.20%	$307	-1.80%	-$251

Figures calculated from (*97*) and (*3*)

However, if this intervention is delayed by as few as five years, the results could be disastrous. Hesitation could make as much as half of the economic decline unavoidable. Historical examples corroborate the benefits of acting early. For example, the gay population in the US and the national initiative in Uganda have shown remarkable success in preventing the epidemic from spreading (*104*).

Macroeconomic estimates of the impact of HIV/AIDS interventions are too limited for regions with higher prevalence, so we did not apply this approach elsewhere.

[18] Provision of ARV therapy in resource-limited settings: The challenges of resistance and adherence: Global HIV/AIDS Program of the World Bank, 17-18 June, 1993
http://www.unaids.org/EN/other/functionalities/Search.asp

Concentrated epidemic package

Brown (*20*) estimated the number of HIV infections that were averted in Thailand's 100% condom programme. In the worst-affected areas in northern Thailand, the number of new HIV cases fell five times between 1991-1993, and the number of new STIs fell ten times between 1991-1995. While 4% of new Thai military conscripts had HIV in 1993, only 0.5% were infected in 2001. Overall, the number of new cases of HIV in Thailand fell from 142,819 in 1991 to 25,790 in 2001, ultimately even reducing the incidence in sex workers (*20, 104*). Based on these figures, Brown estimated that 200,000 infections were averted between 1993-2000.

The costs of the programme were borne both by the private sector and by the government (*20*). The private sector financed information campaigns broadcast through the media costing Int$160 million[19]. The cost of government programmes aimed at brothels rose from Int$11,588,769 in 1991 to Int$93,369,040 in 1996. We assumed that the cost of the programme grew linearly during this period, and remained constant between 1996 and 2000. Discounted at 3%, this programme cost Int$1,738 m 1993-2000. ANB and BCR are shown in Table 4.5.

Table 4.5: Costs and benefits of Thailand's 100% condom programme 1993-2000 (2003 $Int)

	Number of cases averted	Total benefit (millions)	Total cost (millions)	Net-benefit (millions)	Annualised net-benefit (millions)	Benefit-cost ratio
100% condom programme	200,000	$25,925	$1,738	$24,186	$3,455	14.91

Figures based on (*20*)

Increasing the discount rate to 6% decreased the net-benefit to Int$22,162 million. Standardizing the ceiling ratio to Int$3,830 reduced the net-benefit to Int$14,199 million, and the BCR to 9.17.

Interventions in SSA

Microeconomic studies have shown that most individual interventions for combating HIV are highly cost-effective (*105*). Table 4.6 demonstrates this, together with estimated benefit cost ratios.

Many of these figures are likely to underestimate the cost-effectiveness (and benefit cost ratio) of the interventions. For example none of the studies that evaluated preventive measures against vertical transmission considered the knock-on effects on horizontal transmission. The effects of ARV therapy may be underestimated as transmission may be reduced through the reduction in viral loads; also prices are falling rapidly.

Several other interventions not included in this review show promise of being highly cost-effective measures against HIV. Microbicides are being developed that women could use discreetly to protect themselves in the absence of condom use, and may be available as soon as 2007. It has been shown that their benefits in terms of productivity gains and direct cost savings to the health system would be substantial, and are robust to wide variations in assumptions (*106*).

[19] We assumed that this programme cost $25.5 million each year.

Table 4.6: Benefit cost ratios of interventions for SSA

Prevention	Benefit Cost Ratio	Cost per DALY averted Reported (2000 US$)	Adjusted (2003 Int$)
Condom distribution plus STD treatment for sex workers	466	$1	$4
Female condoms targeted to: Sex workers	39	$12	$45
High-risk women	10	$48	$180
Medium risk women	5	$99	$372
Blood safety			
Hospital based screening	93 - 466	$1 - $5	$4 - $19
Strengthening blood transfusion services			
Defer high risk donors	93 - 466	$1 - $5	$8 - $11
Test and defer high risk donors	155 - 233	$2 - $3	$8 - $11
Rapid test	155	$3	$11
Improved transfusion safety with outreach	39 - 47	$10 - $12	$38 - $45
Improved blood collection and transfusion	11	$43	$162
Peer education of sex workers	67 - 116	$4 - $7	$15 - $26
Prevention of mother-to-child transmission			
Single dose nevirapine (universal)	52	$9	$34
ZDV Petra regimen	52	$9	$34
ZDV CDC Thai regimen	6 - 14	$33 - $75	$124 - $282
Formula recommendation	4	$131	$492
Breastfeeding 3 months	3	$171	$642
Formula provision	2	$218	$819
Breastfeeding 6 months	1	$731	$2,748
Diagnosis and treatment of STIs	39	$12	$45
Voluntary counselling and testing	21 - 26	18 - $22	$68 - $82
Treatment and care			
Short course TB treatment for new sputum-smear positive pulmonary patients			
TB Ambulatory care: Malawi, Mozambique, Tanzania '91	155 - 233	$2 - $3	$8 - $11
Uganda, 1995	116 - 233	$2 - $4	$8 - $15
South Africa, 1997	29 - 58	$8 - $16	$30 - $60
IUATLD model: Uganda 1995	116 - 155	$3 - $4	$11 - $15
Malawi, Mozambique, Tanzania, 1991	58 - 116	$4 - $8	$15 - $30
South Africa, 1997	7 - 14	$34 - $68	$127 - $256
Community based DOT	22 - 33	$14 - $21	$53 - $79
Co-trimoxazole prophylaxis for HIV and TB patients	78	$6	$23
Home-based care for people with AIDS			
Community based programme: Tanzania	6	$77	$289
Zambia	5	$99	$372
Health facility based programme: Zambia, 1994	1	$681	$2,560
Tanzania, 2000	1	$786	$2,955
Zimbabwe, 1998	0.3 - 0.9	$469 - $1230	$1,762 - $4,624
Preventive therapy for TB: Isoniazid 6 months	3	$169	$635
Rifampicin plus pyrazinamide 2 months	2	$282	$1,060
Isoniazid plus rifampicin 3 months	2	$288	$1,082
ARV for adults: Senegal and Cote D'Ivoire, 2000	0	$1,100	$4,135
South Africa, 2000	0	$1,800	$6,766

Figures based on (*105*)

When interventions are packaged according to those that complement each other, the cost effectiveness improves further. A recent study shows that integrating TB and HIV services can be done for $1 per person under favourable assumptions (*107*). Further, the cost effectiveness of many interventions has been shown to improve as programmes mature.

Overall package for HIV prevention

The model developed by Stover and colleagues (*100*) estimated baseline HIV prevalence in countries with generalised and concentrated epidemics according to the size of risk group, current practice, and degree of sexual mixing. With no intervention, they predicted that 45.4 million new infections would occur between 2002-2010.

Evidence on the effectiveness of interventions (Table 4.3) to limit the spread of the epidemic was taken from 86 studies found through a literature review. Their effectiveness was defined in terms of their impact on five behaviours: condom use, treatment seeking behaviour for STDs, number of sexual partners, age at first sexual intercourse, and sharing of potentially infected needles. They then estimated costs and outcomes according to coverage levels, many of which varied with prevalence. In total, their model predicted that 63% of infections would be averted if an expanded response costing US$58.77 were put in place.

We applied an estimate for the number of YLLs lost per HIV infection (23.08), and a monetary value per YLL lost for the countries included (Int$4,460), to calculate costs and benefits (Table 4.7).

Table 4.7: Cost and benefits of the UNGASS package of interventions for middle and low- income countries (2003 Int$)

New Infections Baseline 2002-10 (millions)	New Infections Package 2002-10 (millions)	Infections averted 2002-10	Benefits (millions, 2002-10)	Costs (millions, 2002-10)	Net benefit (millions, 2002-10)	Annualised net benefits (millions)	Benefit-Cost Ratio
45.4	16.9	63%	$2,934,148	$58,760	$2,875,389	$359,423	49.9

Figures based on (*100*) and (*3*)

Table 4.7 shows that the implementation of the UNGASS package of HIV/AIDS interventions is substantially beneficial. When the value of a YLL is lowered to Int$3830, the net benefit decreases to Int$2.5 trillion, with a benefit-cost ratio of 42.9.

Stover *et al*. (*100*) stress that the full impact of their programme is achievable only in the presence of strong care and support programmes, and with political commitment to its implementation. More infections are preventable epidemiologically in countries where the epidemic is growing rapidly, such as China and Cameroon, than in countries where it is stable or declining. With full effect, 33% of global infections would be prevented in China and India alone, with 40% prevented in SSA.

4.5 Feasibility

A successful battle against the HIV/AIDS epidemic requires political and social commitment at all levels. This has been developing slowly – as evidenced by the high levels of prevalence in much of SSA, and the relatively few countries which are known for their high commitment to control (such as Uganda and Senegal). HIV/AIDS confronts countries with a unique challenge, since major routes of transmission include those which are illegal, or at least judged morally unacceptable. To the extent that the transmission route has to be openly acknowledged in order for it to be addressed, this poses great challenges to countries reluctant to accept, for example, that homosexual relationships are widespread in prisons, or that all levels of society frequent sex-workers. Commitment can take the form of government support to public health workers, such as meetings set up by the police between public health workers and brothel owners (*20*), and clear public messages. It has been argued that the impact of these measures is greatest when the public is actively involved in spreading these messages through the community because people are more likely to internalise the message and change their behaviour (*104*).

For the HIV/AIDS epidemic to be confronted effectively, financial resources from both higher- and lower-income countries must be increased. The total UNGASS package would cost US$9.2 billion annually by 2005 to provide the expanded response in low- and middle-income countries (*100*). Currently, the Global Fund for AIDS, TB and Malaria provides most of the world's funding to fight AIDS, and has allocated US$2-3 billion towards efforts to control HIV (*1*). Donor support has been increasing at an unprecedented level, with the Bill and Melinda Gates Foundation recently increasing its pledge to fight HIV/AIDS in India to US$200 million (*103*). Other organizations, such as the Clinton Foundation, are successfully negotiating lower prices for ARV medications (*103*). Since 2000, the cost of antiretroviral regimens has fallen from an annual US$10,000 per patient to US$300 (*108*). Considering that the PPP adjusted Gross National Income of OECD countries was $25.6 trillion in 2002, full support for the UNGASS package would require these countries to donate 0.04% (*109*), a share that has been judged feasible (*51, 110*).

Further investment is needed to improve technology to supplement available interventions. Currently, there is no cure or vaccine that would provide protection against the HIV virus. As previously mentioned, a microbicide that women could use secretly before sex to protect themselves against infection could be available by 2007.

Lines of responsibility must be drawn for intervention programmes to be effective. Placing local authorities in charge of promoting awareness and delivering services increases coverage to marginalised groups and raises awareness. Non-state providers have an important role in supplementing government health services. In Uganda, NGOs such as TASO have been successful in promoting awareness through their work with faith-based organisations (*104*). In India, autonomous AIDS control societies have been set up through which public funds for HIV/AIDS services are channelled (*111*). They appear to offer an efficient means of working around the slow Indian state bureaucracy.

Countries and organisations need to ensure that information is continuously collected and analysed for intervention programmes in order to learn from previous mistakes and improve effectiveness and efficiency. AIDS surveillance in Thailand and Uganda allowed these countries to monitor the status of their epidemics, and has been recognised as a major factor contributing to their successes (*104*) (*20*).

General issues of feasibility of implementation are reviewed in section 5.5.

5 Strengthening basic health services

5.1 Identification and description

While the opportunity to scale up basic health services is inclusive of the first two, it provides a comprehensive perspective of the challenge posed by communicable disease in the developing world, as well as including other common conditions. The great majority of health interventions depend for successful and sustained implementation on an infrastructure of basic health services, consisting of community based services, health centres, and local hospitals offering inpatient care. Such a service infrastructure has also been referred to as primary health care (PHC), or a district health system. Relative to other forms of medical care, PHC can be argued to be the most accessible, least costly, and best equipped method to provide effective care for the conditions that most affect global health (*112*). Theoretically, it is estimated that primary care is able to address 90% of health care demands. Although recent international initiatives have tended to be disease or programme specific (eg Roll Back Malaria, the Global Fund for HIV, TB and Malaria, GAVI -Global Alliance for Vaccines and Immunisation; 3 by 5[20]), they all acknowledge their reliance on basic health services. Moreover, there are historical experiences where a strong public health role in health has been related to health outcomes that are much better than might be expected at low levels of income (for example Cuba, Sri Lanka) (*113*) (*114*)[21].

Two types of evidence are available on the costs and benefits of expanding health services: evidence from cross-country analyses of the relationship between health expenditure and health gains; and estimates of the costs and health benefits of packages of interventions.

Regression analysis has been used to measure the effect of economic inputs on health sector outputs in terms of elasticities. To make this link, health must be defined in quantitative terms, and a proxy measure is used such as under-five mortality, maternal mortality, underweight among children under 5, and disease-specific mortality. Public spending in the health sector is commonly used as an independent variable. An advantage of this approach is that it seeks to measure the link between expenditure and health while controlling for other factors that contribute to national health status, such as poverty and education. While an often cited study found that government spending had a small and insignificant impact on under-5 mortality (*115*), recent analyses are beginning to find specific effects on population subgroups (*116*). For example, Gupta and colleagues (*117*) found that spending had a significant impact on child mortality, specifically benefiting population groups living on less than two dollars per day.

There have been several efforts to identify a package of priority interventions to be delivered through local health services, using some mix of criteria including magnitude of the burden, availability of interventions, and cost-effectiveness. These efforts include the World Development Report 1993 (*118*) (its list is reproduced in section 5.2), Better Health in Africa (*119*), the World Health Report 2000 (*112, 120*), and the CMH WG5 (*1*). In general, these efforts identify very similar packages.

[20] Providing anti-retrovirals to 3m people by 2005
[21] though good nutrition and education also contributed to these health gains

5.2 Alleviation of the challenge - interventions

Studies estimating the relationship between increased health sector expenditure and improved health make no assumption on specific interventions: health expenditure is increased in proportion to current patterns.

For a package of interventions to strengthen basic health services, we have chosen to use the WDR 1993 package because its DALY benefit was estimated and the package is still relevant. Table 5.1 lists the interventions in the package. In general, the interventions make few demands on high level care, with the required hospital resources consisting of a capacity for emergency surgery, blood transfusion, and treatment of the more severe cases.

Table 5.1: The WDR 93 minimum health package

Clusters of interventions	Main disease conditions addressed
Public Health	
Expanded programme on immunization	Measles, poliomyelitis, tetanus, whooping cough, yellow fever, hepatitis B
School health programme	Intestinal worms
AIDS prevention programme	Sexually transmitted diseases and AIDS
Tobacco and alcohol control programmes	Lung cancer, cardiovascular disease, cirrhosis, injuries associated with alcohol abuse
Other public health programmes (including family planning, health, and nutrition information)	These are not disease specific
Clinical	
Short course chemotherapy for tuberculosis	Tuberculosis in adults
Management of the sick child	Diarrhoeal diseases, pneumonia and other respiratory infections, malaria, measles, and severe malnutrition
Prenatal and delivery care	Perinatal mortality and morbidity, complications of pregnancy and delivery, low birth weight, unwanted pregnancies, and congenital syphilis and gonorrhea
Family planning	Perinatal and infant mortality and maternal mortality and morbidity
Treatment of sexually transmitted diseases	AIDS, syphilis, gonorrhea, Chlamydia, and other sexually transmitted diseases
Limited care (mainly for adults)	Pain control, infection and minor trauma treatment, and advice to reduce chronic diseases

5.3 Side effects

Positive side effects

The existence of a well functioning system of basic health services may have positive side effects in providing a visible demonstration of the effectiveness of government, and in improving relationships between the government and local people.

Achieving the MDGs related to health will be vital for making gains in other MDGs. As outlined in Figure 2.1, health influences income, nutrition, and access to resources, and can be expected to be an important component of halving the proportion of people who live on less than one dollar per day.

Negative side effects
Comments in earlier sections on the adverse effects of drugs and vaccines apply also here. Drugs and vaccines used in basic health services have mostly been used for many decades, so their safety profiles are well known.

5.4 Economic evaluation

We estimated the costs and benefits of scaling up basic health services drawing on the two sources of data mentioned above: evidence of the relationship between health expenditure and health gains; and estimates of the costs and health benefits of the package of interventions recommended in the 1993 World Development Report.

Increased overall health expenditure

According to the elasticities in their model, Gupta and colleagues (*117*) estimated the expenditures necessary for a cohort of countries to reach the International Development Goal (subsequently adopted as an MDG) to reduce child mortality by two-thirds by 2015. These countries were Heavily Indebted Poor Countries (HIPCs) approved for further aid from the International Monetary Fund (IMF) and World Bank in mid-2001, as they found that it would be especially crucial for these countries to increase preferential spending on the poor for the MDGs to be met. Assuming that income and education levels remained constant, they estimated that public spending on health would need to increase from an average of 2% of GDP in 1999 to 12% of GDP in 2015.

We quantified the expenditure for 13 of these countries assuming that spending increased at a constant rate from levels of GDP[22]. Between 1990-2001, GDP grew by 3.4% in low income countries (*121*) and we assumed that this pattern would continue to 2015 (*66*). Assuming that additional health expenditures would increase linearly between 1999 and 2015, incremental expenditure was calculated and discounted.

We calculated benefits by projecting levels of child mortality into the future, decreasing linearly at an annual rate of 2.67% from a rate of 157 deaths per 1,000 children in 1990, in order to reach the goal by 2015. Deaths avoided were calculated by subtracting this trajectory from a baseline scenario in which child mortality remained constant at 1990 levels. Each child death was associated with 28.41 YLLs, and valued in monetary terms according to the average GNI for these countries (Int$1,407) (*3*). Costs and benefits are shown in table 5.2.

Table 5.2: Costs and benefits of increased health expenditure 2002-2015 (2003 Int $)

Intervention	Under-5 population	Total benefit (millions)	Total cost (millions)	Net-benefit (millions)	Annualised net-benefit (millions)	BCR
Increased overall public spending on health in HIPC group (Int$ 1,470)	27,541,139	$874,492	$225,155	$649,376	$49,952	3.9

Calculated from (*117*) and (*3*)

[22] These countries included: Bolivia, Burkina Faso, The Gambia, Honduras, Madagascar, Mali, Mauritania, Mozambique, Niger, Rwanda, Senegal, Tanzania, and Uganda.

If a 6% discount rate is used, ANB falls to Int$595,437 million, with a BCR of 4.36. If the ceiling ratio is increased to Int$3,830, ANB increases to $2,155,472 million, with a BCR of 10.6.

Results are highly sensitive to the trend of baseline mortality used to calculate deaths averted. If it is assumed that the annual decreases in child mortality (1.1%) that occurred in the developing world during the 1990's continue to 2015 in the absence of intervention (*122*), averted mortality is so reduced that total net-benefit becomes negative (-Int$7.3 billion) (though it should be noted that if this trend does indeed occur, a greater than two third reduction in child mortality might be expected from increased expenditure).

In interpreting these figures, several points should be noted. On the expenditure side, the calculations assume an overall expansion in current patterns of health expenditure. To the extent that expenditures can be better targeted, on high return health interventions and on individuals with the worst health status, the returns are likely to be higher. Determinants of health other than expenditure, such as improvements in education and level of consumption, are not considered and are likely to have a synergistic impact. On the benefit side, the effects of the expenditure increase on child deaths only is included, although service expansion would be expected to benefit a range of population groups. Overall, the cohort of highly-indebted countries in the analysis is expected to produce a modest estimate of the returns to investment. Health systems in financially-constrained countries are notoriously weak, and are likely to require proportionally more investment to scale up health services than wealthier ones.

Package of priority interventions

Bobadilla and colleagues (1994) estimated that the WDR package would cost Int$65 per person in low and middle income countries and would reduce the disease burden by 25%. Based on 2002 estimates from the Global Burden of Disease database, this package would be expected to avert 227,456,368 YLLs each year. The economic benefits of implementing such a package are outlined in Table 5.3.

Table 5.3: Costs and benefits of the 1993 World Development Report Package (2003 Int$)

	Population	Annual Benefits (millions)	Annual Costs (millions)	Annual net-benefit (millions)	BCR
Low and middle income countries (Int$3,830)	909,825,472	$871,158	$337,073	$534,084	2.6

Figures based on (*118*) and (*3*)

The favourable benefit-cost ratio is expected as the framers of this package selected clusters of interventions with strong consideration of their cost-effectiveness, targeted towards groups that were most likely to benefit. By clustering interventions and including those with synergies between them, costs were kept to a minimum. Applying a standard ceiling ratio has no effect since the ceiling ratio is already that for low and middle income countries.

5.5 Feasibility

The growing literature on the relationship between public expenditure on health care and health outcomes (*115, 117*) cautions against easily assuming that increased public expenditure will be translated into improved health outcomes. Analysis of the relationship between public spending and child mortality finds results varying from statistical significance to insignificance (*5*), for a variety of both methodological and policy-related reasons. With respect to the latter, public spending may not be well targeted on the poor who have the worst health outcomes; much of it may not reach the local service provider, being tied up at higher levels and in central hospitals; and service quality is often very poor. Failings may both be a reflection of the overall poor quality of the policy environment, and of more mundane difficulties in managing service provision in settings with very limited capacity, difficult communications, and few trained staff.

The challenge of meeting the MDGs has lead to a recent focus on the difficulties facing health service delivery, and on the constraints that need to be overcome to scale up the coverage of priority health services (*1*) (*123*) (*5*). This body of work directly addresses the managerial challenges in strengthening basic health services. Although evidence is still quite limited on how best to address constraints (*124*), it is good enough to make some suggestions on how best to improve health services, both in the most highly constrained countries (for example, those with very weak governments) and those which are somewhat less constrained. Table 5.4 both identifies constraints by level, and suggests measures to address constraints in settings which are more or less constrained. A key difference between these settings is that the weaker the government system, the greater needs to be the reliance on working outside government channels, using NGOs and the private sector, for example.

Table 5.4 Relaxing constraints: priority actions by type of country

Level of constraint	Highly constrained countries	Least constrained countries
Community and household level	• Encourage community mobilization through NGOs • Use social marketing and retail sector to make effective drugs available to households	• Use incentives to stimulate demand
Health services delivery level	• Build up health care delivery infrastructure through public services and/or agreements with NGO and church providers • Use outreach services and NGOs where public sector difficult to extend	• Improve human resource management policies in order to ensure better staff performance • Strengthen local management
Health sector policy and strategic management level	• Increase degree of management decentralization • Strengthen drug supply and distribution system through public and/or private sector • Greater donor coordination	• Increase degree of management decentralization • Greater donor coordination • Strengthen regulation of private sector
Public policies cutting across sectors		• Give greater autonomy to health sector
Environmental characteristics	• Prepare for possible scale up under improved conditions; maintain links with NGOs; support education and training	• Encourage more pluralist policy process

Source: (*1*)

However, there are also issues of political and financial feasibility. At international level, there has been reluctance to envisage support to a health service development strategy. Political commitment appears to be easier to gain for specific disease control efforts, such as HIV/AIDS and malaria. It may be, however, that the current international focus on extending anti-retroviral treatment to AIDS patients will help change this attitude, since of all priority interventions, ARV treatment is highly dependent on a health service infrastructure. The importance being given to improving service delivery and ensuring it serves the poor is indicated by its choice as the subject of the WDR 2004 (*5*), which emphasises institutional changes to strengthen relationships of accountability between policy makers, service providers, and citizens, as the key to improving service delivery.

Financially, this opportunity faces the most severe financial constraints, since it is the most costly of all three opportunities. There is substantial disagreement over how much countries need to spend to achieve high levels of coverage of priority interventions. The total annual costs estimated for the WDR 1993 package were $12 per capita in low income countries and $22 per capita in middle income countries (US$ 1993). The *Better Health in Africa* cost was $13 per capita in low income African countries (*125*). The CMH report put great stress on adequately costing the full cost of scaling up, including adequate remuneration to health staff, expansion of training, and management and supervisory capacity at all levels. It also included a more extended AIDS package, including treatment. It estimated a total of $38 per capita ($2002) for low income countries ($41 for least developed countries), to achieve the scaling up targets (*17*). This level of expenditure implies on average 5.9% of GNP devoted to health (11.4% for least developed countries), consisting of 2002 total health expenditure, plus the additional costs of raising coverage and quality. It can be noted that the CMH figure for least developed countries is consistent with Gupta et al above, who estimated 12%. The CMH report estimated that donor aid to less developed countries would need to rise by an additional $31 billion a year by 2015, if these country expenditure levels were to be achieved (*17*).

6 Discussion and conclusion

This paper has reviewed the evidence on the economic benefits of good health, specifically in relation to communicable disease, and the economic costs of malaria and HIV/AIDS. It has also sought to estimate the benefits and costs of reducing the burden of communicable disease, considering separately malaria control, HIV/AIDS control, and scaled up basic health services. In order to do this, evidence was drawn from four main sources: macroeconomic studies of the economic cost of disease; microeconomic studies of the costs and health effects of health interventions; estimates of the efficiency of health expenditures with respect to health outcomes; and examples of successful programmes where some data were available on costs and health benefits.

All these sources of data have substantial shortcomings, which must inform the interpretation of the estimates of costs and benefits. In particular:

- The macroeconomic literature is quite inadequate. In the case of malaria, it is very sparse (2 recent studies only) and has yet to generate a critical debate on methods and data. In the case of HIV/AIDS, the literature provides wildly differing estimates, ranging from minimal impact on per capita income to a massive impact.
- The microeconomic literature relates largely to interventions implemented individually in the context of epidemiological trials; evidence of costs and health effects in the context of large scale programme implementation is very limited. Furthermore, health effects have to be translated into a monetary value. We chose to apply the ceiling ratio of one times per capita GNI, but this decision is arbitrary; in sensitivity analyses we applied the GNI for low and middle income countries in order not to disadvantage health gains in poor countries.
- The analysis of the efficiency of health expenditure relates all health expenditure to health outcomes for a single population group, omitting benefits for others.
- Evidence from successful programmes is hard to interpret, since external factors may also have affected changes in health effects.

Macroeconomic estimates of benefits and calculations made from cost-effectiveness evidence cannot of course be assumed to be reflecting the same dimensions of benefits. Macroeconomic benefits allow for interactions over time, where improved health feeds, for example, into increased labour supply quantity and quality, and into changed savings and investment patterns. In contrast, the conversion of health gains into a monetary value reflects an assumption on the value of human life, not necessarily related to its productive potential. Moreover, given the weakness of the evidence base, it would be unwise to read too much into differences between the evidence from these two different sources.

In addition, our estimates suffer from other shortcomings:

- We would have preferred to have estimated costs and benefits over the same time periods, and discounted to present values or calculated an internal rate of return. Given the varied nature of the available data, this was not possible to do consistently
- Available costs were usually costs to the provider, excluding costs to users
- Savings in health care costs that would result from preventive activities were rarely included in the estimates
- We would have liked to have been more explicit on who would benefit under each of the challenges, and in particular on the extent to which the poorest would benefit.

This is partly a question of which groups suffer most from the diseases in question, and partly an issue of the extent to which countries are able or willing to ensure that all population groups benefit from expanded disease control efforts.

This last point bears on the feasibility of the opportunities considered. Increased health expenditure will be translated into improved health outcomes only if the right policies are adopted and well implemented. Low and middle income country health systems often have shortcomings, which mean that they are less efficient at transferring expenditure into health gains than they could be. Thus considerable attention has to be paid to the structures through which health programmes are implemented, as well as to the preferences and knowledge of users. Moreover, the focus of two of the challenges on controlling specific communicable diseases should not be interpreted to indicate that their implementation can avoid the problems and inefficiencies of working through existing health systems. As made clear in the text, important components of both malaria and HIV/AIDS control are dependent on the health system.

Given all these caveats, we highlight and summarise our estimates in Table 6.1. A complete summary of all results is in the Annex. On the basis of the earlier analyses, we have selected a subset of results to include, based on criteria of :

- relevance to a range of countries
- inclusion of a package of interventions.

It should be noted that the per capita costs apply to different populations; in some cases the general population and in others the target groups for particular interventions (as noted in the relevant column). The last two columns show the results of the sensitivity analysis on the DCR and ceiling ratio in terms of its impact on the BCR.

The table suggests that many health interventions and programmes are highly cost beneficial. There is a general pattern, as one might expect, that estimates based on cost-effectiveness data for specific interventions (packages of malaria and HIV interventions) show much higher benefit cost ratios than broader programmes. At least in part this is for methodological reasons – for example underestimation of the necessary costs of system strengthening, and likely overestimation of benefits because of drawing evidence of effectiveness from trial data. However, it is noteworthy that the real life example, that of HIV prevention in Thailand, shows substantial net benefits and a favourable BCR of 15. The WDR package has the highest net benefits of all (partly because it is applied to all low and middle income countries) and a favourable benefit cost ratio, of 2.6. The estimate based on Gupta et al also has a favourable benefit cost ratio, of 3.9, despite three factors that might be expected to reduce it: the costs relate to increasing health expenditure overall but the benefits were estimated for child mortality only (excluding benefits in adult health); the increase in health expenditure represents an increase in the overall pattern of health expenditure, not the targeting to effective interventions; the countries in the analysis are some of the poorest, where it might be expected that the costs of achieving a given health effect are higher given the multiple disadvantages faced by their populations. However, the estimate is highly sensitive to assumptions on the underlying rate of child mortality change.

Table 6.1: Summary of key results (Int$ 2003)

Opportunity, Source, Geographic Region	Per-capita costs (annualised)	Total benefit (annualised, millions)	Total cost (annualised, Millions)	Net-benefit (annualised, millions)	BCR 3% DCR	BCR 6% DR	BCR Rc = Int$3,830
Control of malaria							
Based on evidence from macroeconomic models	$21 per person	$22,996 - $55,359	$11,873	$11,123 - $43,486	1.9 - 4.7	1.8 - 4.3	no ceiling ratio
Package of malaria interventions		$50,417	$2,942	$47,375	26.9	24.7	59.5
Control of HIV/AIDS							
Thai programme of prevention	$28.92 per case averted	$3,704	$248	$3,455	14.9	15.1	9.2
Package for prevention of HIV/AIDS. Six regions (EAP, EAC, LAC, SEA, SAR, SSA)	$11.36 per person	$366,769	$7,345	$359,423	49.9	DCR within model	42.9
Scaled up basic health services							
Increased health expenditure. 13 Highly Indebted Poor Countries	$106.89 per child	$67,269	$17,317	$49,952	3.9	4.4	10.6
WDR (1993) Minimum package. Low and Middle Income Countries	$65 per person	$871,158	$337,073	$534,084	2.6	One year	2.6

Despite uncertainties over the estimates, the table emphasises that there are likely to be high returns from investing in communicable disease control – benefit cost ratios substantially exceeding one. Taken with the currently low coverage of malaria, HIV/AIDS and basic health care programmes in large parts of the developing world, especially SSA, they suggest that communicable disease control is substantially under-resourced. Moreover, investments where health status is low will provide substantial benefits to the poorest populations of the world.

It remains uncertain whether greater returns are achievable from a focused effort to address specific diseases, such as malaria or HIV/AIDS, or from a broader basic health services strategy. However it cannot be emphasised enough that these three approaches are not completely independent – both malaria and HIV/AIDS control must include a substantial component of strengthening basic health services if they are to be successful. While costing sought to allow for this, it is probable that the system strengthening costs required for malaria and HIV specific interventions have not been adequately allowed for, suggesting that in practice there may be less of a difference between disease specific interventions and general health service interventions than suggested in the table.

For reasons of space and focus, this paper has not explored issues of the role of government in addressing communicable disease. However, a strong case can be made for public funding for controlling communicable diseases, on both poverty and efficiency grounds (given positive externalities and public goods arguments).

Finally, it should be noted that the productivity of health expenditure is likely to be greater both in a supportive policy environment, and where complementary investments take place, such as in female education.

ANNEX: Complete summary of results (Int$ 2003)

Opportunity, Source, Geographic Region	Per-capita costs (annualised)	Total annual benefit (m)	Total annual cost (m)	Annual net-benefit (m)	BCR	BCR 6% DR	BCR Rc = $3,830
Control of malaria							
Based on macroeconomic models							
Gallup & Sachs 2001); Jha and Mills (2002)	$21 per person	$55,359	$11,873	$43,486	4.7	4.3	no ceiling ratio
McCarthy et al (2000); Jha and Mills (2002)	$21 per person	$22,996	$11,873	$11,123	1.9	1.8	no ceiling ratio
ITNs for children under 5, Goodman et al. (2000)							
SSA – LIC	$28.47 per child	$6,694	$1,180	$5,513	5.7	5.4	25.6
SSA – MIC	$29.02 per child	$5,308	$435	$4,873	12.2	11.5	25.1
SSA – HIC	$33.50 per child	$6,477	$158	$6,319	41.1	39.1	21.7
SSA – Total	$30.33 per child	$18,479	$1,773	$16,706	10.0	9.5	25.1
*IPTp at ANC visits, Goodman et al. (2000)**							
SSA – LIC	$6.59 per PG	$174	$22	$152	8.0	7.5	36.1
SSA – MIC	$7.29 per PG	$138	$9	$129	15.9	14.8	32.6
SSA – HIC	$12.47 per PG	$168	$5	$164	36.1	34.0	19.1
SSA – Total	$8.78 per PG	$480	$35	$445	12.1	11.3	33.9
*Switch from SP to ACTs, Coleman et al. (2004)**							
SSA	2.98 per malaria case	$19,331	$501	$18,830	38.6	34.3	84.5
*Scaling up ACTs, Coleman et al. (2004)**							
SSA	20.21 per malaria case	$12,130	$634	$11,496	19.1	19.1	41.9
Switch from SP to ACTs in South Africa							
Muheki et al (2004)	-$98.37 per case averted	$0.1	-$0.4	$0.5	Cost-saving	no DCR	Cost-saving
Control of HIV/AIDS							
Based on macroeconomic models. Robalino (2002)							
Algeria	n/a	n/a	n/a	$1,525	n/a	n/a	n/a
Egypt	n/a	n/a	n/a	$2,444	n/a	n/a	n/a
Iran	n/a	n/a	n/a	$3,003	n/a	n/a	n/a
Jordan	n/a	n/a	n/a	$116	n/a	n/a	n/a
Lebanon	n/a	n/a	n/a	$121	n/a	n/a	n/a
Morocco	n/a	n/a	n/a	$788	n/a	n/a	n/a
Tunisia	n/a	n/a	n/a	$712	n/a	n/a	n/a
Yemen	n/a	n/a	n/a	$12	n/a	n/a	n/a

Opportunity, Source, Geographic Region	Per-capita costs (annualised)	Total annual benefit (m)	Total annual cost (m)	Annual net-benefit (m)	BCR	BCR 6% DR	BCR Rc = $3,830
Country experience							
Thailand programme, Brown (2003)	$28.92 per case averted	$3,704	$248	$3,455	14.9	15.1	9.2
Specific interventions, Creese et al (2002) sub-Saharan Africa							
Condom distribution	n/a	n/a	n/a	n/a	466 - 5	n/a	1,019 - 10
Blood safety	n/a	n/a	n/a	n/a	466 - 11	n/a	1,019 - 24
Peer education for sex workers	n/a	n/a	n/a	n/a	116 - 67	n/a	255 - 146
Prevention of MTC transmission	n/a	n/a	n/a	n/a	52 - 1	n/a	113 - 1.39
Treatment of STIs	n/a	n/a	n/a	n/a	39	n/a	85
VCT	n/a	n/a	n/a	n/a	26 - 21	n/a	57 - 46
Short course treatment, TB	n/a	n/a	n/a	n/a	233 - 7	n/a	509 - 15
Co-trimoxazole prophylaxis	n/a	n/a	n/a	n/a	78	n/a	170
Home care	n/a	n/a	n/a	n/a	6 - 0.4	n/a	13 - 0.8
Tuberculosis preventive therapy	n/a	n/a	n/a	n/a	3 - 2	n/a	6 - 3.5
ARV	n/a	n/a	n/a	n/a	0.4 - 0.3	n/a	0.9 - 0.6
Package for prevention of HIV/AIDS, Stover et al (2002)							
Six regions (EAP, EAC, LAC, SEA, SAR, SSA)	$11.36 per person	$366,769	$7,345	$359,423	49.9	DCR within model	42.9
Scaled up basic health services							
Increased health expenditure, HPIC, Gupta (2001)	$106.89 per person	**$67,269	$17,317	$49,952	3.9	4.4	10.6
WDR (1993) Minimum Package, Low and Middle Income Countries	$65 per person	$871,158	$337,073	$534,084	2.6	One year	2.6

***Abbreviations**: MTC: mother-to-child transmission; VCT: voluntary counselling and testing; STIs: sexually transmitted infections; ARV: anti-retroviral therapy; LIC: low income countries; MIC middle income countries; HIC higher income countries; IPT(p): intermittent treatment of pregnant women; SP: Sulfadoxine-pyrimethamine; PG: primigravidae (first pregnancy); ACT: artemisinin-based combination therapy; WDR: World Development Report*

**Adapted from original study*

*** gains in child health only included*

References

1. Jha, P., Mills, A: Improving health outcomes of the poor: Report of Working Group 5 of the Commission on Macroeconomics and Health. World Health Organization, Geneva, 2002, pp. 175.
2. WHO: World Health Report 2003: Shaping the future. WHO, Geneva, 2003, pp. 182.
3. World Bank: World Development Indicators CD-rom. World Bank, 2003.
4. http://www.fic.nih.gov/dcpp/gbd.html. (Disease Control Priorities Project 2004).
5. World Bank: World Development Report 2004. World Bank, Geneva, 2004, pp. 271.
6. WHO: The Africa Malaria Report 2003. UNICEF and World Health Organization, Geneva, 2003, pp. 120.
7. Oliveira-Cruz, V., Kurowski, C., Mills, A.: Delivery of health interventions: searching for synergies within the vertical versus horizontal debate. Journal of international development 15: 67-86 (2003).
8. Ruger, J. P., Jamison, D. T., and Bloom, D. E.: Health and the Economy. *In* Health and the Economy, edited by M. Merson, R. Black and A. Mills. Aspen, Gaithersburg, Maryland, 2001.
9. Bloom, D., Canning, D: The health and the wealth of nations. Science 287: 1207-1209 (2000).
10. Wagstaff, A.: Health spending and aid as escape routes from the vicious circle of poverty and health. British association for the advancement of science, 2002, pp. 22.
11. Alleyne, G. A. O., and Cohen, D.: Health, economic growth, and poverty reduction: Report of Working Group 1 of the Commission on Macroeconomics and Health. World Health Organization, Geneva, 2002, pp. 114.
12. Over, M., Ellis, R. P., Huber, J. H., et al.: The consequences of adult ill-health. *In* The Health of Adults in the Developing World, edited by R. G. A. Feachem, Kjellstrom T, Murray CJL, Over M & Phillips MA. Published for the World Bank by the Oxford University Press, Washington DC, 1992, pp. 161-207.
13. Sauerborn, R., Adams, A., and Hien, M.: Household strategies to cope with the economic costs of illness. Social Science and Medicine 43: 291-301 (1996).
14. Stevens, C. M.: Health and economic development: longer-run view. Social Science and Medicine 11: 809-17 (1977).
15. Folland, S., Goodman, A. C., and Stano, M.: The economics of health and health care. Prentice Hall, Upper Saddle River, NJ, 1997.
16. Klose, T.: The contingent valuation method in health care. Health Policy 47: 97-123 (1999).
17. CMH: Macroeconomics and Health: Investing in health for economic development. World Health Organization, Geneva, 2001, pp. 200.
18. WHO: Investing in Health Research and Development: Report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options. TDR/Gen/96.1, Geneva, 1996.
19. Devlin, N., and Parkin, D.: Does NICE have a cost-effectiveness threshold, and what other factors influence its decisions? Health Economics in press (2004).
20. Brown, P.: Thailand curbs HIV and sexually transmitted diseases. Center for Global Development, 2003.

21. Muheki, C., Barnes, K., and McIntyre, D.: Artemisinin-based combination therapy reduces expenditure on malaria treatment in KwaZulu Natal, South Africa. Work in progress (2004).
22. WHO: Global burden of disease estimates 2002. WHO, 2002, pp. http://www3.who.int/whosis/menu.cfm?path=evidence,burden.
23. UNICEF: State of the World's Children 2003. United Nations, Geneva, 2003, pp. http://www.unicef.org/sowc03/.
24. Snow, R. W., Craig, M., Deichmann, U., et al.: Estimating mortality, morbidity, and disability due to malaria among Africa's non-pregnant population. Bulletin of the World Health Organization 77: 624-640 (1999).
25. Snow, R. W., Armstrong, J. R., Forster, D., et al.: Childhood deaths in Africa: uses and limitations of verbal autopsies. Lancet 340: 351-5 (1992).
26. Breman, J.: The ears of the hippopotamus: manifestations, determinants, and estimates of malaria burden. American Journal of Tropical Medicine and Hygiene 64: 1-11 (2001).
27. Marsh, K., English, M., Crawley, J., et al.: The pathogenesis of severe malaria in African children. Annals of Tropical Medicine and Parasitology 90: 395-402 (1996).
28. Goodman, C. A., Coleman, P.G., Mills, A.J.: Economic analysis of malaria control in sub-Saharan Africa. Global Forum for Health Research, Geneva, 2000, pp. 185.
29. Snow, R. W., Bastos de Azevedo, I., Lowe, B. S., et al.: Severe childhood malaria in two areas of markedly different falciparum transmission in East Africa. Acta Tropica 57: 289-300 (1994).
30. Alonso, P. L., Lindsay, S. W., Armstrong, J. R., et al.: The effect of insecticide-treated bed nets on mortality of Gambian children. Lancet 337: 1499-502 (1991).
31. Shulman, C. E., Graham, W. J., Jilo, H., et al.: Malaria is an important cause of anaemia in primigravidae: evidence from a district hospital in coastal Kenya. Transactions of the Royal Society of Tropical Medicine and Hygiene 90: 535-9 (1996).
32. McCormick, M. C.: The contribution of low birth weight to infant mortality and childhood morbidity. New England Journal of Medicine 312: 82-90 (1985).
33. Alonso, P. L., Lindsay, S. W., Armstrong Schellenberg, J. R., et al.: A malaria control trial using insecticide-treated bed nets and targeted chemoprophylaxis in a rural area of The Gambia, west Africa. 2. Mortality and morbidity from malaria in the study area. Transactions of the Royal Society of Tropical Medicine and Hygiene 2: 13-7 (1993).
34. Molineaux, L.: The impact of parasitic diseases and their control, with an emphasis on malaria and Africa. *In* Health Policy, Social Policy and Mortality Prospects, edited by J. Vallin, Lopez, A. Ordina Editions, Liège, 1985, pp. 13-44.
35. Boissier, M., Knight, J. B., and Sabot, R. H.: Earnings, schooling, ability and cognitive skills. American Economic Review 75: 1016-1030 (1985).
36. Pollitt, E.: Iron deficiency and educational deficiency. Nutrition Reviews 55: 133-41 (1997).
37. Pollitt, E., Saco Pollitt, C., Leibel, R. L., et al.: Iron deficiency and behavioral development in infants and preschool children. American Journal of Clinical Nutrition 43: 555-65 (1986).

38. Soemantri, A. G., Pollitt, E., and Kim, I.: Iron deficiency anemia and educational achievement. American Journal of Clinical Nutrition 42: 1221-8 (1985).
39. Aikins, M. K. S.: Cost-effectiveness analysis of insecticide-impregnated mosquito nets (bednets) used as a malaria control measure: a study from the Gambia. PhD Thesis, Department of Public Health and Policy, London School of Hygiene and Tropical Medicine, University of London, 1995.
40. Chima, R. I., Goodman, C. A., and Mills, A.: The economic impact of malaria in Africa: a critical review of the evidence. Health Policy 63: 17-36 (2003).
41. Ettling, M. B., and Shepard, D. S.: Economic cost of malaria in Rwanda. Tropical Medicine and Parasitology 42: 214-8 (1991).
42. Ettling, M., McFarland, D. A., Schultz, L. J., et al.: Economic impact of malaria in Malawian households. Tropical Medicine and Parasitology 45: 74-9 (1994).
43. Leighton, C., and Foster, R.: Economic impacts of malaria in Kenya and Nigeria. Abt Associates, Health Financing and Sustainability Project, Bethesda, Maryland, 1993.
44. Shepard, D. S., Ettling, M. B., Brinkmann, U., et al.: The economic cost of malaria in Africa. Tropical Medicine and Parasitology 42: 199-203 (1991).
45. Sachs, J., Malaney, P: The economic and social burden of malaria. Nature 415: 680-685 (2002).
46. Audibert, M., Mathonnat, J., and Henry, M.: Social and health determinants of the efficiency of cotton farmers in Northern Cote d'Ivoire. Social Science and Medicine 56: 1705-1717 (2003).
47. Worrall, E., Basu, S., and Hanson, K.: The relationship between socio-economic status and malaria: a review of the literature: Background paper prepared for "Ensuring that malaria control interventions reach the poor", London, 2003.
48. Barlow, R.: The economic effects of malaria eradication. American Economic Review 57(2): 130-48 (1967).
49. Borts, G. H.: Discussion of "The economic effects of malaria eradication" by R. Barlow. American Economic Review 57(2): 149-151 (1967).
50. Barro, R. J.: Economic growth in a cross-section of countries. Quarterly Journal of Economics 106: 407-43 (1991).
51. Gallup, J. L., and Sachs, J. D.: The economic burden of malaria. The American Journal of Tropical Medicine and Hygiene 64: 85-96 (2001).
52. McCarthy, F. D., Wolf, H., and Wu, Y.: The growth costs of malaria. *In* National Bureau of Economic Research Working Paper Series, Cambridge, MA, 2000, pp. 31.
53. Lengeler, C.: Insecticide treated bednets and curtains for malaria control: A Cocherane Review. Swiss Tropical Institute, Basel, Switzerland, 1998, pp. 54.
54. Gülmezoglu, A. M., and Garner, P.: Malaria in pregnancy in endemic areas (Cochrane Review). The Cochrane Library Issue 3: Oxford, Update Software (1998).
55. WHO: Assessment of the safety of artemisinin compounds in pregnancy. WHO, Geneva, 2003, pp. (document WHO/RBM/TDR/Artemisinin/03.1).
56. Attaran, A., Barnes, K., Curtis, C., et al.: WHO, the Global Fund, and medical malpractice in malaria treatment. Lancet 363: 237-293 (2004).
57. Slutsker, L., Chitsulo, L., Macheso, A., et al.: Treatment of malaria fever episodes among children in Malawi: results of a KAP survey. Tropical Medicine and Parasitology 45: 61-4 (1994).

58. WHO: Implementation of the global malaria control strategy - Report of a WHO Study Group on the implementation of the global plan of action for malaria control 1993-2000. WHO, Geneva, 1993.
59. EANMAT: East African Network for Monitoring Antimalarial Treatment, http://www.eanmat.org/, 2004.
60. Bloland, P.: Drug resistance in malaria. WHO, Geneva, 2001, pp. 27.
61. D'Alessandro, U.: Commentary: Treating severe and complicated malaria. BMJ 328: 155 (2004).
62. Hanson, K. G., Goodman, C. G., Lines, J., et al.: The Economics of Malaria Interventions. http://mosquito.who.int/cmc_upload/0/000/015/605/ea_ch2.pdf (2000).
63. International Artemisinin Study Group: Artesunate combinations for treatment of malaria: meta-analysis. Lancet 363: 9-18 (2004).
64. Najera, J. A., Liese, B. H., and Hammer, J.: Malaria. *In* Disease Control Priorities Project, edited by D. Jamison. Oxford University Press, Oxford, 1993.
65. Organisation for Economic Co-operation and Development: (OECD) Development Co-operation Report 2000. (DAC Journal) (2001).
66. World Bank: World Development Report 2003. World Bank, Geneva, 2003, pp. 250.
67. Coleman, P. G., Morel, C. M., Shillcutt, S. D., et al.: A threshold analysis of the cost-effectiveness of artemisinin-based combination therapies in sub-Saharan Africa. American Journal of Tropical Medicine and Hygiene Forthcoming (2004).
68. Fox-Rushby, J.: Disability-adjusted life years (DALYs) for decision-making? An overview of the literature. Office of Health Economics, London, 2002, pp. 172.
69. United Nations: Model life tables for developing countries, New York, 1982.
70. Nájera, J. A., and Hempel, J.: The burden of malaria. WHO CTD/MAL/96.10, 1996.
71. Chavasse, D., Reed, C., and Attawell, K.: Insecticide Treated Net Projects: A Handbook for Managers. Malaria Consortium, London & Liverpool, 1999.
72. D'Alessandro, U., Olaleye, B. O., McGuire, W., et al.: Mortality and morbidity from malaria in Gambian children after introduction of an impregnated bednet programme. Lancet 345: 479-83 (1995).
73. Nevill, C. G., Some, E. S., Mung'ala, V. O., et al.: Insecticide-treated bednets reduce mortality and severe morbidity from malaria among children on the Kenyan coast. Tropical Medicine and International Health 1: 139-46 (1996).
74. Armstrong-Schellenberg, J. R. M., Abdulla, S., Nathan, R., et al.: Effect of large-scale social marketing of insecticide-treated nets on child survival in Tanzania. Lancet 357: 1241-1247 (2001).
75. Wiseman, V., Hawley, W. A., Ter Kuile, F. O., et al.: The cost-effectiveness of permethrin-treated bed nets in an area of intense malaria transmission in western Kenya. American Journal of Tropical Medicine and Hygiene 66 (suppl. 4): 161-167 (2003).
76. Goodman, C. A., Coleman, P. G., and Mills, A. J.: The cost-effectiveness of antenatal malaria prevention in sub- Saharan Africa. American Journal of Tropical Medicine and Hygiene 64: 45-56 (2001).
77. Roper, C., Pearce, R., Bredenkamp, B., et al.: Antifolate antimalarial resistance in southeast Africa: a population-based analysis. Lancet 361: 1174-1181 (2003).

78. Brabin, B. J., Hakimi, M., and Pelletier, D.: An analysis of anemia and pregnancy-related maternal mortality. Journal of Nutrition 131 (suppl): 604S-615S (2001).
79. Kindermans, J.: ACTs: availability and prices. presentation at RBM Partners Meeting, Geneva, 2002.
80. WHO/CTD: Assessment of therapeutic efficacy of antimalarial drugs for uncomplicated falciparum malaria with intense transmission. WHO/MAL/96.1077, Geneva, 1996.
81. Depoortere, E., Guthmann, J. P., Sipilanyambe, N., et al.: Adherence to the combination of sulphadoxine-pyrimethamine and artesunate in the Maheba refugee settlement, Zambia. Tropical Medicine & International Health 9: 62-67 (2004).
82. Malaria Consortium: External evaluation of malaria. Final report, 2002.
83. CIA: The World Factbook. Central Intelligence Agency, Washington DC, 2003.
84. Ainsworth, M., and Over, M.: Confronting AIDS: Public priorities in a global epidemic. Oxford University Press, Oxford, 1999.
85. WHO: The World Health Report. World Health Organization, Geneva, 2002.
86. UNAIDS.: AIDS epidemic update. UNAIDS and WHO, Geneva, 2003, pp. 40.
87. Arndt, C., and Lewis, J. D.: The macro implications of HIV/AIDS in South Africa: A preliminary assessment. Purdue University / World Bank, Geneva, 2000, pp. 18.
88. ICRG: HIV/AIDS as a threat to global security. International Crisis Research Group, New Haven, CT, 2002, pp. 69.
89. Anon: Good news, apparantly: building better models of the prevalence of HIV. The Economist (2004).
90. Pitayanon, S., Knogsin, S., Janjaroen, W.: The economic impact of HIV/AIDS mortality on households in Thailand. *In* The economies of HIV and AIDS: The case of South and Southeast Asia, edited by D. Bloom, Godwin, P. Oxford University Press, Delhi, 1997.
91. Over, M., Randall, P., Ellis, P., et al.: Impact of adult death on household expenditures in Kagera, Tanzania. *In* World Bank working paper. Policy Research Department, Washington D.C., forthcoming.
92. Barnett, T., Blaikie, P.: AIDS in Africa: Its present and future impact. Guilford Press, New York, 1992.
93. Haacker, M.: The economic consequences of HIV/AIDS in southern Africa. International Monetary Fund, Geneva, 2002, pp. 40.
94. Barnett, T., Whiteside, A.: AIDS in the Twenty-First Century: Disease and globalization. Palgrave Macmillan, Basingstoke, 2002.
95. Bell, C., Devarajan, S., Gersbach, H.: The long-run economic costs of AIDS: theory and an application to South Africa, 2003.
96. McPherson, M.: Macroeconomic models and the impact of HIV/AIDS, 2003.
97. Robalino, D. A., Jenkins, C., and El Maroufi, K.: Risks and macroeconomic impacts of HIV/AIDS in the Middle East and North Africa: Why waiting to intervene can be costly. World Bank Policy Research Working paper 2874: 35 (2002).
98. Zerfu, D.: The macroeconomic impact of HIV/AIDS in Ethiopia. Addis Ababa University, Addis Ababa, 2002.
99. Quattek, K.: The economic impact of AIDS in South Africa: a dark cloud on the horizon. Konrad Adenauer Stiftung Occasional Papers, HIV/AIDS, A threat to the African Renaissance? (originally an ING Barings research report), 2000.

100. Stover, J., Walker, N., Garnett, G. P., et al.: Can we reverse the HIV/AIDS pandemic with an expanded response? Lancet 360: 73-77 (2002).
101. Shaw, M.: 'Before we were sleeping but now we are awake: the Stepping Stones workshop programme in the Gambia'. Proceedings of the Global Fund for Health Research: Annual Meeting. Geneva, 2003.
102. Beckerman, K. P.: Long-term findings of HIVNET 012: the next steps. Lancet 362: 842-843 (2003).
103. Sharma, D.: ARV prices nosedive after Clinton brokering. Lancet 362: 1467 (2003).
104. Low-Beer, D., Stoneburner, RL: Behaviour and commumication change in reducing HIV: is Uganda uniqe? African journal of AIDS research 2: 9-21 (2003).
105. Creese, A., Floyd, K., Alban, A., et al.: Cost-effectiveness of HIV/AIDS interventions in Africa: a systematic review of the evidence. Lancet 359: 1635-1642 (2002).
106. Watts, C., Kumaranayake, L., Vickerman, P., et al.: The public health benefits of microbicides in lower-income countries: model projections. The Rockefellar Foundation, New York, 2002, pp. 55.
107. Terris-Prestholt, F., Kumaranayake, L., Ginwalla, R., et al.: The cost-effectiveness of the Zambian ProTEST project: integrating voluntary counselling and testing with tuberculosis activities, 2003.
108. Anon: AIDS: A mixed prognosis. The Economist: 115-117 (2003).
109. World Bank: World Development Indicators online. http://www.worldbank.org/data/dataquery.html (2004).
110. Potts, M., Walsh, J: Tackling India's HIV epidemic: lessons learned from Africa. British Medical Journal 326: 1389-1392 (2003).
111. Ramasundaram, S., Allaudin, K., Charles, B., et al.: Working Paper 25: HIV/AIDS Control in India - Lessons from Tamil Nadu. Commission on Macroeconomics and Health, Working group 5, 2001.
112. Doherty, J., Govender, R: The cost-effectiveness of primary care services in developing countries: A review of the international literature. Background paper: Disease Control Priorities Project: 48 (2004).
113. Halstead, S., Walsh, JA: Good Health at Low Cost. Rockefeller Foundation, New York, 1985.
114. Mehotra, S.: Innocenti Working Paper No. 80: Integrating economic and social policy: good practices from high-achieving countries. UNICEF Innocenti Research Centre, Florence, 2000.
115. Filmer, D., Pritchett, L: The impact of public spending on health: does money matter? Social Science and Medicine 49: 1309-1323 (1999).
116. Rajkumar, A., Swaroop, V: Public spending and outcomes: Does governance matter? World Bank, Washington DC, 2002.
117. Gupta, S., Verhoeven, M., Tiongson, E.: Public spending on health care and the poor. International Monetay Fund Working Paper (2001).
118. WHO: World Development Report 1993: Investing in Health. World Bank, Geneva, 1993, pp. 344.
119. World Bank: Better Health in Africa, Experience and Lessons Learned. World Bank, Washington D.C., 1994, pp. 261.
120. WHO: The World Health Report 2000: Health Systems: Improving performance. World Health Organization, Geneva, 2000, pp. 215.

121. World Bank: World Development Report 2002. World Bank, Geneva, 2002, pp. 249.
122. Black, R. E., Morris, S. S., Bryce, J.: Where and why are 10 million children dying each year? Lancet 361: 2226-2234 (2003).
123. Ranson, M. K., Hanson, K., Oliveira-Cruz, V., et al.: Constraints to expanding access to health interventions: An empirical analysis and country typology. Journal of International Development 15: 15-39 (2003).
124. Oliveira-Cruz, V., Hanson, K., Mills, A.: Approaches to overcoming constraints to effective health service delivery: a review of the evidence. Journal of international development 15 (2003).
125. World Bank: World Development Report 1993. World Bank, Geneva, 1993.