

The economic and social burden of malaria

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Where malaria prospers most, human societies have prospered least. The global distribution of per-capita gross domestic product shows a striking correlation between malaria and poverty, and malaria-endemic countries also have lower rates of economic growth. There are multiple channels by which malaria impedes development, including effects on fertility, population growth, saving and investment, worker productivity, absenteeism, premature mortality and medical costs.

Long before economists attempted to estimate the costs of malaria, natural selection had already demonstrated the phenomenal burden of the disease. Certain genetic polymorphisms, such as sickle cell trait, were selected for because of their protective effect against malaria when inherited from one parent, even though the same allele inherited from both parents is fatal. In essence, the chance of death from malaria was so high as to justify welcoming a potentially fatal mutation into the gene pool^{1–3}.

Given this evolutionary backdrop, it would indeed be surprising if the economic and demographic toll of malaria were not comparably dramatic. Sadly, malaria does little to disappoint. The numbers are staggering: there are 300 to 500 million clinical cases every year, and between one and three million deaths, mostly of children, are attributable to this disease⁴. Every 40 seconds a child dies of malaria, resulting in a daily loss of more than 2,000 young lives worldwide. These estimates render malaria the pre-eminent tropical parasitic disease and one of the top three killers among communicable diseases.

Although the last century witnessed many successful programmes at country level to eliminate the parasite, the world is now facing a rapidly increasing disease burden⁵. This has been attributed to several causes, including population movements into malarious regions, changing agricultural practices including the building of dams and irrigation schemes, deforestation, the weakening of public health systems in some poor countries, and more speculatively, long-term climate changes such as more pronounced El Niño cycles and global warming. Furthermore, resistance to drugs and insecticides used to counter this disease has been evolving in tandem with growing caseloads. With a rapidly growing population in regions with high malaria transmission, it has been estimated that in the absence of effective intervention strategies the number of malaria cases will double over the next 20 years⁴.

Global transmission patterns

The malaria burden is not evenly distributed. The global pattern of malarial transmission suggests a disease centred in the tropics, but with a reach into subtropical regions in five continents. Attempts to eliminate or at least suppress the disease have been an important public health story

through much of the last century. At malaria's furthest reaches, in temperate zones characterized by strong seasonality and cold winters, these attempts have been successful. Beyond any other factors, this reflects the fact that the base case reproduction rate of malaria is considerably lower in temperate regions than in the tropics, so that moderately intensive efforts at vector control and case management can lead to elimination of the disease. The remarkably high transmission rates in sub-Saharan Africa also reflect the particular capacity of Africa's main vector mosquitoes, the *Anopheles gambiae* complex of species, with their remarkable tendency towards human biting (anthropophily).

These climatic patterns of course reflect the natural history of the disease. The malaria parasite is transmitted to the female *Anopheles* mosquito from an infected individual when it takes a blood meal as a prelude to the reproductive process. The parasite must undergo a life-cycle change within the mosquito before it becomes infectious to other individuals in the course of subsequent blood meals. The period required for that life-cycle change increases as the ambient temperature declines, and given the life span of the mosquito, transmission becomes much less likely when the temperature falls below 18 °C. Moreover, malaria parasites cease development completely at temperatures below 16 °C, and many species of vector mosquitoes suspend biting activity at very low temperatures, further reducing the stability of malaria transmission in temperate regions^{6–8}.

Although other climatic features such as rainfall and humidity also affect the stability of transmission⁸, seasonal temperature variation is a predominant factor in explaining the geographical distribution of the disease. Cold winters facilitated effective elimination of malaria infection from much of the temperate zone, leading malariologist Battista Grassi in 1901 to declare malaria a "giant with feet of clay", an obstacle that can readily be eliminated once appropriate interventions become available.

With the benefit of hindsight, we now understand that this optimistic statement is at best a statement concerning temperate-zone malaria. In tropical regions, exposure to mosquitoes may be perennial and frequently includes several contacts with infected vector mosquitoes each night. Such inoculation rates, combined with the long

duration of parasite survival in the host, rapidly saturate local human populations, resulting in universal prevalence and superinfection. This stable pattern of transmission resists amelioration, and vector control efforts that succeed in temperate zones have repeatedly failed to eradicate the parasite from tropical and subtropical regions, although control is possible (ref. 7; and see below). The changing global pattern of malaria transmission from 1946 to 1994 illustrates the success of antimalaria efforts in the more temperate regions of the world and the increased concentration of disease burden in the tropics (Fig. 1). Today, Africa alone accounts for 90% of malaria mortality.

The relationship between poverty and malaria

As a general rule of thumb, where malaria prospers most, human societies have prospered least. The global distribution of per-capita gross domestic product (GDP) in 1995, adjusted for purchasing power, shows a striking and unmistakable correlation between malaria and poverty (Fig. 2). Poverty is concentrated in the tropical and subtropical zones, the same geographical boundaries that most closely frame malaria transmission. The extent of the correlation suggests that malaria and poverty are intimately related. In fact, a comparison of income in malarious and non-malarious countries indicates that average GDP (adjusted to give parity of purchasing power) in malarious countries in 1995 was US\$1,526, compared with US\$8,268 in countries without intensive malaria — more than a fivefold difference⁹. Malaria-endemic countries are not only poorer than non-malarious countries, but they also have lower rates of economic growth. Between 1965 and 1990, countries in which a large proportion of the population lived in regions with *Plasmodium falciparum* malaria experienced an average growth in per-capita GDP of 0.4% per year, whereas average growth in other countries was 2.3% per year⁹.

This correlation can, of course, be explained in several possible ways. Poverty may promote malaria transmission; malaria may cause poverty by impeding economic growth; or causality may run in both directions. It is also possible that the correlation is at least partly spurious, with the tropical climate causing poverty for reasons unrelated to malaria. We tend to favour the explanation that causation runs in both directions, with the causal link from malaria to underdevelopment much more powerful than is generally appreciated.

It is certainly true that poverty itself can be held accountable for some of the intense malaria transmission recorded in the poorest countries. Personal expenditures on prevention methods such as bednets or insecticides, increased funding for government control

programmes, and general development such as increased urbanization can reduce malaria transmission. The elimination of malaria from wealthier countries in the 1930s to 1950s, such as the United States, Italy, Greece and Spain, was a result of both socioeconomic development and intensive antimalaria interventions. Improved housing, especially the provision of screened doors and windows, limits contact between mosquitoes and people. This, combined with efforts at environmental management such as the draining of swampland, which eliminates the breeding grounds of certain vector mosquitoes, and indoor spraying of residual insecticides such as DDT, successfully eliminated malaria from most temperate zone countries¹⁰.

But economic development alone is not enough. Even relatively wealthy countries with high year-round temperatures, such as Oman and the United Arab Emirates, have been unable to eliminate the disease. And within malarious regions, people from relatively wealthy households frequently fall ill from malaria. When malaria incidence within African villages is stratified by household income, there is often little difference across income classes¹¹.

The causation in the other direction, from malaria to poverty, also seems to be robust and powerful. Cross-country regression analysis estimating the long-term impacts of malaria on economic growth and development suggest the significance of the economic burden of the disease⁹. This analysis finds that countries in which a high proportion of the population lived in regions of *P. falciparum* malaria transmission in 1965 had annual economic growth rates that were 1.3% lower than other countries over the period 1965–1990, even after controlling for the other standard growth determinants used in macroeconomic analyses. These other determinants include levels of human capital, life expectancy, initial income, and macroeconomic policy indicators of various kinds as well as geographical factors such as tropical location that could be simultaneously influencing malaria and economic growth. Because this shortfall refers to the annual growth rate, the long-term effect on the level of gross national product (GNP) per capita is the cumulative effect of an annual reduction in growth. In the mathematical formulation used by Gallup and Sachs⁹, the long-term effect can be estimated as reducing the level of GNP per capita in a malarious country by more than half in comparison with a non-malarious country. Table 1 shows the estimated impact of malaria on incomes in thirty-one African countries between 1980 and 1995.

Malaria represents broad social and economic costs

Traditionally, studies that have attempted to estimate the economic burden of malaria have focused on the private and non-

Figure 1 Global distribution of malaria. The changing global distribution of malaria risk from 1946 to 1994 shows a disease burden that is increasingly being confined to tropical regions.

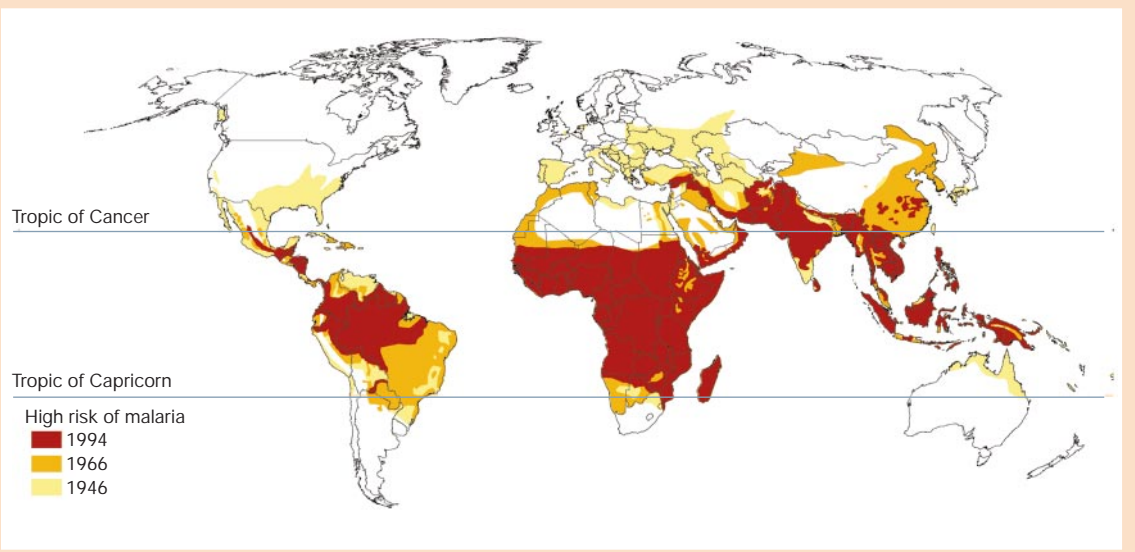
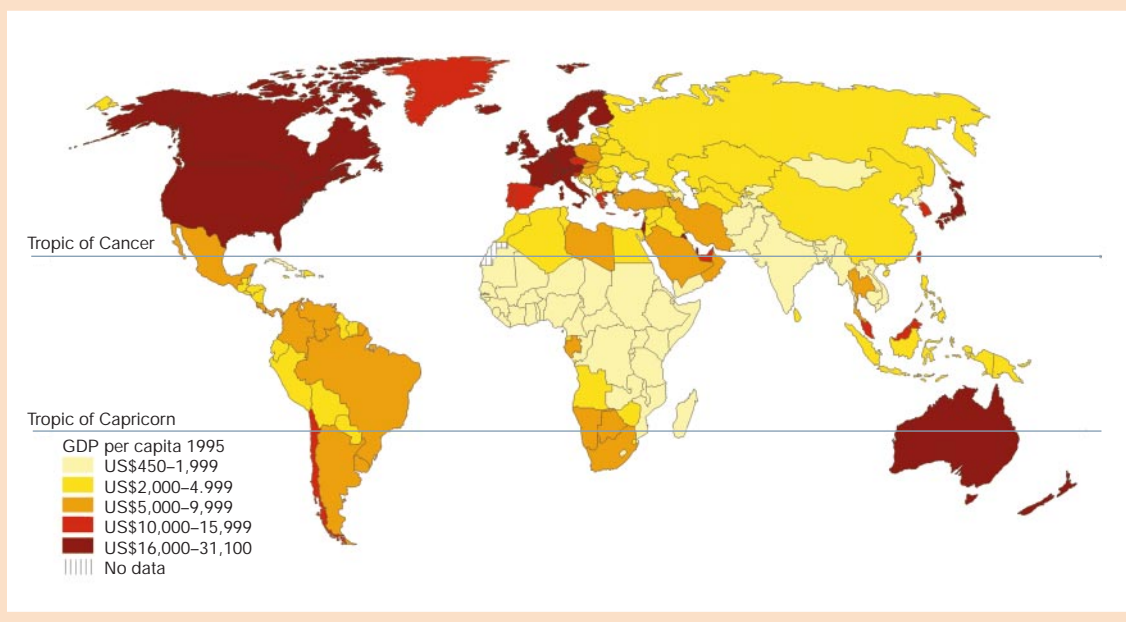


Figure 2 Global distribution of per capita GDP. The global pattern of income distribution is highly uneven, with average income levels significantly lower in tropical regions.



private medical costs associated with the disease, as well as some measure of the income that is foregone as a result of malaria morbidity and mortality. Private medical costs refer to personal expenditures on prevention, diagnosis, treatment and care of the disease. They include such factors as expenditure on bednets, doctor's fees, the cost of anti-malarial drugs, and the cost of transportation to medical facilities and the necessary support provided there. Non-private medical care costs are public expenditures on both prevention and treatment of the disease. They include expenditures by the government on such factors as vector control, health facilities, education and research. Foregone income is generally estimated by calculating the value of lost workdays as a result of malaria and malaria-related illness, based on estimated wages. In the case of mortality, foregone income is estimated by calculating the capitalized value of future lifetime earnings that would have been earned by those who died prematurely as a result of the disease, based on projected incomes for different age groups, basic longevity data and age-specific mortality rates.

These studies have found a burden that is significant and especially severe for those in the lowest income brackets. But the estimates, which average approximately 1% of GDP, simply miss some of the most important ways in which the disease affects long-term economic growth and development. In effect, traditional studies have used accounting techniques which assume that the economic costs of malaria can be determined by the average cost of an individual episode of illness, multiplied by the total number of cases encountered, and adding any fixed costs expended in prevention and treatment. Such techniques might be appropriate when there are a few episodes of disease (for example, episodes of malaria in the United States and Europe resulting from travel in malarious regions), but make little sense when extended to situations of high transmission.

There are at least two broad categories of mechanisms through which malaria can impose economic costs well beyond direct medical costs and foregone incomes. The first is the effects that occur through changes in household behaviour in response to the disease, which can result in broad social costs. These include such factors as schooling, demography, migration and saving. The second are macroeconomic costs that arise specifically in response to the pandemic nature of the disease and that cannot be assessed at a household level. These include the impact of malaria on trade, tourism and foreign direct investment. Below we

explore some of these additional pathways through which malaria affects economic development.

Long-term demographic consequences

Malaria kills more than one million people a year, and perhaps close to three million when the role of malaria in deaths related to other diseases is included. Much of the mortality in endemic areas is concentrated among children under the age of five. In areas of stable endemic transmission about 25% of all-cause mortality in children aged 0 to 4 years has been attributed directly to malaria¹². Furthermore, trials using insecticide-treated bednets in some African countries have shown a reduction in all-cause mortality among infants and children of up to 60%, indicating that in these areas malaria directly and indirectly accounts for an extremely high proportion of infant and child deaths¹³⁻¹⁶.

Aside from the direct demographic consequences of this alarming level of mortality there are also likely to be significant indirect effects. Historical evidence has shown that high infant and child mortality rates are linked closely to high fertility rates. Along with other factors such as household income, female education and the availability of birth control, infant and child mortality are important factors in the fertility decisions of households¹⁷⁻²⁰. The simplest explanation for this link is that parents have additional children to replace the ones that they lose. Another hypothesis, known as the 'child-survivor hypothesis', is that parents base their fertility decisions on a desire for a certain number of surviving children (for example, to guarantee at least one surviving male heir, or one surviving child into the old age of the parents). In this theory, risk-averse households raise fertility by even more than expected mortality, in order to ensure a sufficiently high likelihood of the desired number of surviving children. This theory predicts that a high burden of malaria will lead to a disproportionately high fertility rate and an overall high population growth rate in regions of intense malaria transmission. These predictions are supported by cross-country evidence, although the direct causal linkages from malaria deaths to increased fertility to rapid population growth is circumstantial, and yet to be proved.

A high fertility rate among poor households is also likely to lead to reduced investments in education per child, a phenomenon that economists term the 'quantity-quality trade-off'. A high-fertility environment can also entail especially large human capital costs for women. When women have very high fertility rates, parents may choose to invest less in the education of their daughters, knowing

that they are likely to spend a considerable portion of their working years involved in child-rearing activities rather than in the labour force where they would reap the economic returns to education. Moreover, while the hours they spend caring for a young child may not represent a majority of their workday, women will undoubtedly be limited in their employment choices by the need to be available to the child, with a resulting loss in work opportunities and job experience. Over the long term, such factors can have a sizeable impact on economic growth and productivity.

While it is difficult to estimate the exact responsiveness of fertility and education to malaria-induced mortality, a high-fertility/high-mortality environment presents very high costs at both a household and a national level. At the simplest level, the economic value of resources invested in infants who do not survive can be significant. Estimates of the number of hours parents spend in child-rearing for every year of a child's life and calculations of the productive time 'lost' based on infant and child mortality in high-mortality societies show this to be a substantial cost²¹.

Additional effects will operate through changes in the dependency ratio — the number of dependants per working-age population. If couples are following a child-survivor strategy, at any given time there will be many more young children in the population than are expected to survive into adulthood. This directly lowers GNP per capita (since GNP is produced by adults, whereas GNP per capita is measured relative to the total population). A high dependency ratio has also been shown to have long-term growth impacts through other channels, such as household saving behaviour²².

The acquisition of human capital

Where malaria is highly endemic, adults generally develop partial immunity to the symptoms of the disease. Young children, however, bear a considerable burden in terms of malaria morbidity and mortality. Although this morbidity is most concentrated among pre-school children, school-age children also suffer the effects, resulting in school absenteeism. For example, in Kenya it was found that primary school students miss 11% of school days per year because of malaria, and secondary school students miss 4.3% of school days²³. Another study attributed 13–50% of medically related school absences to the disease²⁴. The adverse effects on schooling are likely to go far beyond the number of days lost per year, as absenteeism increases failure rates, repetition of school years, and drop-out rates.

An even more severe consequence can arise from the impact of malaria on cognitive development and learning ability. Although there is some debate about the direct relationship between malaria and mental functioning, a number of channels have been identified through which malaria can affect cognitive abilities in ways ranging from subtle to profound²⁵. For example, children with malaria are found to have poorer nutritional status than non-malarial children^{26,27}, an outcome that can impair brain development^{28–30}. In at least one area of cognitive development, the performance of fine motor functions, it has been found that parasitaemic children perform worse than non-parasitaemic children³¹.

At an even earlier stage, malaria impacts on fetal development. Pregnant women are particularly likely to be infected by malaria as a result of diminished immunity, and malaria-related anaemia of the mother is related to low birthweight among babies. This is a risk factor for neurosensory, cognitive and behavioural development of children³². Compared with normal birthweight babies, low birthweight babies are two to four times more likely to experience failure in school³³.

There can also be long-term cognitive effects of severe cases of malaria. Cerebral malaria affects approximately 575,000 children a year in Africa, killing 10–40% of patients^{25,34,35}. Of those who survive, 5–20% experience neurological sequelae including behavioural disorders and impairment in the ability to carry out

Table 1 Loss from the economic growth penalty of malaria endemicity in 31 African countries 1980–1995

Country	Aggregate loss (PPP-adjusted US\$ million)*	Per person loss (PPP-adjusted US\$)*	Fraction of actual 1995 income
Benin	1,172	214	18%
Botswana	503	347	5%
Burkina Faso	1,684	162	18%
Burundi	730	117	18%
Cameroon	4,227	318	18%
Central African Rep.	884	270	18%
Chad	995	154	17%
Congo	759	288	18%
Congo, Dem. Rep.	7,125	162	18%
Côte d'Ivoire	4,107	294	18%
Gabon	1,389	1,290	17%
Gambia	251	226	18%
Ghana	5,355	314	18%
Guinea Bissau	152	142	14%
Kenya	5,272	198	18%
Lesotho	0	0	0%
Madagascar	2,280	167	18%
Malawi	1,072	110	18%
Mali	1,222	125	17%
Mauritania	611	269	15%
Mauritius	0	0	0%
Namibia	832	539	10%
Niger	1,457	161	17%
Nigeria	17,315	156	18%
Rwanda	656	102	18%
Senegal	2,426	286	18%
Sierra Leone	366	87	17%
South Africa	4,056	98	1%
Togo	1,166	285	18%
Zambia	1,359	151	18%
Zimbabwe	4,214	383	18%
Total	73,638	185	10%

*Figures are reported in US dollars held constant at 1987 prices and are adjusted for purchasing power parity (PPP), that is, for differences in the local purchasing power of the currency with respect to a fixed market basket of goods and services.

executive functions such as initiating, planning and executing tasks^{25,36,37}. Furthermore, seizures that result from clinical malaria are associated with increased risk of impaired intellectual functioning²⁵.

Human capital constitutes a key factor in economic growth. Modern economic theories have posited that returns to human capital are in fact increasing in scale, with the total impact on economic growth being greater than the sum of the individual contributions. The impact of malaria on economic growth rates through the mechanism of depressing the rate of human capital accumulation could be considerable. Although there have been some estimations of the loss of educational investment expenditures as a result of lost school days³⁸, the overall impact of malaria on human capital development in children remains largely unexplored and unquantified.

The acquisition of physical capital

The direct costs of prevention and treatment of the disease eat into the disposable income of poor families, as do the costs of lost productivity. Whereas economic models suggest that increased risk of illness could, in fact, increase savings if families were trying to protect themselves from vulnerability to economic shocks by building a buffer, there is little evidence to support this idea in the poor, rural households that have been studied. The evidence suggests that malaria decreases household savings as families are forced to hire labour to compensate for days lost to morbidity³⁹.

The long-term demographic impacts of malaria also potentially affect savings rates. If reduced malaria-related infant and child mortality does bring down fertility rates, then the resulting decline in the dependency ratio could lead to a higher savings rate. It has been argued that families with lower dependency ratios, with fewer children to feed and clothe, are more capable of saving and investing, not just in physical capital or capital markets, but also in the human capital of each child through education, as noted above.

Malaria affects the movement of people

Risk of malaria infection has a profound effect on the mobility of human populations and the construction of new settlements, with consequent impact on economic growth and development⁴⁰. Although residents of highly endemic sites generally develop disease-modifying immunity that diminishes malaria-related morbidity and mortality, antigenic diversity may limit this effect geographically. Such acquired immunity, moreover, can be transient and is often lost within a year or so in the absence of re-infection, such as during a period of schooling or employment away from the malarious region. As in the case of migrants, the return of residents to their original endemic homes carries an increased risk of death or disease.

The importance of acquired adult immunity in protecting against malaria morbidity and mortality potentially inhibits the movement of labour between malarious and non-malarious regions. This represents an economic cost because human mobility permits labour to move to regions where it is most productive. By limiting such movement, malaria would interfere with skill matching and generally inhibit maximization of worker productivity. Furthermore, incentives to expand markets into malarious regions of the world will be lost in the event that trade and commercialization expose people to an increased burden of malaria, a factor that can hinder long-term economic development.

Trade and foreign direct investment

Throughout history, malaria has suppressed the economic linkages between malarious and non-malarious regions. In previous centuries this isolating effect may have served to protect malarious countries from European colonizers. But in today's globalized economy, the isolation has more negative effects⁴¹. Although direct measurement of the impact of disease on decision-making by foreign investors is difficult to gauge, failure of investment is likely to be one of the most costly effects of malaria with respect to long-term growth. Investors from non-malarious regions tend to shun malarious regions for fear of contracting the disease — a fear that is sadly well grounded in reality, as evidenced recently by the experience of Billiton, a London-based mining and metals company. In a US\$1.4 billion joint venture investment to build an aluminium smelter in Mozambique, the largest foreign investment so far in that country, the company was faced with 7,000 cases of malaria in two years, and the death of 13 expatriate employees⁴².

Industries such as tourism are particularly hard hit by malaria transmission, as is becoming clearer in countries such as Mozambique and South Africa as they attempt to encourage investment in these areas with limited success. Investments in all sorts of production — in mining, agriculture and manufacturing — may similarly be crippled if the labour force faces a heavy disease burden, or if the burden raises the costs of attracting the needed labour to a malarious region. In an economic era in which international trade and finance is critical for economic development, these adverse effects on foreign trade and investment are likely to be of tremendous macroeconomic importance.

When malaria transmission was suppressed in the subtropical regions of southern Europe in the 1950s, there was a subsequent surge of economic growth. Greece, Portugal and Spain all began a process of accelerated economic development. One of the sources of that growth was increased foreign investment by northern

European firms. Another was greatly increased tourism. Although the linkages from malaria control to increased investment and tourism have not been proven rigorously, the timing and sectoral evidence support the proposition that malaria control played an economically important role.

Malaria and other illnesses

One of the surprising results to emerge from large-scale trials of insecticide-treated bednets is that the reduction in all-cause mortality with the use of bednets is considerably greater than the reduction in malaria-attributed mortality. This might imply that malaria is closely linked to other diseases, either as a direct causal factor, or because malaria renders individuals more susceptible to other infections¹².

The indirect effects of malaria can begin even before birth. As mentioned earlier, pregnant women are at a higher risk of malaria infection, and malarial pregnancy can result in miscarriages, neonatal and infant mortality, low birthweight and congenital infection. Acute and chronic malaria infections can alter the immune system and the body's response to vaccines, and increase vulnerability to other infections.

Furthermore, chronic malaria is an important causal factor in anaemia^{27,43}, which has been shown to have direct physical effects, lowering worker productivity and output^{44,45}. Malaria is also associated with hyper-reactive malarial splenomegaly, chronic renal damage and the nephrotic syndrome, and Burkitt's lymphoma. Increasingly, malaria is becoming a factor in the transmission of human immunodeficiency virus (HIV), the virus that causes AIDS, as children with severe malaria often require blood transfusions, and much of the blood supply in sub-Saharan African countries is infected with HIV. To the extent that malaria is a factor in other illnesses, any assessment of the economic burden of malaria should include the range of costs that are associated with these illnesses.

Looking to the future

Although the failure of earlier attempts at global eradication of malaria led initially to donor fatigue and a weakening of intervention efforts, the lessons of history can serve us well as we look to the future in our battle against the disease. Experience indicates that temperate and tropical malarias can be considered as distinct epidemiological manifestations of a common array of parasites, and although elimination may be a reasonable goal in temperate zones, it has proved unrealistic in many tropical and subtropical environments⁴⁶. However, a range of cost-effective approaches is available to reduce the burden of malaria, including case management, the use of insecticide-treated bednets, indoor residual spraying, and environmental control measures such as larviciding (controlling mosquitoes at the larval stage through the use of chemicals) and filling and draining of breeding sites⁴⁷. Each of these interventions seems to have great value with respect to the health gains achieved per dollar spent and, by extension, would have enormous economic benefits. Effective malaria control programmes can be developed using a combination of these approaches adapted to local needs based on specific ecological, epidemiological, economic and social conditions.

Within its dominion, malaria affects almost every aspect of social and economic endeavour, including fertility, savings and investment rates, crop choices, schooling and migration decisions. Where transmission is intense, the disease creates a complex set of biological and behavioural responses with a long-term effect on economic growth and development that goes well beyond the additive costs of individual cases. Suppressing malaria in poor, highly malarious regions, especially in sub-Saharan Africa, offers the potential to initiate a virtuous cycle in which improved health spurs economic growth, and rising income further benefits human health. The economic evidence also suggests that high priority targets should include port cities, potential tourist destinations,

mining operations and high-value-added agricultural settings. Even when disease incidence is lower in such settings than in other places, the economic benefits of disease control in these locations (through increased tourism, trade and investment) could be enormous. More generally, reducing malaria transmission, and other communicable diseases, in low-income settings may well prove to be among the most effective available spur to overall economic development.

Despite the enormous potential benefits of antimalaria programmes, the level of international spending on malaria control in poor regions has been dismal. While current spending has been running at less than US\$100 million per year, actual needs are more than an order of magnitude greater. Detailed costing estimates prepared by the World Health Organization (WHO) Commission on Macroeconomics and Health find that effective malaria prevention and treatment will require an additional US\$2.5 billion per year as of 2007, increasing to US\$4 billion per year as of 2015. In order to scale up the international effort on malaria control, the WHO and partner institutions have launched a campaign to 'Roll Back Malaria'. This important venture will probably be hampered in its mission as it is still considerably underfunded relative to the need for malaria control and the expected return on such investments in poorer countries. The newly announced Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria may finally deliver some succour, but even that fund remains grossly underfinanced at this point. Nevertheless, we should be optimistic that the new visibility for infectious disease symbolized by such programmes represents but the first step towards putting appropriate resources at the service of those fighting the global burden of this disease. □

1. Luria, S. E. *36 Lectures in Biology* p. 439 (The MIT Press, Cambridge, 1975).
2. Luzzatto, L. Genetics of red cells and susceptibility to malaria. *Blood* **54**, 961–976 (1979).
3. Hill, A. V. S. *et al.* Molecular analysis of the association of HLA-B53 and resistance to severe malaria. *Nature* **360**, 434–439 (1992).
4. Breman, J. The ears of the hippopotamus: manifestations, determinants, and estimates of the malaria burden. *Am. J. Trop. Med. Hyg.* **64**(1,2)S, 1–11 (2001).
5. World Health Organization. Factsheet No. 94 (World Health Organization, Geneva, 1998).
6. Anderson, R. M. & May, R. *Infectious Diseases of Humans: Dynamics and Control* (Oxford Univ. Press, Tokyo, 1991).
7. Colluzzi, M. The clay feet of the malaria giant and its African roots: hypotheses and inferences about origin, spread and control of *Plasmodium falciparum*. *Parassitologia* **41**, 277–283 (1999).
8. Gilles, H. M. & Warrell, D. A. *Bruce-Chwatts Essential Malariology* (Arnold, Boston, 1993).
9. Gallup, J. & Sachs, J. The economic burden of malaria. *Am. J. Trop. Med. Hyg.* **64**(1,2)S, 85–96 (2001).
10. Kitron, U. & Spielman, A. Suppression of transmission of malaria through source reduction: antianopheline measures applied in Israel, the United States and Italy. *Rev. Infec. Dis.* **11**, 391–406 (1989).
11. Filmer, D. Fever and its treatment in the more and less poor in sub-Saharan Africa. Development Research Group (The World Bank, Washington DC, 2000).
12. Snow, R. W., Craig, M., Deichmann, U. & Marsh, K. Estimating mortality, morbidity and disability due to malaria among Africa's non-pregnant population. *Bull. World Health Org.* **77**, 624–640 (1999).
13. Alonso, P. L. *et al.* The effect of insecticide-treated bed nets on mortality of Gambian children. *Lancet* **337**, 1499–1502 (1991).
14. D'Alessandro, U. *et al.* Mortality and morbidity from malaria in Gambian children after introduction of an impregnated bednet programme. *Lancet* **345**, 479–483 (1995).
15. Nevill, C. G. *et al.* Insecticide-treated bednets reduce mortality and severe morbidity from malaria among children on the Kenyan coast. *Trop. Med. Int. Health* **1**, 139–146 (1996).
16. Binka, F. N. Impact of permethrin impregnated bednets on child mortality in Kasseña-Nankana district, Ghana: a randomized controlled trial. *Trop. Med. Int. Health* **1**, 147–154 (1996).
17. Yamada, T. Causal relationships between infant mortality and fertility in developed and less developed countries. *South. Econ. J.* **52**, 364–371 (1985).
18. Galloway, P. R., Lee, R. D. & Hammel, E. A. in *From Death to Birth: Mortality Decline and Reproductive Change* (eds Montgomery, M. R. & Cohen, B.) 182–226 (National Academy Press, Washington DC, 1998).
19. Handa, S. The impact of education, income, and mortality on fertility in Jamaica. *World Dev.* **28**, 173–186 (2000).
20. Rosensweig, M. & Schultz, T. P. Consumer demand and household production: the relationship between fertility and child mortality. *Am. Econ. Rev.* **73**, 38–43 (1983).
21. Reher, D. Wasted investments: some economic implications of childhood mortality patterns. *Popul. Stud.* **49**, 519–536 (1995).
22. Bloom, D. E., Canning, D. & Malaney, P. N. Demographic change and economic growth in Asia. *Popul. Dev. Rev.* **26**(Suppl.), 257–290 (2000).
23. Leighton, C. & Foster, R. Economic impacts of malaria in Kenya and Nigeria. Major Applied Research Paper no 6, HFS project (Abt Associates, Bethesda, 1993).
24. Brooker, S. *et al.* Situation analysis of malaria in school-aged children in Kenya: what can be done? *Parasitol. Today* **16**, 183–186 (2000).
25. Holding, P. A. & Snow, R. W. Impact of *Plasmodium falciparum* malaria on performance and learning: review of the evidence. *Am. J. Trop. Med. Hyg.* **64**(1,2)S, 68–75 (2001).
26. Rowland, M. G., Cole, T. J. & Whitehead, R. G. A quantitative study into the role of infection in determining nutritional status in Gambian village children. *Br. J. Nutr.* **37**, 441–450 (1977).
27. Shiff, C. *et al.* Changes in weight gain and anaemia attributable to malaria in Tanzanian children living under holoendemic conditions. *Trans. R. Soc. Trop. Med. Hyg.* **90**, 262–265 (1996).
28. Lozoff, B. Nutrition and behaviour. *Am. Psychiatry* **44**, 231–236 (1989).
29. McKay, H., Sinisterra, L., McKay, A., Gomez, H. & Lloreda, P. Improving cognitive ability in chronically deprived children. *Science* **200**, 270–278 (1978).
30. Grantham-McGregor, S. M., Powell, C. A., Walker, S. P. & Himes, J. H. Nutritional supplementation, psychosocial stimulation, and mental development of stunted children: the Jamaican study. *Lancet* **338**, 1–5 (1991).
31. Al Serouri, A. W., Grantham-McGregor, S. M., Greenwood, B. & Costello, A. Impact of asymptomatic malaria parasitaemia on cognitive function and school achievement of schoolchildren in the Yemen Republic. *Parasitology* **121**, 337–345 (2000).
32. McCormick, M. C., Brooks-Gunn, J., Workman-Daniels, K., Turner, J. & Peckmah, G. J. The health and development status of very low-birth-weight children at school-age. *J. Am. Med. Assoc.* **267**, 2204–2208 (1992).
33. Taylor, H. G. in *Early Brain Damage: Research Orientations and Clinical Observation* (eds Almi, C. & Fingers, S.) 325–345 (Academic, New York, 1984).
34. Murphy, S. & Breman, J. Gaps in the childhood malaria burden in Africa: cerebral malaria, neurological sequelae, anemia, respiratory distress, hypoglycemia, and complications of pregnancy. *Am. J. Trop. Med. Hyg.* **64**(1,2)S, 57–67 (2001).
35. Greenwood, B. *et al.* Mortality and morbidity from malaria among children in a rural area of The Gambia, West Africa. *Trans. R. Soc. Trop. Med. Hyg.* **81**, 478–486 (1987).
36. Brewster, D. R., Kwiatkowski, D. & White, N. J. Neurological sequelae of cerebral malaria in children. *Lancet* **336**, 1039–1043 (1990).
37. Holding, P. A., Stevenson, J., Pershu, N. & Marsh, K. Cognitive sequelae of malaria with impaired consciousness. *Trans. R. Soc. Trop. Med. Hyg.* **93**, 529–534 (1999).
38. Kere, N. K., Keni, J., Kere, J. F., Bobogare, A. & Webber, R. H. The economic impact of plasmodium falciparum malaria on education investment: a Pacific Island case study. *Southeast Asian J. Trop. Med. Public Health* **24**, 659–663 (1993).
39. Nur, E. The impact of malaria on labour use and efficiency in the Sudan. *Soc. Sci. Med.* **37**, 1115–1119 (1993).
40. Sawyer, D. Economic and social consequences of malaria in new colonization projects in Brazil. *Soc. Sci. Med.* **37**, 1131–1136 (1993).
41. Spielman, A. & DiAntonio, M. *Mosquito* p. 247 (Hyperion, New York, 2001).
42. Choice of evils: as a tropical surge makes a comeback, so, too, does DDT. *Wall St. J.* 26 July (2001).
43. Hedberg, K. *et al.* *Plasmodium falciparum*-associated anemia in children at a large urban hospital in Zaire. *Am. J. Trop. Med. Hyg.* **48**, 365–371 (1993).
44. Scholz, B. D., Gross, R., Schultink, W. & Sastroamidjojo, S. Anaemia is associated with reduced productivity of women workers even in less-physically-strenuous tasks. *Br. J. Nutr.* **77**, 47–57 (1997).
45. Basta, S., Soekirman, S., Karyadi, D. & Scrimshaw, N. S. Iron deficiency anemia and the productivity of adult males in Indonesia. *Am. J. Clin. Nutr.* **32**, 916–925 (1979).
46. Spielman, A., Kitron, U. & Pollack, R. Time limitation and the role of research in the worldwide attempt to eradicate malaria. *J. Med. Entomol.* **30**, 6–19 (1993).
47. Goodman, C. A., Coleman P. G. & Mills, A. J. Cost-effectiveness of malaria control in sub-Saharan Africa. *Lancet* **354**, 378–385 (1999).

Acknowledgements

This work was carried out under Program on Malaria, Economics and Human Affairs, directed by A. Spielman at the Center for International Development. This article has benefited greatly from Dr Spielman's support and ongoing tutelage in the scientific and epidemiological aspects of the malaria disease and vector. We are also grateful to E. Weinstein for valuable insights, to J. Gallup for previous collaboration, and to A. Kiszewski for sharing his entomological expertise. Excellent research assistance was provided by E. Gummerson.