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Draft for Discussion

Interim Report of the Chairman of the Commission on Macroeconomics and Health of the WHO[1]

I. Introduction and motivation of the report

The crisis of public health in the poor countries

A massive public health crisis in many of the world's poorest countries poses one of the great challenges facing the world today. The huge toll of disease and premature death, much of which is readily preventable with existing technologies, causes untold human suffering and throws huge obstacles in the path of long-term economic development. Poor health depresses economic well-being through several direct and indirect channels, including: lower productivity of workers; disruptions of households, enterprises, and communities; destabilization of government budgets; decreased household and enterprise saving and investment; adverse effects on cognitive development and schooling; high fertility rates to compensate for high infant and child mortality rates, with adverse consequences on population size, age structure, and growth rates; and lower investments per child in health and education.

The public health crisis has worsened dramatically in recent years as a result of the HIV/AIDS pandemic. Traditional killer diseases such as malaria, tuberculosis (TB), diarrhea, and respiratory infection, have also surged in many areas and continue to take millions of lives per year in the poorest countries. Hundreds of millions of people have little or no access to medical care. Life expectancy at birth (LEB) in Sub-Saharan Africa is only 50 years, in stark contrast to the 78 years LEB of the high-income countries (World Bank, WDR, 2000). In many of the poorest countries, life expectancy has plummeted in recent years (for example falling in Zambia from 50 years in 1980 to just 43 years in 1998). Experts at the WHO have recently incorporated disability into estimates of life expectancy, by translating each year of disability, depending on its severity, into a fraction of a year of lost life. The resulting concept, termed the disability-adjusted life expectancy (DALE), shows the number of disability-free life years expected at birth. The gap between rich and poor in terms of DALEs is even starker than the gap in the conventional LEBs. In some countries in Africa, the disability-free life expectancy is a shocking 35 years or less. Zambia's DALE stands at 30.3 years, Malawi's at 29.4 years. In those countries, the very struggle for survival itself absorbs the human energies that should otherwise go to enjoyment of life and improvement of economic prospects in the future.

[1] Prepared by Professor Jeffrey Sachs of Harvard University, Chairman of the Commission on Macroeconomics and Health (CMH) of the World Health Organization, for discussion in Paris, November 9 – 10, 2000. Not for Quotation or attribution to the CMH.

Leaders in both the developed and developing countries have underestimated the enormity of the public health crisis. Past global commitments to "Health for All by the Year 2000," famously inaugurated at the World Health Assembly of 1977 and reaffirmed a year later in the Alma Ata Declaration of 1978, have not been fulfilled. Donor governments and multilateral institutions put too much stress on macroeconomic reforms in the poor countries while putting too little effort and financial resources into fighting the growth health crisis. Macroeconomic policy reforms, such as trade liberalization and currency convertibility, while important for the poor countries, did not by themselves produce sustained economic growth in societies heavily burdened by disease. The converse is also true: social investments in health and education did not produce sustained economic growth when the macroeconomic framework was inappropriate. [2] Investments in health and policies to promote economic growth must go hand in hand.

Table 1 shows the economic growth rates of developing countries after 1965, categorized according to income levels and infant mortality rates in that year. Growth is measured as the annual average change of gross national product (GNP) per person.

Table 1. Growth Rate of Per Capita Income, 1965 – 1994 (for given income and infant mortality rate, 1965)

	Initial Infant Mortality Rate, 1965	IMR <= 50	50 < IMR <= 100	100 < IMR <= 150	IMR > 150
Initial Income, 1965					
GDP <= $750		------	3.7	1.0	0.1
$750 < GDP <= $1500		------	3.4	1.1	-0.7
$1500 < GDP <= $3000		5.9	1.8	1.1	2.5
$3000 < GDP <= $6000		2.8	1.7	0.3	------
GDP > $6000		1.9	-0.5	-------	-------

Note: The reported growth rate is the simple average of the GDP growth rates of all countries in the specific cell.

[2] An important case in point, discussed later in the report, is the Indian state of Kerala. This state, for geographical, historical, political, and social reasons made remarkable advances in public health and education despite a low level of income. However, the macroeconomic environment – weak infrastructure, government monopolization of key sectors, restrictions on private trade and investment – meant that the social advances could not translate into rapid economic growth. One outlet has been very high levels of emigration from Kerala to the Middle East, Europe and the United States, as Kerala's healthy and well-educated populace has found employment outside of India.

This is not a coincidence. *Poor health is a direct and important contributor to poor economic performance.* For every income range in 1965, countries with a low infant mortality rate in 1965 experienced higher growth during 1965-95 than did countries with a high infant mortality rate (with only one reversal in the whole table).

The tragic neglect of the public health crisis of the poor countries is especially ironic in the midst of the revolutions in health and information technology. In many cases highly effective and relatively inexpensive technologies already exist to address major killer diseases, yet such effective approaches are dramatically underutilized. In other cases, new and improved technologies are within the reach of modern science, but are not being developed with the speed and urgency that is required, in part because market incentives for R&D are inherently weak in the case of diseases that mainly afflict poor people, such as malaria, HIV/AIDs, and TB. New incentive schemes will be needed to develop new anti-malarial drugs, or vaccines for viral sub-types of HIV/AIDS that are prevalent in developing countries, or new TB treatments with a shorter treatment course with easier compliance

Despite a decade of increasingly urgent pleas by the world's public health community for action against the HIV/AIDS pandemic, and against other killer diseases such as malaria and tuberculosis, the actual mobilization of financial and political resources to address the public health crisis of the poor countries has so far not been achieved. In parts of Sub-Saharan Africa and South Asia, the budgetary expenditures per person on health are around $4 per person per year, compared with more than $1,000 per year (and often much more) in the rich countries. The meager sums include both domestic resource mobilization and all international donor assistance to Ministries of Health to undertake their work. We estimate that international donor assistance to the low-income countries for basic health, including infectious disease control and programs to combat HIV/AIDS has been much less than $1.00 per person per year in those countries.

The Context of Globalization

At the opening of the 21st century, the challenge of public health must be considered in the context of globalization. Globalization has two basic and interconnected meanings. On the one hand, it is the process of increasing economic integration of national economies, characterized by the rising importance of international trade, cross-border finance, and cross-border production systems. On the other side, it is a political process, whereby national governments are increasingly binding their behavior – in economics, environmental management, health standards, intellectual property rights, and other areas – on the basis of international treaties under the umbrella of international institutions. The processes are obviously interlinked: economic integration spurs the promulgation of international treaty obligations, while international agreements especially in trade and finance, spur the economic integration of national economies. Both processes, moreover, are promoted by the fundamental advances in communications, information, and transport technologies.

Globalization offers enormous – indeed unprecedented -- opportunities for poor countries, but also great risks. The opportunities come from the fact that poor countries can increasingly benefit from cross-border inflows of technology and capital from the richer countries, and these inflows of technology and capital can spur rapid economic development. Moreover, the chance to sell products into an expanding world market can be a great spur for economic growth. All of the development success stories of poor countries in the past 30 years (such as China, Korea, Taiwan, Malaysia, Chile, Mauritius, and Botswana) are characterized by export-led growth. Rapid increases of export earnings were reinvested in these countries in improvements in health, education, physical infrastructure, and new businesses.

The risks of globalization are also real. The main risk is that many of the world's poorest countries might be left out of global progress, because of their geographic isolation, or heavy disease burden which frustrates economic development, or political and social instability, or even the adverse effects of market forces. For example, since people and capital can move more easily across national borders, a poor country may suffer more from the outflow of its skilled professionals than it gains from the inflow of capital and technology. The rich countries sometimes encourage "brain drain" by giving visa preferences to the skilled workers of the poor countries, while blocking immigration of unskilled workers. It is estimated that around half of each graduating class of medical students in Ghana, for example, now emigrates almost immediately to higher-paying jobs in Europe, the Middle East, and the United States.

The risks of technological stagnation in the poor countries coupled with brain drain to the rich countries may be magnified by key features of global research and development (R&D). The imbalance in R&D between rich and poor countries is even larger than the imbalance in income. Economist's describe R&D as an "increasing returns to scale activity," in which past technological successes are the breeding ground of new breakthroughs. For that reason, the technologically advanced regions are able to innovate much more rapidly than the poor regions. And if the poor countries face problems that require technologies different from those used in rich countries – for example, technologies to fight malaria rather than cardiovascular disease – then the rapid innovation in the rich countries might not be so helpful, by itself, for the world's poor. Special approaches will be needed to "steer" global science to address the health problems of poor people in poor countries.

Globalization can also entail risks for the rich countries as well. Crisis in poor countries more easily spill over to rich countries through illegal immigration, international criminal networks, illicit drug trafficking, and of course the easier spread of pathogens because of increased international travel. Just as the great epidemics of the past were often carried by international traders, now the pathways of HIV/AIDS, multi-drug-resistant TB, antibiotic-resistance bacteria, West Nile Virus, and other emerging diseases are frequently spurred by international trade and tourism or the misuse of antibiotics and other pharmaceuticals, leading to the cross-border spread of drug-resistant pathogens.

Globalization therefore calls for a deep re-thinking of economic strategies at the national and international levels. The poor countries will have to proceed, broadly speaking, on two fronts. On the one hand, they will have to re-double their efforts to improve their own public health and educational standards, lest they lose their small cohort of skilled labor to international migration. Second, they will have to find new approaches to economic growth, focusing heavily on ways to attract foreign investment and to penetrate new export markets. The developing countries that have succeeded in attracting large-scale foreign investment in the past decade are also the developing countries that have had most success in the new global economy.

At the international level, we will have to re-think international assistance strategies as well as ways that international treaties are negotiated. The poorest countries will need greatly increased foreign assistance to address their health and education crises if they are not to be left further and further behind in the global economy. For a poor country to get on the path of increasing inward investment and technological advancement – rather than on the path of brain drain and collapse – it will have to have a minimally acceptable social and business environment. This includes adequate health and education, as well as capacity to introduce new technologies. As we shall stress, most poor countries will be unable to achieve such conditions without substantial international financial assistance from the rich countries.

International treaties will also have to take into account the new risks and opportunities of a global economy. For example, when the new global system of intellectual property rights was instituted in the Uruguay Round trade negotiations, too little consideration was given to the interests of very poor countries that would be hurt by the extension of patents over essential medicines. There are several areas other areas where international agreements must explicitly protect the rights of the poorest countries. Global leaders have increasingly recognized that globalization requires new international systems for managing the cross-border flows of pathogens, cross-border risks to health from environmental ills, and cross-border risks from inappropriate use of antibiotics.

Fortunately, the worlds' leaders are focusing anew on the health crisis of developing countries, and on the need to mobilize greater financial and human resources to combat the crisis. In April 2000, 19 heads of state of African nations met in Abuja, Nigeria, to dedicate themselves to a new and urgent battle to control malaria. They not only pledged their own countries' resources, but also issued an urgent plea to the world community to support the effort through deep debt relief and at least $1 billion of new funds for malaria control efforts in Africa. Three months later, at the Okinawa Summit in June 2000, the leaders of the G-8 countries stated that:

> Health is key to prosperity. Good health congtributes directly to economic growth whilst poor health drives poverty. Inrfectious and parasitic diseases, most notably HIV/AIDS, TB and malaria, as well as childhood diseases and common infections, threaten to reverse decades of development and to rob an entire generation of hope for a better future. Only through sustained action and coherent

international co-operation to fully mobilize new and existing medical, technical and financial resources, can we strengthen health delivery systems and reach beyond traditional approaches to break the vicious cycle of disease and poverty.

Still more significantly, the 150 world leaders assembled at the Millennium Assembly of the United Nations included the following goals in the United Nations Millennium Declaration:

- To halve, by the year 2015, the proportion of the world's people whose income is less than one dollar a day and the proportion of people who suffer from hunger; and also, by the same date, to halve the proportion of people who are unable to reach, or to afford, safe drinking water.

- To ensure, that by the same date, children everywhere, boys and girls alike, will be able to complete a full course of primary schooling; and that girls and boys will have equal access to all levels of education.

- By the same date, to have reduced maternal mortality by three quarters, and under-5 child mortality by two thirds, of their current rates.

- To have, by then, halted, and begun to reverse, the spread of HIV/AIDS, the scourge of malaria, and other major diseases that afflict humanity.

- To provide special assistance to children orphaned by HIV/AIDS.

- By 2020, to have achieved a significant improvement in the lives of at least 100 million slum dwellers as proposed in the "Cities Without Slums" initiative.

An Interim Report

This **Interim Report of the Commission on Macroeconomics and Health** (CMH) of the World Health Organization aims to assist the international community in preparing a bold but realistic framework for a major attack on the diseases that now block economic and social development in many of the world's poorest countries. The final report of the Commission will be presented in December 2001. In this interim report, we present the growing body of evidence that poor health indeed seriously hinders economic development, and then show that effective technologies exist to reduce the disease burden, but that such technologies are not being applied on an adequate scale because of a lack of political focus in the world community and a lack of adequate financial resources. Both the poor countries themselves and especially the rich countries will have to mobilize greater financial and political resources to back this effort. Health must become a central focus of attention of the political and financial leadership of rich and poor countries -- of Presidents, Prime Ministers and Finance Ministers, in addition to the the valiant but oft-beleaguered Ministers of Health.

The report proceeds in four main sections following the introduction. Section II discusses the manifold linkages of health and development, and especially the ways that improvements in health can contribute to economic growth and economic development more broadly. This section makes clear that the linkages of health and development work in two directions: health affects economic development, while economic development affects health. This two-way causality can create a vicious circle in which poor health and poverty chase each other in a mutually reinforcing manner, and can also make possible a virtuous circle in which improvements in health and economic growth are mutually reinforcing. Development policies, within poor countries and through international cooperation, should ensure that countries are on the virtuous circle of upward development and improving health.

Section III discusses the priorities for health interventions in the poor countries, stressing that a limited number of diseases contribute the vast majority of the excess disease burdens of the poor countries. We focus our attention on 10 major disease categories, which account for the preponderance of the excess disease burden faced by the poorest countries compared with the high-income countries. These are:

- Malaria
- HIV/AIDS
- Tuberculosis
- Acute Respiratory infections
- Diarrheal diseases
- Vaccine-preventable illnesses
- Reproductive Health
- Tropical parasites and helminthic infections
- Nutritional deficiencies
- Tobacco-related illnesses

In each case, existing technologies, if properly applied and utilized within the poor countries, offer highly cost effective and technologically effective means of prevention or treatment. In most cases, as well, increased R&D efforts hold promise for even more effective interventions in the future, this being especially the case because R&D has been so limited to date, so that many promising approaches have still not been explored.

Section IV discusses delivery options, in particular how a new international campaign against these killer diseases can most effectively be organized and sustained, both within countries and regions, and on the international level. In the case of each major disease category, and taking account of the interactions of the various diseases, interventions are necessarily complex, cutting across many different actors with many distinct responsibilities. Proper coordination and management of these efforts is therefore a high priority, as is the steadfast commitment to good science and evidence-based design of intervention programs. An ideological or *a priori* adherence to one approach or another will simply not work in the complex environment of disease control that now challenges the developing world. Any and all approaches will have to be

continually monitored, tested against the evidence and against preconceptions, and updated in a serious and science-based manner.

We also stress that effective public health interventions must give attention to three broad categories of action: prevention, treatment, and research and development for the future. For each of the diseases that we will discuss, no single approach – relying just on prevention, or just on treatment, for example – can be successful. And all efforts will benefit enormously from improved scientific understanding and new technological approaches. Operational research on intervention strategies, and more basic research on new technological approaches, must be a core part of effective interventions.

Section V discusses how the global campaign to improve public health in the poorest countries can be financed. Each region will have to do more on its own, but the financial means within the developing countries will not be sufficient to ensure success. Successful public health interventions require substantial financial support, and this can be even more true in poor countries than rich countries because of the need for special interventions that are often unnecessary in rich-country settings. We estimate that even if poor countries can raise their public health spending to as much as 5 percent of GDP, vastly more than is now being spent in many countries, such a level of outlays would be insufficient to meet the basic health needs of the population. Substantial donor assistance will be required. Since the profound economic and disease challenges facing the poorest countries will be overcome only gradually, we believe that large-scale donor commitment and financial assistance will be required over the course of a generation, though economic progress and fundamental improvements in health will eventually allow the poor countries to achieve sustained growth and favorable health outcomes largely out of their own resources in the future.

II. Public Health and Economic Development

A. The Value of Good Health

Poor health takes an enormous toll on human well being, and the economic "price tag" for societies is enormous, much greater than is typically suspected. There are two parts to that price tag. The first is the pain, suffering, and lost years of life caused by disease. These have an economic price tag – indeed a huge one – in the sense that households are willing to pay a considerable proportion of their income to avoid disease and to diminish the risks of early death. This "willingness to pay" may be used as the economic benchmark for valuing the pain and suffering associated with disease, disability, and premature death. The second part of the price tag is more directly economic: the losses of income, both direct and indirect, incurred as the result of illness, both by the individuals facing episodes of disease or early death, as well as by the broader community through various "spillover" effects. Later generations also pay a heavy price for the burden of disease today, for reasons that we will explain.

Using epidemiological evidence and the support of economic theory, we can make estimates of the overall economic costs to society of particular diseases, or groups of diseases. It is convenient to divide these costs into the following categories: costs borne directly by households incurring disease; costs borne indirectly by the community; and costs borne indirectly by future generations.

A. Costs borne directly by households include:

1. Reduced labor hours due to illness of workers
2. Reduced labor productivity while at work
3. Reduced labor hours due to illness of children in the household
4. Economic value of pain and suffering caused by episodes of illness
5. Economic value of reduced life expectancy caused by premature mortality
6. Household expenditures for disease prevention (e.g. anti-malaria bednets)
7. Household expenditures for medical treatment
8. Excess investments in childrearing due to infant and child mortality
9. Reduced scholastic, cognitive and physical development of children due to episodes of childhood disease

B. Costs borne indirectly by the community include:

1. Disruptions to overall enterprise production due to worker illness
2. Lost economic opportunities (e.g. reduced tourism and foreign investment) due to disease burden in the community
3. Social disorganization due to prevalence of orphans in case of high adult mortality
4. Macroeconomic destabilization caused by high public expenditures on health
5. Increased incidence of extreme poverty, with adverse spillovers to the community

C. Costs borne by future generations include:

1. Lower future incomes due to reduced economic growth
2. More rapid population growth due to high fertility rates (compensating for high mortality rates), with consequences for environmental degradation and other aspects of economic wellbeing

Economic theory suggests ways to add up these costs, and to balance them against the costs of health interventions to reduce the burden of disease. While such calculations are necessarily highly imprecise, they do suggest that the burden of disease in poor countries is vastly greater than is typically believed. This is especially true since a heavy disease burden contributes to reduced economic growth, thereby reducing average incomes of future generations.

Current approaches in the health economics literature tend to estimate only a small fraction of the overall economic costs of disease, giving an gross underestimate of the societal burden of disease. For example, typical burden of disease studies look only at the direct costs of disease to households incurring the disease (category A), and within

that category mainly at items 1, 2, 3, 6, and 7. These studies generally ignore pain and suffering caused by disease (and households' willingness to pay to avoid that pain and suffering), the willingness to pay for increased longevity, the consequences on childhood development of repeated bouts of disease, and the excess investments that parents must make in childrearing when there are high rates of childhood mortality.

Very few studies even attempt to estimate societal consequences beyond those of the households incurring the disease. For example, it is clear that endemic diseases such as malaria or other tropical parasites can render a given area unsuitable for habitation, or for agricultural production, or for tourism. Yet such costs are not included in typical disease burden studies, since such costs are not from episodes of illness itself, but from the effects of illness on potential economic investments. Similarly, the costs to enterprises of high worker absenteeism, lost morale, and disruptions of production due to the loss of workers with key enterprise-specific knowledge – all serious problems of the HIV/AIDS epidemic in Africa – are not captured by typical studies that focus only on the lost wages of sick workers.

Even fewer studies try to assess the third, and maybe largest category of disease burden, the consequences of disease burden on long-term economic growth. Today's disease burden causes not just economic loss today, but also reduced incomes of future generations, by adversely affecting the dynamics of saving, schooling, cognitive development, fertility, population size and age structure, foreign investment and trade, and other processes which affect long-term economic growth.

A popular and extremely useful measure of disease burden is the disability-adjusted life years (DALYs) lost due to disease. The DALY, by itself, is not an economic concept. In rough terms, the DALYs measure the years of premature mortality due to a disease, plus the effective number of years lost due to disabilities, where living one year with a disability is measured as losing a fraction of one year of life, with the fraction depending on these seriousness of the disability. There are many judgments that must be made in calculating DALYs, for example in comparing the burden of disease at various ages, and the burden of disability versus premature mortality. Nonetheless, DALYs offer the best short-hand measure for comparing different diseases in terms of the toll of each disease on mortality and morbidity (including disability).

In some studies, DALYs are turned into an *economic* measure, by assuming that each DALY is worth some multiple of average per capita income. The notion is that such a multiple can include not only the lost incomes of households, but also the costs of medical expenditures and the costs of pain and suffering factored in to the calculation. For this reason, each lost life year is sometimes valued at *two times the average per capita income.* This approach of multiplying DALYs by some multiple of dollars per capita is probably a good starting point for measuring the direct costs of illness and premature mortality to households incurring disease. Notice, however, that DALYs focus on episodes of disease, *not on the overall economic consequences of disease (such as the costs to future economic growth)*. Strictly speaking then, it is not possible to move from DALYs to the economic costs of disease. Nor is it right, strictly speaking, to judge the

priorities for health intervention according to the DALYs per dollar saved, if the DALYs do not include important parts of the economic return to investments in health.

An alternative approach, used recently in some studies of U.S. health care, assigns a dollar value to an added year of life expectancy according to market evidence on the *willingness of households to pay* for reduced risk of mortality. The result is summarized in a "statistical value of a life year," which typically is far higher than one year's average income per person. This measure, however, like the DALY, fails to address the question of how today's burden of disease may affect future generations or even contemporaneous citizens not directly hit by disease.

B. Some Evidence on the Direct Economic Costs of Disease

Even if we focus on the very narrowest part of the disease burden – the lost time incurred from bouts of illness, plus the outlays directly incurred as a result of disease – the costs of disease in the poorest countries are huge. Take the case of malaria, for example. It is estimated that there are between 300 and 500 million clinical cases of malaria per year in Africa, resulting in between 1 and 2 million deaths per year. A recent study (Snow, 1998) has put the numbers towards the lower range, but various studies have shown that successful malaria control reduces a huge amount of disease and death that are attributed in medical records to other causes (such as diarrhea or respiratory infection), so that the real burden of malaria may be much higher than direct estimates of direct malaria-induced deaths and illness.

In any event, if we calculate the most basic economic costs due to this heavy disease burden – household expenditures to avoid malaria (such as bednets, or mosquito coils), household expenditures to treat malaria, and lost household income due to episodes of malaria – the costs turn out to be extremely high, at least in comparison with meager incomes. In the holoendemic regions of Sub-Saharan Africa a reasonable estimate is that malaria causes losses of these kinds on the order of 2 to 4 percent of GNP, with lost incomes being the largest amount. In terms of DALYS, the 1998 burden of malaria in Sub-Saharan Africa is estimated to be around 36.8 million DALYs. Using the criterion that each DALY is worth *twice* the per capita income, and assuming a per capita income in the malarious countries at around $300 dollars per capita, this would imply an annual burden of $22 billion, or around 7.4 percent of Sub-Saharan Africa's GNP of some $300 billion. (Of course if each DALY is evaluated at just one time per capita GNP, the burden is halved, around 3.7 percent of GNP).

As we've stressed, such estimates are likely to be only a fraction of the total burden, even if we are just concerned with the economic costs faced by those directly suffering from the disease. For example, these calculations do not include pain and suffering, but surely 1-2 million lives lost per year (perhaps the deaths of 50 children per 1000 live births) imparts a ferocious toll, with an economic value to be attached (whether the willingness of households to pay to avoid such deaths, if effective control measures were available, or the willingness of donors to make such investments in reduced deaths). There are also questions about the valuation of premature mortality in studies that focus

on the summation of the costs of prevention, treatment, and lost work time. For example, how should we value infant mortality? If a mother has invested 1,000s of hours of time in nuturing a raising a child, and then loses that child to malaria, those hours should be valued, but how? Moreover, these estimates rarely consider the long-term consequences of repeated episodes of malaria on cognitive development, schooling completion, adult productivity in the workplace, etc. The measure is almost always the wage times the lost work time, without asking clearly whether the wage itself has been reduced by the long-term consequences of repeated bouts of the disease.

Of course, malaria is just one part of the disease burden afflicting Sub-Saharan Africa. Similar calculations for other major killer diseases such as HIV/AIDS, diarrheal disease and other discussed below, would offer up large additional direct costs, so that the economic losses of the most basic sort (avoidance, treatment, and lost income) would mount to several percent of GDP, perhaps 15 percent or more in countries with a high disease burden. The 1998 burden of communicable diseases, maternal and perinatal conditions, and nutritional deficiencies, is put at 273 million DALYs, or 0.44 DALYs per person. This compares with 0.008 DALYs per person in the rich countries of North America. In terms of per capita income, if we again assume that each DALY is worth *twice* the per capita income, then the losses in Africa due to disease is approximately 88 percent of GNP.

When the economic burden of disease on households is summarized as a percent of annual income, this obscures the often-devastating effect of disease on the lifetime income of the household, and the effects on poverty within the society, a subject treated at greater length below. Several studies in the United States have shown that a severe episode of disease can push a household into poverty for an extended period of time. The situation in already impoverished countries, with very low insurance coverage, is of course much worse. A serious disease episode of an adult, especially a mother, can have devastating effects on the well being of children within the household. In study after study, death of a mother dramatically raises the probability of death of her young children. The economic dynamics can also be cruel, with a disease episode throwing the family into penury and indebtedness from which it does not recover. Poor health thereby exacerbates poverty by much more than the effects on average income.

C. Indirect Costs of Disease: Current Generation

Standard cost-of-illness studies, or the dollar valuation of DALYs, or even the expanded willingness-to-pay studies, assume that the burden of a disease is the sum of the burdens experienced by the individuals that suffer from the disease (or who risk suffering from the disease, and are thus willing to pay to avoid that risk). But diseases can cause burdens to the current generation that go beyond the costs to the sick individuals themselves. A classic case is malaria. Malaria causes enormous illness, with high direct costs, but it also imposes a huge indirect burden on society by reducing the range of profitable industries. For example, many potential tourist sites are not developed because the malaria burden would scare away the potential clientele. Thus, a tropical coastal area with endemic malaria may experience chronic underdevelopment

that goes far beyond the number of cases of the disease per year. In an extreme case, the region might be abandoned altogether, in which case there would be no direct burden of the disease, but an enormous indirect burden. Notice how hard it would be to measure that indirect effect, since the calculation requires an economic model to ask the counterfactual question: "How much would income and investment be raised if a region were free of malaria."

Throughout history, malarious regions have been cut off from tourism, foreign investment, and international trade for just the reason that the risk of malaria has kept potential business away, but it is rather difficult to estimate exactly how large that cost has been. There are essentially two ways to take a shot at such a calculation. One way is to compare the economic growth of malarious and non-malarious regions of the world, holding constant (or trying to hold constant) other variables that affect economic growth. Gallup and Sachs (2000) take that approach, and find that indeed malarious regions grew less rapidly than non-malarious regions by something over one percentage point per year during the period 1965-90. This cumulates to a loss of more than 20 percent in foregone economic growth due to malaria, according to the regression model, an estimate much greater than the direct losses due to malaria described earlier (and the direct losses would not necessarily produce lost growth of income if the losses were the same percent of GNP in 1965 and 1990). We surmise that these results are capturing some of the indirect losses due to the disease.

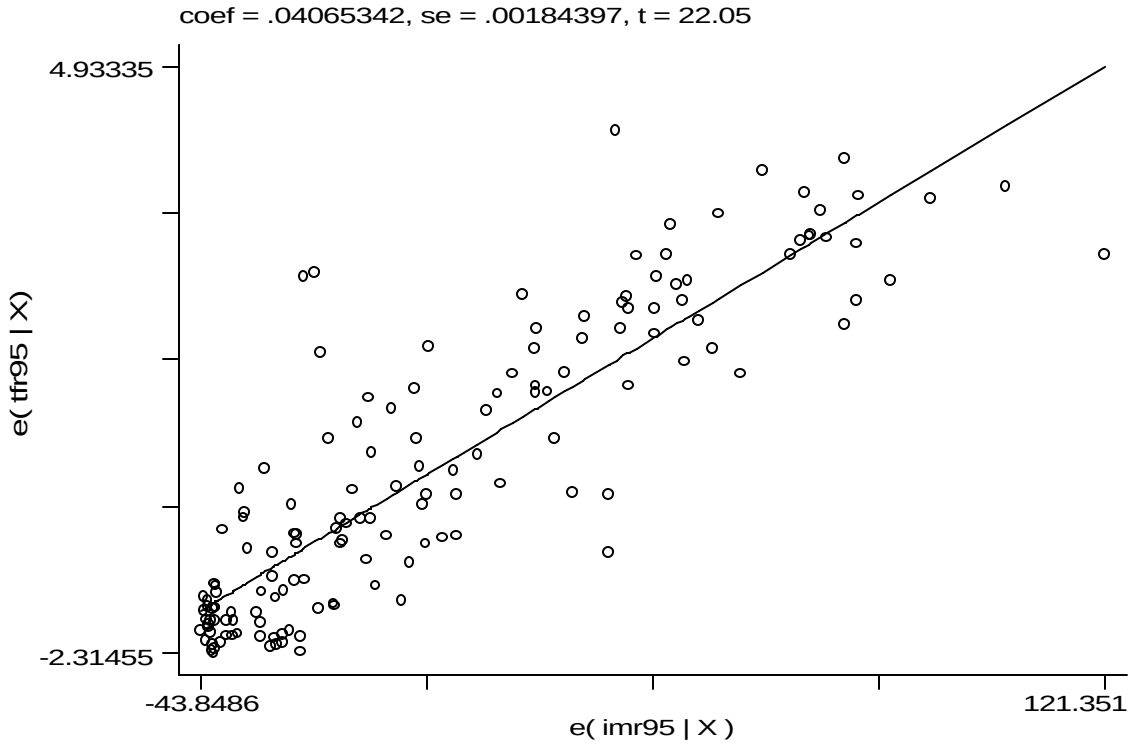
It is very likely that HIV/AIDS will impose enormous indirect costs as well to the contemporaneous generation. Within enterprises hard hit by the pandemic, the loss of enterprise production is likely to go much beyond the direct losses of work time multiplied by the wage. Worker morale suffers heavily in enterprises with large numbers of dying workers. Even the healthy workers lose enormous time at funerals of colleagues, and in helping to train replacement workers. Foreign investors will shun high HIV/AIDS regions just as they shun highly malarious regions. Families are under tremendous strain in areas heavily impacted by HIV/AIDS, and this is causing huge social disruptions that go far beyond the lost wages of ill workers or the direct medical outlays.

D. Indirect Costs of Disease: Future Generations

The illness of one generation is visited upon the children of that generation, "yea down to the seventh generation" as the bible might say. A high disease burden does much more than impose terrible pain, suffering, and economic loss on the present. It also hinders the capacity of society to develop economically, thereby condemning the next generation to a replay of poverty and an unresolved high burden of disease. In essence, a high disease burden in a poor society can create a poverty trap, in which both disease and impoverished are reproduced from one generation to the next. Notice that almost no cost-of-illness study, or calculation of the monetary loss of DALYs even tries to get at this intergenerational consequence of high disease burden.

The discrepancy between the direct costs of illness and the long-term development costs are probably greatest with respect to childhood disease and mortality. A cost-of-illness study might give little or no weight to an infant death, other than the costs of medical treatment that were incurred. A somewhat more elaborate study might include the total lost parental investment of time and effort in the child, on the grounds that the parents will incur those costs once again as they replace the lost child with another. Yet the effects of high infant and childhood mortality (and heavy morbidity) are likely to be much more severe than this, changing the very strategy of households with regard to fertility and investments in the health and education of their children, with highly adverse consequences for long-term development.

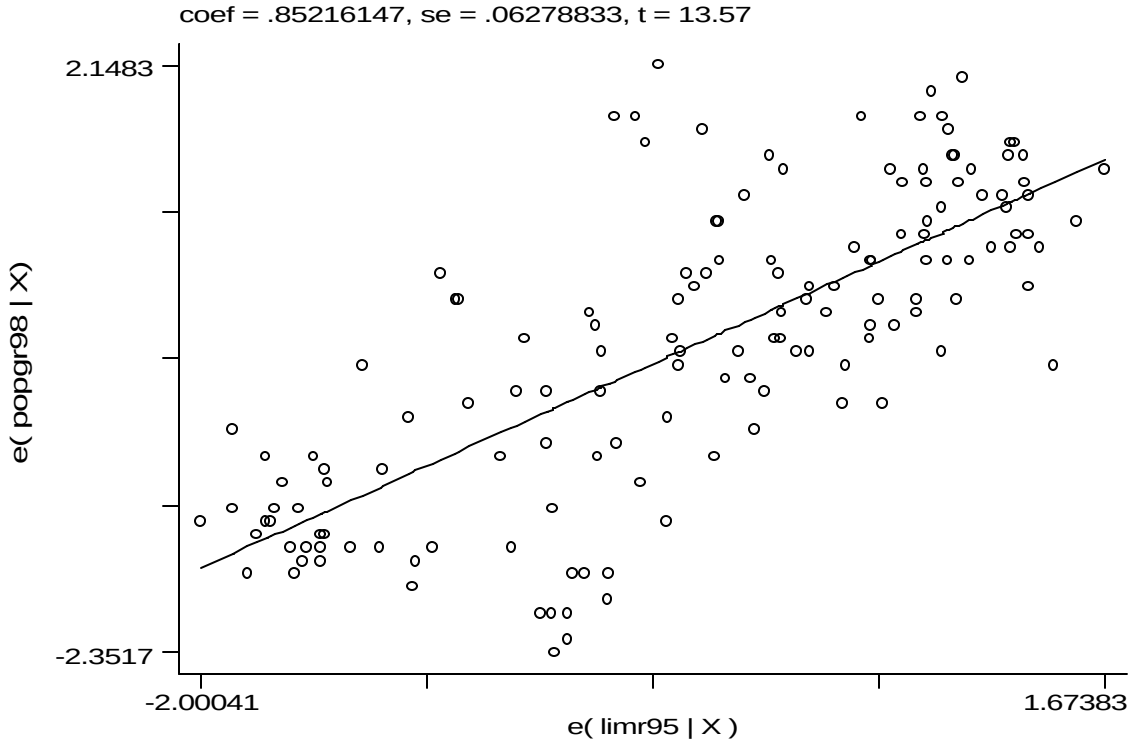
Consider the situation of a very poor household in a rural area facing a high rate of infant and child mortality. Such households tend to have lots of children, to ensure that at least some survive to the old age of the parents, a proposition known in demography as the child survival hypothesis. A scatter plot of infant mortality (on the horizontal access) and total fertility rates (vertical access) for 150 countries in 1995 shows this striking relationship. (The x-axis is the infant mortality rate, per 1000 live births; the y-axis is the total fertility rate).



Of course infant (and child) mortality is just one determinant of fertility rates, alongside other determinants, such as mother's education, mother's opportunity costs of time in child rearing (e.g. market-wage opportunities), and the child's contribution to household production (likely to be higher in rural than urban areas).

High fertility, in turn, forces a "quantity-quality tradeoff," in which more children per couple is accompanied by lower parental investment in each child, especially in terms of the time and income devoted to the child's health and education. In poor families with many children, perhaps only one out of five or six children will be able to complete secondary school; others will be forced to enter the labor force at a very young age, or to work full time in home production, or to marry young before they are able to complete their schooling. In poor families with large numbers of children frequently only the sons are provided with formal health care, and nutrition may be rationed in favor of sons as well. The quality-quantity tradeoff is partly a matter of budget constraints (since there is limited time and income available for child rearing, so fewer resources are devoted to each child when the family is large), and partly a matter of investment planning, since parents will tend to invest less time and income in a child when it faces a higher risk of premature mortality or of life-disabling disease.

The consequences of disease burden go beyond lower levels of investment per child. The "child survival hypothesis" has the implication that high fertility tends to overcompensate for high mortality, leading to rapid population growth. If risk-averse parents want to have at least one surviving son into their old age, it is not enough to have enough sons so that one survives *on average*. It is generally necessary to have several sons so that at least one survives *with high probability*. The result is that on average more than one son survives, and the overall population grows. The positive correlation between infant mortality and overall population growth is shown in the next figure, for 150 countries. (The x-axis is the ln(IMR, 1995), and the y-axis is the population growth rate for the year 1998). Population growth is much higher in the high IMR countries.



It is useful to illustrate the link between high mortality rates and high population growth using a simple numerical example. The technical appendix to this interim report provides further theoretical details and numerical calculations. Suppose here, for purposes of illustration, that each household wants to ensure a survival rate of at least one son with a likelihood of at least 95 percent.[3] Suppose further (just to keep things simple) that households must settle on the number of children before they observe the survival or mortality of each child.[4] Further, if they care just about surviving sons, they will choose to continue to conceive until they reach a target number of sons consistent with the required high probability of the survival of at least one of them.

If the mortality rate is less than 5 percent (50 per 1000 live births), then a household will plan to stop having children after one son is born. The son will have a 95 percent likelihood of surviving. On average the household will have two children, one son and one daughter, resulting in a total fertility rate of 2.[5] If instead the mortality rate is 10 percent (100 per 1000 live births), having one son will give a survival probability of just 90 percent, not high enough for the risk-averse household that wants a 95 percent likelihood. The household will choose to stop after having two sons, or on average four children in total, that is, a total fertility rate of 4.[6] The ramifications for population growth are tremendous. In the first case, with a 5-percent mortality rate, and with a total fertility rate of 2, population growth will tend to be slightly negative. Parents are not replacing themselves on average, since fewer than two children on average will survive to adulthood to replace the two parents. In the second case, with a mortality rate of 10 percent, and a total fertility rate of 4, population growth will be extremely fast, nearly doubling every generation.

Not only will the population grow very rapidly, but the population age structure will be heavily skewed towards young ages, since each parental couple will have four children on average. This will weigh directly on national income per capita, for the simple reason that only (adult-age) workers produce measured GNP, while GNP per capita is measured by dividing output by the *entire* population. The lower is the ratio of

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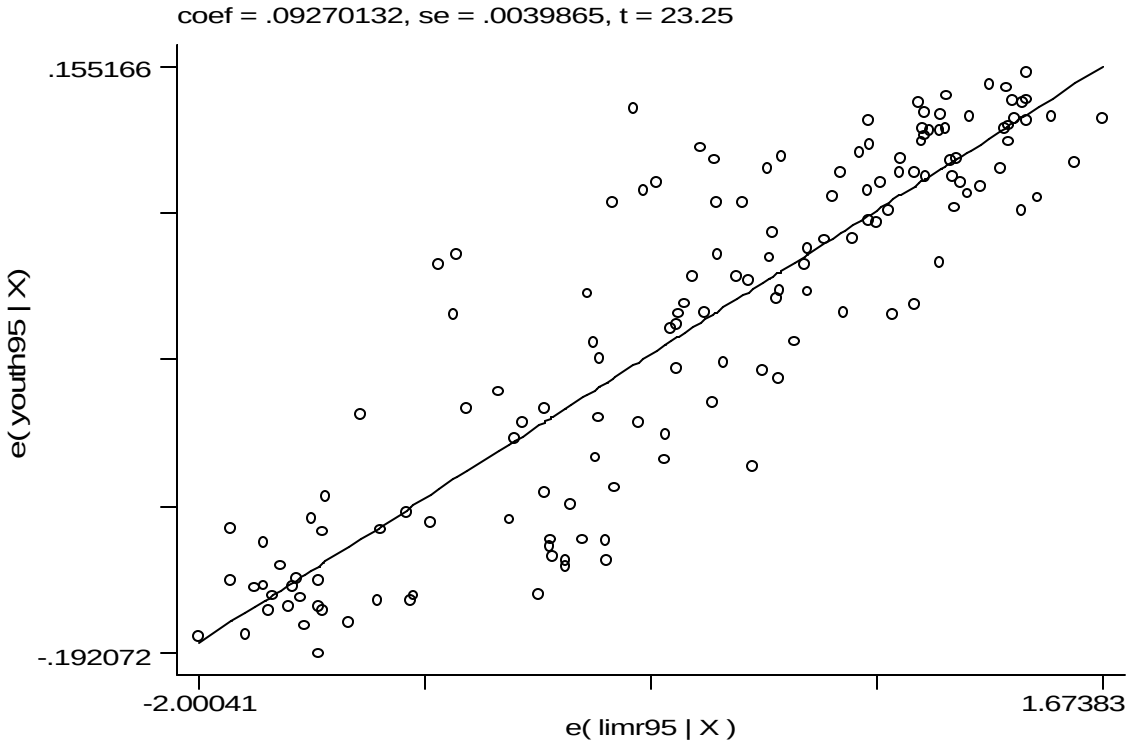
[3] In formal economic analysis, as in the technical appendix to this report, such a household goal would emerge from a maximization of expected utility of the household.

[4] We make this assumption just to keep things simple. Otherwise, households have a sequential decision problem, where the decision to continue having children depends on the survival or mortality of the preceding children. If mortality risk is completely in the first year, for example, then households would follow a simple strategy. They would have children till a son survives to age 1, and then stop. When the risk of mortality continues throughout childhood, then behavior will be more like in the text, where a number of children are conceived first, before observing the eventual survival or mortality of each child. The latter case will require more children on average, as part of the "insurance policy" that at least one son will survive.

[5] Note, of course, that one half of households will have exactly one son, and no daughters; one fourth will have one daughter followed by one son; one eighth will have two daughters, followed by one son; and so forth. The expected number of children, E(n), is given by the formula: $E(n) = \Sigma\ (1/2)^n\ n$, which equals 2.

[6] With a mortality rate of 90 out of 1000, one son would have a survival probability of 0.9. The probability of at least one surviving son if two are born is $1 - (0.1)^2$, which equals 0.99. If a household continues to have sons until 2 are born, the expected number of children is given by the formula:
$E(n) = \Sigma\ n \times (n-1) \times (1/2)^n = 4$.

workers to total population, the lower is GNP per capita for any given level of GNP per worker. In essence, when parents have more mouths to feed, the average consumption per person within the household is reduced. The next figure shows the striking cross-country correlation between infant mortality rates (where the ln(IMR) is shown along the x-axis) and the youth dependency ratio (youth under 15 as a proportion of the total population).



The fact that households have such high fertility rates is also likely to contribute to sharp gender differentiation, with further adverse consequences for long-term development. In societies with very high TFRs, women spend most of their young adult lives having and raising children, rather than participating in the formal labor force. The woman's role is defined around childrearing and home production. If each parental generation anticipates such a role for their own daughters in the next generation, they will be less inclined to invest in their daughters' education (and health), since the returns to such investment accrue mainly to participants in the labor market.

Rapid population growth will have especially adverse effects on economic well being when fixed resources – such as arable land or forests available for firewood – loom large in the production process. In poor rural societies with a high proportion of the population in agriculture, rapid population growth contributes to massive environmental destruction, including deforestation, soil erosion, destruction of biodiversity, and depletion of underground water aquifers. This environmental destruction is exacerbated by the failure of most societies to protect these scarce resources through appropriate incentive systems. Moreover, as each generation of farm family bequeaths a smaller land

plot to their children, the viability of the peasant household as a self-sustaining economic entity is undercut. Much of the massive migration of people from rural to urban areas in the poorest countries results not from new economic opportunities in the urban setting, but from the desperate escape from increasingly over-populated rural areas.

We may summarize by noting that high infant and child mortality rates will tend to do several things to household decisions regarding fertility and investments in their children, all adverse from the point of view of economic development. First, fertility rates will be high to compensate for high mortality rates; and with more children, there will be less investment per child in human capital formation.[7] Gender biases against investments in girls' health and education will be accentuated (or sustained) by the high fertility rates. Second, population growth rates will be high, as will the dependency rates. High dependency ratios will imply a lower GNP per person as the ratio of workers to total population is reduced. Third, rapid population growth may create intense pressures on fixed resources, particular environmental resources such as forests, soils, biodiversity, and fresh water that are often not priced or under-priced.

We have so far described the effects of poor health with regard to the effects on parental investments in children. In addition to these behavioral forces, childhood disease can impair long-term physical and cognitive development, school attainment, and even risks of morbidity and mortality in adulthood, through several physiological channels. Childhood stunting (low height for age), caused for example by repeated bouts of childhood infectious disease, has been associated with lower cognitive attainment and poor school attendance and completion rates. Repeated bouts of malaria can lead to chronic anemia, with highly adverse sequelae on cognitive development (as well as other physical conditions). And of course, micronutrient deficiencies in poor diets can have similar consequences.

Poor health status will adversely affect the accumulation of human capital beyond childhood. When faced with high rates of adult mortality and morbidity, for example, workers may reject on-the-job training or skill upgrading, since these activities generally involve a tradeoff of lower wages today for higher wages over a long future horizon. As the length of the future horizon shrinks (because of expected premature mortality or expected increased morbidity that reduces the likely period of time in the labor force), the incentives for human capital accumulation are therefore diminished. Diseases that impose a high burden of adult mortality and morbidity, such as HIV/AIDS, are likely to discourage investments in human capital at adult ages, for example in tertiary education and on-the-job training. Also, to the extent that experience itself raises productivity (through "learning by doing" on the job), a shorter life span of adults will lower the

[7] Note that infant and child mortality rates are just one of many factors that contribute to fertility choices. The mother's education surely has an independent effect (partly by determining the value of the mother's time in the labor market, and therefore the mother's opportunity cost in having children). Fertility is likely to be higher in rural than urban areas, because in rural areas children are likely to be net economic providers to the household from a young age (working around the farm, or collecting water and firewood), while in urban areas children are likely to be net drains on the household budget (as they are much more likely to be attending school). Access to family counseling, or contraceptives, may be additional factors.

average level of experience of the workforce, and thereby the average level of productivity.

Note also that adult morbidity and mortality are likely to have large and direct adverse effects on the health and education of children within the household. Many studies have shown that infant and child mortality within a household tends to soar after the death of a parent, especially a mother. A considerable amount of human capital accumulation in children takes place within the household rather than at school, as parents teach skills to their children. The sickness or death of a parent can therefore have devastating effects on that inter-generational transmission of knowledge. And of course adult morbidity and mortality often throws a household into financial crisis, forcing children to leave school in order to help replace the lost income or home production caused by the loss of a parent.

What has been said about human capital accumulation generally applies for physical capital accumulation as well. The accumulation of physical capital depends on the saving rate of the economy. A heavy burden of disease is likely to reduce household saving, not only in absolute amounts and as a percent of household income. This is because rate of saving (measured as a percent of household income) is generally a rising function of income among very poor households. (That is, a household at $300 per year per person might manage to save 5 percent of income, or $15, per year, while a household at $600 per year might manage to save 10 percent of income per year, or $60 per year). Also, households will tend to invest less for retirement years if they expect a shorter life span (though they might conceivably invest more in anticipation of higher health care costs in old age).

A heavy disease burden is also likely to have adverse indirect effects on the rate of technological advance in the economy. The most important reason is that technological advance depends crucially on the level of education and skills of the labor force. Both home-grown innovation and technological adoption from abroad depend on a skilled cadre of scientists and engineers. But in a high-disease environment, as we've noted, the level of human capital accumulation is likely to be much lower than low-disease environment, so that the ample supply of engineers and scientists needed for technological progress may well be absent. Another reason why technological advance is likely to be hindered by the disease burden is that much of technological advance in poor countries comes through foreign direct investments (FDI) of high-tech firms based in the rich economies. To the extent that a high disease environment hinders foreign direct investment, the process of technological diffusion through FDI will be frustrated.

E. Poor health and the poverty trap

While health affects the level and growth of GNP per capita, for the reasons we've seen, the income level of the economy also obviously helps to determine the health of the community. This adds a new complexity. A poor society may get caught in a *poverty trap*, in which poor health contributes to the stagnation or decline of GNP per capita, and stagnant or falling GNP leads to continued poor health. This may be

contrasted with a virtuous circle in which rising income per capita helps to boost the level of health, which in turn contributes to faster economic growth. It is the task of economic theory to describe circumstances in which an economy is likely to get stuck in the poverty trap, or alternatively enjoy the benefits of a virtuous circle of rising income and improving public health.

Consider the following scenario, built on our earlier example. Households choose the number of children in order to ensure the high probability of a surviving heir. In a healthy environment, one child will suffice. In an environment of high disease burden (e.g. holoendemic malaria), many children will be desired. The amount of parental investment per child depends negatively on the number of children. When there is only one child, there is a high level of parental investment in the child, and the child ends up with more human capital than the parents. When there are many children, however, parental investment is spread among them, and each ends up with the minimum level of human capital. In the former case, there will be economic growth across generations, while in the later case, there will be a poverty trap.

Now suppose that a one-time massive investment in public health infrastructure could bring the disease burden under control, which in turn would reduce fertility rates and enable the economy to break out of the poverty trap. The initial outlay might be beyond the means of the country, but once positive economic growth starts, the amounts needed for *maintenance* of the program lie within reach of the country. A donor-supported aid program, lasting long enough to secure the country on the positive growth path, could obviously break the vicious circle of poor health and falling GDP per capita.

The notion of a development trap is helpful for understanding the growth dynamics in Africa compared with other parts of the world. Even when Sub-Saharan Africa and parts of East Asia had approximately the same level of GNP per person in the early 1960s, the disease burden in Africa was considerably higher, as were total fertility rates and the youth-dependency ratios.[8] As a consequence, population growth rates outstripped those of East Asia, and GNP per capita declined during the period 1965-95. A study by Bloom and Sachs (1999) attributes a little more than 2 percentage points of the 4 percentage point difference in annual growth rates between Sub-Saharan Africa and East Asia to result from differences in life expectancy (1.19 percentage points), and differences in population dynamics (1.14 percentage points). Unfortunately, the donor world did not come in to help Sub-Saharan Africa to break the vicious circle through improved investments in health.

Ghana and Korea offer a particularly interesting comparative case. Though Korea and Ghana had approximately the same GDP per person in 1965, Korea's infant mortality

[8] Much of Sub-Saharan Africa suffers from an unusually high burden of disease among the group of countries at similarly low levels of income. The disease burden due to malaria, for example, is much more severe in Africa than in the rest of the tropics, almost surely because Africa harbors the most treacherous malaria vector, the anopheles gambiae complex. This, in turn, probably results from the fact that malaria co-evolved with human society in Africa over a very long period, producing remarkable adjustments in the parasite and the vector in the African context.

rate was around half that of Ghana's (57 versus 117), and the life expectancy was 10 years longer (58 versus 48). Partly as a result of these much more favorable health conditions, Korea's total fertility rate in 1965 was just 4.7, compared with 6.8 in Ghana. Korea's population grew by 1.5 percent per year during 1965-95, compared with Ghana's population growth of 2.7 percent per year.[9] In turn, Korea's lower fertility rates and slower population growth rates contributed to much higher rates of human capital accumulation per person, and a much lower dependency ratio by 1995 (youth under 15 constituted 23 percent of Korea's population, compared with a staggering 45 percent of Ghana's population).

Why do some very poor countries succumb to a poverty trap, characterized by very low economic growth, while others do not? We conjecture that the underlying disease ecology probably plays an important role. Countries with holoendemic malaria have, throughout the period of modern economic growth, seemingly been stuck in a low level poverty trap. Other reasons can also play an important role: adverse geographical conditions such as being landlocked or otherwise facing very high costs of transportation to major markets; divisive internal politics; sharp social fragmentation and stratification, which may cause dominant groups in society to prevent adequate investments in the health and education of less powerful groups; macroeconomic instability, for example caused by an overhang of high levels of external indebtedness.

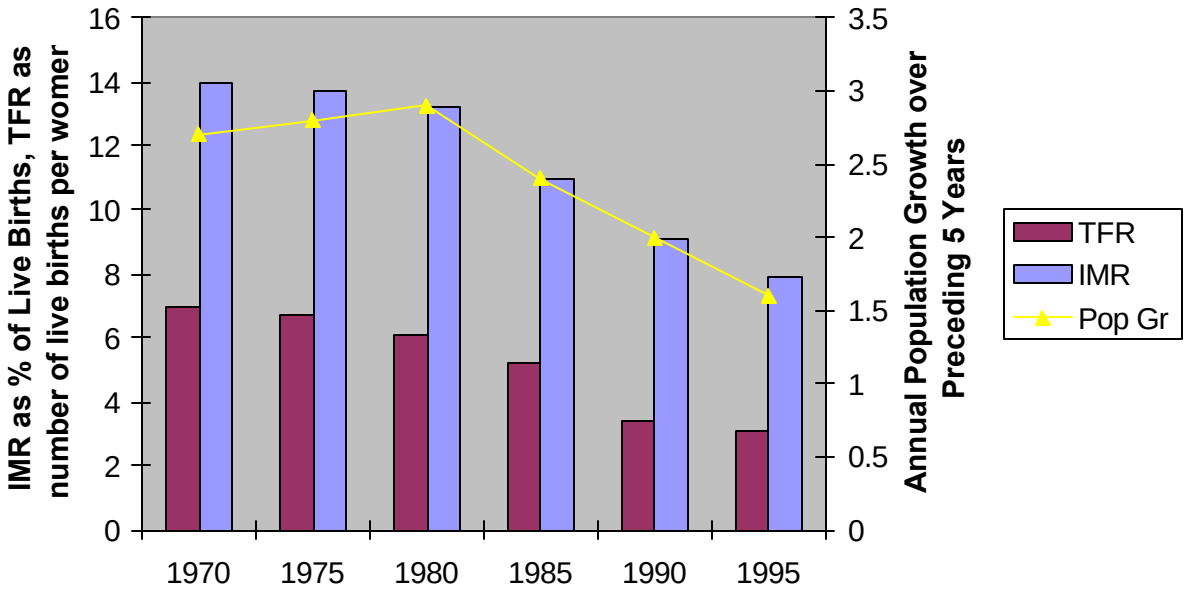
F. Disease Control and Population Control: the Policy Linkages

It is sometimes feared that improved public health in poor countries will simply lead to a population explosion, which will undermine or even reverse entirely the benefits of improved health. We have seen that such fears are overblown. The logic of the demographic transition is that reduced mortality rates, especially among young children, should lead to reduced fertility rates as well. The long-run response of population growth to improvements in health is likely to be an inverse relationship: better health (as measured by reduced infant and child mortality rates) should produce a *lower*, not higher, population growth in the longer term.

This view is probably too optimistic in the short term. A quick drop in infant and child mortality rates is unlikely to be accompanied by a contemporaneous drop in fertility rates such that overall population growth remains the same or even slows. More likely is an outcome where improved health causes a rise in population growth in the short term, and a fall in population growth in the medium term. The analytical question and policy problem, of course, is to specify "short run" and "medium term." Will fertility rates fall alongside mortality rates within a decade? Even faster? Or with a delay of perhaps a generation or more?

[9] Of course, we should not suppose that the health differences explain all of the differences in population dynamics after 1965. Korea also had much higher literacy rates, including of women, and this no doubt contributed directly to the lower fertility rates as well.

Bangladesh is a good example of a country that has recently made astounding progress in reducing fertility rates, linked in part to improvements in infant and child survival. The following graph shows the time paths of total fertility rates (TFR), infant mortality rates (IMR), and population growth rates for five-year intervals during 1970-95 (the population growth rate for 1970, for example, is the annual growth rate of population between 1965 and 1970). The IMR is shown as a percentage rate (e.g. IMR = 14 in 1970 signifies 14 percent death rate of infants, or 140 infant deaths per 1000 live births). During the health transition, which became quite marked around 1985 with a steep decline in IMR, population growth rates *fell consistently*, shown by the average annual population growth rates for each five-year interval. The reduced population growth, of course, mainly reflected a steep drop in TFR, from 7.0 in 1970 to just 3.4 in 1990, and 3.1 in 1995.



The Bangladesh case illustrates that it is possible to improve health outcomes markedly while reducing population growth rates. But the rapid drop in Bangladesh's TFR resulted from a combination of social processes, and was not an automatic response to falling infant mortality rates. The government invested heavily in family planning services and important non-governmental organizations, such as Grameen Bank and BRAC, contributed to improvements in the social conditions of poor women, which in turn contributed to reduced fertility rates. Economic changes, in particular the ongoing process of urbanization, and especially the enormous increase in employment of young women in the export-oriented ready-made-garment sector, also led to delayed marriages of women, and reduced fertility rates within marriage.

The general lesson, known to public health experts for decades, is that the fall in infant and child mortality rates is an important spur to reduced fertility rates, but that family planning programs (and the general empowerment of women through literacy

programs and economic reforms) should accompany the public health measures, to speed the drop in fertility rates in tempo with the decline in mortality rates.

G. The Empirical Evidence Linking Health and Long-term Economic Growth

Two basic approaches have been used to assess the linkages from health to economic growth: (1) macroeconomic growth modeling; and (2) historical research on the links of health and development. We review those approaches here.

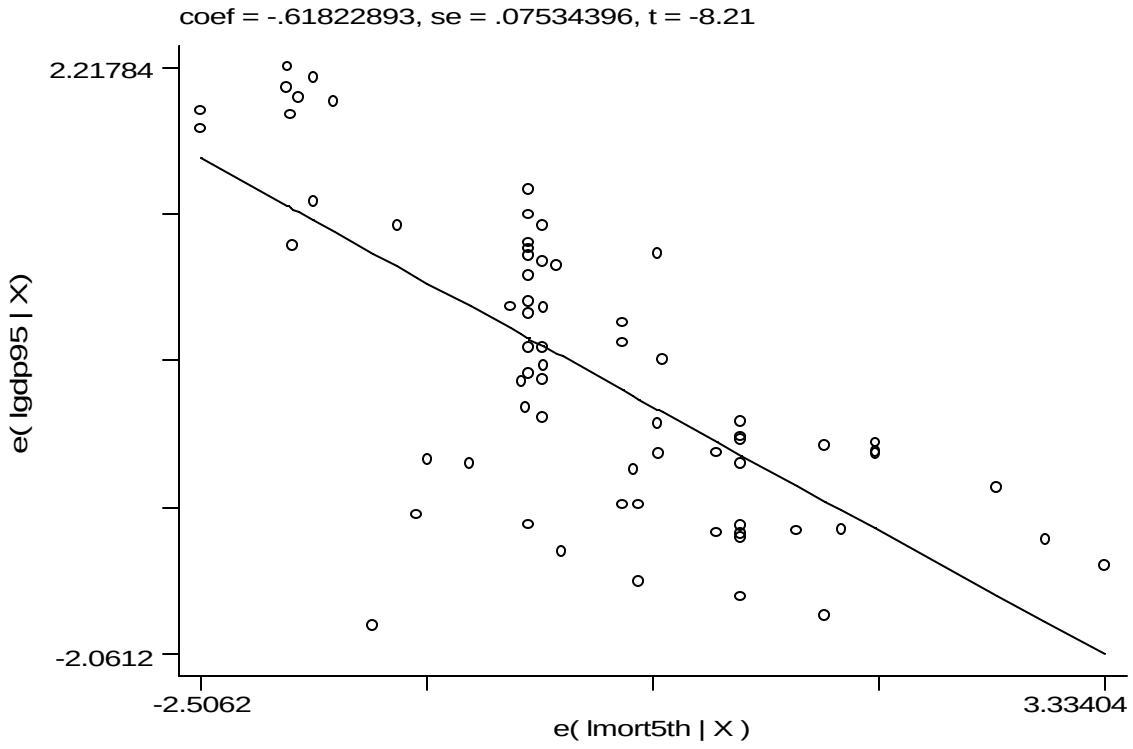
Macroeconomic evidence. The past decade has seen an explosion of empirical work on the cross-country patterns in economic growth. In a typical framework, exemplified by the important and innovative work of Robert Barro (1991, 1995), a country's economic growth rate during an interval of observation is related to a set of explanatory variables, including: initial income (at the start of the interval of observation), initial levels of education, initial levels of health, a set of economic policy measures, and an array of political institutional measures. Thus, as an example, the economy's per capita GNP growth rate during the period during 1965 to 1990 is related to the economy's per capita GNP in 1965, the average years of schooling in the population in 1965, the life expectancy at birth in 1965, the level of government spending as a percent of GNP, the openness of the economy to international trade, the extent of corruption (as measured by surveys), and the stability of government. The model is then estimated econometrically as a cross-sectional multi-regression model, in which each country's growth rate is related to that country's explanatory variables. Studies along these lines have repeatedly shown that the health indicators such as life expectancy in the initial year of observation, are among the most important, if not the most important, variables explaining subsequent economic growth.

A few recent papers have augmented the Barro framework with explicit measurements of disease burden across countries. Both Gallup and Sachs (2000), and McCarthy, Wolf, and Wu (2000), used cross-country measures of malaria prevalence to help explain cross-country growth, controlling as usual for the other economic and political variables. Both studies found that high malaria prevalence was associated with significantly lower rates of economic growth than in non-malarious regions. Indeed, the evidence suggests that regions with holoendemic malaria experienced economic growth that was more than one percentage point per year slower than in non-malarious regions.

Further circumstantial evidence on the role of disease burden in economic growth comes from comparisons of growth rates in the tropics with growth rates in temperate-zone economies. Not only are the tropical countries much poorer than temperate zone countries (Hall and Jones, 1997; Gallup, Sachs, and Mellinger, 1997) , but they have also grown less rapidly during the past 40 years, once again controlling for other determinants of growth such as economic policies. The slower growth in the tropics could have many causes, but a likely candidate is the much higher burden of infectious disease in the tropics – once again, no accident, in view of the importance of vector-borne and water-borne infectious diseases, both of which (in general) tend to have a much higher prevalence in the tropics.

Historical evidence.

Long-term historical processes underscore the linkages between population health and economic growth. Philip Curtin and other historians have collected data on mortality rates in the early 19th century, especially mortality rates of Europeans living in other parts of the world (such as soldiers in colonial armies stationed in the tropics). The data have recently been assembled by Acemoglu, Johnson, and Robinson (2000). The early-19th-century differences in mortality rates, which predate the introduction of modern public health measures, are useful indicators of underlying disease ecology, since they are not much influenced by medical or environmental interventions. The especially high rates of mortality in the tropics are evidence of the long-term burdens of tropical infectious disease. The surprising feature of the data is that the early 19th century mortality rates are highly correlated with income levels at the end of the 20th century! Regions that were high-mortality regions two hundred years ago are, with few exceptions, the very poorest regions of the world today. This result is shown in the scatter plot in Figure XX. On the horizontal access we plot the logarithm of the mortality rate in the early 19th century, and on the y-axis we plot the logarithm of GNP per capita in 1995. *Clearly the high mortality regions in the early 1800s are still the poor regions today.*



Y-axis: Ln(GDP in 1995)
X-axis: Ln(mortality rate, early 1800s) from AJR (2000)

Historians have discussed several key episodes in recent history in which improvements in health have been followed by significant increases in the rate of economic growth. The timing and pattern of these episodes suggest a powerful causal relation between the improvements in health and the subsequent rise in economic growth.

Perhaps the most important of such episodes is the Industrial Revolution itself, which commenced in England in the middle of the 18th century. Historians have long suggested that an agricultural revolution in the 17th and 18th centuries preceded the industrial revolution. Nobel-prize winning economic historian Robert Fogel has traced the links from improved nutrition to improved health (as measured by physical stature of the population) and then from improved health to higher labor productivity. According to Fogel, the improvements in health can explain as much as one third of the total rise in labor productivity over the past two centuries.

An especially fascinating episode of improved health followed by economic boom is the case of the American South in the early decades of the 20th century. In the second half of the 19th century, and especially after the U.S. Civil War, the North and the South of the U.S. were divided between a temperate-zone industrializing economy and a much poorer subtropical-zone economy based on a few primary commodities, mainly cotton, tobacco, corn, and a few other crops. The gap in per capita income between Northern and Southern states actually widened in the years between 1880 to 1910, as Northern industry developed rapidly, while the South remained largely non-industrial, with a large proportion of subsistence farmers. Of course this North-South divide brings to mind the "North-South" divide in the world economy today.

Many factors contributed to the laggard status of the U.S. South, and poor health due to tropical diseases was definitely among them. The warm Southern states suffered from epidemic malaria and yellow fever with an incidence vastly greater than the cooler Northern states. The South also suffered from widespread infection of hookworm, a water-borne parasite that thrives in warmer climates. In all three cases, the etiology of the disease and the mechanisms of disease transmission were not understood in the 19th century. As a result, control measures were extremely limited in the case of yellow fever and malaria, and essentially non-existent in the case of hookworm. The combined effects of these diseases were pernicious, not only on the health status of the population, but also on the economy. Potential investors from Northern states shunned the South for fear of malaria and yellow fever, and regardcd Southern workers as suffering from a "laziness germ" in the case of high hookworm prevalence.

In the early 20th century, the epidemiology and pathology of these diseases were elucidated for the first time, offering a basis for effective disease control for the first-time. Control efforts were launched against all three diseases, based initially on mosquito control in the case of malaria and yellow fever (e.g. drainage of breeding sites), and hygienic measures in the case of hookworm. These efforts were financed and supported by the Rockefeller Sanitary Commission, the precursor of the Rockefeller Foundation. Interestingly, Southern community and political leaders championed these

campaigns with the explicit goal of improving the business environment and thereby attracting "foreign" direct investments from Northern states.

The campaigns were successful in medical terms, as well as in economic terms. By the 1920s, public health in the South had improved markedly. Yellow fever epidemics, which had so terrified Southern populations, were brought to an effective end (the yellow fever vaccine, achieved in 1937 with the support of the Rockefeller Foundation, completed the process of yellow fever control in the U.S.). Hookworm prevalence was substantially reduced as well, as was the burden of malaria. The reputation of the South as an unhealthy environment diminished significantly, and enthusiasm of Northern companies for investing in Southern states increased strongly, marked for example by the large-scale transfer of Northern textile mills to Southern states. In line with this early industrialization, the Southern economies began to enjoy an increase of economic growth, and thereby to begin the process of economic convergence with the North, a process that was substantially completed by the 1980s.

A somewhat similar pattern of lagging industrialization followed by catching up is evident in Southern Europe during the course of the 20th century. In the first half of the century, Northern Europe industrialized while the economies of Southern Europe (Spain, Southern Italy, and Greece) remained agrarian and largely non-industrial, at least in comparison with the North. As in the U.S. South, the heavy burden of malaria in Southern Europe surely played a role in the laggard development of the South, though of course many other factors (politics, climate, resource base) also played a role. Italian scientists and politicians repeatedly referred to the role of malaria as a major culprit in the impoverishment of the mezzigiorno. As in the U.S., malaria control measures followed upon the discovery of the causative agent of the disease (the plasmodium parasite) and the role of anopheline mosquitoes in its transmission. These measures began in earnest in Italy in the 1920s, for example with the drainage of the marshes outside of Rome, but really achieved their success with the introduction of DDT spraying in the 1940s and 1950s. Malaria control was followed by a spurt in foreign investment and an increase in economic growth, as Northern European firms increased dramatically their investments in tourism and manufacturing in Southern Europe. Of course, disease control was but one factor in this acceleration of growth.

The most notable success story in economic development in the past half century is East Asia, where economic growth has been rapid since the mid-1960s in the "tiger economies" of Korea, Taiwan, Hong Kong, and Singapore, and from the mid-1970s in the Southeast Asian economies of Indonesia, Malaysia, and Thailand. The People's Republic of China began to grow rapidly in the early 1980s. It appears that improvements in public health preceded and helped to cause the take off to rapid growth in these cases as well. We noted in Table 2 that while much of East Asia was very poor at the time of its economic takeoff, it had already achieved relatively favorable health and demographic conditions. In Table 4, we show how much these indicators had improved in the lead up to rapid growth. For example, between 1950 and economic takeoff around 1965, Korea's infant mortality rate (IMR) declined from 115 to 57, and the total fertility

rate declined from 5.4 to 4.7. Similarly, between 1950 and economic takeoff around 1980, China's IMR declined from 195 to just 42, and the TFR from 6.2 to 2.5.

These striking improvements in public health resulted from a combination of new technologies and new public policies. The early years after World War II witnessed the widespread introduction of antibiotics and immunizations against childhood diseases. The pesticide DDT was used liberally to fight malaria. The Governments of the region, often with the financial support of the U.S., undertook sustained efforts to build the public health system. China, notably, developed an effective village-level public health effort, built around "barefoot doctors," the principle of universal access to basic medical services, and massive community efforts at environmental management for disease control, such as draining breeding grounds for mosquito vectors, and introducing larvacides and other controls to combat schistosomiasis and other helminthic infections. The East Asian government also directed their efforts explicitly at population control through family planning and the increased use of contraception.

Bloom and Williamson (1997) described the "demographic gifts" that resulted from these policies, of the sort we described earlier. With each household having fewer children, investments per child increased. Population growth slowed, and the share of the population at working age tended to rise (i.e. a fall in the dependency ratio), also leading to a rise in GDP per capita and a rise in household saving rates. The changes helped to trigger the economic takeoff of the region, which of course provided further economic resources to households, communities and the national governments to improve public health still further.

H. Adding up the Economic Benefits of Improved Health: An Illustration

In this section, we put together the microeconomic and macroeconomic benefits of improved health, to estimate the economic returns to a society of a major advance against disease. As a concrete case, we will illustrate the calculation for a specific country, [e.g. Tanzania], to show how large the returns to disease control can be. [This section is still to be completed for a Sub-Saharan African country with a high disease burden, economic stagnation, and good morbidity and mortality data, including cause-of-death estimates].

III. Reducing the disease burden

The quest to reduce the burden of disease must be based on sound scientific knowledge, detailed evidence of best health practices, and intimate attention to local conditions within each community and nation. Health care is intrinsically bound up with local ecology, culture, and socioeconomic conditions, and interventions must be tailored accordingly. There is no shortcut to greatly increased training, mobilization, and financial and technical support of *local expertise* to carry out effective and sustainable health programs. At the same time, broad and internationally applicable scientific principles are vital to establish priorities, to evaluate the effectiveness of alternative

interventions, and to guide the methodologies for surveillance, monitoring, and adjustment of intervention efforts.

Each country and each region will have its own health priorities, to be judged according to careful epidemiological and economic analysis. Nonetheless, several major disease conditions can be identified as the major source of excess disease burden in most of the poorest countries, taking into account that local exceptions and variations surely exist. As is well known, the greatest differences in health outcomes between the rich and the poor countries (measured by morbidity, premature mortality, reduced life expectancy) are due mainly to a group of infectious diseases, some of which are endemic to tropical regions (e.g. malaria) and others of which are better described as diseases of poverty itself (e.g. tuberculosis). The extraordinarily heavy burden of HIV/AIDS in the poorer countries, especially Sub-Saharan Africa, probably reflects a complex mix of biological, culture, and income differences between the hard-hit and the lesser-hit regions.

The evidence on the global burden of disease points to around 10 disease categories which deserve the priority attention in most of the poor countries, recognizing again that differences in the list will occur in individual locales. These 10 conditions are:

- Malaria
- HIV/AIDS
- Tuberculosis
- Acute Respiratory infections
- Diarrheal diseases
- Vaccine-preventable diseases
- Reproductive health
- Tropical parasites and helminthic infections
- Nutritional deficiencies
- Tobacco-related illnesses

Table X reports the DALYs associated with these 10 conditions in various regions of the world, as estimated by WHO, as well as the proportion of total DALYs due to each condition and the group as a whole. Within each geographical region of the world, the WHO distinguishes countries according to their "mortality stratum," separating high-mortality regions from low-mortality regions. Thus, within the Americas, there are low-mortality regions (e.g. the United States) and high-mortality regions (e.g. Peru). We follow the WHO division in the table.

We stress the great uncertainties that surround these estimates, mainly because of the paucity of evidence on morbidity and cause of death in the poorest countries, but also because the long-term effects of various conditions (such as chronic helminthic infection) can not be assessed on the current scientific evidence, and because diseases interact in manifold and complex ways, so that it is often not possible to assign a given state of ill health or a death to a single cause. The number of deaths "due to malaria," for example, may be considerably larger than shown by the table, since the immunosuppressive effects of malaria raise the mortality risks of other diseases. Recent history is replete with

examples in which malaria control interventions reduced all-cause mortality by far more than the direct reduction in deaths classified as due to malaria. The reduction in malaria burden also reduced deaths classified as due to diarrheal diseases, respiratory infection, and other communicable diseases.

Even with these caveats the data are enormously revealing. The 10 conditions that we have identified account for around 46 percent of the DALYs for the world as a whole, and 60 percent of the DALYs of the high-mortality regions as a whole, as shown in the accompanying table.[10] These 10 conditions account for around one-fourth of the total DALYs in the low-mortality regions. Looking at geographic regions, these conditions account for 73 percent of the DALYs of Sub-Saharan Africa, and around half of the DALYs of the high-mortality regions of the Americas, the Middle-East and North Africa (MENA), and South and Southeast Asia (S-E Asia).

HIGH-MORTALITY REGIONS OF THE WORLD

	World	Africa	Americas	MENA	S-E Asia	Total
Population (000,000's)	5962	616	70	348	1219	2254
Total DALYs	1438154	373360	16346	101688	355876	847270
Malaria	44998	36839	23	2727	2748	42337
HIV/AIDS and STDs	109566	82297	757	3062	15329	101444
TB	33287	8721	471	2035	10648	21876
Respiratory	101127	32770	1158	9936	35130	78995
Diarrhea	72063	24322	770	9146	28960	63197
Vaccine-Preventable	67253	30534	244	7578	20810	59165
Maternal and Perinatal	115609	36622	1580	12637	33462	84301
Tropical and Nematode	18845	8511	221	614	5940	15287
Nutrition	44539	11037	715	3415	14672	29838
Tobacco	49288	1900	2264	2136	6014	12314
Category I	607287	271652	5939	51149	167701	496441
Category I + Tobacco	656575	273552	8203	53285	173715	508755
Total as % of DALYs	46	73	50	52	49	60

[10] This table is based on Annex Table 4 of the World Health Report 2000. To make the table, the detailed categories of communicable diseases, maternal and perinatal conditions, and nutritional deficiencies, shown in the WDR table are collapsed into the first nine categories in the table shown in the text. For vaccine-preventable disease, I include the categories of "childhood diseases," meningitis, and hepatitis. For tropical and nematode infections, I also include leprosy, dengue, Japanese encephalitis, and trachoma, which are separate categories in the original WDR table.

LOW-MORTALITY REGIONS OF THE WORLD

		LOW-MORTALITY REGIONS:				
	World	Americas	MENA	Europe	S-E Asia	W Pacific
Population	5962	743	137	872	289	1667
Total DALYs	1438154	109596	20895	136350	56604	267439
Malaria	44998	53	47	2	323	2235
HIV/AIDS and STDs	109566	3262	112	1442	2261	1044
TB	33287	643	225	1258	3453	5832
Respiratory	101127	3046	980	3508	3014	11584
Diarrhea	72063	1744	977	1131	1057	3955
Vaccine-Preventable	67253	1224	563	973	1913	3416
Maternal and Perinatal	115609	5193	1837	2821	6986	14471
Tropical and Nematode	18845	1003	169	20	598	1768
Nutrition	44539	2018	704	1151	2194	8634
Tobacco	49288	6603	840	17084	1425	11022
Category I	607287	18187	5615	12305	21800	52939
Category I + Tobacco	656575	24790	6455	29389	23225	63961
Total as % of DALYs	46	23	31	22	41	24

The infectious diseases impose a relatively low burden of disease in the low-mortality regions. Table XX shows the distribution of worldwide DALYs for each of the 10 conditions according to geographical region. For example, 59 percent of the world's DALYs are in the high-mortality regions, despite those regions having just 38 percent of the world's population. 82 percent of the DALYs due to malaria and 75 percent of the DALYs due to HIV/AIDS are estimated to fall within Sub-Saharan Africa. Overall, Africa has 26 percent of the world's DALYs, though only 10 percent of the world's population. The low mortality regions, with 62 percent of the world's population, have 6 percent of the world's malaria, 7 percent of the world's HIV/AIDS, and 34 percent of the world's TB. If we add all of the infectious diseases, nutrition, and maternal and perinatal conditions, (shown as Category I in the table), the high-mortality regions have 82 percent of the world's DALYs due to these conditions, and the low-mortality regions just 18 percent. On a *per capita basis*, the high-mortality regions have 7.4 times the per capita burden of disease due to Category 1 diseases.

SHARE OF WORLD DALYs BY DISEASE, HIGH-MORTALITY REGIONS

	World	Africa High	Americas High	MENA High	S-E Asia High	All High-Mortality
Population (000,000's)	100	10	1	6	20	38
Total DALYs	100	26	1	7	25	59
Malaria	100	82	0	6	6	94
HIV/AIDS and STDs	100	75	1	3	14	93
TB	100	26	1	6	32	66
Respiratory	100	32	1	10	35	78
Diarrhea	100	34	1	13	40	88
Vaccine-Preventable	100	45	0	11	31	88
Maternal and Perinatal	100	32	1	11	29	73
Tropical and Nematode	100	45	1	3	32	81
Nutrition	100	25	2	8	33	67
Tobacco	100	4	5	4	12	25
Category I	100	45	1	8	28	82

SHARE OF WORLD DALYs BY DISEASE, LOW-MORTALITY REGIONS

	World	Americas Low	MENA Low	Europe Low	S-E Asia Low	W Pacific Low	All Low-Mortality
Population (000,000's)	100	12	2	15	5	28	62
Total DALYs	100	8	1	9	4	19	41
Malaria	100	0	0	0	1	5	6
HIV/AIDS and STDs	100	3	0	1	2	1	7
TB	100	2	1	4	10	18	34
Respiratory	100	3	1	3	3	11	22
Diarrhea	100	2	1	2	1	5	12
Vaccine-Preventable	100	2	1	1	3	5	12
Maternal and Perinatal	100	4	2	2	6	13	27
Tropical and Nematode	100	5	1	0	3	9	19
Nutrition	100	5	2	3	5	19	33
Tobacco	100	13	2	35	3	22	75
Category I	100	3	1	2	4	9	18

Except in very rare cases – smallpox, polio, leprosy, guinea worm, perhaps measles -- the realistic goal is to reduce the disease burden, not to eliminate it entirely. Even the goal of disease control and reduction, of course, represents a profound challenge in many parts of the world and for many disease conditions. HIV/AIDS, malaria, TB, and some of the other conditions have been rising sharply in incidence, prevalence, and as a cause of death, so that reducing the disease burden first requires reversing the current trends. In all cases, we should think about three main categories of disease control efforts: *prevention, treatment, and research*.

Prevention is often the most cost-effective intervention (by far), but is ironically often the most neglected type of intervention as well, partly because poor people may lack the knowledge or means to undertake preventive actions, or because such preventative actions require community or national-level initiatives which are not forthcoming, or because such actions lie outside of the medical system, and are neglected by medical doctors. Treatment of disease, of course, typically lies within the purview of the medical system, but here too many kinds of interventions can best be implemented outside of traditional health facilities – for example in schools or the workplace. Research is surely the most neglected category of all. Every disease category requires an increased research effort – for new, less costly, or more effective forms of prevention (such as vaccines for HIV/AIDS, malaria, and TB); for new treatments (such as anti-malarial drugs to replace those that are being lost to growing drug resistance of the malaria parasite) ; and for improved design and implementation of disease-control programs (so-called operational research), to ensure that control efforts are properly tailored to local conditions and that control efforts are meeting their targeted objectives.

With respect to each disease category, it is worthwhile to list briefly the main issues surrounding prevention, treatment, and research priorities. Of course, far more detailed information is available in the background studies, and in the extensive list of references provided in those background studies.

Malaria. Malaria is estimated to contribute to between 1 million and 2.5 million deaths per year, of which 90 percent or so are in Sub-Saharan Africa. Because of the vector-borne nature of malaria transmission, malaria control requires a complex blend of preventative vector control efforts and treatment efforts. The epidemiology and patho-physiology of the disease are enormously complex and in some ways poorly understood. Malaria is enormously site-specific in its epidemiology, depending on the precise characteristics of the physical environment, the nature of the mosquito species endemic to the region, immunological characteristics of the population, and other factors. Malaria tends to require a minimum ambient temperature for high rates of transmission (often identified around 18 degrees Celsius), and so that malaria is overwhelmingly concentrated in tropical and sub-tropical climates. Theory and history demonstrates that malaria control is vastly easier in sub-tropical environments, such as southern Europe or southern United States, than in the tropical regions.[11] Malaria control is most difficult,

[11] Technically, the base case reproduction rate (BCRR) of the infection was around 1 in many sub-tropical environments where malaria control was successful, so that modest success in reducing disease transmission could reduce the BCRR below 1, thereby stopping the transmission of the disease.

and costly, in parts of tropical Sub-Saharan Africa, where climate and vectorial competence of the endemic species of mosquito lead to holoendemic transmission.

Malaria control efforts throughout Africa have collapsed in the past two decades, leading to high rates of disease burden even in areas that formerly had been under control (such as urban areas). Preventative measures in particular have suffered markedly. Prevention programs focus on controlling mosquito biting behavior, either by reducing the prevalence and survival of mosquitoes (through household spraying, larvaciding of breeding sites, drainage of breeding sites, relocation of habitation and other human activities away from breeding sites), or by introducing mechanical barriers to biting (through insecticide-impregnated bednets, or IBNs, or improvements in housing construction such as use of screen doors). Such programs must be very carefully tailored to the local mosquito and human ecology, as effectiveness depends on such things as: mosquito biting behavior (e.g. biting time of day, inside or outside houses, human versus animal targets), human activity (work outside of the home in the dawn and dusk, location of crops relative to breeding sites, urban or rural setting), mosquito responsiveness to pesticides and other treatments.

One of the most important considerations in vector control programs is that effectiveness generally depends on the level of community coverage of control efforts. It is quite obvious that drainage of mosquito breeding sites will be ineffective if only a small proportion of such sites are drained. Less intuitively, the same is true about insecticide-impregnated bednets. IBNs are much more protective of each individual user when a high proportion of the rest of the village is also using bednets. This is because widespread bednet use in the village not only reduces the frequency of bites per person, but also reduces the *proportion of bites* that are infective. This is a so-called "mass action effect," (or "community effect" or "herd effect") since the effectiveness of the intervention increases markedly as the extent of community coverage rises.[12]

Massive problems afflict also case management of malaria. In many poor countries, individuals and households lack the financial means to secure proper medical attention in the event of malaria. Many have no practical way to reach primary health centers, or to afford the anti-malarial drugs that might be prescribed there but are not provided for free. Mothers often do not bring their children to a doctor until after malaria has reached a very dangerous stage (e.g. cerebral malaria, leading to coma and risk of death). Moreover, throughout Africa and Asia, there is a growing proportion of drug-resistant cases, especially to the least expensive first-line medication, chloroquine. This is already having dire consequences, since many households and governments continue to rely on chloroquine, despite its rising ineffectiveness. The consequences will multiply enormously as second-line drugs (e.g. SP) also are losing effectiveness. There is a

[12] Similar mass action effects are characteristic of immunization campaigns, since immunization coverage not only protects the individuals receiving the immunization but also reduces the probability that non-immunized individuals will become infected because the prevalence of the disease is reduced. Thus, it is generally considered that 80 percent coverage of measles immunization is enough to prevent an epidemic among the non-immunized portion of the community.

dramatically shrinking list of available options, and these are will be available only at a rapidly rising price.

Malaria is a quintessential case where existing technologies could reduce the disease burden markedly (through a combination of vector control and case management), but where there is an urgent need for new research as well. The holy grail for malaria control is a vaccine appropriate for residents living in endemic regions. In addition, research is urgently needed to find new low-cost insecticides, and especially new anti-malarial drugs. Operational research is needed in virtually every high-transmission region to investigate best approaches to vector control and to improved case management, including the use of combination drug therapy to stop or slow the onset of drug resistance.

HIV/AIDS. The number of HIV-positive individuals in the world is now estimated to be 34 million people, of which around 95 percent live in developing countries. An astounding 70 percent or so of all the world's cases are now in Sub-Saharan Africa. In the absence of effective drug therapies (known as *highly active anti-retroviral therapies*, or *HAART,* when combination drug therapies are used, or *anti-retroviral therapy, ARV,* more generally) now employed widely in the rich countries, almost all of the 34 million people are likely to progress to AIDS within a decade, and to die soon after that. The epidemic is continuing to spread at an astounding rate, outstripping earlier epidemiological forecasts of the disease. The number of new HIV-positive cases in 1999 is estimated to be 3.8 million, partly offset by an estimated 2.2 million AIDS deaths, for a net increase of 1.6 million HIV-positive individuals. The HIV/AIDS pandemic threatens to be the worst infectious disease pandemic in world history if it continues its rapid spread throughout the developing world. Already in Southern Africa, an astounding one fourth or more of the adult population is HIV-positive. The prevalence rates are much lower in Asia, but there are fears that HIV/AIDS could spread rapidly in India and other countries in the region.

Most HIV infections are heterosexually transmitted. XX percent of new cases are estimated to result from mother-to-child transmission (transmission from an HIV-positive mother to infant can occur *in utero* before birth; through the exchange of fluids between mother and child at birth; or through breastfeeding in infancy). An estimated XX percent of new HIV cases results from intravenous drug use, and a very small proportion results from other causes (such as intravenous transfusion with infected blood).

Like malaria, an appropriate approach requires urgently scaled-up efforts in prevention, treatment, and new research. Regarding prevention, focus should be on reducing adult-to-adult transmission, mainly sexual transmission but also transmission among intravenous drug users, and on mother-to-child transmission (MCT). In the broadest terms, of course, reduced sexual transmission of the HIV virus generally requires a change in sexual behavior, such as the the use of condoms, or a reduction of frequency of sexual activity with potentially infective partners. Theory and experience suggests a much tighter focus, however. The likelihood of an HIV-positive partner infecting an HIV-negative partner in a single act of sexual intercourse is quite small,

typically less than 1 percent. The risk is increased markedly when one or both partners also suffers from another sexually transmitted disease (STD). This means that *the virus is spread mainly by HIV-positive individuals that engage in a very high frequency of sexual acts with unprotected partnes, and/or high-risk sex, especially in conjunction with an untreated STD.*.

Five types of individuals are most important for transmission of the HIV virus: sex workers, who may have hundreds or thousands of clients per year; very promiscuous individuals, with large numbers of partners (as occurred in the U.S. gay community at the time of the initial outbreak of AIDS); promiscuous individuals with STDs or other risk-factors for high rates of HIV transmission; an HIV-positive spouse with an HIV-negative spouse, eventually leading to the infection of the HIV-negative partner; and an HIV-positive mother giving birth to a child. Most of the effort at preventing adult-to-adult transmission should focus on the first four of these circumstances. While broad public education about AIDS is useful, the key to breaking the epidemic lies with the control of the key transmission points, especially sex workers, individuals with STDs, and households with one HIV-positive adult and one HIV-negative adult. In most places, the predominant channel of transmission is from sex workers to adult males, who in turn transmit the virus to their usual female partners, and from there to newborns. Programs to encourage sex workers to use condoms, therefore, can have a dramatic multiplier effect, as was proved in Thailand. Programs to identify and encourage HIV-positive individuals to use condoms with regular HIV-negative partners, especially spouses, can also have an important effect on the epidemic.

Mother-to-child transmission can be reduced by the use of low-cost anti-retroviral drugs such as AZT and neverapine. The producers of these drugs have even offered to supply them for free in poor countries in well-designed MCT programs. Even with free access to the drugs, however, more studies will be needed about appropriate protocols, that take into account the risks of MCT at various perinatal stages. Should the drugs be administered pre-natally, at birth, or during breastfeeding? What are the right tradeoffs between continued breastfeeding (perhaps with ARVs) or bottlefeeding?

The issue of case management of AIDS patients is daunting, and should be one of the highest priorities of the international community. Since the mid-1990s, combination drug therapies, based on combinations of reverse-transcriptase inhibitors (RTIs) and protease inhibitors (PIs), has proven effective in dramatically reducing the viral load and the onset of illness in HIV-positive patients. These drug therapies cost several thousand dollars per year in the rich countries, and have so far been restricted largely to rich-countries or to a fraction of HIV/AIDS patients in middle-income developing countries. Only a negligible fraction of African victims has so far had any chance to benefit from ARV therapies. Thus, the world is in the stark situation of millions of people facing a death warrant, for all intents and purposes, even though the means to save them exist.

Far too little effort has been made in examining the possibility of a modified ARV strategy in the poorest countries. For example, if the drug combinations were available at marginal production cost rather than patent-protected prices, how much would they cost?

How much could these costs be reduced by supporting the development of new low-cost production facilities to service the African needs? Could a two-drug combination therapy, or a three-drug therapy, leaving out the most expensive drugs (usually the protease inhibitors or nucleoside RTIs) become cost effective and affordable within the African context? What kinds of protocols could be effective when compliance rates are low and side effects of combination therapies can be high? None of these critical questions has been examined by the international community in a objective and complete manner. The evidence that we are developing, discussed below, suggests that an affordable HAART strategy, at a cost below $1000 per year (and probably below $500 per year) can be developed even for very poor countries. Substantial donor assistance will still be necessary.

Appropriate case management goes far beyond HAART. There are important possibilities and options for treating the opportunistic infections associated with AIDS, such as fungal infections (treated with cotramoxizole) or TB (treated with DOTS). In most of Sub-Saharan Africa, little treatment is offered even for the opportunistic infections, and very little operational research has been undertaken to examine the kinds of treatment that would be most needed and effective.

AIDS research deserves the highest international priority alongside funding and operational strategies for prevention and case management. Advances in vaccine design and bioengineering offer several promising approaches to an HIV/AIDS vaccine. One complexity is that the specific viral sub-types in the developing world are different from those in the advanced countries, and these may well require important modifications in vaccine design.[13] The vast majority of research to date has focused on the clades in the U.S. and Europe, though vaccine research supported by the International AIDS Vaccine Initiative (IAVI) has been initiated for the main Southern African sub-type. In addition to vaccine research, there are important needs for continued drug development. Finally, operational research at every stage (prevention strategies and treatment protocols) have been notable for their absence in the African context.

Tuberculosis. Tuberculosis remains one of the major killer diseases in the world, claiming an estimated 1.7 million lives in 1999, despite the fact that existing technologies could dramatically reduce the disease and mortality burdens. About 95 percent of these deaths are in developing countries. The WHO-recommended Directly Observed Therapy Short-Course (DOTS), in an appropriately administered DOTS regimen with full patient compliance, is around 90 percent. Unfortunately, for several reasons related to poverty, poorly functioning health systems, and lack of appropriate actions by TB-affected households, the reach of DOTS remains a small fraction of those suffering from the disease. It is estimated that 1.8 billion people, almost one-third of the world's population, harbors the infective bacterium, *Mycobacterium tuberculosis*, and that among these carriers, approximately 8 million people are suffering from the disease itself. The disease has surged as an opportunistic infection on the back of the HIV/AIDS pandemic.

[13] The main HIV sub-type (or clade) in the U.S.and Europe is HIV1-B. In West Africa, has two epidemics, HIV2 and HIV1-A. The main sub-type of Southern Africa is HIV1-C.

Moreover, treatment has become considerably more complicated in a minority of cases due to multi-drug-resistant (MDR-TB) strains of the infectious agent.

Twenty-two developing countries, with a combined population of 3.6 billion people (or about 62 percent of the global population), account for 80 percent of the incidence of TB. (See WHO Global Tuberculosis Report 1999).[14] Within these 22 programs, the WHO estimates a 72 percent cure rate in the DOTS programmes, compared with a 17 percent cure rate in the non-DOTS areas. There was enormously wide variation in DOTS coverage as of 1997, varying for example from 100 percent coverage in some countries (Kenya, Peru, Tanzania, Uganda) to a relatively high 64 percent population coverage in China, to just 2 percent in India (which accounts for fully 23 percent of worldwide incidence in 1997). DOTS coverage in India is rising rapidly, but was expected to be less than one-third of the population by the end of 1999. Among other high incidence countries, 1997 DOTS coverage was also extremely low in Indonesia, the Philippines, South Africa, and Thailand.

For the world as a whole, only around 42 percent of annual new cases of TB are reported to the WHO (3.4 million out of 8 million new cases), and of these, only around 29 percent were reported under DOTS. Thus, the total reporting of TB under DOTS relative to all new cases is only around 12 percent. DOTS programs are estimated to be available only to around 35 percent of new TB cases, though actual coverage under DOTS is of course even lower, at around XX percent of new cases per year.

Tuberculosis is a complex disease, since the incidence of disease depends not only on infection, but on whether the infection causes active disease. The incidence of disease has been found to depend on age (with special susceptibility in infancy, puberty, and old age), nutritional status (protein deficiency, in particularly, raises the risk of active disease), living conditions (with much higher rates in crowded and poorly ventilated houses and workplaces). In general, rising living standards ameliorates all of these conditions, and thus contributes indirectly to a reduced disease burden. In this sense, TB is clearly a case of a disease that both causes poverty (by reducing household productivity and earning power) and is caused by poverty.

The challenges to TB involve prevention, treatment, and new research. Prevention is best achieved through comprehensive surveillance and timely treatment of new cases, as well as behavioral changes (careful hygiene) by TB patients to reduce the likelihood of spreading the disease within the household or workplace. [Is that correct?]. The main issue for treatment is to expand the coverage of DOTS to a much more substantial proportion of the affected population. Our cost estimates later in this report discuss the modalities and financial implications of wider DOTS coverage. The second challenge for coverage is an expansion of capacity to address MDR TB, which cannot be

[14] In order of incidence, from highest to lowest, among the 22 countries are: India, China, Indonesia, Bangladesh, Pakistan, Nigeria, Philippines, South Africa, Ethiopia, Viet Nam, Russian Federation, Democratic Republic of Congo, Brazil, Tanzania, Kenya, Thailand, Myanmar, Afghanistan, Uganda, Peru, Zimbabwe, and Cambodia.

handled under the standard DOTS protocol. As for new research priorities, the following should be mentioned:

Improved diagnostics. The current test for sputum smear-positivity is often beyond the reach of a rural primary health facility, so alternative low-cost diagnostics would be extremely useful.

Improved drugs and protocols for DOTS therapy. The current protocol is onerous, requiring visits by the patient to a health facility (or health workers to the patient) on a regular basis over a six-month period. Compliance rates suffer accordingly, as does the cost and feasibility of implementing DOTS within a meager public health budget. New drugs may offer the possibility of a shorter course of treatment, and alternative protocols, for example using e-mail or internet connectivity to monitor drug use, could possibly reduce the dependency on frequent visits to the health clinic.

A vaccine for TB. There is currently no available vaccine for prevention or treatment of TB among adults. The Bacille Calmette-Guerin (BCG) vaccine is used in many developing countries to reduce the morbidity and mortality due to TB among children, but this vaccine is not effective in adults.

Diarrheal disease. Diarrheal diseases, characterized by a sudden onset of increased number of stools, usually with reduced form, and with bloody discharge in the case of dysentery, are caused by a wide complex of viral, bacterial, and protozoan microbial infections. Among the bacterial infections are E. coli, shigella, salmonella, campylobacter, and staphylococcus. Viral infections include rotavirus, and Norwalk virus. Protozoan infections include giardia, entamoeba histolytica, and cryptosporidium. The pathways of transmission, and etiology of disease, of course differ according to the infectious agent.

These diseases impose a remarkably high burden of morbidity and mortality, ranking third in total deaths due to infectious diseases behind HIV/AIDS and acute lower respiratory infections (ALRI), with an estimated 2.2 million deaths per year, virtually all in the developing countries, and of these a very high fraction in the tropics.

For most of the relevant infectious agents, diarrheal diseases are prominent in warm-temperature environments, as warmer temperatures encourage the rapid multiplication of bacterial agents (e.g. in contaminated food), and also may facilitate the transmission of microbial agents (e.g. when they are carried by flies or by a water-borne pathway). Thus, diarrheal disease is more prevalent in tropical than temperate ecozones, and within temperate zones, during summer months rather than winter months. Rotavirus, which is more prevalent in the winter in the temperate zones, is an exception to this principle.

Diarrheal diseases are frequently transmitted through a fecal-oral route. Fecal materials containing the microbial agents may infect the water supply directly (for example when defecation is allowed to enter the drinking water of the community), or may get on food when an infected individual that has touched the fecal material subsequently touches food or water, or may be carried by flies from feces to food. For

this reason, hygiene and water availability play a large role in determining the prevalence of diarrheal diseases.

Diarrheal diseases display an intimate two-way causality with undernutrition. On the one hand, dietary insufficiency, especially protein insufficiency, is a major risk factor for the severity (if not the incidence) of many diarrheal diseases. On the other hand, repeated bouts of diarrheal disease can cause massive and life-threatening malnutrition, as the episodes of diarrheal disease may lead to the malabsorption of nutrients which is not recovered in the period between illnesses. Much of the reported stunting and wasting in Sub-Saharan Africa and South Asia is clearly the result of bouts of diarrheal disease rather than dietary insufficiency per se.

As with other disease categories, diarrheal disease requires a strategy that contemplates prevention, case management, and new research, with prevention focused both on the household and community levels. Since the incidence of diarrheal disease depends so much on human behavioral interactions with food, water, and human waste, public education regarding personal hygiene can play a big role in reducing the disease burden. Moreover, mother's education is also critical, to understand the links from hand washing to disease; the maintenance of a latrine to separate waste from the household's water supply; proper food preparation, including boiling water, proper cooking of foods, and the like. In many cases, though, the necessary actions are on the community level, such as protecting the community's water supply (e.g. a tube well) from the infiltration of human wastes. It has been found, as well, that the availability of water, perhaps even more than the quality of the water, is critical. Water-scarce communities have a much higher burden in managing an acceptable level of personal hygiene, including bathing and handwashing. Other preventative actions include: the discontinuance of use of human waste (night soil) as fertilizer; insect control (for example, drainage of breeding sites of flies that carry disease); and promotion of breast feeding.

Treatment is similarly an issue both for households and the community, in the latter case typically at the level of the primary health center for a village. Three types of highly cost-effective treatments are available for most cases of diarrheal disease: oral rehydration therapies to combat dehydration; anti-microbials to combat bacterial and protozoan infections; and in some cases, drugs to reduce secretion and thereby to reduce the risks of extreme dehydration. When mothers are properly trained to recognize the dangers of acute diarrheal disease episodes, and to respond appropriately, they will either be able to administer treatment at home (e.g. in the case of oral rehydration therapy) or be aware of the urgency of bringing the sick child to the clinic.

As with malaria, TB, and HIV/AIDS, there is the need for stepped up research to identify new therapeutics and candidate vaccines for the diarrheal diseases. A near-breakthrough was achieved in 1999 when a vaccine for rotavirus was introduced into the U.S. market. Unfortunately, the vaccine was quickly discontinued on the U.S. market because of some limited evidence suggesting a link of the rotavirus vaccine with increased risk of intussusception. Nonetheless, that vaccine or a related vaccine might still be highly effective in a developing country context, where rotavirus takes the lives of

hundreds of thousands, or perhaps millions, of children per year. Vaccine research is also underway for shigella and other pathogens in diarrheal disease, but as a general matter, the extent of R&D activity falls far short of appropriate levels considering the burden of disease.

Acute Respiratory Infection. As with the case of diarrheal diseases, the acute respiratory infections (ARIs) are a complex of viral, bacterial, fungal and parasitic infections. They impose a remarkably high burden of disease and death, estimated to reach 4 million deaths per year among children in developing countries, and an estimated XX percent of the world's disease burden overall. Bacterial pathogens include: pneumococcal, Hib, and staphylococcal and streptococcal infections. Viral agents include influenza, measles, respiratory syncytial virus (RSV), and varicella. Rickettsial infections are also implicated in infectious pneumonia. As with diarrheal diseases, part of the extraordinary morbidity and mortality rates associated with ARIs in developing countries is due to the interaction of undernutrition (with consequent immunosuppression) and infection. Some cases of ARI are also secondary to HIV/AIDS.

As with the other disease categories, effective control of ARIs requires enhanced measures of prevention, case management, and R&D for new approaches. Prevention of ARIs include medical interventions such as vaccination (e.g. for measles, influenza, pneumococcus and Hib), and environmental actions, ranging from handwashing to improved housing to avoid ARIs and other respiratory diseases resulting from poor ventilation or inhalation of fumes from indoor stoves. Improved nutritional standards, for example through food supplementation programs for young children, can reduce both the incidence and virulence of ARIs. Case management includes adequate diagnosis and access to essential medicines for ARIs, especially the bacterial pathogens, which can often be treated with low-cost antibiotics, but which may be fatal if left untreated. New research and development is urgently needed to develop new and appropriate immunizations for ARIs in developing countries. The new Hib vaccines and the even newer pneumococcal conjugate vaccines must be tested for efficacy in developing countries, and adjusted for target antigens appropriate for the pathogenic strains common to the poor countries. The precise epidemiological linkages between nutrition and ARIs need further elucidation, in order to determine the specific forms of undernutrition or malnutrition that are implicated in increased infectious diseases in the poor countries.

Vaccine preventable diseases. Though the range of vaccine-preventable diseases is large, these diseases are often grouped together in public health discussions because of the common issues related to vaccine delivery. All vaccines share issues of safety, delivery systems, financing, and concern over the extent of community coverage. In most cases, for example, if the vaccine coverage is sufficiently high, then the vaccine not only protects the individual recipient of the vaccine, but also has an "epidemiological" function of breaking the chain of epidemic transmission within the community at large (thus reducing the risks substantially for the non-immunized population as well).

The standard package of vaccine coverage in developing countries is known as the Expanded Program for Immunization (EPI), and covers six vaccines: diptheria,

pertussis, tetanus, polio, BCG (for tuberculosis in young children), and measles. The minimum goal set for community coverage is at least 80 percent of the population, a goal which has been met by all of the rich countries, and by many poor countries. The evidence suggests, however, that coverage has declined markedly in many of the poorest countries in the past decade. A special large-scale program to achieve full eradication of polio is now underway. It is nearing completion, despite many obstacles however in regions of military conflict in Africa and Asia.

At the same time that coverage has declined in the poorest countries, a widening gap has opened between in the kinds of vaccines available in the rich and the poor countries. The EPI package has remained unchanged for more than a decade, while new vaccines have been introduced into the richer countries as a result of breakthroughs in vaccine development. Thus, children in the richer countries are now routinely immunized against Haemophilus influenzae type b (Hib), Hepatitis B, varicella, and recently pneumococcal conjugate vaccine for Streptococcus pneumoniae. Vaccines against yellow fever, hepatitis A, and Japanese encephalitis are also widely available in the richer countries, but relatively little used in the poorer countries.

It is estimated that approximately 3 million people, most children, die each year of vaccine-preventable diseases. This is a combination of undercoverage of the EPI regimen, and lack of uptake of the new vaccines. If we count the deaths due to pneumococcal pneumonia, now preventable with the new pneumococcal conjugate vaccine, the number of vaccine preventable deaths would rise by another 1 million to 1.4 million.

Disease	Annual deaths worldwide (estimated)
Polio	720
Diptheria	5 000
Pertussis	346 000
Measles	888 000
Tetanus	410 000
Haemophilus influenzae b (Hib)	400 000
Hepatitis B	900 000
Yellow Fever	30 000
Total	2 979 720

Source: GAVI (http://www.gavi.org)

The main issues regarding international vaccine policy are financing, delivery (including cold storage and servicing by primary health centers), operational research, and development of new vaccines. With regard to finance, studies show that the coverage of the EPI vaccines and the introduction of the newer vaccines is clearly a matter of income levels among other factors. XX percent of vaccines delivered in Sub-Saharan Africa are purchased by donors, and the traditional donors have not been willing or able to add Hib and HepB (and now pneumoccocal conjugate vaccine) to the list of vaccines that they purchase on behalf of the poorer countries. The newly created Global

Fund for Children's Vaccines, established with a gift from the Bill and Melinda Gates Foundation, will now make possible a substantial increase in vaccine coverage. In the first round of grants announced in September 2000, it is estimated that 600,000 children will receive vaccines that would otherwise not be covered. At the same time, however, it is clear that vaccine delivery systems will need to be reinvigorated in order to achieve these goals. The mere availability of the vaccine per se is insufficient, as the critical supply chains (e.g. cold storage, access of the public to primary health centers) have collapsed or have never existed in some places. Our costing exercises later in the report offer estimates of the overall sums that will be required to expand vaccine coverage to desired levels, in terms of the proportion of the population reached, and the list of vaccines included in national programs.

Operational research is urgently needed to investigate the epidemiology of key vaccine-preventable diseases (e.g. to know the specific etiologies of diarrheal disease and respiratory infection), and the efficacy in the poorer countries of vaccines originally prepared for the U.S., Europe, and Japan. Many of the key diseases targeted for immunization have specific viral sub-types or bacterial serotypes that might render a particular vaccine ineffective in a developing country setting. For example, the pneumococcal conjugate vaccine licensed by the U.S. FDA is seven-valent (i.e., uses seven specific epitopes of the pathogen), but does not stimulate antibodies against two key serotypes (1 and 5) which are thought be responsible for up to a quarter of all cases in many developing countries.

Of course, we have noted in other sections of the report the need for more basic R&D to develop completely new vaccines for major killer diseases – HIV/AIDS, malaria, TB, shigella – and potentially for helminthic infections as well. These needs, and new approaches to stimulating the necessary R&D are discussed at other points of the report.

Helminthic and tropical infections. There are probably well over 1 billion people with helminthic infections, making these the most prevalent infectious diseases in the world. These diseases are often wrongly considered to be mild ailments, since direct mortality rates are low, but the debilitating effects are enormous and are probably grossly underestimated. Hookworm was known as the "Lazy Germ" in the United States South, because of its effects on worker energy, vitality, endurance. As a general matter, the long-term sequelae of helminthic infections include anemia, nutritional deficiencies, and liver disease, potentially serious consequences for overall health, cognitive development, and school attendance and completion rates. There are three major kinds of helminthic infections: roundworms (nematodes), which include hookworm (ancylostomiasis), ascariasis, filariasis, onchocerciasis; tapeworm (cestodes); and flukes (trematodes), including schistosomiasis.

Most of these parasites have complex life cycles, with an important part of the life cycle outside of the human host. Frequently there is a water-borne or food-borne component in the disease transmission, and very often an intermediate vector host. As is typically true for infections with part of the life cycle outside of the human host, climate is a critical dimension of the disease epidemiology. As a general rule, helminthic

infections are concentrated in tropical and sub-tropical climates, where warm weather favors the transmission of the disease. For example, hookworm is transmitted when hookworm larvae living in water or moist soil penetrate the skin of an individual that may be bathing or walking barefoot through the area. The mature hookworm resides in the intestine, and eggs are passed through the feces. The cycle is completed if the eggs find a warm, moist area in which the larvae can develop. The use of human waste as fertilizer (night soil) for crops is one pathway of transmission; the absence of latrines for disposal of human waste is another source.

Helminthic infections are ubiquitous in tropical settings because of an insufficiency of preventative measures, treatment, and research into more effective approaches. Preventative measures include environmental management, such as sanitation to prevent untreated human feces from entering into water reservoirs or fields, and the elimination of the use of night soil as fertilizer. Vector control, such as molluscides to kill the snail vectors that carry schistosomiasis, may also be effective. For many of the helminthic infections there are relatively low cost chemotherapeutic agents, such as thiabendazole and mebendazole for roundworms.

Maternal and Perinatal Care. The WHO estimates that at least 585,000 women die each year as a result of complications from childbirth, and that several million newborns die as well as the result of poorly managed pregnancies and deliveries. Others suffer life-long debilitation from nutritional or traumatic shocks during pregnancy and childbirth. Thus, in addition to the conditions of infectious disease that threaten the survival and wellbeing of infants and young children, pregnancy and childbirth is itself a time of profound risk which needs to be targeted through special interventions.

The main types of interventions are clear, though priorities and modalities for their delivery are much less clear. Mothers need regular monitoring during pregnancy, for nutritional and other stresses that can be life threatening to mother and child alike. Nutritional supplementation is very often needed, as a large number of pregnant women suffer from anemia caused by iron deficiency. Births should be attended by skilled obstetrical workers, to be able to provide emergency care as may be required, and to prevent life-threatening infection and trauma that can accompany child birth. Special medical interventions during pregnancy and childbirth might include: nutritional supplementation, including iron and other nutrients; malaria prophylaxis; anti-retroviral therapies to block mother-to-child transmission of HIV; and precautions against neonatal tetanus.

The urgency of increased care is evident in the following WHO data, which measure for selected countries the estimated lifetime risk of maternal death (from pregnancy or childbirth), the proportion of births that are attended by a skilled attendant, and the number of perinatal deaths (within one week of life) per 1000 births.

Country	Lifetime risk of maternal death 1 woman in:	Skilled attendant at delivery (%)	Perinatal deaths per 1000 births

Chad	9	15	90
Ethiopia	9	8	100
Ghana	18	44	90
India	37	35	65
Pakistan	38	18	70
Yemen	8	16	70

Future progress will require the following steps, with varying priorities across countries:

- increased technical capacity for delivering expert assistance during pregnancy and childbirth.

- Epidemiological research into reasons for high maternal and neonatal mortality rates

- operational research into protocols for nutritional supplementation, monitoring the fetus during pregnancy, disease prophylaxis, reductions in mother-to-child transmission of HIV, etc.

- community based training of nurses and other community workers to assist pregnant mothers and to attend to births.

Nutritional deficiencies. It is well appreciated that malnutrition plays a fundamental role in economic under-development. Poor nutrition saps the physical energy needed for carrying out daily tasks, especially physical labor. Poor nutrition can also contribute to serious debilitation and increased vulnerability to other diseases, especially infectious diseases. Yet despite the critical role of undernutrition in poor health and economic development, the pathways from nutrition to health and economic performance are surprisingly poorly elucidated in the poor countries. Recent discoveries concerning the links from nutrition to health in the developed countries – often supported by detailed cohort data collected over years or decades – have not been matched by similar breakthroughs in the developing countries.

It is common to distinguish three basic kinds of undernutrition: caloric (or energy) insufficiency; protein insufficiency; and micronutrient deficiencies of various sorts. The FAO makes estimates of the extent of caloric insufficiency, which suggest that nearly 1 billion people have an inadequate daily intake of calories. Caloric intake in Sub-Saharan Africa averages an estimated 2,100 calories per adult per day, compared with around 3,400 calories per adult per day in the high-income economies. The average caloric intake in Sub-Saharan Africa appears to have declined slightly during the period 1980 – 1999. Micronutrient deficiencies include Vitamin A, Vitamin C, iron, iodine, and zinc.

Anthropometric indicators (weight for age, height for age, weight for height) are often used as measures of nutritional deficiency. Such measures are important indicators, as they have been shown to be predictive of cognitive and schooling performance among

other outcomes. Nonetheless, they should be handled with extreme care. Poor anthropometric outcomes, such as stunting (low height for age), wasting (low weight for height), and low weight for age (a combination of stunting and wasting), may be indicators of dietary insufficiency, or instead may be secondary to infectious disease, since infectious diseases can lead to malabsorbtion of nutrients, diarrhea, or other factors that cause bodily wasting even when the diet is adequate. Thus, poor anthropometric indicators may or may not be reflections of poor diet as opposed to disease.

Several studies have confirmed the linkages from undernutrition to increased vulnerability to infectious and other diseases, and poor childhood motor and cognitive development. Maternal dietary insufficiency during pregnancy can lead to low-birth weight babies with severe consequences for infant and childhood development. Maternal iron deficiency can result in mental retardation of the child. Adequate nutrition is vital in early childhood. Shortfalls in calories, protein intake, and micronutrients can have lasting effects on growth and cognitive development. Iron deficiency anemia has been negatively associated with cognitive tests of young children. As stressed earlier, poor nutrition may be a reflection of diet or a consequence of disease (such as anemia that is secondary to malaria).

Problems of undernutrition require both dietary improvements and better treatment of infectious diseases (which in turn will lead to better nutritional intake). Interventions to improve diet include: special food supplementation (e.g. during pregnancy, mother-and-child programs, and school meal programs), improvements in the nutritional content of foodstuffs (e.g. improved plant varieties; iodized salt). There is an urgent need for improved monitoring of nutrition levels. Various food subsidy programs should be examined for their nutritional benefit and cost effectiveness. Finally, as in the other major disease catogories, there are critical areas of basic and operational research. Basic research issues include the use of traditional plant breeding and new biotechnologies to enhance the nutritional context of staple products (such as vitamin-enriched rice and maize). Operational research should include, as a high priority, the launch of large-scale cohort studies (such as the Nurses Study of the Harvard School of Public Health), to examine the long-term health impacts of diet, and the interactions of diet and disease, in the ecological and economic context of the poor countries.

Outline: Several kinds of nutritional deficiencies: energy, protein, micronutrient. Undernutrition can be secondary to infectious disease. Anthropometric indicators; other indicators. Consequences of undernutrition: immunosuppression; increased mortality risks associated with diseases such as measles or ALRI. Range of interventions: prenatal supplementation. Vitamin A and other micronutrients. The role of schools (e.g. school meal programs)

Tobacco-related illnesses. Tobacco related illnesses were responsible for around 4 million deaths worldwide in 1998, and current epidemiological estimates suggest that this will rise to around 8 million deaths in the next twenty years. Around two thirds of the 4 million tobacco- related deaths are in developing countries, with the following

breakdown for the low and middle-income countries estimated by the WHO (1998 deaths, in 000s, http://tobacco.who.int/en/health/burden.html):

China 913
Other Western Pacific 64
India 383
Other South and Southeast Asia 197
Europe, low and middle income 735
Eastern Mediterranean 182
Africa 125
Americas 168

These deaths, due to lung cancer, cardiovascular diseases, stroke, pulmonary diseases, diabetes, and other conditions associated with tobacco use, impose an enormous economic cost on individuals and society, and often would require medical interventions well beyond the ability to pay of poor people in poor countries.

While much tobacco related illness is "self inflicted," the result of individual choices to use tobacco, it is a public health priority for several reasons. First, the behavior is addictive, and the tobacco industry spends billions of dollars per year to try to foster the addiction, including among young children. It has especially targeted many fast-growing developing countries in this campaign in the past decade. Second, a significant burden of disease results from passive smoking (or secondhand smoking), where individuals are forced into contact with tobacco smoke of others, for example children who suffer from bronchitis as a result of passive smoking. Third, the behavior is often started or sustained without the tobacco user knowing or understanding the risks. Fourth, the tobacco-related illnesses may impose high financial costs on the rest of society.

From a developing country perspective, *prevention* of tobacco illness through reduced tobacco use is the prime objective of public policy. Four areas of prevention have demonstrated effectiveness:

- Pricing and taxes: smoking is a price-elastic activity. Higher cigarette prices reduce the demand for cigarettes. Therefore, government taxation is an effective means of reducing tobacco usage and tobacco related illness

- Advertising and Sponsorships: tobacco use is susceptible to powerful advertising manipulation, often aimed at vulnerable youth. Many countries have reduced tobacco use through bans on tobacco advertising, or tobacco-industry sponsorship of public events.

- Consumer Information: tobacco use can be reduced by better information to individuals about the risks involved. Many countries have required warnings, and introduced public education campaigns on the risks of tobacco use. Since such

information campaigns are public goods (with little or no private gain to be made by improving the flow of information), they are a public responsibility.

- Smoking Restrictions: the dangers and inconvenience of secondhand smoking have led to the introduction of bans of smoking in public areas, airplanes, offices, and other locations.

IV. Organizing the Fight Against Disease

Controlling the disease burden in the poorest countries will require a suitable strategy and adequate financial resources. We know from painful experience that it is easy to declare international goals for health, but much harder to achieve them. The international scene is littered with failed goals – such as health for all by the year 2000 – or goals that seem to recede as time passes – such as having infant mortality rates by two thirds by the year 2015. The international community comes out with a bold pronouncement, but then fails to follow through on strategy, organization, and finances, as if these goals could take care of themselves. Of course, there are also notable success stories, the greatest of which is the eradication of smallpox, but also great triumphs such as the imminent eradication of polio, the control of onchocerciasis, the tremendous reduction in leprosy and guinea worm, and others as well. Each of those was characteristed by a sensible scientific approach, backed by effective technologies, and critically supported by an organization strategy and adequate international donor support.

The task, to be sure, is not an easy one. The "production" of good health is not a simple mechanical process. It does not depend solely on the medical system – on the availability of doctors or medicines or clinics or hospital beds. Good health is produced through a complex interplay of actions within the household, in the local community, in at the national level, and in the international community. It is produced through actions of the public, private, philanthropic, and NGO sectors. It requires the effective coordination of vast numbers of people to work. This coordination requires, first and foremost adequate financial resources, to give the needed incentives to various health suppliers to do their work. Rich countries, therefore, find ways – mainly through vast expenditures of funds –- to overcome the organizational obstacles. Poor countries, generally, do not. International donor support is therefore vital, but the need for large international flows of donor money of course raises tremendously important issues of monitoring, accountability, and design of efforts.

The field of public health is also a battleground of ideologies. Should disease control be organized according to disease (the so-called "vertical" approach) or according to the effective provision of a wide range of services at the local level (the so-called "horizontal" approach)? Should public health be provided mainly by the public sector, or the private sector, or the public sector with contracting of private service providers? Should poor people be required to pay for services, to promote cost recovery and program sustainability, or should poor people receive health services for free? Should the international community provide mainly technical support, and perhaps start-up funding

for control efforts, or should the international community provide substantial and sustained financing of health systems in poor countries, for up to a generation, or even more? Should international efforts be coordinated among donors, in an overall strategy, or should donors act in a decentralized fashion, funding individual projects of their choosing? Should programs originate from the "bottom up," with lots of community "ownership," or should initiatives originate from the top down, by international agreement of governments and multilateral institutions? Let us try to shed some light on these tendentious issues.

A. Vertical versus Horizontal Programs

Verticalists assert that the major diseases – malaria, HIV/AIDS, TB, and so forth – require separate campaigns to be effective. Smallpox or polio eradication, they point out, was not achieved by a general improvement in health services, but by an extremely targeted control effort, almost a military campaign in focus and organization.[15] Successful efforts require top-down organization, single-minded resolve, and hierarchical accountability, and this will be true, say the verticalists, in cases like malaria control in Sub-Saharan Africa, the extension of DOTS coverage for TB, and an effective program of HIV/AIDS control.

The horizontalists shake their heads in dismay. While they acknowledge that specific interventions can sometimes be effective – especially when there is a narrow geographical target (such as mosquito clearing in the Panama Canal zone) or a "magic bullet" to control the disease such as an effective vaccine – good health generally requires a much richer interplay of individuals, families, communities, and nation. Diseases interact, so that malaria control, diarrheal disease, and acute respiratory infection come as a "package" in poor communities. A top-down approach frustrates community control, reduces the synergies in health delivery when several interacting diseases are present, and generally reduces rather than increases the sustainability of health care provision.

We view this debate as mostly misguided, and by now largely sterile. Both sides are right. The verticalists are 100 percent correct that disease control requires a considerable amount of top-down coordination and supervision, *especially to ensure the provision of many kinds of public goods that are well beyond the capacity of the local community*. Effective control efforts require, among other things: training of large numbers of experts; a cadre of epidemiologists and other specialists that understand the details of the particular disease within the national context; mechanisms for preventing or controlling the spread of disease between communities; operational research to understand the best protocols for disease control; long-term research for the development of new control technologies; and mobilization of resources and political and logistical support from beyond the medical sector (such as for mosquito control operations, or the distribution of condoms to sex workers, or the provision of vitamin supplementation in schools). All of these tasks are way beyond the competency levels of communities or

[15] Indeed the lore of the verticalists points out that it was single-minded resolve of military men that led the original eradication efforts of yellow fever and malaria that permitted the building of the Panama Canal.

sub-national districts, and in many cases well beyond the compentency of individual poor-country governments.

On the other hand, the horizontalists are utterly correct that in the final analysis, most actual health provision takes place at the community or even household level. If a mother doesn't avail herself of primary health services because she doesn't recognize the dire symptoms of her child, or if the primary health clinic (PHC) doctor is never available because he's off in his more lucrative private practice, or if the community does not take the necessary local actions to fight malaria (draining or larviciding breeding grounds, spraying houses, using bednets), then all of the top-down programs will come to naught when the time arrives for real health delivery, not just plans on paper.

The verticalists also make another point that bridges the two camps. Vertical programs can create horizontal, community-based competence in the long-term. Veterans of the smallpox eradication effort – perhaps the ultimate case of vertical intervention -- remind us that the smallpox campaign left behind a long-term community-based capacity in primary health, through the training of the village-level workers that participated in the smallpox campaign. The same is evident in DOTS, where local community groups engaged in tuberculosis case management become the core of a much broader set of community-based primary health activities.

We therefore support, in the most general terms, a matrix organizational design, in which major disease categories have distinct organizational structures within countries, but in which those structures are cross-cut by strong horizontal public health activities (primary health centers, community education) at the various levels of health delivery (primary, district, state, national). For example, a "malaria czar" operating within the Ministry of Health would have a team of malarialogists working at the national level (carrying out training, operational research, epidemiology, monitoring and evaluation of programs), supported by malaria-specific teams at district level. These district-level teams would have expertise in vector control, epidemiology, and case management. They in turn would supervise efforts at the local level. Primary health providers, to be sure, would still be the main point of contact for households facing an episode of suspected malaria, for diagnosis, treatment, and emergency referral to a hospital if necessary. Community organizations would still be responsible for expanding the use of bednets or for local environmental controls (spraying, larviciding, drainage of breeding sites), but under the supervision and guidance of district level officers.

An informal review of countries in Sub-Saharan Africa and Asia suggests that this kind of matrix approach does not now exist, or exists on paper only. In large parts of Africa, malaria control efforts have virtually collapsed during the financial crises of the past 25 years. There are few malaria teams at the national level (or at least few with budgets and staff), and still fewer specialists, if any, at district level. The same, surprisingly, is true in India, where despite a considerable formal structure of public health, there are virtually no entomologists or malariologists operating in most districts around the country. Malaria specialists in India believe that the incidence of malaria may well be 50 times greater than actually reported, so collapsed is the system of national

monitoring (and so serious has been the resurgence of malaria in recent years). This same problems apply to the other disease categories, such as HIV/AIDS, TB, vaccine preventable diseases, and nutritional deficiencies. In each case, we would suggest a vertical structure within the country that intersects with the broad-based public-health delivery at local, district, and national levels.

B. Public versus Private Health Care Delivery

Most health systems in the world rely on a mix of public and private suppliers, where the private suppliers are also subdivided between a profit-oriented sector and a not-for-profit sector that includes church-provided health care, other NGO based care, and philanthropic institutions that subsidize health services. One of the key questions for effective disease control policies in poor countries is how to balance the provision of services between these two sectors. We believe that in poor countries there is a major role for the state in the direct provision of public health services, one that cannot be substituted by the non-state sector or by state contracting with private organizations.

There are two overriding reasons for a large public (governmental) role in the provision of public health in poor countries. First, a considerable amount of public health provision depends on *public goods*, that is, goods that are not readily provided by private markets because of lack of profit motive or lack of property rights, or goods in which private provision is possible but would be highly inefficient. These goods are best provided by the state, or with state subsidization. Second, public health interventions are *merit goods*, that is goods that a fair and decent society should make available to all of its members, even those that are too poor to afford them out of their own incomes. State support for merit goods is basically re-distributional in character. The case for treating health care as merit goods goes beyond simple morality, though. We have seen that by helping the poor to gain access to better health, the cycle of poverty may also be broken, so that a one-time public subsidy (say over the course of one generation) may produce a permanent improvement in economic conditions that obviates the need for such re-distributive actions in the future.

Public goods are pervasive in public health management, in areas such as: basic scientific research, operational research (designing protocols for disease control), disease surveillance, control of epidemic outbreaks, environmental management (e.g. mosquito spraying, water quality control, limitation on leaded gasoline), and training of specialists to perform these tasks. In each of these activities private providers could not easily be compensated for the full social value of their activities. Even in cases where property rights can theoretically be assigned to give necessary market incentives, the assignment of such property rights may be very inefficient compared with direct public provision. For example, if basic scientific discoveries were patentable, there might be more basic scientific research undertaken by the private sector, but the fruits of that research would then be underutilized by society because basic knowledge would be held as a government-protected monopoly. As a result, patent laws have generally barred the patenting of basic scientific discoveries, and the government has been a large backer of

basic scientific research. (Note that the United States will spend around $90 billion of public funds in the year 2000 to support basic science. The National Institutes of Health will account for nearly $20 billion of that).

One major category of public good is the control of communicable disease. In general, when an individual takes an action to reduce the chance of contracting a communicable disease (say, by getting an immunization), there is a direct effect of personal protection, but also a spillover effect in reducing the risk of spreading the infection to the rest of the community. Thus, it has been shown that by immunizing 80 percent of an urban population against measles, the other 20 percent of the population are generally protected against a measles epidemic. (The protected 80 percent break the chain of transmission to the rest).

Unlike immunizations, which at least protect the individual no matter whether others are also immunized, some kinds of protective actions only work for the individual when most of the community is also taking the same actions. Thus, as we mentioned earlier, the use of insecticide-impregnated bednets is highly effective for the individual user only if a high proportion of the overall community is also using bednets. This is because widespread usage serves not only as mechanical protection against biting, but also serves to reduce the proportion of mosquitoes that are carrying the malaria parasite (and thus that are infective). If we think about malaria incidence as depending on the entomological inoculation rate (EIR) -- the product of number of bites per individual times the probability that any individual bite is infective -- an individual bednet user gets the benefit of reducing the first term of the product, while a community of users gets the benefit of reducing both terms. Many environmental interventions, such as draining ditches to eliminate malaria breeding sites or keeping latrines clear of village wells, share the same phenomenon: they are effective only when the entire community participates.

When individuals take decisions on their personal health actions – such as whether to get immunized, or whether to use a bednet – they generally do not consider the effects of their actions on the community at large. That is, they impose externalities – either positive (favorable) or negative (unfavorable) – by their actions that are not factored into their individual incentives. We can predict, for example, that the purely decentralized actions of individual citizens will lead to the underutilization of vaccines and the underutilization of bednets relative to the social optimum. One major type of public good is the intervention of the state to reduce or eliminate these externalities, generally by changing the incentives that individuals face. One way is through regulation: some governments, as in the United States, require immunization coverage as a condition for school attendance. Another way is through state subsidy, such as the free provision of immunizations or bednets. Such examples can be multiplied many times. Governments in rich countries require immunizations; provide public interventions to halt epidemics; provide surveillance of epidemics to guide public interventions; subsidize or freely distribute vaccines or treatments; insist on environmental measures to reduce disease transmission (such as hygienic standards); and so forth. Poor country governments often aim to do the same thing, but typically without the requisite resources.

In very poor societies, governments should also seek to provide health services that poor households cannot afford on their own. An extensive and well-documented history of health interventions shows that when very poor households are forced to pay full costs for the health services that they consume, they cut back sharply on their use of health services, and also shift to lower quality health providers. Very often they revert to low-cost traditional healers that offer no real benefit in controlling disease, but often take what little financial resources the household has for disease control.

The problem is greatly exacerbated by the basic, but pervasive fact, that most people, and poor people particularly, lack the technical knowledge to know what kind of health services they need. A fundamental "asymmetry of information" exists between doctors and the lay population, causing the "market for medical care" to be far less efficient than other markets. Doctors can prescribe things that patients don't need, or fail to provide things that patients do need. Households can't easily judge whether to seek medical help, and if so, of what kind. The information needed to make such decisions is itself a public good, and will generally be underprovided. Thus, households will not know very clearly which doctors or hospitals or procedures are medically effective and which are not.

The 1980s and the 1990s has provided one sobering case after another of the dire limitations of "cost-recovery mechanisms" applied to health care for very poor households. When most of the world's poor and middle-income countries fell into debt crisis in the early 1980s, one of the responses of the creditor community was to push these countries into cutbacks in budget outlays, including cutbacks in budgets of health ministries. Poor countries were encouraged to make their health systems "sustainable" by charging user fees to cover the costs of operations. Often, for example, households started to be charged for the medications that were prescribed at primary health centers. This is an experiment that failed in the poorest countries, as a large literature now documents. Poor households cut back sharply on their utilization of public health services in the face of these user fees. Budget cutbacks also severely constricted community action programs, such as environmental measures for malaria control (e.g. household spraying, and drainage or larvaciding of mosquito breeding grounds), or surveillance and interventions in control of epidemic diseases. When the central government cut back on the free provision of these services, local communities were completely unable to compensate out of local resources.

All of these cases suggest that poor households require a very high degree of subsidization of health services, including full subsidy in the case of very poor households. There are important choices to be made in how that subsidization might be carried out. Should the public sector be the sole provider of health services, providing them below cost for poor households? Should the public sector be a "provider of last resort" for the poor, while the private sector offers health services for the parts of the society that can afford to pay the full costs of health services? Should the public sector provide the subsidies by contracting with private service providers, so that households go to private doctors and clinics, which in turn are reimbursed by the state? Should subsidies be generally applied to the community, or targeted to low-cost households?

Note that targeting can work through a means test (households qualify by registering that they are poor), or by self selection (the public health system provides a lower quality of service – perhaps in the form of longer waiting times -- so that the poor households self-select as users).

The appropriate answers will differ by context, but we still feel able to offer some general guidelines. *We believe that direct public provision of health services for poor households is necessary, through a public system of primary, secondary, and tertiary health-care providers*. Some of the non-medical services provided by the public health system may be privately provided (as when hospitals contract with private suppliers of linens, food, cleaning services), but the core health services should generally be provided by state-financed providers. This is because the system in which the health services are privately provided but publicly subsidized is fraught with very high costs of contracting, monitoring, and quality control, which are especially high when the population to be serviced is very poor, often illiterate, and generally less able to defend their own rights to health care access and quality. As governments impose limits on their payments to the contractual service providers, poor households are very likely to be squeezed out of access to public health services.

At the same time, we generally believe that non-state health-care providers should be free to operate along side, and in competition with, public providers. The private providers would include for-profit providers as well as not-for-profit religious, NGO, and other philanthropic providers of health services. In most poor countries this is already the case, so there could hardly be a return to a pure state-provided model if such ever existed. But aside from private provision being a *fait accompli*, it is generally desirable as well. The non-state sector offers competition, and a market yardstick, for the state sector. It is a crucial safety valve when the state sector breaks down. It offers a mechanism of self-selection for targeting state subsidies to the poor, since the for-profit sector may offer a higher quality of service than the state sector, allowing richer households to self select to the more expensive, but higher-quality services.

The state-run system should have two preeminent responsibilities within a mixed public-private system. First, it should guarantee that all of the public-goods aspects of health care and disease control are being met. Thus, the state system rather than the private system should have responsibility for areas where "mass action" is needed: immunization coverage, environmental controls (e.g. controls on mosquito breeding, water quality), surveillance and interventions for control of epidemics, community use of bednets, community education, quality assurance, and the like. Second, the state system should gurantee the availability of health services to all, especially the poorest who will be priced out of the private market. Targeting of households for subsidization within the state-run system, such as through means testing, should be used very sparingly if at all. Means tests are costly, difficult to administer, and subject to administrative and political abuse, especially in very poor countries where administrative systems are very weak. Many poor people are likely to end up being denied services altogether, as experience has repeatedly shown. A much better mechanism is partial self selection in which richer households opt for the private sector providers of health services.

As we stress in the section on health care financing, the parallel operation of public and private sectors imposes a rigorous market constraint on the salaries that the public sector must pay its own health workers. In a wholly state-run system in a closed society (such as a one-party socialist state that prevented migration), the public sector may be a monopsonistic buyer of health services. That is, as the sole employer of doctors and nurses, the state may be able to procure doctor's services at below-free-market wages. When the private sector operates along side the public sector, or when doctors can migrate internationally, however, the state is no longer a monopsonist. If it underpays its doctors (as most public health systems in poor countries now do), they will leave for the private sector, or leave the country entirely, and the public system will be left as an empty shell. Indeed, the complaint throughout the developing world is that the primary health centers may be standing, but the doctors are not available, since they are off in their private practices or have long ago left the country.

In our increasingly globalized economy, doctors from Africa and Asia are leaving the poorer countries in droves, ending up in the richer countries within the region, or in the oil-kingdoms of the Middle East, or in Europe and the United States (where they often service inner-city hospitals as interns and residents). In parts of Africa and South Asia, half or more of a graduating medical school class departs quickly for the richer countries. In short, in today's increasingly globalized economy, the salaries that public health systems in poor countries will have to pay their doctors will be determined not just in their own private sectors, but actually in the markets of the richer countries.

C. Global Public Goods for Disease Control

Most of the public goods that are needed for disease control can be provided at the local or national level. Some public goods, however, require international effort. This is true, for example, when communicable diseases cross national boundaries, so that cross-bordcr cooperation is needed. Similarly, international efforts are needed to maintain data bases on global health and to identify and diffuse international best practices in health management. Not surprisingly, such functions have been assigned to multilateral institutions, especially the World Health Organization. Perhaps the most important global public goods, however, are the research and development efforts needed to address the health problems of the poorest countries. Such global public goods, however, remain grossly underprovided.

The innovation process inevitably involves a mix of public and private goods, no matter whether it is addressed to problems of rich countries or of poor countries. Thus, in the rich countries, progress in the fight against cancer, cardiovascular disease, and other major killers, depends on a mix of public and private spending, and a complex set of institutions to establish appropriate incentives for innovative activity. As a general rule, basic science is undertaken in public laboratories or in academic institutions supported with public funds. NIH funding in the United States is now nearly $20 billion per year, supporting both intra-mural research (inside NIH) and extra-mural research (outside NIH,

mainly in academic institutions). Applied product development, such as new vaccines and pharmaceuticals, build upon the basic science through an extensive and expensive process of drug identification and testing. Most of this applied activity is undertaken by private firms, especially large pharmaceutical companies and smaller biotechnology companies. Though very expensive, it is driven by the expectation of profits protected by patent rights on new products. In the United States, for example, all drug trials must go through three phases: Phase I to test mainly for safety; Phase II to test for biological response in a limited trial (e.g. immunogenicity of a vaccine); and Phase III is to test for efficacy in a large sample population. These trials may cost tens of millions or hundreds of millions of dollars per each product developed.[16] Successful drugs, however, may be worth billions of dollars in subsequent profits.

Note that there is a global coordination problem involving basic science. The returns to basic science are available to the whole world (since basic science, typically, is not protected by patent rights), but basic science is financed mainly by individual governments. No individual government has the incentive to invest up to the socially optimum scale. [17] Fortunately, there are a few very big countries (especially the United States, but also Japan, United Kingdom, France, among other) that reap enough benefits within their own borders, and enough cross-border cooperation within Europe, to ensure high level of overall support for basic science.

There is also a basic incentive problem at the stage of applied drug development. To the extent that prices are determined by government regulation rather than by the free market, a developer of a new drug faces the risk that government price controls will deprive the producer of the returns to its development efforts. Consider the following. A drug with a potential market of 10 million doses might cost $100 million to develop, and $10 in marginal production costs per dose. At a market price of $20 per dose, the company would recover both the R&D and the marginal production costs. But suppose that *after* $100 million of R&D, and *after* the drug is developed, the government regulator limits the market price to $12 per dose. The pharmaceutical company will still produce and supply the drug (since $12 is greater than the marginal production cost of $10) but the company will end up losing $80 million overall, because it will not recover its R&D outlays. Of course, if the company anticipates this action, it will not undertake the R&D in the first place. (And if the social benefit of the drug is $30 per dose, society will have punished itself heavily by virtue of the "protection" of public regulation of drug pricing). This incentive problem is overcome in practice in two ways. First, pharmaceutical price are set mainly by market forces in the United States. It is no accident that the U.S. market therefore supports a much larger level of applied drug development activity than the European market, which is rife with government regulatory controls on pricing. Second, of course, even in countries with government regulators, at least some care is taken to allow pharmaceutical producers to reap the returns of R&D.

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[16]Note that account should be taken of the failures as well as successes of candidate products in calculating the costs per successful product. See Demasi (1999) for details.

[17]The socially optimum level of investment is at the point where the incremental social returns for the *whole world* equal the incremental investment outlays. Each individual government, however, is likely to compare the incremental returns for the country itself with the incremental investment outlays.

In sum, through the combination of government laboratories, grants to academic centers, patent-protected R&D by private firms, and (at least some) free-market pricing of pharmaceutical products, the rich countries have solved the basic incentive problems of R&D -- with regard to the types of problems targeted by the rich country public and private sectors. While the incentive problems facing R&D probably probably lead to an under-investment in health R&D relative to the social optimum,[18] the levels of R&D outlays, and the rate of innovation, are nonetheless impressive. Global R&D in health research, counting public as well as private outlays, is well over $60 billion per year, and probably 95 percent of that is undertaken within the U.S., Europe, and Japan. The problem, though, is that the vast majority of the world research effort is focused on problems afflicting rich-country populations, such as cancer and cardiovascular disease, and very little is directed at the problems specifically facing poor countries, such as tropical infectious diseases. It is estimated that of the [1,300] new products brought to market by rich- country R&D efforts over the [25] years, only [4] products were directed mainly to tropical disease problems. (cf. MSF, 2000).

This is not to say that poor countries lack any benefits of R&D. They benefit to the extent that they share the same health problems as the rich countries. Thus, poor countries can generally make use of immunizations and drugs that are indicated for problems not specific to rich countries or poor countries. The problem in those cases is that patent-protected prices are often too high to enable their use in poor countries.

When diseases are heavily concentrated in poor countries – such as tropical infectious diseases -- the incentives for R&D are extremely weak, both at the stages of basic science and applied product development. No poor country can afford to support very much basic scientific research, and even in combination these countries lack the resources to finance very much basic research. The combined GNP of the [40] countries with holoendemic malaria is around $300 billion, only around 3.0 percent of U.S. Gross National Product! The incentive problems facing applied product development may be an even more serious constraint. The market for drug products in poor countries is tiny compared to the markets in the rich countries. And most of the drugs are purchased and distributed by governments, often with donor support (since households lack the purchasing power to make the purchases themselves). The free-market purchase of drugs is miniscule compared to the purchases in the rich countries. Since most sales by pharmaceutical companies to poor countries are therefore made to official agencies (either the government or international agencies such as UNICEF), which bargain for low sales prices, the pharmaceutical companies have come to expect that they can not earn money on drug sales to poor countries. In several cases, recently, they have decided to give drugs away at cost or even for free.

All of this means that poor-country problems are neglected by global R&D, both at the stage of basic science and at the stage of applied product development. Estimates in the mid-1990s suggested that total R&D for malaria, for example, totaled just $50 –

[18] See Murphy and Topel (2000) for a recent analysis arguing that R&D in health is below the social optimum.

100 million per year, perhaps one-tenth of one percent of the global R&D effort for a disease that is responsible for two percent or more of the total disease burden. Since R&D is vitally needed and highly promising, new public policy approaches are needed. Approaches to date have focused mainly on support for basic science (through rich-country support for research), and modest subsidization of product development efforts (such as the $X million committed per year to malaria research under the MMV program of WHO). But these efforts have continued to underemphasize the expense and complexity of the product development phase, and the profound lack of incentive faced by the pharmaceutical industry for product development for poor-country problems.

What is needed at this point, more than anything else, is the confidence of the pharmaceutical industry that they can earn profits by developing products for poor countries. One approach would be massive subsidization of product development. But since donor agencies cannot really decide on the scientific viability of individual candidate products, and cannot really monitor the internal R&D efforts of individual companies, it seems that this route is flawed (at least as the exclusive strategy). Lots of money could be given to companies for inappropriate products, or to support R&D that is not truly focused on poor-country problems (except on paper). The companies would still lack the incentive to bring products all the way to market, since they would not believe that there is actually much of a market at the end of the process.

Subsidization of product development should be combined with commitments by the international community to create a viable end-market for new products developed for poor-country problems. Thus, the donor community, for example, could commit now to purchase an effective malaria vaccine at a realistically high price to spur profit-oriented R&D activity. If the donors announced that they will guarantee to pay $10 per dose for 25 million doses of an effective malaria vaccine, the promise of a guaranteed market of $250 million per year for such a product would provide a market inducement for the needed applied development effort. In the jargon, subsidization of R&D is termed a "push mechanism" for drug development, while guaranteeing an end-market for a new product is called a "pull mechanism." *Our argument is that both push and pull mechanisms are needed.*

D. Access to Essential Medicines and Intellectual Property Rights

For many diseases, the problem is not the under-provision of R&D, but rather the lack of poor-country access to existing technologies. Under-provision of R&D is characteristic of diseases that are concentrated in poor countries (e.g. malaria). Lack of access, by contrast, is a problem for diseases that are found in both rich and poor countries (so that rich-countries undertake the needed R&D), but where the poor countries are simply too poor to buy the products developed for the rich-country markets.

Immunizations have been a clear example of the problem in the past twenty years. Vaccines introduced since the 1970s, for example Haemophilus influenzae type-b (Hib) and Hepatitis B, have become routine in the rich countries, while being priced out of the market of the poor countries. The result is that an estimated 400,000 children die each

year of Hib infection, even though a low-cost vaccine is potentially available. The case of anti-retroviral therapies (ARVs) for HIV/AIDS is of course even more visible in public debate these days. New combination drug therapies, we have noted, can hold off AIDS for years, perhaps indefinitely. And yet such therapies cost around $15,000 per year, orders of magnitude more than the ability to pay of poor people living in poor countries.

Access to essential medicines involves three issues. The first is mobilizing donor support to purchase pharmaceutical products for delivery to poor people in poor countries. The Global Fund for Children's Vaccines, for example, aims to narrow, or close, the gap between the rich and poor countries in terms of access to immunizations. The second is establishing appropriate protocols for the use of pharmaceuticals within poor countries. Account must be taken of the specific epidemiology of the disease, the logistical problems of health care delivery (e.g. cold storage for vaccines, low compliance of patients), the interactions of the specific disease with other diseases (e.g. the linkages of the HIV/AIDS pandemic with other sexually transmitted diseases, or the tradeoffs in breastfeeding by HIV-positive mothers in conditions of Sub-Saharan Africa), the specific sub-types of pathogens, and hence the design of drugs and immunizations, and so forth.

The third issue is one of drug pricing by the pharmaceutical producers. Even when donors are responsible, in the end, for purchasing essential medicines on behalf of poor people, the pricing of the products will be key to access. In the rich-country markets we accept the notion that new drugs should receive patent protection so that the temporary monopoly pricing covers the cost of the R&D, thereby creating market incentives for drug innovation. The patent protection results in market prices that are above marginal production costs, with the gap between prices and marginal costs in effect providing to the financial returns to the preceding R&D effort. (It is the anticipation of that gap by the pharmaceutical companies that induces them to undertake R&D for many years before profits start to flow on a particular product).

We recognize and accept that patents create one distortion (temporary monopoly pricing) to solve another problem (the difficulty of capturing the returns to innovation). Poor people in rich-countries generally receive some form of state support to ensure access to essential medicines. *With poor countries, however, the extension of patent rights seems to create a problem without any countervailing benefit*. On the one hand, the patent protection establishes monopolistic prices for pharmaceuticals, but even with monopolistic pricing the poor-country markets are too small to spur much R&D by the major pharamaceuticals. In short, patent protection in the poorest countries may simply establish monopoly profits without any benefit of increased R&D activity! (This point has been made repeatedly in the economics literature, for example by Panagariya, 1999).

From both an equity and an efficiency point of view, a segmented pricing strategy – high prices in the rich countries, to cover R&D, and lower prices for the poor countries, to ensure access – seems warranted. The equity of such market segmentation is clear. The efficiency of such an arrangement comes from the fact that the drugs should be available to any buyer for whom the marginal utility exceeds the marginal production

cost. Marginal cost pricing thereby ensures greater access of the poor, and greater efficiency in the distribution of the product.

There are several ways to promote marginal cost pricing for poor countries. All of these methods require that the markets between rich and poor countries should truly be segmented, that is, the low prices in the poor countries should not be allowed to reduce the market prices in the rich countries – since to do so would undermine the fundamental incentive for the R&D necessary to bring new drugs to market in the first place. The methods for segmenting the markets include:

- Tiered pricing by the pharmaceutical producers, with marginal cost pricing in the poor countries. Tiered pricing would be supported by restrictions on the re-sale of drugs (especially to rich-country markets) that would undermine the pricing in the rich-country markets.

- Voluntary licensing of production technology to producers in the poor-country markets. The pharmaceutical industry would make the patent-protected (and other) technologies available at low cost to producers in designated poor-country markets. In this case, the rich-country pharamaceutical companies would not themselves engage in marketing their products in the poorer countries, thereby avoiding the need to justify tiered pricing to disgruntled consumers in the rich countries (who might suppose that they, too, are entitled to drugs at marginal cost).

- Reliance on the importation of low-cost generics, from countries where patent protection on the products do not apply.

- Compulsory licensing[19], in which the poor country unilaterally assign production and distribution rights to local producers, even over the objection of patent holders in the rich countries. Note that compulsory licensing is an option open to countries under the World Trade Organization rules, in cases of "emergency and extreme urgency," "non-commercial use," and "public interest." Procedural requirements for invoking compulsory licensing are set down in the WTO rules.

We believe that marginal cost pricing is indeed of extreme urgency in many cases, and so would justify a compulsory licensing arrangement. Of course a confrontational approach with pharmaceutical producers may be less effective in the long term, in achieving low-cost availability of pharmaceutical products, than formalized arrangements for tiered pricing and voluntary licensing of technologies.

[19] A "compulsory license" is an authorization given by a national authority to a person, without or against the consent of the title-holder, for the exploitation of a subject matter protected by a patent or other intellectual property rights.

V. Financing the Fight Against Disease

For the past twenty-five years, the international community has made high-minded pledges of support for public health in developing countries, but has failed to follow through on the actions that would be needed to achieve the stated goals. The world community pledged to ensure "Health for All" by the year 2000. It also set targets for reducing infant mortality by two-thirds and maternal mortality by XX, but neither target is on track. More recently, the international community has pledged to cut malaria deaths by one half, and HIV/AIDS cases by half by the year 2010.

At the most fundamental level, the problem is one of money. These goals cost money, and the poor countries lack the money to achieve the goals on their own. The international community has provided much too little financial support to make the goals feasible, hoping that policy reforms in the poor countries would be sufficient. To be sure, achieving the targets also requires policy reforms, sound strategy, effective organization, and political will, but without the needed funding, all the rest will prove insufficient.

This section is devoted to the question of financing a global disease control effort. The CMH will offer some rough estimates of the costs required for a realistic fight against the killer diseases in poor countries, and of the allocation of those costs among poor-country governments, poor-country households, rich-country donor governments, and multilateral agencies. Our very early estimates are that a real fight against the killer diseases will require annual development assistance by the donor world of around $10-$20 billion per year for the low-income countries, sustained for at least one decade (and perhaps two), and provided overwhelmingly in the form of grants rather than debt-creating loans. The money must be real, not headline-grabbing promises pumped up for political effect -- real resources made available in an appropriate and timely way, and at a scale of support that will get the job done.

This level of necessary donor support is vastly greater than the current levels. According to the data collected by the OECD Development Assistance Cooperation (DAC) Secretariat, the 1998 level of official development assistance (ODA) for all health, nutrition, and population programs, from all donors, to all recipient countries, was $3.8 billion (see accompanying Table). This constitutes around 7 percent of the total ODA budget, and signifies approximately $0.82 per person in the developing world. Part of this funding goes to the middle-income developing countries, so that only around $2.5 billion reaches the low income developing countries, around $0.78 per recipient. Of this, $1.3 billion reaches the 619 million people living in the least developed countries (LLDCs), amounting to around $2.15 per person.

All Donor Spending, 1998 ($ millions)	All Recipients	LLDCs	OLICs	LICs
All Health and Population	3837	1331	1237	2569
Basic Health (ALL):	1831	510	732	1243

Medical Service	224	50	74	124
Basic Health (general)	1	0	0	0
Basic Health Care	340	126	112	238
Basic Health Infrastructure	204	59	60	119
Basic Nutrition	106	65	6	71
Infectious Disease Control	231	56	98	155
STD Control including HIV/AIDS	210	49	54	103
Health Education	12	6	1	7
Health Personnel Development	13	11	1	12
Reproductive Health	490	89	326	415
General Health (ALL):	1477	655	448	1102
General Health	188	75	97	172
Health Policy	1233	564	335	899
Medical Education	31	5	4	10
Medical Research	25	10	12	22
Health (not otherwise classified)	0	0	0	0
Population (ALL)	528	166	57	224
Population policies (general)	0	0	0	0
Population policies and administration	194	70	2	72
Family Planning	334	96	55	152
Personnel Development	0	0	0	0
Memo: Infectious Disease Programs	441	106	152	258

These levels of aid, slight as they are, vastly overstate the actual flows of funds available for disease control. Part of the aid is for population policies (e.g. family planning), part is for health policy reform (under the rubric of "General Health") and only a part is for supporting primary health care, including disease control (under the category "Basic Health"). Total spending on Basic Health was less than half of the total ODA under the Health, Nutrition, and Population rubric, and total spending on Basic Health for the LLDCs was only around $510 million. Remarkably, spending for the least developed countries specifically for *infectious disease control* (including HIV/AIDS) was only $106 million in 1998, or roughly $0.16 per recipient. Even this pittance included money for technical advisors in the rich countries, reducing still further the actual sums made available to the poorest countries for the purchase of medical goods and services (e.g. to help buy pharamaceutical products or to help pay for doctors and nurses).

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Perhaps most dismaying and puzzling of all is that despite the huge publicity and anguish surrounding the HIV/AIDS pandemic, the actual donor support for STD control, including HIV/AIDS, in the second half of the 1990s averaged only around $100 million per year for the entire low-income world (of 3.3 billion people). This amounts to around $3 per HIV-positive individual per year in the poor countries, obviously not even a start

at providing the financial base for treatment. Inexplicably, IDA made only three HIV/AIDS loans in the period 1990 - 98, and none in the years 1996-98.

Table 1: Overseas Development Budgets for STD control including HIV-AIDS
Least Developed and Other Low Income Countries (1990-1998)
Thousands of dollars

						ODA loans from World Bank
YEAR	total	total	tied	untied	tech co-op	total
1990	17,711	17,711	9,428	8,282	8,560	0
1991	35,938	35,938	16,310	9,296	10,332	0
1992	121,847	37,847	18,955	7,487	2,612	84,000
1993	42,073	42,073	31,490	3,226	3,070	0
1994	143,868	67,568	29,761	27,908	19,909	76,300
1995	114,779	74,779	21,086	28,644	21,807	40,000
1996	46,138	46,138	26,153	11,654	12,388	0
1997	80,786	80,786	44,640	20,108	16,048	0
1998	102,977	102,977	23,787	17,234	49,379	0

Source: OECD, Development Assistance Committee, Creditor Reporting System (CRS)

A. The Need for Full Costing of Health Provision

Effective health systems are costly to run. Even when vaccines are extremely inexpensive (a few U.S. cents per dose of DPT), or when drugs are donated for free to poor countries, actually getting these products to the needed recipients requires vast, specialized resources. Many reports have stressed, for example, that the falling coverage of immunization in many poor countries has much less to do with the cost of vaccines themselves, and much more to do with the collapse of vaccine supply chains, which will be costly to reconstruct. When we analyze the costs of health coverage, we must take into account the full costs of running the health system – including management, monintoring, oversight, training, and so forth – and not merely the "marginal costs" of additional doses of medicine.

Our strategy for full-cost pricing is the following. *For each of the 10 disease categories* we are analyzing, we construct a package of basic intervention measures and an assumed rate of coverage for the population. We assume that primary, secondary, and tertiary public health facilities are operating with sufficient coverage to be able to supply the basic package of interventions, and we estimate the costs of operating the public-health infrastructure in addition to the costs of each disease package. For malaria, for example, we propose the following package:

- Vector control technology appropriate for local use (insecticide-impregnated bednets (IBNs), residual spraying of insecticides, larviciding and drainage of breeding sites, etc.)

- Case management for uncomplicated malaria (blood smear or diagnostic stick in PHC, followed by prescription of appropriate anti-malaria medication)

- Case management for complicated malaria (referral to secondary or tertiary treatment center)

- Chemoprophylaxis for vulnerable groups (e.g. pregnant women)

Based on an epidemiological model of disease incidence, we estimate the costs of these interventions for an assumed level of community coverage in holoendemic and epidemic malaria regions. We must also add in the costs of the necessary infrastructural support, such as:

- A national-level malaria office within the Ministry of Health, for management, monitoring, evaluation of the national malaria-control program.

- District-level health officers to support PHCs and district-level health facilities in malaria case management

- District-level entomologists to support vector-control programs

- Training programs for malaria-control officers and for primary-health care providers

- Community education programs to explain and promote malaria control efforts, including community control of mosquito breeding sites, household use of IBNs, and appropriate household responses in the event of a malaria episode.

- An operational research program at the national level, to examine changing patterns of vector ecology (e.g. breeding sites of mosquitos; distribution of particular vectors; changing vector behaviors regarding breeding, feeding, and so forth; entomological inoculation rates; susceptibility of vectors to particular insecticides); data management systems (e.g. use of GIS methodologies for analysis and planning); review of case management protocols (e.g. prevalence of drug resistance, success and failure rates of particular interventions).

In addition to such packages for *each disease category*, we need cost estimates for running the basic health-system infrastructure itself. For this purpose, we take a set of key assumptions including number of health facilities, doctors, supplies, management support, operational research, diagnostic laboratories, training centers, community-based efforts, physical infrastructure, and the like that will be needed to ensure widespread access to the key preventative and treatment interventions. We also make various assumptions regarding the target population of these public health measures.

A key set of assumptions regards the costs of personnel in these health systems. It has been usual to take prevailing public-sector salaries for health workers as the basis for

the cost calculations. This is no longer tenable in most poor countries, since public-sector health salaries often lag so far behind the private market that public facilities are unable to recruit and maintain professional staffing. Often the doctors are available for free service provision at the PHCs on paper only, and instead use the public facilities for their own "private" practice (charging fees for access to ostensibly free facilities) or are not available at all for much of their scheduled time at the PHCs. The rising costs of attracting and maintaining quality health care workers is becoming more and more acute, as doctors and nurses are increasingly able to migrate internationally to find better remuneration, or are able more easily to engage in private medical practice. We therefore make our cost calculations based on relatively high, but therefore more realistic costs, of health care provision.

TO BE COMPLETED:

[B. Estimated health benefits of the intervention programs: COVERAGE, EFFECTIVENESS]

[C. Share of costs that can be met within the poor countries: ESTIMATES OF PUBLIC RESOURCES AVAILABLE FOR PUBLIC HEALTH . . . PERHAPS 3-5 PERCENT OF GDP MAXIMUM, ASSUMING FULL RELIEF ON EXTERNAL DEBT]

[D. Share of costs that should be provided by donors: COSTS OF MEETING PROGRAM MINUS RESOURCES THAT CAN BE PROVIDED FROM WITHIN THE COUNTRY]

E. New Approaches to donor assistance

International assistance requires not only more funding, but new forms of delivery as well. Most participants in international aid programs – recipient governments, donor agencies, academic observers – emphasize that aid programs are characterized by excessive fragmentation and much too little scrutiny by independent experts. Much of the funding comes in unhelpful forms – such as tied aid and unneeded technical assistance -- rather the cash funding necessary to procure supplies and services. The World Bank's own Operations Evaluation Department (OED) reviewed the Bank's concessional lending projects recently ("Investing in Health: Development Effectiveness in Health, Nutrition, and Population Sector," 1999) and concluded that the projects were too complex, often failed to meet their goals, and had too little monitoring and evaluation built into the projects to allow for much confidence in their effectiveness.[20]

Some donor agencies notoriously vie for turf, causing program duplication, very high transactions costs, and often long delays. Another basic problem is that donor support is only haphazardly linked to the world scientific community involved in disease

[20] "Because of weak incentives and underdeveloped systems for monitoring and evaluation (M&E) within both the Bank and borrower governments, there is little evidence regarding the impact of Bank investments on system performance or health outcomes." (p. xii, "Investing in Health," 1999).

control. Most donor programs are never independently scrutinized for consistency with existing scientific knowledge, and very few programs are ever given careful external and independent reviews. We have already noted that World Bank programs do not build in the kind of data collection and analysis that would be needed for proper oversight, evaluation, and re-design as necessary of Bank programs in the field. We know of many circumstances in which flawed donor programs in the health sector were designed for political purposes within the donor country (for example to sell a product of a domestic enterprise), or simply were allowed to go forward because of lack of scientific awareness on the part of the donor agencies.

Appropriate programs for HIV/AIDS, malaria, and other disease control efforts will require scientific expertise far beyond the levels available within the donor organizations. The WHO has a special responsibility for mobilizing global science to strengthen donor funded programs. We suggest that WHO be given the lead by donor agencies to coordinate and vet projects in global health policy. The WHO should establish independent expert commissions for disease control in each major disease area: malaria, TB, HIV/AIDS, and so forth. Each expert commission should be charged with reviewing donor projects in the respective areas. Expert commissions would include public health specialists, medical doctors, vector biologists and ecologists (as necessary), epidemiologists, and experts in public health management. Donor support should be based, in significant part, on the judgments of this independent scientific expertise. The expert committees would have rotating memberships to ensure independence of views, and to minimize the risk that any global effort is taken over by a small group of personalities not subject to professional scrutiny.

F. Access to essential medicines

In view of the range of options in reducing drug prices for poor countries, and the lack of clear priority among them, the WHO should propose to the international community a set of international guidelines on pricing, voluntary and compulsory licensing, and the use of generics, in international trade.

[VI. CONCLUSIONS TO BE WRITTEN]

Technical Appendix. The Relationship between Health and Economic Growth

In this appendix we present formal models of the linkages from health to economic growth. The model can be used to illustrate the economic welfare implications and growth implications of disease burden and public health interventions. We begin with an extremely stripped version of the model, to highlight some major points, and then we add bits of realism at the cost of computational complexity. The full version of the model must be solved in a simulation setting.

The simplest version of the health-growth model

We assume a sequence of overlapping generations. In this version, individuals live for up to two periods, though they may die at the end of the first period ("childhood"). The mortality rate in period t is m_t. The number of children born in period t is N_t, of which exactly $N_t/2$ are males. Of the original birth cohort, the number $L_{t+1} = N_t (1-m_t)$ survive to adulthood in period t+1. This is also the size of the labor force in period t+1. A child of generation t receives human capital h_{t+1} from its parents, and produces output in period t+1 equal to its human capital:

(1) $q_{t+1} = h_{t+1}$

Growth of output per adult therefore depends entirely on the growth of human capital per adult.

The total population in period t, P_t, equals number of adults plus the number of children in period t:

(2) $P_t = N_{t-1}(1-m_{t-1}) + N_t$

Each adult household (one male, one female), has F_t children, of which $F_t/2$ are sons and $F_t/2$ are daughters. Thus, the total number of children born in period t is $N_t = F_t [N_{t-1}(1-m_{t1})/2]$. (Note that the divisor 2 occurs because there are half as many households as there are adults N_t).

Population growth g_t is equal to P_t / P_{t-1}, which equals:

$g_t = N_{t-1}(1-m_{t-1}) (1+ F_t/2)/[N_{t-2}(1-m_{t-2})(1+F_{t-1}/2)]$. Since N_{t-1} equals $(F_{t-1}/2)N_{t-2}(1-m_{t-2})$, we can simply further:

(4) $g_t = (F_{t-1}/2) (1-m_{t-1}) (1+F_t/2) / (1+F_{t-1}/2)$

When fertility and mortality rates are unchanging, this leads to the familiar expression: $g = (F/2)(1-m)$, which is sometimes called the gross reproduction rate. Population growth equals on the number of girls per household multiplied by the proportion of girls that survive to the age of childrearing.

Mortality, fertility and population growth

Adults consume part of their income and use part of it to raise children, imparting human capital to the next generation. We'll start with the simplest assumption to motivate the household's choice of fertility rate. We assume that households reap utility from having a male heir (or a female heir).[21] To take one simple formulation, we'll assume that household lifetime utility is:

$U = u(c)\,(1+\Theta)$ with $\Theta > 0$, when at least one son survives to adulthood

$= u(c)$ when no son survives to adulthood

given as:

$EU = u(c)\,(1 + p_t\,\Theta)$ where p_t is the probability of a surviving male heir

Suppose that a household as S sons, and that each has a identical and independent probability of childhood mortality of m. The chance of all S sons dying before adulthood (thereby leaving the parents without an heir) is then m^S, and $p = 1-m^S$.

Households engage in a simple tradeoff. Children are costly to raise, but each additional child raises the probability of a surviving heir. Households trade off the costs of child-raising versus the risks of remaining without heir because of child mortality. Specifically, we'll assume that each child requires a fraction f of potential labor market time. Households are endowed with 2 units of labor (one for each adult) but then use fF_t to raise children. Household labor income, as a result is $h_t(2-fF_t)$, which in turn equals consumption. Households maximize expected utility, subject to the household budget constraint. We assume that for a target of $F_t/2$ sons, they must have F_t total children, half sons and half daughters.[22]

Households choose the level of total fertility F_t (with $F_t / 2$ sons) to maximize $EU = u(c)\,(1 + p_t\,\Theta)$, where $p_t = 1 - m_t^{(F_t/2)}$ and $c_t = h_t\,(2-fF_t)$. The larger is F_t the larger is p_t and the smaller is c_t, so consumption and probability of a surviving heir are balanced against each other. The solution is of the form $F_t = F_t(m_t)$, where F_t is a decreasing step-function of m_t. The higher is the underlying mortality rate, the higher is the total fertility rate.

Consider the following numerical illustration. Suppose that $\Theta = 2$ (lifetime utility is doubled by the survival of a male heir) and $f = 0.05$ (each child requires 5

[21] We can presume that child-age mortality takes place before old-age mortality, so that parents observe whether or not they have a surviving heir, and reap utility accordingly.

[22] Of course, if parents are targeting a certain number of sons, they will act sequentially, having children until the desired number of sons arrive. If the probability of sons is one half, and is independently distributed of preceding births, then a target of S sons will require, on average a total of $2S$ children, half of which are girls. F, the total number of children until S sons are born, will be distributed as $p(F) = (1/2)^F\,B(F-S,S-1)$ where $B(F-S, S-1)$ is the binomial coefficient $(F-1)!/[S!(F-S-1)!]$.

percent of one adult's labor-force time). We set $u(c) = c$ and $h_t = 1$. Then, the optimum fertility choice and population growth rate depends on the child mortality rate in the following way:

Mortality rate (deaths per 1000)	Desired Sons	Total Fertility	Gross Reproduction Rate	Expected Utility	Gross National Product (per capita)
0.0	1	2	1.0	3.80	0.48
50	1	2	0.95	3.74	0.48
100	2	4	1.8	3.66	0.31
200	2	4	1.6	3.61	0.31

The main implications are the following. Total fertility is a rising function of the mortality rate within the range 0 – 200 deaths per 1000 live births. (At very high mortality rates, the total fertility rate falls again, because the high chances of infant death outweigh the slight increased probability of a resulting surviving male heir). For mortality rates of 100 or 200, as shown, the TFR is 4, and population growth is extremely rapid. A gross reproduction rate (GRR) of 1.8 means that population grows by 80% between generations. Expected utility and per capita GNP are both decreasing functions of the mortality rate.

Note the non-linear relationship between population growth and mortality. When mortality falls from 200 to 100, this is not enough of a drop in mortality to induce households to reduce the TFR from 4 to 2. TFR remains unchanged at 4, but the fall in the mortality rate means that a higher proportion of the 4 children (i.e., 90 percent as opposed to 80 percent) survive to adulthood, thereby raising the rate of population growth, from 60 percent in one generation to 80 percent. When the mortality rate falls from 100 to 50, however, the TFR falls from 4 to 2, and this has a huge effect on the population growth rate, which falls from 80 percent in a generation to –5 percent in a generation.[23]

Total output in period t, denoted Q_t, is output per adult worker, h_t, multiplied by the number of households, $N_{t-1}(1-m_{t-1})/2$, multiplied by the amount of labor-force supply of each household, $2 - fFt$. $Q_t = h_t N_{t-1}(1-m_{t-1})(2-fF_t)/2$. Per capita GDP, denoted y_t, is equal to Q_t divided by population P_t: $y_t = h_t N_{t-1}(1-m_{t-1})/[N_{t-1}(1-m_{t-1}) + F_t[N_{t-1}(1-m_{t-1})/2]$. This expression immediately simplifies to:

$$(3) \quad y_t = h_t (1 - f F_t /2) / (1 + F_t/2)$$

[23] With mortality at 50 per 1000, the TFR is 2, but this is below the population replacement rate.

We see immediately the effect of age structure on GNP per capita. Since only adults produce GNP, the GNP per population equals the GNP per full-time adult, in this case h_t, multiplied by the share of time an adult spends in the labor force $(1 - f F_t /2)$, multiplied by the number of adults per population, which is $1/(1+F_t/2)$. A higher fertility rate thus reduces GNP per capita for two reasons: it reduces the share of adult time in the labor force (by raising the share of adult time in childrearing) and it reduces the share of adults in the total population. In the numerical illustration, the rise of total fertility from 2 to 4 reduces the per capita GNP by 36 percent, from 0.48 to 0.31.

The Quality-Quantity Tradeoff and the Health-Poverty Trap

Perhaps the most important implication of high total fertility is not rapid population growth, or even the high ratio of children to adults (and therefore the lower per capita GNP), but the reduced level of human capital that parents impart to each child in large families. For a given level of family income, a higher number of children most likely results in a lower level of human capital per child, something that economists have come to term the "quantity-quality tradeoff" in childrearing. There are several likely reasons for this tradeoff:

1) biological: closer birth spacing results in poor physical well-being of each child
2) budget constraint: parents reduce the financial resources invested per child
3) quality of parental attention: reduced intensity of parent-child interactions

The quantity-quality tradeoff is thus partly automatic (biological), and partly the result of parents' economic decisions when choosing the investments to be made in each child's health and education.

At this stage, we take the simplest assumption, that the tradeoff is automatic: more children in a household implies less human capital accumulation per child. In the next section, we treat the human capital investment as a parental decision, with similar implications. At this stage, we assume a difference equation for human capital in which the child's human capital h_{t+1} is a linear function of parental human capital h_t and a negative function of the total fertility rate F_t. Specifically, we assume:

$$(2) \quad h_{t+1} = \alpha(F_t)\, h_t \qquad \text{with } \alpha(2) > 1$$
$$\alpha(F_t) \text{ decreasing in } F_t, \text{ and}$$
$$\alpha(F_t) < 1 \text{ iff } F_t > F^*$$

According to (2), when the household has two children, the human capital of the offspring are greater than the human capital of the parents, and this becomes the engine of long-term economic growth. When households have many children, however, specifically $F_t > F^*$, where F^* is some threshold, human capital is reduced and there is a decline in per capita income from one generation to the next. If human capital transmission works in this manner, then it is immediately obvious that the level of childhood mortality m will have a profound effect on economic growth. High rates of

mortality will result in high levels of childhood mortality and falling levels of human capital per person:

m_t high $\rightarrow$ F_t high $\rightarrow$ h_{t+1} low

m_t low $\rightarrow$ F_t low $\rightarrow$ h_{t+1} high

It is also easy to see how a society can get stuck in a poverty trap. Suppose, realistically, that the childhood mortality rate depends on two factors: parents' human capital (since parents with higher human capital are more likely to know how to take care of their children's health) and the underlying disease ecology, such as the presence or absence of mosquito vectors that transmit malaria. Specifically, we write:

$$m_t = d / h_t$$

where d represents an index of disease ecology, the exogenous component of mortality. The higher is d, the higher is the mortality rate for any given level of parental human capital. As the human capital of the parents rise, for any given disease ecology, the mortality rate falls, eventually to zero as parental human capital continues to expand.

Now combine the mortality equation with the fertility choice and with the human capital equation:

$$m_t = d / h_t$$

$$h_{t+1} = \alpha (F_t) h_t \qquad \text{where } \alpha < 1 \text{ iff } F_t > F_t^*$$

$$F_t = F_t (m_t)$$

Whenever the disease ecology is so adverse that $d / h_0 > F_0^*$ for some initial period 0, then the economy will fall into a downward spiral. Poor health will produce high fertility and low human capital per child, which in turn will produce poor health the following generation. On the other hand, if $d / h_0 < F_0^*$, then the economy will be caught in an upward spiral, in which fertility rates will be low enough to ensure a rise in human capital per person in the next generation, which in turn will promote improved health, a further reduction in fertility rates, and a further improvement in human capital per person.

Health – Human Capital Tradeoffs when Investment in Children is a Parental Decision

Suppose now that parents decide whether or not to invest in the education of their children. We will assume that parents continue to desire an heir, but that a better educated heir gives higher utility than a poorly educated heir. Thus, parents care, quite plausibly, both about the survival of their children and the level of education of their children.

To be specific, we assume now that human capital is given by the following relationship:

(3) $h_{t+1} = (1 + r e_t) h_t$

where e_t is the parental investment (in units of consumption goods) in the education of the child. The parameter r is the rate of return to investment in education. The level of educational investment is bounded by $0 \quad e_t \quad 1$. The cost of education per child is given by the parameter k, and the time cost of childrearing remains the same at f units per child. We will continue to assume that households care only about male heirs, and invest only in the education of the $F_t / 2$ sons. (We will assume that households invest the identical amount of education in every male child so that there is not a question of *which* heir's human capital is relevant.)

The household's budget constraint is then the following:

(4) $c_t = 2 - f F_t - k (F_t / 2) e_t$

Households are assumed to maximize the following expected utility function:

(5) $EU = u(c_t) [1 + p_t È V(h_{t+1})]$

subject to the budget constraint in (4). According to (5), expected utility now depends on the level of human capital of the heir, according to some utility function $V(h_{t+1})$. Once again, p_t signifies the probability of having a surviving male heir given an initial birth cohort of F_t children (and therefore $F_t / 2$ sons).

Higher mortality rates will cause a lower level of investment in education by optimizing households. As m rises, F_t rises while p_t falls. This raises the cost of education (since more sons must be educated just to achieve one educated heir), and for any number of sons, the probability of any survivors is reduced.

This can be illustrated with a simple numerical example as before. Suppose once again that $u(c_t) = c_t$, and that $V(h_{t+1}) = h_{t+1}$. Set $f = 0.04$, $k = 0.2$, $r = 0.3$, and $È = 1$. Set h_t, the human capital of the parents, equal to 1. Since the cost of education *per son* is 0.2 and the returns are 0.3 for one and only one heir, it will pay to invest in a son's education when there is one and only one son. With more than one son, the parents will choose to set $e_t = 0$. In turn, the household will choose to have one and only one son when the mortality rate is low enough. The implication is the following:

Low childhood mortality	one son	maximum educational investment per son
High childhood mortality	many sons	minimum educational investment per son

The specific values for expected utility are shown in the following table.

Mortality rate (deaths per 1000 births)	Desired number of sons	Expected utility if sons are not educated (e = 0)	Expected utility if sons are educated (e = 1)	Optimum education decision
0.0	1	3.88	4.00	e = 1
100	1	3.69	3.78	e = 0
200	2	3.68	3.22	e = 0
400	3	3.52	2.70	e = 0