4 Diseases of poverty and the 10/90 Gap

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Introduction: What is the 10/90 Gap?

Activists claim that only 10 per cent of global health research is devoted to conditions that account for 90 per cent of the global disease burden – the so-called '10/90 Gap' (Medecins Sans Frontiers, 2001). They argue that virtually all diseases prevalent in low income countries are 'neglected' and that the pharmaceutical industry has invested almost nothing in research and development (R&D) for these diseases.

Citing this alleged imbalance as justification, activists have for some years been calling for a complete redesign of the current R&D paradigm in order to ensure that more attention is paid to these 'neglected diseases' (Love & Hubbard, 2003). This could include measures such as an 'essential research obligation' that would require companies to reinvest a percentage of pharmaceutical sales into R&D for neglected diseases, either directly or through public R&D programs (Medecins Sans Frontiers, 2001), or the creation of a new public entity to direct R&D. This topic is now under discussion by a World Health Organisation working group following the report of its Commission on Intellectual Property, Innovation and Public Health.[1]

But does such an imbalance really exist and what would be the effect of redesigning the R&D system? This chapter investigates the realities of the 10/90 gap and its relation to the diseases of poverty.

Neglected diseases

Many scholars and activists have suggested that because there is little market for treatments for tropical infectious diseases such as leishmaniasis, lymphatic filariasis, Chagas' disease, leprosy, Guinea worm, onchocerciasis and schistosomiasis, there is a consequent lack of suitable drugs. These so-called 'neglected' diseases predominantly effect poor populations in low income countries (Murray *et al.*, 2001), and pose particular social and economic problems for those affected.

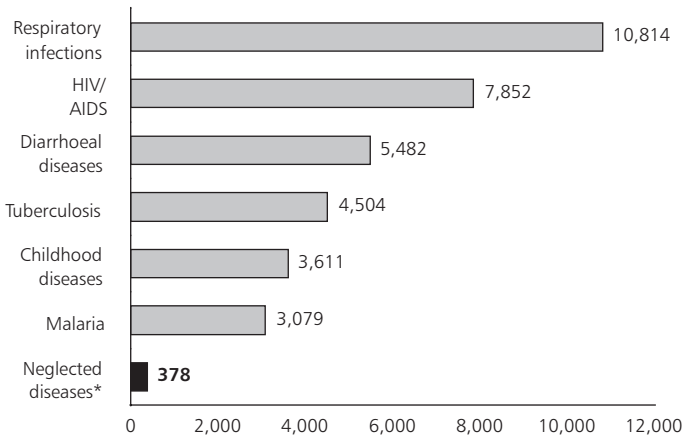
Patrick Trouiller, for example, has pointed out that of the 1,393 total new drugs approved between 1975 and 1999, only 1 per cent (13 drugs) were specifically indicated for a tropical disease (Trouiller et al., 2002). Research conducted by the DND Working Group and the Harvard School of Public Health in 2001 revealed that of the 20 global pharmaceutical companies surveyed, only two had research projects underway for the 'neglected' diseases of Chagas and leishmaniasis (Wirth, 2001)

Neglected diseases are a tiny fraction of total mortality

However, these bare statistics serve to mislead people into thinking that the poor are suffering at the expense of the rich. The reality is that 'neglected' diseases often do not represent the most pressing public health priorities in low income countries. They constitute a small fraction of their total disease burden (Figure 1). According to the 2002 World Health Organisation's (WHO) World Health Report, tropical diseases accounted for only 0.5 per cent of deaths in high-mortality poor countries, and only 0.3 per cent of deaths in low-mortality poor countries.

Moreover, treatments already exist for many of these diseases. Schistostomiasis (bilharzia), which predominantly affects children in Africa, can be treated with praziquantel at a cost of just 8 cents per 600mg tablet (Fenwick, 2006). Onchocerciasis (river blindness) is controllable with ivermectin. A range of treatments exist for lymphatic filariasis (elephantiasis). In fact, the WHO acknowledges that there are

Figure 1 **Number of daily deaths from diseases**[7]



*Neglected diseases are defined as African trypanosomiasis, Chagas disease and leishmaniasis

only three diseases that are genuinely 'neglected': African trypanosomiasis, leishmaniasis and Chagas disease (WHO/IFPMA, 2001).

This notwithstanding, research and development into the diseases of poverty is far from moribund. Several public-private partnerships exist that specifically focus on diseases of poverty. In particular, the Medicines for Malaria Venture (MMV), the Global TB Vaccine Foundation (Aeras),[2] the International Aids Vaccine Initiative (IAVI), and the Infectious Disease Research Institute (IDRI)[3] coordinate publicly-funded R&D projects with private companies. Due in part to these arrangements, there are at least 63 drugs in the R&D pipeline targeting HIV/AIDS, including 15 vaccines (Moran et al., 2005). There are at least 30 more drugs in the R&D pipeline for malaria, and 22 for tuberculosis.[4]

In addition, there are now PPPs that focus on developing drugs for African Trypanosomiasis, Chagas Disease, Leishmaniasis, and Dengue Fever, which have bolstered the number of potential treatments in the R&D pipeline for diseases that disproportionately affect people in poor countries. There are currently at least eight potential treatments in varying stages of clinical trials, and a further 16 in preclinical development.[5]

Research at the London School of Economics shows that the PPP approach has outperformed stand-alone industry efforts in producing drugs that are particularly suited for conditions in less developed countries. PPPs have often proved to be a quicker way to get drugs to market, generally equalling or exceeding industry standards. Finally, it appears that PPPs are more cost-effective than other approaches. For example, the Medicine for Malaria Venture's synthetic peroxide project has moved to Phase I clinical trials for a total cost of US $11.5 million – lower than the industry norm for developing a New Chemical Entity for western markets (Moran et al., 2005).

Most disease in lower-income countries is caused by poverty

Despite this increased activity, it is worth pointing out that a large proportion of illnesses in low-income countries are entirely avoidable or treatable with existing medicines or interventions. Most of the disease burden in low-income countries finds its roots in the consequences of poverty, such as poor nutrition, indoor air pollution and lack of access to proper sanitation and health education. The WHO estimates that diseases associated with poverty account for 45 per cent of the disease burden in the poorest countries (WHO, 2002). They include:

- **Tuberculosis**, **malaria** and **HIV/AIDS**, which account for nearly 18 per cent of the disease burden in the poorest countries (WHO, 2004).

- **Respiratory infections** caused by burning biomass fuels and low-grade coal in poorly ventilated areas also constitute a significant health burden for poor people. According to the WHO, exposure to biomass smoke increases the risk of acute lower respiratory infections (ALRI) in childhood, particularly pneumonia. Globally, ALRI represent the single most important cause of death in children under 5 years and account for at least two million deaths annually in this age group (Bruce et al., 2002).
- **Diarrhoeal diseases**, caused by the poor sanitation which is endemic in economically deprived areas, may be easily and cheaply treated through oral re-hydration therapy. However, diarrhoeal diseases still claim 1.8 million lives each year, (WHO, 1999) and are the second biggest killer of children worldwide, after respiratory infections.
- **Malaria** can be prevented through a combination of indoor residual spraying of dwellings with insecticides, the use of insecticide treated bed nets and the use of prophylactic medicines. Malaria infections can be cured with drugs such as quinine, mefloquine or artemisinin combination therapy (Muheki, et al., 2004; PAHO, 2006).
- **Yellow fever** – a vector-borne, viral disease with high mortality rates – can be prevented by using prophylactic vaccination. An affordable and effective vaccine is available, but nearly all countries in which the disease is enzootic prefer to wait until an epidemic is evident before mass-treatment of the affected population is undertaken (Monath & Nasidi, 1993; Monath 2005). Education can also play an important role in reducing the incidence of insect-borne diseases, for example by encouraging people to remove sources of stagnant water (insect breeding sites) from near their dwellings.
- **Tuberculosis** can be prevented by improving nutrition, and can be treated with DOTS therapy. This method can detect and cure disease in up to 95 per cent of infectious patients, even in the poorest countries (WHO, 1999).

- Education is vital for the prevention of **HIV/AIDS** – and this entails the full engagement of civil society. A combination of anti-retrovirals (ARVs) and good nutrition can help to control the viral load and suppress the symptoms of HIV/AIDS.
- Treatable **childhood diseases** such as polio, measles and pertussis, account for only 0.2 per cent of Disability Adjusted Life Years (DALYs) in high-income countries, while they account for 5.2 per cent of DALYs in high mortality lower income countries (WHO, 2002). Vaccines for these diseases have existed for at least 50 years, yet only 53 per cent of children in sub-Saharan Africa were immunised with the diphtheria-tetanus pertussis (DTP) jab in 2000 (WHO, 2002a).
- **Malnutrition** particularly affects people in poor countries. In particular, micronutrient deficiencies contribute to illness and poor health. For example, as a result of Vitamin A deficiency, 500,000 children become blind each year (WHO, 1995) and many of them die, despite the fact that such outcomes can be avoided by inexpensive, easy-to-administer food supplements (WHO, 1997). Vitamin A deficiency also weakens the immune system, leaving children vulnerable to other illnesses such as diarrhoea and measles. Estimates suggest that Vitamin A deficiency contributes to or causes approximately 800,000 childhood deaths each year (Rice et al., 2004).
- **Dengue** is a mosquito-borne viral infection prevalent in over 100 countries. According to the WHO, two-fifths of the world's population is at risk from dengue, and there are around 50 million infections every year.[6] Dengue can be prevented with a range of techniques to control insects. These include covering water containers and applying insecticides to larval habitats. During the 1950s the principal vector, *Aedes aegypti*, was eradicated from 22 countries in the Americas by the application of DDT.
- **Pertussis** (whooping cough) is a particular threat to infants. Somewhere in the range of 20 to 40 million cases occur every year, mostly in less developed countries, and as a result,

Table 1 **Deaths caused by 'developed country' diseases**[21]

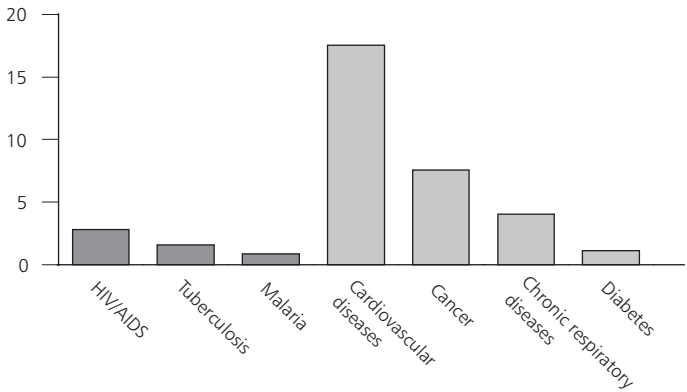
% of deaths caused by/in	*High mortality developing countries*	*Low mortality developing countries*	*Developed countries*
Malignant neoplasms (cancers)	6.3	9.9	21.2
Diabetes	0.6	1.5	1.7
Neuropsychiatric disorders	1.3	1.4	2.9
Cardiovascular diseases	18.9	23.4	47.8
Respiratory diseases (asthma)	4.0	6.7	5.0
Digestive diseases	2.7	3.4	3.7
Total 'developed-countries' diseases	33.8	46.4	82.3

between 200,000 and 400,000 die every year.[7] An effective vaccine against pertussis has existed for some years, but currently 20 per cent of children worldwide do not receive it.

- **Leprosy** was for many centuries an incurable and widespread disease. However, the development and adoption, in the early 1980s, of multidrug therapy (dapsone, rifampicin and clofazimine) has led to a 90 per cent decline in its prevalence.[8]

Poverty-related diseases cause far higher levels of mortality in low-income than high-income countries (Table 1). Most of these diseases and deaths can be prevented with pre-existing treatments and prevention programmes. Diseases for which there is no treatment currently available, such as dengue fever, contribute towards a far smaller proportion of low-income country mortality rates than diseases which are easily preventable or treatable. It is estimated that 88 per cent of child diarrhoeas, 91 per cent of malaria and up to 100 per cent of childhood illness such as measles and tetanus can be prevented among children using existing treatments (Jones et al., 2004). This means that up to 3 million child lives could be saved each year if these medicines could be distributed effectively to all areas of need.

Figure 2 **Projected global deaths by cause** 2005 (all ages), millions



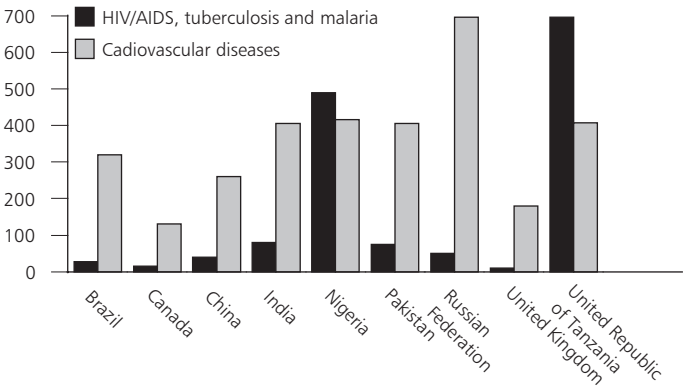
Source: WHO (2005a).

Illnesses of low and high-income countries are converging

Exponents of the 10/90 Gap are also inaccurate when they claim that low-income countries, which constitute the majority of the world's population and disease burden, suffer from completely different diseases than high-income countries. The premise that only 10 per cent of the global health research budget, both private and public, is used for research into 90 per cent of the world's health problems is factually incorrect.

In reality, the nature and spread of diseases suffered in both rich and poor countries is converging rapidly. According to the WHO, ailments such as cardiovascular disease, cancer and diabetes now account for 45 per cent of the global disease burden. Around 80 per cent of this burden now occurs in low and middle-income countries (WHO, 2005a). Chronic diseases cause four out of five deaths in lower-income countries. In absolute terms, more people in the lower-income countries (compared to higher-income countries) die

Figure 3 **Projected death rates by specific causes for selected countries**
2005 (all ages), thousands

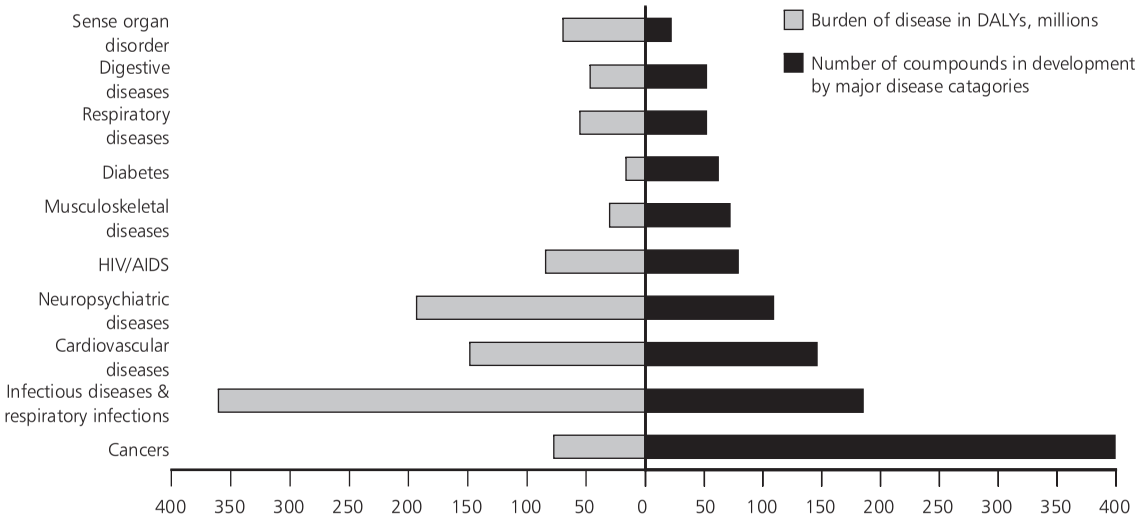


Source: WHO (2005a).

as a result of non-communicable diseases. Cardiovascular diseases are one of the most significant causes of death in lower-income countries (Figures 2 and 3).

The WHO argues that much of this disease burden is attributable to less healthy diets and increasing physical inactivity. This may be so, yet the global rise of chronic diseases is also partly the result of more people living beyond middle age, thanks to greater global economic growth and prosperity. The prevalence of chronic disease, however, does challenge the myth that the current commercial R&D paradigm is failing to produce drugs that meet the needs of the global disease burden. Significant resources currently are being deployed towards developing treatments for cancers, cardiovascular diseases, neuropsychiatric diseases and diabetes. In fact, levels of drug development increasingly reflect the global disease burden, so lower-income countries therefore stand to benefit from drugs that are currently in the R&D pipeline (Figure 4).

Figure 4 **The global disease burden vs. number of compounds in development**



Sources: PhRMA (2005) and WHO (2004)

Lower-income countries also currently benefit from drugs that were originally developed for wealthier markets. Polio, pertussis (whooping cough) and diphtheria, for example, were once endemic in wealthier countries, but have been practically eradicated from these areas due to simple vaccines that were developed a few decades ago.

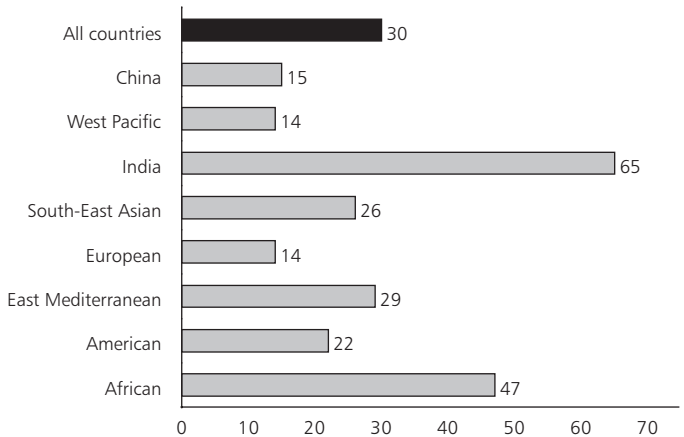
Now, three-quarters of the world's children – including millions in low-income countries – are vaccinated against such diseases, saving at least three million lives a year and preventing long term illness and disability in millions more. Tuberculosis treatments were originally devised to combat the disease in wealthier countries, and many populations in lower-income countries now reap the dividends of this advance in medical science in the form of mass vaccination programmes. HIV/AIDS treatments in the form of ARVs were originally developed with wealthy consumers in mind. Those treatments have now spread to poorer countries which are most affected by the disease, but are unable themselves to bear the cost of R&D for such treatments.

Statins are also an increasingly important tool in the fight against cardiovascular diseases in lower-income countries, with many of these powerful drugs now off-patent and open to generic competition. Again, these treatments originated – and are still being developed – in wealthier countries under the current commercial R&D paradigm.

Access is the real problem – not innovation

If treatments exist for the majority of poor countries' health problems, why then do mortality rates remain so high? Any discussion of this question must address the problem of access to essential medicines, which remains an intractable political and economic problem. According to the WHO, an estimated 30 per cent of the world population lacks regular access to existing drugs, with this figure rising to over 50 per cent in the poorest parts of Africa and Asia (Figure 5).

Figure 5 **Percentage of WHO regions lacking access to essential medicines[29]**



Within these populations, it is the poorest socio-economic groups that disproportionately suffer from a lack of access to existing medicines.[9] The implications of this failure of public health policy on global mortality are profound – according to one study, over 10 million children die unnecessarily each year, almost all in low-income or poor areas of middle income countries, mostly from a short list of preventable diseases such as diarrhoea, measles, malaria and causes related to malnutrition (Black, 2003).

Only one-half (approximately) of sub-Saharan African children are vaccinated against childhood diseases, and in isolated areas that number is as low as one child in 20 (WHO, 2002a). A variety of factors conspire to create this desperate situation, many of them caused by government mismanagement and interference. These

> "An estimated one-third of the world population lacks regular access to essential drugs, with this figure rising to over 50 per cent in the poorest parts of Africa and Asia. And even if drugs are available, weak drug regulation may mean that they are substandard or counterfeit."
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> WHO Medicines Strategy Report 2002–2003

include weak healthcare systems, taxes and tariffs on medicines and inadequate risk pooling mechanisms. These and other barriers to access are discussed in detail in chapter 8.

The 10/90 Gap is a red herring

The evidence presented here suggests that activists who cite the 10/90 gap as justification for the wholesale reform of the R&D paradigm are setting their sights on the wrong target. It is fallacious and misleading to argue that commercial R&D neglects almost entirely the diseases of the poorer parts of the world. Private companies are responsible for developing and producing majority of the drugs that already exist on the WHO's essential medicines list, and hundreds of private research initiatives are currently underway to address the world's biggest killers that impact both rich and poor countries. The so-called 'neglected diseases' rarely constitute a country's most pressing health priorities. The WHO itself has argued that the key factors behind the excessive mortality caused by these diseases include unavailability of health services and failure to use prevention and treatment strategies, rather than the unavailability of medicines (WHO, 1999).

The health problems faced by the world's poorest populations are not caused by the non-existence of drugs specifically related to their problems and diseases. The real problem is ensuring that these populations can actually access vital medicines. Many governments fail their populations in this respect by imposing punitive tariffs and

taxes on medicines, and by failing to foster healthcare systems or functional risk pooling mechanisms. The governments of poor countries also hinder the creation of wealth, imposing obstacles in the way of owning and transferring property, imposing unnecessary regulatory barriers on entrepreneurs and businesses, and restricting trade through extortionate tariffs. It is these and other political failures that have left poor populations without the necessary resources to access the medicines that could so easily transform their quality of life.

Campaigners who cite the 10/90 Gap as the prime mover behind the health problems of the poor are in fact betraying the very people they are attempting to help. In seeking to radically alter the current R&D paradigm, they risk undermining the incentive system that has led to the development of treatments for a great majority of the health problems suffered by both high and low income countries.

Emerging health threats, ranging from drug-resistant strains of AIDS and tuberculosis to avian flu, remind us of the importance of ensuring that the pharmaceutical industry continues to discover and develop new drugs. Innovation is a fragile process, and it can be weakened or thwarted by poor public policies. Heavy taxation, regulation or public vilification of pharmaceutical companies will reduce their incentives to invest in researching these vital drugs, because shareholders will be uncertain of generating a return. If commercial companies are no longer able to prioritise and manage their own R&D spending unmolested by government, the consequences for global health will be tragic.

Furthermore, the public sector offers no panacea for activists who seek to wrest the ability to conduct R&D away from commercial enterprises and towards the public sector. The public sector's trophy cupboard of health R&D successes is almost empty, because governments lack both the technical skills and the ability to pick winners that have rendered many pharmaceutical companies so commercially successful.

In the 1980s, the US Agency for International Development funded research into a vaccine for malaria, which absorbed $60

million and failed to achieve any of its goals. This failure is a neat illustration of the drawbacks to the public procurement of R&D. Because the researchers were operating to the demands of a public sector employer rather than the market, they gave out wildly optimistic statements about the progress of their work in order to ensure a continued supply of funds. Government-funded project directors also have an incentive to fund unpromising work – illustrated by the project leader's demand for further funds, despite the unpromising nature of his early work. Finally, because the recipients of government subsidies are paid before delivery, they remove incentives to properly conclude the research.

By seeking to derail the R&D capabilities of the pharmaceutical industry, exponents of the '10/90 gap' are in danger of creating a self-fulfilling prophesy. A global R&D treaty, in which the profits of pharmaceutical companies are heavily taxed and their intellectual property rights undermined, would be almost certain to have the unintended consequence of effectively turning off the tap of innovation that is essential to dealing with the world's changing health problems.