

European**Voice**

A healthier world: tackling neglected diseases



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CONTENTS

Diagnosing the problem.....	P3-4
Current funding.....	P4-6
Who's who in the search for solutions.....	P7-9
Innovative financing mechanisms.....	P9
The EU's engagement.....	P10
Seeking strategies to reduce suffering.....	P10-11

Written by Peter O'Donnell

SUMMARY

Poverty-related and neglected diseases are a problem too large to be ignored, but responses have so far had only limited success. Even the achievements to date could be under threat if efforts are not stepped up. Policymakers, faced with a mix of scientific, economic and societal challenges, must devise new forms of public-private co-operation. The requirement is not only for improved diagnosis, treatment and prevention, but also for innovative financing – and above all, a coherent political vision.

Sources include:

Neglected disease research and development: the public divide, Policy Cures 2013; global tuberculosis report, World Health Organisation 2013; annual report, the Global Fund to Fight AIDS, Tuberculosis and Malaria 2012; pharmaceutical R&D projects to develop new cures for patients with neglected conditions, International Federation of Pharmaceutical Manufacturers' Associations 2013; the overarching post 2015 agenda, General Affairs Council conclusions 25 June 2013; 2015 and beyond: the role of innovation for health in a new development framework, Global Health Technologies Coalition 2013; Call to EU leadership on global health R&D, DSW, HAI et al 2013; Poverty-related and neglected diseases in Horizon 2020 – gaps and challenges, Global Health Advocates et al 2013;
Images: iStockphoto.com

ACRONYMS

PRNDs – poverty-related and neglected diseases
NTDs – neglected tropical diseases
PDPs – product development partnerships
WHO – World Health Organization
BMGF – Bill and Melinda Gates Foundation
IFPMA – International Federation of Pharmaceutical Manufacturers' Associations
EDCTP – European and Developing Countries Clinical Trials Partnership
UNITAID – a global health initiative

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A European primer on the fight against poverty-related and neglected diseases

Diagnosing the problem

Premature death, pain and poverty

Poverty-related and neglected diseases (PRNDs) cause massive suffering and reinforce poverty – mainly in the developing world, but also in Europe. There are a billion victims of these diseases worldwide, and every year they account for 13.7 million deaths. That is the equivalent of a thousand airliners crashing every week, and killing all their passengers.

The big three PRNDs – HIV/AIDS, tuberculosis (TB) and malaria – cause 230 million new infections every year, and nearly 4 million deaths. Along with other conditions, including neglected tropical diseases (NTDs), they ravage the poorest countries in the world, causing blindness, chronic pain, severe disability, disfigurement and death. 1.5 million children still die each year from diseases that could be prevented by a simple vaccine.

Maternal and perinatal disease accounts for nearly 10% of the global burden of disease, and most maternal deaths occur in low- and middle-income countries. The cumulative effect is to hinder the development and economic growth of affected countries, limiting the ability of infected individuals to work, and pushing their communities further into poverty.

Malaria

There were 200 million cases of malaria across more than 100 countries in 2012, and more than 600,000 deaths – 90% of them in sub-Saharan Africa, and three-quarters of them children under

the age of five. A child dies every minute from malaria, and a pregnant woman each hour. Malaria causes billions of dollars of lost productivity every year – \$12bn per year to Africa's economy alone. It accounts for more than 30% of public healthcare spending in the most affected countries, and it remains a health risk for more than half of the world's population in 2014.

But malaria is a preventable and largely curable disease. It is caused by parasites transmitted through mosquito bites, and can be countered by timely diagnosis, rapid drug treatment, indoor spraying with insecticides, and bed nets to protect against mosquitoes at night.

HIV/AIDS

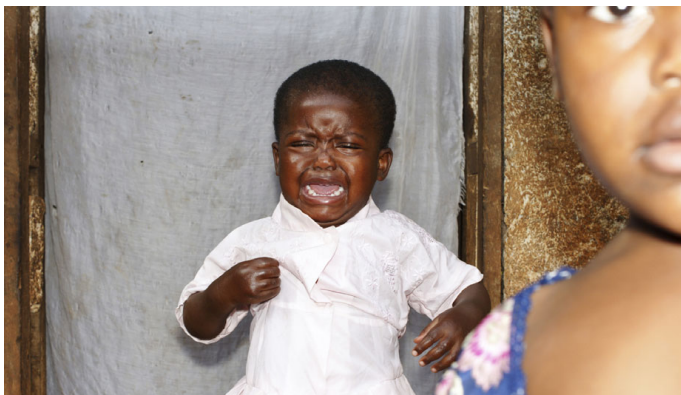
AIDS has so far killed more than 30 million people worldwide. And some 35m are living with HIV, two-thirds of them in sub-Saharan Africa, where, every minute, a young woman is infected with the virus. There were 2.3m new HIV cases in 2012, with more than 131,000 in Europe and Central Asia – including 29,000 in the European Union. Infection rates are rising significantly in the Middle East, North Africa, and Eastern Europe. Only about half of those who need treatment for HIV are currently receiving it, and for every person who gets treatment, two are infected with HIV. In developed countries, key populations at higher risk of infection evade treatment: in Eastern Europe and Central Asia, many drug-users avoid seeking health services for fear of being ostracised or prosecuted.

Tuberculosis

Among infectious diseases, TB is second only to AIDS as a global cause of death. It is closely linked to poverty, and two-thirds of cases occur among people in their most active phase of life. More than 95% of deaths are in the developing world. In 2011 there were 8.7 million new cases of TB and 1.4m deaths. More than one million of the new cases were co-infected with HIV, and 430,000 of those who died from TB had HIV, which creates particular susceptibility to developing TB. A new challenge has also emerged with resistant forms of TB that defeat all standard therapies and even some of the second-line drugs, and that carry immense costs economically. They also pose a real threat to health security, even in Europe. Some 440,000 new cases were identified in 2008.

Other neglected diseases

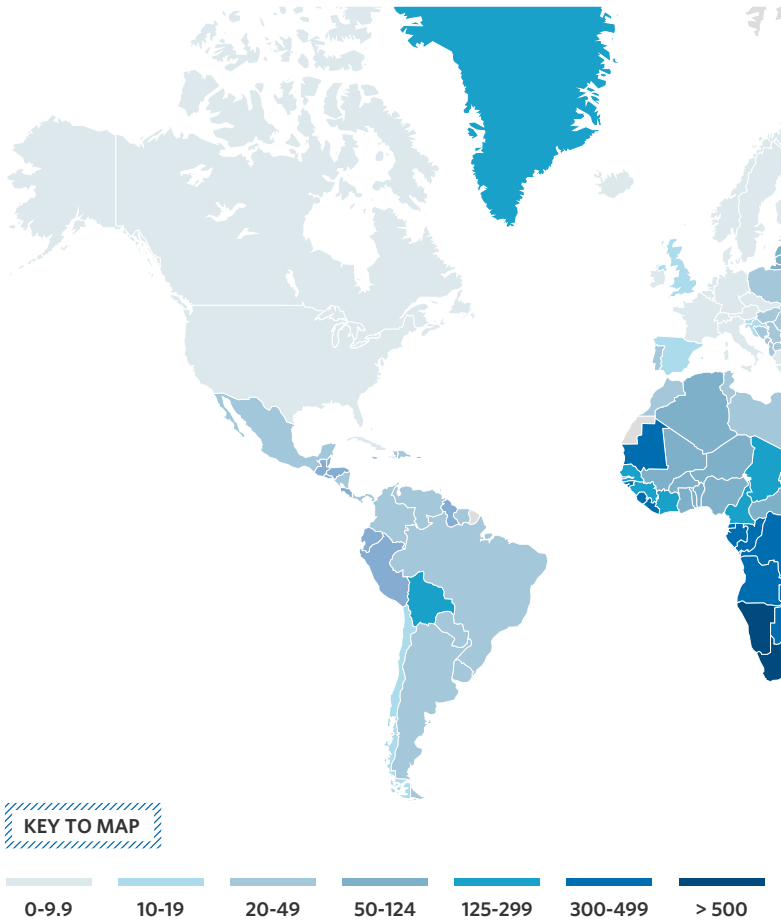
This is a broad category that includes conditions more familiarly known as sleeping sickness, guinea-worm disease, or river blindness. The World Health Organization (WHO) lists 19 conditions: dengue, rabies, Chagas disease, human African trypanosomiasis, leishmaniasis, cysticercosis/taeniasis, dracunculiasis, echinococcosis, foodborne trematodiasis, lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis, Buruli ulcer, leprosy, trachoma, and yaws. Others include diarrhoeal diseases, kinetoplastids, bacterial pneumonia and meningitis, salmonella infections, and rheumatic fever.



“New HIV infections are declining in many of the countries most affected by the epidemic. More and more countries are in a position to target the elimination of malaria from their territories. The world is on course to halve TB mortality by 2015 in comparison with 1990.

Global Fund to Fight AIDS, Tuberculosis and Malaria

Estimated new TB cases (all forms) per 100,000 pop



Current funding

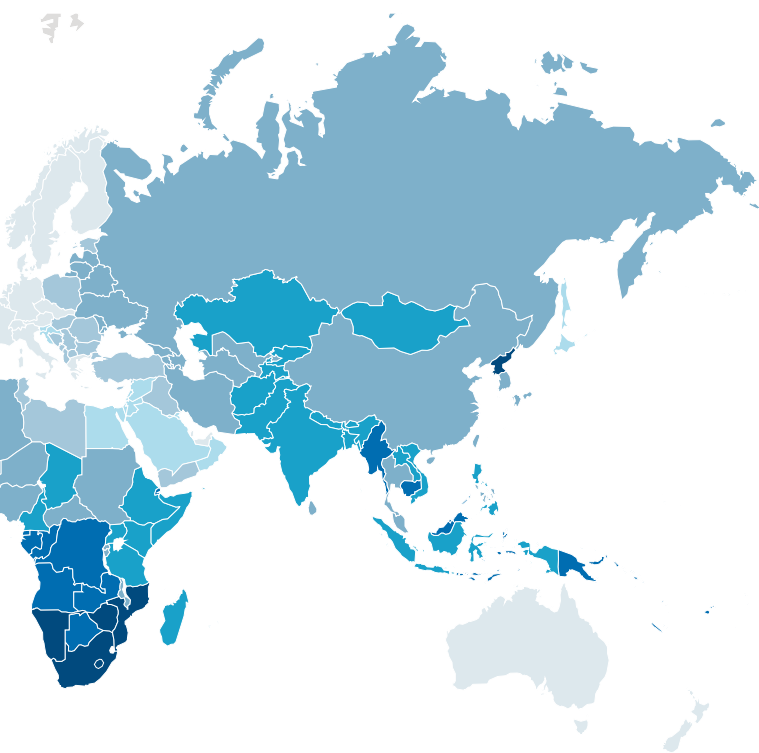
Health and development programmes have already brought transformational improvements over the last decade, providing diagnosis, treatment, and prevention. Organised healthcare provision, along with funding through foreign aid and from philanthropic donors, is bringing relief and hope in many parts of the world.

Worldwide, TB mortality has fallen by 41% since 1990. Malaria cases in the last decade are down by a quarter, and deaths down by more than a third, saving 3.3 million lives. AIDS-related deaths have fallen steadily from their 2002 peak of 2.2m to 1.6m in 2012. Treatment is effective, and wider access averts 700,000 AIDS-related deaths a year. A record 8m people in low- and middle-income countries are currently receiving HIV treatment. And progress on neglected tropical diseases has come from new delivery mechanisms and new vaccines, treatments and diagnostics.

Increased funding

The improvements are largely the result of a steady trend to increase funding for PRNDs over the last decade. Financing for

0 population per year



500
No data /
not applicable

Source: WHO 2013

tuberculosis in disease-endemic countries has risen from less than \$2,000m in 2002 to about \$6,000m in 2013, according to the World Health Organisation. And the Bill and Melinda Gates Foundation (BMGF) has committed more than \$2.5bn in HIV grants to organisations around the world since it was set up in 1997.

A key indicator is the Global Fund to Fight AIDS, Tuberculosis and Malaria, an international financing institution and the main multilateral funder in global health. It channels 82% of international financing for TB, 50% for malaria, and 21% for AIDS. It has supported more than 1,000 programmes in more than 140 countries, providing AIDS treatment for 6.1m people, anti-tuberculosis treatment for 11.2m people and 360m insecticide-treated nets for the prevention of malaria. Its receipts dipped following the economic crisis, but at the end of 2013, world leaders pledged \$12bn over the next three years to the Global Fund to Fight AIDS, Tuberculosis and Malaria.

Limits of resources

The same health improvements are in theory possible for the entire world population. But unnecessary suffering persists widely, partly for lack of resources. Governments of poorer countries are ill-equipped to pay for improved care. And public

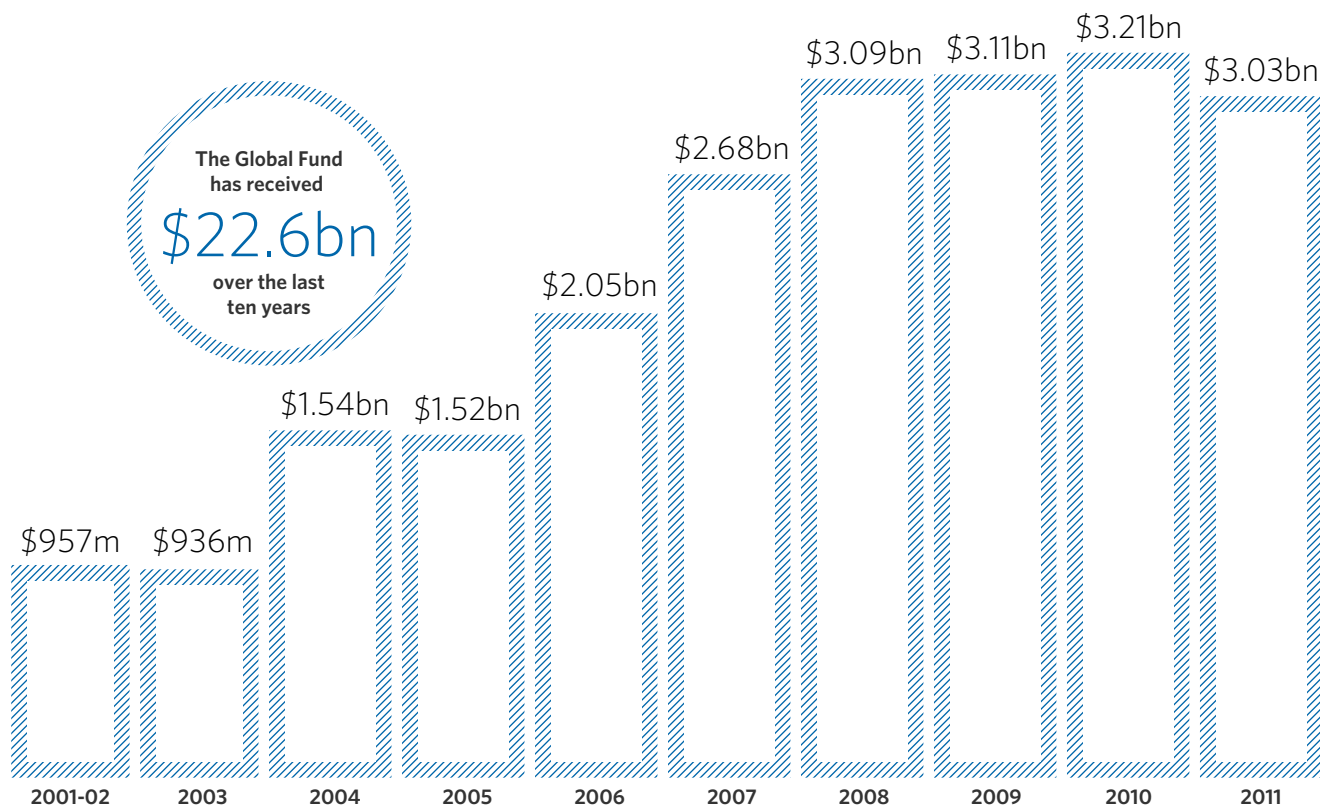
“To supplement domestic funding for tackling TB, international donor funding of about \$2,300 million per year is needed for implementation of existing interventions up to 2015, and \$2,000m per year is needed for research and development. Estimated gaps amount to about \$2,000m per year for implementation between 2013 and 2015.

World Health Assembly May 2014



The Bill and Melinda Gates Foundation (BMGF) is the biggest philanthropic donor to PRNDs. It has committed more than \$1.6 billion to the Global Fund, and it runs numerous research programmes and networks on vaccines for HIV/AIDS and TB, new-generation drug discovery for malaria, TB, and tropical diseases, and control of disease-transmitting mosquitoes.

Contributions made to the Global Fund



Source: The Global Fund

and donor funding is uneven, and not enough to fill all the gaps. As a result, those at risk – or already suffering – are denied access to the care that could help them, and that could often return them to active and productive life.

Limits of infrastructure and strategy

Improvements often also require dramatic upgrading of local infrastructures, and changes in policy priorities and in conditions on the ground – relating to poverty, sanitation, education or conflict. Treatment is often ineffective because care centres or trained staff are lacking (sub-Saharan Africa, with 24% of the global burden of disease, has only 3% of the world’s health workforce), diagnostic capacity is limited, or supply chains are inadequate. WHO emphasises the need for national disease-control programmes to improve co-ordination and integration. It highlights the need to strengthen human resources and to work with other sectors such as education, agriculture and veterinary public health in disease control programmes.

Moving targets

Wider access to treatment, more generous funding, and better health policies will not be enough to lift this burden of disease entirely. Diseases and their causes are moving targets, and often elude the tools available to tackle them. Many current medicines offer incomplete cures, are unsuitable for children, difficult to administer, or unstable in hot climates. Diagnostic tools are

“Global health is under serious threat from the interlinked issues of access to nutrition, food security and climate change. We foster a multidisciplinary approach to address these problems.

The Wellcome Trust

inefficient or costly, and vaccines are lacking or ineffective against many diseases.

Diseases are also constantly evolving, developing resistance that makes many of today’s treatments useless for tomorrow. And new diseases constantly emerge for which no treatment exists. So next-generation approaches are needed, both to meet new challenges, and to overcome a rising tide of resistance to current therapies and techniques.

From palliation to eradication

Tackling PRNDs effectively means not just curing an individual, but tackling the causes of disease too. Many patients successfully treated for malaria remain vulnerable to the malaria parasite: treating the patient does not reduce the incidence of disease. A palliation strategy is not enough, as the burden of repeated treatment will become unaffordable over time in low and middle-income countries. This is all the more true today, when many infectious diseases are spreading more widely than ever before, because of globalisation, unprecedented population movements, and even changing climate patterns. So the ultimate goal is eradication, through combining treatment of individuals with more fundamental changes that can range from neutralising disease vectors (such as the mosquitoes that transmit the malaria parasite) to the creation of vaccines that protect effectively against a disease.

A new toolbox

Combating PRNDs requires renewal and expansion of the tools and techniques for diagnosis, for treatment, and for prevention. After many years of neglect, research is now producing new tools – but not enough, and not always adequate to the task. Research funding in this area is still low in relation to the scale of the challenge.

Prescribing treatment

Who’s who in the search for solutions

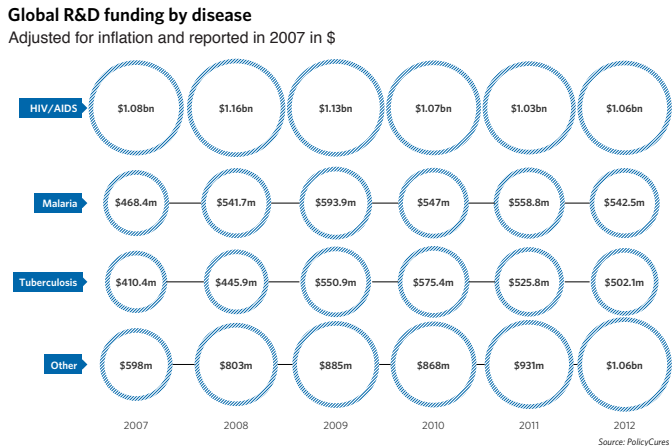
The challenges presented by poverty-related and neglected diseases are widely recognised. The diseases are, primarily, neglected: as the previous section illustrates, not enough treatments exist for them, and those treatments that do exist are not universally accessible because insufficient resources have been devoted to them.

And because they are poverty-related, the limited prospects for commercial profitability have discouraged private-sector research from improved treatments, as this section discusses.

Diverse responses are emerging from a wide range of players. Numerous initiatives are underway in the formal and informal international community – ranging from the European Union and the World Health Organisation to international financing institutions, philanthropic donors, not-for-profit organisations and campaigning non-governmental organisations. Many richer national governments are upgrading their bilateral and multilateral assistance. The healthcare industry is providing tools and researching new ones, principally on a commercial basis, but increasingly in various forms of partnership. And even the poorest national governments are taking some steps to improve conditions for their own populations.

More investment is needed to fund basic research on elusive pathogens such as the ones causing HIV, for the resource-heavy clinical stage 3 trials, as well as for capacity building of national regulators.

Renate Baehr, DSW executive director



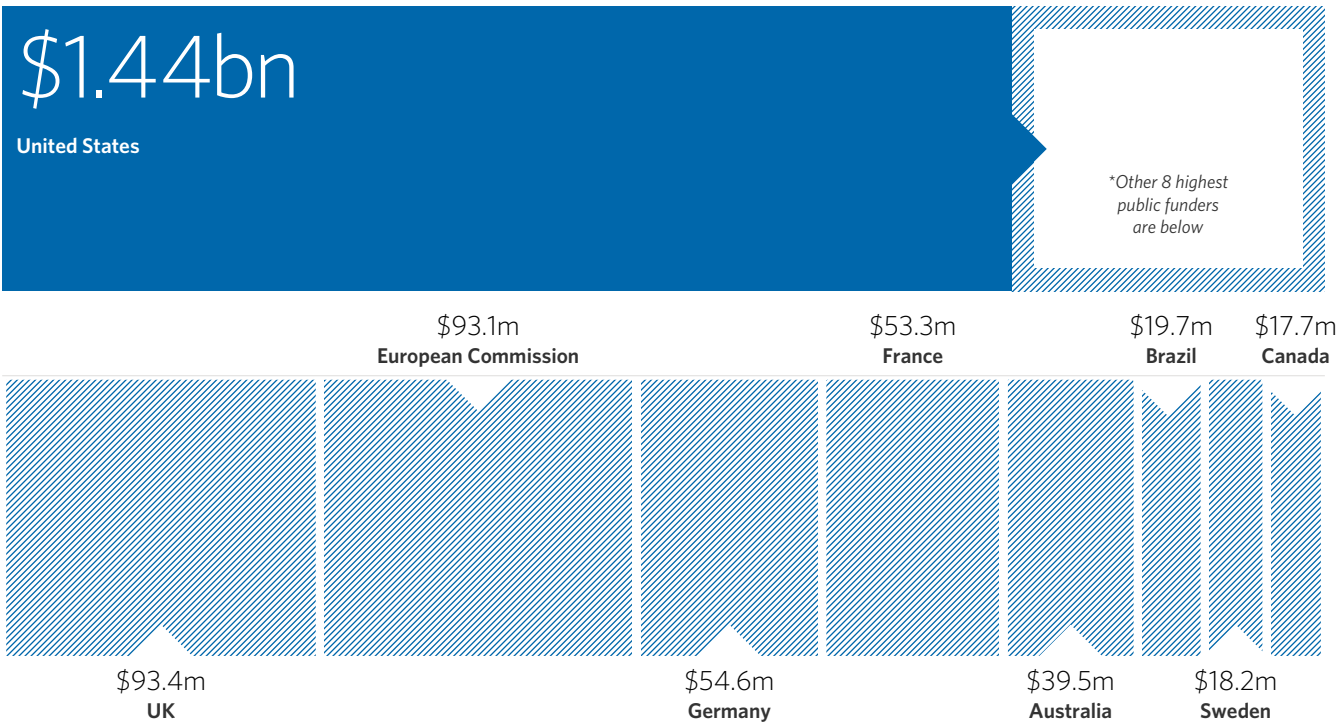
Funding research

The public sector is consistently the largest overall funder of research and development (R&D) for poverty-related and neglected diseases and conditions. Total R&D funding for neglected diseases was \$3.2 billion in 2012. The public sector provides nearly two-thirds (\$2.0bn, 63.2%), followed by the philanthropic sector (\$631 million, 19.9%) and the pharmaceutical industry (\$527.2 million, 16.7%).

Policy Cures is an independent strategic analyst on the creation of new pharmaceuticals for neglected diseases, and produces the leading annual research funding ranking, G-Finder.

Top 10 public funders

Adjusted for inflation and reported in 2007 in \$



Source: PolicyCures

The US government is the leading funder. It contributes around 45% of the total investment in global health R&D each year and 70% of all government investment worldwide. It is the leading funder of R&D for 26 of the 30 most neglected diseases and conditions affecting the developing world

The majority of multinational pharmaceutical companies’ investments in neglected disease R&D in 2012 focused on three diseases: dengue, tuberculosis and malaria.

Getting results

Much of the research is paying off. For some diseases, the pipeline of new candidate products is very promising.

Nearly 100 malaria products are in development, including 37 medicines, 46 vaccine candidates, and a dozen vector control agents.

The member companies of the International Federation of Pharmaceutical Manufacturers' Associations (IFPMA) are currently working on 162 R&D projects focused on new or improved medicines and vaccines for eleven PRNDs, including tuberculosis and malaria. 140 of these projects are product development partnerships involving IFPMA member companies and other partners, the remaining 22 projects are company-only undertakings. Since 2012, the number of medicine and vaccine R&D projects has increased by more than 20%, from 132 to 162.

New tools have a cost

But for success, the process needs continual funding over the years ahead. WHO predicts a shortfall of \$1.3bn per year for research into PRND in 2013-15. Malaria R&D needs in the next decade are projected at between \$5.5 billion and \$8.3bn, with the midpoint averaging around \$700m on an annual basis.

At present, the investment is inadequate to meet the needs. Only 10% of worldwide health research expenditure is used to address the diseases that account for 90% of the world's disease burden. A study of 26 PRNDs that account for 14% of the global disease burden revealed that they benefit from only 1.4% of global health-related R&D expenditure. Research and development for PRNDs falls short of their global public health importance.

Paying for products

The development of effective products is not enough. They then have to be supplied to the people who need them – and that means they have to be paid for.

Some treatments become cheaper with the passage of time, as patents expire and alternative suppliers emerge. AIDS drug costs have dropped 100-fold since 2000 from more than \$10,000 per person per year to less than \$100. Some treatments are supplied by philanthropic donations. IFPMA members have pledged to

donate an average of 14bn treatments in 2011-20 to fight neglected diseases. Efforts are under way to build up local capacity in poorer countries, holding out the prospect of tailored and affordable treatments at lower prices.

But the market alone is not capable of generating needed innovations at affordable prices. “The current innovation model is broken or failing,” as Fanny Voitzwinkler of the campaign group Global Health Advocates puts it. Instead, increasing attention is accorded to the exploration of novel partnership approaches. The Global Health Technologies Coalition urges the creation of a “portfolio of incentives and financing mechanisms to stimulate needed R&D, and the participation of the private sector, at all stages of the product development process”.

Innovative financing mechanisms

A wide range of mechanisms has been created or is under discussion, bringing together different constellations of players from the private, public and philanthropic sectors in different geographical or product areas. The examples here are illustrative, not comprehensive.

- Product development partnerships (PDPs) are offering new prospects for joint action. These are not-for-profit organisations that leverage private-sector expertise and public and philanthropic resources where markets are not lucrative, and drive the development of products intended for low resource settings, so as to bring them onto the market at affordable prices. The top five PDPs – PATH, International AIDS Vaccine Initiative (IAVI), MMV, Global Alliance for TB Drug Development, and Aeras – accounted for more than two-thirds of all PDP funding in 2012, with philanthropic organisations providing most of the money.
- Final trials will start in 2014 on what is billed as “the first-ever drug regimen to treat both drug-sensitive TB and some forms of multi-drug resistant tuberculosis and significantly cut the cost and duration of treatment”. This new combination treatment, known as PaMZ, and making use of a novel agent developed by the Global Alliance for TB Drug Development, is expected to cost less than €100 per patient, instead of the current average cost of around €5,000.
- An ‘advance market commitment’ has been designed to help



“We need to make sure that we are all working together more effectively...We must all forge partnerships, between public bodies and private entities, between countries, sectors and disciplines.

José Manuel Barroso, president of the European Commission

make vaccines available more quickly in developing countries. Donors make financial commitments to help pay for future purchases, which offers manufacturers a guarantee of purchase for vaccines that are developed in line with specified criteria – including supply at affordable prices. This scheme has already promoted the widescale provision of a vaccine for pneumococcal diseases – which kill 1.5m children every year in poorer countries.

- The European Commission is in discussion with non-profit organisations, the European Investment Bank, the European and Developing Countries Clinical Trials Partnership (EDCTP) and BMGF about creating a viable business case to advance TB vaccine development efforts that will balance commercial and public sector interests. The envisaged Global TB Vaccine Partnership would share the technical, financial and market risks in the development and marketing of new, effective and affordable TB vaccines.
- The Global Health Investment Fund finances late-stage development of products to fight PRNDs. It offers its investors a financial return, and is backed by commitments from the Gates Foundation and the Swedish International Development Co-operation Agency to offset potential losses from clinical development.
- A levy on air tickets is one of the funding sources for UNITAID, which is backed by several national governments, and hosted by the WHO. Using its innovative financing, it exerts buy-side market leverage to obtain products at affordable prices for treatment and diagnosis of HIV/AIDS, malaria and tuberculosis in low-income countries.

“A broad-based, concerted effort is needed to develop research capacity, allocate appropriate resources, and encourage stakeholders to work together

World Health Assembly resolution on TB, May 2014

The European Union's engagement in combating PRNDs

One of the leading EU actions in combating PRNDs is the EDCTP, in which 16 European countries and the European Commission partner countries from sub-Saharan Africa in the validation of new drugs and vaccines.

The EU's dedicated research programmes include support to development work on almost 150 PRND products, and calls for new vaccines under Horizon 2020, the EU's funding mechanism for research.

At successive EU-Africa summits, the EU has agreed on co-operation on health and infectious diseases, and it is co-operating with the countries of eastern Europe on diseases and health security under the Eastern Partnership. The recently signed EU-Ukraine association agreement contains binding commitments on public health and communicable diseases.

The EU is also a major donor. It hosted a kick-off meeting in May 2014 for an international immunisation pledging round for 2014-20, and doubled its own commitment.

Council conclusions in 2010 had urged better co-ordination of EU research on global health and the identification of "shared global priorities", and the Commission aims to promote coherence – within its limits – on an agreed research agenda. It co-operates with the European Investment Bank on financing research and on public procurement of vaccines in Africa.

The European Parliament urged increased commitment to tackling PRNDs over its 2009-14 term.

It called for increased support for health services in sub-Saharan Africa and increased contributions to the Global Fund, a focus on immunisation and responses to PRNDs in development co-operation, emphasis on "a comprehensive approach" towards PRNDs in Horizon 2020 and wider scope for EDCTP2, and efforts to counter HIV/AIDS among vulnerable populations in the EU and neighbouring countries.

Prognosis

Seeking strategies to reduce suffering

"It's such a mess, with companies thinking 'market' and public funders thinking 'public good'. There's no strategy for neglected diseases," says Mary Moran of Policy Cures. "Yet it shouldn't be hard, with so much money going into research funding and hundreds of products in the pipeline."

The most frequent suggestion from all sides is that greater collaboration among all parties could improve prospects. "Dramatic progress in global health and development can be made if research institutions, governments, foundations, non-governmental organisations, and private industry join together to generate new discoveries and new technologies," says the Bill and Melinda Gates Foundation.

The UK government's department for international development aims to "improve the effectiveness and efficiency of the global response through international institutions, partnerships and global civil society". The German government "seeks to promote equitable, co-operative and effective action in international forums of global health policy because strong international institutions are a prerequisite for effective and co-ordinated global

action. We can only address the issue of global health policy in close co-operation with our partners."

Hopes for global action

There have been some encouraging signs of joint action. The London Declaration on Neglected Tropical Diseases in 2012 committed the WHO, the World Bank, philanthropists, drug firms and governments to combat nine serious diseases. At the end of 2013, world leaders pledged \$12 billion over the next three years to the Global Fund to Fight AIDS, Tuberculosis and Malaria. WHO has this year backed a number of research demonstration projects to address PRNDs. The replenishment of the international immunisation programme got off to a good start in Brussels in May. The same month, the WHO and the Global Fund agreed to support countries in developing more strategic investments in the fight against HIV, tuberculosis and malaria. And there is support both within the WHO and the EU for incorporating health into new United Nations-backed development goals to be agreed for 2016.

Not so simple

But some major tensions continue to hamper the search for harmony and common strategies. Many countries and

organisations are cautious about collaboration that may lead to centralisation or bureaucratisation, and many are reluctant to abandon their own private agendas. Even the German research ministry, recently hailed by Policy Cures as “an emerging leader” in fighting PRNDs, conditions its enthusiasm for international co-operation: “It is necessary to focus, over the long run, on areas in which Germany is comparatively strong”. There is discussion of a WHO convention on global health that would bind members states to specific levels of delivery, but this is being resisted by many donor countries, partly for fear that momentum might be lost in lengthy discussion of the precise commitments, which could distract attention from substantive action.

Internal divisions also exist. In many countries, different agencies with overlapping responsibilities do not always communicate well. The EU itself is a complex amalgam. Member states have their own views, and the European Parliament approaches PRNDs through at least three different committees. There has been discussion of a European Commission communication on global health, but this is on hold until there is internal consensus that a communication would contain anything of substance. The Commission’s engagement is split across departments responsible for health, research, development and external affairs – provoking European drug firms to say at a recent meeting that EU action in global health policy is “diffuse”. “EU influence over global health requires that the EU find a new alignment of its political, institutional, economic and industrial assets and distinct institutions,” said an industry spokesperson. In the Commission, this critical view found some reflection in the private remarks of a senior official: “Our contribution is not so much in terms of money, but in getting people to talk to one another: regulators, academics, agencies within member state governments, industry – and particularly smaller firms.” Kaitlin Christenson, director of Global Health Technologies Coalition, says the EU is crucial in prompting multiple stakeholders to work together.

Questions need answers

Some key issues remain open, and will need resolution if real progress is to be made against PRNDs.

At international level, tensions are growing rather than receding over how poorer countries will be able to obtain access to the increasingly expensive medicines emerging from the pharmaceutical industry. In particular, there is strong opposition to the spreading practice of tiered pricing – in which drug firms

The Global Health Technologies Coalition brings together non-profit organisations to raise awareness of the need for technologies that save lives in the developing world.

charge different prices in different countries or regions.

The EU has yet to find ways of maximising coherence and fully exploiting its leadership potential in global health debates, and that will largely depend on smarter action by the Commission and the Parliament.

The EU and its member states also have to determine whether their financial support for fighting PRNDs is proportionate to their own wealth. As long as the difficult economic climate persists, uncertainties over funding will impair strategic planning. It remains to be seen how far austerity-hit donors are influenced by arguments that their funding of PNRDs will also bring them benefits in science, jobs, and health security.

The search for new business models will require yet more determination. Recent hopes for major multi-stakeholder collaborations around the development of new antibiotics are already receding in the face of greater complexities than had been anticipated – and the credibility of the private sector as a partner comes under renewed attack each time a new drug industry scandal emerges.

The final form of the sustainable development goals soon to be agreed at the United Nations will influence the battle against PRNDs. This will depend partly on whether health features as a goal (against competing priorities such as energy and environment), and how prominently. It also depends on how far any health reference focuses on health research as well as merely health provision.

There is a consensus that prospects for real progress are good, but this is a crucial moment, and efforts are required to maintain the fragile gains and to extend treatment and prevention. Without those efforts, the fear is that the opportunities for breakthroughs could disappear, and the achievements to date will be jeopardised.





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