



COUGH UP FOR TB!

The Funding of Research for Tuberculosis and
Other Neglected Diseases by the Swedish Government

CAMPAIGN FOR	
ACCESS	
TO	
ESSENTIAL MEDICINES	

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Report highlights

- It is estimated that one billion people suffer from neglected diseases, and that 1.7 million people die each year of tuberculosis (TB) and another million of malaria.
- The aim of this Swedish report is to study the amount of Swedish public funds that are being allocated and disbursed for research and development, both in Sweden and abroad. It includes basic research, further development and applied research, wholly or partly on diagnostics, vaccines and medicines.
- Since the pharmaceutical industry does not regard neglected diseases as an attractive market for its research activities, it is necessary to explore other avenues to stimulate research and development into these diseases.
- We still use the same sputum-based method to diagnose TB that was used in the 1880s when the TB bacillus was originally identified.
- The newest of the medicines currently used for standard treatment was introduced 50 years ago. Moreover, the treatment is lengthy and therefore often interrupted, which leads, in far too many cases, to resistant TB bacteria developing.
- The European Centre for Disease Control (ECDC), situated in Solna outside Stockholm, and the World Health Organization (WHO)'s European office have declared TB to be a 'regional emergency' and have drawn attention to the need to support eight European countries with a high incidence of the disease. Four of these countries are Sweden's neighbours (Russia and the three Baltic states).¹
- In 2007, globally only €351 million was invested in TB research, less than a quarter of the €1.45 billion needed. Of the current spending on TB, about 56% came from public sources and 44% from private ones, with the overwhelming majority of these originating in non-profit organisations such as the Bill and Melinda Gates Foundation.

Swedish research and development funding

- The scope of the original research in this report has been limited to the year 2007 and to research funded by Swedish public funds.

- When different research grants have been considered for inclusion in the study, TB, malaria or any other neglected disease has been stated in the title or has been of central importance in the abstract of the application for grants. A questionnaire concerning funding sources was sent to about 100 researchers/research groups and later to the funders to confirm that the grants were disbursed.
- According to Statistics Sweden, public sector expenditure on medical research was SEK 6.8 billion (€752.8 million) in 2007.
- The total figure for Swedish funding of neglected diseases in 2007 was SEK 89.8 million (€9.93 million).

Is Sweden doing enough?

- As an indication of whether Sweden is contributing adequately, we looked more closely at TB. To calculate Sweden's fair share, that is the amount Sweden should pay for the global TB research effort, Sweden's proportion of global gross national income (GNI) (0.83%) was correlated with the total global TB research and development need: €1.45 billion.
- This calculation puts Sweden's fair share at €6.8 million (or SEK 61.6 million).
- Sweden's actual TB research funding is €5.7 million, or 83.7% of its fair share. Sweden stands out in Europe for coming closer to its fair share than other countries. The contrast is stark in comparison with for example Germany, which funded only 22.5% of its fair share.

Conclusions

- The positive steps taken by Sweden to highlight the importance of innovative incentives for drug research and development in the area of antimicrobial resistance should be commended. The advances made in this area should also be used to explore mechanisms that can stimulate research and development for new diagnostic tests and medicines for drug-resistant TB.
- Sweden should increase its activities to explore innovative financial mechanisms and fund projects to pilot new mechanisms. One such opportunity is the prize fund that has been proposed to stimulate development of a new point-of-care TB test.

¹ Framework Action Plan to Fight Tuberculosis in the European Region, ECDC, February 2008.

Foreword

There is an urgent need for new tools to combat tuberculosis. One third of the world's population, the majority in the poorest countries, are latently infected with tubercle bacilli. As such, they run a high risk of developing tuberculosis during their lifetime, a risk which is steadily increasing due to the added factor of the global HIV/AIDS pandemic. Left untreated, tuberculosis becomes a chronic and deadly disease. The majority of the almost two million people who die each year from tuberculosis do so at the most productive stage of their life. Furthermore, the increasing incidence of drug resistance poses an extra burden on already strained health systems.

In light of this situation, the tools that are used to fight tuberculosis are appallingly inadequate. The present vaccine, BCG, which is the oldest of all vaccines still in use, has proven to be a failure in terms of preventing the spread of the disease. For those who become infected with tuberculosis, treatment depends on a combination of drugs that need to be taken over a period of at least half a year, often accompanied by severe side effects. Despite this, no new drug has been developed for almost half a century. Similarly, diagnostic tests are either inadequate, or too sophisticated and expensive to be used where they are most needed.

Although the development of a new test, vaccine or treatment, is likely to come at a huge cost, it is worth the investment. The World Bank recognised early on that the most cost effective way to combat tuberculosis would be to develop a new vaccine. Furthermore, a rapid and reliable bedside test would shorten the time taken to diagnose new cases and begin treatment which would have the added effect of reducing transmission of the disease. New drugs to treat tuberculosis could also have fewer side effects as well as shorten the time required to cure the disease, which is currently extremely long. Furthermore, the need for new drugs becomes an even more pressing issue in the face of the increasing threat of drug resistance.

This report is important in the sense that it explores the financial prerequisites for the development of these new tools, as well as the availability of funds to achieve this goal. The conclusion drawn is that the research needed to accomplish these tasks is heavily underfunded. It also shows that Sweden, although not currently bearing its 'fair share' of the contribution to such research, does indeed have the potential to take a leading role in this task.

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Stockholm, October 2009

1. Introduction

Every day, in countries where Médecins Sans Frontières (MSF) works, our staff meet people with diseases for which nurses and doctors lack simple tools for diagnosis, treatment or prevention. They may be tuberculosis (TB) in Uzbekistan, sleeping sickness in the Democratic Republic of Congo, malaria in Liberia or Chagas disease in Bolivia. Those suffering from these diseases are often the poorest people, and they often live in the poorest countries. The World Health Organization (WHO) refers to these diseases as ‘neglected diseases’.² They are neglected by all concerned: governments, international organisations, the pharmaceutical industry and the media. The voice of the sick is seldom heard; they have no one to speak on their behalf and they often suffer and die in silence. It is estimated that one billion people suffer from neglected diseases; 1.7 million people die each year of TB and another million of malaria. This human suffering also leads to even greater poverty at both the individual and national level.

Research and development in respect of these diseases has been neglected for many years. Methods and tools for diagnosis, prevention and treatment are often old-fashioned and complicated, sometimes ineffective and even dangerous. The people who have the greatest need of simple diagnostic tests, simplified and less dangerous forms of treatment and prevention are too poor to pay the development costs.

Even though TB and malaria also affect us in the rich part of the world, they are not given priority when different research projects are considered. When basic research is undertaken with public and private support at universities and research institutes, there is no effective international system to transform research findings into applied research and development. The pharmaceutical industry has little financial incentive to invest in these diseases.

This is why few new medicines or vaccines appear and why the ones that are in the pipeline can take between five and 20 years to become available – if they become available at all for poor people in poor countries. In this respect the international community and pharmaceutical industry have clearly failed.

This is of course nothing new. Many have drawn attention to this failing, including MSF through its campaign Access to Essential Medicines.³ A couple of years ago, a commission appointed by WHO that included representatives of governments and the pharmaceutical industry called attention to the need for fundamental changes.⁴ Since then, government working groups have tried to reach agreement on what is needed to stimulate research and development into diseases that primarily affect poor people in countries with few resources.⁵ In 2008, the WHO general assembly adopted a Global Strategy and Plan of Action⁶ that seeks to secure an enhanced and sustainable basis for needs-driven, essential health research and development relevant to diseases that disproportionately affect developing countries. Sweden, as one of the countries that have committed to support the plan, has an important role to play in its implementation and also in stimulating innovative incentives for research and development funding.

Greater public engagement is necessary, but how much money is needed and how should the costs be shared? The first study by MSF on the financing of research was made in Germany in 2008.⁷ It was followed in the same year by a similar study concerning the European Commission’s (EC) support.⁸ Both these studies showed a considerable degree of underfunding compared to the needs calculated by WHO’s Stop TB Partnership⁹ and the Treatment Action Group (TAG),¹⁰ and later reflected in the G-FINDER¹¹ from the George Institute for Public Health.

2 WHO has classified the following as ‘neglected tropical diseases’: Buruli ulcer, Chagas disease, dengue fever, dracunculiasis (Guinea worm), fascioliasis (liver fluke), human African trypanosomiasis (sleeping sickness), leishmaniasis (kala azar), leprosy, filarasis (elephantiasis), onchocerciasis (river blindness), schistosomiasis (bilharzia), some worm diseases (hookworm, strongyloides), trachoma, yaws. The EU designates TB and malaria as ‘poverty-related diseases’ and dengue as a ‘re-emerging’ disease. MSF classifies them all as ‘neglected diseases’. Some suggest that pneumonia should also be included.

3 See MSF’s website: www.msf.org and www.msfaccess.org

4 Public Health Innovation and Intellectual Property Rights, Report of the Commission on Property Rights, Innovation and Public Health WHO, 2006 www.who.int/intellectualproperty/documents/thereport/

5 See WHO Intergovernmental Working Group on Public Health, Innovation and Intellectual Property www.who.int/phi/en.

6 WHA 61.21 A Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property, 24 May 2008 www.who.int/gb/e_waha61.html.

7 Cough up for TB! The Underfunding of Research for Tuberculosis and Other Neglected Diseases by Germany, MSF, April 2008.

8 Cough up for TB! The Underfunding of Research for Tuberculosis and Other Neglected Diseases by the European Commission, MSF, November 2008.

9 www.stoptb.org/globalplan.

10 TAG: A Critical Analysis of Funding Trends 2005–2006, www.treatmentactiongroup.org, updated July 2008.

11 G-FINDER: Global Funding of Innovation for Neglected Diseases, www.thegeorgeinstitute.org/research/health-policy/current-projects/g-find-global-funding-of-innovation-for-neglected-diseases.cfm.

The aim of this Swedish report is to study the amount of Swedish public funds being allocated and disbursed for research and development, both in Sweden and abroad, for neglected diseases, focusing on TB. It includes basic research, further development and applied research, wholly or partly on diagnostics, vaccines and medicines. The study also covers support disbursed by Sweden in the form of multinational or bilateral grants to international organisations and different initiatives that undertake research and development in this field.

We also wish to illustrate how Sweden has acted internationally in these and related matters and the extent to which Sweden lives up to the declarations and commitments it has made. Moreover, the report can be regarded as a point of departure for how future funding corresponds to the objectives stated in the government's research bill of 2008¹² and in its underlying documentation (see box to the right).

Swedish policy commitments to the struggle against infectious diseases

In the *Policy for Global Development*, Sweden's strategy for international development cooperation, six global challenges are identified to which Sweden can contribute. One is infectious diseases, and here mention is made of greater access to medicines, actions that promote health and prevent disease, early-warning systems, and rapid measures to check the spread of diseases.

A study published in 2005, *A Proposed Strategic Action Plan for Swedish Contributions to the Global Struggle Against Infectious Diseases*,¹³ recommends a focus on university and small enterprise-based research and development through generous funding mechanisms channelled via the Swedish International Development Cooperation Agency (Sida) and Sida's department for Research Cooperation (SAREC). It also recommends that all contributions should involve the active participation of developing countries. The Global Fund to Fight AIDS, TB and Malaria (GFATM), Global Alliance for Vaccines and Immunisation (GAVI), European Malaria Vaccine Initiative (EMVI), European and Developing Countries Clinical Trials Partnership (EDCTP) and the Swedish Research Council are identified in particular as cooperating partners.

An interim report by Professor Olle Stendahl for the government bill on research entitled *World Class! Action Plan for Clinical Research*¹⁴ looks for a long-term strategic approach to identifying the most important health problems and prioritising research resources. The report underlines the need for stronger clinical research, special research programmes and international networks, for example in HIV/AIDS, TB and malaria.

According to the government's *research bill*, Swedish research is particularly strong in respect of infections such as HIV/AIDS, bacterial gastro-intestinal and urinary-tract infections, TB and malaria. The bill also states that "in general it is important that government-funded research also takes into consideration research into diseases that have less commercial patentability, for example development of new antibiotics and vaccines and other medicines that are used against infectious and other diseases that particularly affect poor countries."¹⁵

12 Government research bill Prop. 2008/09:50 'A boost for research and innovation', www.regeringen.se.

13 Swedish Government Official Reports (SOU) 2005:107, author Bjarne Bjorvatn, funded by the Swedish government.

14 Swedish Government Official Reports (SOU) 2008:7, author Olle Stendahl, funded by the Swedish government.

15 Government research bill Prop. 2008/09:50 'A boost for research and innovation' page 75-76.

2. The underfunding of research and development

Although it has been estimated that TB, malaria and other neglected diseases account for 12% of the total disease burden in the world, only 21 (1.3%) of the 1,556 new chemical entities that were developed in the 30 years between 1975 and 2004 were intended for these diseases.¹⁶ There is basically one reason for this: people suffering from these diseases are poor and cannot afford to pay for expensive products. They thus constitute an unprofitable market, so the pharmaceutical industry has focused on other diseases and illnesses in which, through patent protection, they can recover the investments they have made and generate a profit.

The Commission on Intellectual Property, Innovation and Health, appointed by WHO, stated that “for diseases affecting millions of poor people in developing countries, patents are not a relevant factor or effective in stimulating research and development.”¹⁷ The pharmaceutical industry itself admits that, ‘as these diseases affect the poorest of the developing world, the opportunities for revenue [...] do not exist or are associated with a greater level of risk, which discourages investment.’¹⁸

Since the pharmaceutical industry does not regard this as an attractive market for its research activities, other methods are necessary to stimulate research and development into these diseases. As early as the mid-1970s, WHO’s Tropical Disease Research and Training (TDR) programme was established. In Europe, the European Commission has included research into neglected diseases in its Seventh Framework Programme (FP7). A number of international product development partnerships, frequently organised as public private partnerships, have been created, for example the Global TB Alliance, New Medicines for TB (NM4TB), Aeras Global TB Vaccine Foundation, Medicines for Malaria Venture (MMV), Foundation for Innovative New Diagnostics (FIND), and Drugs for Neglected Diseases Initiative (DNDi). Further important interventions are the Multilateral Initiative on Malaria Research (MIM), the European Malaria Vaccine Initiative (EMVI) and the TB Vaccine Initiative (TBVI). (See box on Product Development Partnerships on page 9)

When conducting research into neglected diseases it is crucial to separate the costs of research and development from the final price of the product, otherwise the use of the product for poorer people and countries will remain limited, since they cannot afford high prices. Product development partnerships respond to some neglected areas of medical research, but not enough of them, and they do not have stable, predictable funding. Alternative funding mechanisms are necessary. If these product development partnerships make sure that their products are either patent-free or are licensed in a way that makes generic production at least in the poorer countries possible, they can achieve the important goal of making costs for research and development independent from the price of the products.

However, to optimise further research, it is necessary to combine so-called ‘push’ and ‘pull’ mechanisms of research funding. ‘Push’ mechanisms are those such as typical government grants that provide funding up-front for research, and cover its costs irrespective of the outcome. ‘Pull’ mechanisms on the other hand, such as prizes or patents, give a financial incentive that rewards success in research, independent of its costs.

Product development partnerships can only address the ‘push’ mechanism part of research and development funding. To ensure there is also ‘pull’ factor, another method is necessary. One potential solution, suggested by MSF and others, is the concept of providing financial reward through a prize rather than through high prices based on market monopoly. The innovator then has to provide guarantees that the product will be of sufficient quantity and quality and priced at long-term affordable rates in developing countries.

¹⁶ Chirac P, Torrelee E, ‘Global Framework on Essential Health Research and Development’. The Lancet, 2006: 367, 1560–61.

¹⁷ Public Health Innovation and Intellectual Property Rights, Report of the Commission on Property Rights, Innovation and Public Health, www.who.int/intellectualproperty/documents/thereport/enPublicHealthReport.pdf, WHO, 2006, p 22

¹⁸ International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) Feasibility study for a fund for research and development for neglected diseases.

2.1 The diseases

In recent years, increased attention and funding of programmes to prevent and treat neglected diseases has had an impact. We have recently seen the emergence of an effective combination treatment for malaria, improved prevention of infection during pregnancy, simpler methods for diagnosis, and an increase in the use of long-duration impregnated bed nets. A scaling up of treatment has been possible because of increased resources provided for example by the Global Fund to Fight AIDS, Tuberculosis and Malaria. This is naturally good news, but all new medicines are based on a single active substance. There is no fallback medicine to resort to if the malaria parasite develops resistance, which has happened in the past. And although progress has been made in research into vaccines, it will be a long time before a vaccine against malaria becomes available.

The same sputum-based method is used in the diagnosis of TB as was used in the 1880s when the TB bacilli were originally identified. This makes it hard to diagnose the disease in children, who have difficulty providing sputum specimens; and in people infected with HIV, who have few bacteria in their sputum. TB is by far the most common cause of death for people living with HIV/AIDS.

The vaccine used today will soon be 90 years old, and its effectiveness in protecting adults is low. Of the medicines currently used for standard treatment, the most recent was introduced 50 years ago. Moreover, the treatment is lengthy and therefore often interrupted, which leads in far too many cases to resistant TB bacteria developing. Infections with resistant strains require treatment for up to two years using expensive medicines, many of which have side-effects. The transmission of extensively resistant strains of TB particularly affects HIV-positive patients co-infected with TB, and in such cases almost always leads to death.

For many of the other neglected diseases, the situation is even more depressing. Most of them can be prevented (most of the worm diseases), or treated if they are detected in time (onchocerciasis – river blindness – for example), and some (such as Guinea worm) can be eradicated. On the other hand, the treatment of human African trypanosomiasis (sleeping sickness) and leishmaniasis is complicated and has a number of side-effects, and for chronic Chagas disease and Buruli ulcer there is no remedial treatment at all. In general, diagnostic methods are not adapted to the conditions where the diseases are common, so the diagnosis is made at a late stage or not at all, vaccines are not available for any of the neglected diseases, and the effect of other preventive measures is limited by widespread poverty.

TB in Sweden

In the 1800s the disease was the most common single cause of death in Sweden, and was particularly widespread in the Lake Mälaren region. After reaching a peak in 1875, rates of death from the disease decreased in southern Sweden but, at the beginning of the 1900s, three-quarters of the population were still infected. King Oscar II's jubilee fund, established in 1897 when the King had ruled for 25 years, was used to combat TB through the establishment of sanatoria, often located by the sea or in pine forests. It was then the only form of treatment available.

The Swedish National Anti-TB Association was established in 1904 and small artificial flowers – so-called May flowers – were sold from 1907 onwards to raise funds to combat the disease. Preventive BCG vaccinations were introduced in 1927; pasteurisation of milk in 1939; and early diagnosis with the aid of X-ray examinations took place in TB clinics or on busses between 1946 and 1970. The first curative treatment came in 1942–43, after the discovery of streptomycin and para-amino salicylic acid, the latter by a Danish-born Swede, Jørgen Lehman. Universal BCG vaccinations came to an end in 1975 since the number of cases had decreased considerably. However, since then TB has returned, particularly through the increase in immigration to Sweden, and today 550 cases per year are discovered. Of these, every eighth case shows resistance to one or more medicines. During recent years, outbreaks at day nurseries for children have resulted in considerable attention from the media.

TB in the world

WHO estimates that every year, nine million people develop active TB and that 1.7 million die from the disease. We once considered this disease as belonging to the past, but it has become a major threat especially in countries with high prevalence of HIV/AIDS and countries with a history of inadequate treatment and prevention, such as the Baltic or the central Asian states. In addition, there has been an increase in TB bacteria that are resistant to several of the commonly used medicines.

The most important tool we have for detecting TB is microscopy of sputum specimens, which is basically the same method as that used by Robert Koch when he discovered the bacterium almost 130 years ago. In practice, roughly half of all cases are missed; even more where children or people co-infected with HIV are concerned. In the rich part of the world, microscopy is combined with culturing the TB bacilli, but this method is rarely used in poor countries. The BCG vaccine, developed by the Pasteur Institute around 1920, protects only small children and thus has no epidemiological effect since small children rarely pass on the disease.

TB has been treatable with medicines since the mid-1900s. The treatment requires adherence to a strict medical regime for at least six months to ensure complete healing and to avoid the development of resistance. In cases of relapse, treatment often has to include injections of medicines which carry the risk of affecting kidneys and auditory organs. If there is resistance to several medicines, it is necessary to continue treatment for 18 to 24 months with a combination

of medicines, many of which have a large number of severe side-effects, and the patient must be isolated to avoid spreading the disease further. In addition, during recent years extensively resistant strains have been identified. In such cases even treatment with a multitude of medicines has hardly any effect, so the mortality rate is high.

Protracted neglect of research and development into TB has left us in the precarious situation we are in today: the disease is a threat to public health not just in the world's poor countries but also in Sweden.

The European Centre for Disease Control (ECDC), situated in Solna outside Stockholm, and WHO's European office have declared TB to be a 'regional emergency' and have drawn attention to the need to support eight European countries with a high incidence of the disease. Four of these countries are Sweden's neighbours: Russia and the three Baltic states.¹⁹

WHO's European Ministerial Forum has declared that research into TB must be given priority by public national institutions.²⁰ At the 62nd World Health Assembly, WHO adopted a resolution on the prevention and control of multi-drug-resistant TB and extensively-drug-resistant TB. This also includes prioritising research for new TB diagnostics, medicines and vaccines through support for extra financing.²¹

Funding for improved and simplified diagnostics (point-of-care tests) is an even more neglected area where there is urgent need for innovation.

19 Framework Action Plan to Fight Tuberculosis in the European Region, ECDC, February 2008.

20 WHO European Ministerial Forum 'All Against Tuberculosis', Berlin Declaration on Tuberculosis, www.euro.who.int/Document/E91369.pdf, Berlin 2007.

21 apps.who.int/gb/ebwha/pdf_files/A62/A62_R15-en.pdf.

2.2 International funding

For many years it has been clear that research into neglected diseases has been grossly underfunded. In recent years several studies have been published that show just how wide a gap there is between what is needed and what is invested.

Tuberculosis (TB) is the neglected disease for which the situation is best documented. The New York-based Treatment Action Group (TAG) has published a series of studies analysing the global spending and need for TB research and development. The results are striking: in 2007, only €351 million (US \$483 million) were invested, less than a quarter of the actual need of €1.45 billion (US \$2 billion), as defined by TAG. Of the current spending in TB, about 56% comes from public sources and 44% from private ones, with the overwhelming majority of these originating in non-profit organisations such as the Bill and Melinda Gates Foundation.

Regarding funding on an international level, a recently published study called G-FINDER (Global Funding of Innovation for Neglected Diseases) from the George Institute for International Health, funded by the Bill and Melinda Gates Foundation, examined contributions for research into HIV/AIDS and the neglected diseases made by 134 funders in 43 countries in 2007.²² These contributions amounted to €1.8 billion (US \$2.5 billion). Approximately half of that amount was provided for research into HIV/AIDS while for malaria the amount concerned was €342 million (US \$470 million). For TB, the study paints an even darker picture than TAG, showing that only €298 million (US \$410 million) was invested. Most of the research into all the diseases referred to the development of medicines and vaccines: very few resources were allocated to research into diagnostics. According to this study the overall contribution of the pharmaceutical industry, at 9%, was also low.

Product development partnerships, non-profit organisations, make a significant contribution to research and development into neglected diseases. For example, the Drugs for Neglected Diseases Initiative (DNDi), which was established in 2003, launched two patent-free artemisinin combinations for the treatment of malaria in 2007 and 2008, and is working hard on medicines for leishmaniasis, sleeping sickness and Chagas

disease. The EC contribution to DNDi amounted to € 1.7 million (3% of DNDi's budget), however two other product development partnerships focusing specifically on TB: Global Alliance for TB Drug Development, and Aeras Global TB Vaccine Foundation, have received no contributions at all. By contrast, individual countries such as the Netherlands, Great Britain and Ireland are important financiers of partnerships that focus on TB and malaria (Medicines for Malaria Venture and Malaria Vaccine Initiative).

Product Development Partnerships (PDP)

Product development partnerships are seldom involved in conducting research themselves. More often their role is to channel public and private funds into projects, coordinating and integrating the work of industrial, academic and public sector partners, and managing the research portfolios for neglected diseases. Members of these partnerships can be public research facilities, pharmaceutical companies and NGOs.

Among the product development partnerships relevant to the diseases covered in this report are: the *Global Alliance for TB Drug Development* which researches new medicines for the treatment of TB, particularly those that could be used alongside treatment for HIV infection, and those which shorten therapy. *The Foundation for Innovative New Diagnostics (FIND)* which researches diagnostics for TB, malaria and sleeping sickness, and *Aeras Global TB Vaccine Foundation* which focuses on developing new TB vaccines. *The Medicines for Malaria Venture (MMV)* was founded to develop new effective medicines for malaria, and *Drugs for Neglected Diseases Initiative (DNDi)* was initiated by MSF and focuses on malaria and kinetoplastid diseases like the sleeping sickness.

3. Methodology

The scope of the original research in this report has been limited to the year 2007 and to research funded by Swedish public funds. Funding provided through, for example, private Swedish foundations, other countries, international institutions or foundations, such as the Bill and Melinda Gates Foundation, have been excluded. Information on government grants for research and development has been extracted from Statistics Sweden's²³ report and from information provided by each government agency, institution or organisation. Besides this, information has been collected from research workers/research groups themselves and we believe that this method has enabled us to come as close to the truth as possible. Project grants covering several years have been distributed evenly over the years in question (when no other specific information has been given).

Since most of the government resources allocated in Sweden are provided in the form of direct, non-earmarked funds (and only a small proportion as specific project funds), it is difficult to estimate the proportion of this funding that is used for different purposes. This report covers only specific project and not framework funding. Thus, salaries and overhead costs that are part of direct allocations to universities have not been included.

When different research grants have been considered for inclusion in the study, TB, malaria or any other neglected disease have been stated in the title or have been of central importance in the abstract of the application for grants. To gather further information, a questionnaire concerning funding sources was sent to about 100 researchers/research groups to confirm that the grants were disbursed. We also presented the figures to the funders for comments and corrections. Naturally, we cannot be completely certain that we have covered all government-funded Swedish research activities relating to neglected diseases, but any overlooked projects would probably be both financially and operationally limited. Amounts have been converted into SEK (Swedish krona) and Euros using a constant rate for reasons of consistency.²⁴

We have not attached any judgement about the quality of the research, but have merely studied the funding and assumed that assessments of quality have been made by each financing body. Nor have we been able to pinpoint how or when the results of the research can be applied in poor countries.

In addition to this, we have studied Swedish policy documents and reports on research and development in respect of neglected diseases. References to these are made in the report. Moreover, certain documentation has been included that describes and explains Swedish positions on international cooperation.

Finally we have analysed the extent to which Sweden meets its share of the estimated research and development funding needed to cover diagnostics, vaccines and medicines relating to TB.

²³ Statistics Sweden (Statistiska Centralbyrån, SCB) is a government administrative agency tasked to supply official statistics on Sweden for decision making, debate and research www.scb.se

²⁴ Exchange rates for US\$, Euros and Swedish krona have been calculated based on the rate of January 1, 2007.

4. Swedish public funders of research

In 2007 the Swedish Parliament, Riksdagen, allocated SEK 24.7 billion (€2.73 billion) to research and development across all sectors. This amounts to some 0.8% of gross national income or 25% of the total Swedish research and development funds (both private and public). Government funds are first allocated to different departments and thereafter directed to 14 universities and 25 university colleges, to research councils, and to government agencies responsible for sector research. In addition to this, there are a number of public and private research foundations. Only a small amount is allocated to research institutes, which sets Sweden apart by comparison with other countries.

According to Statistics Sweden, public sector expenditure on medical research amounted to approximately 30% of the total public sector research and development funds. This corresponded to SEK 6.8 billion (€752.8 million) in 2007. Approximately 97% of the research funded in this manner is undertaken in the public sector.

We calculate that SEK 89.8 million (€9.93 million) of Swedish public funds were used to finance research and development both in Sweden and abroad during 2007. This represents approximately 0.4% of total public research and development funding. Sida provides the largest contribution of SEK 63.3 million (€7 million), followed by the Swedish Research Council and the Foundation for Strategic Research.

4.1 Ministry of Education and Research

4.1.1 Universities and university colleges

Direct allocations, 'faculty allocations', are related to the volume of education at basic and advanced level, and are estimated to cover 46% of the costs for research and development at universities and university colleges. These allocations, which pay mainly for basic research, have hitherto been distributed by the universities on the basis of their own priorities and without competition or independent assessments of quality. This has strengthened 'free research' but, according to the government research bill of 2008, has also led to shortfalls in the quality and relevance of the research undertaken and to a situation in which the usefulness aspect has not been sufficiently taken into consideration.

The figures regarding how much of the faculty allocations have been used for research and development related to TB, malaria and other neglected diseases have not been possible to obtain and could thus only be estimated based on the total funding from other sources, an information that however was not part of this study.²⁵

4.1.2 Research councils

The Swedish Research Council is the second-largest governmental funder of basic research at universities and university colleges in Sweden. The Council's goal is that Sweden should be a leading research nation, and support is provided to promote the highest levels of quality, development and renewal. In 2007, SEK 2.53 billion (€281 million) was disbursed for funding research, SEK 658 million (€72.85 million) of which was allocated to the field of medicine. Grants related to TB amounted to SEK 6.8 million (€0.76 million), to malaria SEK 2.7 million (€0.3 million), and to other neglected diseases SEK 0.3 million (€0.03 million).

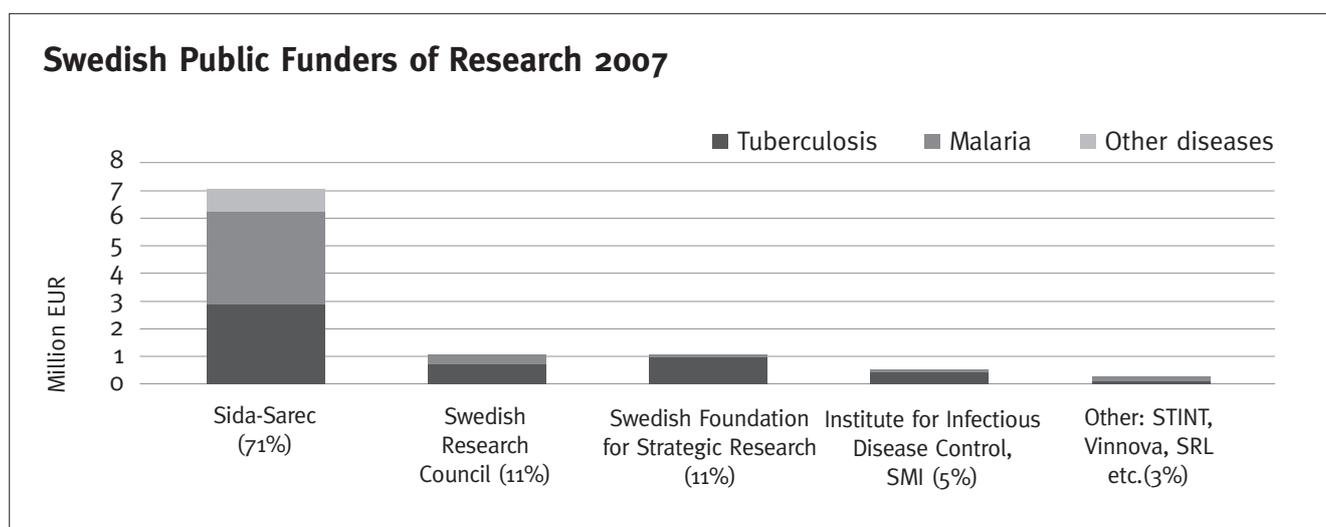
4.1.3 Public foundations

The Swedish Foundation for Strategic Research is an independent public foundation that provides time-limited support for research programmes that can help solve urgent global problems by developing strong research environments of the highest international class.²⁶ It supports, among other things, so-called strategic research centres, which are defined as scientifically focused and geographically co-located research environments designed to bridge the gap between basic and applied research. Support is given as five- to six-year grants of SEK 7–10 million (approximately €0.77–1.1 million) per year. The total amount disbursed in 2007 was SEK 595 million (€65.87 million). Two of eight strategic centres, which focus on life sciences, are engaged to a varying extent in research on neglected diseases. Funding is not earmarked but, according to the recipients, out of the allocated funds approximately SEK 8.7 million (€0.96 million) were used for research primarily into TB and SEK 1 million (€0.11 million) into malaria.

The Swedish Foundation for International Cooperation in Research and Higher Education (STINT) aims to internationalise Swedish higher research in all scientific fields, above all through research exchanges. In 2007, some SEK 40 million (€4.43 million) was disbursed, of which SEK 0.2 million (€0.03 million) went into malaria research.

²⁵ Where possible, figures have been included when they have clearly been accounted for, for example from the Swedish Institute for Disease Control and in grants from the Swedish Research Council, referring to costs of specific research positions

²⁶ The foundation was established in 1994 to support scientific, technological and medical research with the aim of strengthening Sweden's future competitiveness. The funds are based on the returns from the founding capital of SEK 6 billion (app. €664 million) from the former wage-earner funds.



4.2. Ministry for Foreign Affairs

4.2.1 European Union

To fairly represent Sweden's overall contribution to research and development for neglected diseases, it is important to consider contributions made to the EU Commission. The support provided through the European Union for research purposes is financed by the membership fees. The seventh framework programme (FP7) covers the period 2007–2013 with a budget of €50.5 billion over seven years.²⁷ The Swedish Government Agency for Innovation Systems (VINNOVA) is the national contact point for FP7.

According to FP7, medical research in the EU aims to: improve the health of European citizens; boost competitiveness and promote innovation in both the public and private sectors; strengthen the capacity of enterprises active in the health sector, above all within biomedical research, via small and medium-size enterprises; treat new epidemic diseases and develop research capacity in developing countries. More specifically one aim is stated to be translational, research into infectious diseases that transforms research results for the benefit of people's health (HIV/AIDS, TB, malaria, SARS, avian influenza).

Sweden also contributed to EDCTP (European and Developing Countries Clinical Trials Partnership) through the EU membership fee. These contributions, being indirect funding, are not included in the calculations of this report but are covered in the previous MSF study on funding by the European Commission.²⁸ According to that study, €18.7 million was disbursed by

the EC to research on TB, and €17.1 million to malaria in 2007. Since Sweden's percentage contribution to the EU is 2.68%, this would imply Swedish shares of €0.50 million and €0.46 respectively to these two diseases. According to the same study, no resources were allocated to other neglected diseases.

Sweden also made a direct contribution to EDCTP in 2007 of €2.71 million, out of which €2.68 million were unrestricted but €1.11 million were actually directed at a TB project, €0.99 million at different HIV/AIDS projects, and €0.59 million was core funding. Targeted contributions amounted to €18,000 in cash and €8,000 in kind (mainly costs related to meetings).

4.2.2 Swedish International Development Cooperation Agency – Sida

Research support via Sida is intended to help strengthen the research capacity of developing countries; support research relevant for poverty reduction, equitable and sustainable global development; and help strengthen research in Sweden related to development issues. This is to be done through greater cooperation with, and greater engagement in, multilateral organisations including the EU, at which non-earmarked contributions are recommended.

This support, which amounted to SEK 978 million (€108 million) in 2007, is disbursed to some 30 international organisations and just over 30 regional networks and cooperation groups. Sida's department for research cooperation is known as *SAREC* (which after a reorganisation at Sida is now called the Secretariat for Research Cooperation, FORSKSEK). The grants for research into

²⁷ Disbursements from the EU to research in Sweden amounted in 2008 to SEK 1.5 billion (€166 million), of which 54% was allocated to universities and university colleges. This amounted to 4.1% of the total contracted funds and 10% more than the Swedish EU fee for research.

²⁸ Cough up for TB! The Underfunding of Research for Tuberculosis and Other Neglected Diseases by the European Commission, MSF, November 2008

TB amounted to SEK 26.3 million (€2.91 million), and into malaria SEK 29.6 million (€3.27 million) in 2007. A total of SEK 7.5 million (€0.83 million) was allocated for the most neglected diseases, of which SEK 5.7 million (€0.63 million) were allocated to the tropical diseases research and training programme.

Swedish Research Links, a programme that is administered by the Swedish Research Council, promotes cooperation between Swedish researchers and researchers in Asia, the Middle East and southern Africa. SRL's total budget is approximately SEK 35 million (app. €3.87 million). In 2007, researchers working with malaria received support amounting to SEK 0.2 million (€0.02 million) and those working with TB received SEK 0.4 million (€0.04 million).

Via Sida, the *East Europe Committee of the Swedish Health Care Community* financed research cooperation into TB in Belarus with SEK 0.2 million (€0.02 million).

4.3 Ministry of Health and Social Affairs

4.3.1 Swedish Institute for Infectious Disease Control (SMI)

SMI is a national expert agency for monitoring the epidemiological situation and promoting protection against infectious diseases in humans. It is also a reference laboratory for TB and monitors the spread of resistant TB, particularly from Eastern Europe. In this respect, SMI has close links to universities, above all Karolinska Institute and, via Sida, has programmes of cooperation with several countries in Africa concerned with TB.

The total costs of research and development in 2007 were SEK 161 million (€17.82 million), and from the governmental frame contribution SEK 4.2 million (€0.47 million) was used for TB and SEK 0.56 million (€0.06 million) for malaria.

4.4 Swedish Ministry of Enterprise, Energy and Communications

VINNOVA (the Swedish Governmental Agency for Innovation Systems) is a state authority with a particular responsibility for innovations linked to research and development. Its tasks are to fund needs-driven and innovative research for competitive products, services or processes and to strengthen networks. During 2007, VINNOVA supported malaria research and development with SEK 0.9 million (€0.1 million).

4.5 County councils and municipalities

County councils and municipalities finance research in health care to a substantial extent by being responsible for staff and premises. They are partly compensated for their costs by central government, with the aid of an agreement on medical training and research (ALF). It is not possible to obtain exact figures on how much of this is used for different diseases, which is why this financial support is not included in this report.

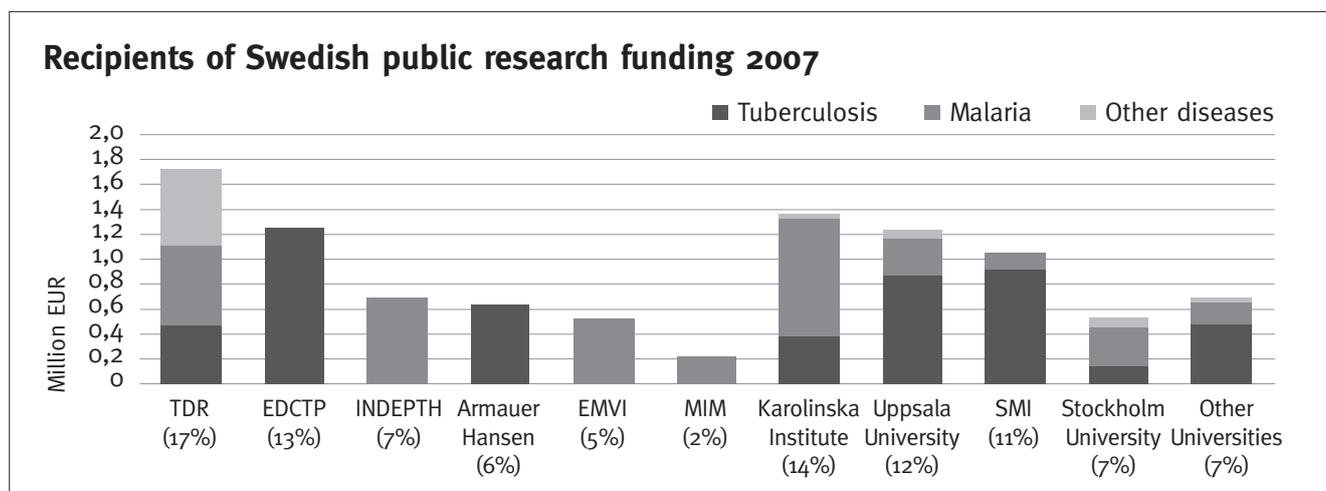
4.6 Summary and financing per disease

We calculate that SEK 44.1 million (€4.88 million) of Swedish public funds were used to finance individual researchers and research groups in Sweden and abroad for neglected diseases in 2007: SEK 25.5 million (€2.83 million) for TB, SEK 16.5 million (€1.83 million) for malaria and SEK 2.1 million (€0.23 million) for all the other diseases together. These figures do not include costs for salaries and university, university college, institution or county council facilities.

Added to this is direct international institutional funding, estimated at SEK 45.7 million (€5.05 million): SEK 21.4 million (€2.37 million) for TB, SEK 18.5 million (€2.05 million) for malaria and SEK 5.7 million (€0.63 million) for the other neglected diseases.

The total figure for Swedish funding of research and development of neglected diseases in 2007, beyond the basic financing by government and counties, was thus SEK 89.8 million (€9.93 million). Out of this, SEK 47 million (€5.19 million) was allocated for TB, SEK 35.1 million (€3.88 million) for malaria and SEK 7.7 million (€0.86 million) for the other neglected diseases grouped together.

5. Recipients of research grants



5.1 Universities and university colleges in Sweden

Much of the basic research into TB and other neglected diseases is undertaken at the six faculties of medicine, especially in the departments of cell and molecular biology, microbiology, immunology, biochemistry and biophysics. Applied research is mainly undertaken at the department or units of medicine and infectious diseases, clinical pharmacology and public health sciences.

However, it is difficult to estimate the amount of salaries and overhead costs allocated specifically to these diseases since the causing micro-organisms often function as interesting models in basic research programmes. Findings can later be important for new or improved diagnostic tools, prophylaxis and treatment, or for further development in other fields. Similarly, it has been difficult to obtain information on allocations to projects that are applied for in competition within the faculty or institution.

Extensive research into TB is being undertaken at the *Karolinska Institutet* (in cooperation with research groups at SMI and Stockholm University) on immune response to mycobacterial infection and structure-based design of antimycobacterial drugs. One of the strategic research centres, Centre for Infectious Medicine, is located at the department of medicine and is working on immune protection and better diagnostic and treatment tools. Public grants for TB amounted to SEK 3.5 million (€0.38 million) in 2007.

Three research groups are working on malaria, one (also in cooperation with Stockholm University) mainly on pathogenic mechanisms, specific treatment to avoid severe malaria and vaccine development. Another group focuses on applied research into methods for prevention and treatment in situations where resources are limited. Both these groups and especially a third one at public health sciences have collaborated extensively with African scientists. Public financial support for malaria amounted to SEK 8.6 million (€0.95 million) in 2007.

Basic research into malaria and to a lesser extent into TB and leishmaniasis is undertaken at the Wennergren Institute, *Stockholm University*, in the department for immunology and in close cooperation with Karolinska Institute and SMI. TB research in biochemistry is also undertaken at the Arrhenius laboratory. In 2007, public funding for TB amounted to SEK 1.4 million (€0.15 million) and for malaria to SEK 2.7 million (€0.20 million).

One of the strategic research centres, RAPID (Rational Approaches to Pathogen Inhibitor Discovery) at *Uppsala University*, pursues extensive research into the pharmaceutical design of antimycobacterial drugs based on structural biology and medical and theoretical chemistry. Research on antimalarial drugs is undertaken in Africa in cooperation with Karolinska Institute and local institutions. Funding for TB reached SEK 8 million (€0.88 million) and for malaria SEK 2.5 million (€0.28 million) in 2007.

Research in *Lund University and Malmö* is undertaken on cellular response to *M. Tuberculosis* and treatment intervention with a funding grant of SEK 1.1 million (€0.12 million). In malaria, the focus is on development of new antimalaria agents and funding amounts to SEK 1.1 million (€0.13 million).

At *Linköping University*, the major interest is in host defence against *M. Tuberculosis* infection. Research was financed with public funding of SEK 2 million (€0.22 million) in 2007.

Minor research in TB and malaria is undertaken at *other universities and university colleges* with public grants amounting in 2007 to SEK 4.4 million (€0.48 million) and SEK 1.6 million (€0.18 million) respectively as well as a small amount of SEK 0.3 million (€0.03 million) for other neglected diseases.

5.1.1 Education and other activities

The Centre for Global Health Research at Umeå University, which was established in cooperation with Karolinska Institute, has been allocated SEK 5.5 million (€0.61 million) each year by the Swedish Council for Working

Life and Social Research for research into diseases that affect poor countries. In addition, a research school with this focus has received support of SEK 2.3 million (€0.24 million) each year from the Swedish Research Council. Research at Umeå University will focus in particular on multi-disciplinary aspects of non-infectious diseases and, at Karolinska Institute, on infectious diseases – in particular HIV/AIDS, TB and malaria – their epidemiology, pathogenesis and effects on public health.

A Centre for Global Health has similarly recently been established at Gothenburg University with some 20 research groups. Its main aim is to produce mucosal vaccines. However, the centre was started after 2007 and has not therefore been included in this report.

5.2 Swedish Institute for Infectious Disease Control (SMI)

Close cooperation has been established with the Karolinska Institute in respect of research into both TB and malaria (see above). The research group is in the forefront of developing new and simplified tools for diagnosis of TB and antimicrobial resistance. In addition, extensive research is being undertaken on monitoring systems for resistant TB. From the institute's research budget, SEK 4.2 million (€0.47 million) was allocated to research on TB and SEK 0.6 million (€0.06 million) to research on malaria (not included in figures below). External public funding for TB amounted to SEK 4.2 million (€0.46 million) and for malaria to SEK 0.6 million (€0.06 million).

5.3 EU organisations

In 2007, Sweden contributed to the *European and Developing Countries Clinical Trials Partnership (EDCTP)*, partly via the EU (membership fee), and partly directly with a new contribution of €1.8 million (of a total of €21.4 million). With this contribution, Sweden was the third-largest new donor after the UK and Netherlands. The aim of the partnership is to develop new or improved diagnostics, medicines, microbicides and vaccines against HIV/AIDS, TB and malaria with a focus on phase II and III studies in cooperation with researchers in Europe and countries in sub-Saharan Africa.

In 2007 the total Swedish contribution was €2.70 million, nearly all of which was unrestricted. However, €1.11 million was allocated to research into vaccines against TB in Uganda where Karolinska Institute and Sida, under a co-funding arrangement, contributed a further €0.10 million in kind. Moreover Karolinska Institute contributed, via co-funding in kind, with €0.09 to EDCTP-supported research into pharmaceutical interactions between TB and HIV drugs in Uganda. These figures are included in the calculations in contrast to similar costs in universities, which were not traceable.

Sweden supports the development of vaccines against malaria through the *European Malaria Vaccine Initiative (EMVI)*, in cooperation with the African Malaria Vaccine Testing Network. In 2007 the contribution amounted to €0.53 million. This made Sweden, together with the Danish International Development Agency, the third-largest donor after the Directorate-General of Development Cooperation Netherlands and Ireland.

Contributions are made indirectly through the EU to the *Innovative Medicines Initiative (IMI)*, an EU-initiated public private partnership between the EU Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA). The EU contribution amounts to €1 billion. However, the amount that can actually be spent on the diseases dealt with in this report is unclear.

5.4 Other international organisations

Sida channels its support to research and development into tropical and other infectious diseases mostly through the *TDR programme of UNICEF/UNDP/World Bank/WHO (Special Programme for Research and Training in Tropical Diseases)*. In 2007, this support amounted to \$3.34 million (€2.53 million) of a total budget of \$36.45 million (€27.63 million), which made Sweden the third-largest donor after the UK and Norway. Swedish research groups are active in several fields included in the TDR programme, above all malaria and TB, which are often co-financed via Sida's programme for development research.

If the contribution to TDR, which is non-earmarked, is broken down in accordance with the percentages given in its budget, this would mean that approximately SEK 4.35 million (€0.48 million) is allocated to TB; SEK 5.6 million (€0.62 million) to malaria, and SEK 5.7 million (€0.63) to other neglected diseases.

A further contribution to research into malaria, in addition to WHO's TDR, is channelled via Sida-SAREC, as a non-earmarked contribution, to the *Multilateral Initiative on Malaria (MIM)*. It amounts to SEK 1.9 million (€0.21 million).

Another international organisation supported by Sweden is the *International Organisation for the Demographic Evaluation of Populations (INDEPTH)*, which pursues research into malaria partly via the *Malaria Clinical Trial Alliance (MCTA)*. The non-earmarked contribution made via Sida-SAREC amounted to SEK 6.2 million (€0.69 million) in 2007.

Sweden also contributed to TB research undertaken at *Armauer Hansen Research Institute* in Addis Ababa, Ethiopia, with SEK 5.8 million (€0.63 million).

No contributions were provided in 2007 to Medicine for Malaria Venture, PATH Malaria Vaccine Initiative, Global Alliance for TB Drug Development, DNDi, Institute for One World Health or Aeras Global TB Vaccine Foundation.

6. Is Sweden doing enough?

This report shows that Sweden is an important funder of research into neglected diseases. The total figure in 2007, beyond the basic financing by government and counties, was SEK 89.8 million (€9.93 million).

This is partly due to the fact that Sweden is an important donor to WHO's TDR programme, EMVI, MIM and, above all, to EDCTP; and partly to the fact that strong Swedish research groups have been developed with a focus that includes immunopathogenesis and the development of medicines on the basis of the structural biology of the pathogens, new diagnostic methods and development of vaccines, and field studies of measures for preventing and treating the diseases. Much of the research work is done in cooperation with international partners, above all in different African countries. In accordance with the Swedish policy for research cooperation, a large amount is also allocated to capacity building in each country and, with the aid of scholarships, a large number of students and post-graduate students have been given the opportunity to undertake postgraduate studies in Sweden. Due to the high quality of the research, the support provided from Swedish public funds has also been increased with funding from major international institutions and/or private financiers.

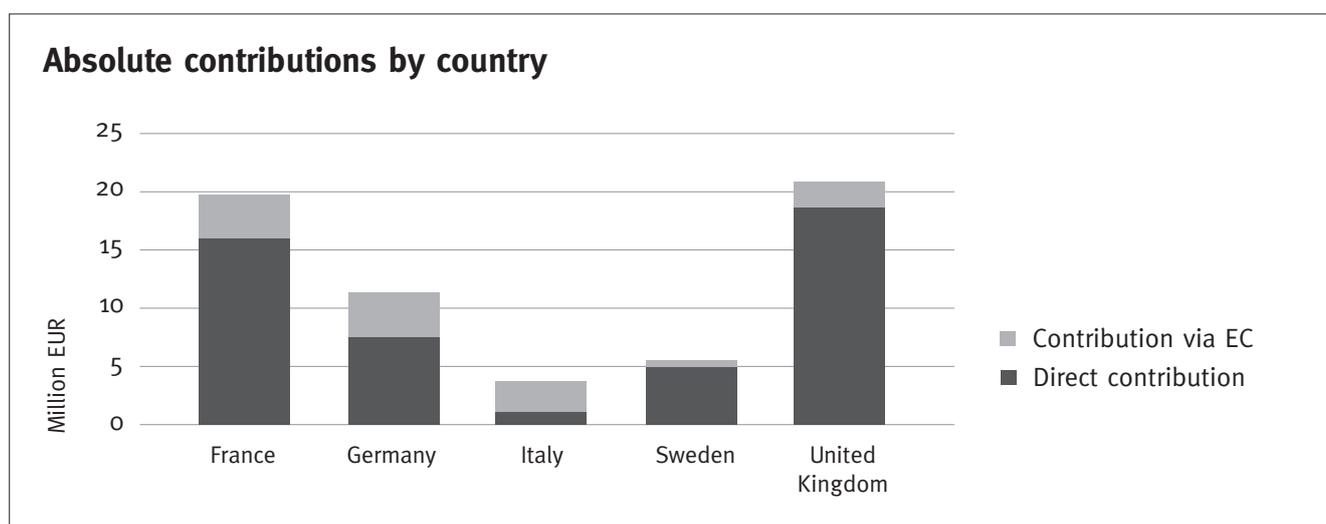
6.1 Swedish support for research into neglected diseases in an international comparison

To calculate Sweden's fair share, that is the amount Sweden should pay for the global TB research efforts,

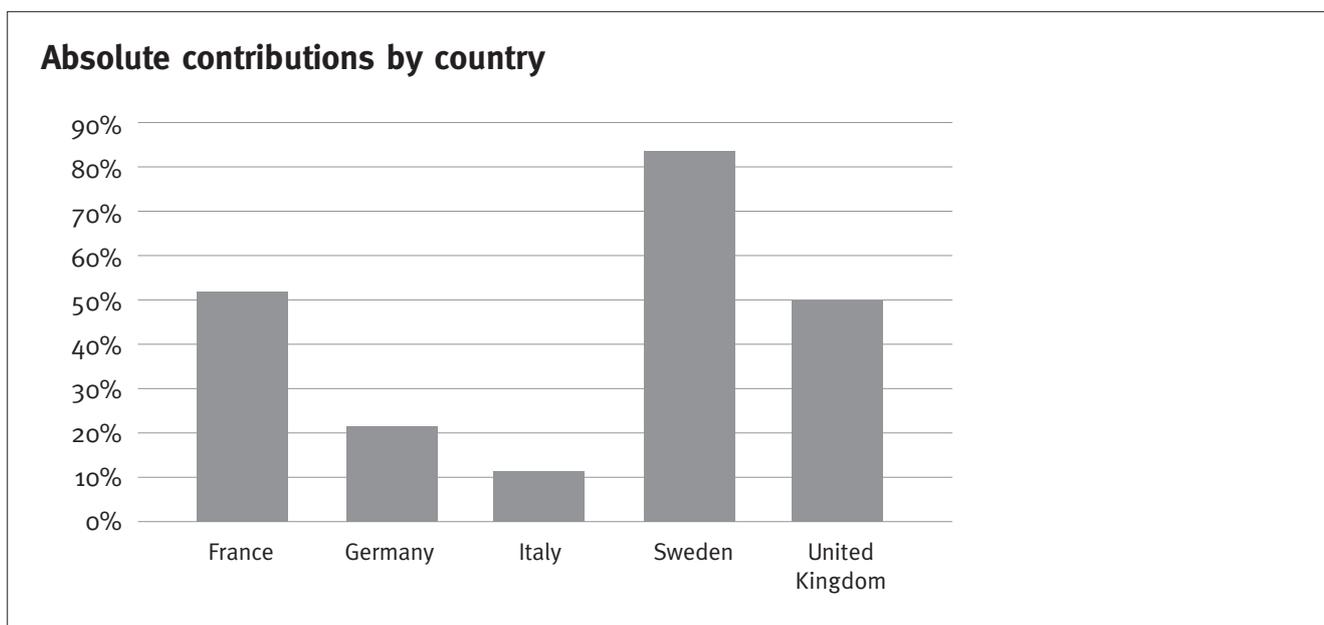
we take Sweden's proportion of international gross national income, (0.83%), and the Treatment Action Group's estimate of funding needs for research into TB (€1.45 billion), assuming that the public contribution to TB research remains at the 2007 level of 56.4%. By this calculation we can conclude that Sweden should contribute at least SEK 61.6 million (€6.8 million).

According to our study, Sweden contributed SEK 47 million (€5.19 million) in 2007, that is 76.3% of its fair share as defined above. For the purpose of comparing individual countries, the Swedish share of the EC's TB research expenditure (2.68% of €18.7 million: €0.5 million) needs to be added to this. Therefore the amount of TB research funding attributed to Sweden is calculated to be €5.7 million, or 83.7% of its fair share. Although it has thus not yet reached its fair share, Sweden stands out in Europe for coming closer to that target than other countries. The contrast is stark in comparison with Germany, for example, whose contribution is estimated to have reached only 22.5% of its fair share.

This is a quite conservative way of calculating Sweden's fair share, since it assumes that the private contributions (profit and non-profit) will rise in proportion to the public funding. If we assume that private funds will not rise any further and all the necessary additional TB research funding is paid for by public funders, we arrive at a Swedish fair share of €10.8 million.²⁹ By this calculation, Sweden would need to double its current investment.



²⁹ 1.45 billion (total TB research and development needs) minus €131 million (private sector contributions) equals €1.32 billion (public sector share of TB research and development needs).



The same calculation was done for four other European countries, as depicted in the figures on pages 16 and 17, and published by Médecins Sans Frontières.³⁰ This comparison shows clearly that Sweden, even though it is funding below its fair share, is still performing better than other EC members.

An increased contribution by the European Union budget is also needed to achieve the goal of adequate global funding for TB research. It currently provides only €18.7 million. Since the European countries examined so far need to more or less triple their contributions to reach their fair share,³¹ a tripling of the funds from the EU budget does not seem an unreasonable request.

Research into other neglected diseases has been neglected to say the least, also in Sweden. A certain amount of support is provided indirectly via WHO's TDR programme, but that is by and large all. Some basic research is being undertaken in Sweden on kinetoplastid diseases, such as Chagas disease and sleeping sickness, but hitherto mainly with funding from foreign sources and via faculty allocations. There are possibilities for improvement, for example through support to product development partnerships that focus on these diseases.

6.2 What can be improved and how?

Why is research into the most neglected diseases also the most neglected form of research? How does this tally with declarations on global responsibility for combating infectious diseases?

Since most Swedish research is done through non-earmarked government allocations made directly to the universities, it is the interest and curiosity of individual researchers and groups of researchers that govern the focus of research. This situation is, in turn, due to several factors: traditional research fields and expertise, access to equipment and research material, the existence of international partners in cooperation, the possibilities of developing research findings, and (not least important) the possibility of obtaining a future career for the individual researcher in the field in question.

One attempt to remedy this situation has been long-term support for the establishment of strategic research centres. Two of these have come to focus wholly or partly on research into malaria and TB, and it should be possible to strengthen these further.

One supplementary approach would be to provide support for international initiatives that focus on bridging the gap between basic and applied research. In several contexts, representatives of the government have spoken warmly of product development partnerships but, despite this, Sweden hardly contributes to any of them.

³⁰ The Underfunding of TB Research Across Europe, MSF, October 2009.

³¹ The Underfunding of TB Research Across Europe, MSF, October 2009.

Sida represents the main public financer of research and development into the diseases covered in this report. It is therefore worrying that major budget cuts have been announced for 2010. An estimated reduction of some 20% is foreseen for research cooperation with developing countries.

Sweden, with its considerable global engagement for example into poverty reduction, democracy and human rights, could increase its own and challenge other countries' contributions to initiate and fund research into diseases that often affect people in conflict zones, which keep people in poverty, and which attract little or no interest from the profit-driven pharmaceutical industry. It is also a field in which considerable effects can be achieved in a relatively short period of time and with limited investment.

It is also important that, in international contexts where issues relating to needs-driven research are discussed, Sweden supports new initiatives that come from emerging economies such as Brazil, South Africa and India.

Research and development funding requires both 'push' and 'pull' mechanisms. Push mechanisms such as traditional grants are a necessary impetus for basic research and will continue to play an important role in the advancement of science and in the development of new products. 'Pull' incentives today are mainly intellectual property rights, which encourage private sector investment in areas where profit can be expected. As we have seen, these have proved ineffective in the research and development neglected diseases. New mechanisms are therefore necessary to complement these, such the proposed prize funds. Patent pools like the one proposed by NGOs or UNITAID can be used to make research easier, and in many cases, possible. But medical innovation is not enough: these mechanisms must also ensure that the products of research and development are made available, affordable and accessible to those who need them.

Alternative financing mechanisms

The current system for stimulating and rewarding research and development of medicines, diagnostics and vaccines relies predominantly on the high prices that can be secured for health products developed through granting monopoly and other intellectual property rights. That the system is broken is no secret. Alternative mechanisms must be explored that stimulate research and development into neglected diseases, but also ensure that any products developed remain affordable and accessible to those in need.

Prize funds

Prize funds stimulate innovation by offering a lump sum or prize as reward, instead of relying on patent protection and sales. In April 2008, at an expert roundtable discussion convened by Médecins Sans Frontières, TB researchers, economists and campaigners showed considerable interest in a proposal for a prize fund that would encourage the development of an easy-to-use point-of-care TB diagnostic test. Ideally the test could be used wherever a patient comes to a health clinic that has limited staff and other resources, be non-invasive and not require blood or sputum, be sensitive enough to detect infection in children and in HIV-infected patients, and specific enough to separate active from latent infection, and be available at a low cost. Such a proposal was subsequently made to WHO by the governments of Barbados and Bolivia with the objective of developing new treatments for Chagas disease, priority vaccines and cancer treatments for developing countries.

Patent pools

Some patent holders make their patents available on a voluntary basis. Researchers and companies can then have easier access to those patents in exchange for a fair payment to the patent holder. The international organisation UNITAID is currently considering establishing a pharmaceutical patent pool, both to boost access to new antiretroviral drugs to treat AIDS in developing countries and to enable the development of fixed-dose combination and paediatric formulations of triple antiretroviral therapy. This could be extended to drugs and medical tools against tuberculosis and other diseases.

6.3 Sweden could take a leading role in developing alternative mechanisms to stimulate and finance research and development for neglected diseases

The government's research bill of 2008 states that some of our greatest challenges are global in character and concern people in both high-income and developing countries. It also states that infectious diseases constitute an obstacle to equitable and sustainable development. Attention is drawn to the need to develop knowledge over national borders and to cooperate with researchers in other countries. We now want to see these fine words transformed into action!

In May 2008, WHO member states (including Sweden) adopted a Global Strategy and Plan of Action for Public Health, Innovation and Intellectual Property looking at how to ensure both innovation and access. It proposed a number of new mechanisms, (some of which are described in the box on page 18) and commits WHO member states to pursuing ideas such as these. During the process leading up to the plan, Sweden's position was rather hesitant regarding the creation of new institutions and commitment to additional funding as well as to suggestions that could involve cooperation on a non-voluntary basis. However, with the adoption of the plan, Sweden indicated a firm commitment to explore ways to secure sustainable financing for the emerging research and development agenda, including exploring innovative financing mechanisms that address the link between the cost of research and development and the price of medical products. It is hoped that this commitment will prevail when the plan moves into its implementation phase. Sweden can play an important role, both financially and technically, in advancing the global strategy and plan of action.

During the 2009 EU Swedish presidency, priority areas are being highlighted within health. Among the issues given particular attention is the matter of antibiotic-resistant bacteria. The challenge is to develop strategies to stimulate development of antibiotics to fight resistant strains of microorganisms. This is especially important considering that pharmaceutical companies have given a low priority to these avenues of research and development. A perception by industry that antibiotics will not be profitable enough has led to dwindling production. Continuing the work of previous presidencies, the new Swedish presidency is investigating new models for financial incentives for the pharmaceutical industry. A number of parallels can be drawn with the TB situation, such as the lack of

incentives for drug research and development leading to a diminishing supply of new drugs, not least for drug-resistant TB. Lessons drawn from the antibiotics experience could be usefully applied to new models for financial incentives to TB.

The global community must focus on research and create market incentives. It is therefore important that the EU does not limit its efforts to certain antibacterials but builds on this initiative to create mechanisms that can stimulate tools for all neglected diseases, including drug-resistant TB.

- It is significant that Sweden contributes an important amount, nearly its 'fair share' to research and development for malaria and TB.
- Sweden should use its political influence within this area and take the opportunity, during its EU presidency and beyond, to encourage other EU member states and the European Commission to follow its example.
- The positive steps Sweden has taken to highlight the importance of innovative incentives for drug research and development in the area of antimicrobial resistance should be commended. The advances made in this area should also be used to explore mechanisms that can stimulate research and development for new diagnostic tests and medicines for drug-resistant TB.
- Sweden should increase its activities to explore innovative financial mechanisms and fund projects to pilot new ones. Sweden could help address the urgent need for a new point-of-care TB test by contributing to a prize fund set up for this purpose.
- Sweden needs to make sure that the products that result from its funding are accessible to the people who need them. Therefore an equitable licensing policy for government-funded research is necessary.

List of abbreviations

BCG	Bacille Calmette-Guérin
CIPiH	Commission on Intellectual Property, Innovation and Health
DNDi	Drugs for Neglected Diseases Initiative
ECDC	European Centre for Disease Control
EDCTP	European and Developing Countries Clinical Trials Partnership
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMVI	European Malaria Vaccine Initiative
EU	European Union
FIND	Foundation for Innovative New Diagnostics
FP7	EU seventh Framework Programme for research and development
GAVI	Global Alliance for Vaccines and Immunisation
GDP	Gross Domestic Product
GFATM	Global Fund against AIDS, TB and Malaria
G-FINDER	Global Funding of Innovation for Neglected Diseases
GNI	Gross National Income
IMI	The Innovative Medicines Initiative
INDEPTH	International Organisation for the Demographic Evaluation of Populations and their Health in Developing Countries
MCTA	Malaria Clinical Trial Alliance
MDR TB	Multi-drug-resistant TB, strains resistant to rifampicin and isoniazid
MIM	Multilateral Initiative on Malaria Research
MMV	Medicines for Malaria Venture
MSF	Medécins Sans Frontières
MVI	Malaria Vaccine Initiative
NIH	National Institutes of Health (USA)
NM₄TB	New Medicines for TB
PATH	Programme for Appropriate Technology in Health
PDP	Product Development Partnership
RAPID	Rational Approaches to Pathogen Inhibitory Discovery
R&D	Research and Development
SAREC	Sida's department for Research Cooperation
SARS	Severe Acute Respiratory Syndrome
Sida	Swedish International Development Cooperation Agency
SMI	Smittskyddsinstitutet/Swedish Institute for Infectious Disease Control
STINT	The Swedish Foundation for International Cooperation in Research and Higher Education
TAG	Treatment Action Group
TB	Tuberculosis
TBVI	TB Vaccine Initiative
TDR	Tropical Diseases Research and Training Programmes
UNDP	United Nations Development Programme
UNICEF	United Nations Children's Fund
VINNOVA	The Swedish Government Agency for Innovation Systems
WHA	World Health Assembly
WHO	World Health Organization
XDR TB	Extensively-drug-resistant TB: strains more resistant than MDR TB

COUGH UP FOR TB!

Every day the medical teams of Médecins Sans Frontières are faced with the lack of adequate or effective tools needed to treat, detect or prevent disease – especially those diseases that predominantly occur in poor countries, such as tuberculosis, malaria or other neglected diseases.

Although governments have repeatedly recognised this disastrous state of affairs, the financial commitments for much needed research and development of drugs, diagnostics and vaccines lag far behind the political rhetoric – raising questions about the seriousness of the international community's response to this crisis in health.

This report examines the contributions of the Swedish Government to the funding of research for neglected diseases with a particular focus on tuberculosis: Worldwide, this disease claims around 1.7 million lives every year. We now face further and more alarming challenges with the emergence of strains that are resistant to standard drugs and the rapid spread of the disease among people living with HIV.

Given that Europe is on the frontline of tuberculosis with the rapid spread of the epidemic in Central Asia, the Caucasus, Eastern Europe, and even within the European Union (EU) in the Baltic States, it is extremely worrying that contributions from European states and the EU are so inadequate. Sweden has made a very respectable contribution towards funding for tuberculosis research and should encourage other EU member states and the European Commission to follow its example.



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