The framework of international health research

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ABSTRACT

Of the global budget for health research, only 10% is spent on the disease burden of 90% of the world's population. Investments in international health research are lacking, hampering health of the poor in particular. Effective vaccines against the world killers HIV, malaria and tuberculosis still do not exist. However, besides scaling up research for new drugs and vaccines, research in health care systems are needed to understand the obstacles to implement new as well as existing interventions to prevent and combat the major health problems of those most in need. The task demands political and private sector commitment.

Only 10% of the global research budget concerns health issues relating to 90% of the world's population. This imbalance contributes to the significant lower health condition in low- and middle-income countries compared to high-income countries. To balance this inequity requires poverty reduction, development and research; research in a broad context, as well as development of new interventions, quality control, and health sector research, which all are necessary to optimise the implementation of already existing interventions.

IMBALANCE

The burden of disease and the research priorities do not balance; of the 90 bio US\$ spent on research globally every year, only 10% is allocated to the health problems mainly concerning the 90% living in low- and middle-income countries: the 10/90 gap [1]. We still lack effective vaccines against the world killers HIV, malaria and tuberculosis. Other examples are insufficient interventions against diar-

Box

Only 10% of the health research budget focus on the diseases 90% of the world's population suffer from

Effective interventions against major health problems in low and middle income countries are lacking

Existing evidence-based interventions are underutilized

International health research includes all the process from basic research to healthcare system research

International health research comprises multiple disciplines such as anthropology, sociology and organisation/ management rhoea, respiratory infections, sexually transmitted diseases, and specific treatments against many tropical diseases are outdated and inefficient. Hence only 16 of the 1393 new entities launched from 1975 to 1999 were targeting tropical diseases, corresponding to 1%. Without patients who can afford to buy the medicine, the research incentive is limited [2]. Poverty also contributes directly to diseases, among others through poor housing conditions, insufficient water, sanitation and hygiene and inadequate nutrition.

DOUBLE BURDEN OF DISEASE

Low- and middle-income countries are particular vulnerable in relation to urbanisation and modernisation. Infections, which are historic in the richer part of the world, are still common in the poor part of the world; and at the same time chronic diseases like cardiovascular diseases, diabetes and cancer are rising. This *double burden of disease* is a new challenge to research in international health [3].

THE FIGHT AGAINST POVERTY AND DISEASES

Poverty-related diseases are a particular burden on international health. Hence, the fight against poverty is an essential part of primary prophylaxis. As shown by the Harvard economist Sachs (2001) and previously by the World Bank (1993) it is also cost effective to invest in health.

We allocate almost 9% of our GDP to health, while most African countries spend no more than 1% and even less on research and development of a GDP, which in few countries exceed 300 US\$ per person per year.

Typically it takes more than 10 years to develop new drugs and only a small fraction makes it to the clinic; hence it is an expensive process, which national governments cannot and will not undertake alone. To register the first malaria vaccine 3 billion US\$ are missing according to United Nations' Development Programme (UNDP). However, the costs due to malaria are estimated to 6 billion US\$ yearly. But even though a vaccine may be cost-effective, investors are lacking, because the return is uncertain, when the target group is mostly African children, who cannot afford to pay for it.

PUBLIC PRIVATE PARTNERSHIPS

Since the 1970's WHO has dominated the research in tropical diseases through the Special Programme for Research and Training in Tropical Diseases (TDR) in collaboration with the World Bank, Unicef and UNDP. Acknowledging the stagnation in international health research and because neither the world community nor the national governments took full responsibility, *public private partnerships* (PPP) have developed over the last decade. The public sector (local governments and international organisations like WHO), the private industry (pharmaceutical and biotech industry) and civil society (academic institutions, private non for profit organisations and philanthropists) have made joint ventures to develop drugs and vaccines targeting infectious diseases in developing countries. Each portfolio has several potential products in various developmental phases [4].

Among the first was Medicines for Malaria Venture managing 21 projects, 10 pre-clinical and clinical projects, like the new synthetic peroxide (RBx11160) in phase III.

Another PPP is Drugs for Neglected Diseases Initiative established by Oswaldo Cruz Foundation, Indian Council for Medical Research, Kenya Medical Research Institute, Malaysia Ministry of Health, Institute Pasteur in France, TDR and Médecins Sans Frontières (Doctors without borders) managing 19 projects in leishmaniasis, African trypanosomiasis, Chagas disease and malaria. The first finished products were artemisinine combination therapy (ACT) containing artesunate/amodiaquine or artesunate/mefloquin against chloroquine-resistant falciparum malaria. WHO has recommended ACT since 2001 and 43 Sub- Saharan countries have approved ACT protocols, but only 15 have started the implementation, and of those only a handful has done it nationwide. Because the price has been a major obstacle, the new products are not patented and in cooperation with Sanofi-Aventis the goal is to provide treatment for 1 US\$ for adults and 0.5 US\$ for children [5].

Today more than 100 PPP exist, of which 20 focus on product development, the remaining on other areas like advocacy and access in relation to international health [4]. The overall objective is to invent new interventions, and to secure they are accessible to the patients in need. The predictable Achilles heal is donor fatigue and lack of long-term financing. If major private funds (Rockefeller Foundation and Bill & Melinda Gates Foundation) withdraw, it is even more important to secure a buffer capacity.

RESEARCH IN BROAD SENSE

Research, as described here, is perceived in the broadest sense: from generating new knowledge and interventions, to monitoring the utilization of existing interventions. Often the coverage of evidencebased interventions is low and it is therefore important to understand the implementation obstacles (under-utilization). One example is that only one in ten HIV-positive pregnant women is offered prevention to stop transmission to the child, although the risk can be reduced from 30% to under 10% [6]. Roll Back Malaria Initiative has a goal to increase insecticide-treated bed net (ITN) coverage to 60% in endemic areas, acknowledging that ITN can halve the mortality among covered children.

Effective implementation takes more than financial resources, commitment is also needed. Molyneux & Weber have formulated a modified "theory of relativity", $e = m \times c^2$, excellency = money \times commitment² [7]. A devastating lack of human resource in the



Figure 1. www.who.int/tdr/media/image.html, research capacity building Image ID: 0210602, Pasteur Institute, Teheran: Dr Sima Rafati and research students working with leishmaniasis.



Figure 2. www.who.int/tdr/media/image.html, research capacity building Image ID: 0110319, National Centre for Genetic Engineering and Biotechnology (BIOTEC), Bangkok: a researcher testing native Thai fungi for antimalaria and anti-TB properties.

Box

By international health we understand the major poverty related health problems in low- and middle-income countries, including classical tropical diseases like tuberculosis, HIV/AIDS, paediatric diseases (including acute respiratory infections and diarrhoea), nutrition related diseases and pregnancy/maternal health problems.

health sector, particularly South of Sahara does not make it any easier.

The research process can be compared to a food chain, from basic molecular research, development of interventions inclusive *good laboratory and manufacturing practice* over clinical research and *good clinical practice* to operational research and health sector research, all parts being necessary. To investigate and implement the last steps, the medical approach must be supplemented by other fields such as anthropology, sociology and organisation/management, e.g. to examine why healthcare systems (do not) work in practice.

ALTERNATIVE HEALTHCARE SYSTEMS

According to Whyte only 47% consults the public health facilities in Uganda [8]. There are more traditional healers and they are easier accessible compared to doctors, which migth be part of the explanation. Further, there are numerous examples of a malfunctioning public healthcare system; the clinics run out of medicine and other materials, the staff is not motivated or does not show up at all (because of poor salary, lack of supervision and unsatisfied patients). Even if treatment and medicine are subsidised for the poorest, patients may have to pay (bribe) and are often told to go to the nearest pharmacy (which could be a day's journey away) to pay for the medicine, the health centre is out of stock of. Hence Mexican and Tanzanian patients often go directly to the pharmacies and save time and consultation fees [9].

DANISH RESEARCH CONTRIBUTIONS

It is of major importance to research in international health, that the countries involved are included in the research process in order to build capacty. One of the initial capacity building programmes for developing countries started in Denmark, Enhancement of Research Capacity [10], a bilateral programme sponsored by Danida. It is a partnership between research institutions in Denmark and host countries cooperating to enhance the capacity to research and to implement international research results and to improve the quality of academic research training.

International health research is carried out by university units like Centre of International Health and Development, including the Centre for Medical Parasitology at University of Copenhagen and institutions like Statens Serum Institute including the Bandim-cohort studies of mothers and children in Guinea-Bissau, and Institute for Health Research and Development (the former Danish Billharziose Laboratory). Other significant contributions are malaria research, including vaccine development in African-European cooperation, and tuberculosis research in vaccines and diagnostics. Further, HIV/AIDS research should be mentioned, especially healthcare system research, which will play an important role when large groups will be enrolled for life long retroviral treatment. Outside the medical society international health research is carried out at the anthropological/ ethnographic institutions/departments at Copenhagen and Aarhus University, Centre for Africa Studies, Centre for Asia Studies and International Studies at RUC. Further, The Faculty of Life Sciences, The Danish Technical University and private consultancies are part of the Danida extended network for international research.

CONCLUSION

If we want to balance burden of disease and research effort, so more than 10% of the global health research focus on the health problems concerning 90% of the world's population, it takes commitment and resources from the public and the private sectors. An overall global prioritised action plan is needed, and WHO's General Assembly in May 2006 decided to initiate this process to overcome the current crises in international health research. There is plenty to go on with – we have no effective vaccines against HIV, malaria or tuberculosis, taking 8 million lives every year, diagnostics and treatments are to a large extent outdated (resistance being one of the reasons) and many healthcare system are not at all used at their optimum. Hopefully UN's Millennium Development Goals for 2015 to fight poverty and diseases can contribute.

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