Mapping of available health research and development data: what's there, what's missing, and what role is there for a global observatory?

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The need to align investments in health research and development (R&D) with public health demands is one of the most pressing global public health challenges. We aim to provide a comprehensive description of available data sources, propose a set of indicators for monitoring the global landscape of health R&D, and present a sample of country indicators on research inputs (investments), processes (clinical trials), and outputs (publications), based on data from international databases. Total global investments in health R&D (both public and private sector) in 2009 reached US$240 billion. Of the US$214 billion invested in high-income countries, 60% of health R&D investments came from the business sector, 30% from the public sector, and about 10% from other sources (including private non-profit organisations). Only about 1% of all health R&D investments were allocated to neglected diseases in 2010. Diseases of relevance to high-income countries were investigated in clinical trials seven-to-eight-times more often than were diseases whose burden lies mainly in low-income and middle-income countries. This report confirms that substantial gaps in the global landscape of health R&D remain, especially for and in low-income and middle-income countries. Too few investments are targeted towards the health needs of these countries. Better data are needed to improve priority setting and coordination for health R&D, ultimately to ensure that resources are allocated to diseases and regions where they are needed the most. The establishment of a global observatory on health R&D, which is being discussed at WHO, could address the absence of a comprehensive and sustainable mechanism for regular global monitoring of health R&D.

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Introduction

In April, 2012, the WHO Consultative Expert Working Group published its report on financing and coordination of research and development (R&D) related to diseases that mainly affect the world's poorest people living in developing countries.[1,2] The report is the latest assessment of potential solutions to the inequity in the distribution of global health research efforts, first described by the Commission on Health Research for Development in 1990 and later referred to as the "10/90 Gap", which indicates that only a small proportion of global health research expenditure is spent on diseases that have a large burden of preventable mortality in low-income and middle-income countries.[3]

Advances in knowledge and technology have contributed substantially to improvements in health,[4,5] but these gains have not been distributed or shared equally, with disparities in life expectancy and burden of disease especially notable between low-income and middle-income countries, and high-income countries.[6] Widespread calls for universal health coverage and to address broader determinants of health show the global imperative to eliminate these avoidable disparities.[7–10] One crucial contributing factor is the inadequate investment in R&D to address the specific health problems of poor populations.[11,12] This well-recognised investment deficit formed the background to the work of the Consultative Expert Working Group and the process that preceded it including an international commission and several year-long multilateral negotiations.[3,13–17] The group's report, which is being discussed by the governing bodies of WHO, recommends a new approach to global health R&D that involves the implementation of three elements focused on meeting the R&D needs of low-income and middle-income countries: guarantee of sustainable financing; coordination of global efforts; and provision of functions to monitor and inform the research processes in the form of a global observatory on health R&D.

A global observatory on health R&D is needed because our understanding of what health R&D is undertaken, and where, by whom, and how, is very scarce, and such knowledge is necessary to improve priority setting and coordination for health R&D.[18,19] In this report, we describe how a global observatory could provide such information. We consider potential data sources for health R&D information; assess data availability and limitations of the available sources; propose a set of potential indicators; and discuss the value that a global observatory would have nationally, regionally, and worldwide.

Methods

Identification of data sources and indicators

Global and regional sources that present up-to-date information about health R&D on an ongoing basis at regular intervals were identified through searches of publications, grey literature, and websites. One-off data collection efforts and analyses were not included. National data sources representing one individual country and data from funding organisations or programmes were excluded because of comparability issues.

We used the Frascati Manual definition of R&D, which is: "Research and experimental development (R&D) comprise creative work undertaken on a systematic basis in order to increase the stock of knowledge, including knowledge of man, culture and society, and the use of this stock of knowledge to devise new applications. It covers three activities: basic research, applied research and experimental development."[20] We analysed the type of data available to develop a set of indicators that could be used to measure and track the global inputs to health R&D (eg, funding and human resources), the R&D processes (eg, clinical trials), the R&D outputs (eg, publications, patents, and products registered), and the final consequences of these outputs (eg, health outcomes). Table 1 presents the proposed set of indicators, links them to existing data sources, and shows some of the data limitations. The indicators can be used to analyse the R&D landscape at different levels, including a particular area of research or a specific disease.

Data sources and analyses

We assessed a subset of the national indicators listed in table 1 by using available data sources, and focused our analysis on R&D expenditure (in 2009–10) related to a

	Description	Limitations
Inputs		
Investments		
UNESCO Institute for Statistics	Biennial survey, re-launched in 2006, which tracks overall R&D expenditures, R&D personnel, and number of researchers reported by non-EU, non-OECD, and non-RICYT countries. Uses data from OECD and RICYT, in addition to the country reporting. Main output is GERD but also includes expenditures by field of science (eg, medical and health sciences)	Limited scope—only particular geographies, disorders, and types of research are covered. Low granularity and level of detail—only up to health and medical R&D. Low comparability because of different methodologies, including varying scope and inclusion criteria
OECD	Annual survey tracking overall R&D expenditures and R&D personnel reported by 42 countries, of which 34 are member countries. Main output is GERD, but also reports expenditures by field of science (medical and health sciences) and socioeconomic objectives (health) by sector of performance	The annual joint OECD–Eurostat–UNESCO questionnaire does not specifically deal with health-related R&D, and relevant numbers have to be extracted from various sections of the databases and built up into an estimated total. OECD and Eurostat do not publish exactly the same selection of data from the responses. Countries do not reply to all sections of the questionnaire. To ensure and incentivise individual country reporting is challenging. Data thereby limit the effects that monitoring or tracking of R&D can have in terms of offering policy support to governments and institutions
Eurostat	Annual survey of EU-27 member state expenditures on overall R&D, of which 6 are not OECD members. Methodology as per UNESCO and OECD (joint questionnaire). Reports totals and health-related R&D	See above
RICYT	Annual survey, started in 1990, mainly tracking overall R&D expenditures, R&D personnel, publications, and patents reported by Portugal, Spain, and 29 countries in the Americas. Reports totals and health-related R&D	See above
G-Finder	Annual survey of R&D disbursements for neglected disease R&D started in 2007. Restricted to 31 neglected diseases and the pharmaceutical devices used to prevent, control, and treat them. Data gathered from 240 public, private, and philanthropic organisations from 34 countries	See above
ASEAN Asia S&T Portal: ST indicators for Asian countries	Indicators for science, technology, and innovation in ASEAN countries: Australia, China, India, Japan, South Korea, and New Zealand. Number of indicators varies depending on country	See above
Organisation of Islamic states: R&D	An overview of the current developments in the OIC member countries measuring human resources in R&D, R&D expenditures, high technology exports, scientific publications, and patent applications	See above
GFHR: monitoring financial flows: global studies published 2001–09	Reports collation and analysis of expenditure data for health R&D with use of OECD, UNESCO, RICYT, and other sources; alternates annually between global surveys and studies focused on specific diseases or public investments by individual countries	See above
African Union/NEPAD: ASTI and AOSTI	The African Science, Technology and Innovation Indicators Initiative is a programme within the African Science and Technology Consolidated Plan of Action being coordinated by NEPAD. Participating countries undertake R&D and innovation surveys, the outcomes of which are captured in the African Innovation Outlook. The first round of R&D and innovation surveys with 19 countries have been finalised	See above
Treatment Action Group reports	Annual survey of tuberculosis R&D investments started in 2005	See above
HIV Vaccines and Microbicides Resource Tracking Working Group reports	Annual survey of HIV/AIDS R&D investments started in 2004	See above
Number of researchers		
UNESCO Institute for Statistics	See above	See above
OECD/Eurostat	See above	See above
RICYT	See above	See above

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	Description	Limitations
(Continued from previous page)		
Processes		
Research projects		
National databases	Some databases created and used by funders or research institutions as a mechanism to manage their research portfolio	Low comparability. Narrow scope. No global or international databases. Although a global database is unlikely to be feasible, agreement on classification might allow harvesting of data
Registered clinical trials		
WHO International Clinical Trials Registry Platform	Provides a single point of access to information about 200 000 clinical trials registered at 15 different national or regional registries worldwide. For the purposes of registration, a clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to assess the effects on health outcomes	Not comprehensive—compliance with registration needs to be improved. Stronger enforcement needed. Registration data are uploaded by trial managers, leading to variable data quality. Data quality and adherence to standards can be improved
Outputs		
Publications		
Thomson Reuters and others	Thomson Reuters' Web of Science covers research published in more than 12 000 scientific journals and conference proceedings and is presently one of the most extensive sources of R&D outputs. Other sources also exist	Broad but not fully comprehensive coverage of the literature. Predominance of publicly funded research. Bias towards reporting of positive results. Lag period between active research and publication. No clear link between publication and inputs (financing)
Medline and PubMed	Medline is the US National Library of Medicine's premier bibliographic database that contains over 19 million references to journal articles in life sciences, with a focus on biomedicine. PubMed comprises more than 22 million citations for biomedical literature from Medline, life science journals, and online books. PubMed provides free access to Medline and links to full text articles when possible	See above
Virtual Health Library (BIREME)	Open access online source of extensive health-related literature for the Latin American and Caribbean region supported by PAHO WHO. Integrates a range of bibliographic and other data sources for the health sciences	See above
Patents		
WIPO (PATENTSCOPE)	Searchable database administered by the WIPO, where more than 14 million patent documents, including over 2 million published international patent applications, can be searched	Not easy to use or interpret the results of searches. Needs specialised training. Predominance of privately funded research
Re:Search (WIPO)	Provides public access to intellectual property for pharmaceutical compounds, technologies, know-how, and data available for research and development for neglected tropical diseases, tuberculosis, and malaria	See above
WIPO GOLD	A free public resource that provides a one-stop gateway to WIPO's global collections of searchable IP data. It aims to facilitate universal access to IP information	See above
National and regional databases	Databases created and used by national and regional patent offices	See above
Products		
National or regional databases	Some databases created and used by national regulatory authorities. These include Drugs@FDA, which provides official information about FDA-approved innovator and generic drugs and therapeutic biological products presently approved for sale in the USA. Another example is the European Medicines Agency, a decentralised agency of the EU, located in London. The agency is responsible for the scientific assessment of drugs developed by pharmaceutical companies for use in the EU	No global or international database. Insufficient scope—only particular diseases or products are included
WHO prequalification system database	Products prequalified by the WHO de-facto regulatory process	See above
Outcome or effect		
Expected or potential and real health outcomes	Effectiveness of technologies or interventions in reducing disease burden. Real-world health benefits achieved that will depend on sales/uptake and adherence. Might be captured by the effective coverage measure	No global or international database. Substantial work is needed to link research contribution to expected and real health effect

UNESCO=United Nations Educational, Scientific and Cultural Organization. R&D=research and development. EU=European Union. OECD=Organisation for Economic Co-operation and Development. RICYT=Ibero-American and Inter-American Network for Science and Technology Indicators. GERD=gross domestic expenditure on research and experimental development. ASEAN= Association of Southeast Asian Nations. ST=science and technology. OIC=Organisation of Islamic Cooperation. GFHR=Global Forum for Health Research. NEPAD=New Partnership for Africa's Development. ASTI=African Science, Technology and Innovation Indicators. AOSTI=African Observatory for Science, Technology and Innovation. PAHO=Pan American Health Organization. WIPO=World Intellectual Property Organization. IP=intellectual property.

Table 1: **Indicators and sample of information sources**

country's wealth, a sample of registered actively recruiting (in August, 2012) clinical trials, and publications indexed by the Web of Science (2002–11).

This subset of indicators was selected on the basis of data availability, the need to balance inputs and outputs, and the desire to cover the different stages of the R&D continuum. We decided not to include researchers, patents, products, or estimates of health outcomes. We used total gross domestic expenditure on research and experimental development (GERD); total health GERD;

	DALYs ratio
Type III diseases: disease burden is at least 35 times higher in low-income and middle-income countries than in high-income countries	
Chagas disease	1869·1
Trachoma	1358·3
Trypanosomiasis	867·1
Lymphatic filariasis	569·5
Diphtheria	390·2
Vitamin A deficiency	338·6
Measles	266·9
Tetanus	264·1
Malaria	185·1
Onchocerciasis	152·1
Leishmaniasis	122·7
Leprosy	118·2
Maternal haemorrhage	114·7
Syphilis	78·0
Hypertensive disorders of pregnancy	60·1
Japanese encephalitis	58·6
Ascariasis	55·0
Abortion*	41·5
Iodine deficiency	39·6
Schistosomiasis	38·8
Pertussis	37·4
Type II diseases: disease burden is 3–35-times higher in low-income and middle-income countries than in high-income countries	
Obstructed labour	34·7
Trichuriasis	33·4
Tuberculosis	31·6
Diarrhoeal diseases	29·5
Protein energy malnutrition	24·2
Dengue	20·3
Meningitis	18·4
Hookworm disease	18·2
HIV/AIDS	17·1
Birth asphyxia and birth trauma	15·4
Lower respiratory tract infections	13·5
Low birthweight	10·6
Maternal sepsis	8·4
Cataracts	7·1
Rheumatic heart disease	7·1
Upper respiratory infections	5·8
Hepatitis B	4·6
Iron-deficiency anaemia	4·4
Peptic ulcer disease	4·0
Type I diseases: disease burden is no more than 3 times higher in low-income and middle-income countries than in high-income countries	
Otitis media	2·55
Epilepsy	2·44
Nephritis and nephrosis	2·39
Glaucoma	2·03
Appendicitis	1·96
Schizophrenia	1·73
Cervical cancer	1·68
Refractive errors	1·65
Oesophageal cancer	1·58
Hypertensive heart disease	1·54
Cerebrovascular disease	1·49
Bipolar affective disorder	1·49
Benign prostatic hypertrophy	1·41
Asthma	1·39
Panic disorder	1·38
Lower back pain	1·37
Chronic obstructive pulmonary disease	1·34
Obsessive-compulsive disorder	1·29
Liver cancer	1·28
Inflammatory heart disease	1·27
Mouth and oropharynx cancers	1·27
Gout	1·22
Cirrhosis of the liver	1·19
Ischaemic heart disease	1·18
Stomach cancer	1·10
Leukaemia	1·09
Post-traumatic stress disorder	1·03
Hepatitis C	1·01
Unipolar depressive disorders	1·00
Adult-onset hearing loss	0·99
Macular degeneration and other sense disorders	0·93
Diabetes mellitus	0·80
Alcohol use disorders	0·80
Migraine	0·80
Osteoarthritis	0·79
Rheumatoid arthritis	0·74
Insomnia (primary)	0·67
Lymphomas and multiple myeloma	0·67
Multiple sclerosis	0·67
Drug use disorders	0·63
Ovary cancer	0·47
Breast cancer	0·45
Other malignant neoplasms	0·44
Bladder cancer	0·40
Tracheal, bronchial, and lung cancers	0·38
Corpus uteri cancer	0·31
Colon and rectum cancers	0·30
Alzheimer's disease and other dementias	0·28
Prostate cancer	0·28
Pancreatic cancer	0·27
Parkinson's disease	0·26
Melanoma and other skin cancers	0·20

Data are from reference 6. The diseases are listed according to their relative burden in low-income and middle-income countries compared with high-income countries, with those with the highest relative burden being listed first within each category. Values are DALYs per 100 000 population in low-income and middle-income countries divided by DALYs per 100 000 population in high-income countries—ie, the ratio of DALYs. A calculation of the DALYs in each World Bank income group can be found in reference 24. DALY=disability-adjusted life-year. *Disability and mortality caused by abortions.

Table 2: **List of type III, II, and I diseases based on Global Burden of Disease data**

percentages of health R&D expenditure funded by business, public, and other sources; neglected disease R&D funding; number of registered, actively recruiting clinical trials; and number of publications attributed to institutions in countries. The countries included were the 192 United Nations member states (based on membership in 2010); they were categorised further according to income brackets—low-income, lower-middle-income, upper-middle-income, and high-income—on the basis of the World Bank classification for the 2010 financial year.

To measure GERD, data for 192 countries from 2008–10 were extracted from the online database of the United Nations Educational, Scientific and Cultural Organization Institute for Statistics. Data for health R&D were taken from the Organisation for Economic Co-operation and Development and Eurostat databases, which together cover 49 countries and were updated in March, 2012, and with data generally from 2009. Health GERD, like GERD itself, encompasses all R&D in each country as reported by the units doing the work. To calculate percentages of health R&D expenditure funded by business, public, and other sources, some simplifying assumptions were necessary—notably, that all health R&D carried out by industrial firms was financed by business. Another data source reported by R&D funders instead of performers also exists, and would have given somewhat different estimates. The data are mainly derived from national R&D surveys as reported in the annual joint Organisation for Economic Co-operation and Development–Eurostat–United Nations Educational, Scientific and Cultural Organization Institute for Statistics questionnaire. No single category for health R&D exists, and totals need to be generated from expenditure items available for different sectors of the economy. These surveys are based on the methods and definitions of the Frascati Manual.[20] Additional health-related R&D expenditure data were found in national R&D surveys and, for some countries, specific estimation approaches were needed (appendix).

To calculate the total health R&D investments worldwide, data had to be found for countries not reporting to Eurostat or the Organisation for Economic Co-operation and Development. For several of these countries, data were available from United Nations Educational, Scientific and Cultural Organization Institute for Statistics sources on total R&D done in the medical sciences. For countries without such data, health GERD was extrapolated from the average proportion of health R&D of total GERD from the relevant income group of countries, which is a similar approach to that used in previous studies.[21,22] For countries with no R&D expenditure data, the average proportion of gross domestic product (GDP) for R&D in the relevant income group of countries was used to extrapolate GERD; health GERD was then extrapolated as explained previously. Estimates of GERD for large oil-producing economies were based on the average proportion of GDP invested in R&D in Kuwait and Saudi Arabia, since this group of countries seems to invest less on research than do other countries with similar incomes.

Bibliometric data were commissioned from Thomson Reuters' Web of Science database and analysed by Thomson Reuters (Evidence). Academic papers for all topics and for applied health research (all categories of clinical medicine and health sciences, but not basic biomedical research, based on journal classification) for 2002–11 were included. Papers were linked to countries by all listed affiliations. Data for the number of ongoing clinical trials were based on a 5% random sample on August 10, 2012, of all interventional, actively recruiting trials from the International Clinical Trials Registry Platform, which is described in detail elsewhere.[23]

For more on **Web of Science** see http://thomsonreuters.com/products_services/science/science_products/a-z/web_of_science

A specific aim was to assess the relevance of R&D related to improving health in low-income and middle-income countries with the categories of disease types first described by the Commission on Macroeconomics and Health: diseases for which the burden lies overwhelmingly or exclusively in low-income countries (type III diseases), diseases for which the main burden lies in low-income countries (type II diseases), or diseases for which the burden is similar in low-income and in wealthier countries (type I diseases).[15] This categorisation has been used most frequently with a focus on neglected tropical diseases as a typical example of type III diseases, as was done when this typology was introduced.[15] We applied this classification with the 2011 G-FINDER report to extract data for research done in 2010 into 31 neglected diseases, from basic research through to clinical trials. The G-FINDER report presents funding for diseases in US$. Since the data we present for total GERD are in current purchasing power parity-adjusted dollars, for consistency we adjusted the G-FINDER data to account for this factor by using 2010 purchasing power parity values from the World Bank database. We have adhered to the G-FINDER definition of a neglected disease in our assessment of investments.[19]

See **Online** for appendix

We developed a new, additional approach to operationalise the categorisation of diseases to type I, II, or III diseases, on the basis of the disorders or diseases presented in the 2004 Global Burden of Diseases report.[6] The number of disability-adjusted life-years caused by each disease was calculated for all low-income and middle-income countries combined per person. The number of disability-adjusted life-years was also calculated for all high-income countries combined per person. A ratio was then calculated for each disease: the number of disability-adjusted life-years per person in low-income and middle-income countries divided by the number per person in high-income countries. These ratios were then ranked from high to low, where a ratio of 1·0 indicates that the disease is found in equal measure in low-and-middle-income countries and high-income countries. From this list, diseases were categorised subjectively with the following ranges of ratios: type I diseases 0·0 to less

	GERD total in millions current PPP$		GERD as a % of GDP	GERD per person	Health GERD 2010 or latest year				Neglected diseases research investments			Ongoing clinical trials		Publications in all fields 2002–11		Health publications 2002–11		Proportion of publications in health (%)
	2010 or latest year available	Estimates	2010 or latest year available	2010 or latest year available	Millions PPP$	Estimates (millions PPP$)	% of GDP	% of GERD	Public and philanthropic thousands PPP$	Public thousands PPP$ values	Public per GDP (% of GDP)	Estimated number of trials	Estimate per million people	Total	Per million people	Total	Per million people	
Low-income countries																		
Afghanistan	..	65	..	..	..	6	..	..	..	..	..	0	0	172	5·0	121	3·5	70·3%
Bangladesh	..	447	..	..	..	41	..	..	..	..	..	60	0·4	7219	48·5	2042	13·7	28·3%
Benin	..	25	..	..	..	2	..	..	..	..	..	0	0	1347	152·2	373	42·1	27·7%
Burkina Faso	39	..	0·21%	2·42	..	4	..	..	..	..	..	40	2·3	1723	104·6	730	44·3	42·4%
Burma	..	0	..	..	..	0	..	..	..	..	..	20	0·4	..	..	..	..	..
Burundi	..	9	..	..	..	1	..	..	..	..	..	0	0	114	13·6	34	4·1	29·8%
Cambodia	..	56	..	..	..	5	..	..	..	..	..	20	1·4	870	61·5	486	34·4	55·9%
Central African Republic	..	6	..	..	..	1	..	..	..	..	..	0	0	192	43·6	85	19·3	44·3%
Chad	..	30	..	..	..	3	..	..	..	..	..	0	0	154	13·7	44	3·9	28·6%
Comoros	..	1	..	..	..	0	..	..	..	..	..	0	0	31	42·2	14	19·1	45·2%
Democratic Republic of the Congo	..	42	..	..	..	4	..	..	..	..	..	0	0	434	6·6	248	3·8	57·1%
Eritrea	..	5	..	..	..	0	..	..	..	..	..	0	0	222	42·3	49	9·3	22·1%
Ethiopia	210	..	0·24%	2·53	33	..	0·04%	15·5%	..	..	..	20	0·2	4046	48·8	1316	15·9	32·5%
The Gambia	0·5	..	0·02%	0·29	..	0	..	..	..	..	..	20	10·9	808	467·5	540	312·4	66·8%
Guinea	..	20	..	..	..	2	..	..	..	..	..	0	0	197	19·7	96	9·6	48·7%
Guinea-Bissau	..	3	..	..	..	0	..	..	..	..	..	0	0	211	139·3	166	109·6	78·7%
Haiti	..	20	..	..	..	2	..	..	..	..	..	20	2·0	223	22·3	165	16·5	74·0%
Kenya	..	121	..	..	..	11	..	..	..	..	..	40	0·9	8339	205·8	3004	74·1	36·0%
Kyrgyzstan	20	..	0·16%	3·71	2	..	0·01%	8·3%	..	..	..	0	0	496	91·0	88	16·2	17·7%
Liberia	..	4	..	..	..	0	..	..	..	..	..	0	0	48	12·0	29	7·3	60·4%
Madagascar	29	..	0·15%	1·44	2	..	0·01%	8·4%	..	..	..	0	0	1252	60·4	328	15·8	26·2%
Malawi	..	24	..	..	..	2	..	..	..	..	..	60	3·8	1858	124·7	1157	77·6	62·3%

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	GERD total in millions current PPP$		GERD as a % of GDP	GERD per person	Health GERD 2010 or latest year				Neglected diseases research investments			Ongoing clinical trials		Publications in all fields 2002–11		Health publications 2002–11		Pro-portion of pub-lications in health (%)
	2010 or latest year available	Estimates	2010 or latest year avail-able	2010 or latest year available	Millions PPP$	Esti-mates (millions PPP$)	% of GDP	% of GERD	Public and philan-thropic thousands PPP$	Public thousands PPP$ values	Public per GDP (% of GDP)	Esti-mated number of trials	Esti-mate per million people	Total	Per million people	Total	Per million people	
(Continued from previous page)																		
Mali	..	30	..	..	..	3	..	..	..	..	..	20	1·2	950	61·8	443	28·8	46·6%
Mozambique	..	39	..	..	..	4	..	..	..	..	..	20	0·8	803	34·3	401	17·1	49·9%
Nepal	..	65	..	..	..	6	..	..	..	..	..	20	0·6	2336	78·0	1180	39·4	50·5%
Niger	..	20	..	..	..	2	..	..	..	..	..	0	0	589	38·0	158	10·2	26·8%
North Korea	..	0	..	..	..	0	..	..	..	..	..	0	0	..	..	..	..	..
Rwanda	..	22	..	..	..	2	..	..	7	7	0·00006%	20	1·8	396	37·3	205	19·3	51·8%
Sierra Leone	..	9	..	..	..	1	..	..	..	..	..	0	0	120	20·5	48	8·2	40·0%
Somalia	..	0	..	..	..	0	..	..	..	..	..	0	0	..	..	..	..	..
Tajikistan	12	..	0·09%	1·80	1		0%	4·8%	..	..	..	0	0	412	59·9	37	5·4	9·0%
Tanzania	..	114	..	..	..	11	..	..	141	141	0·00024%	60	1·3	4273	98·2	2063	47·4	48·3%
Togo	..	11	..	..	..	1	..	..	..	..	..	0	0	410	68·0	161	26·7	39·3%
Uganda	165	..	0·41%	5·10	15	..	0·04%	9·4%	..	..	..	20	0·6	4005	119·8	2171	65·0	54·2%
Zimbabwe	..	..	..	..	..	0	..	..	..	..	..	40	3·0	2246	179·4	778	62·2	34·6%
Total for low-income countries	475	1191	0·18%	..	53	114	..	9·3%	149	149	..	280	0·3	46 496	65·2	18 760	26·3	40·3%
Total (data plus estimates)	..	1666	..	..	..	167	..	..	..	..	..	..	..	..	..	..	..	..
Lower-middle income countries																		
Angola	..	319	..	..	..	37	..	..	..	..	..	0	0	181	9·5	81	4·2	44·8%
Armenia	44	..	0·27%	14·35	2	..	0·01%	3·5%	..	..	..	60	19·3	4709	1522·9	227	73·4	4·8%
Belize	..	7	..	..	..	1	..	..	..	..	..	0	0	99	287·2	23	66·7	23·2%
Bhutan	..	11	..	..	..	1	..	..	..	..	..	0	0	148	203·9	26	35·8	17·6%
Bolivia	72	..	0·16%	7·37	1	..	0%	1·2%	..	..	..	0	0	1567	157·8	410	41·3	26·2%
Cameroon	..	130	..	..	..	15	..	..	..	..	..	40	2·0	4182	213·4	1228	62·7	29·4%
Cape Verde	..	6	..	..	..	1	..	..	..	..	..	0	0	46	92·7	6	12·1	13·0%

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	GERD total in millions current PPP$		GERD as a % of GDP	GERD per person	Health GERD 2010 or latest year				Neglected diseases research investments			Ongoing clinical trials		Publications in all fields 2002–11		Health publications 2002–11		Proportion of publications in health (%)
	2010 or latest year available	Estimates	2010 or latest year available	2010 or latest year available	Millions PPP$	Estimates (millions PPP$)	% of GDP	% of GERD	Public and philanthropic thousands PPP$	Public thousands PPP$ values	Public per GDP (% of GDP)	Estimated number of trials	Estimate per million people	Total	Per million people	Total	Per million people	
(Continued from previous page)																		
Congo (Brazzaville)	..	50	..	..	..	6	..	..	..	..	..	0	0	682	168·7	332	82·1	48·7%
Côte d'Ivoire	..	108	..	..	..	13	..	..	..	..	..	20	1·0	1625	82·3	637	32·3	39·2%
Djibouti	..	0	..	..	..	0	..	..	..	..	..	0	0	35	393·7	19	213·7	54·3%
Egypt	998	..	0·21%	12·52	..	117	..	..	..	..	..	80	1·0	39 697	489·4	9442	116·4	23·8%
El Salvador	31	..	0·08%	5·08	5	..	0·01%	15·0%	..	..	..	0	0	235	37·9	122	19·7	51·9%
Federated States of Micronesia	..	1	..	..	..	0	..	..	..	..	..	0	0	68	612·3	20	180·1	29·4%
Fiji	..	12	..	..	..	1	..	..	..	..	..	0	0	741	861·0	133	154·5	17·9%
Georgia	..	65	..	..	..	8	..	..	..	..	..	60	13·6	3462	777·5	393	88·3	11·4%
Ghana	..	116	..	..	..	14	..	..	20	20	0·00006%	40	1·6	3065	125·7	1215	49·8	39·6%
Guatemala	37	..	0·06%	2·62	14	..	0·02%	37·3%	..	..	..	20	1·3	723	50·2	455	31·6	62·9%
Guyana	..	8	..	..	..	1	..	..	..	..	..	0	0	165	218·7	53	70·2	32·1%
Honduras	..	86	..	..	..	10	..	..	..	..	..	0	0	326	42·9	168	22·1	51·5%
India*	33042	..	0·80%	26·98	4886	..	0·13%	16·6%	76 261	76 261	0·00185%	1520	1·2	315 842	257·9	51 474	42·0	16·3%
Indonesia	809	..	0·08%	3·41	..	95	..	..	..	..	..	40	0·2	7409	30·9	1662	6·9	22·4%
Iraq	..	331	..	..	..	39	..	..	..	..	..	20	0·6	1717	53·6	516	16·1	30·1%
Kiribati	..	1	..	..	..	0	..	..	..	..	..	0	0	5	50·2	1	10·0	20·0%
Laos	..	46	..	..	..	5	..	..	..	..	..	0	0	562	90·6	232	37·4	41·3%
Lesotho	1	..	0·03%	0·45	..	0	..	..	..	..	..	0	0	147	67·7	43	19·8	29·3%
Marshall Islands	..	0	..	..	..	0	..	..	..	..	..	0	0	27	500·0	12	222·2	44·4%
Mauritania	..	25	..	..	..	3	..	..	..	..	..	0	0	182	52·6	28	8·1	15·4%
Moldova	54	..	0·53%	14·99	6	..	0·06%	11·2%	..	..	..	20	5·7	2130	598·0	130	36·5	6·1%
Mongolia	25	..	0·24%	9·28	2	..	0·02%	8·2%	..	..	..	20	7·0	1030	373·7	211	76·6	20·5%
Morocco	..	443	..	..	..	0	..	..	..	..	..	0	0	11 552	355·6	2630	81·0	22·8%
Nicaragua	..	47	..	..	..	5	..	..	..	..	..	0	0	477	82·4	197	34·0	41·3%
Nigeria	..	1092	..	..	..	128	..	..	218	218	0·00006%	20	0·1	15 607	98·5	5377	33·9	34·5%
Pakistan	2066	..	0·46%	12·12	..	242	..	..	..	..	..	40	0·2	25 003	144·0	5323	30·7	21·3%
Papua New Guinea	..	49	..	..	..	6	..	..	..	..	..	0	0	726	105·9	339	49·4	46·7%
Paraguay	18	..	0·06%	2·84	4	..	0·01%	22·1%	..	..	..	20	3·0	391	60·6	203	31·5	51·9%
Philippines	..	1072	..	..	..	126	..	..	..	..	..	220	2·3	6452	69·2	1471	15·8	22·8%
Samoa	..	2	..	..	..	0	..	..	..	..	..	0	0	31	169·3	4	21·8	12·9%

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(Continued from previous page)																		
São Tomé and Principe	··	1	··	··	··	0	··	··	··	··	··	0	0	19	114·9	11	66·5	57·9%
Senegal	81	··	0·37%	6·89	··	10	··	··	··	··	··	20	1·5	2371	190·7	894	71·9	37·7%
Solomon Islands	··	4	··	··	··	0	··	··	··	··	··	0	0	93	172·8	34	63·2	36·6%
Sri Lanka	106	··	0·11%	5·16	18	··	0·02%	17·3%	··	··	··	0	0	3507	169·8	1122	54·3	32·0%
Sudan	··	285	··	··	··	33	··	··	··	··	··	0	0	1686	38·7	680	15·6	40·3%
Swaziland	··	18	··	··	··	2	··	··	··	··	··	0	0	251	237·8	71	67·3	28·3%
Syria	··	313	··	··	··	37	··	··	··	··	··	0	0	2014	98·5	355	17·4	17·6%
Timor-Leste	··	5	··	··	··	1	··	··	··	··	··	0	0	··		··	··	··
Tonga	··	1	··	··	··	0	··	··	··	··	··	0	0	36	346·0	25	240·3	69·4%
Turkmenistan	··	121	··	··	··	14	··	··	··	··	··	0	0	70	13·9	5	1·0	7·1%
Tuvalu	··	0	··	··	··	0	··	··	··	··	··	0	0	··	··	··	··	··
Uzbekistan	··	254	··	··	··	30	··	··	··	··	··	0	0	3204	112·2	188	6·6	5·9%
Ukraine	2514	··	0·86%	54·98	118	··	0·04%	4·7%	··	··	··	380	8·4	43 694	952·5	1245	27·1	2·8
Vanuatu	··	3	··	··	··	0	··	··	··	··	··	0	0	126	525·8	35	146·0	27·8%
Vietnam	··	807	··	··	··	95	··	··	··	··	··	120	1·4	8069	92·8	1819	20·9	22·5%
Yemen	··	184	··	··	··	22	··	··	··	··	··	0	0	710	29·5	262	10·9	36·9%
Zambia	58	··	0·34%	4·72	··	7	··	··	··	··	··	60	4·4	1341	103·7	731	56·6	54·5%
Totals for lower-middle-income countries	39 955	5705	0·29%	··	5055	1177	··	11·7%	76 499	76 499	··	2220	0·9	518 237	206·3	92 320	36·7	17·8%
Total (data plus estimates)	··	45 660	··	··	··	6232	··	··	··	··	··	··	··	··	··	··	··	··
Upper-middle-income countries																		
Albania	40	··	0·15%	12·52	··	4	··	··	··	··	··	0	0	600	187·2	164	51·2	27·3%
Algeria	··	1780	··	··	··	187	··	··	··	··	··	0	0	11 064	311·9	581	16·4	5·3%
Antigua and Barbuda	··	9	··	··	··	1	··	··	··	··	··	0	0	32	360·7	21	236·7	65·6%
Argentina	3499	··	0·60%	87·34	458	··	0·08%	13·1%	2962	2962	0·00046%	460	11·2	60 898	1506·9	12 024	297·5	19·7%
Azerbaijan	212	··	0·25%	23·41	10	··	0·01%	4·9%	··	··	··	0	0	3022	333·8	101	11·2	3·3%
Belarus	783	··	0·64%	81·23	47	··	0·04%	6·0%	··	··	··	40	4·2	9927	1046·0	642	67·7	6·5%

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	2010 or latest year available	Estimates	2010 or latest year available	2010 or latest year available	Millions PPP$	Estimates (millions PPP$)	% of GDP	% of GERD	Public and philanthropic thousands PPP$	Public thousands PPP$ values	Public per GDP (% of GDP)	Estimated number of trials	Estimate per million people	Total	Per million people	Total	Per million people	
(Continued from previous page)																		
Bosnia and Herzegovina	7	..	0·02%	1·87	..	1	..	..	..	..	..	20	5·4	2275	605·0	1060	281·9	46·6%
Botswana	..	166	..	..	..	16	..	..	..	..	..	0	0	1668	831·1	332	165·4	19·9%
Brazil*	26017	..	1·19%	133·45	1945	..	0·09%	7·5%	4376	4376	0·00020%	1240	6·3	233005	1195·2	70477	361·5	30·2%
Bulgaria	626	..	0·60%	83·48	82	..	0·08%	13·1%	..	..	..	460	61·9	19500	2588·2	2216	294·1	11·4%
Chile	964	..	0·39%	57·37	89	..	0·04%	9·3%	874	874	0·00032%	320	18·4	37863	2212·4	7328	428·2	19·4%
China*	178981	..	1·77%	132·87	8825	..	0·09%	4·9%	5689	5689	0·00006%	2760	2·0	937601	700·8	114750	85·8	12·2%
Colombia	680	..	0·16%	14·68	..	76	..	..	6971	6971	0·00160%	280	5·9	15967	344·9	3915	84·6	24·5%
Costa Rica	279	..	0·54%	60·76	12	..	0·02%	4·4%	..	..	..	20	4·2	3476	746·1	896	192·3	25·8%
Cuba	..	694	0·61%	..	..	68	..	..	..	..	..	0	0	7263	645·1	1804	160·2	24·8%
Dominica	..	5	..	..	..	1	..	..	..	..	..	0	0	64	944·6	24	354·2	37·5%
Dominican Republic	..	552	..	..	..	54	..	..	..	..	..	0	0	308	31·0	176	17·7	57·1%
Ecuador	282	..	0·26%	20·09	25	..	0·02%	9·0%	..	..	..	0	0	2435	168·3	626	43·3	25·7%
Gabon	136	..	0·64%	91·86	..	13	..	..	..	..	..	20	12·8	795	528·1	363	241·1	45·7%
Grenada	..	7	..	..	..	1	..	..	..	..	..	0	0	275	2631·9	183	1751·4	66·5%
Iran	6434	..	0·79%	89·01	..	678	..	..	23	23	0·00000%	620	8·2	93937	1269·9	18207	246·1	19·4%
Jamaica	..	125	..	..	..	13	..	..	..	..	..	0	0	1664	615·8	966	357·5	58·1%
Jordan	135	..	0·42%	23·10	..	14	..	..	..	..	..	60	9·5	8211	1357·9	2053	339·5	25·0%
Kazakhstan	421	..	0·23%	26·57	..	44	..	..	..	..	..	20	1·2	2433	149·1	190	11·6	7·8%
Latvia	221	..	0·60%	98·22	17	..	0·05%	10·4%	4	4	0·00001%	340	153·2	3931	1755·7	585	261·3	14·9%
Lebanon	..	354	..	..	..	35	..	..	..	..	..	60	14·0	5747	1359·4	2594	613·6	45·1%
Libya	..	0	..	..	..	0	..	..	..	..	..	0	0	987	155·3	268	42·2	27·2%
Lithuania	482	..	0·80%	145·07	64	..	0·11%	13·5%	..	..	..	340	104·5	14249	4335·2	2066	628·6	14·5%
Macedonia	51	..	0·23%	24·65	13	..	0·06%	26·2%	..	..	..	40	19·4	1684	817·3	399	193·6	23·7%
Malaysia	..	2490	..	..	..	262	..	..	1222	1222	0·00029%	260	8·9	31175	1097·7	5686	200·2	18·2%
Maldives	..	15	..	..	..	2	..	..	..	..	..	0	0	37	117·1	13	41·2	35·1%
Mauritius	..	104	..	..	..	11	..	..	..	..	..	0	0	567	442·6	91	71·0	16·0%
Mexico*	6133	..	0·40%	54·74	988	..	0·06%	14·6%	3882	3882	0·00024%	560	4·8	79893	704·4	14607	128·8	18·3%
Montenegro	..	49	..	..	..	5	..	..	..	..	..	0	0	..	..	..	..	..
Namibia	..	89	..	..	..	9	..	..	..	..	..	0	0	709	310·5	48	21·0	6·8%
Palau	..	2	..	..	..	0	..	..	..	..	..	0	0	60	2930·8	17	830·4	28·3%
Panama	93	..	0·19%	26·46	..	9	..	..	..	..	0·00000%	20	5·5	2117	602·0	279	79·3	13·2%
Peru	..	1651	..	..	..	162	..	..	..	..	..	300	10·1	4635	159·4	1848	63·6	39·9%

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	2010 or latest year available	Estimates	2010 or latest year available	2010 or latest year available	Millions PPP$	Estimates (millions PPP$)	% of GDP	% of GERD	Public and philanthropic thousands PPP$	Public thousands PPP$ values	Public per GDP (% of GDP)	Estimated number of trials	Estimate per million people	Total	Per million people	Total	Per million people	
(Continued from previous page)																		
Romania	1463	..	0·47%	68·09	169	..	0·05%	11·4%	..	..	..	400	18·8	42 103	1963·9	4062	189·5	9·6%
Russia	32 838	..	1·16%	229·70	1142	..	0·04%	3·5%	..	..	..	820	5·8	264 930	1866·8	16 900	119·1	6·4%
Serbia	746	..	0·92%	75·74	37	..	0·05%	4·9%	..	..	..	280	30·7	18 028	2472·5	4531	621·4	25·1%
Seychelles	..	13	..	..	..	1	..	..	..	..	..	0	0	177	2045·7	53	612·5	29·9%
South Africa	4708	..	0·93%	95·46	703	..	0·14%	14·9%	11 059	10 929	0·00207%	820	16·2	61 312	1226·5	13 454	269·1	21·9%
Saint Kitts and Nevis	..	5	..	..	..	0	..	..	..	..	..	0	0	34	648·8	9	171·7	26·5%
Saint Lucia	..	10	..	..	..	1	..	..	..	..	..	0	0	22	126·4	9	51·7	40·9%
Saint Vincent and the Grenadines	..	7	..	..	..	1	..	..	..	..	..	0	0	11	100·6	3	27·4	27·3%
Suriname	..	25	..	..	..	3	..	..	..	..	..	0	0	80	152·5	38	72·4	47·5%
Thailand	..	3518	..	..	..	371	..	..	2261	2261	0·00038%	420	6·0	36 446	527·3	11 461	165·8	31·4%
Tunisia	1064	..	1·10%	102·67	..	112	..	..	..	..	..	20	1·9	17 303	1640·2	4243	402·2	24·5%
Turkey	9582	..	0·84%	131·71	1832	..	0·18%	20·8%	7	..	0·00000%	380	5·1	168 849	2320·9	67 525	928·1	40·0%
Uruguay	188	..	0·43%	56·09	9	..	0·02%	5·9%	..	..	..	0	0	5125	1526·8	1048	312·2	20·4%
Venezuela	..	2099	..	..	..	205	..	..	..	..	..	20	0·7	11 809	409·6	2498	86·6	21·2%
Total for upper-middle-income countries	277 759	13 073	0·60%	..	16 470	2399	..	10·5%	39 331	39 193	..	5840	2·4	2 226 303	908·1	393 434	160·5	17·7%
Total (data plus estimates)	..	290 831	..	..	..	18 869	..	..	..	..	..	..	..	..	..	..	..	..
High-income countries																		
Andorra	..	0	..	..	..	0	..	..	..	..	..	0	0	38	447·1	20	235·3	52·6%
Australia	19 029	..	2·37%	884·50	3294	..	0·39%	17·3%	18 892	18 781	0·00221%	2500	109·2	323 308	14 498·2	104 170	4671·3	32·2%
Austria	9254	..	2·76%	1102·52	1150	..	0·35%	13·0%	1695	0	0·00000%	1360	161·8	99 810	11 896·6	34 095	4063·9	34·2%
Bahrain†	..	29	..	..	..	5	..	..	..	..	..	20	15·2	1100	871·7	443	351·1	40·3%
Barbados	..	..	..	..	..	..	..	..	..	..	..	0	0·0	569	2003·5	215	757·0	37·8%
Belgium	8154	..	1·99%	761·22	2224	..	0·56%	27·7%	3951	3951	0·00096%	1400	127·9	146 240	13 421·7	46 606	4277·4	31·9%
Brunei†	..	19	..	..	..	3	..	..	..	..	..	20	48·5	419	1050·3	112	280·8	26·7%
Canada	23 970	..	1·80%	704·66	5513	..	0·43%	22·5%	8003	7995	0·00060%	2920	84·1	478 525	14 022·2	143 052	4191·9	29·9%
Croatia	630	..	0·73%	143·18	126	..	0·14%	17·0%	..	..	..	160	36·4	24 708	5592·6	5835	1320·7	23·6%
Cyprus	124	..	0·50%	112·15	7	..	0·03%	5·6%	..	..	..	0	0·0	4487	5582·3	711	884·6	15·8%

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	2010 or latest year available	Estimates	2010 or latest year available	2010 or latest year available	Millions PPP$	Estimates (millions PPP$)	% of GDP	% of GERD	Public and philanthropic thousands PPP$	Public thousands PPP$ values	Public per GDP (% of GDP)	Estimated number of trials	Estimate per million people	Total	Per million people	Total	Per million people	
(Continued from previous page)																		
Czech Republic	4152	..	1·61%	395·67	364	..	0·14%	9·1%	..	..	..	1360	128·7	72 224	6865·5	11 778	1119·6	16·3%
Denmark	6816	..	3·06%	1228·07	1892	..	0·89%	29·2%	6073	6073	0·00273%	1560	279·5	102 128	18 409·1	36 243	6533·0	35·5%
Equatorial Guinea†	..	23	..	..	..	4	..	..	..	..	..	0	0·0	32	45·7	18	25·7	56·3%
Estonia	443	..	1·60%	330·59	39	..	0·14%	8·8%	..	..	..	300	224·5	9870	7364·8	1676	1250·6	17·0%
Finland	7589	..	3·88%	1414·61	612	..	0·32%	8·2%	61	61	0·00003%	920	170·6	91 056	16 977·4	29 623	5523·2	32·5%
France‡	49 991	..	2·26%	796·19	7479	..	0·34%	15·2%	37 125	35 295	0·00159%	4160	62·9	581 615	8937·5	148 462	2281·4	25·5%
Germany	86 210	..	2·82%	1047·47	12 729	..	0·43%	15·3%	35 515	35 435	0·00116%	4840	59·5	809 704	9901·4	230 941	2824·0	28·5%
Greece*‡	1814	..	0·56%	160·32	160	..	0·05%	8·8%	..	..	..	800	70·5	88 225	7796·8	31 185	2756·0	35·3%
Hungary	2383	..	1·16%	238·67	592	..	0·29%	25·1%	..	..	..	1340	134·6	51 486	5148·6	11 291	1129·1	21·9%
Iceland	334	..	2·64%	1073·79	128	..	1·01%	32·3%	..	..	..	40	123·0	5744	18 060·6	1943	6109·3	33·8%
Ireland	3246	..	1·79%	726·19	592	..	0·33%	19·1%	5758	5758	0·00318%	540	118·0	50 218	11 223·5	14 960	3343·5	29·8%
Israel	9589	..	4·40%	1292·63	998	..	0·49%	10·9%	..	..	..	1140	144·7	114 256	14 987·1	34 459	4520·0	30·2%
Italy	24 269	..	1·26%	400·81	3642	..	0·19%	14·8%	1437	1437	0·00007%	3480	57·4	449 421	7430·5	149 161	2466·1	33·2%
Japan	137 314	..	3·36%	1085·04	18 439	..	0·45%	13·4%	6659	6659	0·00015%	4720	37·2	767 178	6019·4	209 132	1640·9	27·3%
Kuwait	..	150	0·11%	..	..	26	..	..	32	32	0·00002%	0	0·0	6000	2192·4	2356	860·9	39·3%
Liechtenstein	..	0	..	..	..	0	..	..	..	..	..	0	0·0	356	10171·4	112	3200·0	31·5%
Luxembourg	713	..	1·63%	1405·26	40	..	0·10%	5·9%	1415	1415	0·00324%	0	0·0	3126	6166·3	978	1929·2	31·3%
Malta	68	..	0·62%	163·59	13	..	0·13%	23·2%	..	..	..	0	0·0	936	2250·0	327	786·1	34·9%
Monaco	..	0	..	..	..	0	..	..	..	..	..	0	0·0	643	17 520·4	218	5940·1	33·9%
Netherlands	12 822	..	1·83%	771·82	3378	..	0·50%	27·3%	17 546	16 349	0·00233%	2780	165·4	263 335	15 848·9	101 613	6115·6	38·6%
New Zealand	1646	..	1·30%	380·88	239	..	0·19%	14·7%	1281	1281	0·00097%	700	157·1	61 070	13 981·9	16 795	3845·2	27·5%
Norway	4742	..	1·69%	971·18	875	..	0·33%	18·6%	9254	9254	0·00331%	640	129·2	76 789	15 705·7	25 232	5160·7	32·9%
Oman†	..	73	..	..	..	13	..	..	..	..	..	20	6·9	3275	1177·0	838	301·2	25·6%
Poland	5588	..	0·74%	145·98	540	..	0·07%	11·1%	..	..	..	1320	34·6	162 025	4243·3	28 394	743·6	17·5%
Portugal	4305	..	1·59%	403·22	573	..	0·22%	13·2%	155	0	0·00000%	540	50·8	68 875	6474·8	11 088	1042·4	16·1%
Qatar†	..	132	..	..	..	23	..	..	..	..	..	40	21·4	1932	1098·5	762	433·3	39·4%
San Marino	..	0	..	..	..	0	..	..	..	..	..	0	0	22	733·3	9	300·0	40·9%
Saudi Arabia	504	..	0·08%	18·78	..	87	..	..	..	..	..	80	2·8	22 415	816·6	7514	273·8	33·5%
Singapore	5776	..	2·27%	1167·85	841	..	0·34%	14·6%	..	..	..	380	73·3	71 047	13 994·7	13 342	2628·1	18·8%
Slovakia	800	..	0·63%	146·39	75	..	0·06%	9·3%	..	..	..	280	51·4	25 181	4637·3	3358	618·4	13·3%
Slovenia	1162	..	2·11%	572·51	248	..	0·45%	24·1%	..	..	..	200	97·3	26 084	12 732·7	5027	2453·9	19·3%

(Continues on next page)

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	GERD total in millions current PPP$		GERD as a % of GDP	GERD per person	Health GERD 2010 or latest year				Neglected diseases research investments			Ongoing clinical trials		Publications in all fields 2002–11		Health publications 2002–11		Pro-portion of pub-lications in health (%)
	2010 or latest year available	Estimates	2010 or latest year avail-able	2010 or latest year available	Millions PPP$	Esti-mates (millions PPP$)	% of GDP	% of GERD	Public and philan-thropic thousands PPP$	Public thousands PPP$ values	Public per GDP (% of GDP)	Esti-mated number of trials	Esti-mate per million people	Total	Per million people	Total	Per million people	
(Continued from previous page)																		
Spain	20386	..	1·37%	442·44	3827	..	0·26%	18·6%	16001	14656	0·00100%	3920	84·2	364508	7911·9	88061	1911·4	24·2%
South Korea	53185	..	3·74%	1103·80	5758	..	0·40%	10·8%	1977	1968	0·00014%	1560	31·7	306150	6196·1	66324	1342·3	21·7%
Sweden	12536	..	3·43%	1336·46	2177	..	0·63%	17·4%	15053	15053	0·00408%	1600	168·8	182039	19411·0	65057	6937·1	35·7%
Switzerland	10525	..	2·99%	1389·80	4237	..	1·16%	40·3%	20240	9306	0·00256%	700	88·9	190785	24377·9	59991	7665·5	31·4%
The Bahamas†	..	10	..	..	..	2	..	..	..	..	..	0	0	125	364·6	38	110·8	30·4%
Trinidad and Tobago	18	..	0·05%	13·57	0	..	0%	2·3%	..	..	..	0	0	1524	1136·1	561	418·2	36·8%
United Arab Emirates†	..	341	..	..	..	59	..	..	..	..	..	40	5·1	7179	955·7	1899	252·8	26·5%
UK‡	39138	..	1·76%	630·89	12123	..	0·57%	30·7%	241730	161552	0·00727%	4840	76·9	851193	13677·9	270265	4342·9	31·8%
USA§	401576	..	2·86%	1305·15	118844	..	0·84%	29·4%	1852183	1389411	0·00962%	14300	44·9	3163533	10226·4	1033452	3340·7	32·7%
Total for high-income countries	970800	778	1·88%	..	214182	222	..	17·0%	2302037	1741722	..	42300	37·2	10132508	9283·8	3049742	2794·3	30·1%
Total (data plus estimates)	..	971578	..	..	..	214404	..	..	..	..	..	..	..	..	..	..	..	..
Overall totals																		
EU-27 total	304753	..	1·91%	..	54808	..	..	18·0%	383518	297039	..	19600	38·8	4583569	9130·6	1329829	2649·0	29·0%
USA	401576	..	2·86%	..	118844	..	..	29·6%	1852183	138941	..	14300	44·9	3163533	10226·4	1033452	3340·7	32·7%
Other high-income countries total	267263	778	2·49%	..	40862	222	..	15·3%	66339	55276	..	12500	39·4	2465189	7836·9	695390	2210·7	28·2%
BRICS total	275585	..	1·39%	..	17501	..	..	6·4%	97385	97255	..	5380	1·8	1812690	614·6	267055	90·5	14·7%
Others total	39112	19969	0·46%	..	3744	3690	..	12·4%	18589	18582	..	2940	1·0	898563	333·6	228530	84·8	25·4%
Total for all countries	1288989	20746	1·77%	..	235760	3912	..	18·0%	2418015	1857563	..	47620	6·8	12923544	1909·3	3554256	525·1	27·5%
Total for all countries (data plus estimates)	..	1309735	..	..	..	239672	..	..	..	..	..	..	..	..	..	..	..	..

Nauru is not classified by the World Bank. South Sudan is not included because it was not a member state of the United Nations in 2010. GERD=gross domestic expenditure on research and experimental development. PPP=purchasing power parity. GDP=gross domestic product. BRICS=Brazil, Russia, India, China, and South Africa. *Brazil, India, China, Mexico, and Greece's very broad health GERD estimates are based on health research and development intensity in earlier years. †Health GERD for large oil-producing economies is based on the average proportion of GDP invested in research and development in Kuwait and Saudi Arabia. ‡France, Greece, and the UK are partially based on funder-reported data. §Health GERD data for the USA from 2008 from recently improved surveys.

Table 3: **Country health research and development indicators**

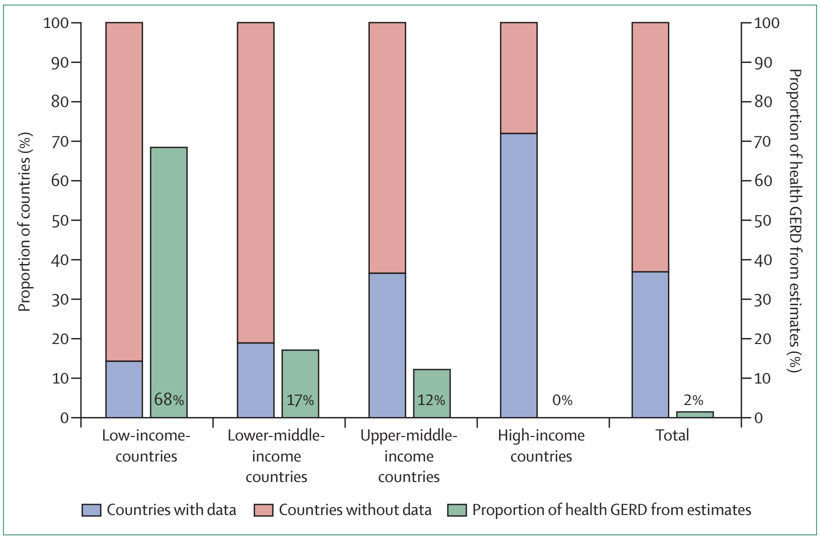

***Figure 1:* Data availability for health research and development investments in international databases**
Proportion of countries with and without data for health research and development investments and proportion of total health research and development investments (health GERD) based on indirect estimates in the four different income groups of countries. GERD=gross domestic expenditure on research and experimental development.

than 3·0; type II diseases at least 3·0 to less than 35·0; and type III diseases at least 35·0 (table 2). This approach is useful because it allows for the development of indicators that show how much R&D is being done for diseases whose burden lies mainly in low-income and middle-income countries, in high-income countries, or in both, which lies at the heart of the problem of inequities in the global distribution of health R&D. To exemplify this idea, we applied this approach to our analyses of the global distribution of clinical trials. The cutoff points suggested here are not intended to be prescriptive and were chosen to enable categorisation of diseases in a transparent manner. We would suggest that they form the basis for further discussion and refinement of this categorisation.

Data availability

Substantial information gaps were apparent for all the assessed health R&D indicators, especially for and in low-income and middle-income countries, where disease burden is greatest. The availability of data for countries' investments—ie, what they report and how comprehensively and what is available in international databases—in R&D in general and in health R&D varied widely (table 3). Data for health R&D investments were found for only 37% of all countries. Data availability for this indicator was particularly poor for low-income countries, lower-middle-income countries, and upper-middle-income countries (14%, 19%, and 37%, respectively) and was much better for high-income countries (72%). Countries with small populations account for most of the missing data for high-income countries. Since the high-income countries with large populations contribute most financially to R&D in both relative and absolute terms, the proportion of estimated total health R&D investments that had to be extrapolated was low: only 2% (figure 1).

For the other indicators assessed—clinical trials and publications—important information gaps also exist. Although clinical trials registration is now broadly considered an ethical and scientific responsibility, caveats remain in the enforcement of trial registration, mainly in low-income and middle-income countries.[23] The sample we used in Thomson Reuters' Web of Knowledge database covers 2956 peer-reviewed journals; however, its coverage of national journals in the native language addressing problems of local interest is incomplete, and a linguistic bias exists in access to publication in English language journals for authors from low-income and middle-income countries.[25]

R&D investments

We estimated the global total investment in health R&D (both public and private sector) to be roughly $240 billion purchasing power parity-adjusted dollars in 2009, with 89·5% ($214 billion) coming from high-income countries, 7·9% ($19 billion) from upper-middle-income countries, 2·6% ($6·2 billion) from lower-middle-income countries, and only 0·1% ($0·2 billion) from low-income countries (table 3). The countries contributing the most in absolute terms were the USA ($119 billion), Japan ($18 billion), Germany ($13 billion), and the UK ($12 billion). The countries contributing the most in relative terms as a proportion of GDP were Switzerland (1·16%), Iceland (1·01%), Denmark (0·89%), the USA (0·84%), and Sweden (0·63%). In general, countries' investments in health research were related to their wealth (GDP per person; figure 2A).

Calculation of disaggregated estimates for health R&D expenditure funded by business, public, and other sources could only be done for a small subset of mainly high-income countries. The countries for which these values could be estimated contributed 90% of all health GERD. In the high-income countries combined, about 60% of health R&D expenditure came from the business sector, 30% from the public sector, and 10% from other sources (including private non-profit organisations). The relative proportions of funding sources vary substantially between countries (figure 3). As is the case for total health R&D investments, publicly funded health R&D largely corresponded to countries' wealth (figure 2B).

Clinical trials and publications

We assessed the volume of ongoing global clinical trial activity—ie, the number of actively recruiting trials registered on the International Clinical Trials Registry Platform, and the number of publications in health journals indexed by Web of Science. Denmark, Estonia, Finland, Sweden, and the Netherlands had the highest number of trials per person, whereas Switzerland, Sweden, Denmark, the Netherlands, and Iceland ranked

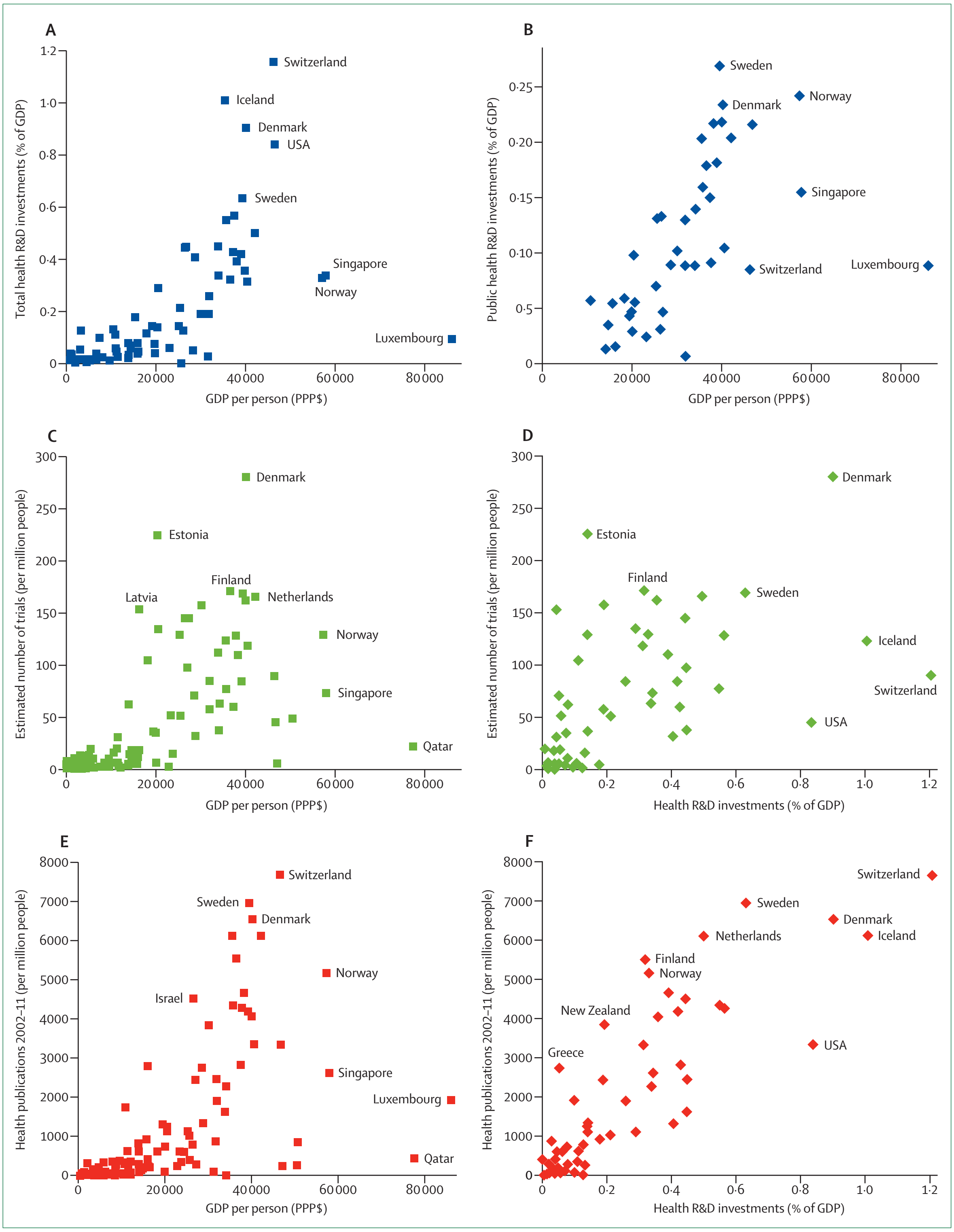

Figure 2: **Health R&D investments, clinical trials, publications, and wealth**

(A) Total health R&D investments related to GDP per person (2010) in 70 countries. (B) Publicly (government) funded health R&D investments related to GDP per person (2010) in 44 countries. (C) Estimated number of ongoing clinical trials on the International Clinical Trials Registry Platform per million people (2012) related to GDP per person (2010) in 103 countries. (D) Estimated number of ongoing clinical trials on the International Clinical Trials Registry Platform per million people (2012) related to total health R&D investments (2010 or 2009) in 56 countries. (E) Number of publications in health-related journals in 2002–11 related to GDP per person (2010) in 174 countries (data from Thomson Reuters: Web of Science [Evidence]). (F) Number of publications in health-related journals in 2002–11 related to total health R&D investments (2010 or 2009) in 70 countries. R&D=research and development. GDP=gross domestic product. PPP$=purchasing power parity-adjusted dollars.

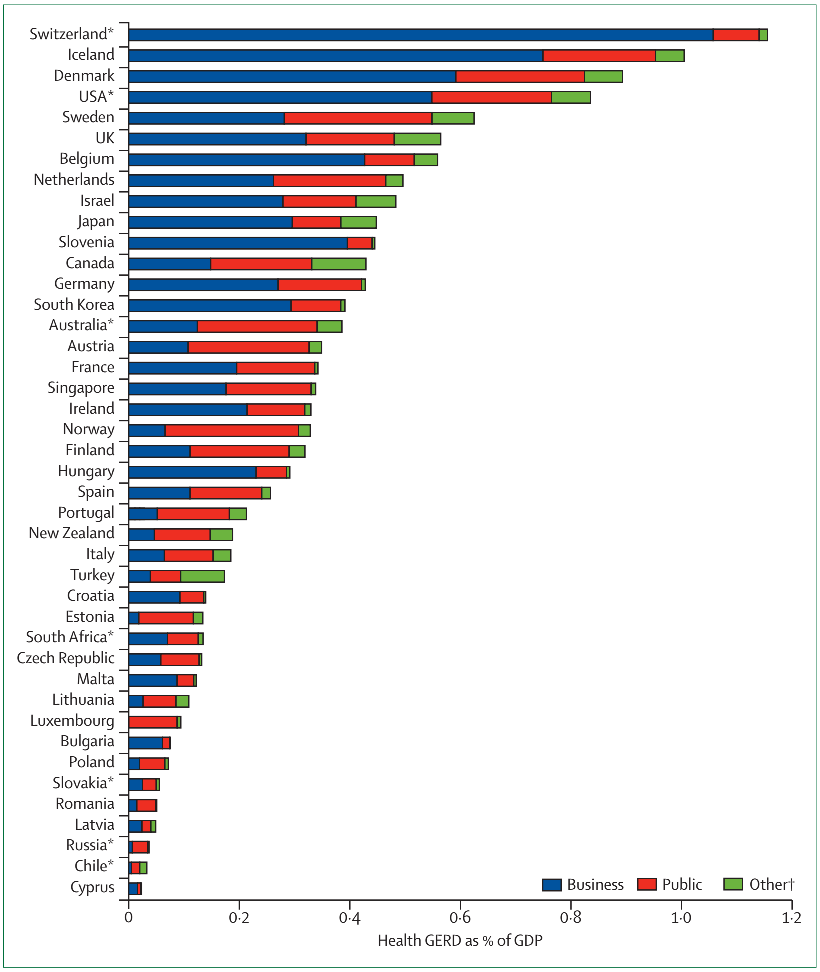

***Figure 3:* Health GERD by estimated broad funding source**

Data are from 2009 unless indicated otherwise. GERD= gross domestic expenditure on research and experimental development. GDP=gross domestic product. *Indicates data from different years: Slovakia 2010; Russia 2009–10; Australia and South Africa 2008–09; Switzerland, USA, and Chile 2008. †"Other" encompasses estimated research and development funds received by government, higher education, and private non-profit institutions from higher education (including the institutional funds of private universities), private non-profit organisations, and from abroad.

highest for publications per person (table 3). An association was noted between both ongoing trials and number of publications and a country's wealth (figures 2C and 2E). Similarly, a link was reported between a country's health R&D investments and both ongoing trials and the number of publications (figures 2D and 2F).

R&D profiles

Many of the health R&D indicators were linked to wealth—ie, the richer the country, the greater their R&D investments, volume of ongoing clinical trials, and number of publications. However, some indicators seemed to be less dependent on country income than others. Although a weak relation was noted between wealth and health R&D investments as a proportion of total R&D investments, with richer countries usually investing relatively more on health research than poorer countries, this proportion varied widely (figure 4A). Similarly, no strong association was reported between a country's wealth and the proportion of publicly funded health R&D (figure 4B). This finding shows the role of private sector health R&D investments in individual countries (figure 3), notably the pharmaceutical industry, and suggests that variations exist that depend on countries' industrial structures, on past and present political decisions, and on the priorities of governments and multinational corporations. No clear relation was recorded between a country's wealth and the proportion of health-related publications as a total of all research publications (figure 4C). Countries seem to have different health R&D profiles: in some countries, health R&D constituted a small proportion of the total R&D investments, but health publications constituted a large share of publications, and vice versa (figure 4D).

Research to address unmet needs

Available data and indicators for assessment of countries' contributions to the health R&D needs of low-income and middle-income countries are scarce. One method to assess this factor is to study countries' investments in R&D aimed at developing health products for neglected diseases as defined by the G-FINDER report.[19] Global public and philanthropic investments for neglected disease R&D were $2·4 billion purchasing power parity-adjusted dollars in 2010, which is roughly 1% of total global health R&D investments (table 3). Countries' public investments in neglected disease R&D varied greatly, and no clear association was reported between countries' wealth or public health R&D investments and the amount of investment in neglected disease R&D, indicating that different countries set different priorities (figures 5A and 5B).

The distributions of ongoing clinical trial research and health-related publications are alternative measures to assess what health R&D is being prioritised. We analysed the number of trials relative to the burden of disease. There were more trials for non-communicable diseases than for infectious diseases and injuries, and more trials for type I diseases than for type II and type III diseases—both by a factor of 7–8 when measured in proportion to the burden of disease. Similarly, more trials recruited in high-income countries than in low-income and middle-income countries (table 4). The proportion of health-related publications with authors from high-income countries was 84% in 2011, an 8% decrease compared with 2002 when the proportion was 92%; 18% and 4% for upper-middle-income and lower-middle-income countries—10% and 2% increases from the 2002 values, respectively; and less than 1% for low-income countries, which was similar to the proportion in 2002 (figure 6).

Investments compared with norms

The Consultative Expert Working Group report concluded with recommendations about countries' investment

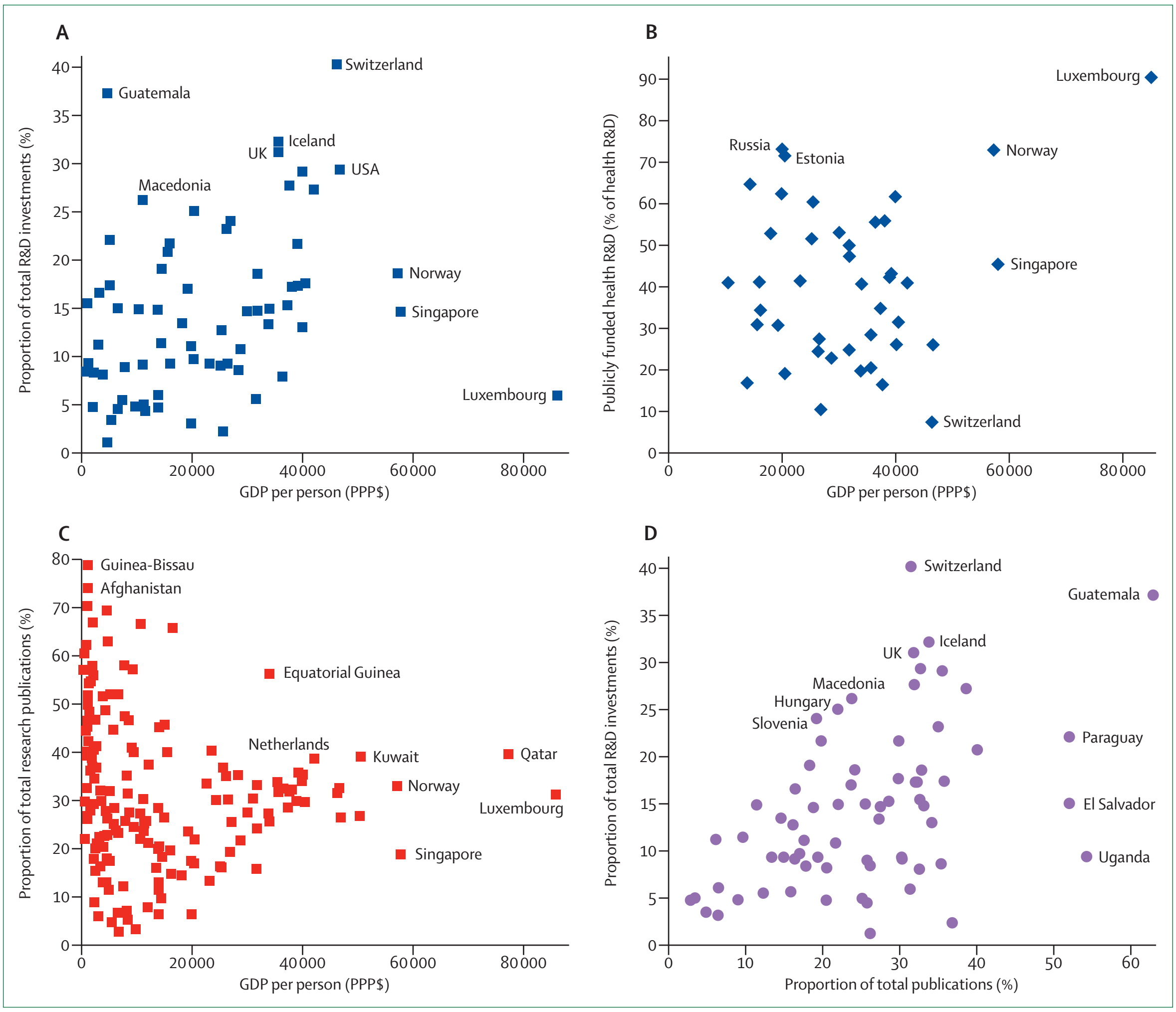

Figure 4: **Health R&D investments and publications as proportion of total**
(A) Health R&D investments as proportion of total R&D investments related to GDP per person (2010) in 70 countries. (B) Proportion of publicly funded health R&D investments related to GDP per person (2010) in 41 countries. (C) Number of publications published in health-related journals in 2002–11 as a proportion of the total number of publications related to GDP per person (2010) in 174 countries (data from Thomson Reuters: Web of Science [Evidence]). (D) Proportion of total R&D investments for health in relation to proportion of total publications in health. R&D=research and development. GDP=gross domestic product. PPP$=purchasing power parity-adjusted dollars.

levels in health R&D.[1,11] Governments in developing and developed countries were recommended to invest 0·05–0·1% and 0·15–0·2% of GDP on total health R&D, respectively, and at least 0·01% on research on products to meet the specific health needs of developing countries. These targets are roughly in line with the 2% target of governmental health expenditures proposed by the Commission on Health Research for Development and later endorsed by the World Health Assembly.[3,26]

We compared countries' public investments to these targets, recognising the caveats regarding the sporadic nature of the available data (figure 5C). Based on available evidence, the data show large variations and many countries do not meet the targets. Several countries are meeting the general recommendation of investing at least 0·15–0·2% of GDP on total health R&D, but many do not. Notable differences also exist between countries' contributions towards neglected disease R&D when compared with total public health R&D investments.

Persistent R&D gaps

Global investments in health R&D are increasing and reached $240 billion purchasing power parity-adjusted dollars in 2010, with $26 billion of this amount spent in low-income and middle-income countries. Estimates of the global total of health R&D investments have been reported at intervals from 1986 (US$30 billion invested, of which $1·6 billion was devoted to the health problems in low-income and middle-income countries) through to 2005 ($160 billion invested, including $5 billion in low-income and middle-income countries).[3,21,22,27–30] However, despite this overall growth in health R&D, our findings show a persistent imbalance between R&D investments and needs-based priorities as measured by all R&D indicators (research inputs, processes, and outputs). R&D investments in neglected disease research account for only 1% of overall health R&D investments; proportions of ongoing clinical trials addressing type II and III diseases are low; and the geographical distributions of health R&D investments, clinical trial research, and health research publications are heavily skewed towards high-income countries.

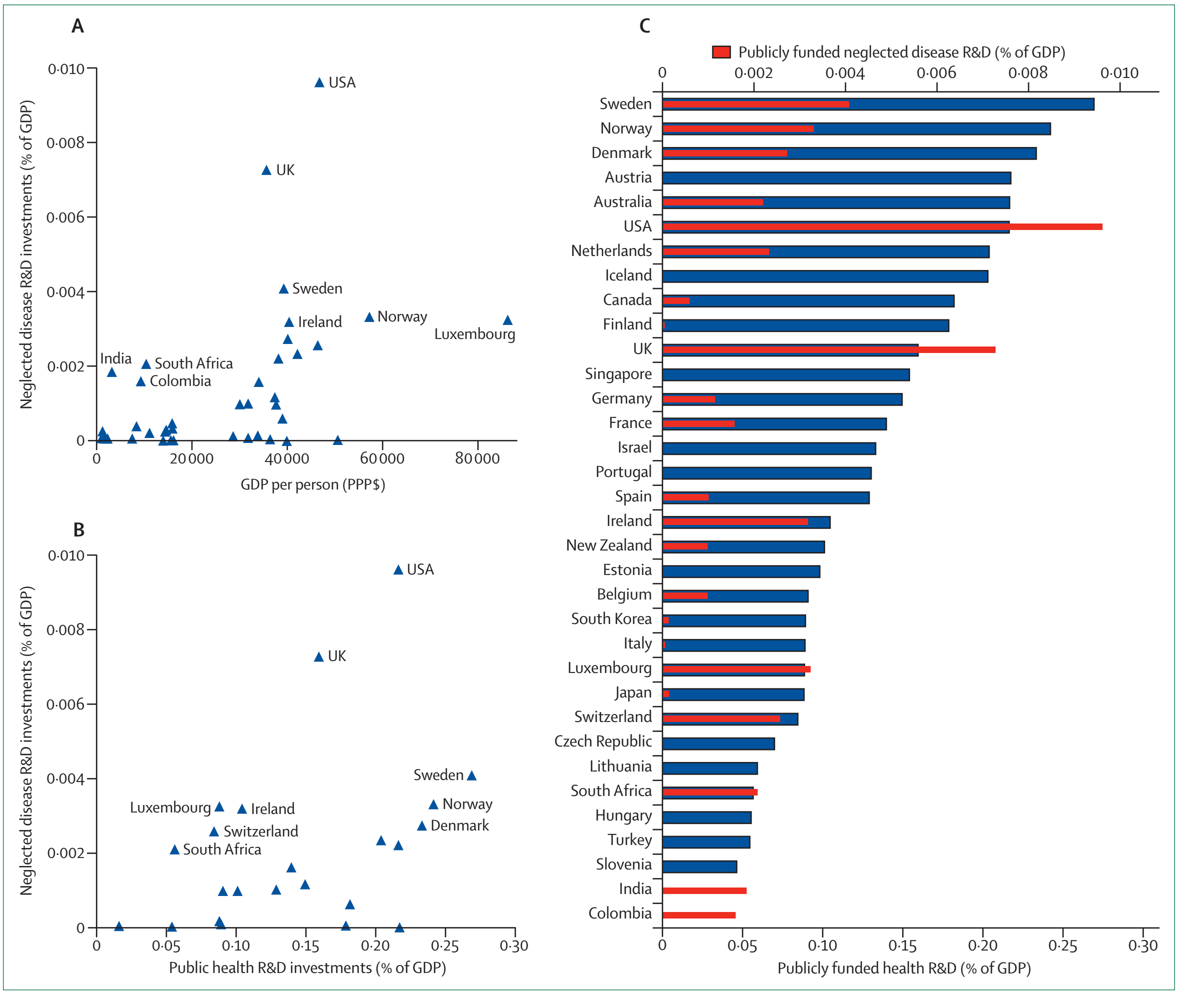

Figure 5: **Investments in neglected disease R&D**
(A) Investments in neglected disease R&D in 2010 related to GDP per person (2010) in 38 countries (data from G-FINDER report).[19] (B) Investments in neglected disease research in 2010 related to total public investments in health R&D (2009–10) in 24 countries. (C) Comparison of public investments in total health R&D (blue bars, lower x-axis) and in neglected disease R&D (red, narrow bars, upper x-axis) in 34 countries. R&D=research and development. GDP=gross domestic product. PPP$=purchasing power parity-adjusted dollars.

	Disease group			Disease type			Country of recruitment			
	NCDs	Communicable, maternal, perinatal, and nutritional disorders	Injuries	Type I	Type II	Type III	High-income countries	Upper-middle-income countries	Lower-middle-income countries	Low-income countries
Estimated number of trials per million DALYs	52·4	7·4	6·0	45·7	6·1	5·5	292·7	13·4	3·0	0·8
Proportion of all trials	87·3%	10·1%	2·6%	89·0%	9·1%	1·9%	89·0%	12·3%	4·7%	0·6%
Estimated number of trials per million people	..	..	..	..	..	..	37·2	2·4	0·9	0·3

Percentages in the table do not add up to 100% because categories are not mutually exclusive. NCD=non-communicable disease. DALY=disability-adjusted life-year.

Table 4: **Distribution of clinical trials in the WHO International Clinical Trials Registry Platform**

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Thus, although the nature of the 10/90 gap has changed since the 1990s, the gap itself very much remains.[3,12]

Since most health research indicators are related to a country's wealth, economic development might gradually improve the situation and start to rectify inequities. However, investments in health and in health R&D are important drivers and requirements for economic development.[15] Investments in health R&D for unmet health needs are necessary to meet the goal of universal health coverage, which poses challenges at three different levels. The first is to achieve universal coverage of existing health interventions,[31] which needs improved delivery and investments in health systems and health services research, including the growing area of implementation research.[32] The second challenge is to devise ways to treat patients and avert disease burden that are more effective or less costly than available interventions, which necessitates investments in clinical and behavioural research.[13] The third challenge is to discover and develop new technologies that address unmet health needs.[5] Balanced investments in these different domains of health research are prerequisites to achieve universal health coverage.

In view of the universality of health, most new knowledge that results from health R&D can be thought of as a shared global public good.[11,33] Since existing incentive systems do not generate sufficient R&D to address the needs of low-income and middle-income countries, the public sector needs to play an active part by contributing to R&D that is relevant to the needs of these countries. Given a basic level of capacity, countries also have the potential to benefit extensively from each other's contributions. Countries' prioritisation of health R&D over other R&D areas varies widely. We believe that globally agreed norms might be necessary to secure collective action, especially to meet the needs identified by the Consultative Expert Working Group. Investments at comparable levels, with each country contributing to global health R&D, would aid the conceptualisation of health R&D as a collectively shared public good.[11,33] Monitoring of countries' contributions towards health R&D is crucial to ensure that the output is truly a shared public good, and that countries are able to account for their investment strategies.[30,34] Furthermore, as our analyses show, although wealth is a predictor for the size of a country's national health research portfolio, it is not a predetermining factor for the shape of the national health research portfolio. These interesting differences suggest that strategic or policy decisions have been made, and are available to countries to orientate their R&D towards health priorities.

Existing information gaps

We have proposed a set of health R&D indicators to allow for better monitoring and analysis of existing priorities and of countries' performance. A broad set of indicators allows for a triangulation approach, in which different types of information provide different windows of understanding into the R&D landscape. However, several challenges persist in data availability and applicability for collation of such a set of indicators.

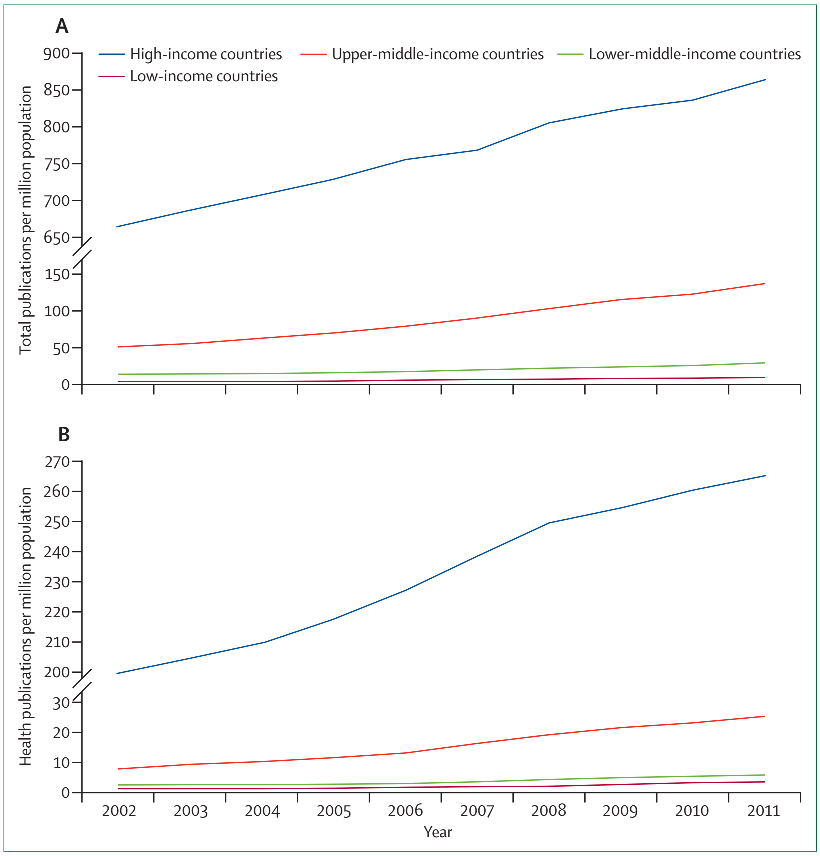

Figure 6: **Trends in annual publication outputs, 2002–11**
(A) Trends in annual number of total scientific publications in 2002–11 in different income groups. (B) Trends in health-related publications in 2002–11 in different income groups. Note the break point in the vertical axis on each graph. Data taken from Thomson Reuters: Web of Science (Evidence).

Data sources for monitoring of health R&D are collected mainly by regional or other international economic organisations and by national statistics offices. Thus, indicators mostly have an economic investment focus. No international efforts are assessing the R&D landscape from a health sector perspective. The Organisation for Economic Co-operation and Development and Eurostat have the most comprehensive survey to collect national investment data, but many countries do not report the full dataset. Consequently, the estimation of health R&D expenditures for a given year is laborious and imprecise. Preparations are underway to revise the Frascati Manual, and the needs of national health R&D policy makers should be included in the updated framework for international surveys and in the guidelines for health accounts.[20]

For non-Organisation for Economic Co-operation and Development countries, the available data for R&D investments are sporadic, incomplete, and inconsistent.

Our estimates for countries such as Brazil, India, and China are uncertain and are based on data collected several years ago. These countries seem to have increased their investments in health R&D recently, and our estimates should therefore be interpreted with caution. R&D in the Americas is covered by the regular surveys of the Ibero-American and Inter-American Network for Science and Technology Indicators. No regular, comprehensive reports yet exist that detail health-related R&D investments for countries in Africa or Asia. However, R&D and innovation surveys are planned through the African Science, Technology and Innovation Indicators Initiative, and an African Observatory for Science, Technology and Innovation is in development to provide regular reporting.[35]

More generally, access to all health R&D data sources remains incomplete, particularly in poor countries where the need for such information is the greatest. Capacity to collate and manage these data sources needs to be supported, combined with appropriate incentives to provide the data with a minimum additional burden. Incentives should be created for researchers, research institutions, and research funders to contribute information.

Our proposed set of indicators can be used at the most aggregated level—ie, total health R&D in a country and its main general sources. However, funding allocation decisions that affect health R&D are made at lower levels—eg, within a disease area, within one domain of health R&D, and by different public and private sector participants. Thus, the potential for further disaggregation of information is important and needs agreement on a common health R&D classification system. Although efforts are underway to better align these classification systems across countries,[36] and new initiatives to map existing classification systems to a common standard are in development,[18] no international standards for health R&D classification yet exist.[18]

Notwithstanding these challenges, accessibility to data for health R&D has increased greatly in recent years. Our analysis was undertaken without new surveys being done, and took advantage of online resources and databases such as the Organisation for Economic Co-operation and Development and United Nations Educational, Scientific and Cultural Organization Institute for Statistics databases, the International Clinical Trials Registry Platform, and Web of Science. However, these related sources of information are fragmented and need standardised linkages, because all sources of information have their own strengths and weaknesses (table 1). Triangulation—bringing together of several indicators—would allow mitigation of some of these limitations.

A global observatory on health R&D

The creation of a global observatory on health R&D, as recommended by the Consultative Expert Working Group and outlined in a draft resolution for discussion at the 66th World Health Assembly in May, 2013, could address the information gaps.[1,37,38] The functions of such an observatory could include monitoring and reporting of financial flows in support of global health needs; integration of information about R&D financial flows with product pipelines and other resources that support innovation and access to medical technologies; provision of information, reports, and analyses to inform policy makers, funders, researchers and benchmark activities and guide R&D priority setting, with a special focus on low-income and middle-income countries and their health needs; creation of a space to convene stakeholders; initiation of collecting, disseminating, and developing good practices, norms, and standards; and provision of support nationally to build capacity in the monitoring, stewardship, governance, and management of health R&D and innovation. Together, these functions would be expected to lead to improved mechanisms for R&D priority setting and decision making, and to greater efficiency in innovation through enhanced transparency on existing R&D efforts.[12] In Europe, Orphanet, funded jointly by the European Commission, the French National Institute of Health and Medical Research, and the French Directorate General for Health, provides a recent example of how a portal with observatory functions can add value to research, diagnosis, product development, and treatment in a defined disease area, such as orphan diseases.[39]

Substantial technical challenges exist in the establishment of such an observatory, and to add value, a global platform of this type requires long-term commitment and sustainable sources of support. Past efforts, such as the Global Forum for Health Research's monitoring functions, were unsustainable. The development of a global observatory could be approached in a phased manner, and initial research would need to be done to understand user needs (eg, governments, researchers, research funders, civil society, and the private sector); identify the incentives needed to generate support for the initiative; and analyse how existing initiatives might be complemented, integrated, or scaled up to meet requirements. Assessment of the costs of a global observatory needs more work, but the costs of such work would be modest compared with the potentially beneficial ramifications if R&D coordination is improved.[1]

Any global observatory needs to build on the principle of data harvesting whenever possible, rather than being the primary collector or generator of data. It should collaborate, as appropriate, with the Organisation for Economic Co-operation and Development, Eurostat, or the United Nations Educational, Scientific and Cultural Organization to assess and improve existing survey methodology with respect to the needs of the health sector. As indicated by the scarce data available in poor countries, efforts to improve global monitoring and reporting should also rely on supporting capacity at the country level to manage national health R&D portfolios. Whereas technical support to undertake research is available in research institutes or academic units, far fewer resources are available to support national research governance capacity. Work is being undertaken by the Council on Health Research for Development through Health Research Web to create a platform to allow reporting of a range of data related to health research, including financing, and to support the management of research portfolios.[40] This approach should also be seen in conjunction with efforts by the United Nations Educational, Scientific and Cultural Organization to introduce and improve R&D surveys in low-income countries. The identification of a package of support for countries to develop their own observatories and manage their own R&D programmes could create both the necessary incentives for enhanced reporting of data, and a way for countries to engage in supporting the development of a global observatory.

Conclusions

The persistent nature of the gap between health R&D needs and the R&D that is presently funded and undertaken calls for managed approaches to the allocation of scarce health research resources. Health R&D funders, both public and private, should be able to access appropriate and accurate information about health R&D inputs, processes, and outputs. To achieve this aim, national, regional, and global monitoring of health R&D must be strengthened.[38] A global observatory on health R&D would be helpful, and could ultimately enable adequate financing for priority areas, aid efficient use and targeting of low resources, and improve investment decisions through avoidance of duplication and improvement in coordination. Increased transparency would enable countries to be accountable for public investments in health R&D and make knowledge more widely available so that researchers can more easily identify research projects that are similar to their own and make incremental improvements to existing research. Recent negotiations at WHO suggest that member states are supportive of a global observatory on health R&D,[41] which is an encouraging development for global health equity and the achievement of universal health coverage. These plans should now be implemented to secure a sustainable solution for regular mapping of health R&D.[42]

Contributors

J-AR and RFT coordinated the collaboration, data collection, and analyses. SR and ME identified data sources and collected data for research investments. AJY advised on the methodology and analysis of the health GERD data. RFV analysed clinical trials data. J-AR, CÅ, JG, DE, SAM, and RFT contributed to the design of the study and the writing of the report. All authors contributed to and approved the final report.

Conflicts of interest

We declare that we have no conflicts of interest.

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