Biomedical Research and the Regional Burden of Disease

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Abstract
Most biomedical research is carried out in developed countries that have relatively low mortality rates among both adults and children, and its subject profile tends to reflect the pattern of the burden of disease in those countries. This is very different from that prevailing world-wide, where communicable diseases still account for over 40% of the burden – although this is decreasing – and the imbalance has been the subject of criticism by bodies such as the Global Forum for Health Research. This study sought to investigate whether the distribution of research outputs during the last eight years in the 14 individual world regions, as defined by the World Health Organization, reflected the burden of 13 specific diseases. These were based on careful definitions of filters that selectively identified relevant papers in the Science Citation Index. Time trends in research were examined to see if there was progress towards a more equitable distribution of effort.

Introduction: the burden of disease

Countries carry out biomedical research primarily in order to support the provision of clinical care to their citizens, either directly through the acquisition or application of up-to-date knowledge or through the underpinning of medical education in universities. Ideally, one would expect the balance of research effort to reflect the local burden of disease, so that tropical countries, for example, would emphasise research on the diseases endemic to their regions and do relatively less on ones that are rarely encountered. There have been some studies of this relationship, which have suggested that the research agenda is driven more by the personal interests of local researchers than the needs of local people (Arunachalam, 1997; 1998). In Canada and the USA however, it has been found (Gross *et al*., 1999; Lamarre-Cliché *et al*., 2001) that the research agenda actually does take account of the burden of disease for north Americans, especially if this is measured in DALYs (*v.i.*). Nevertheless, there have been claims (Marshall, 1997) that it should give greater emphasis to Parkinson's Disease and some of the other degenerative diseases that affect many Americans, rather than to AIDS which was seen as less important nationally. Advocates for diabetes and cardiology research were also active.
This is a complex issue because not only can research in an area such as AIDS benefit work on other communicable diseases (which are often under-researched), but it may also reflect the availability of qualified researchers and of suitable subjects for experiment. Moreover, it can be seen with hindsight that the relatively large US research effort on AIDS in the mid-1990s (the budget was nearly $1.5 billion in 1994) anticipated the huge incidence of the disease in other countries, particularly in sub-Saharan Africa but now also in Asia (UNAIDS, 2004).

On an international level, the Global Forum for Health Research (2004a) has made a powerful case for the distribution of biomedical research by subject to reflect the relative overall burden of disease. It describes the "10-90 gap" that occurs because 90% of world biomedical research (measured by expenditure) is on the diseases, such as cancer and heart disease, that mainly affect only 10% of the world's population, and *vice versa*. This stricture applies with particular force to the 48% of this expenditure (Global Forum, 2004b) incurred by the large pharmaceutical companies, which is essentially directed to the development of new drugs that will sell in the lucrative markets of the USA and Canada, Western Europe and Japan. There are, of course, some notable exceptions to these criticisms, as we shall see. The high relative commitment of the UK to research on malaria, for example, reflects a strong tradition of tropical medicine research stemming from past imperial needs and present eleemosynary policies, especially at the Wellcome Trust (Anderson *et al*., 1996; Marshall, 2000).

Much previous discussion of the relationship between disease burden and research has been based on the budgets allocated to research topics. However these are extremely difficult to determine (Anderson *et al*., 1996), partly because there are so many sources of funding and subject areas overlap,

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currencies alter in relative value and financial years differ. It seems worthwhile, therefore, to see if bibliometrics can provide data that will allow the relationship to be examined between the burden of disease and research commitments, as represented by the numbers of published papers, both world-wide and in particular countries or regions. Such a technique has been used (Lewison *et al*., 2005) for the estimation of the worldwide resources devoted to some specific diseases, including four of the ones studied here.

Measures of the burden of disease need to take account of both disability and premature mortality. One such measure is the Disability-Adjusted Life Year or DALY (Murray and Lopez, 1996). DALYs are the sum of Years of Life Lost (YLLs) and Years of Living with a Disability (YLDs) for a given condition. As measured for the Global Burden of Disease study of the World Health Organization (WHO), YLLs are standardised to take account of the current life expectancy at birth enjoyed by the Japanese (80 years for males, 82.5 for females). They also give a higher weighting to the lives of young adults over those of young children and the elderly, see Figure 1.

Figure 1. Years of Life Lost attributed by WHO to a death at different ages for the Global Burden of Disease study (Murray and Lopez, 1996).

Some other YLL determinations, such as those in Australia, are calculated slightly differently (Mathers *et al*., 1999). YLDs are based on various disabilities being assigned a factor between zero and unity according to severity, for example severe anaemia = 0.1, rheumatoid arthritis = 0.2, deafness = 0.33, blindness = 0.63, quadriplegia = 0.9.

DALYs have been calculated by the WHO for 1990 and for 2000 and allocated to communicable or non-communicable disease areas or to injuries. DALYs can also be attributed to lifestyle factors, such as unsafe sex, or the use of tobacco or alcohol; these three causes were estimated, for example, (WHO, 2002) to be responsible respectively for 6.3%, 4.1% and 4.0% of DALYs in 2000. They can also be allocated geographically by major region. Murray and Lopez (1996) gave breakdowns for eight major world regions; latterly (WHO, 2002) the world has been divided up into 14 regions, based on WHO area offices and five mortality strata, see Table 1.

Methodology: the measurement of disease-related research commitments

The Science Citation Index (SCI) has the great advantage for analytical purposes of including all the addresses on each paper, but it also suffers from some biases against biomedical papers written in languages other than English and not published in the "international" literature. As a result much clinical research, particularly from developing countries, but also from European countries where English is not routinely used for the communication of scientific results (this would exclude Scandinavia), is under-represented. However it is likely that the under-representation will be reasonably uniform as between different subject areas, although those where there is a high proportion of relatively basic research may not suffer so much from the SCI bias.

Table 1. WHO regions used for analysis, with allocation to mortality strata (MS), their populations (million) and GDPs (year 2000, $1995 billion)

Region	**MS**	**Pop, m**	**GDP**	**Region**	**MS**	**Pop, m**	**GDP**
African	D	294	217	European	A	412	10564
	E	346	257		B	218	495
American	A	325	9742		C	243	490
	B	431	1822	South East	B	294	398
	D	71	109	Asian	D	1242	690
Eastern	B	139	505	Western	A	154	6292
Mediterranean	D	343	207	Pacific	B	1533	1914

Mortality strata: A = very low adult and child; B = low adult and child; C = low child, high adult; D = high adult and child; E = high child, very high adult

Accordingly, it is possible to gauge the relative amount of research effort in a country or region on a given subject from a comparison with its total biomedical output of papers in the SCI. The latter is conveniently measured by the application of an address keyword filter to the index; the process is described by Lewison and Paraje (2004). Papers in specific subject areas need to be identified by means of a custom-designed filter, based on specialist journals and title words. This process has also been described in detail (Lewison, 1996), together with methods for the "calibration" of the filter in terms of its precision, *p* (or specificity) and recall, *r* (or sensitivity). Ideally, these coefficients should be close to unity; in practice values over 90% are usually acceptable. In this study, 13 disease areas were chosen for analysis, so as to cover a good range of both communicable and non-communicable diseases and disorders; they are listed in Table 2.

Table 2. List of 13 disease areas selected for study, with the codes used for their "filters" and their precision, *p*, and recall, *r*.

Disease area	**Code**	**p**	**r**	Disease area	**Code**	**p**	**r**
AIDS/HIV research	AIDSR	0.97	0.99	Malaria	MALAR	0.89	0.98
Arthritis & rheumat	ARTHR	0.98	0.88	Multiple sclerosis	MULSC	0.95	0.93
Cardiology	CARDI	0.92	0.88	Oncology	ONCOL	0.95	0.90
Dentistry	DENTA	0.98	0.88	Parkinson's disease	PARKI	0.93	0.76
Dermatology	DERMA	0.81	0.85	Renal medicine	RENAL	0.94	0.94
Diabetes	DIABE	0.97	0.83	Respiratory med.	RESPI	0.97	0.89
Hepatology	HEPAT	1.00	0.99				

Each of the filters was defined by an expert in the subject in partnership with a bibliometrician (the author); this ensured that the definition was accurate. Some of the filters were revised versions, designed to take account of additional specialist journals and new technical terms such as recently-discovered genes.

Relative Commitment (RC) is then the ratio of the percentage of world output from a region in a subject area to its percentage presence in biomedical research. For example, the UK output of biomedical research in recent years is about 10% of the world total, but its output of malaria papers is almost 20% (both measured on an integer count basis), so its RC for malaria research is 2.0.

Results and comments

Biomedical research outputs from the 14 WHO regions vary greatly in size, but are closely related to the gross domestic products of the regions. Figure 2 shows this relationship, with the abscissa representing (to a log scale) GDP in 2000 (United Nations, 2002) and the ordinate the mean annual output from 2000-03 of SCI papers. There are some outliers: AFR-E does relatively more research than expected; this is largely because of South Africa. Eastern Europe also performs well in relation to its resources. On the other hand SEA-B and EMR-B under-perform, mainly because of the relatively low outputs from Indonesia, Iran and Saudi Arabia.

There have been some changes in the percentage presence of the regions in biomedical research output in recent years, see Table 3. The most noticeable changes in output have been decreases in the USA (AMR-A region), despite the much increased expenditure of the National Institutes of Health, and increases in China (WPR-B). Western Europe (EUR-A) has also increased its share of global output, and this has been greater than that of AMR-A in four of the last six years.

Table 3. Percentage presence (integer counts) of 14 WHO regions in world biomedical research in 1992-95 and in 2000-03, and the change between them.

Region	**92-95**	**00-03**	**Change**	**Region**	**92-95**	**00-03**	**Change**
AFR-D	0.2	0.3	0.0	EUR-A	41.0	42.9	1.9
AFR-E	0.8	0.7	-0.1	EUR-B	1.3	2.3	0.9
AMR-A	46.0	42.8	-3.2	EUR-C	2.1	1.9	-0.2
AMR-B	1.7	2.8	1.2	SEA-B	0.2	0.3	0.1
AMR-D	0.1	0.1	0.0	SEA-D	1.1	1.3	0.2
EMR-B	0.4	0.5	0.2	WPR-A	12.3	13.6	1.4
EMR-D	0.3	0.3	0.0	WPR-B	1.2	3.6	2.4

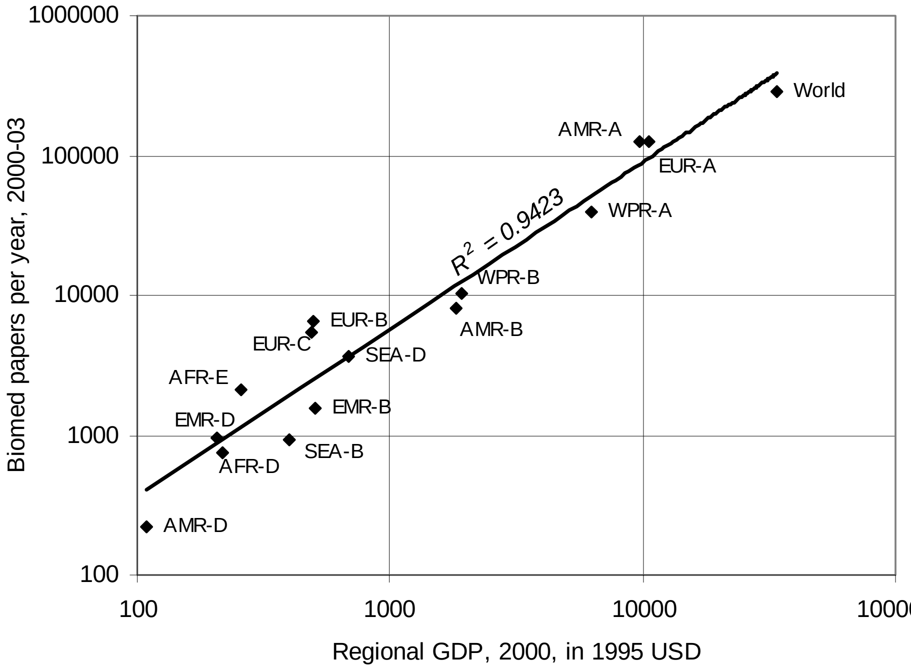

Figure 2. Relationship between biomedical research outputs of 14 WHO regions and their gross domestic products.

Because of the great imbalance between GDP *per caput* in different regions, and the much greater disease burden in poor countries than in rich ones, there is a disproportionate amount of research output in relation to DALYs in the three developed regions (AMR-A, EUR-A and WPR-A). The results of these calculations are given in Table 4. The figures in the right-hand column show the imbalance between research and disease burden very starkly. There is a ratio of more than 500:1 between the best and worst regions in this respect.

Table 4. The 14 WHO regions, with their populations, disease burden in 2000 (DALYs), biomedical research outputs, and ratios of these to their population and their disease burden.

	Pop, m million	DALYs billion	DALYs/pop x 100	Research 2000-03	Res/pop per mill.	Res/DALY x 109
World	6045	1467	24	289835	47.9	198
AFR-D	294	148	50	753	2.6	5
AFR-E	346	210	61	2090	6.0	10
AMR-A	325	47	14	123991	381.3	2665
AMR-B	431	81	19	8154	18.9	100
AMR-D	71	17	24	224	3.1	13
EMR-B	139	23	17	1574	11.3	68
EMR-D	343	113	33	959	2.8	8
EUR-A	412	53	13	124291	301.7	2342
EUR-B	218	39	18	6558	30.0	168
EUR-C	243	59	24	5389	22.2	91
SEA-B	294	61	21	938	3.2	15
SEA-D	1242	358	29	3657	2.9	10
WPR-A	154	16	11	39536	256.1	2406
WPR-B	1533	241	16	10358	6.8	43

These disparities are by now reasonably well known, although perhaps mainly to experts and advocates. The issue that this paper seeks to explore, however, is a little different: is the research output from the world's different regions, small or large, actually on the diseases that are relevant to them?

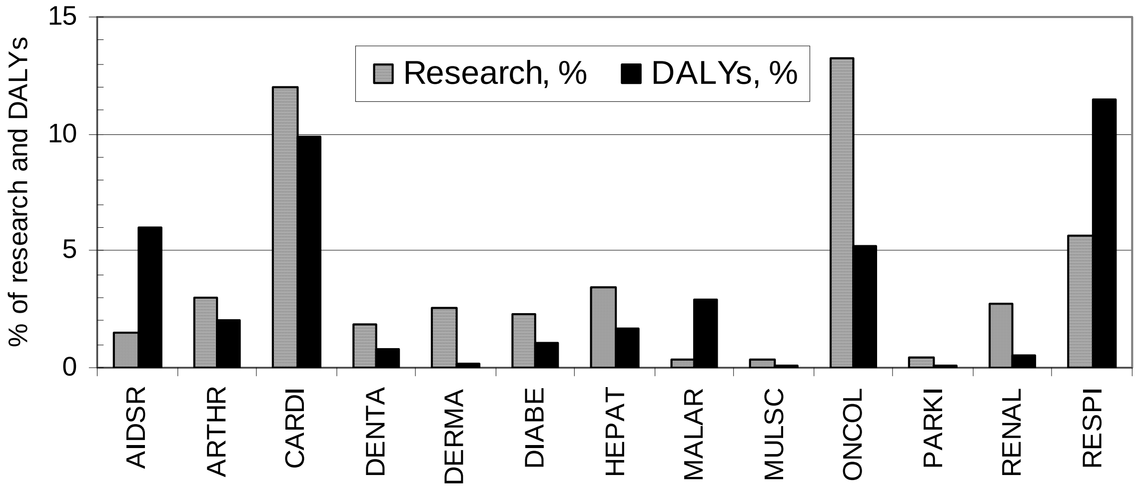

Figure 3. Comparison between world research outputs (1996-2003) and world disease burden (DALYs, 2000) for 13 disease areas (for codes, see Table 2).

To consider this issue, we first examine the overall outputs of research in the 13 disease areas of Table 2, and compare them with the global burden of disease attributable to each of them. The results are shown in chart form in Figure 3. The 13 disease areas in total account for 42% of total DALYs (the burden from many communicable diseases has not been analysed, nor has that from injuries) and the corresponding research outputs for 50%, though there may be some overlap between subject areas. Clearly, the biggest imbalances are in oncology, dermatology and renal medicine (relatively over-researched) and in AIDS and respiratory diseases (under-researched). Malaria is also under-researched, and the deficiency is well known and is being addressed, notably by the Bill and Melinda Gates Foundation. Are recent changes in output tending to narrow these gaps between research need and output? Some data are shown in Table 5.

Table 5. Comparison of the changes in the disease burden, from 1990 to 2000, and changes in output of research in 13 disease areas, from 1996-99 to 2000-03.

	DALYs,%		**Research, %**			**DALYs,%**		**Research, %**	
	1990	**2000**	**96-99**	**00-03**		**1990**	**2000**	**96-99**	**00-03**
AIDSR	0.81	6.03	1.62	1.39	MALAR	2.30	2.88	0.38	0.38
ARTHR	1.37	2.03	3.01	3.06	MULSC	0.10	0.10	0.39	0.40
CARDI	9.66	9.85	12.08	11.86	ONCOL	5.11	5.23	13.14	13.39
DENTA	0.81	0.81	1.88	1.87	PARKI	0.08	0.11	0.39	0.47
DERMA	n.a.	0.19	2.58	2.49	RENAL	0.62	0.56	2.83	2.71
DIABE	0.81	1.05	2.21	2.28	RESPI	13.48	11.46	5.64	5.60
HEPAT	1.59	1.70	3.65	3.33					

The burden of AIDS/HIV has increased enormously during the last decade (more than seven-fold) and it is continuing to rise rapidly, especially in sub-Saharan Africa (Balter, 1999; Gottlieb, 2000; Klausner *et al*., 2003; UNAIDS, 2004). The amount of AIDS research, however, is showing a decline, both relatively and even absolutely (–8%). Other diseases on the increase are arthritis (+48%), Parkinson's (+43%), diabetes (+31%) and malaria (+25%). For these, research is expanding slightly relative to biomedicine except for malaria, though even here absolute output in 2003 was 27% higher than in 1996, and 10% more relative to biomedical production. By contrast, the burden of respiratory diseases is now declining (–15%) as is that from renal disease (–10%), and the corresponding research efforts are also diminishing somewhat. That for respiratory diseases is, however, much below the share that would seem appropriate, as was noted above.

Table 6. Relative burden of 13 different diseases (for codes, see Table 2) in 14 world regions (for codes, see Table 1) in 2000. Incidences > 4 x the world mean shown **bold and boxed**; > 2 x world mean in **bold**; 1.41 x world mean in *italics*.

	AIDSR	**ARTHR**	**CARDI**	**DENTA**	**DERMA**	**DIABE**	**HEPAT**	**MALAR**	**MULSC**	**ONCOL**	**PARKI**	**RENAL**	**RESPI**
AFR-D	1.40	0.35	0.37	0.31	1.30	0.23	0.46	**4.28**	0.36	0.38	0.19	0.78	0.96
AFR-E	**4.34**	0.27	0.29	0.33	1.19	0.21	0.38	**2.93**	0.20	0.35	0.17	0.65	0.88
AMR-A	0.17	**2.04**	*1.52*	1.20	**2.17**	**2.83**	0.89	0.00	**2.48**	**2.28**	**4.53**	0.91	0.90
AMR-B	0.24	1.32	0.90	*1.44*	*1.47*	**2.10**	1.04	0.04	1.27	1.06	0.57	1.07	0.80
AMR-D	1.09	0.86	0.58	1.15	*1.58*	1.23	1.32	0.04	0.91	0.97	0.39	*1.70*	0.88
EMR-B	0.01	1.04	1.30	**2.48**	0.58	*1.72*	0.59	0.07	*1.47*	0.90	1.01	0.93	0.72
EMR-D	0.25	0.52	0.79	0.94	0.75	0.70	0.66	0.61	0.64	0.48	1.40	1.19	1.08
EUR-A	0.07	**2.27**	*1.76*	*1.47*	**2.21**	*1.94*	1.38	0.00	**3.00**	**3.08**	**4.96**	0.66	0.91
EUR-B	0.02	*1.86*	**2.22**	*1.60*	1.08	1.28	1.32	0.02	*1.58*	*1.64*	*1.53*	1.25	0.99
EUR-C	0.18	*1.58*	**2.82**	1.17	*1.74*	1.09	1.18	0.00	*1.47*	*1.77*	1.23	0.66	0.60
SEA-B	0.50	1.26	1.01	*1.73*	**2.12**	*1.70*	1.37	0.20	1.05	0.94	0.81	1.39	0.74
SEA-D	0.55	0.70	1.01	1.06	0.49	0.91	0.88	0.32	0.77	0.57	0.49	0.93	1.12
WPR-A	0.01	**2.94**	*1.48*	*1.49*	*1.42*	**2.18**	*1.90*	0.00	*1.84*	**3.19**	**5.98**	1.07	0.99
WPR-B	0.14	*1.65*	1.18	1.14	0.37	1.10	*1.90*	0.06	*1.46*	*1.68*	0.99	*1.41*	1.23

We now calculate the relative burden from the different diseases in each of the regions, expressing them as a ratio of the percentage burden for the world, see Table 6. For example, in AFR-E, 26.2% of the overall disease burden is caused by AIDS compared with 6.0% worldwide, so the ratio is 4.34. Regions suffering particularly from certain diseases have their ratios printed in different type.

The patterns are fairly clear: developed regions with very low adult and child mortality suffer disproportionately from Parkinson's disease, cancer, multiple sclerosis (MS), arthritis and diabetes, followed by skin disorders and heart disease. African countries, by contrast, are afflicted primarily by AIDS and malaria, and to a much lesser extent from skin disorders. These, and diabetes, are the highest relative burdens in Latin America. In Eastern Europe, heart disease poses relatively the biggest burden, followed by arthritis, cancer and MS. Dental problems seem to occur relatively most in the regions with low adult and child mortality (mortality stratum = B), especially in the Eastern Mediterranean region (the oil-rich countries).

But do the relative commitments to research in these different regions reflect these health burdens? Table 7 shows the RC values for research on the different diseases and in the different regions.

Table 7. Relative Commitments to research on 13 different diseases (for codes, see Table 2) in 14 world regions (for codes, see Table 1) in 1996-2003. RCs > 4 x the world mean shown **bold and boxed**; > 2 x world mean in **bold**; > 1.41 x world mean in *italics*.

	AIDSR	ARTHR	CARDI	DENTA	DERMA	DIABE	HEPAT	MALAR	MULSC	ONCOL	PARKI	RENAL	RESPI
AFR-D	**4.05**	0.29	0.31	0.55	0.74	0.85	0.63	**32.4**	0.05	0.28	0.20	0.40	0.72
AFR-E	**5.91**	0.44	0.49	1.17	0.59	0.45	0.60	**14.1**	0.11	0.58	0.23	0.45	1.30
AMR-A	1.28	0.88	0.96	0.86	0.75	0.89	0.67	0.77	1.02	0.98	0.91	0.87	0.99
AMR-B	0.93	0.89	0.70	1.38	0.89	0.97	0.90	**2.60**	0.47	0.55	0.74	0.97	0.78
AMR-D	**2.07**	0.40	0.33	0.88	1.25	0.10	0.53	**7.04**	0.47	0.39	0.00	0.33	1.10
EMR-B	0.34	0.99	0.72	*1.94*	*1.43*	1.33	1.02	1.30	0.56	0.69	0.46	**2.00**	1.02
EMR-D	0.64	0.78	0.44	0.98	0.96	1.05	1.22	**3.56**	0.36	0.66	0.32	1.22	0.66
EUR-A	0.96	1.11	1.00	0.97	1.12	1.06	0.85	1.10	1.21	0.87	1.16	1.01	0.99
EUR-B	0.27	0.97	0.95	1.33	1.05	1.05	1.03	0.28	0.89	0.84	0.51	*1.52*	0.85
EUR-C	0.45	0.40	0.60	0.38	0.46	0.49	0.63	0.23	0.45	0.58	0.73	0.41	0.54
SEA-B	**4.09**	0.61	0.30	**2.32**	0.87	0.55	1.04	**26.7**	0.13	0.42	0.05	0.78	0.63
SEA-D	0.79	0.42	0.49	0.85	0.79	1.14	1.19	**4.82**	0.16	0.72	0.64	0.79	0.91
WPR-A	0.50	1.07	1.07	1.10	0.92	1.08	1.33	0.90	0.65	1.15	1.03	1.02	0.95
WPR-B	0.48	0.71	0.81	1.09	0.78	0.76	*1.56*	**2.07**	0.44	1.15	0.73	0.93	0.86

Some regions show an RC less than unity for all the diseases analysed: this means that they are preferentially working on other biomedical subjects and diseases. The most conspicuous departures from the world norm of RC = unity are for malaria and for AIDS. Africa and SEA-B (mainly Thailand, where the Wellcome Trust has a big presence) have much the highest relative commitments to research on both diseases, especially malaria. The oil-rich Eastern Mediterranean countries specialise in renal medicine and dentistry (the latter being particularly appropriate for them). The high adult mortality countries of Eastern Europe (mainly Russia) appear to be rather neglecting research on heart disease, arthritis and cancer, which are imposing the highest health burdens on their citizens relative to the rest of the world.

The question of whether each region is maintaining a research portfolio appropriate for its disease pattern could be considered with the help of a table of the ratios of the percentage of biomedical research to the percentage of all DALYs for each disease. However this would give a misleading picture. For example, all but two regions show an apparently excessive commitment to malaria research (the average is 85 times the percentage burden!) but overall the disease is substantially under-researched. And for cardiology, apart from South Africa, the ratios are almost all below unity yet the disease overall is not under-researched – see Figure 3. It is better to consider the actual percentages of biomedical research and of DALYs for each region, because some ratios are high but the actual amount of research on a disease is really quite small so that the overall portfolio is not seriously distorted.

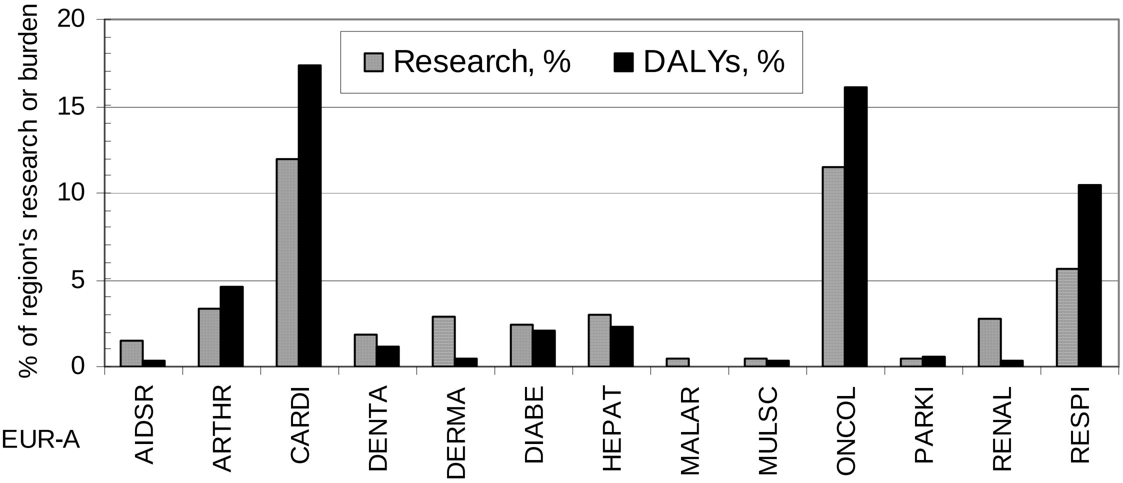

Figure 4. Comparison between Western European (EUR-A) research outputs (1996-2003) and disease burden (2000) for 13 disease areas (for codes, see Table 2).

Figure 4, for Western Europe, shows that there is reasonable agreement between the burden of disease and the amount of research, but the two biggest disease burdens (from heart disease and cancer) are actually under-researched – as is respiratory disease. The apparent over-commitment worldwide to cardiology and oncology (Figure 3) may not be relevant to the bodies that support such research in Western Europe, notably the collecting charities. They can still make a credible appeal for more funds on the basis of Figure 4.

The situation in Africa is different. As we have seen, the major burdens are from AIDS and malaria, but the research portfolios of AFR-D and AFR-E diverge, see Figures 5 and 6.

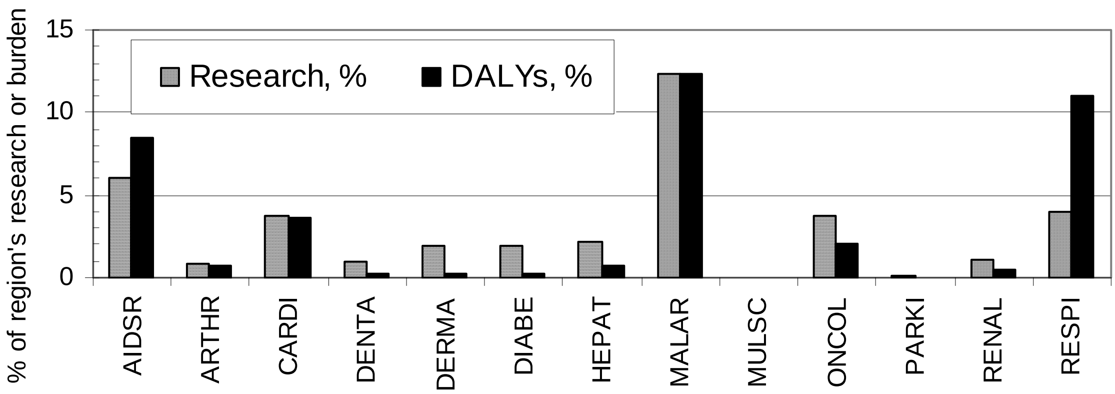

Figure 5. Comparison between African (AFR-D) - mainly west African - research outputs (1996-2003) and disease burden (2000) for 13 disease areas (for codes, see Table 2).

Apart from the under-researching of respiratory diseases, which is almost universal, the west African research portfolio actually matches its current burden of disease quite well. In contrast, AFR-E, dominated by South Africa, seems to be neglecting the problems of AIDS, giving less attention to malaria than might appear desirable, and to be continuing the pattern of research dominated by the diseases of developed countries – cancer, heart disease, dentistry, hepatology and renal medicine.

Discussion

This paper has shown that bibliometrics can play a useful role in demonstrating whether the biomedical research portfolios of the world, and of individual regions within it, are informed by the needs created by their changing patterns of disease. Of course, one would not expect exact proportionality, and research in some basic sciences will contribute to the understanding of many different diseases (see Marshall, 1997); much of this will have been excluded from the subject-based filters used here. Health services research can also be of widespread benefit to treatment.

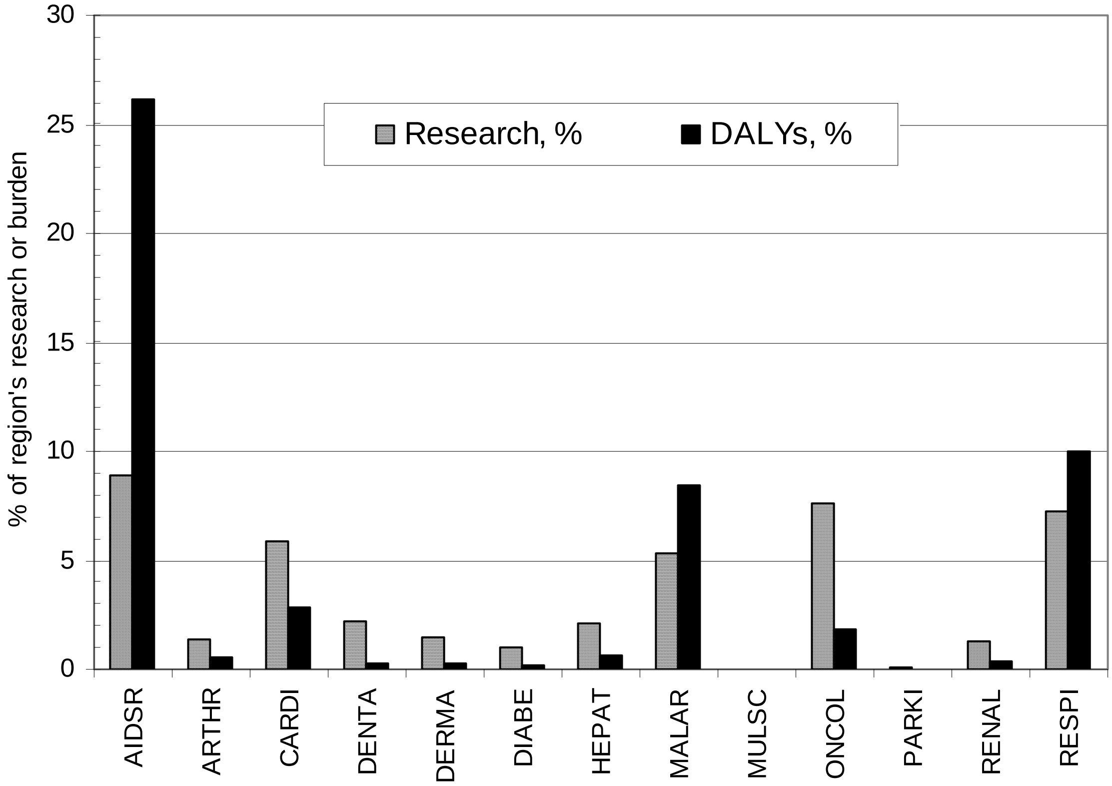

Figure 6. Comparison between African (AFR-E) - mainly South African - research outputs (1996-2003) and disease burden (2000) for 13 disease areas (for codes, see Table 2).

Some of these results may appear anomalous, but they are actually a direct consequence of the very unequal division of the world into regions whose characteristics are quite different. A much-simplified example will make this more evident. Suppose that the world population of 6 billion is divided into just two regions, a rich one *A* with one tenth of the population but performing 90% of the research, and a poor one *B* with 90% of the population but doing only one tenth of the research. Suppose further that *A* has 10 DALYs *per caput* and *B*, 40 DALYs *per caput*. Then the world total of DALYs will be 600 m x 10 + 5400 m x 40 = 6 + 216 = 222 bn. Now consider a disease of the rich region, *P* (*e.g*., cancer) that causes 30% of the DALYs in *A* but only 5% in *B*. It will be responsible for 0.3 x 6 + 0.05 x 216 = 12.6 bn DALYs, or 5.7% of the total. Suppose that it is the subject of 20% of the research in *A* and just 1% in *B*; in both regions it is apparently under-researched in relation to that region's burden. But it will generate 0.2 x 90 + 0.01 x 10 out of every 100 biomedical papers published, or 18.1%. This means that disease *P* is over-researched by a factor of 3.2.

Conversely another disease, *Q*, that primarily affects the poor region (*e.g*., AIDS or malaria), causing 1% of DALYs in *A* but 30% in *B*, will pose a total burden of 0.01 x 6 + 0.3 x 216 = 64.9 bn DALYs, or 29.2% of the total. If *A* devotes 10% of its research to *Q* and *B*, 50%, then it will account for 9 + 5 = 14% of the papers, and will appear globally under-researched, but over-researched in both *A* and *B*. Thus it is inevitable that the diseases of poor regions will appear to be under-researched, and those of rich regions over-researched, yet at the same time there will be justifiable complaints in rich regions that the research portfolio is unrepresentative of their disease burden as occurred in the USA in the 1990s (Marshall, 1997).

The main difficulty in this approach is that research portfolios are not in fact set at the regional level but at that of the individual country, so that each country with an actively-managed biomedical research programme would need to have an accurate picture of its burden of disease. At present few do so, and the main health indicators available are death rates from different causes. Reliance on them alone will mean that debilitating but non-fatal diseases such as arthritis and mental disorders are unfairly overlooked. There is therefore a need to develop national indicators comparable to DALYs and to use them both for policy-making and for advocacy, especially by patient groups. The numbers of patients affected by a disease provide one indicator but clearly a rather imperfect one.

What is appropriate at the regional and national level may also be relevant at the local level. The pattern of disease often varies across a country, particularly where it is geographically diverse, or there are pronounced differences between the inhabitants of different areas, or of their diets. It may therefore be useful for biomedical grant-giving bodies to take clinical need more into account in their decisions, so that the research can be applied to the direct benefit of local patients. But this is a subject for another study.

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