UK investments in global infectious disease research 1997–2010: a case study

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Summary

Background **Infectious diseases account for 15 million deaths per year worldwide, and disproportionately affect young people, elderly people, and the poorest sections of society. We aimed to describe the investments awarded to UK institutions for infectious disease research.**

Methods **We systematically searched databases and websites for information on research studies from funding institutions and created a comprehensive database of infectious disease research projects for the period 1997–2010. We categorised studies and funding by disease, cross-cutting theme, and by a research and development value chain describing the type of science. Regression analyses were reported with Spearman's rank correlation coefficient to establish the relation between research investment, mortality, and disease burden as measured by disability-adjusted life years (DALYs).**

Findings **We identified 6170 funded studies, with a total research investment of UK£2·6 billion. Studies with a clear global health component represented 35·6% of all funding (£927 million). By disease, HIV received £461 million (17·7%), malaria £346 million (13·3%), tuberculosis £149 million (5·7%), influenza £80 million (3·1%), and hepatitis C £60 million (2·3%). We compared funding with disease burden (DALYs and mortality) to show low levels of investment relative to burden for gastrointestinal infections (£254 million, 9·7%), some neglected tropical diseases (£184 million, 7·1%), and antimicrobial resistance (£96 million, 3·7%). Virology was the highest funded category (£1 billion, 38·4%). Leading funding sources were the Wellcome Trust (£688 million, 26·4%) and the Medical Research Council (£673 million, 25·8%).**

Interpretation **Research funding has to be aligned with prevailing and projected global infectious disease burden. Funding agencies and industry need to openly document their research investments to redress any inequities in resource allocation.**

Funding **None.**

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Introduction

Infectious diseases cause a high burden of largely avoidable morbidity and mortality worldwide, and place substantial strain on the limited health budgets, health systems, and economies of affected countries. WHO figures[1] for low-income countries suggest that infections of the lower respiratory tract are the leading cause of death, followed by ischaemic heart disease, with diarrhoeal disease the third highest and HIV/AIDS the fourth highest cause of death. Although infectious disease control is of the utmost importance for human health, global health security, economic stability, and international development do not have a comprehensive surveillance system to document and monitor infectious disease research investments.

Many factors affect the fairly low level of investment in research and development for infectious diseases and maternal, neonatal, and child health. These factors include market failure[2–4] because of low financial opportunities for private investors, risks of research (especially in children and pregnant women), and fragmented infrastructure to do trials for infections and disorders affecting populations in low-income countries. Funding for these diseases has been from donor governments, philanthropic organisations, and public–private partnerships.

Infections do not recognise borders. Investment in research and development for infectious diseases produces global public benefits that have a positive effect both locally and worldwide, irrespective of the site of the work or the location of the institution receiving an award, bringing substantial health, social, and economic benefit.[2,5]

In view of the scarcity of resources available, funds for research and development should take into account the local and global burdens of disease. Since 2007, the G-FINDER project, originally commissioned by the Bill & Melinda Gates Foundation, annually surveys global neglected disease research and development expenditure.[6,7] Studies to assess the research spend according to the burden of disease, with data sourced from Australia, Canada, Spain, and the USA,[8–11] have had difficulties because of poor data availability. The UK is the second largest investor in global health, but there has been no detailed analysis of its research investment. A study by the UK Clinical Research Collaboration considered the broad direction of research funding across all medical specialties, but was restricted to one financial year.[12] Investments from the UK pharmaceutical industry (a key

See Online for appendix

investor in infectious disease research) are poorly documented, partly because of commercial sensitivity.[12]

There are large gaps in our quantification of the worldwide spend on infectious disease research and the translation of funds along the research and development value chain into health policy and practice. We present an in-depth analysis examining the investments awarded to UK institutions for all infectious disease research, over the 14 year period from 1997 to 2010. The aims of our study were to quantify awards to UK institutions for local and global infectious disease research; to establish the clinical diseases, specialties, and study types targeted by the major funders; and to identify potential areas of historical and current underinvestment.

Methods

Data sources

We obtained data from several sources for studies where funding was awarded between 1997 and 2010. Variables collected included study title, abstract, funding awarded to the study, lead institution, principal investigator, and year of award. 70 principal investigators were contacted individually for further information where needed. We include in the appendix the full list of keywords used to search databases and websites belonging to funding agencies. We also searched ClinicalTrials.gov, the National Research Register, and the Association of Medical Research Charities database.

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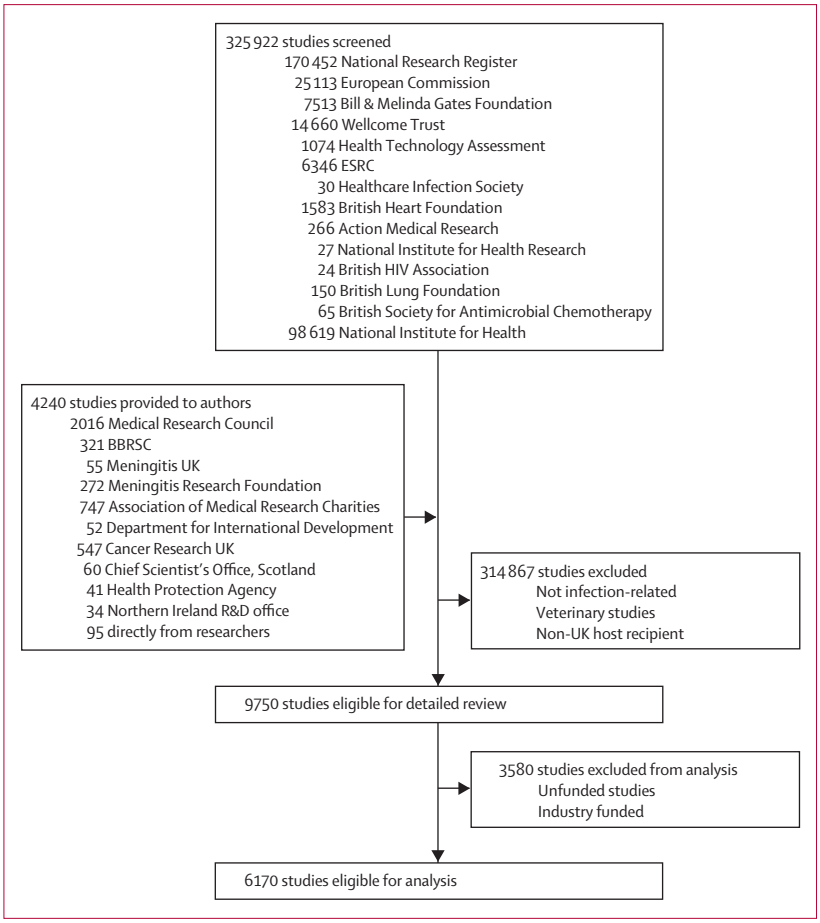

Figure 1: **Sources and numbers of studies screened**
ESRC=Economic and Social Research Council. BBSRC=Biotechnology and Biological Sciences Research Council.

Inclusion criteria

We used the study title and abstract (where present) as a filter, and included all infection-related studies with funding awarded in the period 1997–2010, studies where the lead institution was based in the UK, and infrastructure grants with a clear purpose for infectious disease research. This period was selected on the basis of accurate data availability, which enabled us to suitably compare our results with the WHO burden estimates of 2004 and 2008. We excluded studies not immediately relevant to infection, veterinary infectious disease research studies (unless there was a clear zoonotic component), studies where viral vectors were used to investigate non-communicable diseases, grants for symposia or meetings, and studies where there were UK contributions (eg, as a collaborator) but the funding was awarded to a non-UK institution. Where there was uncertainty, the study author was contacted or further details were sourced from the internet. Of the studies included in the final database, all had a title and 58% had an abstract. We excluded open-access data from the pharmaceutical industry since it was clearly under-representative.

Data management

Grants awarded in a currency other than pounds sterling were converted to UK pounds using the mean exchange rate in the year of the award. All grant funding amounts were adjusted for inflation and reported in 2010 UK pounds. Grants were not modified according to levels of overheads applied to the award. For multicentre studies, any distribution of funding from the lead centre where the award was made to other study sites was not documented. Unfunded studies were excluded from our analysis.

Each study in the database was reviewed by MGH and assigned to as many primary disease categories as appropriate (appendix). Within each category, topic-specific subsections were documented.

Studies were also allocated to one of four research and development categories: pre-clinical; phase 1, 2, or 3; product development; and operational research (appendix). All studies were categorised and subsequently double-checked by JRF. Provisional datasets were circulated to all authors for review and comment. MKC and FBW further verified a random sample of 10% of the data (663 studies) in a third round of checks. The fixed marginal κ score was 0·950 suggesting high agreement between the authors when categorising studies. All differences on inclusion or categorisation were discussed between MGH and the author who flagged the study, and where there was still disagreement, the data were

	Investment (total), £ (%)	Studies, n (%)	Investment (1997–2004)		2004 mortality, n (%)	2004 DALYs, n (%)	Investment (2005–10)		2008 mortality (projected), n (%)	2008 DALYs (projected), n (%)
			£ (%)	n (%)			£ (%)	n (%)		
Disease system										
Gastrointestinal infections	254 006 242 (9·7%)	799 (12·9%)	130 548 965 (9·5%)	498 (12·6%)	2 169 764 (22·2%)	76 789 182 (25·1%)	123 457 277 (10·0%)	301 (13·5%)	1 691 818 (19·8%)	59 244 563 (22·2%)
Haematological infections	413 489 870 (15·9%)	742 (12·0%)	190 188 198 (13·9%)	504 (12·8%)	889 186 (9·1%)	33 976 026 (11·1%)	223 301 672 (18·0%)	238 (10·7%)	836 624 (9·8%)	32 342 189 (12·1%)
Hepatic infections	73 965 716 (2·8%)	322 (5·2%)	48 859 066 (3·6%)	251 (6·4%)	199 792 (2·0%)	4 769 299 (1·6%)	25 106 651 (2·0%)	71 (3·2%)	172 068 (2·0%)	3 907 550 (1·5%)
Neglected tropical diseases	184 446 162 (7·1%)	392 (6·4%)	113 018 076 (8·3%)	267 (6·8%)	182 153 (1·9%)	18 323 958 (6·0%)	71 428 087 (5·8%)	125 (5·6%)	149 693 (1·8%)	14 969 564 (5·6%)
Neurological infections	101 363 708 (3·9%)	339 (5·5%)	62 685 767 (4·6%)	241 (6·1%)	392 292 (4·0%)	13 099 105 (4·3%)	38 677 941 (3·1%)	98 (4·4%)	314 617 (3·7%)	10 231 400 (3·8%)
Ocular infections	7 407 218 (0·3%)	36 (0·6%)	3 574 775 (0·3%)	27 (0·7%)	173 (0·0%)	1 722 990 (0·6%)	3 832 443 (0·3%)	9 (0·4%)	153 (0·0%)	1 487 567 (0·6%)
Respiratory infections	410 705 744 (15·8%)	1190 (19·3%)	197 356 636 (14·4%)	737 (18·7%)	4 258 563 (43·5%)	97 786 126 (32·0%)	213 349 109 (17·2%)	453 (20·3%)	3 815 503 (44·7%)	81 583 751 (30·6%)
Sexually-transmitted infections	138 581 653 (5·3%)	380 (6·2%)	96 118 502 (7·0%)	259 (6·6%)	396 717 (4·1%)	14 144 219 (4·6%)	42 463 150 (3·4%)	121 (5·4%)	393 239 (4·6%)	13 186 581 (4·9%)
HIV	460 547 457 (17·7%)	760 (12·3%)	243 453 711 (17·8%)	479 (12·2%)	2 039 727 (20·8%)	58 512 843 (19·1%)	217 093 746 (17·5%)	281 (12·6%)	2 242 597 (26·3%)	64 661 516 (24·2%)
Overall	2 606 482 941	6170	1 367 696 262	3941	9 786 907	305 863 590	1 238 786 678	2229	8 533 171	266 845 840
Specific infection										
African trypanosomiasis	48 082 259 (2·6%)	116 (2·9%)	25 831 831 (2·7%)	73 (2·7%)	52 347 (0·8%)	1 672 728 (0·8%)	22 250 428 (2·6%)	43 (3·2%)	44 490 (0·7%)	1 408 517 (0·7%)
Aspergillus	4 853 858 (0·3%)	26 (0·7%)	3 950 124 (0·4%)	27 (1·0%)	..	..	933 213 (0·1%)	4 (0·3%)	..	..
Campylobacter	24 116 021 (1·3%)	87 (2·2%)	12 072 058 (1·3%)	47 (1·8%)	..	..	12 198 511 (1·4%)	43 (3·2%)	..	..
Candida	1 219 072 (0·1%)	8 (0·2%)	237 210 (0·0%)	8 (0·3%)	..	..	1 028 298 (0·1%)	2 (0·1%)	..	..
Chagas disease	3 448 856 (0·2%)	15 (0·4%)	2 522 761 (0·3%)	12 (0·5%)	11 367 (0·2%)	429 873 (0·2%)	926 096 (0·1%)	3 (0·2%)	10 066 (0·2%)	341 578 (0·2%)
Chlamydia	21 702 378 (1·2%)	112 (2·8%)	17 462 388 (1·8%)	73 (2·7%)	8889 (0·1%)	3 748 198 (1·8%)	4 239 990 (0·5%)	39 (2·9%)	7421 (0·1%)	3 420 418 (1·8%)
Clostridium	29 751 310 (1·6%)	72 (1·8%)	5 164 027 (0·5%)	23 (0·9%)	..	..	25 199 334 (2·9%)	51 (3·8%)	..	..
Cytomegalovirus	28 369 415 (1·6%)	68 (1·7%)	18 988 235 (2·0%)	60 (2·3%)	..	..	9 581 430 (1·1%)	14 (1·0%)	..	..
Dengue	43 742 101 (2·4%)	28 (0·7%)	4 430 589 (0·5%)	15 (0·6%)	18 104 (0·3%)	669 648 (0·3%)	39 311 513 (4·5%)	13 (1·0%)	12 899 (0·2%)	470 201 (0·2%)
Diphtheria	139 863 (0·0%)	2 (0·1%)	139 863 (0·0%)	2 (0·1%)	5091 (0·1%)	173 575 (0·1%)	0 (0·0%)	0 (0·0%)	3933 (0·1%)	132 303 (0·1%)
Escherichia coli	25 589 407 (1·4%)	106 (2·7%)	15 852 833 (1·7%)	74 (2·8%)	..	..	9 760 027 (1·1%)	33 (2·4%)	..	..
Epstein-Barr virus	45 310 414 (2·5%)	147 (3·7%)	32 961 882 (3·5%)	114 (4·3%)	..	..	12 348 532 (1·4%)	33 (2·4%)	..	..
Gonorrhoea	948 399 (0·1%)	18 (0·5%)	768 377 (0·1%)	14 (0·5%)	559 (0·0%)	3 549 976 (1·7%)	180 021 (0·0%)	4 (0·3%)	474 (0·0%)	3 316 666 (1·7%)
Helicobacter	15 109 554 (0·8%)	101 (2·6%)	12 924 723 (1·4%)	96 (3·6%)	..	..	2 262 304 (0·3%)	13 (1·0%)	..	..
Helminths	47 026 454 (2·6%)	114 (2·9%)	25 762 808 (2·7%)	77 (2·9%)	47 858 (0·8%)	11 660 451 (5·5%)	21 263 645 (2·4%)	37 (2·7%)	41 357 (0·7%)	9 609 061 (4·9%)
Hepatitis B	11 768 095 (0·6%)	68 (1·7%)	9 829 208 (1·0%)	57 (2·1%)	104 606 (1·7%)	2 067 533 (1·0%)	1 938 888 (0·2%)	11 (0·8%)	88 653 (1·5%)	1 668 641 (0·9%)
Hepatitis C	59 727 829 (3·3%)	235 (5·9%)	38 124 617 (4·0%)	182 (6·8%)	54 099 (0·9%)	994 622 (0·5%)	21 603 212 (2·5%)	53 (3·9%)	46 906 (0·8%)	782 184 (0·4%)

(Continues on next page)

	Investment (total), £ (%)	Studies, n (%)	Investment (1997–2004)		2004 mortality, n (%)	2004 DALYs, n (%)	Investment (2005–10)		2008 mortality (projected), n (%)	2008 DALYs (projected), n (%)
			£ (%)	n (%)			£ (%)	n (%)		
(Continued from previous page)										
HIV	460 547 457 (25·3%)	760 (19·2%)	243 453 711 (25·6%)	479 (18·0%)	2 039 727 (32·2%)	58 512 843 (27·7%)	217 093 746 (24·9%)	281 (20·7%)	2 242 597 (37·7%)	64 661 516 (33·3%)
Human papillomavirus	57 795 110 (3·2%)	150 (3·8%)	41 452 682 (4·4%)	108 (4·1%)	268 245 (4·2%)	3 719 348 (1·8%)	16 342 428 (1·9%)	42 (3·1%)	286 451 (4·8%)	3 906 185 (2·0%)
Herpes simplex virus	22 063 300 (1·2%)	48 (1·2%)	18 201 738 (1·9%)	57 (2·1%)	..	..	4 694 523 (0·5%)	13 (1·0%)	..	..
Influenza	79 763 001 (4·4%)	140 (3·5%)	29 388 916 (3·1%)	42 (1·6%)	..	..	50 629 034 (5·8%)	101 (7·4%)	..	..
Leishmaniasis	36 027 609 (2·0%)	75 (1·9%)	16 156 050 (1·7%)	47 (1·8%)	46 862 (0·7%)	1 974 465 (0·9%)	19 871 559 (2·3%)	28 (2·1%)	35 881 (0·6%)	1 486 268 (0·8%)
Leprosy	623 080 (0·0%)	2 (0·1%)	623 080 (0·1%)	2 (0·1%)	5442 (0·1%)	193 803 (0·1%)	0 (0·0%)	0 (0·0%)	4847 (0·1%)	166 371 (0·1%)
Listeria	4 751 097 (0·3%)	10 (0·3%)	3 947 669 (0·4%)	8 (0·3%)	..	..	803 428 (0·1%)	2 (0·1%)	..	..
Lymphatic filariasis	51 112 541 (2·8%)	16 (0·4%)	3 679 045 (0·4%)	10 (0·4%)	290 (0·0%)	5 940 641 (2·8%)	47 433 496 (5·4%)	6 (0·4%)	252 (0·0%)	4 878 733 (2·5%)
Malaria	346 180 494 (19·0%)	501 (12·7%)	165 764 640 (17·4%)	340 (12·8%)	889 186 (14·0%)	33 976 026 (16·1%)	180 415 854 (20·7%)	161 (11·9%)	836 624 (14·1%)	32 342 189 (16·6%)
Measles	2 597 677 (0·1%)	9 (0·2%)	1 630 534 (0·2%)	7 (0·3%)	423 710 (6·7%)	14 852 775 (7·0%)	967 143 (0·1%)	2 (0·1%)	327 744 (5·5%)	11 255 332 (5·8%)
Meningitis	54 078 664 (3·0%)	223 (5·6%)	35 650 075 (3·7%)	152 (5·7%)	339 945 (5·4%)	11 426 377 (5·4%)	18 428 589 (2·1%)	71 (5·2%)	270 127 (4·5%)	8 822 883 (4·5%)
Norovirus	5 102 250 (0·3%)	12 (0·3%)	1 250 218 (0·1%)	6 (0·2%)	..	..	3 852 031 (0·4%)	6 (0·4%)	..	..
Onchocerciasis	1 338 978 (0·1%)	4 (0·1%)	1 338 978 (0·1%)	4 (0·2%)	65 (0·0%)	388 576 (0·2%)	0 (0·0%)	0 (0·0%)	60 (0·0%)	348 364 (0·2%)
Pertussis	2 432 158 (0·1%)	9 (0·2%)	1 658 797 (0·2%)	7 (0·3%)	254 497 (4·0%)	9 881 667 (4·7%)	773 361 (0·1%)	2 (0·1%)	194 096 (3·3%)	7 589 588 (3·9%)
Polio	1 189 984 (0·1%)	4 (0·1%)	247 880 (0·0%)	2 (0·1%)	1195 (0·0%)	34 399 (0·0%)	942 103 (0·1%)	2 (0·1%)	1095 (0·0%)	26 455 (0·0%)
Pseudomonas	6 473 237 (0·4%)	43 (1·1%)	3 417 409 (0·4%)	36 (1·4%)	..	..	3 170 837 (0·4%)	12 (0·9%)	..	..
Rotavirus	5 883 445 (0·3%)	18 (0·5%)	3 026 257 (0·3%)	15 (0·6%)	..	..	3 063 635 (0·4%)	5 (0·4%)	..	..
Respiratory syncytial virus	16 899 738 (0·9%)	45 (1·1%)	11 187 246 (1·2%)	37 (1·4%)	..	..	6 158 406 (0·7%)	13 (1·0%)	..	..
Salmonella	55 716 287 (3·1%)	145 (3·7%)	31 145 306 (3·3%)	81 (3·0%)	..	..	24 656 054 (2·8%)	65 (4·8%)	..	..
Schistosomiasis	38 677 801 (2·1%)	46 (1·2%)	35 08658 117 (3·7%)	38 (1·4%)	41 087 (0·6%)	1 707 144 (0·8%)	3 591 684 (0·4%)	8 (0·6%)	36 509 (0·6%)	1 456 725 (0·7%)
Shigella	3 292 442 (0·2%)	9 (0·2%)	1 886 751 (0·2%)	4 (0·2%)	..	..	1 405 691 (0·2%)	5 (0·4%)	..	..
Syphilis	1 061 560 (0·1%)	5 (0·1%)	775 444 (0·1%)	3 (0·1%)	99 167 (1·6%)	2 846 113 (1·3%)	286 117 (0·0%)	2 (0·1%)	81 164 (1·4%)	2 305 151 (1·2%)
Tetanus	1 228 583 (0·1%)	6 (0·2%)	1 228 583 (0·1%)	6 (0·2%)	162 867 (2·6%)	5 283 485 (2·5%)	0 (0·0%)	0 (0·0%)	128 258 (2·2%)	4 190 231 (2·2%)
Trachoma	1 928 640 (0·1%)	3 (0·1%)	608 792 (0·1%)	1 (0·0%)	108 (0·0%)	1 334 414 (0·6%)	1 319 848 (0·2%)	2 (0·1%)	93 (0·0%)	1 139 203 (0·6%)
Tuberculosis	148 801 691 (8·2%)	327 (8·3%)	70 024 830 (7·4%)	202 (7·6%)	1 463 792 (23·1%)	34 216 721 (16·2%)	78 776 861 (9·0%)	125 (9·2%)	1 249 975 (21·0%)	28 696 686 (14·8%)
Varicella zoster virus	4 186 583 (0·2%)	20 (0·5%)	2 131 877 (0·2%)	18 (0·7%)	..	..	2 264 526 (0·3%)	6 (0·4%)	..	..
Total infections	1 820 658 688	3953	951 986 157	2666	6 339 105	211 255 401	871 966 395	1356	5 951 972	194 421 449
Overall	2 606 482 941	6170	1 367 696 262	3941	9 786 907	305 863 590	1 238 786 678	2229	8 533 171	266 845 840

All investment reported in 2010 UK pounds. DALYS=disability-adjusted life-years.

Table 1: **Investment in cross-cutting theme and disease with associated measures of burden**

referred to a third author (MKC, FBW, or JRF) for their consideration and final decision.

Funding organisations were allocated to one of 26 categories (appendix). Categories were defined by the authors, initially based on a pilot of this work in 2006 and further refined based on the total research investment of the funder and the providence of the investor's funds. The category of antimicrobial resistance includes antibacterial, antiviral, and antifungal resistance. Reference to diagnostics includes screening programmes. Reference to sexually transmitted infections excludes HIV. Neglected tropical diseases were categorised based on the infections focused on by WHO. Reference to cross-cutting themes includes areas of research that apply to several infectious diseases such as antimicrobial resistance, drug development, and vaccination.

Data were sourced over 3 years (September, 2007, to December, 2010). Data categorisation was done between December, 2010, and April, 2012. Data were analysed between October, 2011, and May, 2012.

Statistical analysis

Microsoft Excel versions 2000 and 2007 were used for the categorisation of studies. Where needed, data were exported into Microsoft Access (versions 2000 and 2007) and specific keyword queries used to select precise sections of the data for analysis. Statistical analysis and generation of figures and graphs were done with Stata (version 11). Regression analyses were reported with Spearman's rank correlation coefficient (r) to establish the relation between research investment, mortality, and disease burden as measured by disability-adjusted life years (DALYs).[13]

Role of the funding source

There was no funding source for this study. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

We identified 320 470 studies that were suitable for screening. Of these, 6170 funded studies met our inclusion criteria (figure 1). The funding for these studies represented a total research investment of UK£2·6 billion (figure 1). Worldwide, gastrointestinal disease represents a similar burden of mortality and DALYs as HIV but receives roughly half the research funding.[1] Investment is similar when classified by research themes, health burden, and research. Table 1 shows a detailed breakdown of the investment by disease and cross-cutting themes, and the burden data. There are prominent disparities between investment and burden of specific diseases. The type of science funded by each institution

For the **list of neglected tropical diseases focused on by WHO** see http://www.who.int/neglected_diseases/diseases/en/

	Investment, £ (%)	Studies, n (%)	Pre-clinical		Phase 1–3		Product development		Operational research	
			£ (%)	n (%)	£ (%)	n (%)	£ (%)	n (%)	£ (%)	n (%)
Public funding	1 393 972 967 (53·5%)	2281 (37·0%)	..	..	..	..	..	..	..	..
Biotechnology and Biological Sciences Research Council	186 268 429 (7·1%)	578 (9·4%)	186 243 256 (100·0%)	576 (99·7%)	0 (0·0%)	0 (0·0%)	0 (0·0%)	0 (0·0%)	25 173 (0·0%)	2 (0·3%)
UK Government, non Department of Health	144 831 562 (5·6%)	237 (3·8%)	12 858 143 (8·9%)	74 (31·2%)	59 803 751 (41·3%)	6 (2·5%)	5 979 916 (4·1%)	34 (14·3%)	66 189 752 (45·7%)	123 (51·9%)
Department of Health	134 961 745 (5·2%)	285 (4·6%)	14 317 188 (10·6%)	28 (9·8%)	6 840 563 (5·1%)	7 (2·5%)	20 373 031 (15·1%)	40 (14·0%)	93 430 963 (69·2%)	210 (73·7%)
Medical Research Council	672 895 698 (25·8%)	962 (15·6%)	527 370 055 (78·4%)	738 (76·7%)	42 323 395 (6·3%)	43 (4·5%)	27 578 378 (4·1%)	35 (3·6%)	75 623 870 (11·2%)	146 (15·2%)
European Commission	255 015 533 (9·8%)	219 (3·5%)	187 782 118 (73·6%)	164 (74·9%)	0 (0·0%)	0 (0·0%)	12 680 401 (5·0%)	14 (6·4%)	54 553 014 (21·4%)	41 (18·7%)
Philanthropy	1 108 966 983 (42·5%)	2879 (46·7%)	..	..	..	..	..	..	..	..
Bill & Melinda Gates Foundation	220 923 242 (8·5%)	39 (0·6%)	40 318 109 (18·2%)	8 (20·5%)	4 747 473 (2·1%)	5 (12·8%)	5 407 891 (2·4%)	4 (10·3%)	170 449 769 (77·2%)	22 (56·4%)
Charity	199 703 382 (7·7%)	855 (13·9%)	136 625 522 (68·4%)	529 (61·9%)	4 993 262 (2·5%)	40 (4·7%)	3 620 490 (1·8%)	35 (4·1%)	54 464 109 (27·3%)	251 (29·4%)
Wellcome Trust	688 340 359 (26·4%)	1985 (32·2%)	486 184 312 (70·6%)	1524 (76·8%)	17 647 229 (2·6%)	17 (0·9%)	41 427 765 (6·0%)	70 (3·5%)	143 081 054 (20·8%)	374 (18·8%)
Other	103 542 992 (4·0%)	1010 (16·4%)	37 344 165 (36·1%)	401 (39·7%)	10 471 721 (10·1%)	27 (2·7%)	15 810 957 (15·3%)	103 (10·2%)	39 916 149 (38·6%)	479 (47·4%)
Overall	2 606 482 941	6170	..	..	..	..	..	..	..	..

All investment reported in 2010 UK pounds.

Table 2: **Investment by funding source and research and development phase**

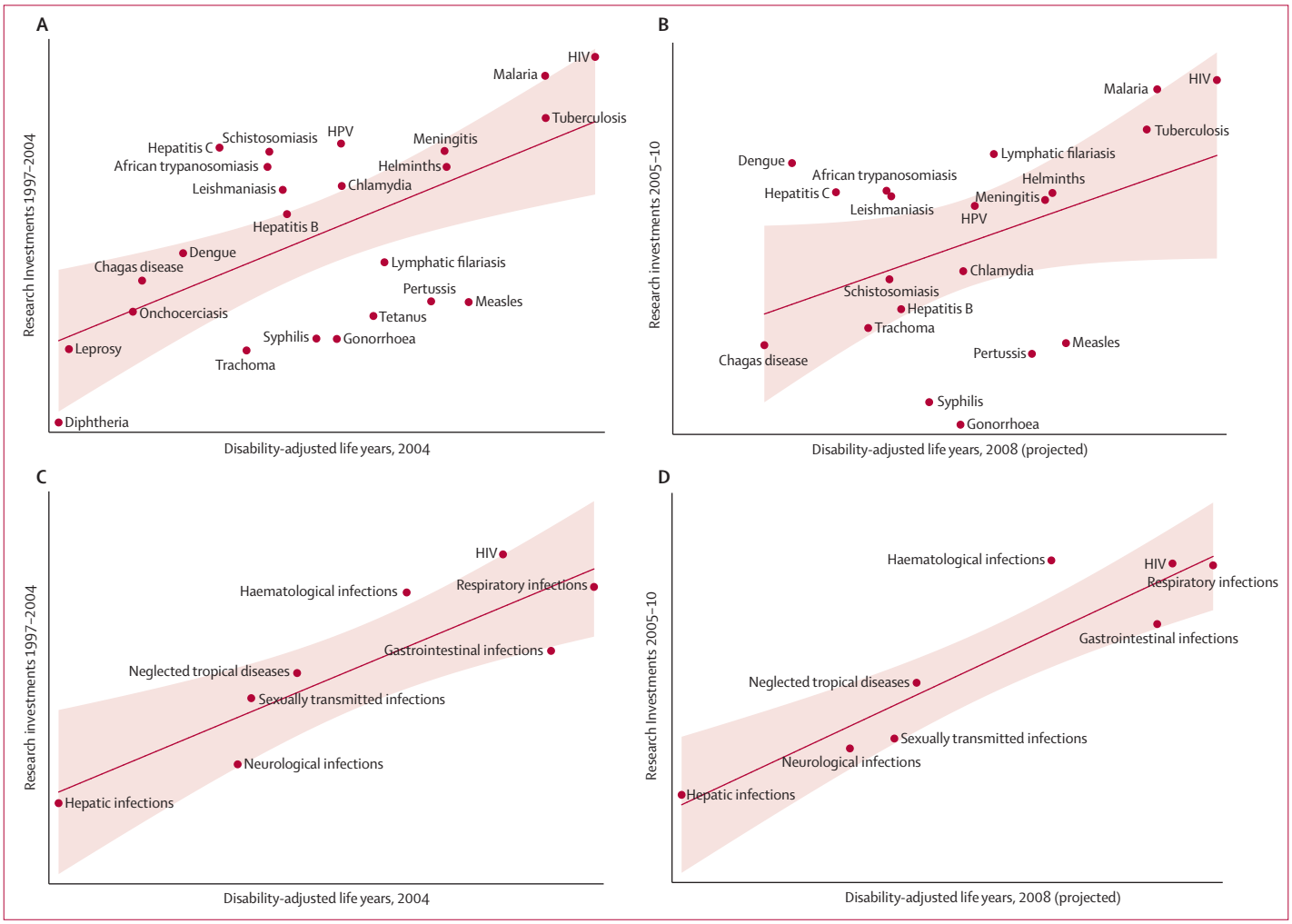

Figure 2: **Association between investment and DALYs**
Association between investment in specific infection and DALYs in 2004 (Spearman's correlation coefficient [*r*] 0·5908 [A]). Investment in specific infection and DALYs in 2008 (*r* 0·3688; p=0·0999 [B]). Investment in disease system and DALYs in 2004 (*r* 0·8810 [C]). Investment in disease system and DALYs in 2008 (*r* 0·8333) using a logarithmic scale (D). DALYs=disability-adjusted life-years. HPV=human papillomavirus.

varies according to their priorities. Wellcome Trust funds a greater number of preclinical studies, whereas the UK Government research portfolios are more focused on operational and implementation research (table 2).

More than a third of the total funding (£927·3 million) had an explicit global health component. This represents a minimum estimate because the distinction between locally focused and global research was not always clear. Mean funding for all infectious diseases was £186·2 million per year (SD £75·8 million). Mean funding awarded per study was £422 445 (SD £1 316 020) with median funding per study substantially lower at £158 059 (IQR £49 657–£352 754).

Regression analysis between disease system and infection against DALYs shows a clear misalignment between investment and worldwide burden (figure 2), with a moderate association of specific infection research funding to DALYs in 2004 (*r* 0·5270) and a worsening association in 2008 (*r* 0·3203). Conversely, there is a positive association between infection by disease system and DALYs in 2004 (*r* 0·8810) and 2008 (*r* 0·8333). Considering their burden according to DALYs in 2004 and 2008, trachoma, syphilis, and gonorrhoea are among the infections that are most underfunded, relative to all infections in the study. Hepatitis C, African trypanosomiasis, leishmaniasis, and malaria are among the infections that are most overfunded.

Funding for research with a clear paediatric focus was £87·1 million (3·3%), whereas investment for geriatric research was £7·2 million (0·3%). Health-care-associated infections attracted £53·3 million (2·0%) of research funding.

When analysed by research and development pipeline (figure 3), £1·6 billion (62·5%) of the investment was allocated to preclinical research, with smaller amounts (£146·8 million, 5·6%) allocated to clinical trial research

and development stages (phases 1–3). Intervention and product development studies attracted 5·1% of investment (£132·9 million); these include phase 4 trials and the post-clinical trial assessment of medicines and devices in health care. Operational research studies attracted 26·8% of investment (£697·7 million). The relative contributions of each research and development value chain remained similar over the study period.

Seven institutions accounted for 88·4% of the total funding. The Wellcome Trust was the leading funder of infectious disease research, investing £688·3 million (26·4%) across 1985 studies, followed by the Medical Research Council investing a total of £672·9 million (25·8%) across 962 studies (appendix). Other prominent funding sources included the Biotechnology and Biological Sciences Research Council (BBSRC), the UK Department of Health, the European Commission, the Bill & Melinda Gates Foundation, and the combined investments of smaller charitable foundations.

The Bill & Melinda Gates Foundation awarded the largest mean grant per study (£5·7 million), followed by the European Commission (£1·2 million), the Medical Research Council (£699 000), the UK governmental departments (£611 104), the UK Department of Health (£473 500), the Wellcome Trust (£346 771), and the BBSRC (£322 262). A notable example of the type of grants awarded by the Bill & Melinda Gates Foundation is the £20 million donation in 2002 to establish the Schistosomiasis Control Initiative at Imperial College London.

Sources of funding by research phase vary greatly (table 2). The Medical Research Council was the leading funder of HIV and virology research, with £360 million of investments (36·0%). The Wellcome Trust is the leading funder of malaria and parasitology with £275 million (41·7%), as well as bacteriology research, with £176 million (30·1%). The BBSRC is the leading funder of mycology research with £14·8 million (30·5%) and the UK Department of Health is the leading funder of research into prion disease with £20·2 million (60·2%).

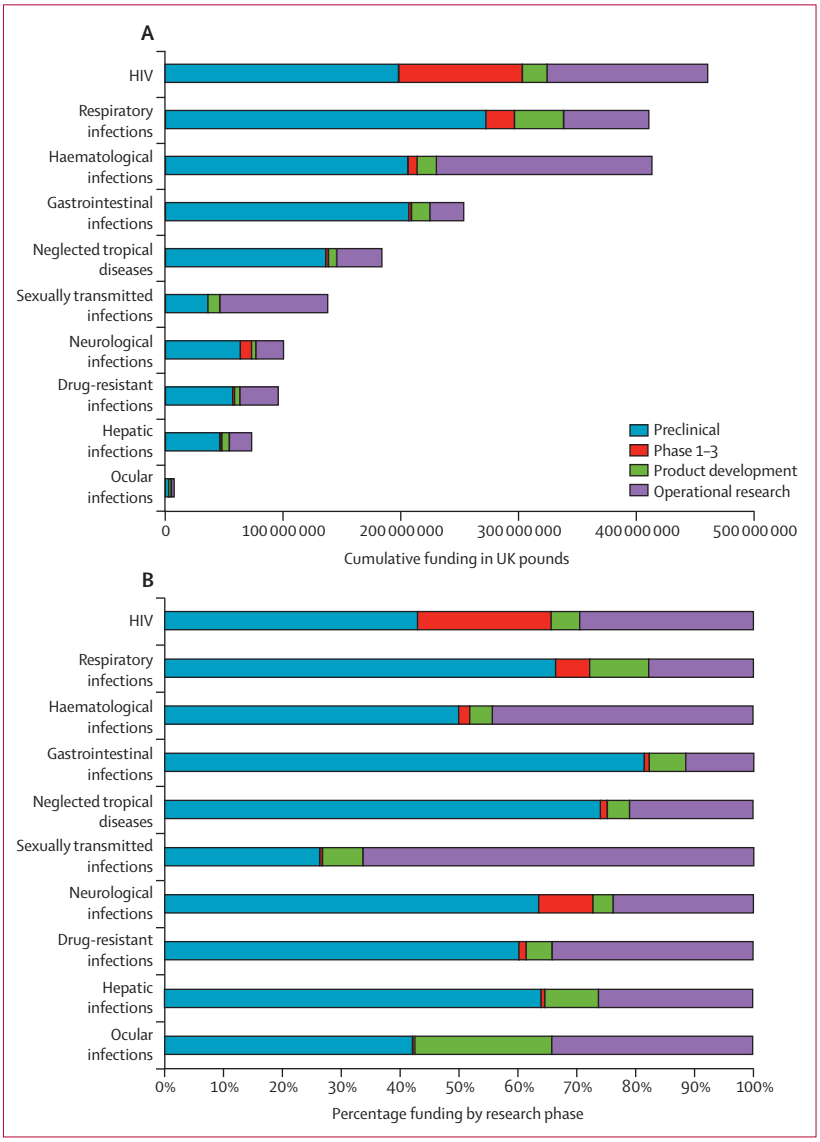

Figure 3: **Distribution of cumulative funding by disease system and breakdown by research pipeline (A), and proportional breakdown of research pipeline within disease system (B)**

Discussion

We identified 6170 funded studies, with a total research investment of £2·6 billion. Studies with a clear global health component represented 35·6% of all funding (£927 million), and the Wellcome Trust and Medical Research Council were the two leading funding sources. Preclinical research accounted for £1·6 billion (62·5%) of the total research and development investment. We highlight several major areas where there might be underinvestment—namely, for research focusing explicitly on infections in elderly people (£7·2 million, 0·3%) and in children (£87·1 million, 3·3%). Investment in some of the neglected tropical diseases, gastrointestinal infections, and sexually transmitted infections excluding HIV are also far lower than their global burden of disease would warrant.

Investment for drug-resistance-related research seems inadequate, since antimicrobial resistance across all areas of infection has been described by WHO as a global public health emergency affecting all countries.[14] Despite the expansion of the directly observed treatment short-course (DOTS) programme for tuberculosis, multidrug-resistant tuberculosis is spreading unabated such that WHO now considers strains of extensively drug-resistant tuberculosis to be "virtually untreatable".[15] Future research investment in this area should increase in line with projected burden.

WHO data suggest that gastrointestinal infections and diarrhoeal disease account for high disease burden and mortality worldwide.[1] However, the research spend for these disorders is substantially lower than other high burden and high profile diseases, such as HIV and malaria. In view of their relative burden, gastrointestinal infections,

For the **Schistosomiasis Control Initiative** see http://www.imperial.ac.uk/schisto

and sexually transmitted infections should therefore be assigned a higher priority for improved research investment by funding organisations. There might be a reasonable argument for a proportionate increase in research related to health-care-associated infections, although there is also a lack of good quality data about burden in this area, particularly in low-income countries.

The burden of infectious diseases is particularly heavy on children, with 64% of worldwide deaths in children younger than 5 years related to infection.[16] We show two key shortcomings for global infectious disease research in relation to children. First, investment in research for infections in children is generally very low, although malaria and vaccines, which mostly relate to children, attracted fairly high levels of funding. From 1997 to 2010, studies specifically focusing on infectious diseases in children attracted £87·1 million across 307 studies, representing 3·3% of the total funding across 5·0% of the total studies. Second, studies relating to nutrition and paediatric infectious diseases were poorly funded despite the huge burden of morbidity and mortality worldwide in children due to malnutrition—a major cause of immune deficiency.[17] Paediatric infectious disease studies with a nutrition component attracted £4·3 million across nine studies, representing only 5·0% of paediatrics funding and 0·2% of total funding.

Analysis by research and development value chain shows that the UK has invested heavily in preclinical research, but invested relatively small amounts in phase 1–4 trials or product development. This discrepancy might represent a strength of UK institutions in preclinical science, but it also highlights a need to strengthen research capacity further along the research and development value chain. There is also a need to obtain comparable data from other countries to understand whether this spending pattern is representative. It would also be useful to gauge whether funders consider they receive a lack of high quality clinical grant applications compared with those in basic science. We noted a lack of readily available data from the pharmaceutical industry, greatly underestimating funding for clinical trials of pharmaceutical products; but this will probably make little difference to estimates of funding for operational research.

Linking investments to disease burden to optimise the allocation of limited research funds is a challenging endeavour. Our findings could be used to develop transparent and objective methods to better couple research investment to burden of disease. Earlier analyses have broadly concluded that the financial spend is appropriate when DALYs are used as a measure of burden, but using measures of incidence or prevalence as a marker for burden of disease were insufficient[8–11] in view of the unreliability of incidence data and that improved management of infections with a high mortality rate often lead to an increase in prevalence.[18] However, defining an appropriate amount of research investment for each disease category is challenging, since different levels of investment might be needed to address diseases with a similar level of public health burden. Emerging infections with unpredictable future disease burden such as prion disease, viral haemorrhagic fevers, or pandemic influenza present particular challenges when establishing relative priority for investment.

Our findings are consistent with earlier studies that focused mainly on research and development spending for global infectious disease,[7] showing the UK to be a leading funder of research and development, along with the USA and European Commission, and showing private sector contributions to neglected disease research to be an estimated US$503 million (£325·4 million) in 2010. Although there is no breakdown by country, the data are categorised by disease area, with tuberculosis, malaria, and dengue attracting the most private investment. Investment by the pharmaceutical industry could affect how other funders invest in research and development for infectious disease (no industry data is included in this analysis because of difficulties in openly accessing funding information),[8] whereas research charities have their own specific areas of focus that might constrain their ability to invest beyond selected diseases. A study of official development assistance allocated for neglected tropical diseases shows low investment levels accounting for only 0·6% of annual health assistance between 2003 and 2007.[19]

Tracking the overall spend on all areas of global health financing is a complex task. This conclusion was based on several factors including fragmentation of data and paucity of detailed information from the private sector. A Global Health Resource Tracking Working Group reported in 2006 that calculating the amount of funding allocated to global health was too difficult owing to several factors including tracking the large and diverse number of public and private sources of funding, and the nature of poorly designed donor accounting structures.[20] A 2009 study investigating global health funding recommended the provision of detailed descriptions of the funding provided to improve the efficiency, accountability, performance, and equity of resource allocation of the many actors that populate the global health landscape.[21] One key recommendation of the Global Health Resource Tracking Working Group was to implement improved tracking and monitoring of global health financing. Within research, this improvement can be achieved both worldwide and nationally, as earlier studies and our report show in the area of infectious diseases.

An important question inspiring our project is whether the right research is being funded. Although the competitive research process used by most funders when awarding grants can help ensure that the funded portfolio is of a high quality, absence of explicit resource allocation criteria means funding for research and development might not reach areas of highest burden. Funding agencies do have their own areas of focus, and thus UK funding agents might have factored other countries'

investments into their own investment strategy. Data from other countries is essential to complete the mapping of investments. WHO budgets and global disease burden have been the centre of much debate.[22–24] The low profile of neglected tropical diseases despite a high disease burden against other tropical diseases such as malaria has been highlighted.[25–27] Studies have also explored ways to maximise the effect of operational research on policy and practice.[28] Our findings build on these earlier studies and contribute to policy discussions relating to investment in research. They also inform funders of funding patterns among organisations financing research and development, which can help prevent suboptimum investment of limited resources.

Showing the relation between health burden and research funding allows identification of areas of under-investment. However, we cannot state with certainty that these gaps represent areas of neglect without factoring in several considerations. These factors include the feasibility of doing the research, the cost of the technologies involved, the presence or absence of suitable infrastructure and appropriately skilled individuals, local political and social conditions, and uncertainty around the accuracy of the estimates of disease burden.

Our analysis has several limitations. We rely on the accuracy of the original data from the funding organisations; although checks were made on any apparent discrepancies or obvious errors, any interpretation of these original data is potentially flawed. No attempt was made to investigate any contribution of indirect and estate costs (including the introduction of full economic costing formulae in the UK), and currency conversions for donations in US dollars or Euros might not be precisely representative of the funding awarded because of fluctuations in financial markets across 1 year. Unless the information was clearly documented, we do not have data to assess how much funding was distributed from the lead institution to study partners.

Study numbers will be slightly inaccurate owing to difficulties ascertaining whether the funding was related to project extension or new study, and whether the funding was for a site as part of a multicentre study. Differences in study reference numbers were used as a guide to distinguish between new studies and extensions and effort made to identify multicentre trials.

Details of private sector research funding are difficult to obtain and analyse in the level of detail we were able to apply to data obtained from public sector and charitable foundations. The National Research Register lists awards of research of direct relevance to the NHS from 1997 to 2007. The register closed at the end of 2007. We could not openly access data for pharmaceutical industry in-house research and development investment, since much of this information is considered commercially sensitive. Individual awards of many millions of pounds for research into specific diseases could skew the results. There are no data from the Chief Scientist Office (Scotland) from 2008 to 2010, which might underestimate overall figures for research and development.

We cannot ascertain what proportion of a grant should be allocated to each of the allocated disease categories. Hence, there might be disagreement about how the categories have been assigned. Some studies could not be allocated to categories since there was no clear implication of association with that category—for example hepatitis B could not be allocated to sexually transmitted infections unless this factor was suggested in the study title or abstract, owing to the pathogen's many modes of transmission. Creation of disease categories and allocation of studies to the categories is subjective.

Burden measures are typically an estimate, since data could be missing, unobtainable, or subject to a different classification system or case diagnosis. Our analysis cannot easily account for the cross-disciplinary or geographical effect of research.

Our report presents the latest figures on investments in local and global infectious disease research awarded to UK institutions between 1997 and 2010 (panel). Neglected tropical diseases, gastrointestinal infections, sexually transmitted infections, and antimicrobial resistance seem to be areas warranting increased investment. We will make the entire database and figures available online to assist policy makers, funding organisations, and fellow researchers in the identification of research gaps and infectious disease priorities (see margin link). We urge funding organisations to make their investment portfolios

For the **Research Investements in Global Health database** see http://www.researchinvestments.org

***Panel:* Research in context**

Systematic review

We searched PubMed for articles published at any time with the search terms "investments in research" and "infectious disease burden", as well as "burden" and specific infectious diseases or cross-cutting themes. We also searched for published reports with the same search terms. No publication investigating the investments in infectious disease research by the UK over time was identified.

Interpretation

Our study is the first to do a detailed assessment that the infectious disease research investments made by funding organisations to UK institutions. Health research investment decisions need to balance strategic insight into the burden of disease with judgments on scientific quality and novelty. We identify inconsistencies of investment compared with the global burden of infection, suggesting the need for strategies to redress this imbalance. The scientific and public health community, as well as governments and health departments, need to ensure limited resources are allocated appropriately and strategically. We encourage the support of similar open-access databases for non-communicable diseases and other countries, as well as further work comparing research funding with disease burden.

openly accessible on this website by reporting their successful grants each year, as we have seen with the clinical trials registry ClinicalTrials.gov. We encourage the development of similar databases for non-communicable diseases and other countries, as well as further work on comparing research funding to disease burden.

High-quality research can allow substantial improvements in redressing the infectious disease burden. As emphasised by the neglected tropical diseases movement, increased funding and better-informed resource allocation could help control, eliminate, and eradicate infectious diseases.[29] The scientific and public health community, as well as governments and health departments, need to ensure limited resources are allocated appropriately and strategically, particularly with regards to health care and the alleviation of infectious disease morbidity and mortality.

Contributors

MGH designed the study and collated the dataset. JRF undertook data analysis and created the graphs and figures with input from MGH and RA. MGH, JRF, and RA interpreted the data and wrote the first draft. MGH, JRF, and RA refined the analysis and paper with input from FBW, MKC, and ACH. All authors reviewed and approved the final version. MGH is guarantor of the paper.

Conflicts of interest

RA has received research funding from the Medical Research Council, the National Institute for Health Research and the UK Department for International Development. RA is a member of the Medical Research Council Global Health Group. MGH works for the Infectious Disease Research Network, which has supported this work and is funded by the UK Department of Health. JRF has received funds from the Wellcome Trust and is a steering group member for the Infectious Disease Research Network. MKC has received funding from the Medical Research Council and the Bill & Melinda Gates Foundation. FBW has received funds from UCLH Charitable Foundation. ACH has received funds from the Medical Research Council, the Wellcome Trust, the UK Department of Health, the National Institute of Health Research and the Biotechnology and Biological Sciences Research Council.

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