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.

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 figures1 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, there is no 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 failure4–6 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.2,3

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.27 Studies to assess the research spend according to the burden of disease, with data sourced from Australia, Canada, Spain, and the USA,3–11 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
investor in infectious disease research) are poorly documented, partly because of commercial sensitivity. 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 there was still disagreement, the data were circulated to all authors for review and comment. MKC double-checked by JRF. Provisional datasets were 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 MGH and the author who flagged the study, and differences on inclusion or categorisation were discussed between the authors when categorising studies. All marginal κ scores 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 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...
| Disease system                          | Investment (total), £ (n %) | Studies, n (%) | 2004 mortality, n (%) | 2004 DALYs, n (%) | Investment (2005-10), £ (n %) | 2008 mortality, n (%) | 2008 DALYs, n (%) |
|----------------------------------------|-----------------------------|----------------|-----------------------|-------------------|------------------------------|----------------------|-------------------|
| **Gastrointestinal infections**        |                             |                |                       |                   |                              |                      |                   |
| Gastroenteritis                         | 254 006 242 (9·7%)          | 799 (12·9%)    | 130 488 965 (9·5%)    | 498 (12·6%)       | 2 169 764 (22·2%)            | 76 789 182 (25·1%)   | 1 245 727 (10·0%) |
| Helminths                              | 41 488 870 (15·9%)          | 742 (12·0%)    | 190 188 198 (13·9%)   | 594 (12·8%)       | 889 186 (9·1%)              | 33 976 026 (11·1%)   | 223 306 472 (18·0%) |
| Hepatic infections                      | 73 965 716 (2·8%)           | 322 (5·2%)     | 48 559 066 (3·6%)     | 253 (6·4%)        | 199 792 (2·0%)              | 4 769 299 (1·6%)     | 25 106 651 (2·0%) |
| *Helicobacter*                          |                             |                |                       |                   |                              |                      |                   |
| *Campylobacter*                         | 184 446 162 (7·1%)          | 392 (6·4%)     | 113 018 676 (8·3%)    | 267 (6·8%)        | 182 153 (1·9%)              | 18 323 958 (6·0%)    | 71 428 087 (5·8%) |
| *Salmonella*                            | 101 363 708 (3·9%)          | 339 (5·5%)     | 62 685 765 (4·6%)     | 241 (6·1%)        | 392 292 (4·0%)              | 13 099 105 (4·3%)    | 38 676 941 (3·1%) |
| *Shigella*                              | 7 407 218 (0·3%)            | 36 (0·6%)      | 3 574 775 (2·7%)      | 27 (0·6%)         | 173 (0·6%)                  | 1 722 990 (0·6%)     | 382 443 (0·3%)   |
| *Entamoeba*                             | 410 705 744 (15·8%)         | 190 (3·0%)     | 197 356 636 (14·4%)   | 73 (2·8%)         | 4 258 563 (45·3%)           | 97 786 126 (32·0%)   | 213 349 109 (17·2%) |
| *Salmonella*                            | 138 516 533 (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%) |
| *Campylobacter*                         |                             |                |                       |                   |                              |                      |                   |
| Ocular infections                       | 1 120 072 (0·1%)            | 8 (0·1%)       | 237 210 (0·8%)        | 8 (0·6%)          | 1 028 298 (0·1%)            |                      |                   |
| Chagas disease                          | 3 448 856 (0·2%)            | 15 (0·0%)      | 2 227 761 (0·8%)      | 12 (0·6%)         | 11 367 (0·1%)               | 429 873 (0·2%)       | 926 096 (0·1%)   |
| *Chlamydia*                             | 21 702 378 (1·2%)           | 112 (1·8%)     | 17 462 388 (2·8%)     | 73 (2·7%)         | 888 997 (1·8%)              | 37 489 198 (1·8%)    | 422 399 900 (5·0%) |
| *Clostridium*                           | 28 751 310 (1·6%)           | 72 (1·3%)      | 5 164 027 (1·8%)      | 29 (1·1%)         | 25 199 334 (1·4%)           |                      |                   |
| *Cytomegalovirus*                       | 28 369 415 (1·6%)           | 68 (1·7%)      | 18 888 235 (2·0%)     | 60 (2·3%)         | 9 581 430 (1·1%)            |                      |                   |
| *Dengue*                                | 43 742 101 (2·4%)           | 28 (0·7%)      | 4 430 589 (0·6%)      | 15 (0·3%)         | 18 104 (0·6%)               | 669 648 (0·3%)       | 39 311 513 (4·5%) |
| *Diptheria*                             | 139 883 (0·0%)              | 2 (0·0%)       | 139 863 (0·0%)        | 2 (0·0%)          | 5 091 (0·0%)                | 1 735 75 (0·0%)      | 0 (0·0%)         |
| *Escherichia coli*                      | 25 589 407 (1·4%)           | 106 (2·7%)     | 15 852 833 (2·6%)     | 74 (2·8%)         | 9 760 027 (2·4%)            |                      |                   |
| *Epstein-Barr virus*                    | 45 310 414 (2·5%)           | 147 (3·7%)     | 32 961 882 (5·3%)     | 114 (4·3%)        | 12 348 532 (3·4%)           |                      |                   |
| *Gonorrhoea*                            | 948 399 (0·1%)              | 18 (0·1%)      | 768 377 (0·1%)        | 14 (0·0%)         | 559 (0·0%)                  | 3 549 976 (0·1%)     | 180 021 (0·0%)   |
| *Helicobacter*                          | 15 109 554 (0·8%)           | 101 (2·6%)     | 12 942 723 (3·1%)     | 96 (3·6%)         | 2 262 304 (0·3%)            |                      |                   |
| *Helminths*                             | 47 025 464 (1·4%)           | 114 (2·9%)     | 25 762 808 (2·7%)     | 77 (2·9%)         | 47 828 (5·5%)               | 11 660 451 (2·4%)    | 21 265 645 (2·7%) |
| *Hepatitis B*                           | 11 768 095 (0·6%)           | 68 (1·0%)      | 9 829 208 (1·6%)      | 57 (1·7%)         | 104 606 (1·7%)              | 2 067 333 (1·0%)     | 1 938 888 (0·2%) |
| *Hepatitis C*                           | 59 727 829 (3·3%)           | 235 (5·9%)     | 38 124 517 (6·8%)     | 182 (9·0%)        | 54 099 (0·5%)               | 994 622 (0·5%)       | 21 605 212 (2·5%) |

(Continues on next page)
| Disease                  | 2004 mortality, n (%) | 2004 DALYs, n (%) | Investment (2005–10), £ (%) | 2008 mortality (projected), n (%) | 2008 DALYs (projected), n (%) |
|-------------------------|-----------------------|------------------|-----------------------------|-----------------------------------|-------------------------------|
| HIV                     | (25·3%)               | (19·2%)          | 460 547 457 (25·6%)         | 243 457 371 (18·0%)               | 203 972 727 (22·2%)           |
| Human papillomavirus    | (3·2%)                | (3·8%)           | 57 951 110 (4·4%)           | 142 612 848 (4·2%)                | 268 245 (2·8%)                |
| Herpes simplex virus    | (1·2%)                | (1·2%)           | 22 063 300 (1·9%)           | 18 201 738 (2·1%)                 | 37 193 148 (1·8%)             |
| Influenza               | (4·4%)                | (3·5%)           | 79 763 001 (3·1%)           | 29 388 168 (3·6%)                 | 16 342 428 (4·2%)             |
| Leishmaniasis           | (2·0%)                | (1·9%)           | 36 072 609 (1·7%)           | 15 165 650 (1·8%)                 | 46 945 232 (3·1%)             |
| Leprosy                 | (0·0%)                | (0·1%)           | 6 230 080 (0·1%)            | 6 230 080 (0·1%)                  | 5 442 (0·1%)                  |
| Listeria                | (0·3%)                | (0·3%)           | 4 751 657 (0·3%)            | 3 947 669 (0·3%)                  | 8 034 282 (0·1%)              |
| Lymphatic filariasis    | (2·8%)                | (0·4%)           | 51 112 541 (17·4%)          | 3 679 045 (1·2%)                  | 290 (0·2%)                    |
| Malaria                 | (19·0%)               | (12·8%)          | 346 180 494 (14·0%)         | 165 764 640 (12·8%)               | 883 186 (14·0%)               |
| Measles                 | (0·1%)                | (0·2%)           | 2 597 677 (0·2%)            | 1 630 534 (0·2%)                  | 423 710 (0·2%)                |
| Meningitis              | (3·9%)                | (3·7%)           | 54 078 664 (3·7%)           | 35 650 075 (3·7%)                 | 339 945 (3·7%)                |
| Norovirus               | (1·0%)                | (0·4%)           | 5 102 325 (0·4%)            | 1 250 218 (0·4%)                  | 6 (0·0%)                      |
| Onchocerciasis          | (0·1%)                | (0·2%)           | 1 328 978 (0·2%)            | 1 328 978 (0·2%)                  | 65 (0·2%)                     |
| Pertussis               | (0·1%)                | (0·2%)           | 2 432 358 (0·2%)            | 1 657 979 (0·3%)                  | 254 497 (0·3%)                |
| Polio                   | (0·1%)                | (0·1%)           | 1 189 984 (0·1%)            | 247 880 (0·1%)                    | 119 (0·0%)                    |
| Pseudomonas             | (0·4%)                | (1·1%)           | 6 473 237 (1·4%)            | 3 417 409 (1·4%)                  | 3 170 837 (0·4%)              |
| Rotavirus               | (0·3%)                | (0·5%)           | 5 883 445 (0·3%)            | 3 026 257 (0·3%)                  | 15 (0·0%)                     |
| Respiratory syncytial virus | (0·9%)     | (1·2%)           | 16 899 738 (1·2%)           | 11 817 246 (1·2%)                 | 254 497 (0·3%)                |
| Salmonella              | (3·1%)                | (3·7%)           | 55 716 287 (3·7%)           | 31 416 306 (3·7%)                 | 81 (0·0%)                     |
| Schistosomiasis         | (2·1%)                | (3·7%)           | 38 677 801 (3·7%)           | 35 086 117 (3·7%)                 | 41 087 (0·6%)                 |
| Shigella                | (0·2%)                | (0·2%)           | 3 292 442 (0·2%)            | 1 887 561 (0·2%)                  | 4 (0·0%)                      |
| Syphilis                | (0·1%)                | (0·1%)           | 1 061 560 (0·1%)            | 775 444 (0·1%)                    | 199 167 (0·1%)                |
| Tetanus                 | (0·1%)                | (0·2%)           | 1 228 583 (0·2%)            | 1 228 583 (0·2%)                  | 162 867 (0·2%)                |
| Trachoma                | (0·1%)                | (0·1%)           | 1 928 640 (0·1%)            | 608 792 (0·1%)                    | 108 (0·0%)                    |
| Tuberculosis            | (8·2%)                | (7·4%)           | 1 488 601 691 (8·2%)        | 70 024 803 (7·4%)                 | 1 465 792 (8·2%)              |
| Varicella zoster virus  | (0·2%)                | (0·5%)           | 4 186 583 (0·5%)            | 2 112 877 (0·5%)                  | 18 (0·0%)                     |
| Total infections        | (3·8%)                | (0·9%)           | 1 820 658 688 (3·8%)        | 953 985 167 (0·9%)                | 633 105 (0·9%)                |
| Overall                 | (2004)                | (2008)           | (2005–10)                   | (projected)                       | (projected)                   |

*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 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).11

**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 320470 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 and evaluation of the research investments were performed on a per-institution basis.

![Table 2: Investment by funding source and research and development phase](http://www.who.int/neglected_diseases/diseases/en/)

**For the list of neglected tropical diseases focused on by WHO see http://www.who.int/neglected_diseases/diseases/en/**
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), £4·6 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%).

**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. 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”. 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. 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,
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.18 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 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.19 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),7 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 2007.20

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.21 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.22 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.7–9 Studies have also explored ways to maximise the effect of operational research on policy and practice.29 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 open 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.
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.28 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
MHG designed the study and collated the dataset. JRF undertook data analysis and created the graphs and figures with input from MHG and RA. MHG, JRF, and RA interpreted the data and wrote the first draft. MHG, JRF, and RA refined the analysis and paper with input from FBW, MKC, and ACH. All authors reviewed and approved the final version. MHG 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. MHG 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 funding from the Medical Research Council Global Health Group. MGH works for the Infectious Disease Research and Training in Tropical Diseases 2012. Global Report for Maternal and Perinatal Health. The Lancet. Progress and challenges in neglected tropical 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.

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