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Funding healthcare-associated infection research: a systematic analysis of UK research investments, 1997–2010☆

M.G. Head [a,*], J.R. Fitchett [b], A.H. Holmes [c], R. Atun [d]

[a] University College London, Research Department of Infection and Population Health, London, UK
[b] King's College London, Department for Infectious Diseases, London, UK
[c] Centre of Infection Prevention and Management, Faculty of Medicine, Imperial College, Hammersmith Hospital, London, UK
[d] Harvard School of Public Health, Harvard University, Boston, MA, USA

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SUMMARY

Background: Healthcare-associated infections (HCAIs) are a cause of high health and economic burden in the UK. The number of HCAI research studies funded in the UK, and the associated amount of investment, has not previously been analysed.
Aim: To assess the level of research funding awarded to UK institutions for HCAI research and the relationship of funded research to clinical and public health burden of HCAIs.
Methods: Databases and websites were systematically searched for information on how infectious disease research studies were funded for the period 1997–2010. Studies specifically related to HCAI research were identified and categorized in terms of funding by pathogen, disease, and by a research and development value chain describing the type of science.
Findings: The overall dataset included 6165 studies (total investment £2.6 billion) of which £57.7 million was clearly directed towards HCAI research across 297 studies (2.2% of total spend, 2.1% of total studies). Of the HCAI-related projects, 45 studies had a specific focus on MRSA (£10.3 million), 14 towards *Clostridium difficile* (£10.7 million), two towards pneumonia (£0.3 million) and 103 studies related to surgical infections (£14.1 million). Mean and median study funding was £194,129 (standard deviation: £429,723) and £52,684 (interquartile range: £9,168 to £201,658) respectively. Award size ranged from £108 to £50.0 million.
Conclusions: Research investment for HCAIs has gradually increased in the study period, but remains low due to the health, economic, and social burden of HCAI. Research for hospital-acquired pneumonia, behavioural interventions, economic analyses, and research on emerging pathogens exhibiting antimicrobial resistance remain underfunded.

Introduction

Healthcare-associated infections (HCAIs) account for a significant burden of disease in the UK. Meticillin-resistant *Staphylococcus aureus* (MRSA) infections, which were the subject of much media attention, peaked in 2003, but in

* Corresponding author. Address: University College London, Research Department of Infection and Population Health, UCL Royal Free Campus, London NW3 2PF, UK. Tel.: +44 (0) 20 7794 0500x38822.
E-mail address: m.head@ucl.ac.uk (M.G. Head).

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England since 2006 there has been a decline in the rate of MRSA bloodstream infection.[1] Similarly, rates of *Clostridium difficile* infection have been decreasing year on year in the UK since 2008, though they still number almost 15,000 per year, and there are global concerns about antimicrobial resistance; for example, carbapenem-resistant *Acinetobacter baumannii* is increasing in prevalence and is notable in particular for its ability to cause infections in immunocompromised patients.[2–4] Norovirus is a common pathogen in hospitals, often causing outbreaks that require the closures of wards in England and beyond with consequent significant economic burden.[5] Viral hepatitis may be transmitted by multiple routes and in numerous different settings, including within the healthcare setting – one review reported on 33 hepatitis B virus outbreaks that involved 471 patients, with 16 fatal cases.[6] In the UK, there has also been neonatal mortality associated with outbreaks of pseudomonas.[7]

The true economic burden of HCAIs across UK hospitals and other healthcare providers is difficult to establish – the most recent estimate published in 2000 suggested that the annual cost of HCAIs in the UK was approximately £1 billion.[8] Antimicrobial resistance (AMR) has also led to substantial morbidity, mortality and financial impact on hospitals and other healthcare institutions. Globally, infection prevention and control has become a priority for healthcare organizations, and institutional management of HCAIs is recognized as being critical to improving quality of care and patient safety.[9]

In the USA, the total annual costs of HCAIs is thought to be greater than US$9.8 billion, with surgical site infections contributing to a third of these costs, and approximately 50% of the incidence is thought to be preventable.[10] The infection rates for HCAIs vary greatly by country.[11] Globally, there is a high burden of antimicrobial resistance bacteria.[12] Healthcare-associated bloodstream infections and pneumonia have been shown to greatly increase mortality and the length of stay in intensive care units.[13] Modelling studies have typically been limited to studying transmission pathways in the UK, USA and The Netherlands, rather than the health, economic, and societal cost of HCAIs.[14] There are few data on the burden of HCAIs in low-income countries.[15]

Between 1997 and 2010, UK research institutions received around £2.6 billion of public and philanthropic funding for infectious disease research from a variety of national and international funding sources.[16] In this study, we estimate research funding awarded to UK institutions specifically for HCAI research, with temporal trends, and assess the relationship of funded research to clinical and public health burden of HCAIs.

Methods

We analysed all the studies funded in a 14-year period (1997–2010 inclusive) that were clearly relevant to, or had specific mention of, healthcare-associated infectious disease. No private sector (commercial) funding was included in this analysis as few data are publicly available.

The analysis presented here is a subset of a larger study on funding of infectious diseases in the UK, and as such the methods have been described in detail elsewhere, but are discussed here briefly.[16] The overarching dataset was developed following a detailed and systematic search of all the studies for infectious disease research from the major sources of public and charitable funding for infectious disease research studies, including the Wellcome Trust, Medical Research Council, and other research councils, UK government departments, European Commission, the Bill and Melinda Gates Foundation, and other research charities. We developed the dataset by (a) downloading all data from the funder website and manually filtering the infectious disease studies; or (b) searching open access databases on the funder website for infection-related keyword terms; or (c) contacting the funder directly and requesting details of their infection studies. Funders were identified through the authors' knowledge of the research and development landscape and searches of the Internet. M.G.H. performed the majority of data extraction, with support from J.R.F. Each study was assigned to as many primary disease categories as appropriate.[17] Within each category, topic-specific subsections (including specific pathogen or disease) were documented. Studies were also allocated to one of four research and development categories: preclinical; phase I, II, or III; product development; and implementation and operational research (including surveillance, epidemiology and statistical and modelling projects; for definitions and examples see ResIn[18]). Funders were considered either in their own right, or for convenience; some were grouped into categories, such as in-house university funding, research charities, and government departments. In total, 26 funder categories were used. Studies were excluded if: (i) they were not immediately relevant to infection; (ii) they were veterinary infectious disease research studies; (iii) they concerned the use of viral vectors to investigate non-communicable diseases; (iv) they were grants for symposia or meetings; or (v) they included UK researchers, but with the funding awarded to and administered through a non-UK institution. Studies were categorized as HCAI research where there was specific mention of, or a clear implication of relevance to, HCAIs in the title or abstract. Unfunded studies were excluded. 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 awards were adjusted for inflation and reported in 2010 UK pounds. Analysis was carried out in Microsoft Excel and Access (versions 2000 and 2007) and Stata (version 11).

Results

We identified 6165 studies funded within the 14-year study period and covering all infectious disease research, representing a total investment of £2.6 billion. There were 297 studies of relevance to HCAI research, comprising in number 2.1% of total infectious disease research projects. These 297 studies were awarded £57.7 million, 2.2% of the total spend, with a median award of £52,684 (interquartile range: £9,168 to 201,658) and mean award of £194,129 (standard deviation: £429,723) (Table I). Award size ranged from £108 to £50.0 million.

Of the 297 HCAI projects (Table I), MRSA was the most-studied pathogen across 45 studies (15.2%), and these received £10.3 million (17.9%) of investment. There were 14 *C. difficile* studies (4.7%), which received investment of £10.7 million (18.5%), whereas acinetobacter investment totalled £0.3 million across four studies, viral hepatitis investment

Table I
Investments in healthcare-associated infection (HCAI) research areas by sum, numbers of studies, median and mean award and top funder

Disease	No. of studies	% of HCAI study no.	Total funding	% of HCAI funding	Mean award, £ (SD)	Median award, £ (IQR)	Top funder, millions (%)
HCAI	297	NA	£57,656,313	NA	194,129 (429,723)	52,684 (9,168–201,658)	Department of Health, 14.3 (24.9)
Pathogen							
MRSA	45	15.2%	£10,311,703	17.9%	229,149 (610,810)	50,410 (4,566–155,478)	Medical Research Council, 4.3 (41.9)
Clostridium difficile	14	4.7%	£10,658,337	18.5%	761,309 (1,269,328)	122,202 (5,396–1,176,072)	European Commission, 6.7 (63.1)
Norovirus	1	0.3%	£684	0	684 (NA)	684 (NA)	NHS Trust (NA)
Acinetobacter	4	1.3%	£341,518	0.6%	85,379 (158,998)	7,959 (3,675–167,083)	Medical Research Council, 0.3 (94.8)
Hepatitis	13	4.4%	£2,032,137	3.5%	156,318 (118,904)	153,325 (66,747–197,873)	Department of Health, 0.5 (24.9)
Pneumonia	2	0.7%	£300,800	0.5%	150,400 (70,372)	150,400 (100,639–200,160)	Wellcome Trust, 0.3 (100%)
Prion	6	2.0%	£3,717,911	6.4%	619,651 (398,861)	644,033 (249,122–972,600)	Department of Health, 2.7 (73.8)
Pseudomonas	7	2.4%	£1,146,868	2.0%	163,838 (137,562)	253,336 (13,813–254,591)	BBSRC, 1.1 (96.0)
Infection group							
Antimicrobial resistance	71	23.9%	£15,578,161	27.0%	219,411 (496,690)	91,602 (11,708–227,408)	Medical Research Council, 4.4 (28.5)
Behavioural	18	6.1%	£3,145,060	5.5%	174,725 (244,696)	15,967 (7,888–342,018)	Department of Health, 1.1 (36.4)
Catheter-related	14	4.7%	£3,582,006	6.2%	255,859 (430,777)	57,402 (22,900–323,559)	Department of Health, 2.6 (71.7)
Cleaning and decontamination	17	5.7%	£5,012,072	8.7%	294,827 (368,736)	144,918 (32,835–374,646)	Department of Health, 3.4 (68.3)
Diagnostics	27	9.1%	£4,342,730	7.5%	160,842 (41,462)	41,462 (4,145–130,218)	Department of Health, 3.2 (74.9)
Economics	12	4.0%	£1,481,225	2.6%	123,435 (181,743)	53,584 (25,397–157,767)	Department of Health, 1.0 (69.2)
Enteric	20	6.7%	£6,518,628	11.3%	325,931 (677,894)	13,194 (2,798–224,592)	European Commission, 2.5 (37.8)
Geriatrics	3	1.0%	£525,251	0.9%	175,084 (40,530)	155,478 (148,084–221,690)	Department of Health, 0.2 (42.2)
Paediatrics	15	5.1%	£413,028	0.7%	27,535 (26,572)	15,077 (4,567–44,874)	Charity, 0.3 (74.3)
Respiratory	18	6.1%	£2,559,453	4.4%	142,192 (108,175)	155,484 (13,813–231,865)	BBSRC, 1.1 (43.1)
Surgery	103	34.7%	£14,145,700	24.5%	137,337 (200,539)	49,895 (7,604–166,156)	Medical Research Council, 3.2 (23.0)
Therapeutics	20	6.7%	£2,464,179	4.3%	123,208 (182,963)	71,623 (21,783–141,113)	Medical Research Council, 0.7 (30.9)
Vaccinology	8	2.7%	£254,480	0.4%	31,810 (34,307)	23,444 (9,218–40,714)	Charity, 0.1 (57.8)

SD, standard deviation; IQR, interquartile range; MRSA, meticillin-resistant *Staphylococcus aureus*; NHS, National Health Service; NA, not applicable; BBSRC, Biotechnology and Biological Sciences Research Council.

totalled £2.0 million across 13 studies, pseudomonas investment totalled £1.1 million across seven studies, and norovirus specifically as HCAI received only £684 in one small study. Hospital-acquired pneumonia received investment totalling £0.3 million across just two studies, and prion research received £3.7 million across six studies.

By cross-cutting theme (Table I), 71 studies (23.9%) focused on antimicrobial resistance, with an investment of £15.6 million (27.0%), and surgical infections were investigated in 103 studies (34.7%), with an investment of £14.1 million (24.5%). Studies related to behavioural sciences received £3.1 million (5.5%) investment across 18 studies (6.1%), whereas catheter-related research received £3.5 million (6.2%) across 14 (4.7%) studies – of these studies, six were clearly related to urinary catheters, four to venous catheters and four were unclear. There were 17 studies (5.7%) considering cleaning regimens or decontamination procedures, receiving £5.0 million (8.7%) of investment. There were no studies specifically relating to HCAI and global health, nor were there any studies relating to HCAI and rotavirus or streptococcal infection.

Overall funding appears to have increased over time (Figure 1), with an increasing focus on antimicrobial resistance research.[19] Along the research and development value chain (Table II; Figure 2), preclinical research received £23.5 million across 97 studies, phase I–III studies received £1.1 million across 12 studies, product development research received £6.8 million across 34 studies, and implementation and operational research received £26.2 million across 154 studies. The UK Department of Health provided the greatest quantities of investment in HCAI research (£14.3 million, 24.9%), followed by the European Commission (Figure 3).

Discussion

This study is the first systematic analysis of research funding for HCAIs in the UK. Over the 14-year study period 1997–2010, 297 studies were identified for HCAIs where public funding had been awarded to a UK institution. The most-studied pathogen was MRSA (45 studies, £10.3 million). There was a focus on surgical infections (103 studies, £14.1 million) and antimicrobial resistance (71 studies, £15.6 million). The small median award of HCAI research studies (and wide interquartile ranges, difference from the mean and associated standard deviation) demonstrates that there were numerous relatively small grants, set alongside a few large investments. The UK Department of Health was the leading investor in HCAI research. The total investment (2.1% of the dataset) appears to be relatively low as compared with research funding awarded to some other infectious diseases, considering that HCAIs constitute one of the major complications for patients following hospitalization or contact with other healthcare providers.[16]

The increase in preclinical science awards for HCAI research in the later years of this dataset may reflect the improvements in laboratory technologies that enable preclinical outputs to be effectively incorporated within a hospital environment, and thus dovetail with pieces of translational research that aim to be of direct benefit to patients. The majority of these studies relates to point-of-care diagnostics and susceptibility testing.

The UK Chief Medical Officer has described antimicrobial resistance as a public health emergency, and although approximately one-quarter of all HCAI funding was related to antimicrobial resistance research, this only totals £15.6 million and is relatively poorly funded across all of infectious disease research within this dataset.[19,20] Much of the funding for AMR research was for MRSA, in a time period when incidence of MRSA peaked and then fell; given around half the MRSA-related HCAI studies (albeit less than one-third of the funding) related to translational research, it is entirely possible that research had an impact on this decline.[1] However, the emergence of highly resistant Gram-negative bacteria poses a real threat to patients in both healthcare settings and in the community, and warrants larger research investment.[19,20]

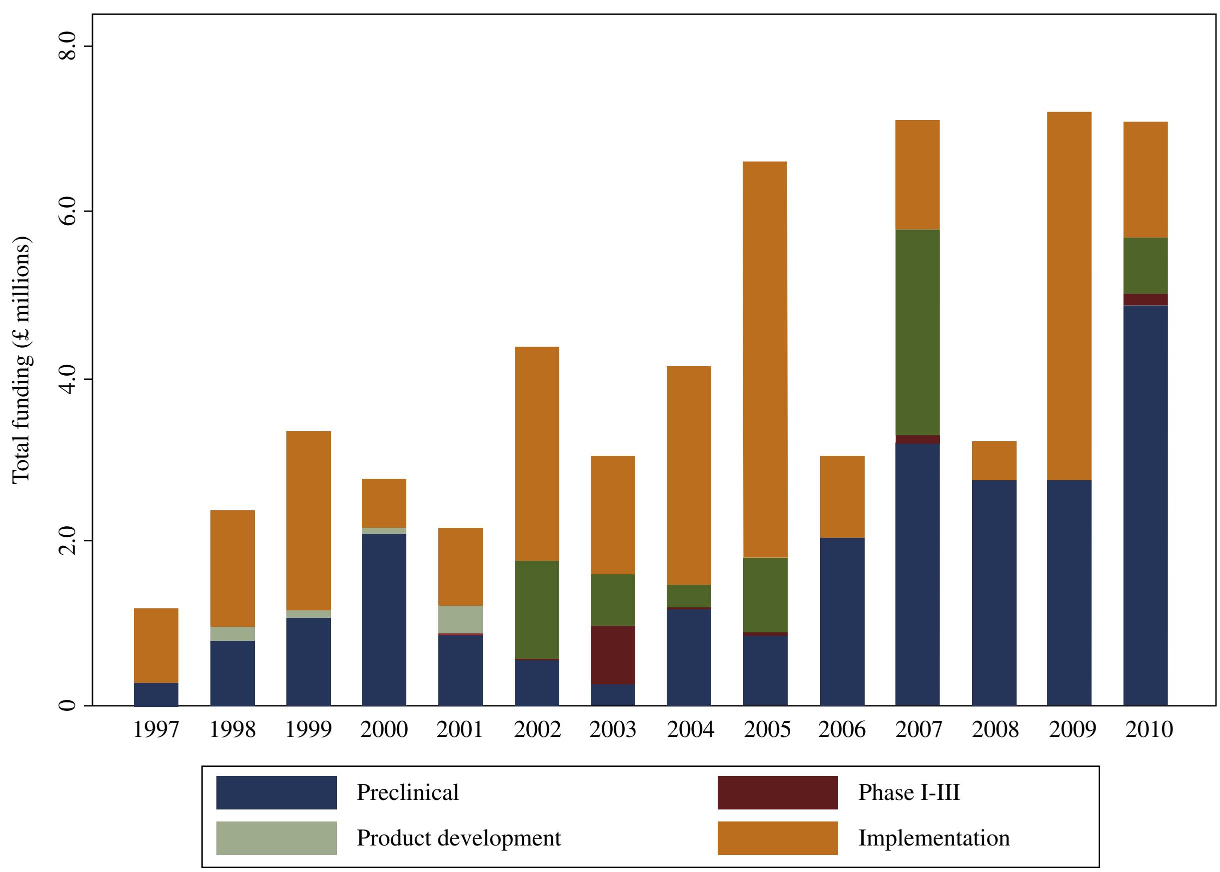

Figure 1. Sum investment over time by type of science.

Table II
Investments in healthcare-associated infection (HCAI) research areas by type of science

Disease	No. of studies	Total funding	Preclinical		Phase I–III		Product development		Operational	
			Study numbers	Funding	Study numbers	Funding	Study numbers	Funding	Study numbers	Funding
HCAI	297	£57,656,313	97	£23,498,978	12	£1,090,842	34	£6,769,284	154	£26,297,279
Pathogen										
MRSA	45	£10,311,703	14	£6,115,836	1	£653,912	2	£383,468	28	£3,158,485
Clostridium difficile	14	£10,658,337	6	£4,481,194	0	£0	0	£0	8	£6,177,144
Norovirus	1	£684	0	£0	0	£0	0	£0	1	£684
Acinetobacter	4	£341,518	4	£341,518	0	£0	0	£0	0	£0
Hepatitis	13	£2,032,137	5	£729,894	0	£0	1	£231,831	7	£1,070,413
Pneumonia	2	£300,800	2	£300,800	0	£0	0	£0	0	£0
Prion	6	£3,717,911	1	£249,122	0	£0	0	£0	5	£3,468,789
Pseudomonas	7	£1,146,868	7	£1,146,868	0	£0	0	£0	0	£0
Infection group										
Antimicrobial resistance	71	£15,578,161	26	£9,072,594	0	£0	7	£886,555	38	£5,619,011
Behavioural	18	£3,145,060	0	£0	0	£0	1	£572,511	17	£2,572,550
Catheter-related	14	£3,582,006	5	£1,207,042	0	£0	3	£2,167,734	6	£207,230
Cleaning and decontamination	17	£5,012,072	4	£129,594	0	£0	3	£378,370	10	£4,504,107
Diagnostics	27	£4,342,730	12	£1,020,859	0	£0	6	£1,039,782	9	£2,282,088
Economics	12	£1,481,225	0	£0	0	£0	0	£0	12	£1,481,225
Enteric	20	£6,518,628	8	£4,582,107	0	£0	2	£18,623	10	£1,917,897
Geriatrics	3	£525,251	0	£0	0	£0	0	£0	3	£525,251
Paediatrics	15	£413,028	1	£41,462	7	£151,588	1	£56,814	6	£163,164
Respiratory	18	£2,559,453	10	£1,679,532	1	£107,282	1	£6,171	6	£766,468
Surgery	103	£14,145,700	36	£6,868,113	10	£956,900	12	£1,852,062	45	£4,468,623
Therapeutics	20	£2,464,179	4	£1,296,707	2	£167,373	10	£773,573	4	£226,525
Vaccinology	8	£254,480	0	£0	8	£254,480	0	£0	0	£0

MRSA, meticillin-resistant *Staphylococcus aureus*.

Research funding for behavioural sciences that explored HCAI typically included studies relating to hand hygiene or attitudes to specific aspects of infection control (e.g. visitor compliance with restricted movements around a ward); however, research investment in this area was very limited. The evaluation of the UK national CleanYourHands campaign, one of the largest HCAI research studies, concluded that the campaign had an important role in reducing the rates of some HCAIs; however, there are clear gaps in our knowledge of positive behavioural change in relation to infection control, and further research is needed to understand which behavioural interventions are effective in healthcare settings.[21]

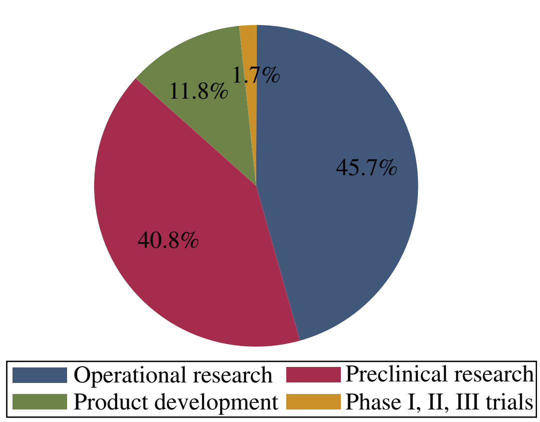

Figure 2. Proportion of investment in healthcare-associated infection research by type of science.

There were few studies related to cleaning and decontamination. The challenges of keeping a healthcare environment clean are complex, and the definition of 'clean' varies across settings. Spores originating from *C. difficile* complicate cleaning regimens and the most effective ways of dealing with them are not entirely clear – for example, whereas one study found that altering the cleaning regimen contributed to a decrease in *C. difficile* infections, another review did not.[22,23] There is a wide range of cleaning products available, and many have not been assessed against patient outcome and queries over the toxicity and effectiveness of disinfectants against detergents.[24] The median award (£144,918, as against £52,684 for all HCAIs) indicates that larger investments were made for cleaning research, although some of these awards were for research that explored decontamination in relation to prions. Implementation of the most effective cleaning policies are likely to be inexpensive without requiring complex technologies, and perhaps even a small updated portfolio of research to build upon the existing published work in this area might be relatively high impact and cost-effective, and therefore may be considered by funders and healthcare institutions.

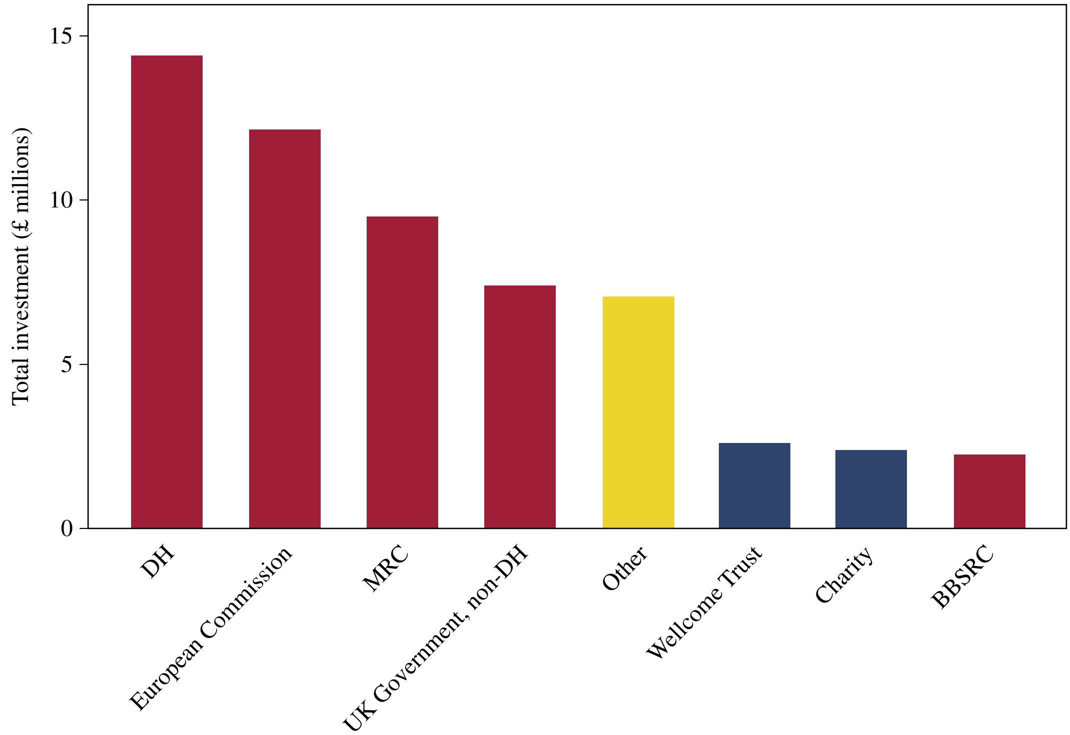

Figure 3. Total investment in healthcare-associated infection research 1997–2010 by the major funders. 'Other' includes contributions from a variety of funders, with the majority from the government of Northern Ireland, hospital research and development funding and Scottish government funding (despite being part of the UK, Northern Ireland and Scotland local governments offer localized funding for biomedical research). DH, UK Department of Health; MRC, Medical Research Council; BBSRC, Biotechnology and Biological Sciences Research Council.

There is limited research into the economic and societal burden of HCAIs, and even the most recent efforts are now somewhat dated.[8] There is a real need for new studies in the UK to estimate more precisely the economic and societal burden of HCAIs so that research and healthcare resources can be appropriately allocated in line with the burden. There are clear acknowledged complexities in carrying out such studies, but accurately counting the cost of infection is crucial.[9]

Infections related to surgery were the most commonly studied aspect of HCAIs in this dataset. Nearly half of the funding (around one-third of the studies) was related to laboratory work in relation to surgery, with the most studied area being implementation and operational research. Several of these studies researched the impact of viruses from the herpes family (in particular the Epstein–Barr virus and cytomegalovirus).

There was very little research specifically on hospital-acquired pneumonia, although some of the research reported here will have an association with pneumonia, such as the studies looking at staphylococci and pseudomonas. Respiratory tract infections have been identified as the most common HCAI in acute hospitals, with ventilator-associated pneumonia associated with high mortality and increased length of stay in hospital.[25] Thus it would seem prudent to increase investments that specifically investigate pneumonia. Research into pseudomonas infection itself was minimal – although the burden is likely to be fairly small, outbreaks can be high impact in terms of neonatal fatalities and subsequent negative media coverage of the hospital(s) involved.[7] Norovirus infections are a source of high disease burden, particularly across the winter months, yet only one small study that focused on this pathogen in a healthcare setting was funded.

The research, and the background for the research, into prion disease with particular reference to Creutzfeldt–Jakob disease is somewhat different to other areas. All six studies were funded in years 1997–2000, with no investments thereafter. These years coincide with the peak of notifications, declining since then, and the media coverage surrounding 'mad cow disease' was at its most widespread during that period. To date, there have been 176 notifications in total, and all of these patients have died, with a peak of 28 deaths in 2000 and five deaths in 2011. It is suggested that the decline in numbers to very few new notifications will continue, although a second 'wave' cannot be ruled out.[26] There may be little appetite among funders and researchers to invest money and time to continue significant efforts into researching Creutzfeldt–Jakob disease unless there is perceived to be a genuine threat that an epidemic will emerge.

It is of particular interest that we found no studies specifically relating to HCAIs in a global health context, despite around one-third of total investment in infectious disease research being related to global health studies and/or pathogens.[16] It is difficult to assess associations with other areas of research that are not directly related to HCAIs, but which nonetheless have an impact, and this may be the case with some of the studies that had a focus on important pathogens in low-income countries but that did not specify an HCAI component to the work or indicate HCAI transmission. We also did not specifically search for health systems research, which in a low-income setting may well have an impact on local incidence of HCAIs.

The study has several limitations, which have been highlighted and discussed in detail elsewhere.[16] There were few publicly available data from the pharmaceutical industry. Hence, there is a data gap in relation to funding of clinical trials and development of new therapeutics, vaccines, and diagnostics, which the pharmaceutical and biotechnology industries are financing. We rely on the original data being complete and accurate, and are unable to take into account distribution of funds from the lead institution to collaborating partners, nor can we assess quantity of each award given to overheads or the impact of the introduction of full-economic costing. Moreover, assigning studies to categories is a subjective and imperfect process – although we used two researchers when assigning findings to categories in order to reduce inter-observer error. Our study focuses on UK-led investments – we do not know whether similar patterns (e.g. a lack of public or charitably funded clinical trials, and focus on MRSA and surgical infections) would also emerge if the analysis were repeated for other high-income countries. Owing to the large amount of work involved and lack of funded staff time, it has not been possible to update the analysis to include award data up to 2013. Nor did we assess any impact of these investments, via outputs such as publications or patents.

An environment of more rapid transmission of infectious diseases across borders, weak health systems and inadequate surveillance creates an imperative for international collaborations to effectively manage and control transmission of infections across borders to increase the availability and reliability of HCAI-related data and knowledge.[27] The Global Burden of Disease Study illustrates the usefulness of such collaborations.[28] There is a paucity of information available on HCAI transmission in low-income settings that have weak health systems, and this is something that needs to be addressed urgently with tailored surveillance systems in order to identify the most pressing priorities and develop suitable interventions. Further research in these settings on the feasibility and impact of cost-effective interventions – such as education on handwashing and provision of soap – might also yield some useful information on behavioural interventions that could increase the adoption of these interventions.

There is a need for funders of other countries to provide similarly detailed information of funded studies, in order to build a global database of research studies for infections generally and HCAI specifically, in order to identify true research gaps, reduce unnecessary duplication of research, pinpoint where there is infrastructure and capacity for specific types of research requiring technology or skills, and to inform priority setting globally.

The UK has received significant investments in the area of HCAI research, albeit less than is warranted by the actual burden of disease and threat of drug resistance. The Department of Health has led the investments in this area, with support from other funding bodies such as the Medical Research Council, although the quantities of funding have often been modest. MRSA and infections related to surgery have been relatively well studied (within the limits of available funding), but research for hospital-acquired pneumonia, Gram-negative organisms, behavioural interventions, cleaning studies, and economic analyses warrant greater attention from funders and policy-makers. Research is also needed for modelling studies to explore the future threats to the welfare of patients in healthcare settings, such as from Gram-negative organisms and antimicrobial resistance.

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Conflict of interest statement/funding
M.G.H. works for the Infectious Disease Research Network, which has supported this study and is funded by the UK Department of Health. J.R.F. has received funds from the Wellcome Trust, and is a steering group member for the Infectious Disease Research Network. R.A. has received research funding from the Medical Research Council, the National Institute for Health Research and the UK Department for International Development. R.A. is a member of the Medical Research Council Global Health Group. A.H. is supported by the National Institute for Health Research, the National Centre for Infection Prevention and Management (CIPM) funded by the UK Clinical Research Council, the BRC, the European Commission, and the Health Foundation, and has also received funding from the European Centre for Disease Prevention and Control and bioMérieux.

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