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Research Paper

Mapping pneumonia research: A systematic analysis of UK investments and published outputs 1997–2013

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ABSTRACT

Background: The burden of pneumonia continues to be substantial, particularly among the poorest in global society. We describe here the trends for UK pneumonia R&D investment and published outputs, and correlate with 2013 global mortality.
Methods: Data related to awards to UK institutions for pneumonia research from 1997 to 2013 were systematically sourced and categorised by disease area and type of science. Investment was compared to mortality figures in 2010 and 2013 for pneumonia, tuberculosis and influenza. Investment was also compared to publication data.
Results: Of all infectious disease research between 2011 and 2013 (£917.0 million), £28.8 million (3.1%) was for pneumonia. This was an absolute and proportionate increase from previous time periods. Translational pneumonia research (33.3%) received increased funding compared with 1997–2010 where funding was almost entirely preclinical (87.5%, here 30.9%), but high-burden areas such as paediatrics, elderly care and antimicrobial resistance received little investment. Annual investment remains volatile; publication temporal trends show a consistent increase. When comparing investment to global burden with a novel 'investment by mortality observed' metric, tuberculosis (£48.36) and influenza (£484.21) receive relatively more funding than pneumonia (£43.08), despite investment for pneumonia greatly increasing in 2013 compared to 2010 (£7.39). Limitations include a lack of private sector data and the need for careful interpretation of the comparisons with burden, plus categorisation is subjective.
Conclusions: There has been a welcome increase for pneumonia funding awarded to UK institutions in 2011–2013 compared with 1997–2010, along with increases for more translational research. Published outputs relating to pneumonia rose steadily from 1997 to 2013. Investment relative to mortality for pneumonia has increased, but it remains low compared to other respiratory infections and clear inequities remain. Analyses that measure investments in pneumonia can provide an insight into funding trends and research gaps.
Research in context: Pneumonia continues to be a high-burden illness around the globe. This paper shows that although research funding is increasing in the UK (between 1997 and 2013), it remains poorly funded compared to other important respiratory infectious diseases such as tuberculosis and influenza. Publications about pneumonia have been steadily increasing over time, indicating continuing academic and clinical interest in the topic. Though global mortality of pneumonia is declining, it should still be an area of high priority for funders, policymakers and researchers.

1. Introduction

Despite documented complexities with epidemiological definitions and clinical diagnosis (Scott et al., 2012), the global burden of pneumonia,

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including healthcare-associated and ventilator-associated pneumonia, clearly remains significant. Estimates from the Global Burden of Disease Study 2013 (GBD 2013) suggested that although mortality from the main pneumonia-causing pathogens was decreasing worldwide, there were still at least 785,000 deaths globally from pneumococcal pneumonia, respiratory syncytial virus and *Haemophilus influenzae* pneumonia in 2013 with much of this burden in low- and middle-income countries (GBD 2013 Mortality and Causes of Death Collaborators, 2014), although other analyses considered mortality to be greater (Kovacs et al., 2015). In GBD 2013 figures, there were a further 105,000 deaths from influenza, where pneumonia is a significant secondary complication from primary infection, and an estimated 2 million deaths from lower respiratory tract infections of unknown aetiology (GBD 2013 Mortality and Causes of Death Collaborators, 2014). The GBD study also attributed 76.7 million disability-adjusted life-years (DALYs) to pneumonia and pneumococcal disease in 2010, again with the poorest sectors of society bearing the majority of this burden (Murray et al., 2012). Though there is an increasing prevalence of non-communicable disease and injuries in middle and lower-income countries (GBD 2013 Mortality and Causes of Death Collaborators, 2014), projections from the World Health Organization (WHO) estimate deaths from lower respiratory tract infections will remain among the top 4 leading causes of deaths in 2015 and 2030 (World Health Organization, 2013a).

Part of the solution to overcoming these challenges is to invest in research. The UK is consistently rated among the top three investors in neglected disease research (Policy Cures, 2014a), and UK-based authors are generally prolific at contributing to the published evidence base (Yao et al., 2014). Thus the activity of UK institutions is likely to be of significant national and international importance. The Research Investments in Global Health study (ResIn, www.researchinvestments.org) has previously reported on infectious disease research investments awarded to UK institutions between 1997 and 2010 (Head et al., 2013), also specifically highlighting the limited and fractured nature of pneumonia and pneumococcal research (Head et al., 2014a,b). There is a paucity in the systematic tracking of global investments in health research and development (R&D), with noted mismatches between the global burden of pneumonia and research investment (Rudan et al., 2011), and only one study of limited scope highlighting product and technology-related R&D of bacterial pneumonia in low-income settings (Policy Cures, 2014b).

We present an update to the ResIn study, covering awards for pneumonia and pneumococcal-research from 2011 to 2013, with reference to previously published data from 1997 to 2010 for context. We highlight the trends in both total investment and temporal drift in funding by type of science. Furthermore, we compare investment against global mortality of disease and describe bibliometrics trends for pneumonia-related publications as a surrogate of research output. We discuss some clear challenges and evidence gaps, and review potential ways forward.

2. Methods

Our methods for the analysis covering 1997–2010 are described in detail elsewhere (Head et al., 2013, 2014b), and have been updated for the 2011–2013 analyses.

2.1. Data collection

We systematically sourced information on funding decisions from the major public and philanthropic funding bodies for infectious disease research (http://researchinvestments.org/about-the-study/study-methodology/). Private sector investment is not included due to insufficient information in the public domain. Data was obtained either by searching online for the institution's portfolio of awards, or requested directly from the funder.

2.2. Data categorisation and handling

The study team identified the infection-related awards led by a UK institution and categorised them by disease area, by specific pathogen and by type of science according to their position along the R&D value chain. R&D categories were: preclinical research, phase I-III trials, intervention and product development studies, translational (previously referred to as implementation and operational research), and cross-disciplinary awards. The cross-disciplinary category has been newly created for the 2011–2013 analysis, reflecting the notable increase in the number of studies with significant components covering two distinct types of science. We have not yet retrospectively applied this new category to the 1997–2010 dataset though do not anticipate revisions to greatly impact on observed trends in investment. Further detail on data categorisation is available on the study website, alongside the full list of included funders and the search keywords used. Information collected on each award included study title and abstract (where available), the lead institution and principal investigator, funder, year of award and total funding awarded. As per previous analyses (Head et al., 2013), and similar to approaches recommended by others (Young et al., 2015), awards originating from an international funder 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 2013 UK pounds.

Each study was categorised by author MGH. Awards for pneumonia and pneumococcal-related research are included here. There were random checks by at least two other individuals on 20% samples of the data to reduce observer error, with differences reported and corrected, and any remaining differences settled by consensus. Datasets were also sent out to all authors for review and comment.

2.3. Data analysis

Burden data was sourced from the GBD study (GBD 2013 Mortality and Causes of Death Collaborators, 2014; Lozano et al., 2012). UK investment and global mortality for pneumonia, tuberculosis and influenza was analysed by comparing the sum funding across 2005–2009 with 2010 burden, and funding across 2008–2012 with 2013 burden. Findings were reported as an 'investment by mortality observed' metric. The dataset was assembled in Microsoft Excel 2013 and Stata (V13) was used for further statistical analysis. Spearman's rank correlation coefficient (rho) was used to assess correlation.

2.4. Bibliometrics

The publications database Scopus® (http://www.scopus.com/) was used to search for publications incorporating the keywords 'pneumonia' or 'pneumococcal', published between 1997 and 2013 and including at least one author affiliated to a UK institution. Search results were exported and conditional formatting equations used to identify papers with a UK individual listed as first or last author; this was a proxy measure for significant involvement from the UK and thus used to compare with funding trends. Since most awards in our dataset are either less than one year, or between two and three years in duration, a likely publication yield for each year of investment was calculated by using the total publications in the four years after the award, and this produced an 'investment per publication' metric. Temporal trends, citation numbers and type of publication were also considered. Microsoft Excel 2013 and 2011 was used to assemble the bibliometrics dataset, and Graphpad Prism 6 (http://www.graphpad.com/scientific-software/prism/) produced the figures.

3. Results

Total research funding for all infectious diseases awarded to UK institutions between 2011 and 2013 was £917.0 million across 1232

awards (Table 1). Of this, £145.2 million (15.8%) and 219 awards (17.8%) were related to respiratory infections. Pneumonia and pneumococcal research received £28.8 million (3.1% of total and 19.9% of respiratory infections funding) across 35 awards (2.8% of total and 16.0% of respiratory infections) (Table 1). By comparison across 2011–2013, tuberculosis received £71.1 million (7.8% of total and 49.0% of respiratory infections funding) from 83 awards (37.9% of respiratory infections) and influenza received £39.1 million (4.3% of total and 26.9% of respiratory infections funding) across 53 awards (24.2% of respiratory infections).

These findings represent an approximately three-fold total and proportional increase from 1997 to 2010, where we reported that pneumonia-related research represented 6.6% of all respiratory infections and 1.1% of all infectious disease research funding (Head et al., 2014b). Total funding for pneumonia across the three-year period of 2011–2013 is greater than total funding across the fourteen year period of 1997–2010, with mean annual pneumonia funding in this update time period is £9.6 million compared with £2.0 million previously. The mean annual number of awards has increased slightly from 7 to 12 and the median award size has increased from £137,389 to £335,210 (Interquartile range £196,000–642,463). Similarly, the total annual investment in infectious disease research has increased by 64.6% in the period 2011–2013, compared with 1997–2010, despite similar numbers of awards. Investment and year were moderately correlated (rho 0.6152, $p = 0.0086$), research output and year were strongly correlated (rho 0.9798, $p = 0.0001$) and investment was moderately correlated with research output (rho 0.6107, $p = 0.0092$).

Of the 35 pneumonia studies, 12 focused on *Streptococcus pneumoniae*. Eight awards focused on vaccine research, with 3 awards each concerned with diagnostics and therapeutics. Two awards had a specific focus on paediatrics, with no awards focusing on elderly care. Eight awards were clearly related to global health (Table 1). Temporal trends, building on previously published data (Head et al., 2014a), show an inconsistent long-term approach but significant increases in investment in recent years (Fig. 1).

Previously, Wellcome Trust was the leading funder of UK-awarded pneumonia research (44.8% of the total 1997–2010, now 15.9%) (Head et al., 2014b). In this update (Table 2), the European Commission provided the largest proportion of pneumonia research investments (31.2%) through 6 large awards, of which 5 were preclinical, amounting to £9.2 million; during 1997–2010 they supported just two studies. The second largest contribution was from the Bill & Melinda Gates Foundation, which provided £7.4 million (26.6%) of investment across 5 awards, 4 of which were translational; during 1997–2010 there were no awards from the Bill and Melinda Gates Foundation to UK institutions for pneumonia.

There have been changes in pneumonia investment trends when considering the type of science along the R&D pipeline. Previously, 87.5% of the funding was devoted to preclinical research (Head et al., 2014a). Across 2011–2013 (Table 3, Fig. 2), preclinical research now accounted 30.9% of investment, with comparable amounts awarded to intervention and product development studies (32.7%) and translational research (33.3%).

The 'investment by mortality observed' metric for pneumonia is much greater in 2013 (£43.08) than 2010 (£7.39), though remains less than tuberculosis (£48.36) and influenza (£484.21) across both years (Table 4).

There were 8400 publications related to pneumonia that contained a first and/or last UK-affiliated author. Temporal trends show a steady increase in publication numbers per year between 1997 and 2013 (Fig. 1), with the majority of publications being original articles (4771, 56.8%) or reviews (1759, 20.9%) (Fig. 3a). In 1997, there were 250 publications, and in 2013 there were 792, a more than three-fold increase. The 'R&D investment per publication' metric demonstrated great variability year on year, with a peak of £2395 in 2005 and a low of £395 in 2007, and median investment across 1997–2009 of £779 per publication (Table 5). Citations of pneumonia publications included in this dataset increased over time from 1997 (5874) until 2008 (16,862, an increase of almost three-fold) (Fig. 3b). For comparison, equivalent median investment per publication for tuberculosis was £6335 (range £1822–15,824), and £4100 (range £314–20,074) for influenza. Tuberculosis publication numbers (8194) and temporal trends were broadly similar to that of pneumonia, whilst influenza publications (4864) and citations were fewer but with notable increases around the time of concerns around the H5N1 strain, and then the H1N1 pandemic strain (supplementary information).

4. Discussion

Annual pneumonia funding was considerably greater in the period 2011–2013 compared to the period 1997–2010, yet the increase in number of awards remains modest with the pattern of investment appearing to favour larger individual grants (a trend reflected across all infectious disease research). There has been a notable shift in the type of science funded, which previously was almost entirely devoted to preclinical research but now represents a balance of preclinical, intervention and product development, and translational research. There are still relatively few studies funded by public and philanthropic institutions that focus on tools to control pneumonia such as vaccines, diagnostics and novel therapeutics, and minimal investment specifically for paediatric, elderly care or antimicrobial resistance research.

The European Commission and Bill and Melinda Gates Foundation are now the leading funders of pneumonia research awarded to UK institutions (though the MRC and Wellcome Trust each contributed the greater number of awards), highlighting an important shift in funding policy and advocacy by global health organisations. Compared to global mortality, pneumonia R&D funding is improving, as we observe increased investment and decreased mortality. Tuberculosis and influenza receive greater R&D investments in absolute terms and also relative to their attributable burden of disease. Bibliometrics trends for pneumonia show a broadly steady annual increase from 1997 to 2013, but with great variability when assessed using the 'R&D investment per publication' metric as applied here. The similar temporal increase in citation numbers could be taken to indicate that one use of the pneumonia publications is to continuously inform the development of other published outputs, some of which will have resulted from the funding analysed here; however, publications have variable impact and further bibliometrics should be developed to evaluate use of publications in informing other areas of knowledge such as policy development. Linkage between individual investment and their published outputs would be one area to develop to more closely map the extent of any relationship between them.

The increase in investment in this high-burden and priority area is clearly positive. It remains to be seen whether the trend of funding consortia, programme grants and other large project grants, particularly in areas of research beyond preclinical science, will reap the benefits of increased impact and ultimately provide a greater contribution to the reduction of disease burden than has been observed so far. The burden of pneumonia is decreasing, although it remains a focus of policy and advocacy groups such as the WHO and Bill & Melinda Gates Foundation (Bill and Melinda Gates Foundation, 2015; World Health Organization, 2013b), and accelerating the reductions in incidence will arguably require a sustained increased level of investment in both research and implementation. The lack of phase I-III clinical trials is concerning, though this is an area where the private sector traditionally invests, at least in high-income settings. Investments in innovative products with the potential to impact on health would be a pragmatic approach for future research, though the roll-out of research and any subsequent implementation must be appropriate. The European and Developing Countries Clinical Trials Partnership and the Global Fund have been influential in this area in particular for HIV, tuberculosis and malaria. Operational research is important to optimise the distribution and

Table 1
Summary of investment information relating to infectious diseases and pneumonia research 2011–2013.

Disease	1997–2010				2011–2013					
	Number of awards	Percentage of all respiratory infection or pneumonia research	Total funding, £	Percentage of all respiratory infection or pneumonia research	Number of awards	Percentage of all respiratory infection or pneumonia research	Total funding, £	Percentage of all respiratory infection or pneumonia research	Mean award, £ (SD)	Median award, £ (IQR)
All Infectious disease	6165[+]	n/a	2,807,982,764[+]	n/a	1232	n/a	916,960,747	n/a	744,286 (1,360,777)	315,918 (156,283–779,794)
All respiratory infectious disease	1010[+]	n/a	410,732,999[+]	n/a	219	n/a	145,182,110		662,932 (1,104,659)	319,019 (170,095–726,046)
Pneumonia	102[+]	10.1%	27,788,770[+]	6.8%	35	16.0%	28,849,125	19.9%	824,260 (1,340,046)	335,210 (196,000–642,463)
Pneumococcal	26	25.5%	4,417,895	15.9%	12	34.3%	8,944,883	31.0%	745,406 (1,207,254)	412,769 (261,084–647,062)
Disease areas and products[*]										
Antimicrobial resistance	12	11.8%	2,899,479	10.4%	1	2.86%	4218	0.01%	n/a	n/a
Diagnostics	5	4.9%	335,993	1.2%	3	8.57%	6,814,845	23.62%	2,271,615 (3,624,003)	319,019 (42,617–6,453,209)
Geriatrics	1	1.0%	7933	0.0%	0	n/a	0	n/a	n/a	n/a
Global health	12	11.8%	4,626,308	16.6%	8	22.86%	17,437,921	60.45%	2,179,740 (2,241,692)	1,039,549 (598,711–3,651,835)
Healthcare-associated infections	2	2.0%	313,651	1.1%	2	5.71%	361,636	1.25%	n/a	n/a
HIV	7	6.9%	1,397,599	5.0%	1	2.86%	404,523	1.40%	n/a	n/a
Paediatrics	9	8.8%	1,733,415	6.2%	2	5.71%	3,331,750	11.55%	n/a	n/a
Therapeutics	4	3.9%	1,050,241	3.8%	3	8.57%	1,166,680	4.04%	388,893 (235,729)	319,019 (196,000–651,661)
Vaccinology	9	8.8%	5,364,389	19.3%	8	22.86%	10,371,078	35.95%	1,296,385 (1,447,016)	604,472 (443,647–1,757,426)

[*] Percentages in "disease areas and products" are calculated as a fraction of all pneumonia research rather than all respiratory infection research. Because awards can cover more than one disease area or product category, the sum of these column percentages may exceed 100%.

[+] Data published previously but here corrected for 2013 inflation (Head et al., 2013, 2014b).

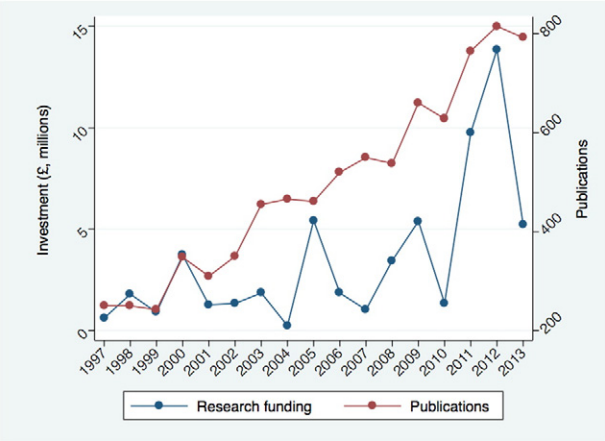

Fig. 1. Sum research investment and publications for pneumonia, by year.

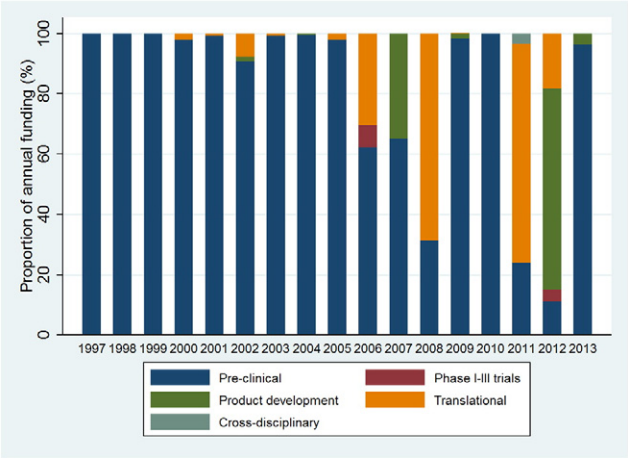

Fig. 2. Proportion of research investment for pneumonia R&D, by year and by type of science. * 1997–2010 data previously published (Head et al., 2014a).

accessibility of pneumonia treatments such as antibiotics in the community and oxygen in hospitals, as is the development of new vaccines to protect against strains of pneumococcus not covered by the current multivalent conjugate vaccines. The Bill & Melinda Gates Foundation has invested significantly in research to define the aetiology of pneumonia in children in low-income countries over this period (Levine et al., 2012). As GBD 2013 illustrates (GBD 2013 Mortality and Causes of Death Collaborators, 2014), the large proportion of lower respiratory tract infections with unknown aetiology remains a challenge for many suffering from suspected pneumonia (Prendergast and Papenburg, 2013; Murdoch et al., 2012; Enne et al., 2014). Rapid point of care tests demonstrating high specificity and sensitivity are urgently needed, with a focus on products that are suitable for use in low-income healthcare and community settings. Advances in nanotechnology research may yield highly specific new assays (Howes et al., 2014); however, they may emphasise the clinical uncertainty that identifying the bacteria does not necessarily mean it is the pathogen causing the illness (Enne et al., 2014). In terms of advocacy, building capacity and attracting increased funding, there may be an opportunity to learn from established research communities receiving proportionately greater R&D investment, such as those who work on tuberculosis and influenza. The area of pneumonia, though large, lacks a single-disease advocacy body to focus attention on the likely returns on research investments in this area. Elsewhere, a detailed analysis of research priorities suggested that health policy and systems research to improve

Table 2
Pneumonia research investments 2011–2013, by funder.

Disease	Number of awards 2011–2013	Percentage of total	Total funding 2011–2013	Percentage of total	Mean award £ (SD)	Median award £ (IQR)
All pneumonia investment	35		£28,849,125		824,260 (1,340,046)	335,210 (196,000-642,463)
BBSRC	2	5.71%	£1,060,870	3.68%	n/a	n/a
Bill and Melinda Gates Foundation	5	14.3%	£7,360,368	25.51%	1,472,074 (1,767,709)	656,391 (603,102-1,422,707)
European Commission	6	17.1%	£9,185,732	31.84%	1,530,955 (2,533,903)	188,121 (170,095-2,101,297)
Medical Research Council	9	25.7%	£5,617,685	19.47%	624,187 (821,816)	273,432 (235,476-564,749)
National Institute for Health Research	2	5.71%	£941,053	3.26%	n/a	n/a
Wellcome Trust	8	22.9%	£4,592,214	15.92%	574,026 (622,481)	363,534 (302,855-485,644)
Other	3	8.57%	£91,202	0.32%	30,400 (22,691)	42,617 (4218-44,367)

Table 3
Pneumonia research investments 2011–2013, by type of science.

Disease	Number of awards 2011–2013	Percentage of total	Total funding 2011–2013	Percentage of total	Mean award £ (SD)	Median award £ (IQR)
All pneumonia investment	35		£28,849,125		824,260 (1,340,046)	335,210 (196,000-642,463)
Pre-clinical	22	62.9%	£8,917,385	30.9%	405,335 (424,894)	280,062 (188,121-564,749)
Phase I-III	1	2.86%	£554,959	1.92%	n/a	n/a
Intervention and product development	3	8.57%	£9,426,000	32.7%	3,142,000 (3,144,551)	2776,792 (196,000-6,453,209)
Translational	8	22.9%	£9,615,570	33.3%	1,201,946 (1,514,565)	530,457 (235,154-1,757,426)
Cross-disciplinary	1	2.86%	£335,210	1.16%	n/a	n/a

Table 4
Relationship between research investment and mortality for pneumonia, tuberculosis and influenza.

Infection	Year	Numbers of deaths	Investment 5 years beforehand	R&D investment per death
Pneumonia*	2010	2,319,100	£17,146,396	£7.39
	2013	784,600	£33,802,448	£43.08
Tuberculosis	2010	1,196,000	£86,338,770	£72.19
	2013	1,290,300	£62,399,586	£48.36
Influenza	2010	507,900	£51,991,733	£102.37
	2013	105,000	£50,841,831	£484.21

* Pneumonia mortality data includes pneumococcal pneumonia/*H. influenzae* type b pneumonia/respiratory syncytial virus pneumonia.

Table 5
R&D investment for pneumonia and pneumonia-related published outputs.

Year	Funding	Publications	Likely publication yield	UK pound per publication
1997	£611,493	250	1150	£532
1998	£1,794,230	250	1250	£1435
1999	£896,453	242	1463	£613
2000	£3,719,166	348	1581	£2352
2001	£1,264,689	310	1732	£730
2002	£1,332,194	350	1902	£700
2003	£1,853,285	455	1997	£928
2004	£239,056	466	2069	£116
2005	£5,431,788	461	2268	£2395
2006	£1,851,883	520	2376	£779
2007	£1,023,629	550	2591	£395
2008	£3,449,233	538	2868	£1203
2009	£5,389,863	660	3000	£1797
2010	£1,345,555	628	n/a	n/a
2011	£9,763,953	765	n/a	n/a
2012	£13,853,844	815	n/a	n/a
2013	£5,231,327	792	n/a	n/a

access and coverage by the existing interventions (such as vaccine and therapeutic delivery) were key in the short term, as well as epidemiological research to address the most important gaps in knowledge (Rudan et al., 2011).

Antimicrobial resistance is an under-resourced area across all investments for infectious disease research (Head et al., 2014c; Head, 2014), and pneumonia is no exception. Globally, resistance to *S. pneumoniae* is increasing. Recent trends have concerned the Centers for Disease Control and Prevention (CDC) in the US who made specific reference to this area in their unprecedented 2013 Threat Report (Centers for Disease Control and Prevention, 2013), as well as being a focus of the WHO 2014 global report on surveillance (World Health Organization, 2014). It is imperative to increase development in the R&D pipeline of novel antibacterial therapies active major causes of pneumonia including *S. pneumoniae*, *Staphylococcus aureus*, and *Klebsiella pneumoniae*, especially those that are acquired in-hospital, where the pathogens are highly selected for resistance. It is also important to broaden the selection of agents to treat viral pneumonia, particularly disease caused by influenza, para-influenza and respiratory syncytial virus. The economic impact of infectious disease is notoriously difficult to quantify (Fonkwo, 2008), though the annual economic burden of pneumonia in Europe has been estimated at €10.1 million (Welte et al., 2012), and treating hospitalised cases of community-acquired pneumonia in the US results in mean costs of $15,385 per patient across over one million annual patient episodes (Sato et al., 2013).

There are recognised difficulties with any comprehensive analysis of R&D data (Young et al., 2015), and the limitations of this study have been described in detail previously (Head et al., 2013, 2014b). An important point to reiterate here is the lack of private sector data. Gaps in knowledge here will likely mask the true total investments for, in particular, preclinical research and clinical trials for key advances in vaccine, diagnostic and therapeutic development. There may also be funds dedicated to respiratory infectious disease in any of the three NIHR-funded Biomedical Research Units with a respiratory focus that may not be listed as separate awards and thus not included here. We do not take into account the proportion of each award dedicated to each of the categories that may be applied to a single study. We also do not investigate the distribution of funds from the lead institution to any collaborating partners, nor do we take account of funding intended for covering indirect or estate costs or any overheads. A basic sensitivity

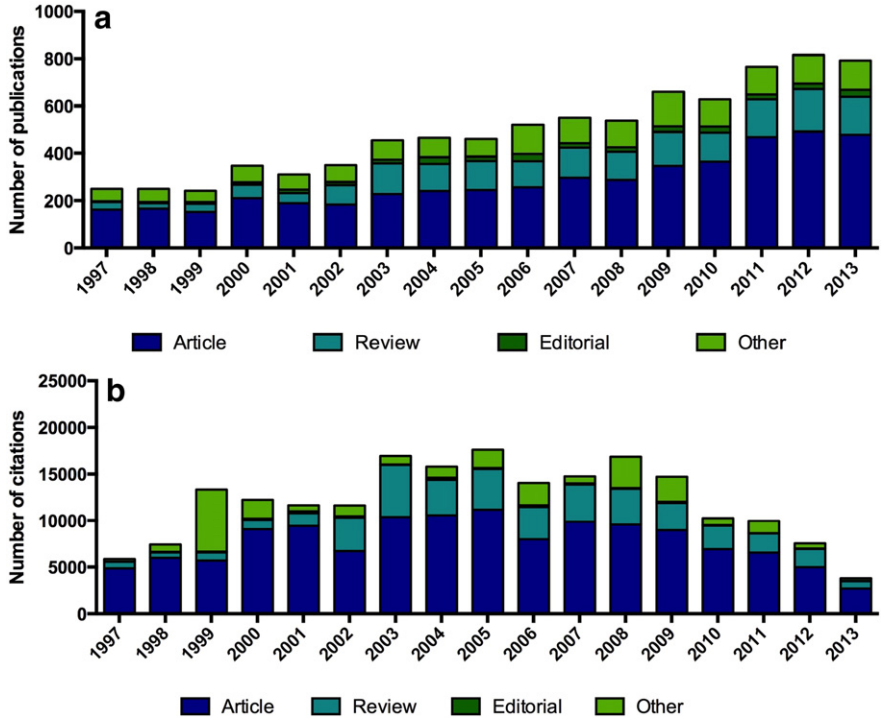

Fig. 3. a) Number of publications by year and publication type, b) number of citations, by year and publication type.

analysis suggests that the Research Councils introduction of full economic costing in 2004 has not greatly skewed the size of awards and the volatility in total and temporal trends remain when considering pneumonia funding with and without BBSRC and MRC data, though there may be implications for other areas of infectious disease research. The impact of the stochastic nature of research funding is also difficult to quantify. We rely on study titles and abstracts to provide specific mention of pneumonia or alternatively clearly imply the study is related to pneumonia. It is difficult to quantify the level of funding missed in our data collection exercise, however this is mitigated by the fact that all major public and philanthropic funders of UK research, and dozens more awarding bodies, have supplied data. The metric development for investment by mortality and published outputs needs further development and validation, and application to other disease areas to allow direct comparisons.

Despite recent sum and relative increases, funding available for pneumonia research remains disproportionately low, when compared with the global burden of disease. There are no sustained comprehensive efforts to track global pneumonia-related R&D investments, and this should be tackled in order to allow simpler identification of research and evidence gaps. Other countries, particularly the US which is the largest investor in global health, have pneumonia portfolios that may cover areas where the UK is not investing. A multi-country analysis, similar to that carried out in the UK by the ResIn study, is warranted to provide a comprehensive global investment surveillance system for health R&D. A more detailed breakdown of bibliometrics trends and linkage to investments data, plus identification of additional measures of research impact, across all infectious diseases and non-communicable disease, would allow for greater scrutiny of how research investments are allocated and how well they perform, openly assess accountability, and ultimately allocate limited resources wisely.

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Ethical approval

An ethics statement was not required for this work.

Contributors

MGH and JRF designed the study. MGH wrote the draft manuscript. JRF produced the statistical analysis. JNH and MGH carried out the bibliometrics analysis. SCC, RA, JAGS, and MLN contributed to data interpretation. All authors reviewed and contributed to draft and final versions.

Competing interests

No authors have any competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ebiom.2015.06.024.

References

Bill and Melinda Gates Foundation, 2015. 2015 Gates Annual Letter. Our Big Bet For The Future. http://www.gatesnotes.com/2015-annual-letter?page=5&lang=en (accessed 16 June 2015).

Centers for Disease Control and Prevention, 2013. Antibiotic resistance threats in the United States, 2013. http://www.cdc.gov/drugresistance/threat-report-2013/ (accessed 16 June 2015).

Enne, V.I., Personne, Y., Grgic, L., Gant, V., Zumla, A., 2014. Aetiology of hospital-acquired pneumonia and trends in antimicrobial resistance. Curr. Opin. Pulm. Med. 20, 252–258.

Fonkwo, P.N., 2008. Pricing infectious disease. The economic and health implications of infectious diseases. EMBO Rep. 9 (Suppl. 1), S13–S17.

GBD 2013 Mortality and Causes of Death Collaborators, 2014. Global, regional, and national age–sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 385, 117–171.

Head, M.G., 2014. Gross underinvestment in antibacterial research. Lancet Infect. Dis. 14, 788–789.

Head, M.G., Fitchett, J.R., Cooke, M.K., Wurie, F.B., Hayward, A.C., Atun, R., 2013. UK investments in global infectious disease research 1997–2010: a case study. Lancet Infect. Dis. 13, 55–64.

Head, M.G., Fitchett, J.R., Newell, M.-L., Scott, J.A.G., Clarke, S.C., Atun, R., 2014a. Investment in pneumonia and pneumococcal research. Lancet Infect. Dis. 14, 1037–1038.

Head, M.G., Fitchett, J.R., Cooke, M.K., et al., 2014b. Investments in respiratory infectious disease research 1997–2010: a systematic analysis of UK funding. BMJ Open 4 (e004600-e004600).

Head, M.G., Fitchett, J.R., Cooke, M.K., et al., 2014c. Systematic analysis of funding awarded for antimicrobial resistance research to institutions in the UK, 1997–2010. J. Antimicrob. Chemother. 69, 548–554.

Howes, P.D., Rana, S., Stevens, M.M., 2014. Plasmonic nanomaterials for biodiagnostics. Chem. Soc. Rev. 43, 3835–3853.

Kovacs, S.D., Mullholland, K., Bosch, J., et al., 2015. Deconstructing the differences: a comparison of GBD 2010 and CHERG's approach to estimating the mortality burden of diarrhea, pneumonia, and their etiologies. BMC Infect. Dis. 15, 16.

Levine, O.S., O'Brien, K.L., Deloria-Knoll, M., et al., 2012. The Pneumonia Etiology Research for Child Health Project: a 21st century childhood pneumonia etiology study. Clin. Infect. Dis. 54 (Suppl. 2), S93–S101.

Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., Abraham, J., Adair, T., Aggarwal, R., Ahn, S.Y., Alvarado, M., Anderson, H.R., Anderson, L.M., Andrews, K.G., Atkinson, C., Baddour, L.M., Barker-Collo, S., Bartels, D.H., Bell, M.L., Benjamin, E.J., Bennett, D., Bhalla, K., Bikbov, B., 2012. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2095–2128.

Murdoch, D.R., O'Brien, K.L., Driscoll, A.J., Karron, R.A., Bhat, N., 2012. Laboratory methods for determining pneumonia etiology in children. Clin. Infect. Dis. 54 (Suppl. 2), S146–S152.

Murray, C.J.L., Vos, T., Lozano, R., et al., 2012. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 380, 2197–2223.

Policy Cures, 2014a. Neglected disease research and development: emerging trends. Sydney. http://www.policycures.org/gfinder.html (accessed 16 June 2015).

Policy Cures, 2014b. G-finder diseases product and technologies. https://g-finder.policycures.org/gfinder_report/registered/docs/G-FINDER_R&D Matrix_updated_2011.pdf (accessed 16 June 2014).

Prendergast, C., Papenburg, J., 2013. Rapid antigen-based testing for respiratory syncytial virus: moving diagnostics from bench to bedside? Future Microbiol. 8, 435–444.

Rudan, I., El Arifeen, S., Bhutta, Z.A., et al., 2011. Setting research priorities to reduce global mortality from childhood pneumonia by 2015. PLoS Med. 8, e1001099.

Sato, R., Gomez Rey, G., Nelson, S., Pinsky, B., 2013. Community-acquired pneumonia episode costs by age and risk in commercially insured US adults aged ≥50 years. Appl. Health Econ. Health Policy 11, 251–258.

Scott, J.A.G., Wonodi, C., Moïsi, J.C., et al., 2012. The definition of pneumonia, the assessment of severity, and clinical standardization in the Pneumonia Etiology Research for Child Health Study. Clin. Infect. Dis. 54 (Suppl. 2), S109–S116.

Welte, T., Torres, A., Nathwani, D., 2012. Clinical and economic burden of community-acquired pneumonia among adults in Europe. Thorax 67, 71–79.

World Health Organization, 2013a. All cause mortality estimates for 2000–2012. http://www.who.int/healthinfo/global_burden_disease/estimates/en/index1.html (accessed 16 June 2015).

World Health Organization, 2013b. Priority medicines for Europe and the world — 'a public health approach to innovation'. http://www.who.int/medicines/areas/priority_medicines/BP6_22Pneumo.pdf (accessed 12 June 2015).

World Health Organization, 2014. Antimicrobial Resistance: Global Report on Surveillance 2014. World Health Organization, Geneva (http://www.who.int/drugresistance/documents/surveillancereport/en/, accessed 16 June 2015).

Yao, Q., Chen, K., Yao, L., et al., 2014. Scientometric trends and knowledge maps of global health systems research. Health Res. Policy Syst. 12, 26.

Young, A.J., Terry, R.F., Røttingen, J.-A., Viergever, R.F., 2015. Global trends in health research and development expenditures — the challenge of making reliable estimates for international comparison. Health Res. Policy Syst. 13, 7.