Southampton



ASSESSING GLOBAL INVESTMENTS IN PNEUMONIA RESEARCH 2000-2015

Report authored by Dr Rebecca J. Brown and Dr Michael G. Head, University of Southampton, UK, on behalf of the Research Investments in Global Health Study Team

ResIn
Research Investments in Global Hea





SCHOOL OF PUBLIC HEALTH

THE STUDY TEAM



Dr Rebecca J Brown

Rebecca is a Research Fellow within the Faculty of Medicine at the University of Southampton. She has an undergraduate degree in biochemistry and postgraduate degree in immunology. Rebecca completed her PhD in clinical microbiology at Cardiff University during which she worked closely with Public Health England to monitor epidemiology of *Mycoplasma pneumoniae* infections, develop diagnostics and molecular typing methods for human Mycoplasma species, and has been involved in implementing research into clinical practice.



Dr Michael G Head

Michael is a Senior Research Fellow within the Faculty of Medicine at the University of Southampton and previously spent 11 years at University College London. He has an undergraduate degree in biomedical science and postgraduate degree in epidemiology. Michael has published widely on the topic of research financing and carried out his PhD on this topic at the University of Amsterdam. He also has research interests in scabies and planetary health.



Professor Rifat Atun, Harvard
University



Professor James Batchelor,
University of
Southampton



Dr Stuart Clarke, University of Southampton



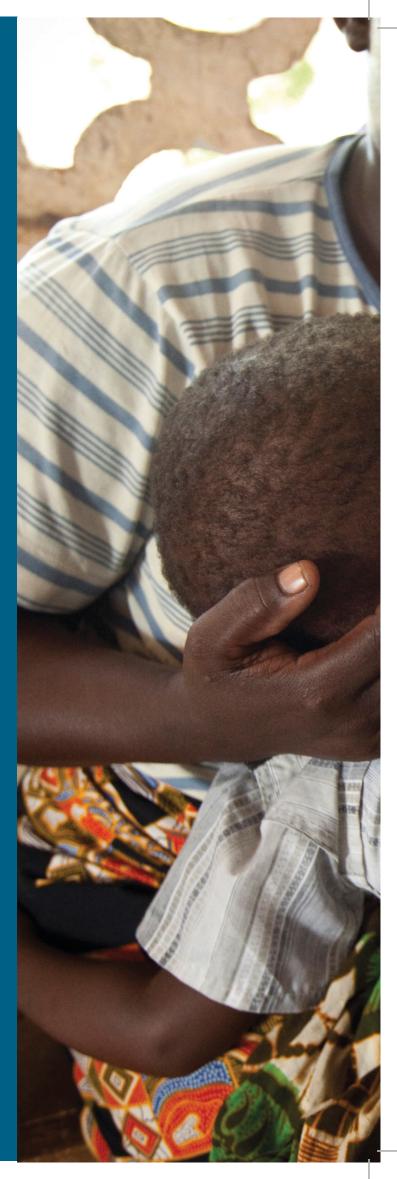
Dr Joseph Fitchett, Harvard
<u>Univ</u>ersity



Professor Marie-Louise Newell, University of Southampton



Professor Anthony Scott, London School of Hygiene & Tropical Medicine





FOREWORD

The need to align investments in health research and development (R&D) with public health demands remains one of the most pressing challenges in global public health. But mapping R&D can feel like staring into a black hole as there are few standards in research classification and often limited capacity to report such data.

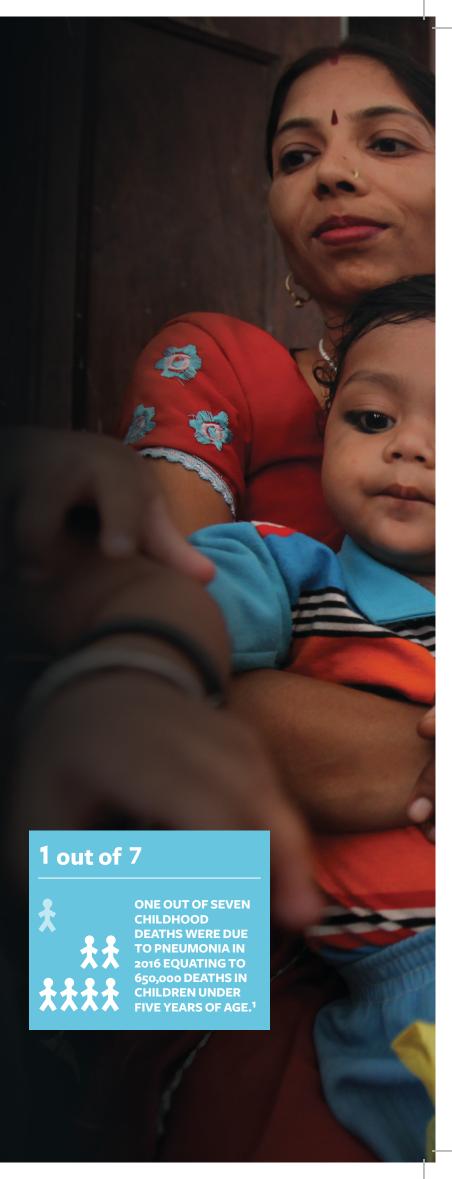
Yet making difficult choices and prioritising research between the multiple diseases is as important today as it has ever been. This is particularly necessary in those areas where R&D funding is already limited due to market failure such as for the poverty related neglected diseases. We know that collectively the funds available for R&D in this area is reaching a plateau at a time when a number of infectious diseases, those that cause pneumonia among them, are adding additional demands to the R&D system with growing antimicrobial resistance. Therefore, we will need to get smarter at thinking inside this funding box. This was the driving factor for the World Health Organization (WHO) in creating a global observatory on health R&D launched in 2017. The Observatory aims at providing R&D data to: review and query information on current trends, for example, in investment in health R&D, products in the pipeline and clinical trials; look at comparisons of R&D activities between countries, diseases and in relation to relevant information such as burden of disease or macroeconomic indicators and review global indicators on health R&D in the context of the Sustainable Development Goals.

However, the map of R&D activity and the priorities that a resource such as the Observatory can identify is reliant on those data that are out in the public domain. So the work that groups like the Research Investments in Global Health study is undertaking and the analysis it provides are very valuable both in supporting our understanding of global R&D trends, informing policy making and developing the methodology necessary to grow the important field of R&D tracking.



Robert Terry, WHO

Robert Terry is the Manager of Research Policy at TDR – the Special Programme for Research and Training in Tropical Diseases. He has published a number of articles on mapping R&D resources and worked to develop the original concept for a global health R&D observatory at the WHO.





REPORT HIGHLIGHTS

THE FUNDING LANDSCAPE TO ADDRESS PNEUMONIA

Research targeting pneumonia is limited

Research targeting pneumonia represents a very small proportion of overall infection-related research funding, approximately 3% of the estimated \$100 billion invested between 2000 and 2015.

Pneumonia claims 13% of childhood deaths

Pneumonia is responsible for approximately 13% of all childhood deaths worldwide and yet received limited research investment and additionally only received approximately 2% of available development assistance for health funding.²





Increasing threat of antimicrobial resistance

Resistance to antimicrobials is a severe threat to the effectiveness of treatments for pneumonia however, there was limited investment in this area of research, with the majority of funding relating to a couple of large clinical trials.



Funding for related re

Funding for pneumoniarelated research increased

Funding for pneumonia-related research has increased from \$67.0 million in 2000 to \$483.6 million in 2015. As a funding channel, the Bill & Melinda Gates Foundation have been the predominant funder of pneumonia-related research since 2008.



Child pneumonia deaths have decreased at a slower pace than other leading causes of mortality and accounts for the vast majority of the burden of pneumonia-related disease but the portfolio of research in this area accounts for approximately one third of funding for pneumonia-related research.



THE GEOGRAPHY OF PNEUMONIA RESEARCH FUNDING



EXECUTIVE SUMARY

IN 2016, ACCORDING TO THE GLOBAL BURDEN OF DISEASE STUDY, ONE OUT OF SEVEN CHILDHOOD DEATHS WERE DUE TO PNEUMONIA, ACCOUNTING FOR AN ESTIMATED 650,000 DEATHS IN CHILDREN UNDER FIVE YEARS OF AGE.¹

ALTHOUGH THE ESTIMATED ANNUAL NUMBER OF CHILD DEATHS FROM PNEUMONIA HAS DECREASED BY 47% BETWEEN 2000 AND 2015, PNEUMONIA REMAINS A SIGNIFICANT BURDEN TO HEALTH.²

Mortality due to pneumonia is strongly linked to povertyrelated factors with approximately 80% of deaths concentrated in countries in sub-Saharan Africa and South Asia.²

Aside from vaccination, pneumonia remains challenging to prevent, diagnose, and treat in low-income countries with the current tools and methods that are available. Pneumonia is a complex disease caused by a multitude of pathogens including bacteria, viruses and fungi. Vaccines can prevent the leading causes of pneumonia, particularly the pneumococcal and Hib vaccines. By the end of 2016, the pneumococcal vaccine had been introduced in 134 countries with a global coverage estimated at 42%.3 In comparison, the Hib vaccine had a global coverage of 70% across 191 countries. ⁴ Antibiotics can successfully treat most bacterial pneumonia cases when care is sought quickly; however, their use remains low. 5 Antibiotics need to be available and accessible to effectively treat pneumonia; however, inappropriate treatment with antibiotics has significant consequences and overuse of antibiotics is known to lead to the development of antibiotic resistance.5

Research is crucial to generate new knowledge and tools that can improve prevention and treatment strategies for pneumonia as well as aid understanding of global, national and local epidemiology and sociocultural impacts on the burden of pneumonia disease.

Our vision is to utilise dynamic, real-time data to promote evidence-informed policymaking and to support priority countries in rapidly enacting recommendations to develop national 'pneumonia action plans'. Through the analysis of research funding trends, gaps in research and investment in relation to pneumonia can be identified and utilised to develop priorities for future work.

Funding for pneumonia-related research was identified from public and philanthropic organisations providing investment for research related to health. Awards were classified as pneumonia research studies if they: i) referred to pneumonia in the title and abstract and were clearly focused on pneumonia disease with an infectious aetiology or, ii) focused on pneumococcal disease or, iii) referred to severe respiratory infectious disease (e.g. lower respiratory tract infection, hospitalisation due to influenza or respiratory syncytial virus) and in the opinion of the authors, likely to be related to pneumonia. Reference to pneumonia awards and investments refers to this working definition.

Overall, \$3.0 billion was invested in pneumonia-related research between 2000 and 2015 across 2,034 individual awards and a broad temporal increase was observed. Prior to 2008, the USA National Institutes of Health (NIH) were the predominant funder of pneumonia-related research however, since 2008, following the inception of the pneumonia group at the Bill & Melinda Gates Foundation, the Foundation became the dominant investor.

In comparison to other key infectious diseases, pneumonia appears relatively underfunded, receiving only 3.0% of an estimated \$100 billion invested in all infectious disease research between 2000 and 2015 across the G20 countries. Indeed, pneumonia receives lower levels of investment per

global death than HIV, tuberculosis, malaria and enteric diseases. Limited funding \$164 million has been invested for research on the diagnosis of pneumonia compared to \$839 million and \$857.5 million for research in therapeutics and vaccines for pneumonia, respectively.

Despite the high burden of pneumonia in children, the portfolio of research in this area accounts for only 34.4% of the investment in pneumonia-related research. However, investment in paediatric pneumonia research increased between 2000 and 2015 and by 2015 represented 76.4% of the total pneumonia research funding for that year.

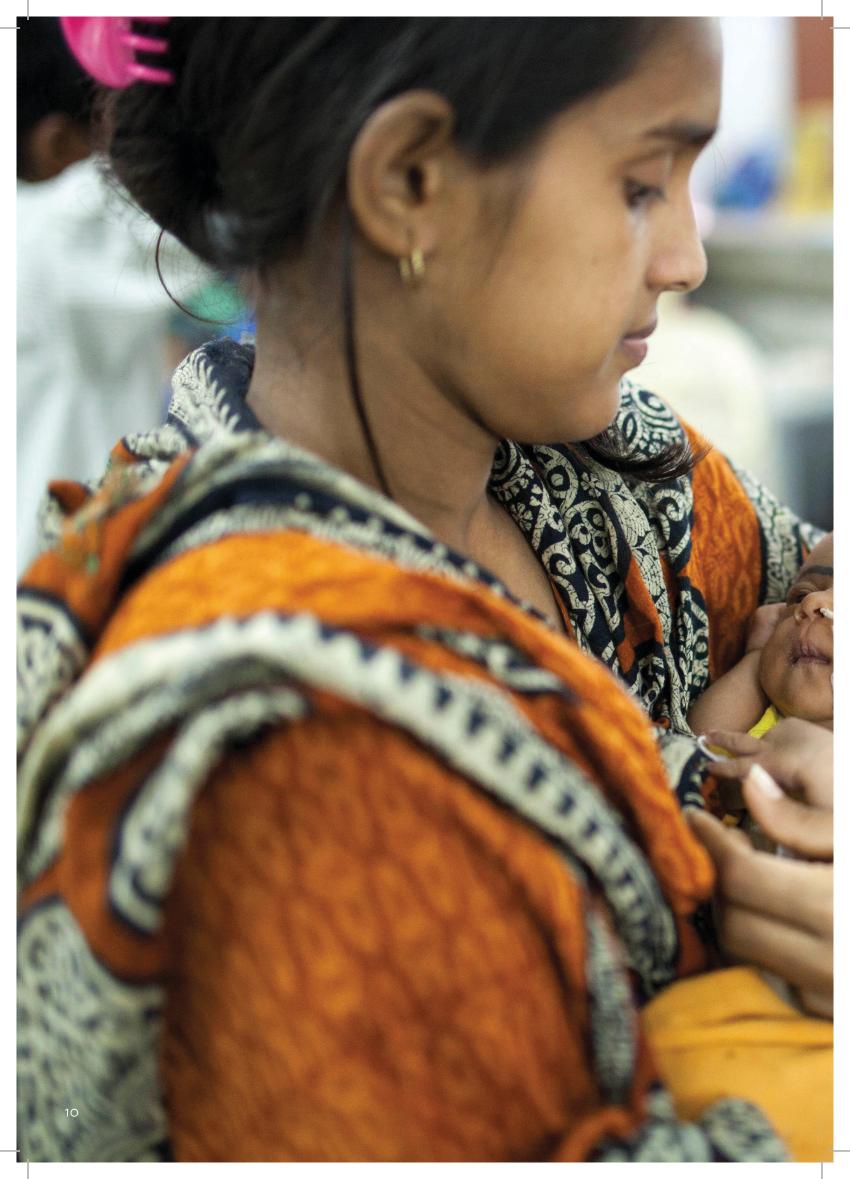
Antimicrobial resistance (AMR) is a growing concern for all infectious diseases and pneumonia is no exception, with four key pneumonia-causing pathogens included in the "WHO Priority Pathogens List for R&D of New Antibiotics". Despite this, limited research has focused on AMR in relation to pneumonia between 2000 and 2015.

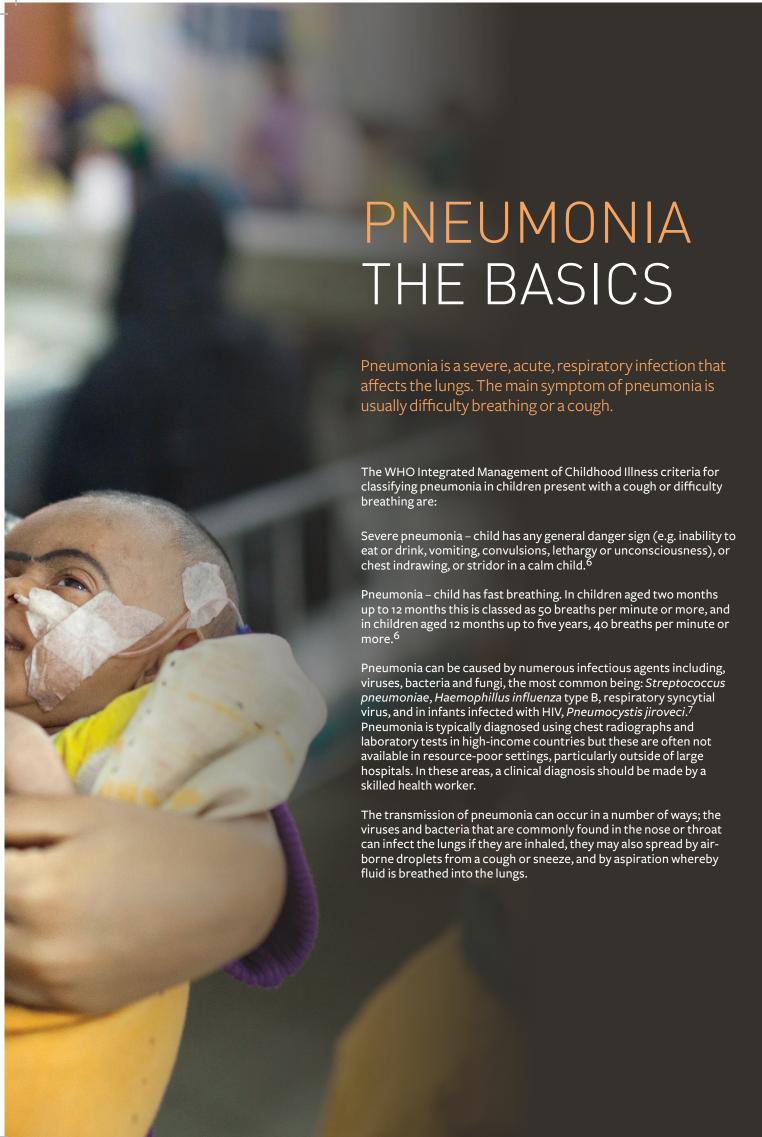
Pneumonia-related research investment was limited in low-income countries despite bearing approximately 80% of the burden of pneumonia disease. Investments with a focus on sub-Saharan Africa represented a majority of this but many nations in this region were not the focus of any pneumonia-related research funded by the G20 countries. There are clearly social and political difficulties in investing in certain countries; however, there are also large populations vulnerable to the high burden of pneumonia disease. Capacity-strengthening and educational initiatives may help to address these inequalities.

The analyses presented here form part of the most comprehensive data set of global investments in infection-related research undertaken to date. Overall, research into pneumonia is lower than warranted by its burden of disease, and arguably, pneumonia has a relatively low profile compared to other infectious diseases such as HIV and malaria. Promotion of research in pneumonia, including community health and social science research along with country-specific research on delivery strategies, overcoming barriers to interventions and on better ways for implementation will ultimately help prevent and reduce child deaths due to pneumonia.

IN THIS REPORT

This report summarises public and philanthropic funding for pneumonia-related research by the G20 countries between 2000 and 2015 and provides detail of findings in specific areas: funding for diagnostics, therapeutics and vaccine research, research with a focus on the paediatric community, antimicrobial resistance, and funding of pneumonia research in high-risk areas.







THE STUDY IN CONTEXT

Pneumonia is the single largest infectious killer of children worldwide and is particularly prevalent in sub-Saharan Africa and South Asia.

Although the annual number of childhood deaths from pneumonia decreased by 47% between 2000 and 2015, pneumonia remains a significant burden and in fact, child deaths due to pneumonia exceeded the proportion of child deaths from HIV, malaria, and measles combined.²

Furthermore, the rate of reduction of deaths due to pneumonia is slower than has been achieved for other childhood killers, including measles (85%) and enteric diseases (57%). 8

In the Democratic Republic of Congo and Chad, pneumonia claimed more children's lives in 2013 than in 1990. Conversely deaths caused by measles fell by more than 70% in both countries. This demonstrates a need to subsequently re-energise and target efforts to tackle child deaths caused by pneumonia in sub-Saharan Africa in order to move closer to ending preventable child deaths. Mortality due to pneumonia is strongly linked to poverty-related factors, such as poor nutrition, indoor air pollution, and lack of access to proper sanitation and health education.

In higher-income countries, pneumonia is a disease that overwhelmingly threatens the lives of the elderly or people who are already sick but many children still develop pneumonia. One hundred years ago, pneumonia was a global plague and was one of the principal causes of death among children of Europe and the USA. However, rising living standards and improved access to health care have dramatically changed this. Pneumonia remains a health risk for children in high-income countries but the risks of fatality are skewed towards poor children in lower-income countries.

Pneumonia has a complex aetiology with numerous causative pathogens. Vaccines, particularly the pneumococcal conjugate vaccine (protecting against various disease causing strains of S. pneumoniae) and the Hib vaccine (protecting against H. influenzae type b) can protect against most cases of pneumonia caused by these pathogens and have been widely implanted with global coverages estimated at 42% and 70%, respectively.^{3,4} However, these vaccines only protect against particular pneumonia-causing pathogens. The diagnosis of pneumonia can be difficult, particularly in low-income settings and especially in children. Furthermore, the determination of the causative pathogen of pneumonia is important to define the treatment strategy for an individual. Antibiotics can successfully treat most cases of bacterial pneumonia when care is sought quickly; however, their use remains low. 5 Antibiotics need to be available and accessible to effectively treat pneumonia but inappropriate treatment with antibiotics has significant consequences and overuse of antibiotics is known to lead to the development of resistance.7

Research is crucial to generate new knowledge and tools that can improve the prevention, diagnosis and treatment strategies for pneumonia as well as aid understanding of global, national and local epidemiology and the sociocultural impact on the burden of pneumonia disease. Funding for pneumonia-related research was identified from public and philanthropic organisations providing investment for research related to health.

International funding to support global health interventions and programmes has grown substantially since 1996 but they have not necessarily aligned with trends in disease burden. In 2011, only 2% of development assistance for health funding was allocated to pneumonia in comparison to the burden of disease which accounted for an estimated 13% of child deaths worldwide.¹

The G20 is the central forum for international cooperation on financial and economic issues. The G20 countries account for more than four fifths of gross world product and three quarters of global trade, and are home to almost two thirds of the world's population. The meeting of the G20 countries under the German Presidency (2017) set a milestone for strengthening global health in response to the recent infectious disease pandemics. This was the first time that the G20 have jointly taken responsibility for global health and they are promoting the strengthening of the WHO and the development of strong national health care systems. Through the 2017 Leaders' Summit, a declaration was made by the leaders' to safeguard against health crises, strengthen health systems and combat AMR. Although no specific reference to pneumonia appeared on the agenda for the G20 in 2017, their recommendations demonstrate the increasing prioritisation of global health among world leaders.

This report summarises public and philanthropic funding for pneumonia-related research by the G20 countries between 2000 and 2015. Additionally, it provides in-depth analysis and further detail of specific areas relating to pneumonia: funding for diagnosis, therapeutics and vaccine research, research with a focus on the paediatric community, AMR, and funding of pneumonia research in the high-risk areas of sub-Saharan Africa, Pakistan and India.

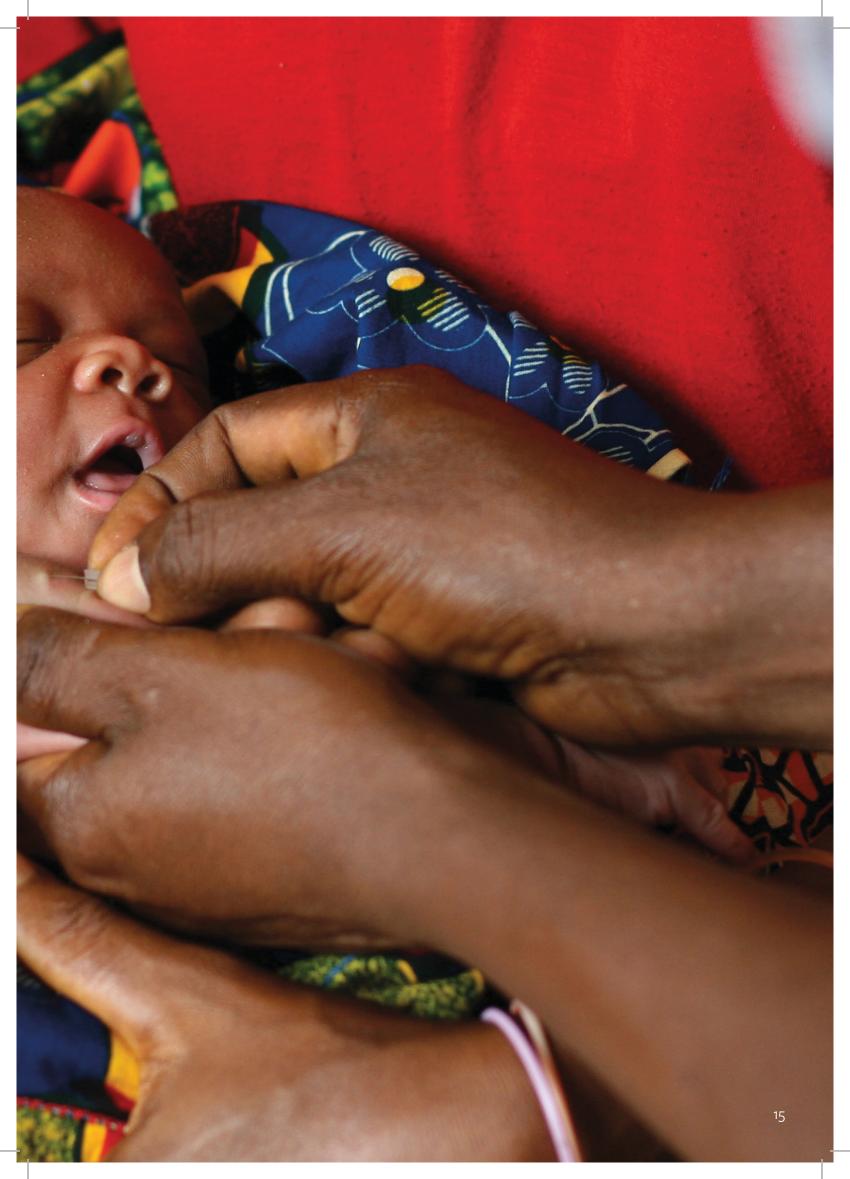
RESEARCH ACTIVITIES

The Research Investments in Global Health (ResIn) study was set up to describe trends in funding for health research, specifically research for infectious diseases. Previous analysis focused on infectious disease research in the UK and showed the pneumonia portfolio of research to be significantly underfunded compared to the global burden of disease.¹¹

This report provides a detailed analysis of pneumonia research funding across the G2o countries. The following activities were planned and delivered:

- Research awards with focuses on pneumonia and infectious diseases from funders across the G2o countries were collated and categorised; trends in funding were examined.
- Associations between burden of disease and research investments for pneumonia and other selected infectious diseases were examined to provide a metric indicating the relative level of spend compared to the burden of disease.
- Detailed analysis of pneumonia-related research funding for tools and products (diagnosis, therapeutics and vaccines) was performed along with assessment of funding for AMR research in the context of pneumonia.
- Specific analysis examining funding for paediatric pneumonia was performed to characterise the extent and sources of investment in this high-risk age group.
- The geography of pneumonia-related research in sub-Saharan Africa was illustrated to characterise the extent and location of pneumonia research in this high-burden setting.

The results from these activities were combined to help identify gaps in research and investment in relation to pneumonia and to develop priorities for future work.



APPROACHES TO THE WORK

The methodology used in this report builds on previously published work by the ResIn study that describes UK investments relating to infectious disease research.¹¹

Within this analysis research was defined as discrete projects that generated new knowledge about a specific area of focus.

Funders

Research funders were identified across the G20 countries from a number of sources including: funders that we had prior knowledge of, existing funding databases, searches of the internet, and contact with relevant in-country stakeholders.

The G2o comprises of: Argentina, Australia, Brazil, Canada, China, France, Germany, India, Indonesia, Italy, Japan, Mexico, Russia, Saudi Arabia, South Africa, South Korea, Turkey, the UK, the USA, and the European Union (EU). In this analysis, the contributions of the individual EU member states and the countries invited to the G2o summit in 2015 are included. In 2015, the invited counties were: Azerbaijan, Malaysia, Senegal, Singapore, Spain and Zimbabwe

Handling data

Each individual award was extensively characterised. Funding amounts have been adjusted for 2015 inflation and, where required, have been currency converted into US dollars. Comparisons with the burden of disease used 2015 data from the Global Burden of Disease study (GBD 2015). ¹² In this report the burden of pneumonia is based on GBD 2015 estimates of lower respiratory tract infections, which encompasses a full range of pneumonia aetiologies. ¹²

Inclusion criteria

- Funding from public and philanthropic organisations.
- Funding organisation within the G20 countries.
- Commitment to fund between 2000 and 2015 (inclusive).
- Awards focused on pneumonia with an infectious aetiology.
- Awards focused on pneumococcal disease.
- Awards focused on severe respiratory disease likely to be related to pneumonia.
- Award types project grants, programme grants or consortia grants, fellowships, and pump-priming or pilot projects that had a clear research component.
- Research from pre-clinical to public health studies.
- Implementation research (e.g. assessing the impact of pneumococcal vaccine introduction).

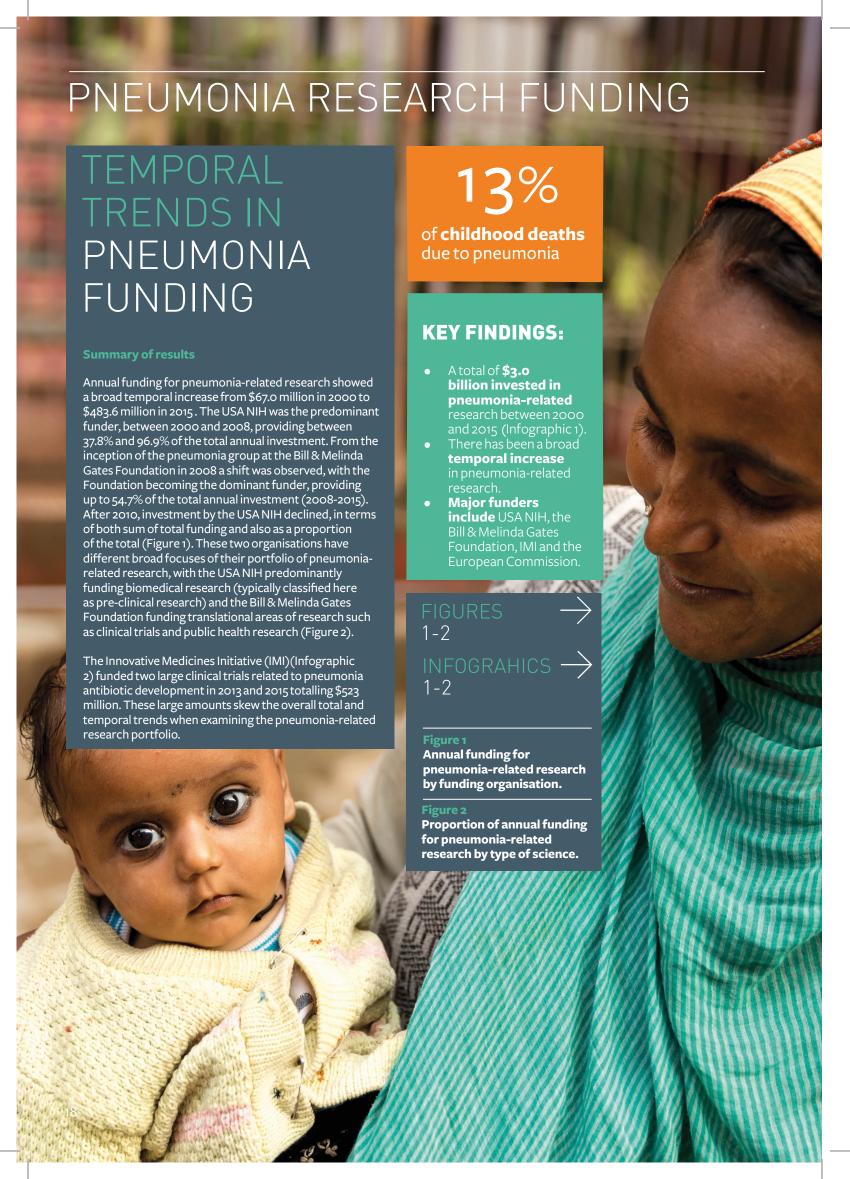
Exclusion criteria

- Funding from private sector and industry.
- Implementation activity (e.g. financing the distribution of vaccines).

Limitations

- Since there is no uniform way of reporting researchrelated investments across funding organisations, not all data points are available for each individual award.
- Investments from the private sector and industry are typically not openly available and are therefore difficult to document and are not included in this analysis.





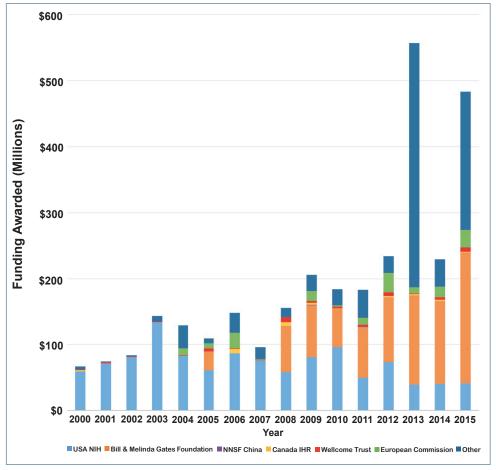


Figure 1 Annual funding by funding organisation

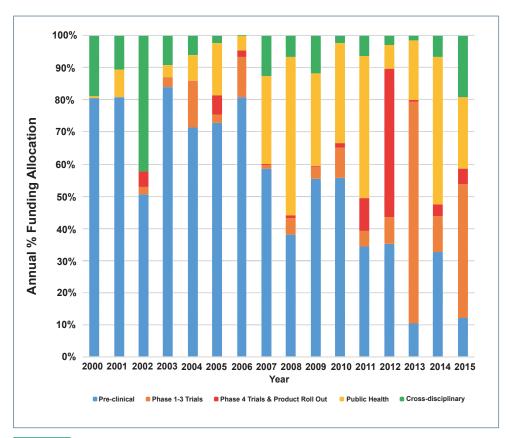


Figure 2 Proportion of annual funding by type of science

\$3.0bn

invested in pneumonia-related research between 2000 & 2015



individual awards for pneumoniarelated research

Infographic 1

INNOVATIVE MEDICINES INITIATIVE (IMI) FUNDING

There were two IMI awards that represent 16.9% of all investment in pneumoniarelated research between 2000 and 2015.

\$335.5m / 2013



for one IMI clinical trial related to **Staphylococcus aureus therapeutics**



\$187.5m

for one IMI clinical trial related to **Pseudomonas aeruginosa therapeutics**

Infographic 2

PNEUMONIA RESEARCH FUNDING

PNEUMONIA

AND OTHER **INFECTIOUS** DISEASES

Summary of results

An estimated \$100 billion has been invested by public and philanthropic organisations for all infectious disease research between 2000 and 2015 across the G20 countries.

- \$37.9 billion (37.9%) focused on HIV
- \$5.6 billion (5.6%) focused on tuberculosis
- \$4.5 billion (4.5%) focused on influenza \$4.3 billion (4.3%) focused on malaria \$3.0 billion (3.0%) focused on
- pneumonia

ASSOCIATIONS WITH BURDEN OF DISEASE

Investments for research into key infectious diseases were compared to the global burden of these diseases to give an indication of the relative level of spend. The total funding for HIV, tuberculosis, malaria, enteric diseases and pneumonia was assess against mortality in 2015.

Summary of results

The burden of pneumonia, as measured by mortality, has decreased over time along with observed increases in research funding (Figure 3). Research may have contributed to this reduction in disease burden however, there are numerous other efforts that are also responsible and may have had a larger impact on the burden of disease, such as implementation policy, economic development (including improved nutrition, housing and access to health care), and availability of vaccinations. 13 Compared to mortality for HIV, tuberculosis, malaria and enteric diseases, pneumonia received lower levels of investment per death (Figure 4).

KEY FINDING:

underfunded compared to other key infectious diseases and its disease

3 & 4

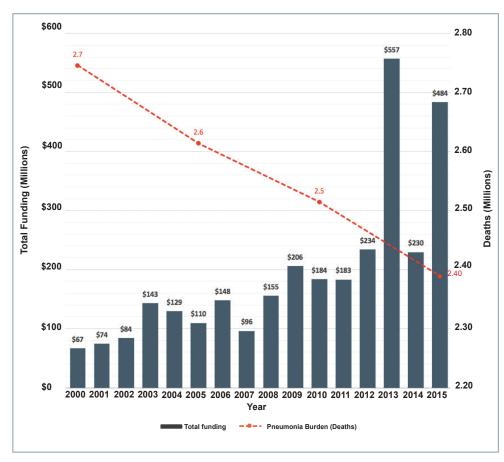
Figure 3

Annual funding for pneumonia-related research compared to all-age pneumonia-related deaths.

Funding for selected infectious diseases per allage deaths (2015).







Research funding compared to **all-age pneumonia-related deaths**

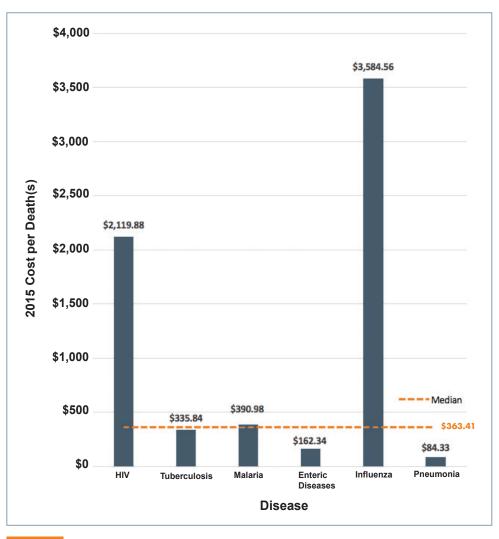


Figure 4 Infectious diseases funding per all-age deaths

PNEUMONIA RESEARCH FUNDING

DIAGNOSIS, THERAPEUTICS AND VACCINES

Improving the diagnosis, therapeutics and vaccines for the detection, treatment and prevention of pneumonia is critical for the reduction of the disease burden and are therefore areas of interest for scientific research. The portfolio of pneumonia-related research generated in this study was analysed to assess contributions from funders to these three key areas.

Summary of results

A total of \$164 million was invested in research relating to the diagnosis of pneumonia across 148 individual awards. This represented 5.3% of the total investment in pneumonia-related research between 2000 and 2015 (Infographic 3). Within this set of awards, 22.3% were funded by the USA NIH equating to \$53.8 million and 19.6% were funded by the Bill & Melinda Gates Foundation, \$38.9 million. Furthermore, the European Commission funded 12 awards which contributed approximately one quarter of the investment in this area. There were large fluctuations in annual investment for diagnosis research, ranging from no funding in 2001 to \$35.2 million in 2012 (Figure 5).

Research into therapeutics equates to \$839 million, representing 27.2% of the total investment in pneumoniarelated research across 302 individual awards (Infographic 3). The majority of these awards, 59.3%, had a pre-clinical research focus, however this only represents \$162.8 million of the investment in this area. Conversely, \$592.3 million of the investment was for clinical trials across 12.9% of the awards. This large proportion of investment in pneumonia-therapeutic research is skewed somewhat by two large awards for clinical trials provided by the IMI totalling \$522.9 million, making IMI the largest single funder of therapeutic research despite the small portfolio of awards. The second largest funder of therapeutic research is the USA NIH followed by the European Commission and then the Bill & Melinda Gates Foundation (Table 1). Overall, annual investment in therapeutic research increased between 2000 and 2015 (Figure 5).

Vaccine-related research represents 27.8% of investment in pneumonia-related research equating to \$857.5 million across 339 individual awards (Infographic 3). The Bill & Melinda Gates Foundation is the largest single funder of pneumonia vaccine research, providing investment of \$545.4 million across 91 individual awards. In comparison, the second largest funder, the USA NIH, provides \$190.5 million, although this investment was spread over a similar number of individual awards. Funding from any other source was limited, including from other high-profile funders such as the Wellcome Trust and the European Commission (Table 1). Funding for pneumonia-related vaccine research has increased between 2000 and 2015, with a large majority of investment, \$681.7 million, occurring between 2008 and 2015 (Figure 5).

KEY FINDINGS:

- A total of \$1.86 billion invested in diagnosis, therapeutic and vaccine research for pneumonia between 2000 and 2015.
- The Bill & Melinda
 Gates Foundation
 was the major funder
 of vaccine research
 relating to pneumonia.
- Limited funding has been invested in research for the diagnosis of pneumonia.

FIGURE -5 INFOGRAPHIC -

TABLE

Figure 5

Annual funding for diagnosis, pneumonia-related therapeutic & vaccine research between 2000 and 2015.

Table 1

Total investment in research by funding organisation for diagnosis, therapeutics, and vaccines for pneumonia 2000-2015. Percentages represent proportion of investment in the specific area of research (e.g. percentage of pneumonia therapeutics investment).

DEFINITIONS

Diagnosis – includes both diagnosis and diagnostics and refers to any award attempting to improve the identification of pneumonia. This may include the use of biomarkers, assessment of point of care diagnostics, revised approaches to clinician diagnosis, and screening studies.

Therapeutics – includes all aspects of drug design, assessment of antibiotics, antivirals and antifungal drugs, and other forms of treatment.

Vaccines – refers to pre-clinical and clinical assessment of immunisation, including roll out of vaccine programmes and behavioural and social science studies concerning attitudes and uptake of vaccination.





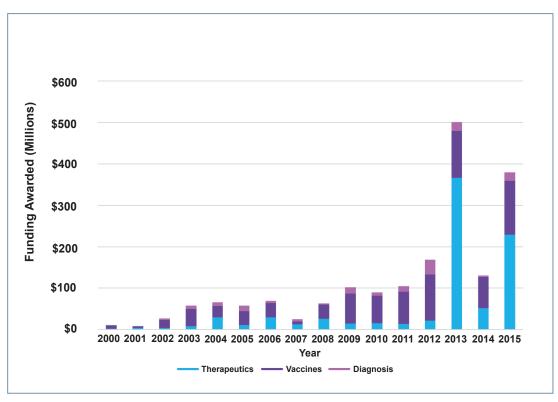


Figure 5 Funding awarded for diagnosis, therapeutics and vaccines



\$164m / 2000-2015

invested in research for the diagnosis of pneumonia

\$839m / 2000-2015



invested in therapeutic research for pneumonia



\$857.5m / 2000-2015

invested in vaccine research for pneumonia

Infographic 3

Funding Organisation	Diagnosis	Therapeutics	Vaccines
USANIH	\$53.8 million (32.9%)	\$135.7 million (16.2%)	\$190.5 million (22.2%)
	33 awards	108 awards	88 awards
Bill & Melinda Gates	\$38.9 million (23.8%)	\$40.8 million (4.9%)	\$545.4 million (63.3%)
Foundation	29 awards	21 awards	91 awards
European Commission	\$42.9 million (26.3%)	\$52.7 million (6.3%)	\$15.6 million (1.8%
	12 awards	13 awards	5 awards
IMI	\$0 (0%)	\$522.9 million (62.3%)	\$0 (0%)
	o awards	2 awards	o awards
Wellcome Trust	\$1.1 million (0.6%)	\$15.7 million (1.9%)	\$10.8 million (1.3%)
	2 awards	11 awards	11 awards

Table 1

PNEUMONIA RESEARCH FUNDING

PAEDIATRIC PNEUMONIA

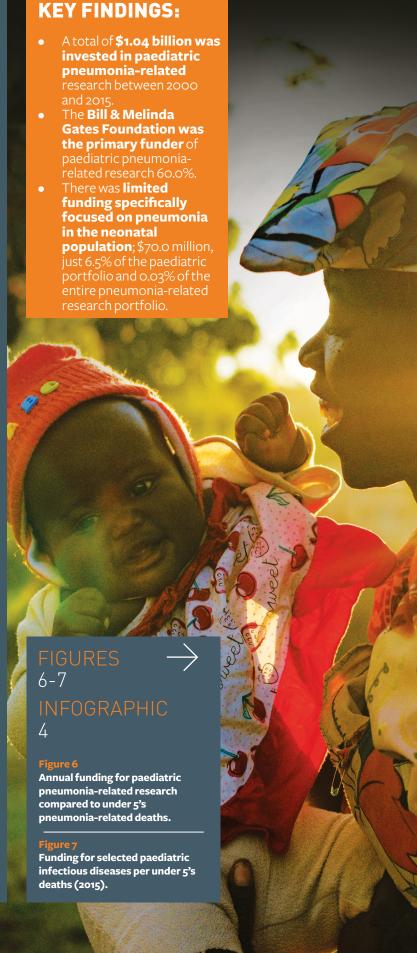
Pneumonia remains the world's leading cause of death among children under five years old with a majority of these deaths occurring in low-income countries, particularly in sub-Saharan Africa and South Asia. Neonates are particularly vulnerable to pneumonia; in 2016, neonatal mortality accounted for 24% of all paediatric pneumonia deaths.² Awards related to paediatric pneumonia were identified and explored further, compared to the overall portfolio of pneumonia-related research and other key infectious diseases that have a high burden of disease in children. Investment levels alongside the burden of disease were also examined.

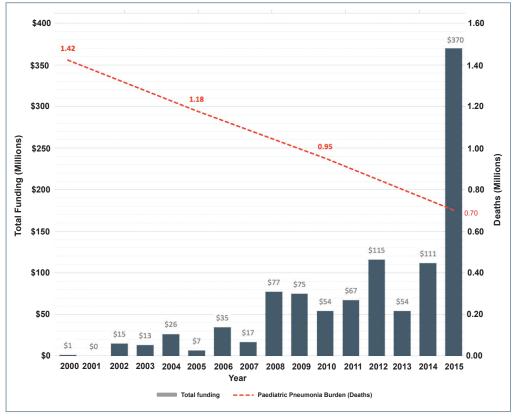
Summary of results

Research into paediatric pneumonia contributed 34.4% of the total investment in pneumonia-related research equating to \$1.04 billion, and comprised 316 individual awards. Investment in paediatric pneumonia research increased between 2000 and 2015 from \$1.05 million to \$369.7 million, respectively (Figure 6), and by 2015 represented 76.4% of the total pneumonia-related research funding. In 2015, there was a large investment by IMI representing 50.7% of the annual investment in paediatric pneumonia research for that single year. The Bill & Melinda Gates Foundation are the major single funder of paediatric pneumonia research providing 60.0% of the total funding in this area, \$622.9 million. Overall, 40.4% of paediatric pneumonia research had a public health focus. Within the paediatric portfolio, there were 29 awards totalling an investment of \$70.0 million that had a clear focus on pneumonia in the neonatal population. It is important to note that although other research awards may not be directed at the paediatric community or have a clear paediatric focus, their findings may be translated to, impact on, and benefit the paediatric community.

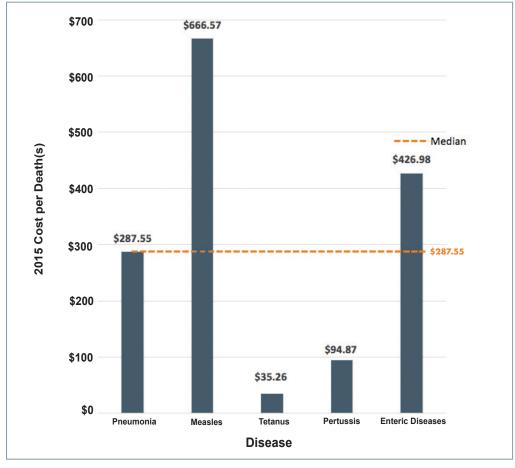
In comparison to other infectious diseases that are of importance in paediatrics, such as measles, tetanus, pertussis and enteric diseases, only enteric diseases received more total funding, \$3.2 billion, than pneumonia between 2000 and 2015 (Infographic 4). However, when looking at the relative level of spend compared to the burden of these diseases in the underfive population, both measles and enteric diseases received more funding per global death than pneumonia (Figure 7).

The burden of paediatric pneumonia, as measured by mortality in under five year olds, has decreased over time along with observed increases in paediatric pneumonia-related research funding (Figure 6). As for all-age pneumonia burden, there have been numerous efforts to reduce the burden of disease of which research is one contributor. ¹³ Even though the burden of paediatric pneumonia is declining and research investment has increased, pneumonia is still a leading contributor to paediatric mortality.





Paediatric infectious diseases funding per under 5's deaths Figure 6



Pneumonia-related research funding compared to **under 5's deaths** Figure 7

TOTAL ALL-AGE **FUNDING BETWEEN** 2000-2015 FOR CHILDHOOD-RELATED DISEASES \$3.0bn **Pneumonia DEATHS**: 700,554 | **DALYs**: 60.2 million Measles \$625.8m **DEATHS**: 62,588 | **DALYs**: 53.3 million \$13.5m **DEATHS**: 25,497 | **DALYs**: 2.2 million **Pertussis** \$77.5m **DEATHS**: 54,493 | **DALYs**: 4.7 million **Enteric DEATHS**: 498,889 | **DALYs**: 45.1 million * disease burden in under 5's (2015)

Infographic 4

PNEUMONIA RESEARCH FUNDING

ANTIMICROBIAL RESISTANCE AND PNEUMONIA

AMR affects nearly all infectious diseases, and in pneumonia it has a great health impact, especially in neonates. ¹⁴ Four key pneumonia-causing pathogens (*P. aeruginosa, S. aureus, S. pneumoniae*, and *H. influenza*) (Infographic 5) have been included in the "WHO Priority Pathogens List for R&D of New Antibiotics" (2017) indicating the public health need for research into new antibiotics and treatments for these pathogens.

Summary of results

Limited research has focused on AMR in relation to pneumonia between 2000 and 2015; a total of \$667.9 million across 151 individual awards. A major contribution to this investment were the two awards for clinical trials of therapeutics (which had an AMR component) funded by IMI in 2013 and 2015. This equates to \$522.9 million and 78.3% of pneumonia AMR research. The remaining pneumonia AMR research portfolio represents 4.7% of all pneumonia-related research, totalling \$145 million. Annual investment has remained limited for this research area, with small annual fluctuations between 2000 and 2015, with the exception of the two IMI awards (Figure 8). A majority of the individual awards, 114 awards, for pneumonia AMR research were pre-clinical totalling \$115.9 million of the investment in this research area. After the IMI, the second largest funder was the USA NIH, \$75.9 million, followed by the European Commission, \$22.9 million, the Wellcome Trust, \$13.0 million, and the Bill & Melinda Gates Foundation, \$6.7 million.

Despite the impact of AMR on pneumonia in neonates and the paediatric population, only \$2.8 million of the investment in pneumonia AMR research had a focus on neonates and \$192.1 million had a focus on the wider paediatric community.

KEY FINDINGS:

- A total of \$667.9 million was invested in pneumonia-related AMR research.
- Two clinical trials with AMR components represented 78.3% of all pneumonia-related AMR research
- There was limited funding specifically focused on pneumoniarelated AMR research in the paediatric and neonate populations.

FIGURE 9



Figure 8 Annual funding for pneumonia-related AMR research between 2000 and 2015. Highlighted bars indicate years that include IMI funding.



KEY PATHOGENS OF FOCUS FOR PNEUMONIA AMR RESEARCH BETWEEN 2000 AND 2015

\$44.8m



Streptococcus pneumoniae

46 awards

Pseudomonas aeruginosa 26 awards



Staphylococcus aureus 19 awards



\$350.9m

\$39.1m



Klebsiella pneumoniae 47 awards

Infographic 5

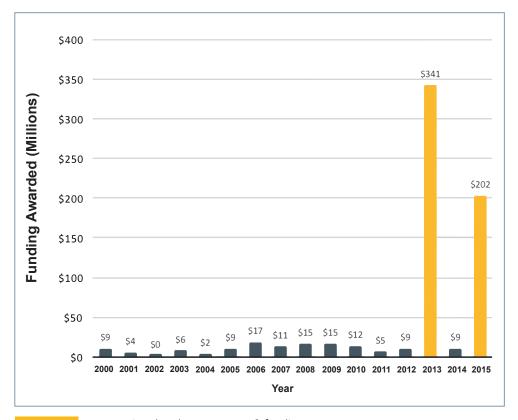


Figure 8 Pneumonia-related AMR research funding THE GEOGRAPHY
OF PNEUMONIA INVESTMENTS

Approximately 80% of the disease burden of pneumonia is in low-income countries, particularly sub-Saharan Africa and South Asia. Here we have explored the country of focus of research awards for pneumonia, concentrating on sub-Saharan Africa, India and Pakistan, to map the investment in pneumonia-related research in the context of these countries.

\$82,002,325

\$18,778,497

COUNTRIES RECEIVING FUNDING FOR PNEUMONIA RESEARCH (2000-2015)		
1 Gambia	\$75,538,334	
2 Nigeria	\$26,385,082	
3 Uganda	\$24,748,559	
4 South Africa	\$23,827,947	
5 Mali	\$21,192,133	
6 Ethiopia	\$18,204,254	
7 Mozambique	\$16,504,448	
8 Malawi	\$12,623,545	
9 Kenya	\$7,749,782	
Democratic Republic of Congo	\$5,749,500	
11 Ghana	\$5,303,107	
12 Benin	\$5,249,500	
13 Ivory Coast	\$5,249,500	
14 Togo	\$2,063,227	
IS Rwanda	\$1,240,692	
16 Tanzania	\$1,087,591	
7 Cantral African Republic	\$1,087,300	
18 Lesotho	\$1,087,300	
19 Madagascar	\$1,087,300	
20 Burkina Faso	\$808,064	
21 Zambia	\$417,400	
22 Zimbabwe	\$417,400	
3 Guinea-Bissau	\$228,035	



Summary of results

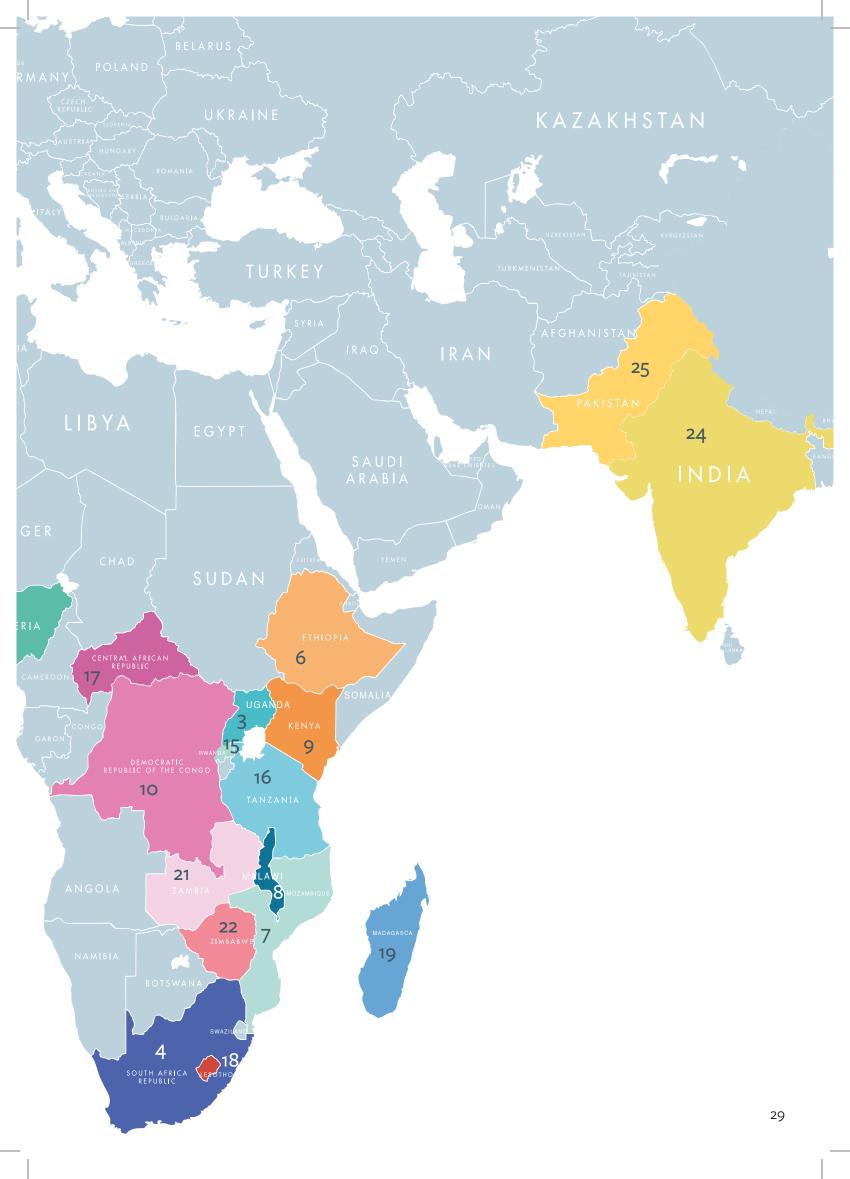
From 2000-2015, \$258.3 million was invested in pneumoniarelated research focused on low-income countries (as defined by the World Bank). This represents 8.4% of the total pneumonia-related research investment.

There was \$257.9 million of investment in pneumonia-related research with a clear focus on sub-Saharan Africa. Whilst there were numerous counties where very little to no investment was identified, Gambia was the main focus for research investment followed by Nigeria, Uganda, South Africa, and Mali. This may be explained by the presence of UK Medical Research Council-funded research centres in both Gambia and Uganda.

There was \$82.0 million invested in pneumonia-related research with a focus on India, including funding from the Indian Council of Medical Research and \$18.8 million had a focus on Pakistan.

24 India

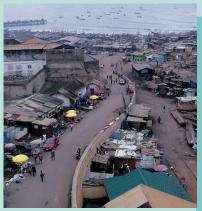
25 Pakistan



CASE STUDY:

PNEUMONIA IN GHANA – A NEED TO RAISE THE PROFILE*

Premise: Michael Head received a 2017 Global Partnerships award from the University of Southampton to travel to Accra, Ghana (August 2017) to initiate collaborations and discussions with academic, clinical and policy colleagues, reflecting on the problems and priorities of pneumonia in Ghana. The lessons learnt through this partnership award and the identification of priority research areas framed within their local context, can be used as a template across other key low-income settings.



BACKGROUND

The burden of pneumonia in Ghana is lower than some sub-Saharan Africa countries but there are still around 5,000 pneumonia-related deaths annually in children under five years of age. 15 This makes pneumonia the third greatest cause of death in this age group in Ghana. As a country, Ghana ranks 11th out of 45 sub-Saharan Africa countries for receiving public and philanthropic research investment, totalling \$5.3 million, related to pneumonia. The country is politically stable and has undergone several peaceful democratic changes in government. It also has a substantial health infrastructure which includes regional, district and sub-district hospitals and a widely-implemented community health programme, as well as a centralised system for ethical approvals and a research register.

GHANA

THE PROBLEM

Community healthcare officers have often received little training, there will typically be no doctor on site, and cases of pneumonia are often misdiagnosed. Even if pneumonia is correctly diagnosed, antibiotics are not freely available in the community setting. Patients/parents will need to buy from drug peddlers or travel to the nearest pharmacy and pay for a prescription. Thus treatment may not always reach the patient.

In a children's hospital in Accra, the mortality associated with pneumonia was high, and possibly even rising between 2003 and 2013, accounting for 18% of deaths in children under five years of age. ¹⁶ Many Ghanaians in rural settings have little easy access to hospital care and rely on the community health programme for healthcare.

Absence of appropriate diagnosis means that eventually many of these patients will end up in district or teaching hospitals with a worsening infection. Here the challenge in Ghana is the subjective diagnosis of pneumonia between clinicians; they may be constrained by a lack of routine access to basic radiological and microbiological investigations. The patient will usually be sick enough to be admitted, and prescribed amoxicillin, despite not knowing the likely aetiology and patterns of resistance and whether it will be effective. In a teaching hospital there may be specialist respiratory physicians available, but they are not routinely called to assess cases of pneumonia upon admission, and typically only see the patient up to ten days later. The patient may have remained on amoxicillin all this time and not improved, and many children at this point may die. District and regional hospitals rarely have respiratory specialists.

Ghana has national standard treatment guidelines (as per WHO recommendations) for the management of diseases as well as an

been implemented across the country since 2012 with a schedule of three doses given at six, ten and 14 weeks post birth, and in 2016 has an estimated vaccine coverage of 93% in infants receiving three doses of pathogens.

INTERVENTIONS

Awareness and use of national guidelines varies, with healthcare practitioners often relying solely on clinical judgement and experience, as well as international guidelines that are partially adjusted for the local context.

RESEARCH **FUNDING**

There is a limited evidence base that specifically addresses pneumonia in Ghana. Through our analysis four awards were identified across three projects for pneumonia-related research focused on Ghana invested by funders within the G20 countries between 2000 and 2015.

- associated with invasive disease in Kumasi, Ghana. A preclinical, Wellcome Trust grant totalling \$102,487 (2001-



The collaborations established through this award have led to the development of the Ghana Southampton Pneumonia Partnership. Members of this group are:

Mercy Abbey, Research and Development Division, Ghana Health

Service, Accra, Ghana Seth Kwaku Afagbedzi, School of Public Health, University of Ghana,

Accra, Ghana
Jane Afriyie-Mensah, Department of
Medicine and Therapeutics, Korle-Bu
Teaching Hospital, Accra, Ghana
David Antwi-Agyei, Ghana Health
Services, Kumasi, Ghana; Kirchuffs
Atengble, PACKS Africa, Accra, Ghana Ebenezer Badoe, Department of Child Health, University of Ghana James Batchelor, Faculty of

Medicine, University of Southampton,
Southampton, UK
Eric S Donkor, Department of Medical
Microbiology, University of Ghana,
Accra, Ghana
Reuben Esena, School of Public
Health, University of Ghana, Accra,

Ghana **Bamenla Q Goka**, Department of Child Health, University of Ghana,

Accra, Ghana

Michael G Head, Faculty of

Medicine, University of Southampton,

Southampton, UK **Appiah-Korang Labi**, Department of Medical Microbiology, Korle-Bu
Teaching Hospital, Accra Ghana **Edmund Nartey**, Centre for Tropical Clinical Pharmacology & Therapeutics, University of Ghana, Accra, Ghana **Isabella Sagoe-Moses**, Family Health Division, Ghana Health Service, Accra,

Edem MA Tette, Department of Community Health, School of Public Health, University of Ghana

Interventions that take into account the local context, allow local ownership of the research and forge close links with policy stakeholders are important in maximising uptake and use of research findings.





There are opportunities to correctly diagnose and treat cases of pneumonia in vulnerable patients at their first contact with a healthcare facility in the community, and further opportunities to improve care and reduce mortality in the hospital setting.



the pneumococcal conjugate vaccine, arguably little has changed in Ghana since a 2008 effort at highlighting priority areas globally for pneumonia. Improvements in policy and practice underpinned by high-quality data, epidemiology, and a renewed focus stakeholders are both overdue and vital to progress the efforts to reduce incidence and mortality of

THE WIDER PICTURE

This body of work has established that pneumonia is relatively underfunded compared to other high profile infectious diseases such as HIV, tuberculosis and malaria, particularly when examined in the context of the global burden of disease.

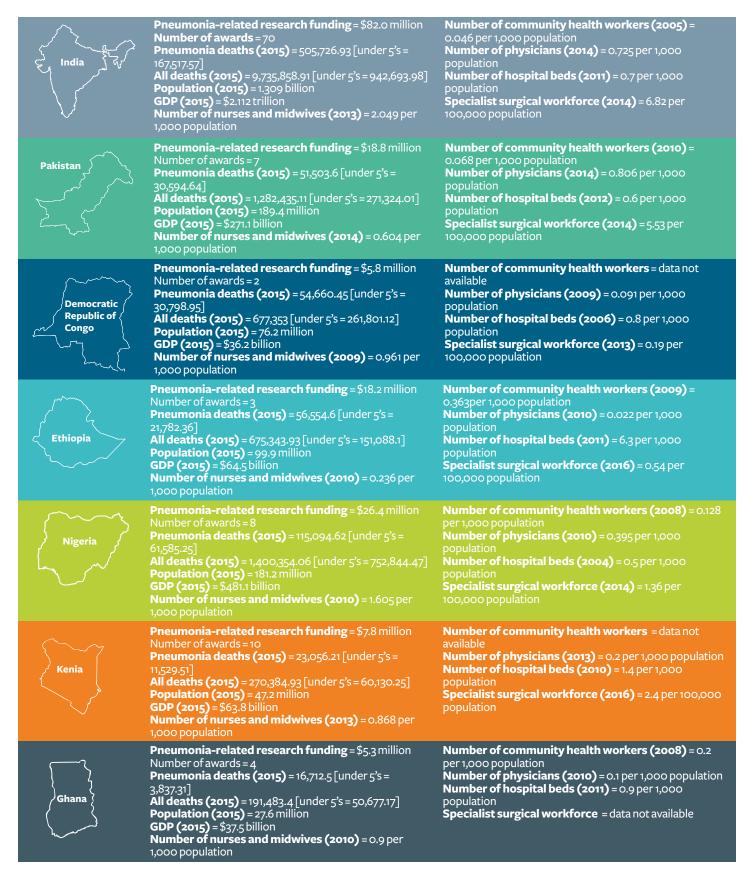
The predominant funder of pneumonia research is the Bill & Melinda Gates Foundation and there is little sustained public or philanthropic funding from other investors.

Therefore, it is important to consider funding motivations for infectious disease research and to identify mechanisms that might increase the overall portfolio for pneumonia research.

It is also important to work in close partnership with stakeholders in priority countries in order to raise the profile of pneumonia and improve the development of policies that address pneumonia case prevention, identification and management.



SELECTED PRIORITY COUNTRY PROFILES



STAKEHOLDER ENGAGEMENT

The engagement of key stakeholders is integral to the ResIn Study and has been a focus of the study over the last two years. ¹⁹ ResIn contributes to the UK Health Funders Forum run by the UK Collaborative on Development Sciences.







































EUROPE



OUR VISION:

OUR VISION IS TO UTILISE DYNAMIC, REAL-TIME DATA TO PROMOTE EVIDENCE-INFORMED HEALTH POLICYMAKING.

Moving forward, we propose an innovative, multi-disciplinary programme of research that can create a learning health system and translate into rapid and sustainable benefits for patients, decreasing inequalities in vulnerable populations, and reducing pneumonia and other disease burdens. Through this work we want to enable in-country capacity building to collate country-specific data relating to research funding, the impact and outputs of research, and research capacity. This will allow countries to be self-sufficient and able to use data to inform evidence-based policy decisions, ultimately improving patient care and reducing the burden of disease.

Our objectives are to:

- Update and enhance descriptions of global public and philanthropic funding trends for health research.
- Reflect upon the drivers for research investment decisions.
- Create a self-sustaining knowledge transfer network of multi-disciplinary colleagues in priority high-disease burden countries.
- Map the profile of healthcare facilities in priority countries to indicate centres of ongoing and previous research, current research capacity, readiness for future health research, and epidemic preparedness.
- Utilise surveys of policy, clinical and academic colleagues in priority countries to identify
 national uptake and local contextual barriers to the use of health policies within local health
 systems.
- Identify sustainable approaches to ensure the flow of knowledge from national and international health research into evidence-informed policymaking in each priority country.



References

- 1. GBD 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017; 390: 1151-210.
- 2. Institute for Health Metrics and Evaluation (IHME). Pushing the Pace: Progress and Challenges in Fighting Childhood Pneumonia. Seattle, WA: IHME, 2014.
- 3. WHO. Pneumococcal conjugate 3rd dose (PCV) immunization coverage. 2017. http://www.who.int/gho/immunization/pneumococcal/en/ (accessed 15/11/2017).
- 4. WHO. Immunization coverage. 2017. http://www.who.int/mediacentre/factsheets/fs378/en/ (accessed 15/11/2017).
- 5. WHO and UNICEF. Ending Preventable Child Deaths from Pneumonia and Diarrhoea by 2025. The integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD). Geneva, Switzerland, 2013.
- 6. WHO. Integrated Management of Childhood Illness Chart Booklet. 2014.
- 7. WHO. Pneumonia fact sheet. 2016. http://www.who.int/mediacentre/factsheets/fs331/en/(accessed 15/11/2017).
- 8. Save the Children. Fighting for Breath. A call to action on childhood pneumonia. London, UK, 2017.
- 9. G2o. Participants of the G2o Summit in Hamburg in 2017. 2017. https://
- www.g2o.org/Webs/G2o/EN/G2o/Participants/participants_node. html;jsessionid=049F4DC19FDBD9AFDoC1FD1AC1C715DD.s6t1 (accessed 15/11/2017).
- 10. G20. Berlin Declaration of the G20 Health Ministers. Together Today for a Healthy Tomorrow. Berlin, Germany, 2017.
- 11. M. G. Head, J. R. Fitchett, V. Nageshwaran et al. Research Investments in global health: a systematic analysis of UK infectious diseases research funding and global health metrics, 1997-2015. EBioMedicine 2016; 3: 180-190.
- 12. Institute of Health Metrics and Evaluation (IHME), GBD Results Tool, Seattle WA. http://ghdx.healthdata.org/gbd-results-tool (accessed 15/11/2017)
- 13. J. A. Scott, W. A. Brooks, J. S. Peiris, D. Holtzman, E. K. Mulholland. Pneumonia research to reduce childhood mortality in the developing world. The Journal of clinical investigation 2008; 118(4): 1291-300.
- 14. Keith Klugman. Vaccines and antibiotic resistance: a conversation with Dr. Keith Klugman. In: Team L, editor.; 2017.
- 15. Gbd Lri Collaborators. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory tract infections in 195 countries: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet Infectious diseases 2017; 17(11): 1133-61.
- 16. E. M. Tette, M. Neizer, M. Y. Nyarko, E. K. Sifah, E. T. Nartey, E. S. Donkor. Changing Patterns of Disease and Mortality at the Children's Hospital, Accra: Are Infections Rising? PloS one 2016; 11(4): e0150387.

- 17. WHO and UNICEF. Data, statistics and graphics for immunization, vaccines and biologicals. 2017. http://www.who.int/immunization/monitoring_surveillance/data/en/ (accessed 15/11/2017).
- 18. M. Abbey, S.K. Afagbedzi, J. Afriyie-Mensah et al. Pneumonia in Ghana a need to raise the profile. International Health 2018, 10(1): 4-7.
- 19. M.G. Head and R.J. Brown. The activity of the Research Investments in Global Health study and ways forward within the global funding and policy landscape. BMC Proceedings. 2016; 10(Suppl8): 59.

Acknowledgements

We would like to acknowledge funding from the Bill & Melinda Gates Foundation (OPP1127615). We would also like to thank the input of: Professor James Batchelor (University of Southampton, study Principal Investigator from October 2017), Dr Stuart Clarke (University of Southampton, study Principal Investigator from October 2015 – September 2017), Professor Marie-Louise Newell (University of Southampton, co-applicant), Professor Rifat Atun (Harvard University, co-applicant), Dr Joseph Fitchett (Harvard University, co-applicant), and Professor Anthony Scott (London School of Hygiene and Tropical Medicine, co-applicant).

We would further like to acknowledge the cooperation of numerous funders in our countries of focus, and also UberResearch for facilitating access to the Dimensions database (https://dimensions.uberresearch.com).

Copyright 2018 $\, @$ Research Investments in Global Health Study.

This report was written by the Research Investments in Global Health Study Team, a research project funded by the Bill & Melinda Gates Foundation and hosted at the University of Southampton, UK. Collaborating partners include the London School of Hygiene and Tropical Medicine (UK) and Harvard University (UK).

All rights reserved. This report can be copied in an unaltered form, with the copyright statement intact, for any non-commercial purposes. The use of extracts, data figures or tables from this report is allowed for non-commercial purposes provided suitable acknowledgement of the Report is made in accordance with standard academic practices.

Suggested citation: Research Investments in Global Health Study (ResIn). Sizing up Pneumonia Research: Assessing Global Investments in Pneumonia Research 2000-2015. Southampton, UK: ResIn, 2018.



For more information

www.researchinvestments.org

Rebecca Brown, rebecca.brown@soton.ac.uk Michael Head, m.head@soton.ac.uk Telephone: +44 (0)2382 359 759

Research Investments in Global Health Study Clinical Informatics Research Unit Care of the National Blood and Transplant Service Mail point 852, Coxford Road Southampton SO16 5AF, United Kingdom