

Research Synthesis: Public Funding of Pharmaceutical R&D

v1.0 researched and written by Marcela Vieira, edited by Suerie Moon, last updated April 2019

Introduction

The literature on public funding for pharmaceutical research and development (R&D) is considerable* and has been increasing in the past decade. This review focuses on public funding; a full picture of total expenditures on health R&D is beyond the scope of this review, as are commercial sector expenditures.

Search terms

Pharmaceutical/medicine/health/biomedical and public funding/financing, public sector, contribution, research and development

Synthesis of the literature

The identified literature focused mainly on 3 topics: i) mapping public funding of pharmaceutical R&D, ii) analyzing how public funding compares to public health needs, and iii) documenting the contributions of public funding to drug development. Despite an increase in the number of studies aiming to document the role of public funding in drug development in recent years, the information available is fragmented, incomplete and difficult to find. Some studies estimated spending on broader health research and more targeted pharmaceutical research jointly, as these can be difficult to disentangle; in such cases, this review uses the broader term “health research” to refer to the findings.

i. Mapping public funding of pharmaceutical/health R&D

Several studies and data sources provide information on public funding of overall health R&D or with focus by disease area, both globally and at national or regional level. Most of the studies with a focus at the national level are related to the United States and the United Kingdom, the two largest public funders of health R&D, and only a few provide information about other regions and countries.

Global estimates: WHO’s Global Observatory on Health R&D centralizes data sources on health R&D activities, including grants for health research by major funders (World RePORT) and funding flows for health R&D by country (expressed as gross domestic expenditure on R&D (GERD) and GERD in the health and medical sciences (health GERD)). Røttingen et al. (2013) mapped global investments in health R&D from all sectors in 2009 and found a total of US\$240

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billion spent, out of which 89% (US\$214 billion) was invested in high-income countries. Of this total, 60% came from the commercial sector, 30% from the public sector, and about 10% from other sources (including the philanthropic sector).

Viergever and Hendriks (2016) identified 55 major public and philanthropic funders of health research globally that together spent \$93 billion, of which 40% (\$37 billion) was spent by the 10 largest funding organizations. The largest funder was the United States National Institutes of Health (\$26.1 billion), followed by the European Commission (\$3.7 billion), and the United Kingdom Medical Research Council (\$1.3 billion). The largest philanthropic funder was the Wellcome Trust (\$909.1 million), and the largest multilateral funder was the World Health Organization (\$135.0 million).

Estimates by disease area: Policy Cures Research's G-FINDER project has conducted since 2008 an annual survey mapping global public, private, and philanthropic R&D expenditures for neglected diseases, defined as: "those predominantly affecting developing countries, for which products are needed but there is an insufficient commercial incentive to stimulate R&D". The last survey conducted in 2017 included R&D investments in 33 diseases from 197 organizations, amounting to a total of \$3.5 billion of which \$2.3 billion (65%) came from the public sector, \$692m (19%) from philanthropic funders and \$554m (16%) from the private sector.

The Resource Tracking for HIV Prevention R&D Working Group (RTWG) has tracked R&D investments for biomedical HIV prevention options since 2000. In 2017, total investment was \$1.13 billion, with the US public sector contributing \$830 million (73.5%) and the philanthropic sector \$164 million (14.5%).

The Treatment Action Group (TAG, 2018) mapped trends in global research funding for tuberculosis (TB) from 2005–2017, tracking how much public, private, philanthropic, and multilateral institutions spend across six areas of research: basic science, diagnostics, drugs vaccines, operational research, and infrastructure/unspecified projects. Findings show total global investment in TB research over the 13 years adds up to \$7.8 billion. In 2017, 66% (\$510 million) came from public sources, 19% (\$145 million) from philanthropies, 11% (\$85 million) from private industry, and 4% (\$32 million) from multilateral entities. Tomlinson and Low (2019) mapped research funding for tuberculosis in South Africa from domestic and foreign sources. They found that the South African government invested more than most countries in TB research as a percentage of GDP or GERD, even though it was low in absolute terms and still much lower than its share of the global TB burden.

Simpkin et al. (2017) identified the major international, European Union, US and UK public and philanthropic funding programs for antibiotic R&D. The study found that most funding was available for basic science and preclinical research, while there was limited late-stage funding of clinical development, and almost no funding for the transition of products from early clinical phases to commercialization.

Estimates by country: In the US, a US Government Accountability Office (GAO, 2017) study on the drug industry covering global spending on R&D by the private and public sectors from 2008 to 2014 found that in 2014 company-reported R&D spending amounted to \$89 billion while US federal government spending was around \$28 billion. Most of the companies' spending was directed to drug development and most of the federal spending was directed to basic research.

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Research America (2018) mapped investments in health R&D from all sectors in the US from 2013 to 2017 and found that in 2017 the total amount was \$182.3 billion, with the private sector accounting for 67% of total spending, followed by the federal government at 22%. GHTC and Policy Cures Research (2017) analyzed US government funding for global health R&D and the health impact and economic returns from these investments, including their contributions to the development of new health technologies. They found that the US government invested \$14 billion in R&D for global health between 2007 and 2015, helping advance 42 new technologies approved since 2000 and supporting 128 promising products in late-stage development.

In the UK, Cooksey (2006) provided an overview of UK health research funding and highlighted gaps to ensure UK health priorities are considered through all types of research and in the translation of health research to practice, concluding with a set of recommendations to address these gaps. The UK Clinical Research Collaboration (2015, 2012 and 2006) published three reports on health research in the UK, providing an overview of health research activity across all areas of health and disease funded by the largest government and philanthropic health-related research funders. Results show that in 2014, 64 public and philanthropic funding organizations spent £3bn (£2bn directly on research projects and £1bn on infrastructure), out of an estimated total of £8.5bn spent on health R&D in the UK. Sussex et al. (2016) estimated the effect of government and philanthropic biomedical and health research expenditure in the UK on subsequent private pharmaceutical sector R&D expenditure and found that a 1% increase in public sector expenditure is associated with a 0.81% increase in private sector expenditure.

A few studies provide information related to other countries in Europe. Salud Por Derecho (2019) analyzed public funding of biomedical R&D in Spain and the transfer of knowledge from the public to the private sector. The findings show that expenditures in health R&D in Spain in 2014 amounted to a total of 2.5 billion euros and were overall higher in the public and philanthropic sector (62%) than in the private sector (38%). Van Hecke and Gils (2019) provided an overview of publicly funded biomedical research in Belgium, which amounted to 575 million euros in 2015 in direct funds, most of which was directed to Belgium universities, with industry receiving 59 million euros. The authors also provided information about tax incentives for the industry, which amounted to 872 million euros in 2016, and also included the reimbursement of purchase of medicines by the public health system as a public contribution to pharmaceutical R&D, which represented a total of 4.32 billion euros in 2017. Viergever and Hendriks (2014) provided information on funding programs issued by the Netherlands Organisation for Health Research and Development (ZonMw), amounting to an average of 215 million euros annually. They highlighted that the allocation of public funds is targeted to areas where new knowledge or products are needed, especially when these areas are not considered profitable for the private sector.

In Asia, Dondona et al. (2017) estimated the total annual funding available for health research in India in 2011-12 at US\$ 1.42 billion, including 0.02% from the public sector and 79% by the Indian pharmaceutical industry. Dara and Sangamwar (2014) provided a landscape of patents related to various drug therapeutic targets and anticancer technologies from 10 Indian publicly-funded research organizations over a period of 13 years (1990 - 2013). Qiu et al. (2014) investigated public funding and private investment into Chinese pharmaceutical R&D from 2002-2010, finding that the vast majority of R&D investment was from private sources and public funding was invested in less developed provinces. Chen et al. (2015) provided data regarding rare disease biomedical research in China related to 366 projects (involving 32 rare diseases) funded by the National

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Natural Science Foundation of China (NSFC) from 1999 to 2007, with annual funding of about 10 million RMB. The authors compared the data to government-funded biomedical research programs for rare diseases the USA, EU, and Japan, showing that the expenditures in China represented about 10% of similar funding in the USA. Hsieh and Löfgren (2009) conducted an analysis of biopharmaceutical innovation and industrial development in South Korea, Singapore, and Taiwan and found that “governments employ a range of industrial policies to promote the biopharmaceutical industry, including public investment in biomedical hubs, research funding, and R&D tax credits.” The authors concluded that “the most important feature of the biopharmaceutical industry in these countries is the dominant role of the public sector.”

In Africa, Kebede (2014) conducted a survey to map the expenditures on health research by 847 research institutions in 42 sub-Saharan African countries for the biennium 2005–2006, which amounted to a total of US\$ 302 million. Most were external funders, followed by government ministries, non-profit institutions, and industry.

ii. Analyzing how public funding of health R&D compares to public health needs

The allocation of public funding in comparison to the disease burden has been a long-standing issue in the literature, with most of the identified papers focusing their analysis in the US, especially in relation to NIH funding, and a few in the UK. It should be noted that there are discussions about other criteria to take into consideration when discussing the allocation of public research funds, such as complementarity with funding by others, but it falls beyond the scope of this review.

At global level, the above-mentioned study by Røttingen et al. (2013) also analyzed total health R&D investments across diseases and how it aligns to the global disease burden, concluding that only about 1% of all health R&D investments were allocated to neglected diseases in 2010.

In the US, Sampat et al. (2013) conducted an analysis of the allocation of NIH funding across diseases, highlighting that previous empirical studies had been significantly hindered by data constraints. The NIH had recognized these shortcomings and in 2008 created a data system in response. The authors analyzed data from this new system to assess the relationship between NIH funding and deaths and hospitalizations in the US associated with 107 diseases, and found a strong relationship. Hanna (2015) analyzed the NIH allocation of public research funding among 29 diseases and concluded that NIH's allocation of research funding is disproportionate to the disease burden in the US, with results showing that infectious diseases are overfunded, and lifestyle/environmental health conditions are underfunded. Another study by Karimkhani et al. (2014) analyzed grants from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) for 15 skin conditions and how they compared to global disease burden, concluding that grant funding was well-matched for 5 of the 15 studied skin diseases, while 2 skin diseases were over-represented and 7 were under-represented.

In the UK, Head et al. (2016) conducted a systematic analysis of research funding for infectious diseases from public and philanthropic organizations between 1997 and 2013 and compared the investments with global mortality, disability-adjusted life years (DALYs) and years lived with disability (YLD), finding that acute hepatitis C, leishmaniasis and African trypanosomiasis received comparatively high levels of funding while pneumonia, shigellosis, pertussis, cholera, and syphilis were poorly funded. Ward et al. (2013) compared the national burden of disease with R&D funding from public and philanthropic sectors in the UK, and concluded that disease areas

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representing the biggest burden were generally associated with the most funding and research output.

Beyond the US and the UK, the above-mentioned study by Dondona et al. (2017) concluded that public funding for health research in India was extremely small and had considerable mismatches with the major causes of disease burden in the country. Kinge et al. (2014) analyzed the correlation between the Norwegian investment in health research and the burden of disease, using both Norwegian and global burden of disease estimates and concluded that Norwegian research investments appeared aligned with the Norwegian disease burden, while the correlation with the global disease burden was much lower.

In Latin America, Martinez et al. (2012) analyzed the funding between 2003 and 2010 of Mexico's national health research agency (National Council on Science and Technology - CONACYT), and compared it with two indicators of the national disease burden - number of deaths and DALYs - to conclude that they were weakly correlated with the funding for health research. Maceira et al. (2010) described the national public health research systems in five Latin American countries (Argentina, Bolivia, Chile, Paraguay, and Uruguay), highlighting that none of them had explicit mechanisms for prioritization of health research. The authors concluded that problems such as nutrition, environment, violence and accidents received little attention in most countries, despite accounting for a significant amount of the health burden. Paraje (2010) assessed the allocation of public funds for health research in Chile between 2002 and 2006 and concluded that the funding allocation was not prioritizing the disease burden in the country.

iii. Documenting the contributions of public funding to drug development and conditions attached to public funding

Another main topic discussed in the identified literature is the contribution of public funding to drug development. Most of the identified papers focused their analysis in the US and the UK, with few but an increasing number of studies covering other countries.

Generally, Mazzucato and Semieniuk (2017) questioned common perceptions related to the role of the public sector in innovation by discussing evidence from different fields of the economy. They showed that public funding is strongly present across the entire innovation chain, not only in basic research. They also argued that public actors take an “entrepreneurial and lead investor role... willing and able to take on extreme risks,” including in funding early-stage start-ups, questioning the perception that it is private venture capital that takes most of the risk. In the health sector, the authors discussed the evidence related to US NIH funding for health R&D and how it has enabled the biotechnology revolution and the development of most innovative drugs approved by the FDA over the years.

With a focus on the US, Cleary et al. (2018) examined the contribution of NIH funding to drug development and found that it contributed to every one of the 210 new molecular entities (NMEs) approved by the FDA from 2010-2016, concluding that the NIH contribution to research associated with new drug approvals is greater than previously appreciated. Blume-Kohout (2012) investigated the relationship between expenditures from the NIH and pharmaceutical innovation from 1975 to 2006 and found that a 10% increase in targeted, disease-specific NIH funding produced a 4.5% increase in the number of related drugs entering clinical testing (phase I trials), but found no evidence that it increased the number of related treatments investigated in late-stage (phase III) trials.

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Azoulay et al. (2019) measured the commercial output associated with publicly funded research, analyzing information contained in patents in the US. The authors used the information to explicitly link NIH grants with the publications they supported and the patents that cited those publications. They measured the impact of NIH research funding on patenting by biopharmaceutical companies from 1980 to 2012 and concluded that NIH funding spurred the development of private-sector patents: a \$10 million boost in NIH funding led to a net increase of 2.7 patents. Results also showed that “half of the patents resulting from NIH funding were for disease applications distinct from the one that funded the initial research,” adding information about the “cross-disease spillover effects of NIH funding.” The authors then conclude that “by looking only within the same disease area when measuring impact, the prior literature in this area appears to have missed almost half of the total impact of basic research funding.”

Sampat and Lichtenberg (2011) analyzed the role of public and private sectors in pharmaceutical innovation and provided empirical data on the contribution of the US federal government to drug development “linking data on drug approval, patents, and consumers’ drug spending to information on publications and patents emanating from public-sector research.” Overall, the authors found that direct government funding was more important in the development of “priority-review” drugs (described as the most innovative new drugs) than for “standard-review” drugs. The study also showed that government funding also played an indirect role by funding basic underlying research in almost half of the drugs approved and in almost two-thirds of priority-review drugs.

In addition, several studies analyzed the role of public funding related to the development of medicines identified as particularly important. Chakravarthy et al. (2016) investigated the public- and private-sector contributions in the US to the research and development of the 25 “most transformational” drugs in the past 25 years and found that only 4 drugs were almost completely researched and developed by the private sector. For the others, there were contributions from both sectors, with one sector or the other dominating particular phases of the R&D continuum; for example, 54% of basic science milestones were achieved predominantly by the public sector and 27% by the private sector. Kesselheim et al. (2015) studied the developmental histories of 26 drugs or drug classes approved by the US FDA between 1984 and 2009 that were judged to be transformative (defined as pharmaceuticals that are both innovative and have groundbreaking effects on patient care) and found that many were based on discoveries made by academic researchers who were supported by federal government funding; others were jointly developed in both publicly funded and commercial institutions; and the fewest number of drugs had originated solely within pharmaceutical industry research programs.

The NIH (2000) analyzed the effectiveness of its funding of biomedical research for product development; it investigated 5 top-selling drugs and concluded that NIH-funded research played a critical role in the development of each of them, complementing industry investments. Reichert and Milne (2002) performed an assessment of the relationship between private and public sector expenditures in the discovery and development of 21 “impact” drugs in the US and concluded that due to mixed methods and incomplete data, previous attempts to measure the relative contribution of the public and private sectors to the R&D of therapeutically important drugs were flawed. Cockburn and Henderson (1996) examined the relationship between public and private funding for drug development in the US using data from authorship of publications related to the development of 21 drugs. Their findings showed a “significant reciprocal

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interaction” between authors from public and private institutions and the authors conclude by rejecting a “simple ‘linear’ dichotomous model in which the public sector performs basic research and the private sector exploits it.” Cockburn and Henderson (2001) also evaluated the impact of US public funding of health R&D on the pharmaceutical industry by analyzing data from academic studies showing that “public sector science creates new knowledge and new tools, and produces large numbers of highly trained researchers, all of which are a direct and important input to private sector research.” The authors concluded that “measured quite narrowly in terms of its effect on private sector R&D, the rate of return to public funding of biomedical sciences may be as high as 30% per year.”

With a focus on applied research, Stevens et al. (2011) analyzed the direct role of the public sector in the applied-research phase of drugs and vaccines over the past 40 years and identified 153 new FDA-approved drugs, vaccines, or new indications for existing drugs that were discovered through research carried out by public-sector researchers, more than half of which were used in the treatment or prevention of cancer or infectious diseases. The authors concluded that drugs discovered by public sector researchers were expected to have a disproportionately large therapeutic effect and that public-sector research had a more immediate effect on improving public health than was previously realized.

Focusing on a specific medicine, the Treatment Action Group (TAG, 2018) mapped public and philanthropic funding in the development of bedaquiline (a TB treatment). While the total amount invested in R&D for bedaquiline was not disclosed by the originator company Janssen, the study listed public and philanthropic investments that contributed to the clinical development and uptake of the medicine, as well as financial incentives from which Janssen benefited to develop the drug. Garber et al. (1992) investigated the US federal public and private roles in the development of alglucerase therapy for Gaucher disease, a rare disease, and concluded that the government supported or performed much of the research that made it possible to develop the treatment, while removing much of the risk for pharmaceutical companies.

In the EU, Lincker et al. (2014) investigated the profile and geographical origin of the organizations involved in the recent development of new medicines in the European Union (EU). They analyzed data from 94 medicinal products approved containing a new active substance (NAS) between 2010 and 2012 and found that large or intermediate-sized pharmaceutical companies accounted for 49% of the products (large, 28%; intermediate-sized, 21%), SMEs for 27%, academic/public bodies/PPPs accounted for 17%, and private-private collaborations accounted for 7%. The respective figures for orphan products revealed a higher proportion (61%) of SMEs as originators, with large or intermediate-sized pharmaceutical companies accounting for 22%, and academic/public bodies/PPPs accounting for 11%. With regard to the region where the innovative research resulting in these products occurred, 45% of the originators were based in North America and 37% in Europe. International projects, the majority of which were transatlantic collaborations, accounted for 8%, and other countries (Japan, China, Israel, and Australia) accounted for the remaining 10%. There were no apparent major differences in the geographical origin of orphan versus non-orphan products.

In the UK, Head et al. (2015) conducted a systematic analysis of public funding for infectious disease research studies in the UK from 1997–2010, amounting to a total investment of £2.6 billion, of which £76.9 million (3.0%) was directed towards viral hepatitis, the focus of the study.

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Preclinical research received £50.3 million (65.4%), whilst implementation and operational research received £19.4 million (25.3%). Stopaids and Global Justice Now (2017) analyzed UK government health R&D spending and the contribution to the development of many medicines, arguing that the public is paying twice: first through the substantial funding of health R&D which amounted to £2.3 billion in 2015, and second through the purchase of the medicines by the public health system (NHS), which spent more than £1bn in 2016 alone on medicines developed with significant reliance on UK public research funding. The study detailed the UK public funding of specific medicines, i.e. abiraterone (an effective drug for treating advanced prostate cancer) and the whole class of monoclonal antibodies (MABs), including alemtuzumab, adalimumab, and infliximab.

A few studies addressed the issue of conditions attached to public funding of health R&D. The main condition identified in the literature is related to the dissemination of the findings in open access publications. McElfish et al. (2018) presented an overview of the policies and requirements of 11 major health research agencies in the US regarding dissemination of results to academic and lay communities and the participants of the research. They found that several agencies have policies for academic dissemination but only a few have the same for dissemination to research participants and the lay communities. Tschider (2014) analyzed the implementation of the condition of “open access publication” of the results of publicly funded research in US NIH funding agreements and found that principal investigators have partially complied with this depository requirement, and the NIH have signaled an intent to enforce grant agreement terms and conditions by stopping funding deposits and engaging in legal action. Bakker et al. (2017) also analyzed the condition of “open access publication” present in public funding of health research in Canada focusing on compliance and barriers to open access publishing (mainly costs of publishing) using as a case study the research for multiple sclerosis.

The above-mentioned report by Tomlinson and Low (2019) also focused on the access conditions placed on products resulting from publicly funded research in South Africa. The authors concluded that “while funding agreements typically include provisions on access and affordability, these provisions are not always clear and may turn out to be hard to enforce.” The above-mentioned article by Van Hecke and Gils (2019) analyzed the conditions applied to public funding in Belgium and found that there are few conditions set, the main being with regard to open access publications and no conditions with regard to availability and affordable pricing of medicines. The above-mentioned report by Stopaids and Global Justice Now (2017) also analyzed the conditions on UK public funding for R&D and concluded there is an absence of safeguards to ensure the accessibility and affordability of medicines that derive from publicly funded R&D.

A KEI (2018) briefing note analyzed provisions in the US related to obligations for federal contractors, including: i) requirement to disclose inventions discovered with federal funding; ii) requirement of local production, that is, that the invention be manufactured substantially in the United States; iii) requirement of practical application of the invention, specifically that “its benefits are available to the public on reasonable terms”, iv) March-In Rights and the Royalty-Free Right. Treasure et al. (2014) analyzed petitions presented to the NIH to exercise its march-in rights related to products developed with government funding since 1980, especially to address exceedingly high prices or inadequate supply of interventions whose development was based heavily on government funding, particularly pharmaceutical products and medical devices. They found that in the 33 years since the passage of Bayh-Dole, such march-in rights

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petitions to the NIH had been seriously considered for only 4 products and were rejected each time.

The UCL Institute for Innovation and Public Purpose (2018) published a policy report with a section on “Achieving public return through conditionality”, in which the authors mentioned a few examples of conditions that could be attached to public funding to achieve a more just sharing of the rewards, such as “reinvesting a greater share of profits from innovative products to support future R&D; a commitment to share knowledge and fully disclose data related to R&D, including expenditures and data from failed clinical trials; the possibility of the public retaining a golden share from intellectual property rights (and on occasion equity of profits); and a requirement that manufacturers supply treatments on reasonable terms.” So et al. (2008) analyzed 30 years of experience in the US with the implementation and shortcomings of the Bayh-Dole Act of 1980 to make a series of recommendations to other countries seeking to implement similar legislation, highlighting the need to adopt policies and safeguards serving the public interest that could be attached to government-supported research. Among the options, they suggested: i) transparency in the patenting and licensing of publicly funded research; ii) no exclusive licensing unless necessary for commercialization; iii) government authority to issue additional licenses; iv) government use rights and v) ensuring consumer access to end products.

Conditionality was also raised in several United Nations reports. The report of the WHO Fair Pricing Forum (2017) suggested that governments should attach conditions to research funding so that public funding is explicitly taken into account in pricing discussions and the results are made publicly available. The final report of the United Nations Secretary General’s High-level Panel on Access to Medicines (2016) mentioned explicitly that data sharing and data access should be conditions on public funding and recommended the adoption of other conditions to promote availability and affordability. The final report of the WHO Consultative Expert Working Group on Research and Development: Financing and Coordination - CEWG (2012) suggested that funders or research organizations adopt licensing conditions that permit non-exclusive licensing or prescribe a low target price for a product, especially where the public sector has funded most of the R&D. The WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (2011) recommended promoting public access to the results of government-funded research by publication in open access databases and further dissemination of publicly- or donor-funded inventions and know-how.

Research gaps

- Information on national policies for innovation and public R&D investment, particularly in advanced economies with established R&D activity.
- More information on public spending in health R&D beyond the US and EU
- Information on any conditions attached to public funding of R&D (e.g. relating to affordability or availability of end products), including in laws, policies or contracts, and compliance with or enforcement of such conditions

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Azoulay, Pierre, Joshua S Graff Zivin, Danielle Li, and Bhaven N Sampat. 2019. "Public R&D Investments and Private-Sector Patenting: Evidence from NIH Funding Rules." *The Review of Economic Studies* 86 (1): 117–52. <https://doi.org/10.1093/restud/rdy034>.

Abstract: We quantify the impact of scientific grant funding at the National Institutes of Health (NIH) on patenting by pharmaceutical and biotechnology firms. Our article makes two contributions. First, we use newly constructed bibliometric data to develop a method for flexibly linking specific grant expenditures to private-sector innovations. Second, we take advantage of idiosyncratic rigidities in the rules governing NIH peer review to generate exogenous variation in funding across research areas. Our results show that NIH funding spurs the development of private-sector patents: a \$10 million boost in NIH funding leads to a net increase of 2.7 patents. Though valuing patents is difficult, we report a range of estimates for the private value of these patents using different approaches.

Bakker, Caitlin, Carol Stephenson, Erin Stephenson, and Debbie Chaves. 2017. "Public Funding and Open Access to Research: A Review of Canadian Multiple Sclerosis Research." *Journal of Medical Internet Research* 19 (2): e52. <https://doi.org/10.2196/jmir.6250>.

Abstract: **Background:** Multiple sclerosis (MS), a progressive demyelinating disease of the brain and spinal cord, is the leading cause of nontraumatic neurological damage in young adults. Canada has one of the highest reported incidents of MS, with estimates between 55 and 240 per 100,000 individuals. Between 2009 and 2014, the MS Society of Canada provided over Can \$90 million to researchers and, since 2013, has encouraged researchers to make both current and previous research products openly available. **Objective:** The goal of the study was to determine the open access (OA) cost implications and repository policies of journals frequently used by a sample of MS researchers. This study benchmarked current publishing preferences by MS Society of Canada researchers by examining the OA full-text availability of journal articles written by researchers funded between 2009 and 2014. **Methods:** Researchers were identified from the 2009 to 2014 annual MS Society of Canada Research Summaries. Articles were identified through searches in Web of Science, Scopus, Medline and Embase (both via OVID). Journal level analysis included comparison of OA policies, including article processing charges (APCs) and repository policies. Data were analyzed using descriptive statistics. **Results:** There were 758 articles analyzed in this study, of which 288 (38.0%) were OA articles. The majority of authors were still relying on journal policies for deposit in PubMed Central or availability on publisher websites for OA. Gold OA journals accounted for 10.2% of the journals in this study and were associated with significantly lower APCs (US \$1900) than in hybrid journals (US \$3000). Review of the journal self-archiving options highlighted the complexity of stipulations that authors would have to navigate to legally deposit a version of their article. **Conclusions:** This study found that there are currently researcher- and publisher-imposed barriers to both the gold and green roads to OA. These results provide a current benchmark against which efforts to enhance openness can be measured and can serve as a reference point in future assessments of the impact of OA policies within this field. With funding agencies worldwide releasing OA mandates, future success in compliance will require changes to how researchers and publishers approach production and dissemination of research.

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Blume-Kohout, Margaret E. 2012. "Does Targeted, Disease-Specific Public Research Funding Influence Pharmaceutical Innovation?" *Journal of Policy Analysis and Management: [The Journal of the Association for Public Policy Analysis and Management]* 31 (3): 641–60. <http://www.jstor.org/stable/41653819>.

Abstract: Public funding for biomedical research is often justified as a means to encourage development of more (and better) treatments for disease. However, few studies have investigated the relationship between these expenditures and downstream pharmaceutical innovation. In particular, although recent analyses have shown a clear contribution of federally funded research to drug development, there exists little evidence to suggest that increasing targeted public research funding for any specific disease will result in increased development of drugs to treat that disease. This paper evaluates the impact of changes in the allocation of U.S. National Institutes of Health (NIH) extramural research grant funding across diseases on the number of drugs entering clinical testing to treat those diseases, using new longitudinal data on NIH extramural research grants awarded by disease for years 1975 through 2006. Results from a variety of distributed lag models indicate that a sustained 10 percent increase in targeted, disease-specific NIH funding yields approximately a 4.5 percent increase in the number of related drugs entering clinical testing (phase I trials) after a lag of up to 12 years, reflecting the continuing influence of NIH funding on discovery and testing of new molecular entities. In contrast, we do not see evidence that increases in NIH extramural grant funding for research focused on specific diseases will increase the number of related treatments investigated in the more expensive, late-stage (phase III) trials.

Chakravarthy, Ranjana, Kristina Cotter, Joseph DiMasi, Christopher-Paul Milne, and Nils Wendel. 2016. "Public- and Private-Sector Contributions to the Research and Development of the Most Transformational Drugs in the Past 25 Years: From Theory to Therapy." *Therapeutic Innovation & Regulatory Science* 50 (6): 759–68. <https://doi.org/10.1177/2168479016648730>.

Abstract: Background: With available funding from the public sector decreasing while medical needs and scientific complexity increase, private-sector collaborations with academia and government have become increasingly key in furthering medical innovation. Nonetheless, some skeptics diminish the contribution of the private sector to the discovery and development of truly innovative drugs on the one hand, while on the other hand they assert that research and development (R&D) of new medicines could and should be exclusively within control (at least financially) of the government. This begs the question, How much government funding would be needed to replace industry new drug R&D spending? **Methods:** We address the respective roles of the private and public sectors in drug development by examining a diverse array of evidentiary materials on the history of 19 individual drugs, 6 drug classes, and 1 drug combination identified as the most transformative drugs in health care over the past 25 years by a survey of over 200 physicians. **Results:** Only 4 of the individual drugs appear to have been almost completely researched and developed by one sector. One sector or the other, however, did dominate particular phases of the R&D continuum. For example, 54% of basic science milestones were achieved predominantly by the public sector and 27% by the private sector. For discovery milestones, it was 15% by the public sector and 58% by the private sector. The private sector was also dominant in achieving the major milestones for both the production and drug development phases (81% and 73% of the drugs reviewed, respectively). For 19% to 27% of the case histories for the various categories, dominance of one sector versus the other could not be determined. On the question of replacing industry's spending on the R&D of medicines, we estimate quite

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conservatively that the amount that would have to be spent by government would be nearly double the budget of the National Institutes of Health just to maintain the flow of the most innovative drug approvals and would have to increase nearly 2.5 times that level to maintain the development of all new drugs. Conclusions: Our analysis indicates that industry's contributions to the R&D of innovative drugs go beyond development and marketing and include basic and applied science, discovery technologies, and manufacturing protocols, and that without private investment in the applied sciences there would be no return on public investment in basic science.

Chen, Kai, Lan Yao, and Zhiyong Liu. 2015. "Towards Government-Funded Special Biomedical Research Programs to Combat Rare Diseases in China." *Bioscience Trends* 9 (2): 88–90. <https://doi.org/10.5582/bst.2015.01048>.

Abstract: Rare diseases are rarely conditions that are often debilitating and even life-threatening, which was identified by the World Health Organization (WHO) with a prevalence of 0.65-1%. 5,000- 7,000 rare diseases are thought to exist, which account for around 10% of diseases for individuals worldwide. It is estimated that over 10 million people were patients with rare disease in China. During the past years, public awareness of rare diseases has in fact heightened with the launching of campaigns by patients' organizations and spontaneous efforts by members of the public, not only in developed countries and regions including United States of America (USA), the European Union (EU), and in Japan, but also in China. However, the features of missed or delayed diagnosis, shortage of effective drugs, and the high cost of currently available drugs for rare diseases make it an important public health issue and a challenge to medical care worldwide. To combat rare disease, the government should assume the responsibility of taking on the important task of promoting the sustained development of a system of medical care for and research into rare diseases. Government- funded special biomedical research programs in the USA, EU, and Japan may serve as a reference for China coping with rare diseases. The government-funded special biomedical research programs consisting of leading clinicians and researchers to enhance basic and applied research on rare diseases were expected to be launched in China.

Cockburn, I., and R. Henderson. 2001. "Publicly Funded Science and the Productivity of the Pharmaceutical Industry." In *Innovation Policy and the Economy*. Vol. 1. MIT Press. <http://www.nber.org/chapters/c10775>.

Abstract: U.S. taxpayers funded \$14.8 billion of health related research last year, four times the amount that was spent in 1970 in real terms. In this paper we evaluate the impact of these huge expenditures on the technological performance of the pharmaceutical industry. While it is very difficult to be precise about the pay- offs from publicly funded research, we conclude from a survey of a wide variety of quantitative and qualitative academic studies that the returns from this investment have been large, and may be growing even larger. Public sector science creates new knowledge and new tools, and produces large numbers of highly trained researchers, all of which are a direct and important input to private sector research. But this is not a one way street: the downstream industry is closely linked with upstream institutions, and knowledge, materials, and people flow in both directions. One important contribution of public science is that it sustains an environment in which for- profit firms can conduct their own basic research, which in turn contributes to the global pool of knowledge. Measured quite narrowly in terms of its effect on private sector R&D, the rate of return to public funding of biomedical sciences may be

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as high as 30% per year. Large as this figure is, these calculations are likely an underestimate, since they fail to fully capture the wider impact of pharmaceutical innovation on health and well-being. Indeed, the best may be yet to come: the revolution in molecular biology that began in publicly funded laboratories 25 years ago and continues to be driven by the academic research promises dramatic advances in the treatment of disease.

Cockburn, I., and R. Henderson. 1996. "Public-Private Interaction in Pharmaceutical Research." Proceedings of the National Academy of Sciences 93 (23): 12725–30. <https://doi.org/10.1073/pnas.93.23.12725>.

Abstract: We empirically examine interaction between the public and private sectors in pharmaceutical research using qualitative data on the drug discovery process and quantitative data on the incidence of coauthorship between public and private institutions. We find evidence of significant reciprocal interaction, and reject a simple "linear" dichotomous model in which the public sector performs basic research and the private sector exploits it. Linkages to the public sector differ across firms, reflecting variation in internal incentives and policy choices, and the nature of these linkages correlates with their research performance.

Cooksey, David. 2006. A Review of UK Health Research Funding. London: Stationery Office. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/228984/0118404881.pdf.

Abstract: Not available.

Extracts from the executive summary: The Review found that the UK Health Research system has many strengths. The quality of the health research base, combined with a national health service, creates a major selling point that attracts R&D investment from the pharmaceutical and biotechnology industries, which form a major part of the UK knowledge economy. In recent years, the UK Government has taken a number of actions to ensure the UK remains at the forefront of health research and a location of choice for the pharmaceuticals industry to locate its R&D. These actions include the creation of the UK Clinical Research Collaboration (UKCRC) to improve the infrastructure for clinical and medical research; the creation of the Joint MRC/NHS Health Research Delivery Group in the 2004 Spending Review to enable a more joined up approach between Government funders of medical and clinical research; the creation of a new strategy for research in the NHS in England, Best Research for Best Health (BRfBH); and the establishment of MRC Technology, to manage and commercially develop intellectual property arising from the basic research carried out by the MRC's directly-supported scientists. The Review found, however, that the UK is at risk of failing to reap the full economic, health and social benefits that the UK's public investment in health research should generate. There is no overarching UK health research strategy to ensure UK health priorities are considered through all types of research and there are two key gaps in the translation of health research. The Review also found that the wider funding arrangements for supporting translation of ideas from conception to practice could be more coherent or comprehensive and, where arrangements exist, they do not function well. The Review identified cultural, institutional and financial barriers to translating research into practice in the publicly funded research arena. But it also found that, in the private sector, the pharmaceuticals industry is facing increasing challenges in translating research into health and economic benefit. The Review has sought to make recommendations

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that will increase the translation of R&D into health and economic benefit for the UK, both in the public and private sectors.

Dandona, Lalit, Rakhi Dandona, Ganil Kumar, Krycia Cowling, Pritty Titus, Vishwa Mohan Katoch, and Soumya Swaminathan. 2017. "Mapping of Health Research Funding in India." *The National Medical Journal of India* 30 (6): 309. <https://doi.org/10.4103/0970-258X.239069>.

Abstract: Background. We aimed to estimate the total annual funding available for health research in India. We also examined the trends of funding for health research since 2001 by major national and international agencies. Methods. We did a retrospective survey of 1150 health research institutions in India to estimate the quantum of funding over 5 years. We explored the Prowess database for industry spending on health research and development and gathered data from key funding agencies. All amounts were converted to 2015 constant US\$. Results. The total health research funding available in India in 2011–12 was US\$ 1.42 billion, 0.09% of the gross domestic product (GDP) including only 0.02% from public sources. The average annual increase of funding over the previous 5 years (2007–08 to 2011–12) was 8.8%. 95% of this funding was from Indian sources, including 79% by the Indian pharmaceutical industry. Of the total funding, only 3.2% was available for public health research. From 2006–10 to 2011–15 the funding for health research in India by the three major international agencies cumulatively decreased by 40.8%. The non-industry funding for non-communicable diseases doubled from 2007–08 to 2011–12, but the funding for some of the leading causes of disease burden, including neonatal disorders, cardiovascular disease, chronic respiratory disease, mental health, musculoskeletal disorders and injuries was substantially lower than their contribution to the disease burden. Conclusion. The total funding available for health research in India is lower than previous estimates, and only a miniscule proportion is available for public health research. The non-industry funding for health research in India, which is predominantly from public resources, is extremely small, and had considerable mismatches with the major causes of disease burden. The magnitude of public funding for health research and its appropriate allocation should be addressed at the highest policy level.

Dara, Ajay, and Abhay T Sangamwar. 2014. "Anticancer Patent Landscape and Technology Assessment of Indian Public-Funded Research Institutes and Organizations." *Expert Opinion on Therapeutic Patents* 24 (8): 893–912. <https://doi.org/10.1517/13543776.2014.926329>.

Abstract: Introduction: This review discusses the various drug therapeutic targets and latest technologies of anticancer patents from 10 Indian public-funded research organizations covering more than 150 esteemed institutes. We have identified and reported the leading assignee and inventors along with their collaboration network and, thereby, have analyzed the various patent trends, geographical distributions, citation maps, Derwent World Patents Index, international patent classification analysis and the like. Areas covered: This article provides the insights of 1905 patent documents from 191 families and discusses in-depth anticancer technology through categorization studies at the level of drug discovery, drug development and treatment and diagnosis. In addition, various cancer targets were correlated with recent technologies so as to identify the white spaces for upcoming technologies. Expert opinion: Over a period of 13 years (1990 – 2013) the main focus of Indian cancer research was in the field of synthetic chemistry and natural extracts followed by the pharmaceutical compositions and combinations, whereas, the white spaces for future cancer remedy were identified from research

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in the areas of cancer stem cell lines, vaccines, gene therapy, nano formulations with targeted drug delivery systems as core and latest technologies.

Cleary, Ekaterina Galkina, Jennifer M. Beierlein, Navleen Surjit Khanuja, Laura M. McNamee, and Fred D. Ledley. 2018. "Contribution of NIH Funding to New Drug Approvals 2010–2016." Proceedings of the National Academy of Sciences 115 (10): 2329–34. <https://doi.org/10.1073/pnas.1715368115>.

Abstract: This work examines the contribution of NIH funding to published research associated with 210 new molecular entities (NMEs) approved by the Food and Drug Administration from 2010–2016. We identified >2 million publications in PubMed related to the 210 NMEs (n = 131,092) or their 151 known biological targets (n = 1,966,281). Of these, >600,000 (29%) were associated with NIH-funded projects in RePORTER. This funding included >200,000 fiscal years of NIH project support (1985–2016) and project costs >\$100 billion (2000–2016), representing ~20% of the NIH budget over this period. NIH funding contributed to every one of the NMEs approved from 2010–2016 and was focused primarily on the drug targets rather than on the NMEs themselves. There were 84 first-in-class products approved in this interval, associated with >\$64 billion of NIH-funded projects. The percentage of fiscal years of project funding identified through target searches, but not drug searches, was greater for NMEs discovered through targeted screening than through phenotypic methods (95% versus 82%). For targeted NMEs, funding related to targets preceded funding related to the NMEs, consistent with the expectation that basic research provides validated targets for targeted screening. This analysis, which captures basic research on biological targets as well as applied research on NMEs, suggests that the NIH contribution to research associated with new drug approvals is greater than previously appreciated and highlights the risk of reducing federal funding for basic biomedical research.

Garber, Alan M., and United States, eds. 1992. Federal and Private Roles in the Development and Provision of Alglucerase Therapy for Gaucher Disease. Background Paper / Office of Technology Assessment. Washington, DC: Office of Technology Assessment. <https://ota.fas.org/reports/9214.pdf>.

Foreword: The effort to discover and develop new pharmaceuticals is a risky and costly enterprise. For diseases that affect few patients, the barriers to development maybe especially great, since the drugs' small markets may make it difficult for firms to recoup their initial research and development investments. The Federal Government has sought to reduce these barriers through incentives first adopted in the Orphan Drug Act of 1983 (Public Law 97-414). The transfer of technology from Federal laboratories such as the National Institutes of Health to the pharmaceutical industry can also reduce the cost and risk of drug development for firms. Although such incentives may result in important new therapies, their price to patients and insurers may still be high. As part of our assessment, Government Policies and Pharmaceutical Research and Development, requested by the House Committee on Energy and Commerce and its Subcommittee on Health and the Environment and the Subcommittee on Antitrust, Monopolies, and Business Rights of the Senate Committee on the Judiciary, OTA commissioned researchers at Stanford University to examine the development and provision of alglucerase, an important new treatment for Gaucher disease. Gaucher disease is a rare inherited disorder in which the body lacks an enzyme necessary to break down fats. This background paper describes the development of alglucerase, illustrates the role that both the Federal Government and private sector can have in making new therapies available for orphan diseases, and lays out some

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of the tradeoffs that can exist between developing new medical technologies and controlling health care costs.

GHTC, and Policy Cures Research. 2017. "Return on Innovation: Why Global Health R&D Is a Smart Investment for the United States." <https://www.ghtcoalition.org/pdf/Return-on-innovation-Why-global-health-R-D-is-a-smart-investment-for-the-United-States.pdf>.

Summary: This report provides an in-depth analysis of US government funding for global health research and development (R&D), as well as analysis of health impact and economic returns from these investments. First, it looks at US government investments in global health R&D over time and outlines funding trends, including implications of emergency R&D investments versus sustainable funding. It also looks at key US agencies fueling research efforts and examines their contributions to novel global health technologies. Next, the report analyzes the health impact of tools supported by US government investments, with case studies highlighting treatments delivered, lives saved, and cost savings. Finally, it considers direct returns to the United States from government investments in global health R&D, including economic growth, job creation, and American health security. We hope this report will inform Congress, Executive Branch, and other key stakeholders as they make policy and budget decisions that affect the future of US leadership in global health R&D.

Hanna, Michael. 2015. "Matching Taxpayer Funding to Population Health Needs." *Circulation Research* 116 (8): 1296–1300. <https://doi.org/10.1161/CIRCRESAHA.114.305585>.

Summary: In an era of economic recession and budget cutbacks, Americans may be curious to know how the government is distributing their taxes for medical research, relative to their health needs. Previous reports recommended that the National Institutes of Health (NIH) allocate funding proportional to the burden-of-illness from diseases and conditions. But the most recent publicly available data on burden-of-illness and NIH funding show that infectious diseases are still overfunded relative to their health burden on the American population, especially HIV/AIDS. By contrast, several lifestyle/environmental health conditions are still underfunded, including importantly: chronic obstructive pulmonary disease, lung cancer, stroke, heart disease, depression, violence, and road injury. NIH's allocation of research funding is often disproportionate to the current health needs of the American people. Greater decision-making involvement of Congress and the public would be helpful, if Americans want their taxes spent fairly on the illnesses that actually burden their health.

Head, M. G., J. R. Fitchett, G. S. Cooke, G. R. Foster, and R. Atun. 2015. "Systematic Analysis of Funding Awarded for Viral Hepatitis-Related Research to Institutions in the United Kingdom, 1997- 2010." *Journal of Viral Hepatitis* 22 (3): 230–37. <https://doi.org/10.1111/jvh.12300>.

Summary: Viral hepatitis is responsible for great health, social and economic burden both globally and in the UK. This study aimed to assess the research funding awarded to UK institutions for viral hepatitis research and the relationship of funded research to clinical and public health burden of viral hepatitis. Databases and websites were systematically searched for information on infectious disease research studies funded for the period 1997–2010. Studies specifically related to viral hepatitis research were identified and categorized in terms of funding by pathogen, disease and by a research and development value chain describing the type of science. The overall data set included 6165 studies (total investment £2.6 billion) of which £76.9

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million (3.0%) was directed towards viral hepatitis across 323 studies (5.2%). By pathogen, there were four studies specifically investigating hepatitis A (£3.8 million), 69 studies for hepatitis B (21.4%) with total investment of £14.7 million (19.1%) and 236 (73.1%) hepatitis C studies (£62.7 million, 81.5%). There were 4 studies investigating hepatitis G, and none specifying hepatitis D or E. By associated area, viral hepatitis and therapeutics research received £17.0 million, vaccinology £3.1 million and diagnostics £2.9 million. Preclinical research received £50.3 million (65.4%) across 173 studies, whilst implementation and operational research received £19.4 million (25.3%) across 128 studies. The UK is engaged in much hepatology research, but there are areas where the burden is great and may require greater focus, such as hepatitis E, development of a vaccine for hepatitis C, and further research into hepatitis-associated cancers. Private sector data, and funding information from other countries, would also be useful in priority setting.

Head, Michael G., Joseph R. Fitchett, Vaitehi Nageshwaran, Nina Kumari, Andrew Hayward, and Rifat Atun. 2016. "Research Investments in Global Health: A Systematic Analysis of UK Infectious Disease Research Funding and Global Health Metrics, 1997–2013." *EBioMedicine* 3 (January): 180–90. <https://doi.org/10.1016/j.ebiom.2015.12.016>.

Abstract: Background: Infectious diseases account for a significant global burden of disease and substantial investment in research and development. This paper presents a systematic assessment of research investments awarded to UK institutions and global health metrics assessing disease burden. Methods: We systematically sourced research funding data awarded from public and philanthropic organisations between 1997 and 2013. We screened awards for relevance to infection and categorised data by type of science, disease area and specific pathogen. Investments were compared with mortality, disability-adjusted life years (DALYs) and years lived with disability (YLD) across three time points. Findings: Between 1997–2013, there were 7398 awards with a total investment of £3.7 billion. An increase in research funding across 2011–2013 was observed for most disease areas, with notable exceptions being sexually transmitted infections and sepsis research where funding decreased. Most funding remains for pre-clinical research (£2.2 billion, 59.4%). Relative to global mortality, DALYs and YLDs, acute hepatitis C, leishmaniosis and African trypanosomiasis received comparatively high levels of funding. Pneumonia, shigellosis, pertussis, cholera and syphilis were poorly funded across all health metrics. Tuberculosis (TB) consistently attracts relatively less funding than HIV and malaria. Interpretation: Most infections have received increases in research investment, alongside decreases in global burden of disease in 2013. The UK demonstrates research strengths in some neglected tropical diseases such as African trypanosomiasis and leishmaniosis, but syphilis, cholera, shigellosis and pneumonia remain poorly funded relative to their global burden. Acute hepatitis C appears well funded but the figures do not adequately take into account projected future chronic burdens for this condition. These findings can help to inform global policymakers on resource allocation for research investment.

Hsieh, Chee-Ruey, and Hans Löfgren. 2009. "Biopharmaceutical Innovation and Industrial Developments in South Korea, Singapore and Taiwan." *Australian Health Review: A Publication of the Australian Hospital Association* 33 (2): 245–57. <https://doi.org/10.1071/AH090245>.

Abstract: South Korea, Singapore and Taiwan are well known as export-oriented developmental states which for decades employed industrial policy to target particular industries for government support. In the past fifteen years, these three countries all identified the biopharmaceutical industry as a strategic sector. This article explores, through economic

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analysis, the rationale for this decision and the strategies chosen for linking into the global bio-economy with the objective of catching up in biopharmaceuticals. The paper identifies three comparative advantages enjoyed by these countries in the biopharma sector: (1) public investments in basic research; (2) private investments in phase 1 clinical trials; and (3) a potentially significant contract research industry managing latter-stage clinical trials. Governments employ a range of industrial policies, consistent with these comparative advantages, to promote the biopharmaceutical industry, including public investment in biomedical hubs, research funding and research and development (R&D) tax credits. We argue that the most important feature of the biopharmaceutical industry in these countries is the dominant role of the public sector. That these countries have made progress in innovative capabilities is illustrated by input measures such as R&D expenditure as share of gross domestic product, number of patents granted and clinical trials, and volume of foreign direct investment. In contrast, output indicators such as approval of new chemical entities suggest that the process of catching up has only just commenced. Pharmaceutical innovation is at the stage of mainly generating inputs to integrated processes controlled by the globally incumbent firms.

Karimkhani, Chante, Lindsay N. Boyers, David J. Margolis, Mohsen Naghavi, Roderick J. Hay, Hywel

C. Williams, Luigi Naldi, et al. 2014. "Comparing Cutaneous Research Funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases with 2010 Global Burden of Disease Results." Edited by Andrzej T. Slominski. PLoS ONE 9 (7): e102122. <https://doi.org/10.1371/journal.pone.0102122>.

Abstract: Importance: Disease burden data helps guide research prioritization. Objective: To determine the extent to which grants issued by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) reflect disease burden, measured by disability-adjusted life years (DALYs) from Global Burden of Disease (GBD) 2010 project. Design: Two investigators independently assessed 15 skin conditions studied by GBD 2010 in the NIAMS database for grants issued in 2013. The 15 skin diseases were matched to their respective DALYs from GBD 2010. Setting: The United States NIAMS database and GBD 2010 skin condition disability data. Main Outcome(s) and Measure(s): Relationship of NIAMS grant database topic funding with percent total GBD 2010 DALY and DALY rank for 15 skin conditions. Results: During fiscal year 2013, 1,443 NIAMS grants were issued at a total value of \$424 million. Of these grants, 17.7% covered skin topics. Of the total skin disease funding, 82% (91 grants) were categorized as "general cutaneous research." Psoriasis, leprosy, and "other skin and subcutaneous diseases" (i.e.; immunobullous disorders, vitiligo, and hidradenitis suppurativa) were over-represented when funding was compared with disability. Conversely, cellulitis, decubitus ulcer, urticaria, acne vulgaris, viral skin diseases, fungal skin diseases, scabies, and melanoma were under-represented. Conditions for which disability and funding appeared well-matched were dermatitis, squamous and basal cell carcinoma, pruritus, bacterial skin diseases, and alopecia areata. Conclusions and Relevance: Degree of representation in NIAMS is partly correlated with DALY metrics. Grant funding was well-matched with disability metrics for five of the 15 studied skin diseases, while two skin diseases were over-represented and seven were under-represented. Global burden estimates provide increasingly transparent and important information for investigating and prioritizing national research funding allocations.

Kebede, Derege, Chris Zielinski, Peter Ebongue Mbondji, Issa Sanou, Wenceslas Kouvidila, and Paul-Samson Lusamba-Dikassa. 2014. "Expenditures on Health Research in Sub-Saharan African

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Countries: Results of a Questionnaire-Based Survey.” *Journal of the Royal Society of Medicine* 107 (1_suppl): 77–84. <https://doi.org/10.1177/0141076814530601>.

Abstract: Objective: To estimate the sources of funds for health research (revenue) and the uses of these funds (expenditure). Design: A structured questionnaire was used to solicit financial information from health research institutions. Setting: Forty-two sub-Saharan African countries. Participants: Key informants in 847 health research institutions in the 42 sub-Saharan African countries. Main outcome measures: Expenditure on health research by institutions, funders and subject areas. Results: An estimated total of US\$ 302 million was spent on health research by institutions that responded to the survey in the World Health Organization (WHO) African Region for the biennium 2005–2006. The most notable funders for health research activities were external funding, ministries of health, other government ministries, own funds and non-profit institutions. Most types of health research performers spent significant portions of their resources on in-house research, with medical schools spending 82% and government agencies 62%. Hospitals spent 38% of their resources on management, and other institutions (universities, firms, etc.) spent 87% of their resources on capital investment. Research on human immunodeficiency virus/tuberculosis and malaria accounted for 30% of funds, followed by research on other communicable diseases and maternal, perinatal and nutritional conditions (23%). Conclusions: Research on major health problems of the Region, such as communicable diseases, accounts for most of the research expenditures. However, the total expenditure is very low compared with other WHO regions.

Kesselheim, Aaron S., Yongtian Tina Tan, and Jerry Avorn. 2015. “The Roles of Academia, Rare Diseases, and Repurposing in the Development of the Most Transformative Drugs.” *Health Affairs* 34 (2): 286–93. <https://doi.org/10.1377/hlthaff.2014.1038>.

Abstract: Transformative drugs, defined as pharmaceuticals that are both innovative and have groundbreaking effects on patient care, are the “holy grail” of drug research and development. The sources of drug innovation are often debated, with pharmaceutical manufacturers arguing that high drug prices support innovative output from their sector. We studied the developmental histories of twenty-six drugs or drug classes approved by the Food and Drug Administration between 1984 and 2009 that were judged by expert physicians to be transformative (in two cases, the first drug in a transformative class was approved before 1984). Most of the twenty-six were first approved early in the study period; only four were approved in 2000 or later. Many were based on discoveries made by academic researchers who were supported by federal government funding. Others were jointly developed in both publicly funded and commercial institutions; the fewest number of drugs had originated solely within pharmaceutical industry research programs. Nine of the twenty-six (35 percent) were repurposed from products developed for other indications, and ten (38 percent) were developed for rare diseases before much broader applicability was found. The insights from these case studies provide an experience-based foundation for policies to encourage the development of future transformative drugs.

Kinge, Jonas Minet, Ingrid Roxrud, Stein Emil Vollset, Vegard Skirbekk, and John-Arne Røttingen. 2014. “Are the Norwegian Health Research Investments in Line with the Disease Burden?” *Health Research Policy and Systems* 12 (1): 64. <https://doi.org/10.1186/1478-4505-12-64>.

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Abstract: Background: The relationship between research funding across therapeutic areas and the burden of disease in Norway has not been investigated. Further, few studies have looked at the association between national research investments and the global disease burden. The aim of the present study was to analyze the correlation between a significant part of Norwegian investment in health research and the burden of disease across therapeutic areas, using both Norwegian and global burden of disease estimates. Methods: We used research investment records for 2012 from the Research Council of Norway, and the investment records distributed through liaison committees between regional health authorities and universities. Both were classified by the Health Research Classification System (HRCS). Furthermore, we used the years of life lost and Disability Adjusted Life Years (DALYs) for Norway and globally from the Global Burden of Disease 2010 project. We created a matrix to match the expenditures by HRCS with the values from the Global Burden of Disease project. Results: Disease-specific research funding increased with the Norwegian burden of disease measured as years of life lost (correlation coefficient = 0.73). Similar findings were done when the Norwegian disease burden was measured as DALYs (correlation coefficient = 0.62). The correlation between research funding and the global disease burden was low both when years of life lost (correlation coefficient = 0.11) and DALYs (correlation coefficient = 0.12) were used. Generally, when the disease burden was relatively high in Norway compared with the rest of the world, research investments were also high. Conclusions: Across therapeutic areas, the Norwegian research investments appeared aligned with the Norwegian disease burden. The correlation between the Norwegian research investments and the global disease burden was much lower.

Knowledge Ecology International. 2018. "Bayh-Dole Obligations to Disclose Federal Funding in Patented Inventions." KEI Briefing Note: 2018:1. Available: <https://www.keionline.org/wp-content/uploads/2018/03/KEI-Briefing-Note-2018-1.pdf>

Abstract: Not available.

Description: Provides an analysis of provisions in the Bayh-Dole Act and federal regulations and guidelines related to obligations for contractors of federal funding, including: i) requirement to disclose inventions discovered with federal funding; ii) requirement of local production, that is, that the invention be manufactured substantially in the United States; iii) requirement of practical application of the invention, specifically that "its benefits are ... available to the public on reasonable terms.", iv) March-In Rights and the Royalty-Free Right.

Lincker, Helene, Constantinos Ziogas, Melanie Carr, Nuria Porta, and Hans-Georg Eichler. 2014. "Where Do New Medicines Originate from in the EU?" *Nature Reviews Drug Discovery* 13 (2): 92–93. <https://doi.org/10.1038/nrd4232>.

Abstract: Not available.

Extracts: We have investigated the profile and geographical origin of the organizations involved in the recent development of new medicines in the European Union (EU). We compiled a list of medicinal products for human use containing a new active substance (NAS) that received a positive opinion from the licensing committee — the Committee for Medicinal Products for Human Use (CHMP) — at the European Medicines Agency (EMA) between 2010 and 2012. Between 2010 and 2012, 94 MAAs for medicinal products containing an NAS, as defined in this analysis, received a positive opinion from the CHMP. The number of MAAs approved in 2011 and

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2012 was considerably higher (37 and 36 approvals, respectively) than in 2010 (21 approvals). Eighteen of the products overall were orphan medicines, and the percentage of orphan applications was, on average, 19% (19% in 2010, 13% in 2011 and 25% in 2012).

When the products were tracked back through development to their origin, large or intermediate-sized pharmaceutical companies accounted for 49% of the products (large, 28%; intermediate-sized, 21%), SMEs for 27%, and academic/public bodies/PPPs accounted for 17%. Private-private collaborations accounted for 7%. The respective figures for orphan products revealed a higher proportion (61%) of SMEs as originators, with large or intermediate-sized pharmaceutical companies accounting for 22%, and academic/public bodies/PPPs accounting for 11%. With regard to the region where the innovative research resulting in these products occurred, 45% of the originators were based in North America (United States and Canada) and 37% in Europe (including Switzerland). International projects, the majority of which were transatlantic collaborations, accounted for 8%, and other countries (Japan, China, Israel and Australia) accounted for the remaining 10%, with a gradual increase over the period analysed (5% in 2010, 8% in 2011, 14% in 2012). There were no apparent major differences in the geographical origin of orphan versus non-orphan products. Overall, although large and intermediate-sized companies still represent the main engine for commercializing new medicines, SMEs, academic institutions, public bodies and PPPs represent an important source of innovation and enrich the product pipelines of larger companies.

Maceira, Daniel, Guillermo Paraje, Fernando Aramayo, Sergio Duarte Masi, and Delia Sánchez. 2010. "[Public financing of health research in five Latin American countries]." *Revista Panamericana De Salud Publica = Pan American Journal of Public Health* 27 (6): 442-51.

https://www.scielosp.org/scielo.php?script=sci_arttext&pid=S1020-49892010000600005&lng=en&nrm=iso&tlng=en.

Abstract: OBJECTIVES: Describe the public subsystems of the national health research systems (SNIS) in five Latin American countries (Argentina, Bolivia, Chile, Paraguay, and Uruguay), emphasizing the types of institutional arrangements in place in each country to promote, develop, and sustain their SNIS, as well as explicit or implicit mechanisms for prioritizing health research projects. METHODS: The bodies responsible for managing the public resources allocated to finance health research projects in the five countries studied were identified. The types of projects financed were then analyzed-using a matrix constructed by area and object of study-, certain characteristics of the principal investigators, and the sums allocated between 2002 and 2006. RESULTS: Only the countries with greater resources or better developed networks of investigators have formal structures for allocating funds with regular calls for proposals and fixed rules. None of them has explicit comprehensive mechanisms for prioritizing health research. Moreover, the health research priorities in the countries vary widely. In this regard, it is significant that problems such as "nutrition and the environment" or "violence and accidents" receive little attention in most countries. The same holds true for a number of public health issues in some countries. In contrast, the research in the "hard sciences" absorbs up to one-third of the total resources for research. CONCLUSIONS: Many questions arise about the ability of these countries to adapt and generate new knowledge, as well as the nearly nonexistent research on social, economic, and cultural determinants, or on health services and systems that have a high impact on groups with limited access to health care. Explicit priorities

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should be set with stakeholders for the health research agenda, and mechanisms should be adopted for monitoring and following up health research financing by subject and area of study.

Martínez-Martínez, Eduardo, María Luisa Zaragoza, Elmer Solano, Brenda Figueroa, Patricia Zúñiga, and Juan P. Laclette. 2012. "Health Research Funding in Mexico: The Need for a Long-Term Agenda." Edited by Sten H. Vermund. PLoS ONE 7 (12): e51195. <https://doi.org/10.1371/journal.pone.0051195>.

Abstract: Background: The legal framework and funding mechanisms of the national health research system were recently reformed in Mexico. A study of the resource allocation for health research is still missing. We identified the health research areas funded by the National Council on Science and Technology (CONACYT) and examined whether research funding has been aligned to national health problems. Methods and Findings: We collected the information to create a database of research grant projects supported through the three main Sectoral Funds managed by CONACYT between 2003 and 2010. The health-related projects were identified and classified according to their methodological approach and research objective. A correlation analysis was carried out to evaluate the association between disease-specific funding and two indicators of disease burden. From 2003 to 2010, research grant funding increased by 32% at a compound annual growth rate of 3.5%. By research objective, the budget fluctuated annually resulting in modest increments or even decrements during the period under analysis. The basic science category received the largest share of funding (29%) while the less funded category was violence and accidents (1.4%). The number of deaths ($\rho=0.51$; $P<0.001$) and disability-adjusted life years (DALYs; $\rho=0.33$; $P=0.004$) were weakly correlated with the funding for health research. Considering the two indicators, poisonings and infectious and parasitic diseases were among the most overfunded conditions. In contrast, congenital anomalies, road traffic accidents, cerebrovascular disease, and chronic obstructive pulmonary disease were the most underfunded conditions. Conclusions: Although the health research funding has grown since the creation of CONACYT sectoral funds, the financial effort is still low in comparison to other Latin American countries with similar development. Furthermore, the great diversity of the funded topics compromises the efficacy of the investment. Better mechanisms of research priority-setting are required to adjust the research portfolio to the new health panorama of Mexican population.

Mazzucato, Mariana, and Gregor Semieniuk. 2017. "Public Financing of Innovation: New Questions." *Oxford Review of Economic Policy* 33 (1): 24–48. <https://doi.org/10.1093/oxrep/grw036>.

Abstract: Economic theory justifies policy when there are concrete market failures. The article shows how in the case of innovation, successful policies that have led to radical innovations have been more about market shaping and creating through direct and pervasive public financing, rather than market fixing. The paper reviews and discusses evidence for this in three key areas: (i) the presence of finance from public sources across the entire innovation chain; (ii) the concept of 'mission-oriented' policies that have created new technological and industrial landscapes; and (iii) the entrepreneurial and lead investor role of public actors, willing and able to take on extreme risks, independent of the business cycle. We further illustrate these three characteristics for the case of clean technology, and discuss how a market-creating and -shaping perspective may be useful for understanding the financing of transformative innovation needed for confronting contemporary societal challenges.

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McElfish, Pearl A., Rachel S. Purvis, M. Kathryn Stewart, Laura James, Karen H. Kim Yeary, and Christopher R. Long. 2018. "Health Research Funding Agencies' Policies, Recommendations, and Tools for Dissemination." *Progress in Community Health Partnerships: Research, Education, and Action* 12 (4): 473–82. <http://muse.jhu.edu/article/716655>.

Abstract: THE PROBLEM: Dissemination is a key component of translational research. However, research participants rarely receive findings from the studies in which they have participated. Funding agencies have a significant amount of influence to promote research dissemination through requirements, recommendations, and tools. However, it is not clear to what extent current funding agencies promote dissemination to study participants. Purpose of Article: A review of major health research funders was conducted to ascertain the current policies, recommendations, and tools related to 1) academic dissemination, 2) lay community dissemination, and 3) returning results to research participants. KEY POINTS: Several agencies have policies, recommendations, and tools for academic dissemination; however, few have the same policies, recommendations, and tools for dissemination to research participants and the lay communities they are recruited from. CONCLUSIONS: Funding agencies have a unique opportunity to encourage the dissemination of research results to research participants and lay community audiences by developing policies to increase dissemination of grantees' research findings.

NIH Office of Science Policy. 2000. "NIH Contributions to Pharmaceutical Development: Case Study Analysis of the Top-Selling Drugs." in *Rx R&D Myths: The Case Against Drug Industry's R&D "Scare Card,"* Public Citizen, Congress Watch. <https://www.citizen.org/sites/default/files/rdmyths.pdf>.

Abstract: Not Available.

Description: NIH staff members conducted a study to analyze the effectiveness of the US NIH public funding of biomedical research using product development as measure. The study investigated 5 top- selling drugs and concluded that NIH-funded research played a critical role in the development of each of them, complementing industry investments.

Paraje, Guillermo. 2010. "[Public financing of health research in Chile]." *Revista Medica De Chile* 138 (1): 36–43. https://scielo.conicyt.cl/scielo.php?script=sci_arttext&pid=S0034-98872010000100005&lng=en&nrm=iso&tlng=en.

Abstract: BACKGROUND: In Chile, researchers can apply to public research funds through specific research projects and must compete with other professionals of other disciplines.

AIM: To perform a critical assessment of the allocation of public funds for health research in Chile by a public institution called CONICYT. **MATERIAL AND METHODS:** A database was constructed with health projects financed by CONICYT, between 2002 and 2006. Projects were classified (according to their titles) in three methodological categories and nine topics. Age, gender and region where the main researcher is based, were also recorded. **RESULTS:** 768 research projects were analyzed. Biomedical, clinical and public health research projects accounted for 66, 24 and 10% of allocated funds, respectively. Main researchers were female in 31 % of projects, their mean age was 52 years and 76% worked in the Metropolitan region. **CONCLUSIONS:** These results show

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that some objectives of the National Research System lead by CONICYT, such as using research as a tool for regional development and allocating funds for conditions with a large burden, are not been met.

Qiu, Lan, Zi-Ya Chen, Deng-Yu Lu, Hao Hu, and Yi-Tao Wang. 2014. "Public Funding and Private Investment for R&D: A Survey in China's Pharmaceutical Industry." *Health Research Policy and Systems* 12 (1): 27. <https://doi.org/10.1186/1478-4505-12-27>.

Abstract: **Background:** In recent years, China has experienced tremendous growth in its pharmaceutical industry. Both the Chinese government and private investors are motivated to invest into pharmaceutical research and development (R&D). However, studies regarding the different behaviors of public and private investment in pharmaceutical R&D are scarce. Therefore, this paper aims to investigate the current situation of public funding and private investment into Chinese pharmaceutical R&D. **Methods:** The primary data used in the research were obtained from the China High-tech Industry Statistics Yearbook (2002–2012) and China Statistical Yearbook of Science and Technology (2002–2012). We analyzed public funding and private investment in five aspects: total investment in the industry, funding sources of the whole industry, differences between provinces, difference in subsectors, and private equity/venture capital investment. **Results:** The vast majority of R&D investment was from private sources. There is a significantly positive correlation between public funding and private investment in different provinces of China. However, public funding was likely to be invested into less developed provinces with abundant natural herbal resources. Compared with the chemical medicine subsector, traditional Chinese medicine and biopharmaceutical subsectors obtained more public funding. Further, the effect of the government was focused on private equity and venture capital investment although private fund is the mainstream of this type of investment. **Conclusions:** Public funding and private investment play different but complementary roles in pharmaceutical R&D in China. While being less than private investment, public funding shows its significance in R&D investment. With rapid growth of the industry, the pharmaceutical R&D investment in China is expected to increase steadily from both public and private sources.

Reichert, Janice M., and Christopher-Paul Milne. 2002. "Public and Private Sector Contributions to the Discovery and Development of 'Impact' Drugs." *American Journal of Therapeutics* 9 (6): 543–55. https://journals.lww.com/americantherapeutics/Fulltext/2002/11000/Public_and_Private_Sector_Contributions_to_the.16.aspx.

Abstract: Recently, well-publicized reports by Public Citizen and the Joint Economic Committee (JEC) of the US Congress questioned the role of the drug industry in the discovery and development of therapeutically important drugs. To gain a better understanding of the relative roles of the public and private sectors in pharmaceutical innovation, the Tufts Center for the Study of Drug Development evaluated the underlying National Institutes of Health (NIH) and academic research cited in the Public Citizen and JEC reports and performed its own assessment of the relationship between the private and public sectors in drug discovery and development of 21 "impact" drugs. We found that, ultimately, any attempt to measure the relative contribution of the public and private sectors to the research and development (R&D) of therapeutically important drugs by output alone, such as counting publications or even product approvals, is flawed. Several key factors (e.g., degree of uncertainty, expected market value, potential social benefit) affect investment decisions and determine whether public or private sector funds, or

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both, are most appropriate. Because of the competitiveness and complexity of today's R&D environment, both sectors are increasingly challenged to show returns on their investment and the traditional boundaries separating the roles of the private and public research spheres have become increasingly blurred. What remains clear, however, is that the process still starts with good science and ends with good medicine.

Research!America. 2018. "U.S. Investments in Medical and Health Research and Development 2013

- 2017." Research!America.

https://www.researchamerica.org/sites/default/files/Policy_Advocacy/2013-2017InvestmentReportFall2018.pdf.

Abstract: Not available.

Extracts from introduction: Investment in medical and health research and development (R&D) in the U.S. grew by \$38.8 billion or 27% from 2013 to 2017. The industry continues to invest more than any other sector, accounting for 67% of total spending in 2017, followed by the federal government at 22%. Federal investments increased from 2016 to 2017, the second year of growth after a dip from 2014 to 2015. Overall, federal investment increased by \$6.1 billion or 18.4% from 2013 to 2017, but growth has been uneven across federal health agencies. Investment by other sectors, including academic and research institutions, foundations, state and local governments, and voluntary health associations and professional societies, also increased from 2013 to 2017.

Røttingen, John-Arne, Sadie Regmi, Mari Eide, Alison J Young, Roderik F Viergever, Christine Årdal, Javier Guzman, Danny Edwards, Stephen A Matlin, and Robert F Terry. 2013. "Mapping of Available Health Research and Development Data: What's There, What's Missing, and What Role Is There for a Global Observatory?" *The Lancet* 382 (9900): 1286–1307. [https://doi.org/10.1016/S0140-6736\(13\)61046-6](https://doi.org/10.1016/S0140-6736(13)61046-6).

Summary: The need to align investments in health research and development (R&D) with public health demands is one of the most pressing global public health challenges. We aim to provide a comprehensive description of available data sources, propose a set of indicators for monitoring the global landscape of health R&D, and present a sample of country indicators on research inputs (investments), processes (clinical trials), and outputs (publications), based on data from international databases. Total global investments in health R&D (both public and private sector) in 2009 reached US\$240 billion. Of the US\$214 billion invested in high-income countries, 60% of health R&D investments came from the business sector, 30% from the public sector, and about 10% from other sources (including private non-profit organisations). Only about 1% of all health R&D investments were allocated to neglected diseases in 2010. Diseases of relevance to high-income countries were investigated in clinical trials seven-to-eight-times more often than were diseases whose burden lies mainly in low-income and middle-income countries. This report confirms that substantial gaps in the global landscape of health R&D remain, especially for and in low-income and middle-income countries. Too few investments are targeted towards the health needs of these countries. Better data are needed to improve priority setting and coordination for health R&D, ultimately to ensure that resources are allocated to diseases and regions where they are needed the most. The establishment of a global observatory on health

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R&D, which is being discussed at WHO, could address the absence of a comprehensive and sustainable mechanism for regular global monitoring of health R&D.

Salud por Derecho. 2019. "Interés público en la innovación biomédica." Salud por Derecho. https://saludporderecho.org/wp-content/uploads/2019/01/Interes_Publico_Inovacion_Biomedica.pdf.

Abstract: Not available.

Extracts from executive summary: Biomedical research involves several stakeholders that configure a value chain where each of the links proves essential in the public and private sphere. Nevertheless, the result of this research is frequently transferred to or remains in the hands of, the private sector, while the public sector loses its capacity to influence such crucial matters as price or management of intellectual property, despite the fact that it is the main purchaser of the resulting medicines and healthcare products. This study starts with the premise that innovation in health must be affordable, accessible, efficient and of quality, and elements such as high prices and current mechanisms for managing biomedical intellectual property cannot be a barrier that prevents us from reaching all those who need it irrespective of their socioeconomic situation or their place of residence. The public sector is not a passive actor in biomedical innovation. On the contrary, it actively participates in many phases of development. It is true that the public role in the development is not the same for all technologies and, in certain cases, the presence of industry can also be important. But it is generally the case that the public contribution is made invisible when the private sector acquires or appropriates technologies and knowledge. This study questions to what extent is the public interest vanish from the transaction with the private sector, and if there are mechanisms in Spain that allow for certain conditions that can protect it. The study focuses primarily on two areas: public funding of biomedical R&D in Spain and the transfer of knowledge from the public to the private space.

Sampat, Bhaven N., Kristin Buterbaugh, and Marcel Perl. 2013. "New Evidence on the Allocation of NIH Funds across Diseases: New Evidence on the Allocation of NIH Funds across Diseases." *Milbank Quarterly* 91 (1): 163–85. <https://doi.org/10.1111/milq.12005>.

Abstract: Context: The responsiveness of NIH (National Institutes of Health) funding to disease burden is a long-standing issue of policy interest. Previous analyses of this issue have been hindered by data constraints, have not specified channels through which the NIH funding process could be responsive to disease considerations, and have not examined differences across NIH institutes and centers. Methods: We collected data from the NIH's new RCDC (Research, Condition, and Disease Categorization) database on funding for 107 diseases in 2008 and linked these to data on deaths and hospitalizations for these diseases. We used RCDC data and information from another NIH database—RePORTER—to determine institute-specific funding for these diseases and also funding by award type. We used these data to examine the overall responsiveness of NIH funding to disease burden, within-institute responsiveness, and the responsiveness of different types of NIH awards. Findings: Overall, we found a strong and statistically significant relationship between NIH funding and deaths and hospitalizations associated with a disease. We detected some evidence that more "applied" grant mechanisms—in particular, funding for clinical trials—are more responsive than other types of funding. We also found evidence of differences across institutes in their extent of responsiveness. Conclusions: Overall, the data suggest that NIH funding is responsive to the two measures of disease burden.

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More applied grant mechanisms also may serve as “safety valves” in the allocation process, allowing Congress, disease advocacy groups, and others to apply pressure to address particular health priorities in a more fine-grained way than is possible through investigator-initiated “basic” research grants alone.

Sampat, Bhaven N., and Frank R. Lichtenberg. 2011. “What Are The Respective Roles Of The Public And Private Sectors In Pharmaceutical Innovation?” *Health Affairs* 30 (2): 332–39. <https://doi.org/10.1377/hlthaff.2009.0917>.

Abstract: What are the respective roles of the public and private sectors in drug development? This question is at the heart of some policy proposals, such as those that would give the government a share of profits from drugs at least partly developed with federal research dollars. This paper provides empirical data on these issues, using information included in the patents on drugs approved between 1988 and 2005. Overall, we find that direct government funding is more important in the development of “priority-review” drugs—sometimes described as the most innovative new drugs—than it is for “standard-review” drugs. Government funding has played an indirect role—for example, by funding basic underlying research that is built on in the drug discovery process—in almost half of the drugs approved and in almost two-thirds of priority-review drugs. Our analyses should help inform thinking about the returns on public research funding—a topic of long-standing interest to economists, policy makers, and health advocates.

Simpkin, Victoria L, Matthew J Renwick, Ruth Kelly, and Elias Mossialos. 2017. “Incentivising Innovation in Antibiotic Drug Discovery and Development: Progress, Challenges and next Steps.” *The Journal of Antibiotics* 70 (12): 1087–96. <https://doi.org/10.1038/ja.2017.124>.

Abstract: Political momentum and funding for combatting antimicrobial resistance (AMR) continues to build. Numerous major international and national initiatives aimed at financially incentivising the research and development (R&D) of antibiotics have been implemented. However, it remains unclear how to effectively strengthen the current set of incentive programmes to further accelerate antibiotic innovation. Based on a literature review and expert input, this study first identifies and assesses the major international, European Union, US and UK antibiotic R&D funding programmes. These programmes are then evaluated across market and public health criteria necessary for comprehensively improving the antibiotic market. The current set of incentive programmes are an important initial step to improving the economic feasibility of antibiotic development. However, there appears to be a lack of global coordination across all initiatives, which risks duplicating efforts, leaving funding gaps in the value chain and overlooking important AMR goals. This study finds that incentive programmes are overly committed to early-stage push funding of basic science and preclinical research, while there is limited late-stage push funding of clinical development. Moreover, there are almost no pull incentives to facilitate transition of antibiotic products from early clinical phases to commercialisation, focus developer concentration on the highest priority antibiotics and attract large pharmaceutical companies to invest in the market. Finally, it seems that antibiotic sustainability and patient access requirements are poorly integrated into the array of incentive mechanisms.

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So, Anthony D, Bhaven N Sampat, Arti K Rai, Robert Cook-Deegan, Jerome H Reichman, Robert Weissman, and Amy Kapczynski. 2008. "Is Bayh-Dole Good for Developing Countries? Lessons from the US Experience." PLoS Biology 6 (10): e262. <https://doi.org/10.1371/journal.pbio.0060262>.

Abstract: Not available.

Extracts: Recently, countries from China and Brazil to Malaysia and South Africa have passed laws promoting the patenting of publicly funded research, and a similar proposal is under legislative consideration in India. These initiatives are modeled in part on the United States Bayh-Dole Act of 1980. Bayh-Dole (BD) encouraged American universities to acquire patents on inventions resulting from government-funded research and to issue exclusive licenses to private firms, on the assumption that exclusive licensing creates incentives to commercialize these inventions. A broader hope of BD, and the initiatives emulating it, was that patenting and licensing of public sector research would spur science-based economic growth as well as national competitiveness. And while it was not an explicit goal of BD, some of the emulation initiatives also aim to generate revenues for public sector research institutions. We believe government-supported research should be managed in the public interest. We also believe that some of the claims favoring BD-type initiatives overstate the Act's contributions to growth in US innovation. Important concerns and safeguards—learned from nearly 30 years of experience in the US—have been largely overlooked. Furthermore, both patent law and science have changed considerably since BD was adopted in 1980. Other countries seeking to emulate that legislation need to consider this new context.

Stevens, Ashley J., Jonathan J. Jensen, Katrine Wyller, Patrick C. Kilgore, Sabarni Chatterjee, and Mark L. Rohrbaugh. 2011. "The Role of Public-Sector Research in the Discovery of Drugs and Vaccines." *New England Journal of Medicine* 364 (6): 535–41. <https://doi.org/10.1056/NEJMsa1008268>.

Abstract: **BACKGROUND:** Historically, public-sector researchers have performed the upstream, basic research that elucidated the underlying mechanisms of disease and identified promising points of intervention, whereas corporate researchers have performed the downstream, applied research resulting in the discovery of drugs for the treatment of diseases and have carried out development activities to bring them to market. However, the boundaries between the roles of the public and private sectors have shifted substantially since the dawn of the biotechnology era, and the public sector now has a much more direct role in the applied-research phase of drug discovery. **METHODS:** We identified new drugs and vaccines approved by the Food and Drug Administration (FDA) that were discovered by public-sector research institutions (PSRIs) and classified them according to their therapeutic category and potential therapeutic effect. **RESULTS:** We found that during the past 40 years, 153 new FDA-approved drugs, vaccines, or new indications for existing drugs were discovered through research carried out in PSRIs. These drugs included 93 small-molecule drugs, 36 biologic agents, 15 vaccines, 8 in vivo diagnostic materials, and 1 over-the-counter drug. More than half of these drugs have been used in the treatment or prevention of cancer or infectious diseases. PSRI-discovered drugs are expected to have a disproportionately large therapeutic effect. **CONCLUSIONS:** Public-sector research has had a more immediate effect on improving public health than was previously realized.

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STOPAIDS and Global Justice Now. 2017. "Pills and Profits: How Drug Companies Make a Killing out of Public Research." <https://stopaids.org.uk/resources/pills-and-profits-how-drug-companies-make-a-killing-out-public-research/>.

Abstract: Not available.

Extracts from executive summary: UK taxpayers and patients worldwide are being denied the medicines they need, despite the public sector playing a pivotal role in the discovery of new medicines. The UK government is the second largest funder country, after the US, for research and development (R&D) in diseases that predominantly affect poor countries. Across all areas of health R&D, the UK government spent £2.3 billion on health R&D in 2015 alone. Globally, it is estimated that the public pays for two-thirds of all upfront drug R&D costs, with around a third of new medicines originating in public research institutions. On top of this, many medicines developed by pharmaceutical companies are often built upon a large body of scientific work undertaken and paid for by the taxpayer. This report illustrates that even when the UK government has funded a substantial proportion of the R&D for innovative medicines, there is no guarantee of an equitable public return on this public investment. That is to say, no guarantee that patients in the UK and beyond will be able to access the medicine at an affordable price, and be able to make use of the data, knowledge, and technologies generated in the research process.

Conditions on UK public funding for R&D: There is a clear lack of safeguards to ensure the accessibility and affordability of medicines that derive from publicly funded R&D. Though there are some guidelines on public funding in these departments, they are usually vague and fall far short of concrete guarantees that products developed with public funding will be made available at an affordable price to patients in the UK and beyond.

UK public funding of specific medicines: UK public funding has played a substantial role in the discovery and development of highly effective and often life-saving treatments. The following examples show that the high prices charged by pharmaceutical companies for these very effective medicines have severely restricted access for the patients that need them, despite this upfront investment by taxpayers: Abiraterone, Alemtuzumab, Adalimumab, Infliximab.

R&D initiatives that safeguard accessibility: The UK has made some positive progress towards models of R&D that offer better public returns. The UK is the largest contributor to the Drugs for Neglected Diseases initiative (DNDi), which was set up to develop new medicines for diseases that predominantly affect people in the global south.

Recommendations: Here are 5 recommendations for the UK government to safeguard access to publicly funded medicines: Attach public interest conditions to all UK health R&D grants so that medicines that benefit from public funds are affordable for patients and the NHS. Introduce transparency: enforce standardised measures for reporting the costs of R&D, so that the UK government can determine a fair price for medicines. Enable effective governance and accountability so that the government prioritises public health over commercial interests and citizens can hold the government to account for doing so. Drive international progress on R&D by supporting the establishment of a global biomedical R&D convention and enabling the market entry of generic drugs. Invest in new approaches to R&D, such as the use of grants and

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prizes that fully cover the cost of R&D and do not allow for high prices as a mechanism to finance drug development.

Sussex, Jon, Yan Feng, Jorge Mestre-Ferrandiz, Michele Pistollato, Marco Hafner, Peter Burridge, and Jonathan Grant. 2016. "Quantifying the Economic Impact of Government and Charity Funding of Medical Research on Private Research and Development Funding in the United Kingdom." *BMC Medicine* 14 (1): 32. <https://doi.org/10.1186/s12916-016-0564-z>.

Abstract: Background: Government- and charity-funded medical research and private sector research and development (R&D) are widely held to be complements. The only attempts to measure this complementarity so far have used data from the United States of America and are inevitably increasingly out of date. This study estimates the magnitude of the effect of government and charity biomedical and health research expenditure in the United Kingdom (UK), separately and in total, on subsequent private pharmaceutical sector R&D expenditure in the UK. Methods: The results for this study are obtained by fitting an econometric vector error correction model (VECM) to time series for biomedical and health R&D expenditure in the UK for ten disease areas (including 'other') for the government, charity and private sectors. The VECM model describes the relationship between public (i.e. government and charities combined) sector expenditure, private sector expenditure and global pharmaceutical sales as a combination of a long-term equilibrium and short-term movements. Results: There is a statistically significant complementary relationship between public biomedical and health research expenditure and private pharmaceutical R&D expenditure. A 1 % increase in public sector expenditure is associated in the best-fit model with a 0.81 % increase in private sector expenditure. Sensitivity analysis produces a similar and statistically significant result with a slightly smaller positive elasticity of 0.68. Overall, every additional £1 of public research expenditure is associated with an additional £0.83–£1.07 of private sector R&D spend in the UK; 44 % of that additional private sector expenditure occurs within 1 year, with the remainder accumulating over decades. This spillover effect implies a real annual rate of return (in terms of economic impact) to public biomedical and health research in the UK of 15–18 %. When combined with previous estimates of the health gain that results from public medical research in cancer and cardiovascular disease, the total rate of return would be around 24–28 %. Conclusion: Overall, this suggests that government and charity funded research in the UK crowds in additional private sector R&D in the UK. The implied historical returns from UK government and charity funded investment in medical research in the UK compare favourably with the rates of return achieved on investments in the rest of the UK economy and are greatly in excess of the 3.5 % real annual rate of return required by the UK government to public investments generally.

Tomlinson, Catherine, and Marcus Low. 2019. "Tuberculosis Innovation Approaches in South Africa and Strategies to Secure Public Returns." *Fix the Patent Laws*. <https://www.fixthepatentlaws.org/wp-content/uploads/2019/04/Tuberculosis-innovation-approaches-in-South-Africa-and-strategies-to-secure-public-returns-Tomlinson-and-Low.pdf>.

Abstract: Not available.

Extracts from executive summary: Recognising the urgent need for new health technologies to address TB in South Africa and the strong political will to address TB needs in this country, we undertook this analysis to gain greater understanding of the TB innovation landscape in South

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Africa. We also sought to understand whether adequate safeguards are in place to ensure that public financing for TB R&D serves public interest – for example by ensuring that health technologies developed with public financing are affordable and accessible. Findings: There was wide agreement among interviewees that TB research is underfunded in South Africa. South African government investment in medical research increased significantly from 2012 to 2014, after which it stagnated and then declined from the 2016/2017 to the 2017/2018 fiscal year. However, funding specifically for TB research increased significantly in 2016 and 2017, suggesting increased prioritisation of TB research in this period. Even though South Africa invests more than most countries in TB research measured as a percentage of GDP or GERD, absolute investment is low compared to wealthy countries such as the United States. Arguably, South African government investment in TB research is insufficient given the country's severe TB burden.

A key focus of our research was ownership of intellectual property generated from publicly funded research and access conditions placed on products resulting from publicly funded research. While funders and research entities in South Africa have some flexibility to negotiate terms on a case-by-case basis, these negotiations take place within parameters set by predominantly the Intellectual Property from Publicly Financed Research and Development Act (IPR Act), but also other key documents depending on the specific donor – examples include the SAMRC's Socially Responsible licensing guidelines and the Grand Challenges Canada Global Access Policy. Between these various laws, policies and guidelines, and considering the nature of the TB market, most interviewees are satisfied that products resulting from publicly funded TB research in South Africa will be affordable and available in the areas where it is most needed – put another way, the perception is that there is no incentive for companies to develop TB products that are unaffordable. However, while funding agreements typically include provisions on access and affordability, these provisions are not always clear and may turn out to be hard to enforce should the need arise given the ambiguity around key terms and limited capacity for oversight of industry behaviour across low- and middle-income countries (LMICs).

Treasure, Carolyn L., Jerry Avorn, and Aaron S. Kesselheim. 2014. "What Is the Public's Right to Access Medical Discoveries Based on Federally Funded Research?" *JAMA* 311 (9): 907. <https://doi.org/10.1001/jama.2014.404>.

Abstract: Not available.

Extracts: To spur translational development of federally funded inventions, Congress enacted the Bayh-Dole Act in 1980, which allowed universities to patent the results of federally funded research and then license these patents to commercial entities. The legislation included an escape clause to protect the public interest, providing funding agencies with so-called march-in rights to reclaim the invention and offer new licenses if the original licensees did not bring the product to market adequately or otherwise failed to meet the needs of US consumers. Since the Bayh-Dole legislation was passed in 1980, public interest groups or policy makers have sought to use these march-in rights to address exceedingly high prices or inadequate supply of interventions whose development was based heavily on government funding, particularly pharmaceutical products and medical devices. However, in the 33 years since the passage of Bayh-Dole, such march-in rights petitions to the NIH have been seriously considered for only 4 products—and were rejected each time.

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Treatment Action Group. 2018. "Tuberculosis Research Funding Trends 2005-2017." Treatment Action Group.
http://www.treatmentactiongroup.org/sites/default/files/tb_funding_2018_final.pdf.

Abstract: Not available.

Extracts from executive summary: Treatment Action Group (TAG) has been tracking global investment in tuberculosis (TB) research and development (R&D) since 2005. In this report, we present data on TB research funding trends from 2005 to 2017. Sixty-six percent (\$510 million) of global TB funding in 2017 came from public sources, 19% (\$145 million) from philanthropies, 11% (\$85 million) from private industry, and 4% (\$32 million) from multilateral entities. Public funding showed the greatest growth over 2016 levels, with an increase of \$27 million. The U.S. government remains by far the largest funder of TB research, having invested \$312 million in 2017 through eight different agencies. This accounts for 40% of global TB R&D funding and 62% of all public funding— more than all other governments added together. The European Union invested \$37 million, the United Kingdom \$36 million, Germany and Canada \$19 million each, India \$17 million, and South Korea \$15 million. No other countries reported spending more than \$10 million in 2017. The Bill and Melinda Gates Foundation (Gates Foundation) was the second largest funder of TB research in 2017, with an investment of \$128 million. This is multiple times more than the contribution from any government except for the United States, is more than all private sector investments combined, and makes up 17% of total TB research funding. The next largest funder after the U.S. government and the Gates Foundation was Unitaid, with an investment of \$29 million. With an investment of \$23 million in 2017, the pharmaceutical company Otsuka ranks sixth overall and was the top private- sector investor in TB R&D. It is one of four pharmaceutical companies in the top 20 funders. Together, these four companies contributed \$66 million of the total \$85 million reported by private- sector groups in 2017.

Treatment ActionGroup. 2018. "The Price of Bedaquiline."
http://www.treatmentactiongroup.org/sites/default/files/reality_check_bedaquiline_10_16_18.pdf

Abstract: Not available.

Extracts: In December 2012, bedaquiline (Sirturo) became the first new tuberculosis (TB) drug from a new drug class to receive approval by the U.S. Food and Drug Administration (FDA) in 40 years. The amount Janssen has invested in the research and development (R&D) of bedaquiline is not known due to a lack of transparency on the part of the company. Janssen has not made details of its expenditures on bedaquiline R&D public by, for example, publishing the costs of clinical trials or other R&D activities. In addition to its own investments, the company has also benefited from substantial public investments in bedaquiline (see Tables 1 and 2). These publicly funded studies were necessary to inform the appropriate clinical use of bedaquiline, and some were even required to fulfill Janssen's regulatory requirements. In addition to the public contributions underwriting bedaquiline's development accounted for in Table 1, a substantial amount of public time and money has been invested in creating an enabling environment for the uptake of bedaquiline at the country level.

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Tschider, Charlotte A. 2014. "Innovation in the Public Sphere: Reimagining Law and Economics to Solve the National Institutes of Health Publishing Controversy." *Journal of Law and the Biosciences* 1 (3): 281–315. <https://doi.org/10.1093/jlb/lisu025>.

Abstract: The National Institutes of Health (NIH) are responsible for the largest proportion of biological science funding in the United States. To protect the public interest in access to publicly funded scientific research, the NIH amended terms and conditions in funding agreements after 2009, requiring funded Principal Investigators to deposit published copies of research in PubMed, an Open Access repository. Principal Investigators have partially complied with this depository requirement, and the NIH have signaled an intent to enforce grant agreement terms and conditions by stopping funding deposits and engaging in legal action. The global economic value of accessible knowledge offers a unique opportunity for courts to evaluate the impact of enforcing 'openness' contract terms and conditions within domestic and international economies for public and economic benefit. Through judicial enforcement of Open Access terms and conditions, the United States can increase economic efficiency for university libraries, academic participants, and public consumers, while accelerating global innovation, improving financial returns on science funding investments, and advancing more efficient scientific publishing models.

UCL Institute for Innovation and Public Purpose. 2018. "The People's Prescription: Re-Imagining Health Innovation to Deliver Public Value." IIPP, Global Justice Now, Just Treatment, STOPAIDS. <https://www.ucl.ac.uk/bartlett/public-purpose/wp2018-10>.

Abstract: Not available.

Extracts from executive summary: Achieving public return through conditionality. If value is created collectively through the involvement of different actors, then the rewards should also be shared to ensure sustainable capital and resources for continued innovation. Instead, under the current system, the public sector plays an essential role in funding the upstream high-risk research, while the downstream profits disproportionately go to the private sector. A more just sharing of rewards needs to be based on a reinvigorated concept of 'public value' – in other words value that is both created and shared by the public. This could happen in various ways, including attaching conditions on public funding such as reinvesting profits from innovative products to support future R&D (rather than being hoarded); a commitment to share knowledge and fully disclose data related to R&D, including expenditures and data from failed clinical trials; the possibility of the public retaining a golden share from IPR (and on occasion equity of profits); and a requirement that manufacturers supply treatments on reasonable terms.

UK Health Research Collaboration. 2015. "UK Health Research Analysis 2014, 2009/2010 and 2006." <https://www.ukcrc.org/research-coordination/health-research-analysis/uk-health-research-analysis/>.

Abstract: Not available.

Description: The first UK Health Research Analysis report, published in 2006, was the first ever national analysis of health research. It provides an overview of all types of health research activity across all areas of health and disease in the UK, funded by the largest government and charity

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health-related research funders. A bespoke Health Research Classification System (HRCS) was developed to allow meaningful comparisons to be made across the different funders' research portfolios. The second UK Health Research Report, published in 2012 compares what the funders spent on health research in 2004/2005 with the data from 2009/2010. This immediately highlights that direct spend on health research projects by these 12 organisations is 50% higher in real terms in 2009/2010 compared with 2004/2005. The third report of the Health Research Analysis (2014) is now available to download. This report builds on the basis of the previous analyses in 2004/05 and 2009/10 and has expanded this third volume to include 64 charitable and public funders of medical research in the UK. As with previous reports, the data relates to a 'snapshot' of health research spend in 2014. However, as the third in the series we have the opportunity of ongoing trends in research funding over the ten-year reporting period. The dataset for this report has now been released for public use on the HRCS Online website (please see useful links section on right).

United Nations Secretary-General's High-Level Panel on Access to Medicines. 2016. "Report: Promoting Innovation and Access to Health Technologies."
<https://static1.squarespace.com/static/562094dee4b0d00c1a3ef761/t/57d9c6ebf5e231b2f02cd3d4/1473890031320/UNSG+HLP+Report+FINAL+12+Sept+2016.pdf>.

Abstract: Not available.

Extracts from executive summary: The policies of public funders of health technology R&D can also play an important role in enhancing health technology innovation and access. The United States, for instance, holds a central position in health technology innovation. The country's R&D and access policies influence other actors, including private and public sector donors and foundations, and have an impact on access to the fruits of technology worldwide. The introduction of the 1980 Bayh-Dole Act in the United States significantly changed academic research by allowing universities and public research institutions to patent the results of federally-funded research and license private enterprises to develop them. However, limiting access to academic discoveries can obstruct follow-on innovation and force taxpayers to pay twice for the benefits of publicly-funded research. Strong, enforceable policies on data sharing and data access should be a condition of public grants. Public funding agencies should strongly encourage patenting and licensing practices that benefit public health, including the use of non-exclusive licences, the donation of intellectual property rights, participation in public sector patent pools and other mechanisms that maximize innovation while promoting access. Open models of innovation can also lower entry hurdles and accelerate the pace of development of health technologies, including those needed to combat emerging infectious diseases. Recommendations: Public funders of research must require that knowledge generated from such research be made freely and widely available through publication in peer-reviewed literature and seek broad, online public access to such research. Universities and research institutions that receive public funding must prioritize public health objectives over financial returns in their patenting and licensing practices. Such practices may include publication, non-exclusive licensing, donations of intellectual property and participation in public sector patent pools, among others. Sufficient incentives must be in place in these practices to make it attractive for developers to underwrite the cost of bringing a product to market at affordable prices that ensure broad availability. Universities and research institutions that receive public funding should adopt policies and approaches that catalyse innovation and create flexible

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models of collaboration that advance biomedical research and generate knowledge for the benefit of the public.

United States Government Accountability Office. 2017. "Drug Industry: Profits, Research and Development Spending, and Merger and Acquisition Deals." GAO-18-40. <https://www.gao.gov/assets/690/688472.pdf>.

Abstract: Not available.

Extract from summary: What GAO Found: From 2008 through 2014, worldwide company-reported R&D spending, most of which went to drug development (rather than research), increased slightly from \$82 billion to \$89 billion in 2015 dollars. During the same period, federal spending, which funded a greater amount of basic research relative to industry, remained stable at around \$28 billion. In addition to grants, several federal tax provisions provided incentives for industry R&D spending, including the orphan drug credit, available for companies developing drugs intended to treat rare diseases, which increased more than five-fold from 2005 through 2014.

Van Hecke, Martine, and Ben van Gils. 2019. "Médicaments : Vous les payez deux fois." Test Santé 149. <https://www.test-aankoop.be/overzichtspagina?type=magazine-articles>.

Abstract: Not available.

Summary: The article gives an overview of public expenses for biomedical research and tax incentives to promote research & development in Belgium.

Public funded biomedical research - In 2015, in Belgium, public funded biomedical research was performed for an amount of 575 million euros. This money is mostly Belgian money, but part of it is paid by the European Commission. Most of the public resources go to our universities. Industry (all industry active in the medical domain, but the largest part of it are pharmaceutical & biotech companies) received 59 million euros of public money.

There are little conditions set by the authorities or at least not the conditions we would like them to impose. Funds are not divided according to medical and public health priorities, there are no conditions with regard to availability and affordable pricing of medicines. There are conditions with

regard to open access to publications, but this is only a legal obligation in the French-speaking part of Belgium, it's generally poorly monitored, and there are delays because of conditions some scientific journals set. There are no conditions (yet) with regard to open data. The article gives some examples of medicines developed by one of our universities, and estimations of the money received by the university on one hand, and sales of the company on the other hand. Next to that, there are also examples mentioned of amounts of money companies received for research projects.

Tax incentives - In Belgium, there are different kinds of tax incentives to promote research & development. Some of them can also be used by the public sector, but it's mainly the profit sector using those advantages. There has been an analysis of the effects of these incentives,

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namely if these tax incentives promote extra R&D by the company receiving the advantage. For some of them, there is a positive effect, for others there is no or a very doubtful effect.

The total amount of tax incentives for the industry in the medical domain is 872 million euros (2016) (here also medical sector, larger than the pharmaceutical industry, because of refusal of the authorities to give more detailed figures). The largest amount is for a benefit that's called patent box, the tax deduction of 80% of gross patent income: 606 million euros. There is no benefit for society, it's used as a way for multinationals to "optimize" the taxes they need to pay. This system has been introduced at the demand of the pharmaceutical industry. Belgium has been obliged to change this system and did so, but it's still possible to use it for a couple of years and it has been replaced by another (quite similar) system.

Expenses for medicines - The article also mentions the amount of money spent by our social security system, in 2017 an amount of 4,32 billion euros. Patients also pay a considerable amount of money out of pocket for medicines, more or less 150 euros per year.

Viergever, Roderik F., and Thom C. C. Hendriks. 2014. "[Targeted public funding for health research in the Netherlands]." *Nederlands Tijdschrift Voor Geneeskunde* 159: A8174.

Abstract: The Dutch government funds health research in several ways. One component of public funding consists of funding programmes issued by the Netherlands Organisation for Health Research and Development (ZonMw). The majority of ZonMw's programmes provide funding for research in specific health research areas. Such targeted funding plays an important role in addressing knowledge gaps and in generating products for which there is a need. Good governance of the allocation of targeted funding for health research requires three elements: a research agenda, an overview of the health research currently being conducted, and a transparent decision-making process regarding the distribution of funds. In this article, we describe how public funding for health research is organized in the Netherlands and how the allocation of targeted funds is governed. By describing the questions that the current model of governance raises, we take a first step towards a debate about the governance of targeted public funding for health research in the Netherlands.

Viergever, Roderik F., and Thom C. C. Hendriks. 2016. "The 10 Largest Public and Philanthropic Funders of Health Research in the World: What They Fund and How They Distribute Their Funds." *Health Research Policy and Systems* 14 (1): 12. <https://doi.org/10.1186/s12961-015-0074-z>.

Abstract: Background: Little is known about who the main public and philanthropic funders of health research are globally, what they fund and how they decide what gets funded. This study aims to identify the 10 largest public and philanthropic health research funding organizations in the world, to report on what they fund, and on how they distribute their funds. Methods: The world's key health research funding organizations were identified through a search strategy aimed at identifying different types of funding organizations. Organizations were ranked by their reported total annual health research expenditures. For the 10 largest funding organizations, data were collected on (1) funding amounts allocated towards 20 health areas, and (2) schemes employed for distributing funding (intramural/extramural, project/'people'/organizational and targeted/untargeted funding). Data collection consisted of a review of reports and websites and interviews with representatives of funding organizations. Data collection was challenging; data were often not reported or reported using different classification systems. Results: Overall, 55 key

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health research funding organizations were identified. The 10 largest funding organizations together funded research for \$37.1 billion, constituting 40% of all public and philanthropic health research spending globally. The largest funder was the United States National Institutes of Health (\$26.1 billion), followed by the European Commission (\$3.7 billion), and the United Kingdom Medical Research Council (\$1.3 billion). The largest philanthropic funder was the Wellcome Trust (\$909.1 million), the largest funder of health research through official development assistance was USAID (\$186.4 million), and the largest multilateral funder was the World Health Organization (\$135.0 million). Funding distribution mechanisms and funding patterns varied substantially between the 10 largest funders. Conclusions: There is a need for increased transparency about who the main funders of health research are globally, what they fund and how they decide on what gets funded, and for improving the evidence base for various funding models. Data on organizations' funding patterns and funding distribution mechanisms are often not available, and when they are, they are reported using different classification systems. To start increasing transparency in health research funding, we have established www.healthresearchfunders.org that lists health research funding organizations worldwide and their health research expenditures.

Ward, Derek, Orsolina Martino, Claire Packer, Sue Simpson, and Andrew Stevens. 2013. "Burden of Disease, Research Funding and Innovation in the UK: Do New Health Technologies Reflect Research Inputs and Need?" *Journal of Health Services Research & Policy* 18 (1_suppl): 7–13. <https://doi.org/10.1177/1355819613476015>.

Abstract: Objectives: New and emerging health technologies (innovation outputs) do not always reflect conditions representing the greatest disease burden. We examine the role of research and development (R&D) funding in this relationship, considering whether areas with fewer innovative outputs receive an appropriate share of funding relative to their disease burden. Methods: We report a retrospective observational study, comparing burden of disease with R&D funding and innovation output. UK disability-adjusted life years (DALYs) and deaths came from the World Health Organization (WHO) 2004 Global Burden of Disease estimates; funding estimates from the UK Clinical Research Collaboration's 2006 Health Research Analysis; and innovation output was estimated by the number of new and emerging technologies reported by the National Institute for Health Research (NIHR) Horizon Scanning Centre between 2000 and 2009. Results: Disease areas representing the biggest burden were generally associated with the most funding and innovation output; cancer, neuropsychiatric conditions and cardiovascular disease together comprised approximately two-thirds of DALYs, funding and reported technologies. Compared with DALYs, funding and technologies were disproportionately high for cancer, and technologies alone were disproportionately high for musculoskeletal conditions and endocrine/metabolic diseases. Neuropsychiatric conditions had comparatively few technologies compared to both DALYs and funding. The relationship between DALYs and innovation output appeared to be mediated by R&D funding. Conclusions: The relationship between burden of disease and new and emerging health technologies for different disease areas is partly dependent on the associated level of R&D funding (input). Discrepancies among key groups may reflect differential focus of research funding across disease areas.

World Health Organization. 2011. "Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property." WHO. <https://www.who.int/phi/publications/gspa-phi/en/>.

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Abstract: Not available.

Description: This document represents a reader-friendly and consolidated version of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA-PHI). It includes original the GSPA-PHI document as agreed by Member States, along with the finalized, agreed list of stakeholders, time frames and progress indicators. Both resolutions (i.e. WHA61.21 and WHA62.16) are also provided as annexes. This consolidated version makes the GSPA-PHI more accessible and at the same time helps to promote the GSPA-PHI, as requested by operative paragraph [4(2)] of resolution WHA61.21, which requests the WHO Director-General to support the effective promotion and implementation of the GSPA-PHI.

World Health Organization. 2012. "Report of the Consultative Expert Working Group on Research and Development: Financing and Coordination. Research and Development to Meet Health Needs in Developing Countries: Strengthening Global Financing and Coordination." World Health Organization. https://www.who.int/phi/cewg_report/en/.

Abstract: Not available.

Description: The Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG) was established by the World Health Assembly (WHA) in 2010. The CEWG submitted its final report to the 65th World Health Assembly. The report is now available in English, French, Spanish, Russian, Arabic and Chinese.

World Health Organization. 2017. "Fair Pricing Forum 2017 Meeting Report." World Health Organization. https://www.who.int/medicines/access/fair_pricing/fair_price_report/en/.

Abstract: Not available.

Description: The Forum took place in Amsterdam, the Netherlands, on 11 May 2017, and was co-sponsored by the Dutch Ministry of Health, Welfare and Sport and WHO. and is co-sponsored by the Dutch Ministry of Health, Welfare and Sport and WHO. The main aim of the Forum was to enable stakeholders to discuss options for a fairer pricing system that is sustainable for both health systems and the pharmaceutical industries. Member States, non-governmental and patient organizations, and the pharmaceutical industry discussed key issues, such as developing alternative approaches for research and development (R&D) and business models for innovation; facilitating collaboration among payers by expanding current networks to include other relevant stakeholders and countries; increasing exchange of information, for example to assess the value of new products; promoting transparency of prices paid, R&D costs, production costs, and profit margins.

** For the purposes of this review, we have established three categories to describe the state of the literature: thin, considerable, and rich.*

- *Thin: There are relatively few papers and/or there are not many recent papers and/or there are clear gaps*
- *Considerable: There are several papers and/or there are a handful of recent papers and/or there are some clear gaps*

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- *Rich: There is a wealth of papers on the topic and/or papers continue to be published that address this issue area and/or there are less obvious gaps*

Scope: While many of these issues can touch a variety of sectors, this review focuses on medicines. The term medicines is used to cover the category of health technologies, including drugs, biologics (including vaccines), and diagnostic devices.

Disclaimer: The research syntheses aim to provide a concise, comprehensive overview of the current state of research on a specific topic. They seek to cover the main studies in the academic and grey literature, but are not systematic reviews capturing all published studies on a topic. As with any research synthesis, they also reflect the judgments of the researchers. The length and detail vary by topic. Each synthesis will undergo open peer review, and be updated periodically based on feedback received on important missing studies and/or new research. Selected topics focus on national and international-level policies, while recognizing that other determinants of access operate at sub-national level. Work is ongoing on additional topics. We welcome suggestions on the current syntheses and/or on new topics to cover.

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