EMERGING TECHNOLOGIES FOR THE POOR: HOW NANOMEDICINE AND PUBLIC PRIVATE PARTNERSHIPS ARE USED TO ADDRESS DISEASES OF POVERTY

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EMERGING TECHNOLOGIES FOR THE POOR:
HOW NANOMEDICINE AND PUBLIC PRIVATE PARTNERSHIPS
ARE USED TO ADDRESS DISEASES OF POVERTY

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LIST OF ABBREVIATIONS

BoD Burden of Disease

DALY Disability Adjusted Life Years

DoP Diseases of Poverty

G-FINDER Global Funding of Innovation for Neglected Diseases

IHME Institute for Health Metrics and Evaluation

IOR Interorganizational Relationship

NGO Non-governmental Organization

NIH USA National Institutes of Health

NM Nanomedicine

NTD Neglected Tropical Diseases

PDP Product Development Partnership

PPP Public Private Partnership

R&D Research and Development

WHO World Health Organization

WoS Web of Science

SUMMARY

Decreasing the number of people who die from preventable illnesses and reducing poverty and inequality are major public goods that are being addressed from a variety of angles. One way that policy makers and scholars are trying to improve global health is by developing new health technologies that will decrease poverty and inequality. This dissertation investigates whether nanotechnologies for medical applications (NM) are used to address diseases of poverty (DoP) and the role that public-private partnerships (PPP) play in NM research. If scientists are developing nanotechnology based vaccines and medicines for DoP, then I can conclude that the technology is helping to decrease poverty and inequality.

There are two parts to my analysis. The first part of my dissertation analyses the landscape of NM DoP research, and then I test how USA medicine sales, disease burden, and DoP correlate with the number of NM publications and patents. I find that there is some NM research on DoP, especially for high-profile DoP such as malaria, tuberculosis and HIV/AIDS, but overall there is less R&D on DoP than non-DoP. However, I cannot determine if USA medicine sales and disease burden have any relationship to research output.

In the second part of my dissertation, I examine the role of formal PPPs for developing DoP medicines. Many think the formal health PPPs can overcome the various market failures associated with developing medicines for DoP. I analyze PPP websites, and I interview PPP managers/scientists about their research portfolios, their relationships with nanotechnology, and how they believe PPPs are addressing inequality in health

R&D. I find that managers/scientists at PPPs have a variety of opinions about nanotechnology, but the general consensus is that nanotechnology will not be used in the near-term for DoP medicines. PPP managers/scientists believe that the technology is too expensive for DoP medicines and it will take too long to approve NMs. Instead of using nanotechnology, most PPPs are in favor of using traditional technologies.

CHAPTER 1: INTRODUCTION

Ensuring that people are healthy is one of the major global public goods, and for millennia, doctors have tried a variety of techniques to keep people from getting sick (Feachem & Sachs, 2002). Many of the most deadly diseases were eliminated through a variety of technologies and social improvements such as better medications, new treatment regimens, and cleaner communities that prevented pestilence from spreading. Despite the improvements in overall health, the advancements in healthcare are not evenly distributed. Many medical discoveries only target diseases of the rich while other medicines are too expensive for impoverished communities to purchase. At one point, scholars estimated that there was a "10-90 gap." This dissertation explores how an emerging technology, nanotechnology, is used to address DoP and the role that PPPs have in this research. Chapter 1 gives a brief overview of the literature, research questions, methods, and the significance of the study. I start by discussing the main literature used in the dissertation. I review the public health literature; science, technology, and innovation policy literature; and public policy/administration literatures. Then, I give an overview of the three main research questions of the dissertation and the methods I use to address these questions. I use both quantitative and qualitative data from publications, patents, websites, and interviews. Finally, the last section of the chapter outlines the significance of this study. Overview of Literature

There are about 40 DoP (Global Forum for Health Research, 2004), and the health literature attributes a large proportion of global healthcare inequality to the lack of a profitable market associated with DoP (Stevens, 2007). Scholars reason that

biotechnology and pharmaceutical companies will not develop new medicines to target DoP if they cannot recoup their R&D expenses. As a result, there is a lack of R&D and medicines for DoP. The research gap is a major market failure that needs to be addressed in order to improve the global public health (Feachem & Sachs, 2002).

To correct the market imbalances, many scholars believe that special organizational structures, such as PPPs, are necessary (Moran, Guzman, Ropars, & Illmer, 2010; World Health Organization, 2010a). PPPs can provide research funds, connect companies to government health organizations, participate in manufacturing, and assist with distribution and marketing (Glennerster, Kremer, & Williams, 2006; Widdus, 2001). These efforts can spur new DoP drug development and make the current medicines for DoP more accessible.

The term "public-private partnership" was first used about 40 years ago, and now the PPP is a very common organizational structure that is promoted by politicians and scholars (Bovaird, 2004). PPP scholarship arises from several disciplines, but this dissertation examines PPPs from a public management and administration viewpoint because it most clearly defines PPPs. From this discipline, PPPs are defined as "working arrangements based on a mutual commitment (over and above that implied in any contract) between a public sector organization with any organization outside of the public sector" (Bovaird, 2004). This dissertation focuses on a subset of PPPs that conduct R&D for DoP. These formal PPPs are operationally and legally institutionally independent from the collaborating organizations, and they are extremely influential for DoP research (Hanlin et al., 2007). One study estimates that 75% of all research on DoP is done by formal health PPPs (Moran, 2005).

There are a variety of formal PPPs, but a goal shared by many them is drug discovery. Scientists have long believed that new and emerging technologies could revolutionize healthcare and improve lives. However, emerging technologies are often associated with high-tech societies, and rarely have scientists worried about the distributional consequences of the technology. Therefore, there is an interesting intersection between PPPs, emerging technologies, and DoP. According to current academic theory, PPPs can act as the conduit for emerging technologies to address DoP because the PPPs resolve the market failure associated with DoP research (Glennerster et al., 2006). PPPs lower the barrier to entry for drug development, they reduce uncertainty in R&D, and they help knowledge flow between the manufacturers and patients. This gives incentives for public and private organizations to fund DoP research. Unfortunately, there are no studies that examine the relationship between emerging technologies and PPP. This dissertation helps scholars better understand the relationship between emerging technologies, DOP, and PPPs.

Research Questions

There are several different research questions in this dissertation. The first part of the dissertation measures the amount of nanomedicine (NM) research that is conducted and then assesses inequality in NM research. I use three different measurements to understand inequality in NM R&D. First, I test whether NM publications and patents have any relation to USA medicine sales. The USA is the biggest market for pharmaceutical companies (about 53%) (World Health Organization, 2004), and it drives pharmaceutical innovation (Blume-Kohout, 2012). As a result, I test the extent that USA

medicine sales relate to NM R&D. I expect that NM research is more likely to address diseases with large markets as opposed to small markets.

Q1.1: Do diseases with high USA medicine sales have more NM R&D than diseases with low medicine sales?

H1.1: High USA medicine sales for a disease are associated with more NM publications and patents for that disease.

The second dimension of health inequality that I investigate is disease burden. Disease burden measures the severity of an illness on a population. In order to best improve global health, doctors and scientists need to develop medicines that treat illnesses with high disease burdens. However, if diseases with small disease burden have more NM R&D than diseases with large disease burden, then NM R&D is not greatly improving global health inequality, and only a minority of the population are benefitting from the technology.

Similarly, I explore if there is more research on diseases with increasing disease burden. I have not found studies that exam the change in disease burden with relation to R&D, and as a result, I do not have a good hypothesis of this relationship. It is possible that scientists focus on diseases with increasing disease burden because the diseases are more serious and they require greater attention. However, it is also possible that scientists study diseases with decreasing disease burden because scientists have developed treatments for those illnesses and the areas are viable for research.

Q1.2: Does disease burden for a specific disease correlate with the amount of NM research and development for that disease? Do diseases with growing disease burden receive more research attention?

H1.2a: Diseases with high burden of disease have more NM publications and patents.

H1.2b: Diseases that have increasing disease burden have more publications and patents.

A third dimension of public health that I investigate is whether diseases of the rich are studied more than DoP. If there is less NM R&D for DoP compared to non-DoP, holding other factors such as disease burden constant, then NM is increasing health inequality.

Q1.3: Is there less NM research for DoP than other diseases?

H1.3a: There are fewer NM publications and patents on DoP compared to other diseases, controlling for medicine sales and disease burden.

H1.3b: DoP with more PPP funding (hotdop) have more NM publications and patents than other DoP with less PPP funding.

After understanding the scale of NM research and inequality, I investigate the role that PPPs play in DoP research. As stated before, studies show that PPPs are the most important organizations for DoP research (Moran, 2005), and therefore, I expect that PPPs will be a major source of NM DoP research.

Q2: Do formalized PPPs study DOP more than other organizations?

H2.1: NM DoP research is more likely to be conducted by formalized PPPs than other organizations, controlling for variables such as drug sales, disease burden, and whether the illness is a disease of poverty.

As I examined publications and patents, however, I found that fewer than 100 out of 81,000 NM publications were authored or funded by a PPP. Rather, universities and

government agencies conducted most of the NM research. The lack of PPP involvement in NM research forced me to shift my attention from studying the importance of PPPs in NM research to studying the difference between PPP and NM research. I looked for different patterns in the research, partnering organizations, and subject categories.

H2.2: PPPs' publications focus on different diseases than NM publications.

H2.3: PPPs' publications focus on different fields and sub-disciplines than NM publications.

H2.4: PPPs partner with different organizations than NM researchers.

I also investigated if PPPs and NM scholars have different integration and specialization scores. The integration and specialization scores measure the extent that knowledge is being integrated into research. Many scientists believe that research with higher integration scores and lower specialization scores are more likely to lead to innovative research because this type of research has higher knowledge cross-fertilization across disciplines that helps the advancement of science (Hollingsworth, 2008; Moed, Glanzel, & Schmoch, 2005; Rafols & Meyer, 2008). Since nanotechnology is a new and emerging technology, it should have higher integration scores than other areas of science. Do NM publications have higher integration and specialization scores than PPP publications?

H2.5: PPP publications have lower integration scores than NM publications.

H2.6: PPP publications have higher specialization scores than NM publications.

Finally, the third set of questions examines the factors that influence formal PPP funding and research portfolio decisions. How do PPPs decide the types of projects to pursue? Do PPPs think NM is a viable field? The goal of these questions is to explain and contextualize the previous research finding. I use a mixture of primary and secondary

data sources (such as websites and reports) and phone interviews to understand the motivations of formal PPPs.

Data and Methods

I use both quantitative and qualitative data to study the extent that NM and formal PPPs are addressing DoP. For the quantitative analysis, I used publication and patent data from Web of Science (WoS), PubMed and PatStat. All three databases are commonly used in these types of analyses (Huang, Notten, & Rasters, 2008). From my analysis, which is described in more detail in Chapter 3, I found that WoS has about 81,800 NM publications and PubMed has about 58,400 PubMed NM publications from 2000-2012. PatStat is much smaller than both PubMed and WoS, and it only has about 15,500 NM patents from 2000-2009.

After collecting my bibliometric data, I compare the dependent variables to burden of disease, USA medicine sales, and DoP. These data came from the World Health Organization (WHO), Bloomberg Finance L.P., Policy Cures and the BioVentures for Global Health. I find that only the dummy variable for DoP has any significant impact on NM R&D.

The qualitative data analysis comes from two sources. First, I analyzed the websites of all 28 formal PPPs. Overall, the PPP websites give very detailed descriptions of their mission and the importance of the PPP model. Next, I conducted phone interviews of PPP managers and scientists. In the interviews, I asked the respondents a variety of topics ranging from their research portfolios and patenting practices, to the importance of nanotechnology for DoP.

Significance of Study

This dissertation fills a unique hole in the literature. First, it brings together research from three different areas to shed light on the potential for emerging technologies to address poverty and inequality. This dissertation impacts public and non-profit management and contributes to the body of knowledge on PPPs for technology development. Over the past 30 years, PPPs have gained prominence; the PPP is now a very common organizational structure used for service delivery, policy coordination, resource mobilization, and management (Bovaird, 2004). This study specifically looks at a new type of PPP that focuses on product development for medicines and vaccines. This new type of partnership began forming about 15 years ago, but there are very few studies about it (De Pinho Campos, Norman, & Jadad, 2011). Recently, Hanlin et al. examined two PPPs, the International AIDS Vaccine Initiative and the Malaria Vaccines Initiative, and find that PPPs are important because they act as brokers and knowledge integrators as well as play a crucial role in getting technology to poor individuals (Hanlin, Chataway, & Smith, 2007). This dissertation extends our knowledge about PPPs by looking at the ways they interact with emerging technologies such as NM.

Another discipline that this study will push forward is health policy scholarship. Currently, there is not a clear understanding of health inequality. Some studies show that the gap is widening, especially in sub-Saharan Africa countries (Kilama, 2009), while other studies show that the research gap is shrinking (Stevens, 2007). This study will not directly solve this controversy, but it does give more insight on inequality within medicine research.

Moreover, the health policy literature is unclear about the connection between societal needs and research output for emerging technologies. Many global health scholars believe that the lack of R&D for diseases that afflict the poor is one of the biggest challenges in public health (Feachem & Sachs, 2002). A 2011 study examines the relationship between NIH disease-specific funding and disease burden. The study finds that only 33% of the variation in funding can be attributed to disease burden (Gillum et al., 2011). Another study by Lichtenberg examines the relationship between disease burden and the number of drugs to treat diseases and finds that only disease burden in high-income countries affects the number of medicines that are developed (Lichtenberg, 2005). Similarly, Vanderelst and Speybroeck find that only high-income disease burden impacts the number of scientific publications. Low income diseases, even if they have large disease burden, do not have a significant impact on drug R&D (Vanderelst & Speybroeck, 2013). These studies explain research priorities across science, but they do not examine research inequalities in new and emerging technologies. Will nanotechnology follow the same trend as science in general, or is there a new pattern of research with emerging technologies?

Finally, this dissertation will help scholars better understand if scientists are developing nanotechnologies that decrease poverty and inequality. Over the past 15 years, there has been some hope that nanotechnology could be used to reduce poverty. South Africa's nanotechnology initiative, for example, targets social issues in water, energy, and health (Department of Science and Technology South Africa, 2005), and the Salamanca-Buentello et al. study finds that there are ten major applications of nanotechnology in developing countries (Salamanca-Buentello et al., 2005). The

emphasis on using nanotechnology for poverty alleviation should make it more likely that nanotechnology will help the poor compared to other technologies, but this hypothesis needs to be examined. This study tests whether nanotechnologies are being developed that could decrease poverty and inequality.

Outline of Dissertation

This dissertation has six chapters. Chapter 2 discusses the relevant literature related to this study. First, I define DoP, and then I give a brief history of PPPs and show how they are important organizational structures to address DoP. For this part of the literature review, I draw on literature from new public management, management, and health policy. Next, I use the science and innovation policy literature to describe emerging technologies and compare nanotechnology to the current definition of emerging technology. I conclude that nanotechnology is a good example of an emerging technology and that it is an important technology to examine research inequality.

Chapter 3 describes the data and methods used in the dissertation. I use data from WoS, PubMed, PatStat, Bloomberg Finance L.P., and the WHO. The mixed-method approach employs negative binomial Poisson regression analysis, website content analysis, and semi-structured interviews of scientists and PPP managers.

Chapters 4 and 5 discuss the research findings. Chapter 4 focuses on the findings from the quantitative data while Chapter 5 gives the results from the qualitative data. In these chapters, I specifically address whether the hypotheses were rejected or accepted. I also discuss other findings that were not part of my original hypotheses. Finally, in Chapter 6, I summarize my research results and discuss policy implications of my study.

CHAPTER 2: BACKGROUND/LITERATURE REVIEW

Introduction

The goal of this chapter is to give a brief overview of the literature and intellectual foundations of the dissertation. This study measures the amount of inequality in NM research and the role of formal PPPs in addressing the research imbalance. To understand these questions, I begin by reviewing the literature on global public health and DoP. I discuss the definitions of public goods, public health, and DoP; I then provide the reasons why a health research gap arose. Next, I review the literature on PPPs. PPPs are the most prominent institutions doing research on DoP (Moran et al., 2010), and the literature review explains the purpose of PPPs and how these organizations address many of the market failures associated with DoP. The PPP literature is a convergence of several disciplines; however, I focus the literature review on the definition of PPP, as well as on the role of PPP in the public management and public policy fields.

The third section of this chapter gives background on emerging technologies and NM. The term "emerging technology" is a buzzword that is often used to describe new technologies, but the term it is not clearly operationalized. Cozzens et al. give four characteristics of emerging technologies, and from their definition I show that nanotechnology is a good example of an emerging technology (Cozzens et al., 2010). Finally, I highlight previous studies on medical research inequality and DoP. These studies examine the relationship between disease burden, research output, and pharmaceutical innovation. Although there are some studies on research inequality, there

are no studies that specifically analyze research inequality in NM or the role of PPP in R&D for emerging technologies.

Global Health and Diseases of Poverty

Doctors have treated patients for centuries, and governments have always been concerned with outbreaks of diseases. However, with the rise of rapid global transportation during the 1800s, government officials had a new impetuous to solve global health problems because the diseases could easily spread to new populations (Birn, 2009). Today, improving global health is still one of the major public goods that concern the world community.

A pure public good has two qualities; it is non-rivalrous and non-exclusive (Feachem & Sachs, 2002). Health, therefore, is not considered a public good by most economists because it is very exclusive. Only an individual feels the benefits of good health, and others cannot share in the benefits of someone else's health. However, public health is argued to be a public good because when health is viewed as an aggregate good, then public health is non-rivalrous and non-exclusive (Feachem & Sachs, 2002). If a country has a healthy population, then the whole nation benefits from the low risks of disease and illness.

A major focus of global public health is addressing the global public good of improving the health of the poor and eliminating many DoP. A disease of poverty is a disease that predominantly affects the poor. The WHO Special Programme for Research and Training in Tropical Diseases (WHO-TDR) defines DoP as "diseases that affect mostly the poor in developing countries" (World Health Organization, 2010a). The WHO divides DoP in two classes. First, there are the "big three" DoP: malaria, HIV/AIDS, and

tuberculosis. These diseases receive the most attention from the global community, and there is significant investment in eradicating them (World Health Organization, 2010a). It is estimated that 63% of DoP drug development is for the "big three" DoP (Ponder, 2012). The other diseases that the WHO classifies as DoP are neglected tropical diseases (NTD). There are 17 NTD, and these diseases, which are "a proxy for poverty and disadvantage, affect populations with low visibility and little political voice; [These diseases] do not travel widely; cause stigma and discrimination, especially among girls and women; have important impact on morbidity and mortality; are relatively neglected by research; [and] can be controlled, prevented, and possibly eliminated using effective and feasible solutions" (World Health Organization, 2010b).

In addition to the "big three" and NTD, BIO Ventures for Global Health, a non-profit that specializes in accelerating research on medicines for developing countries, classifies diseases such as diarrheal diseases, cholera, and typhoid fever, as DoP (Ponder, 2012). Policy Cures, another health nonprofit, lists 31 neglected diseases. This nonprofit considers an illness a disease of poverty if it meets three conditions: "the disease disproportionately affects people in developing countries, there is a need for a new products, [and] there is a market failure" (Moran et al., 2010). Table 1 lists the DoP identified by the WHO, Policy Cures, and BioVentures for Global Health.

TABLE 1 LIST OF DISEASES OF POVERTY

"Big Three" Diseases	Neglected Tropical Diseases		Other Diseases of Poverty	
Tuberculosis	Buruli Ulcer	Leprosy	Podoconiosis	Typhoid Fever
HIV/AIDS	Chagas disease	Lymphatic filariasis	Snakebite	Pneumococcal Disease
Malaria	Cysticercosis	Onchocerciasis	Strongyloidiasis	Cryptosporidium
	Dengue/Severe dengue	Schistosomiasis	Diarrheal Disease	EAggEC
	Dracunculiasis (guinea-worm)	Sleeping Sickness	Cholera	Giardia
	Echinococcosis	Soil transmitted helminthiasis	ETEC	Roundworm
	Fascioliasis	Trachoma	Rotavirus	Hookworm
	Human African Trypanosomiasis	Yaws	Shigellosis	Whipworm
	Leishmaniasis		Salmonella infections	Rheumatic Fever

Causes of Diseases of Poverty

In general, scholars believe that DoP arise from two market failures. First, the market fails to account for the negative externalities associated with DoP. The pharmaceutical companies focus their attention on medicines that will generate large profits and fail to do R&D on illnesses that mainly affect poorer populations and have large negative externalities. For example, diseases from developing countries can easily spread to other parts of the world, and by neglecting DoP, the world community puts itself at risk of spreading the disease (Kremer, 2002).

A second market failure associated with DoP is that there is a time-inconsistency problem for pharmaceutical companies. To produce medicines for DoP requires a large initial investment in R&D, but once the drug companies produce the medicines, the customers "have every incentive to use their powers as dominant purchasers to keep prices down to maximize access to these life-saving products" (Berndt & Hurvitz, 2005). As a result, pharmaceutical companies are hesitant to conduct R&D for DoP because the

market can demand a lower cost once the medicine has been produced. This leads to many neglected illnesses.

Not all scholars think that DoP pose a serious risk. Stevens argues that labeling neglected diseases as a serious public health concern is unnecessary because many neglected diseases have effective medicines (Stevens, 2007). He writes that most DoP have drugs in the pipeline or effective treatments that are currently available. For example, rotavirus has four vaccines in the pipeline, and yaws, a bacterial infection that affects bone and cartilage, already has effective medicines on the market (Ponder, 2012).

In addition, Stevens points out that many neglected diseases do not pose the greatest health risk to individuals in developing countries. For example, in 2004, the neglected disease Chagas only caused of 3,000 disability adjusted life years (DALYs) in low income countries while road accidents caused 16.7 million DALYs (World Health Organization, 2008). Rather than focusing on diseases that affect only a few people, Stevens suggests the world community could concentrate on issues such as road accidents that have bigger impacts on global health.

Finally, Stevens argues that the research gap is irrelevant because diseases of the rich and poor are converging (Stevens, 2007). Cardiovascular disease and other lifestyle diseases are quickly becoming the most serious illnesses in developing countries. Therefore, the need for research on DoP is not as relevant as research on lifestyle illnesses.

Public-Private Partnerships

For hundreds of years, governments have partnered with private organizations. An early example of the public sector working alongside the private sector is the relationship

of the Netherlands with the Dutch East India Company. The Dutch East India Company was a private sector company, yet it was an agent of the Netherlands and often performed government functions such as negotiating treaties, coining money, and governing the colonies. During WWII, governments relied heavily on the private industry for the war movement, and after the war, the private sector was crucial for international development (Hounshell, 1992). Despite the long history of the public and private sectors working together, the term "public-private partnership" was first used about 40 years ago. Since then, the phrase has grown in prominence, and now it is widely used by politicians, businesspeople, and non-profit organizations (Bovaird, 2004).

However, many scholars debate whether PPPs are a new phenomenon or simply a relabeling of old organizational patterns that have been around for a long time (Graeme A. Hodge, 2010). The scholars who believe that PPPs are not a new phenomenon say that individuals only use the term PPP because it has positive connotations compared to phrases such as privatization and outsourcing. Instead of a politician saying that the government will "privatize industries," they prefer to discuss "partnering with industry and civil society organizations" (Hodge, 2009; Khanom, 2010). In response to these criticisms, other scholars counter that the current structure and emphasis of PPPs is a new phenomenon. In the past twenty years, dozens of governments established PPP agencies and these partnerships are working in new areas such as vaccine development and clinical trials (Farrugia, Reynolds, & Orr, 2008).

PPP scholarship comes from several academic disciplines. First, many scholars view PPPs as stemming from neoliberal economics and new public management. Neoliberal economics and new public management favor a smaller government so that

market forces can be the main mode for change. These theories believe that the private sector can allocate resources more efficiently than the public sector, and as a result, there is a push towards privatization of government services and deregulating industries in order to give them more freedom to operate (Bovaird, 2004; Miraftab, 2004). According to neoliberal economics and new public management, PPPs are the conduit for the government to privatize many services.

Another field that PPP scholarship draws from is economics and game theory. In game theory, cooperation helps individuals pursue their own self-interests (McQuaid, 2000), and as a result, partnerships arise to help an individual achieve a higher utility. PPPs are one type of cooperation that helps two organizations achieve a more positive outcome.

Similarly, in the public administration and management literature, scholars discuss the importance of interorganizational relationships (IOR) because networks and connectedness are essential for the survival and performance of organizations (Khanom, 2010; Oliver, 1990). One definition of IOR is "relatively enduring transactions, flows, and linkages that occur among or between an organization and one or more organizations in its environment" (Oliver, 1990). PPPs can be considered a subset of IOR (Edelenbos & Klijn, 2007). The management literature also describes PPPs as cross-sector partnerships (Selsky & Parker, 2005) and joint partnership (Hall, 1991, p. 219).

Definition of Public Private Partnership

One heavily cited definition of a PPP is "working arrangements based on a mutual commitment (over and above that implied in any contract) between a public sector organization with any organization outside of the public sector" (Bovaird, 2004). This

definition is broad, and it allows PPPs to be between a government entity and any non-government entity such as a company, nonprofit organization, or local community group.

A key part of Bovaird's definition is that the mutual commitment between organizations has to be "over and beyond that implied by a normal contract"(Bovaird, 2004). Bovaird does not expound upon the level of interaction necessary to be classified as "over and beyond" a normal contract, but he suggests that the firms must make a commitment for a close and ongoing relationship that is not based purely on a monetary transactions or monitoring/ enforcement agreements (Bovaird, 2004). In a normal government contract, the government sets the boundaries of the project and acts as the principal that watches over the agents as they complete a task. In essence, "the Government acts as commissioning party, lays down the characteristics of the project and contracts out the construction and exploitation to a private contractor on the basis of a clear-cut and straightforward programme of requirements" (Van Ham & Koppenjan, 2001). Contract-based government relationships have led to a "hollow state" in which the government uses third parties to provide public services (Milward & Provan, 2000). This type of relationship is not a partnership but rather normal government interaction with the private sector.

Some criticize Bovaird's broad definition of PPPs because it makes it difficult to understand how PPPs operate, and it hides underlying power distributions within them. PPPs do not necessarily consist of equally powerful organizations; rather, there is a wide range of power and resource distribution within PPPs (McQuaid, 2000; Miraftab, 2004). For example, a PPP could be between a strong government agency and a weak civil society organization. In this type of relationship, there is not a partnership but a

government directive. One scholar says that "the terminology sloppiness in debates about PPPs fosters convenient ambiguities in defining the roles and expectation of each partner" (Miraftab, 2004). As a result, I narrow the types of PPPs for this study to formal public-private partnerships (see the next section for a more thorough discussion of formal PPPs).

The literature gives a number of reasons that public-partnerships form. First, as the world gets more complex, a single organization does not have the resources and knowledge to solve problems, and so in order to accomplish their goals, organizations partner together (McQuaid, 2000; Van Ham & Koppenjan, 2001). This reason for establishing partnership is especially relevant when examining emerging technologies. Emerging technologies are at the forefront of knowledge, and a variety of sectors must work together to develop the technology (Cozzens et al., 2010). PPPs help transfer knowledge between organizations and sectors. A classic example of multiple stakeholders working together to develop an emerging technology occurred with the personal computer. Throughout the twentieth century, government labs, universities, and companies were all involved in developing computers (Bovaird, 2004). They set standards, designed manufacturing processes, and set the pace for the improvements in microprocessing technology.

A second reason that organizations form PPPs is that a group of organizations are better at overcoming market deficiencies than a single actor (McQuaid, 2000; Van Ham & Koppenjan, 2001). For example, some innovations have high technical risk that prevent them from being economically attractive, and other innovations have low monetary return or take a long time to develop. PPPs can circumvent these barriers by

spreading the risks of failure over multiple parties and projects, so that they will have limited exposure and liability (Greve, 2006). Partnerships also improve the economies of scale and increase the scope of the individual organization (Bovaird, 2004). Most health R&D PPPs have expert scientific boards from different sectors that help them make prudent decisions about research portfolios. PPPs can also pool resources from several sources and invest in multiple projects at once. In contrast, smaller organizations do not have the personnel and financial resources to work on multiple projects simultaneously (Moran et al., 2010).

Finally, PPPs build new organizational structures "capable of generating new technologies" (Chataway et al., 2010) and new social interactions (Chataway, Tait, & Wield, 2007). These new structures give these organizations more legitimacy to operate, allow them to have a greater impact, and brings together techniques and ideas from different sectors (McQuaid, 2000; Selsky & Parker, 2005).

However, not all scholars think that PPPs are beneficial for development. Miraftab describes PPPs as Trojan Horses because they can hide unequal power relationships that lead to the community partners being marginalized by the dominant partner. In low-income countries, often the agendas of foreign governments and researchers take priority because those entities have the money and influence to direct the PPP (Miraftab, 2004). Rather than thinking of PPPs as a panacea to problems, Miraftab suggests that PPPs focus on social, economic and cultural conditions (Miraftab, 2004). Simply forming a PPP does not guarantee equitable outcomes.

Types of Partnerships

There are several typologies to describe the different variations of PPPs. One typology proposed by Brinkerhoff characterizes PPPs on two dimensions: mutuality and organizational identity. Brinkerhoff recognizes that partnerships fall on a continuum ranging from simple contracts to full PPPs. Brinkerhoff believes that only organizations that have high mutuality and organizational identity are PPPs (J. M. Brinkerhoff, 2002). Another typology of partnerships focuses on the particular sectors involved in the partnership and whether the partnership solves a resource dependence problem or shares a similar social platform (Selsky & Parker, 2005). Moreover, scholars describe the various purposes of PPPs. They can do policy design, policy evaluation and monitoring, implementation, capacity building, activism, and resource mobilization (Bovaird, 2004; D. W. Brinkerhoff & Brinkerhoff, 2011). They can also help with innovation by increasing the cooperation and knowledge linkages between organizations.

Due to the broad range of PPPs and their functions, this dissertation will focus on a subset of PPPs called formal PPPs. Based on the definition of PPP by Hanlin et al., I define formal a public-private partnership as a partnership between government and non-government organizations that is operationally and legally independent from the collaborating organizations after it is formed (Hanlin et al., 2007). In these PPPs, several public and private organizations join together to start a separate non-profit entity. Formal PPPs are a good unit of analysis because they are easy to identify. Most formal PPPs identify themselves as PPPs, and they give information about their structure. Also, there is a growing body of literature that discusses formal PPPs and how they operate. For example, over the past five years, Policy Cures tracked formal PPPs' funding, and they

maintain a database of funding flows to and from these organizations (Moran et al., 2010). Finally, formal PPPs are very active in DoP research, so it is important to study them.

An example of a formal PPP is a product development partnership (PDP). PDPs gained prominence as organizations that conduct disease of poverty R&D (Moran et al., 2010). Chataway et al. defines PDPs as "a technology push initiative aimed at providing new science and technology based products for neglected diseases" (Chataway, Hanlin, Muraguri, & Wamae, 2009). Moran estimates that in 2004, 75% of R&D projects for neglected diseases were conducted by PDPs (Moran, 2005), and that 14 PDPs spent $262 million on neglected disease R&D in 2007 (Moran et al., 2010). Two prominent formal PPPs conducting research on DoP are the International Aids Vaccine Initiative and the Malaria Vaccine Initiative.

Emerging Technologies

Another topic this dissertation explores is the role of emerging technologies to address poverty and inequality. In the literature, there is no clear definition of emerging technology; the term is rarely operationalized, and it is used across disciplines without a clear academic basis (Cozzens et al., 2010; Veletsianos, 2010). The term emerging technologies first appeared in the literature in the 1960s and became more widely used in the 1990s (Cozzens et al., 2010); however, the concept of an emerging technology has a longer history. Kondratieff discusses the "long waves of technical change", and Schumpeter writes about creative destruction (Avila-Robinson & Miyazaki, 2011). Both of these concepts deal with new technology and the way it changes society.

As stated before, there is no clear definition of emerging technology; however, when the various definitions are systematically analyzed, there are four main characteristics of emerging technologies (Cozzens et al., 2010). First, emerging technologies are characterized by fast and recent growth (Cozzens et al., 2010). If the technology languishes for a long time or it has a slow adoption then it is not an emerging technology. The second characteristic of emerging technologies is that it is a transition or change to something new (Cozzens et al., 2010). Like fast growth, novelty is an important aspect of emerging technologies. The third characteristic of emerging technology is that it has an economic or market potential (Cozzens et al., 2010). Even if an innovation is a superior technology than a previous product, it is not considered an emerging technology unless it has market potential. Finally, emerging technologies must be based on scientific innovation or breakthrough. There are many innovations that are important, but they are not based on scientific breakthroughs, and as a result, they are not considered an emerging technology (Cozzens et al., 2010). For example, there are organizational innovations, such as the assembly line, that are important innovations but not based on scientific breakthroughs. As a result, those technologies are not considered emerging technologies.

Nanotechnology

One technology that has received a lot of attention as an emerging technology is nanotechnology (Youtie, Iacopetta, & Graham, 2008). Nanotechnology is "science, engineering, and technology conducted at the nanoscale, which is about 1nm-100nm" (nano.gov). At the nanoscale, matter has different properties, such as conductivity, color, and reactivity, which allows for novel research and the creation of new products. Many

people think the novel properties of nanoscale materials will transform science and engineering. One scientist said that nanotechnology could be as transformational as "the steam engine in the 18th century, electricity in the 20th century, and the Internet in contemporary society"(Hassan, 2005). Because of the large potential of nanotechnology, significant investments have been made in the field. In 2000, the USA established the National Nanotechnology Initiative with an initial funding of $475 million. That funding level has steadily grown and in 2013 the NNI received $1.8 billion dollars (nano.gov). Europe and China have made similar large investments in nanotechnology. By 2004, about 62 countries had some type of nanotechnology initiative (Maclurcan, 2010a).

The excitement about nanotechnology is not only in rich countries. There is emphasis on nanotechnology R&D centers in low-income countries, and several developing nations started nanotechnology initiatives. Many scientists believe that nanotechnology can have major benefits for poor and marginalized communities, and that nanotechnology research in low-income countries is essential for creating context-specific technologies (Singer, Salamanca-Buentello, & Daar, 2005). Some believe that if low-income countries do not conduct nanotechnology R&D, then the nanotechnology revolution will pass them by. In one study, researchers asked nanotechnology experts which nanotechnologies could have the greatest benefit for developing countries. The scientists responded with applications that ranged from improved solar cells to cheaper construction materials (Salamanca-Buentello et al., 2005).

Nanotechnology as an Emerging Technology

As stated before there are four qualities of emerging technology: fast recent growth, transition/change to something new, market or economic potential, and

increasing science-based-ness. Nanotechnology fits all the definitions of emerging technology, and hence, it is a good case to use in this dissertation. The principles taken from the nanotechnology case can then be generalized to other emerging technologies that also follow a similar development path as nanotechnology.

The first characteristic of emerging technology is that it has fast recent growth. Throughout the 2000s, nanotechnology saw immense R&D. It is estimated that in 1990, there were about 2000 nanotechnology publications and 400 nanotechnology patents. By 2005, there were about 56,000 nanotechnology articles in WoS and 12,200 nanotechnology patents in MicroData and International Patent Documentation Center (INPADOC). Moreover, the number of country nanotechnology programs went from 0 in 1999 to 62 by 2004 (Maclurcan, 2010a).

The second characteristic of emerging technologies, a transition/change to something new, has been debated within the nanotechnology literature. Some scientists argue that working at the nanoscale is not new; rather, chemists have operated at the nano-level for centuries. For example, the Romans used gold and silver nanoparticles in paint pigments for glass (Maclurcan, 2005). Also, sol-gel processes (a method of making solid substance from small particles), which were first used in the 1800s, contain nanoparticles (Baer, Burrows, & El-Azab, 2003; Hench & West, 1990). Moreover, in personal interviews, scientists often say that nanotechnology is just a buzzword and that although it is interesting, it is not new. Despite the criticism, nanotechnology research has some features that are different from older scientific traditions. Nanotechnology researchers use new equipment, such as scanning electron microscopes, which allows them to better understand physics and chemistry at the nanoscale. Scientists also have the

capabilities to build nano devices from the "bottom up" as opposed to relying strictly on top-down processes. Finally, although chemistry and other processes operate at the nanoscale, current researchers have a certain level of precision that allow scientists to actually manipulate individual atoms and molecules (Maclurcan, 2005).

The third reason that nanotechnology is an emerging technology is because it is estimated that nanotechnology products will have a large market. Early in the 2000s, experts predicted that nano-enabled products could have a market of more than $2 trillion by 2015 (Berger, 2007). Currently, there are over 1,300 nano-enabled products on the market, ranging from lip balm to water recreation vehicles (Woodrow Wilson International Center, 2012).

Finally, nanotechnology is a science-based technology. A variety of fields such as chemistry, physics, and material science make up the field of nanotechnology. The scientific nature of nanotechnology is evident in the number of Nobel Prizes nanotechnology scientists have received. In 1996, Robert Curl, Harold Kroto, and Richard Smalley won the Nobel Prize in chemistry for "discovering" the fullerene, a nanoparticle. Later, in 2007, Albert Fert and Peter Grunberg won the Nobel Prize in Physics for research on magnetism and resistance at the nano-scale. Most recently, in 2010, another Nobel Prize in Physics was awarded to Andre Geim and Konstantin Novoselov for making graphene, another nano material ("Nobelprize.org," 2012).

Nanomedicine

A large portion of the nanotechnology field is focused on medical applications. NM has roots back to Richard Feynman, who is often identified as the father of nanotechnology (Freitas, 2005). In his famous speech, "Plenty of Room at the Bottom,"

Feynman describes a future where little robots are surgeons inside the body. He predicted that one day, doctors could "put the mechanical surgeon inside the blood vessel and it goes into the heart and 'looks' around….It finds out which valve is the faulty one and takes a little knife and slices it out. Other small machines might be permanently incorporated in the body to assist some inadequately functioning organ" (Feynman, 1959). Today, we are not close to realizing Feynman's dream of surgeons in the body, but scientists are designing cheap and more sensitive diagnostics tools, novel drug delivery systems, and implants/prosthetics (Freitas, 2005; Guo, Zhou, Porter, & Robinson, 2014).

Despite the major efforts of scientists and funding agencies to use nanotechnology to address healthcare needs, one criticism is that nanotechnology may not be the best tool to fix health problems (Invernizzi, 2006). Some will argue that genes, hormones, and proteins may hold the key to new medicines and that nanotechnology is not as important. Also, many of the DoP already have viable prevention and treatment options, but these diseases remain a problem due to social factors rather than the lack of medicines and vaccines (Invernizzi, 2006). Therefore, a technical solution, such as nanotechnology, will not be able to solve the problems.

In response to these criticisms, scholars note that NM is a broad platform technology and can be incorporated into a plethora of medicines (Best & Khushf, 2006; Freitas, 2005). As a result, it will work alongside other health research that focuses on genes and hormones. Moreover, as drug resistance grows for many common medicines, NM can serve as a platform to create resistance free medicines and vaccines (Santos-Magalhães & Mosqueira, 2010). Finally, the worry that nanotechnology is irrelevant for low-income countries is not substantiated by many nanotechnology scientists. From the

Salamanca-Buentello et al. study, three of the top ten poverty-alleviating nanotechnologies relate to NM (Salamanca-Buentello et al., 2005).

Other Studies

Over the past ten years, more scholars have tried to understand the gap in health care research and the impacts of disease burden on research priorities. In 2005, Lictchenberg studied the relationship between disease burden and pharmaceutical innovation. He operationalizes pharmaceutical innovation by counting the number of drugs that were developed to treat a particular disease and the number of new drugs launched around the world. He finds that "pharmaceutical innovation is positively related to the burden of disease in developed countries but not to the burden of disease in developing countries" (Lichtenberg, 2005). He reasons that the gap in pharmaceutical innovation occurs because there are few incentives for pharmaceutical companies to manufacture drugs for the poor (Lichtenberg, 2005).

In 2011, Gillum et al. examined the relationship between the NIH disease funding and disease burden with other variables such as public interest, charity funding, and disease-specific articles in PubMed. The NIH is the largest sponsor of biomedical research, and their research priorities have major impacts on R&D. Gillum et al. find that the most significant factor in determining NIH funding levels is the burden of disease (Gillum et al., 2011), while other factors such as public interest and charity revenue have a significant yet smaller effect on NIH funding.

Another study by Vanderelst and Speybroeck examines the relationship between disease burden and publications. They show that funding level is correlated with research output; the more money that is spent to fund research on a disease, the more scientific

publications on that disease. Next, they examine how disease burden affects research funding. They find that diseases that predominantly affect high-income countries drive research priorities and that high income diseases tend to be overfunded relative to their disease burden (Vanderelst & Speybroeck, 2013).

Other studies examine the role that nanotechnology could have on reducing poverty. First, many studies question whether nanotechnology can decrease inequality and poverty. Cozzens et al. examine nanotechnology in the energy, water, and agri-food sectors. The authors find that there is some work on nanotechnologies that could benefit the poor, but the socio-technical system of many poor countries does not match the technology that was developed (S. Cozzens et al., 2013). Another study by Invernizzi discusses the role that nanotechnology will have on employment. She predicts that nanotechnology could increase inequality because many middle wage jobs will be destroyed by the nanotechnology revolution (Invernizzi, 2011).

Finally, there have been some bibliometric studies on NM (Chen & Guan, 2011; Wagner, Dullaart, Bock, & Zweck, 2006). These papers give a general overview of global NM trends, and they find that NM publications have grown exponentially grown over the past ten years. Chen & Guan go on to show that the USA, Germany, France, and Italy are world leaders in NM. China is a latecomer to NM research, but it is quickly growing in importance (Chen & Guan, 2011).

Conclusion

This dissertation draws upon disparate sources of knowledge in order to understand new phenomena. Nanotechnology has been hailed as an emerging technology that will have positive impacts on poor communities, but this assertion has not been fully

tested. This dissertation measures research inequality in NM and the role of PPPs in R&D for new medicines and vaccines. I use literature from a variety of disciplines, such as public administration, public health, and science policy. The public administration literature gives a foundation for my investigation of PPPs, and the public health literature helps me analyze DoP. From there, I add information about emerging technologies and nanotechnology from science policy. The next chapter reviews the data and methods of this dissertation.

CHAPTER 3: DATA SOURCES AND METHODS

Introduction

Scholars believe PPPs are necessary to develop medicines for DoP (Reich, 2000). Scholars reason that DoP do not have a large market and that pharmaceutical companies have little incentive to develop drugs for these illnesses since they will be unable to recoup research expenditures. As a result, governments, companies, and nonprofit organizations must partner together to develop medicines for these diseases.

In this dissertation, I analyze the extent of NM research for DoP and the role PPPs play in that research. For this analysis, I use secondary data analysis, bibliometrics, website content analysis, and interviews. The secondary data and the bibliometrics are used in the quantitative data analysis and the data comes from the WHO, Policy Cures, Bloomberg Finance L.P., the Institute for Health Metrics and Evaluation (IHME), WoS, PatStat, and PubMed. The website content analysis and interviews of scientists and PPP managers are used to inform the quantitative data and to describe the role of PPPs in DoP research.

In this chapter, I discuss the data collection methods and how I cleaned and analyzed the quantitative and qualitative data. I used a software program called VantagePoint to manipulate, clean and sort the bibliometric data, and then I used Stata and Excel to merge the data and statistically analyze it. For the website content analysis and interviews, I used a software package called Nvivo to code, sort, and analyze the data.

Data for Independent Variables

WHO and IMHE

In 2008, the WHO released statistics on the global burden of disease. The data gives information on BoD based on age, gender, and county income level. Later, IMHE released updated BoD estimation for 1990, 2005, and 2010. In this analysis, BoD is one of the major independent variables used to understand the relationship between BoD and NM publications and patents.

The 2008 WHO BoD dataset contains 136 diseases/injuries, and the updated IMHE dataset contains BoD data on 291 diseases/injuries and 1160 disease sequelae. The data has a variety of demographic information such as age, world region, and gender. Table 2 lists all the diseases used in the analysis. It contains all the illnesses from the 2008 WHO dataset, but excludes BoD statistics from injuries such as falls, automobile accidents, and war.

TABLE 2 LIST OF DISEASES USED IN THE ANALYSIS (*= DISEASE OF POVERTY)

Abortion	Hypertensive disorders	Other musculoskeletal disorders
Alcohol use disorders	Hypertensive heart disease	Other neoplasms
Alzheimer and other dementias	Inflammatory heart disease	other neuropsychiatric diseases
Appendicitis	Insomnia (primary)	other oral diseases
Ascariasis (roundworm)*	Intestinal nematode infections*	Other respiratory diseases
Asthma	Iodine deficiency	Otitis media
Benign prostatic hypertrophy	Iron-deficiency anemia	Ovary cancer
Bipolar affective disorder	Ischemic heart disease	Pancreas cancer
Birth asphyxia and birth trauma	Japanese encephalitis*	Panic disorder
Bladder cancer	Leishmaniasis*	Parkinson disease
Breast cancer	Leprosy*	Peptic ulcer disease
Buruli ulcer*	Leukemia	Perinatal conditions*
Cardiovascular diseases	Liver cancer (hepatic cancer)	Periodontal disease
Cataracts	Lower back pain	Pertussis*
Cerebrovascular disease	Lower respiratory infect. (pneumonia)*	Pneumonia*
Cervix uteri cancer	Lymphatic filariasis*	Poliomyelitis
Chagas disease*	Lymphomas, multiple myeloma	Post-traumatic stress disorder
Chlamydia	Macular degeneration and other	Prematurity and low birth weight
Cholera*	Malaria*	Prostate cancer
Chronic obstructive pulmonary dis.	Malignant neoplasms	Protein-energy malnutrition
Cirrhosis of the liver	Maternal conditions	Refractive errors
Colon/rectum cancer	Maternal hemorrhage	Respiratory diseases
Congenital abnormalities	Maternal sepsis	Respiratory infections
Corpus uteri cancer	Measles	Rheumatic heart disease
Cysticercosis*	Melanoma and other skin cancers	Rheumatoid arthritis
Dengue*	Meningitis	Rotavirus*
Dental caries	mental retardation, lead-caused	Salmonella enterica*
Diabetes mellitus	Migraine	Salmonella Infection*
Diarrheal diseases*	Mouth and oropharynx cancers	Schistosomiasis*
Digestive diseases	Multiple sclerosis	Schizophrenia
Diphtheria	Musculoskeletal diseases	Sense organ disorders
Drug use disorders	Neonatal infect. and other conditions*	Shigellosis*
Dysentery	Nephritis/nephrosis	Skin diseases
eaGGec*	Neuropsychiatric disorders	STDs excluding HIV
Echinococcosis*	Noncommunicable conditions	Stomach cancer
Edentulism	Nutritional deficiencies	Syphilis
Epilepsy	Nutritional/endocrine disorders	Tetanus
ETEC*	Obsessive-compulsive disorder	Trachea/bronchus/lung cancers
Fascioliasis*	Obstructed labor	Trachoma*
Giardiasis*	Oesophagus cancer	Trichuriasis (whipworm)*
Glaucoma	Onchocerciasis*	Trypanosomiasis*
Gonorrhoea	Oral diseases	Tuberculosis*
Gout	Osteoarthritis	Typhoid fever*
Hearing loss, adult onset	Other cardiovascular diseases	Unipolar depressive disorders
Hepatitis B	Other digestive diseases	Upper respiratory infections
Hepatitis C	Other genitourinary system diseases	Vitamin A deficiency
HIV/AIDS*	other malignant neoplasm	Yaws*
Hookworm disease*	Other maternal conditions	

One key independent variable I use in the analysis is disability adjusted life years (DALY). A DALY is a measure of BoD[1], and it equals *years of life lost* (YLL) plus *years lost due to disability* (YLD). See Equation 1 for mathematical explanation.

EQUATION 1 DISABILITY ADJUSTED LIFE YEARS CALCULATION

$$DALY = YLL + YLD$$

$$YLL = deaths * life\ expectancy$$

$$YLD = incidence\ rate * disease\ duration * weight\ factor$$

(Cooper, Osotimehin, Kaufman, & Forrester, 1998)

DALYs are a good measure of disease burden because they include both mortality rates and disability due to disease. There are several diseases that are highly disabling yet have low morality rates. If disease burden is only measured by mortality rates, then the impact of chronic disease on a person's wellbeing is underestimated. Another reason I use DALYs in this analysis is that it is a standard measure for disease burden (Murray et al., 2012), which makes it easier to compare my results with previous studies. Finally, DALY data is free, and it is one of the few health statistics with reliable global coverage.

Even though DALYs are a standard measure for disease burden, it has been criticized. Some scholars comment that DALYs are inaccurate because there is not enough information to generate DALY measurements for some diseases and countries. The extrapolation that scientists use to generate DALYs overestimates the severity of some diseases and discounts the importance of others. For example, one study estimates

[1] Another common measure used in health evaluations is quality adjusted life years (QALY). A QALY measures the health gains due to interventions (Mathers, Ezzati, & Lopez, 2007). DALYs and QALYs are calculated differently, and as a result, they emphasize different facets of health. Health professionals desire to maximize QALY and minimize DALYs (Gold, Stevenson, & Fryback, 2002). Since I am concerned with how much life is lost due to illness, I use DALYs in the analysis.

that DALYs underestimate ischemic heart disease by 27% due to a lack of accurate health records (Cooper, Osotimehin, Kaufman, & Forrester, 1998). Another criticism is that DALYs disadvantage the poor and those with less access to resources. A blind person in a poor country would face very different struggles than a blind person in a rich country; however, they would each have the same DALY. Similarly, some believe that disability weight assignments should not be constant across individuals. Even in the same country, individuals experience disabilities differently, and it is difficult to compare the pain across individuals (Anand & Hanson, 1997). Despite these criticisms, DALYs are one of the most accurate measures of disease burden.

Table 3 is an illustrative list of burden of disease measurements in DALYs.

In the analysis, there are two variables related to DALYs. First, I use the updated IHME 2010 DALYs (bod2010) to measure the disease burden. Secondly, I create a variable called *increase* to measure the difference in disease burden between 2005 and 2010. This variable will help me determine if scientists are focusing more on diseases that have an increasing or decreasing disease burden. Currently, there is no research that examines the change in disease burden in relation to R&D; as a result, this variable will help me explore the relationship between NM publications and the change in disease burden.

TABLE 3 DISEASES WITH HIGHEST WORLDWIDE DALY IN 2010

Disease	DALY	%Total
Ischemic heart disease	129,819,898	5.2
Low back pain	83,063,498	3.3
Malaria	82,685,191	3.3
Preterm birth complications	76,981,719	3.1
Chronic obstructive pulmonary disease	76,731,358	3.1
HIV/AIDS	66,599,553	2.7
Major depressive disorder	63,179,254	2.5
Hemorrhagic and other non-ischemic stroke	62,842,897	2.5
Neonatal encephalopathy	50,149,575	2
Tuberculosis	49,396,246	2
Diabetes mellitus	46,823,256	1.9
Iron-deficiency anemia	45,338,235	1.8
Sepsis and other infectious disorders of newborn baby	44,236,491	1.8
Ischemic stroke	39,389,407	1.6
Self-harm	36,654,294	1.5
Falls	35,385,079	1.4
Protein-energy malnutrition	34,874,497	1.4
Neck pain	33,640,233	1.3
Trachea, bronchus, and lung cancers	32,404,655	1.3

Diseases of Poverty

DoP are diseases that predominantly affect the poor. I compiled a list of DoP from three organizations: the WHO, BioVentures for Global Health, and Policy Cures. In Table 2, the diseases marked with a * are DoP. In this analysis, I test whether there is more NM research for non-DoP than DoP. In the regression analysis, I use a dummy variable *dop* to represent DoP. For more information on DoP, see Chapter 2.

G-FINDER

The Global Funding of Innovation for Neglected Diseases (G-FINDER) database is a free online database that contains funding information for 31 neglected diseases from over 50 countries and 240 organizations. For the past five years, Policy Cures, the organization that develops G-FINDER, surveyed public and private organizations to

understand the global flow of funding and resources for DoP R&D (Moran et al., 2011). The G-FINDER database contains data on a variety of metrics such as DoP R&D funding by disease, recipient organization, year, type of funding organization, and country. In the analysis, I use a variable called *hotdop* to represent global R&D interest in DoP.

USA Pharmaceutical Sales

The global pharmaceutical drug market is opaque and heterogeneous. Drug companies often do not report their exact medicine sale figures, and sometimes the figures that are reported do not match the reality (Clifford & Creswell, 2009; Simoens, 2011). Pharmaceutical companies donate medicine or use special formulas to determine the cost of medicine in a country, which alters the sales reports. As a result, it is difficult to aggregate medicine sales across companies and disease areas (Frank, 2001).

Despite the lack of data on global medicine sales, there is accurate data about USA drug sales. Bloomberg Finance L.P. collects information on pharmaceutical companies, medicine sales, and medicine pipelines. They also aggregate the data to report USA pharmaceutical sales across many disease categories. Bloomberg Finance L.P. is one of the largest financial data news corporations. It controls about "a third of the 16 billion global financial data market" (Clifford & Creswell, 2009).

Even though I am limited to USA medicine sales, I am able to understand many things about the world market from this limited dataset. USA medicine sales are a good proxy for originator drug firms' market. In 2000, the USA was 53% of the world's healthcare market (World Health Organization, 2004); other high-income countries, which have a similar disease profile as the USA, made up 36% of global pharmaceutical consumption (World Health Organization, 2004). Moreover, the USA is the most

innovative country for pharmaceutical development, so medicine sales and priorities in the USA can direct global markets. As one scholar says, "Emerging markets' emphasis on generic medicines coupled with European countries' price regulations means that U.S. consumers continue to provide originator firms with more revenue per person than consumers in other countries" (Blume-Kohout, 2012). As a result, I include USA sales in the analysis as a proxy for the market size for new and innovative medicines.

To find information on disease market size, I search for medicine sales of major illnesses in Bloomberg's drug database. Each disease search produces a list of applicable medicines that treat the disease and information such as the active molecule, manufacturer, sales volume, and sales in dollars for those medicines. I collected annual sales from 2006-present. Out of the 136 diseases in the WHO burden of disease data, Bloomberg has financial data for 58 diseases. In the regression analysis I use the variable *usasales2010* to represent 2010 USA sales.

Data for Dependent Variables

Web of Science

The dependent variables in this study come from three different databases: WoS, PubMed, and PatStat. WoS is a prominent scholarly publication database that indexes over 14,000 journals in natural sciences, social sciences, and humanities (Thomson Reuters, 2012). The database is used in numerous bibliometric studies, and scholars have developed tools to analyze scientific trends within WoS (Leydesdorff, Carley, & Rafols, 2013). The database has become such a central repository for scholarly work that pay structures, scientific research incentives, and science policy are based on whether an article is published in a WoS indexed journal (Weingart, 2005).

For this dissertation, I used a WoS nanotechnology database created by Arora et al. (2012). From 2000-2012, Arora et al. found 770,000 WoS nanotechnology articles. I then used a NM keyword strategy to extract all the NM articles from their database using the health keyword strategy in Table 4. There are about 81,800 NM articles from 2000-2012.

Moreover, I searched WoS for articles written or funded by formal PPPs. Details about this search are found in the PPP section below. The PPP search was used to compare NM research to PPP research.

PubMed

PubMed is a journal database that focuses on health and biomedical journals. It is run by the USA National Institutes of Health (NIH) (National Institutes of Health, 2013), and it indexes 5,600 journals from 1946 until the present. PubMed has several features that make it a good a database for this study. First, it is a free and easy to access comprehensive database of biomedical and health journals. Several other studies use PubMed as a database in their health-related bibliometric studies (Bonaccorsi & Daraio, 2003; Falagas et al., 2006). In addition, the NIH requires that all NIH-sponsored research be available on PubMed (National Institutes of Health, 2014). Since the NIH is the largest funder of medical research, PubMed is a major repository for biomedical research.

To find nanotechnology articles in PubMed, I used the same keyword search strategy created by Arora et al. (2012). I did my search on March 6, 2013, on all available fields. From 2000-2012, PubMed had 224,500 nanotechnology articles.

Once I had the nanotechnology articles from PubMed, I searched for the health articles using the same health keywords strategy that I used for the WoS search (the

keyword strategy is found in Table 4). There were 58,360 NM articles from 2000-2012 in PubMed.

PatStat

The European Worldwide Patent Statistical Database (PatStat) is an openly available database of worldwide patents. It has data from over 100 countries and contains about 60 million patent applications (EPO, 2011). PatStat is commonly used by other bibliometric studies, and it is one of the standard databases used in patent analyses (Hullmann & Meyer, 2003; Maclurcan, 2010b).

The nanotechnology patent database was created using the same search terms as Arora et al. (2012). I then used the health keyword strategy (Table 4) to find the NM patents. However, in addition to the keyword search, I searched for NM patents based on their International Patent Classification (IPC) code. I extracted articles with the IPC code A61. A61 is the patent classification for medical and hygiene patents. Within A61, I excluded veterinary patents.

Unlike the WoS and PubMed databases, PatStat has complete patent data only from 2000-2009. As a result, instead of using 2010 data for patents, I analyze 2009 patents. Using 2009 data does not introduce too much bias into the results because there is a high data correlation between the years. For example, the correlation between 2009 and 2008 patent data is 0.98. PatStat only has 13,000 NM patents, while WoS has 81,812 and PubMed has 58,630 NM articles. Despite the differences in size, NM still represents 13% of the nanotechnology patent database. In comparison, NM is 11% of the nanotechnology WoS database. Figure 1 shows the number of NM articles in all three databases from 2000 until 2012. In general, there is a steady exponential growth in the

number of NM publications and patents. In addition, the graph shows that there are significantly more publications than patents for each year.

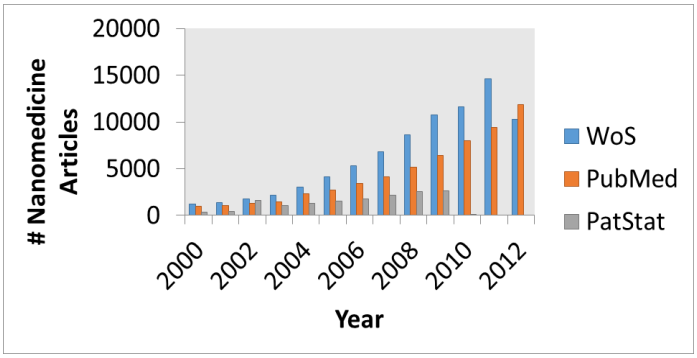

FIGURE 1 NM PUBLICATIONS IN WEB OF SCIENCE, PUBMED, AND PATSTAT

Comparison Group

In order to better understand the nature of NM R&D, I compare it to a random set of WoS publications from 2009 and 2010. The 2009 articles were given to me directly from Thompson Reuters (the owners of WoS), and I generated a random set of 2010 articles by downloading all the articles that had the randomly generated number 29 in the digital object identifier (DOI). There were 40,000 random articles in 2009 and 1,376 in 2010.

Methods

Health Keyword Strategy

My search strategy for NM was similar to many other nano/bio bibliometric studies (Chen & Guan, 2011; A. Porter, Youtie, Shapira, & Schoeneck, 2007). To create the search keywords, I first developed a large list of keywords that could possible generate NM articles by reviewing highly cited NM articles (Invernizzi, 2006; Wagner et al., 2006). Then, I removed the keywords that generated fewer than 100 articles and

keywords that did not contribute any unique articles. This step ensured that the keywords are encompassing and generate "a sizable quantity of articles" (A. Porter, Youtie, Shapira, & Schoeneck, 2007). By removing these keywords, I reduced the number of keywords in my search strategy from about 150 phrases to 29 phrases while only losing 5% of the articles.

Next, I verified the accuracy of each keyword by testing if it generated relevant NM articles. Each keyword had to correctly identify 70% of the articles as NM in order for it to stay in the search strategy. In general, 70% keyword accuracy is a benchmark used by other bibliometric scholars (as discussed in personal correspondence with Alan Porter). For example, two inaccurate keywords were *health* and *surgery*. Though these keywords appear to be closely related to medical articles, they generate a lot of non-medical research. Additionally, I edited several keywords so that they would be more specific. For example, I edited "dental" so that it excluded articles that contained "accidental" but did not have any relationship to health.

In each iteration of the search strategy, I asked a NM expert to verify that the search generated NM articles. I gave the NM expert a random set of papers from my search, and she classified them as NM. She also gave a brief explanation of why the paper was or was not NM. Through this process, I further refined and removed words to better reflect the actual NM literature. For example, in the first set of nanotechnology searches, I included words like *toxicology*. After talking with the expert and reading various definitions of NM, I realized that nanotechnology toxicology studies are not considered NM. As a consequence, I narrowed my results to exclude nanotechnology toxicology reports.

After I developed the keyword strategy, I used it to search the nanotechnology databases I previously created in WoS, PatStat, and PubMed. Table 4 contains the final list of health keywords that I used in search.

TABLE 4 HEALTH KEYWORD SEARCH TERMS

alzheimer	dental	neuron
anemia	disease	orthopedic
antibiotic	dopamine	pharma
antitumor	drug	physiological
blood	HIV	skin
brain	insulin	therapeutic
cancer	liver	tissue
cholesterol	measles	vaccine
clinic	medicine	wound

Disease Search Strategy

Next, I developed a set of keywords to find specific diseases within NM publications and patents. I used the WHO BoD study as a list of the world's major illnesses (see Table 2). Then, I looked for alternative names for each disease in WebMD to make the search robust. In general, most diseases had unique names; therefore, they were easy find and code in the database. However, it was difficult find keywords to classify some illnesses such as obstructed labor or maternal hypertensive disorders. From the list of diseases, I built a thesaurus to search the NM database (see Appendix A for the list of disease search terms). About 24,500 NM articles, or about 30%, related to a specific disease. The other 70% of articles relate to healthcare, but they cannot be associated with a specific disease.

PPP Search and Analysis

My first set of hypotheses examined the role that formal PPPs play in NM. My hypothesis was that formal PPPs are major actors in DoP NM research because other studies found that 75% of DoP research was conducted by formal PPPs. However, as described in Chapter 4, very few PPPs did research on nanotechnology. As a result, I compared PPP and NM research by asking several different types of questions. For example: Are they focusing on different diseases? Is the research concentrated in different areas of science? To compare PPP and NM research, I first created a list of formal health PPPs from Policy Cures and the broader literature on PPPs. Then I downloaded all the articles written by formal health PPPs in WoS[2]. Overall, I searched for articles from 28 different formal PPP organizations in WoS. Table 5 lists all of the PPPs that I used in this study.

[2] For this part of the analysis, I did not use PatStat and PubMed. I could not use PatStat because I did not have access to the database. I did not use PubMed because many of the analysis tools in this study are only available for WoS.

TABLE 5 LIST OF FORMAL HEALTH PUBLIC-PRIVATE PARTNERSHIPS

List of formal PPPs	
Aeras	International AIDS Vaccine Initiative (IAVI)
BuruliVacConsortium	International Partnership for Microbicides (IPM)
Consortium for Parasitic Drug Delivery	International Vaccine Institute (IVI)
Drugs for Neglected Diseases initiative (DNDi)	Malaria Vaccine Initiative (MVI)
European Vaccine Initiative (EVI)	Medicines for Malaria Venture (MMV)
European and Developing Countries Clinical Trials Partnership	Meningitis Vaccine Project (MVP)
European Solutions Enterprise on Neglected Diseases	Novartis Institute for Tropical Diseases
Foundation for Innovative New Diagnostics (FIND)	OneWorld Health (OWH)
Global Solutions for Infectious Diseases	Program for Appropriate Technology in Health (PATH)
Global Alliance for TB Drug Development (TB Alliance)	Sabin Vaccine Institute
Global Alliance for Vaccines and Immunisation	The Vizier Project
Global HIV Vaccine Enterprise	TI Pharma
Infectious Disease Research Institute (IDRI)	TuBerculosis Vaccine Initiative (TBVI)
Innovative Vector Control Consortium (IVCC)	WHO: Special Programme for Research and Training in Tropical Diseases (WHO/TDR)

Once I had the PPP and NM databases, I conducted several analyses to compare the two sets of articles. First, I compared NM and PPP articles to determine if they focus on different diseases and subject areas, and if they utilize disparate sources of knowledge. Second, I mapped each population's research to determine the relationship between scientific fields and sub-disciplines based on factors such as co-authorship and citation patterns. These maps were made using the protocol described by Rafols et al. (Rafols, Porter, & Leydesdorff, 2010).

Then, I calculated the integration and specializations score of the PPP articles and NM articles. The integration score describes the breadth of knowledge that is used to write an article. If the authors use a variety of articles from very disparate fields to write a paper, then the paper will have a high integration score. However, if the author does not

cite papers from other disciplines, then the paper has a low integration score because it only draws knowledge from a narrow set of fields. Integration scores are calculated using the citations from each article (A. L. Porter & Rafols, 2009). Equation 2 shows how to calculate the integration score. S_{if} is the cosine similarity matrix between two different subject categories and P_i is "the proportion of references citing the subject category *i* in a given paper" (A. L. Porter & Rafols, 2009)

EQUATION 2 CALCULATING INTEGRATION SCORE

$$I = 1 - \sum_{i,j} s_{ij} p_i p_j$$

The specialization score measures the diversity of a group of articles based on where they are published. If a scientist publishes articles in journals ranging from economics to nuclear physics, then the scientist is not specialized. However if a scientist only publishes in journals in one narrow field, then that scientist is very specialized. Specialization is another way to describe the interdisciplinarity of a set of papers spanning fields, and it shows the potential influence of a set of paper. Interdisciplinarity is important because many scholars believe that the most innovative scientific discoveries occur at the boundaries of traditional disciplines (Hollingsworth, 2008; Moed et al., 2005). Equation 3 shows how to calculate the specialization. The equation to calculate specialization is very similar to the equation to calculate integration, but instead of using the subject categories of the cited journals, specialization uses the proportion of subject categories for the journals in which the articles are published.

EQUATION 3 CALCULATE SPECIALIZATION

$$S = 1 - \sum_{i,j} s_{ij} p_i p_j$$

The results of the integration and specialization score analysis are found in Chapter 4.

Qualitative Data

As I analyzed the quantitative analysis, I simultaneously collected and analyzed qualitative data. The qualitative data comes from two main sources; first, I examined the websites of the formal PPPs, and second, I conducted semi-structured interviews of PPP scientists and managers. Traditionally, a website is one of the main information portals of a PPP; as a result, a PPP would put a lot of relevant information on the website that I could not obtain during an interview. For example, most of the websites discuss how the organization was founded, but many interviewees did not know the history of their organization. A weakness of using a PPP website is that it provides a narrow image of the organization. PPPs design their websites to portray their organization favorably, so it is unlikely that the websites will discuss the failures of the PPPs. Also, the websites will not provide information on topics that are not central to the mission of the organization. Therefore, subjects such as NM do not appear on most PPP websites. For each website, I downloaded the relevant text and uploaded it to Nvivo (qualitative data management software) to be coded and analyzed. I followed standard content analysis procedures in order to extract the necessary information (Krippendorf, 1980). For more information on my coding procedures, see Table 7.

The interviews help offset the deficits of the websites and allow me to triangulate my information from two types of sources. I selected my interview participants through a variety of purposive sampling techniques. First, I identified major PPPs involved in drug research for neglected diseases. Policy Cures maintains a comprehensive list of these organizations, and I contacted all 28 of them for interviews. I tried to interview executives and managers at the various PPPs, but sometimes I spoke with media/public outreach officials. I also interviewed scientists that partnered with PPPs. To schedule an interview, I sent all the active PPPs emails requesting an interview, and I directly called several of them. Appendix B shows a sample of the email contact letter and the letter outlining the participants' rights, and Table 6 shows the response rate of interviews. I conducted 14 interviews of managers/scientists of 10 PPPs and 3 universities. My overall response rate was 34%, but the response rate of the PPPs was slightly higher at 41%. I interviewed 10 out of the 24 current PPPs. Four of the 28 PPPs are either defunct or they merged with another organization. The few PPPs that declined the interview stated that their organizations did not conduct research, and as a result, they did not feel their opinion would be useful for the dissertation.

TABLE 6 RESPONSE RATE FOR EMAIL INTERVIEW REQUESTS

# of requests	# of interviews	# of PPPs interviewed	Overall Response Rate
41	14	10	34%

There are some non-response biases associated with this study because the individuals who participated in the interviews have different characteristics from the participants who did not respond to the interview requests. One source of non-response bias is that I was not able to interview Asian-based PPPs. Rather, I interviewed ten

people at American PPPs and five people at European PPPs. Although the study would be stronger if I interviewed an Asian-based PPP, there are only two Asian PPPs, and therefore, the non-response is not severe. Another non-response bias is that none of the PPP founders agreed to an interview. The PPP founders could have a different perspective on PPPs compared to scientists and senior executives, and as a consequence, there is a potential for biased results.

I checked for other possible non-response biases, and there is no evidence that the study suffers from any others. I interviewed PPPs that focused on a variety of diseases such as TB, Malaria, HIV/AIDS, buruli, and leishmaniasis, and I interviewed managers at both large, globally renowned PPPs and smaller PPPs. I also interviewed both scientists and communications specialists, which allowed me to get opinions across job descriptions. Finally, I interviews scientists and managers who work at old and new PPPs.

I conducted 30-minute to 1-hour semi-structured interviews. Table 8 gives a list of the interview questions. I recorded and transcribed all the interviews and uploaded them into Nvivo for analysis. Table 7 shows the coding scheme used on the qualitative data. The initial codes were developed based on the major themes of the dissertation, and they covered a variety of topics such as the research funding and R&D portfolios of the PPPs. As new themes arose in the qualitative data, more codes were added to the project. The recording units for the analysis are sentences and paragraphs because it allows the codes to capture the whole idea of the particular portion of text.

Table 7 Codes for qualitative data

Codes	Code Explanation
Disease of poverty	Any mention of a disease of poverty
Diseases	Any mention to a non-DoP
Drug Delivery	Any mention to drug delivery systems
Funding	information on who funds the PPP or how much money they have
Future	any reference to the future (i.e. the future of the PPP or DoP research)
Governance	Information on the governance structure of the PPP
History	History/origins of the PPP start?
International	Any mention to countries working with PPP
Model	Explanation of the PPP model and why it is important
Nanotechnology	Any reference to nanotechnology
Partners	Who is the PPP working with?
Portfolio	Information on the research projects
Publishing/patenting	Information on publishing and patenting habits of organization or researcher.
Scientist	Any reference to a specific researcher
Sensors	Any reference to sensor technology
Skills	Mentioning a specific skill of scientists or the PPP

Table 8 Interview questions

Interview Questions	
Introduction/ Background	What is your background? What do you do within your organization? Give a brief overview of your organization?
Research/ Focus	What is your research? Who funds your research? How did you choose your research area? What are some successes you have had in your research? Who are your research partners? How long have you been working in this area? What types of project will you do in the future?
Nanomedicine	Are you doing any work in NM? Why (or why not) are you doing work in NM? Do you think NM is useful for DoP?
PPP	Do you consider your organization a public private partnership? If so why? What is the structure of your PPP? Who funds the PPP? Where do PPPs fit within research and drug discovery? Are PPPs necessary to find medicines for diseases of poverty? How does your organization use patents, and publications? How does your PPP choose its research foci? Do you think PPPs are the new normal for drug development Do you collaborate/talk with other PPPs? All PPPs seemed to spring up at the same time. Do you have any clues why?
DoP	In your opinion what are the most problematic diseases of poverty? What research areas are necessary to reduce the burden of disease from diseases of poverty?

Data Analysis

As mentioned before, I used several different types of software to analyze the data. To sort, clean and search the bibliometric data, I primarily used VantagePoint, which is a text mining software that specializes in organizing and analyzing text based data. Within VantagePoint, created search thesauri, filtered the R&D to relevant topics, and cleaned the data so that I could verify that authoring institutions. I also used several macros to calculate the integration and specialization scores of the various datasets. After cleaning and sorting the data in VantagePoint, I exported the data to Microsoft Excel and Stata for further analysis.

For the analysis, I did a 2010 cross sectional analysis of NM. I chose 2010 because nanotechnology had at least 10 years to develop as a field. Scholars had time to fund, complete and publish their research results in WoS indexed journals. As a result, I can better assess NM as a field. In addition there is accurate 2010 BoD and USA medicine sales data. The fidelity of the data gives the analysis more power.

Regression Techniques

The dependent variables in this analysis, the number of publications and patents per disease area, are count data that have Poisson distributions. Therefore, I use Poisson regression techniques as opposed to ordinary least squares regression to analyze the data (Coxe et al., 2009). Figure 2 shows the distribution of the WoS 2010 NM data. Most of the disease areas are associated with very few articles and therefore the density of articles is close to 0 publication. However, there are a few diseases, such as breast cancer, that have many publications and extend the tail of the table.

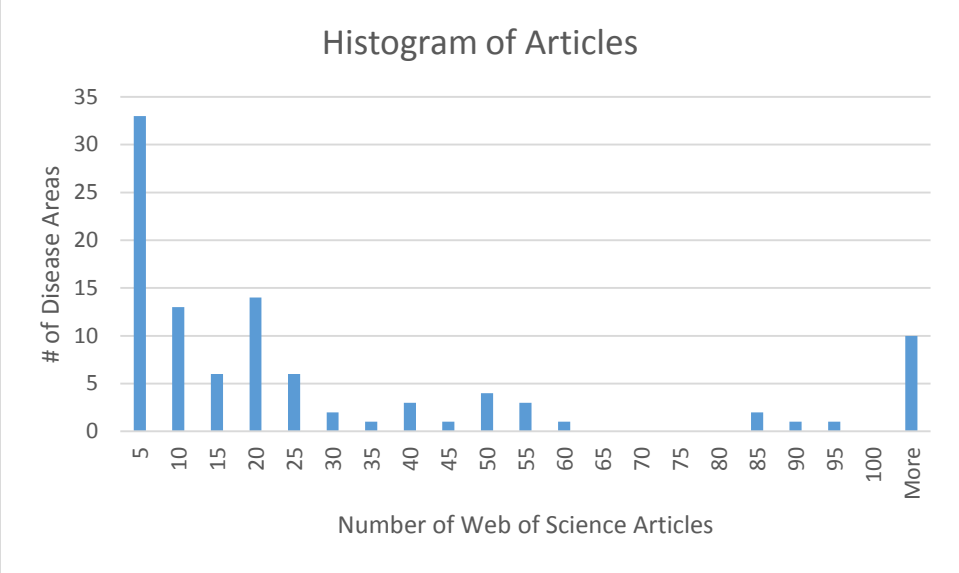

FIGURE 2 DISTRIBUTION OF 2010 WEB OF SCIENCE NM DATA

The Poisson distribution is given by Equation 4. It "gives the probability of observing a given value, y, of variable Y" where μ is the mean of the number of publications/patents (Coxe et al., 2009). The typical regression model takes the form of Equation 5.

EQUATION 4 POISSON MASS DISTRIBUTION FUNCTION

$$P(Y = y|\mu) = \frac{\mu^y}{y!}e^{-\mu}$$

EQUATION 5 TYPICAL REGRESSION MODEL WITH POISSON DISTRIBUTION

$$\ln(\hat{\mu}) = b_0 + b_1 * x_1 + b_2 * x_2 + \cdots + b_p * x_p$$

One major assumption in Poisson models is that the mean and variance of the dependent variables are equal. If they are not equal, as in this case, scholars recommend using negative binomial regression models (Coxe et al., 2009). Table 9shows the mean and variance for the various dependent variables in this study.

Another assumption with Poisson analyses is that the dependent variables do not have excessive zeroes due to a secondary process. For example, if I modeled the number

of patents made by a scientist, the analysis could suffer from excess zeroes because some scientists never patent a technology. Therefore in this type of analysis, I first have to find the probability of a scientist patenting research (a logistic regression) and then I can use the Poisson analysis to test the probability that a scientist has more than 0 patents. This type of regression is called a zero inflated negative binomial regression. For this analysis, I find that the data is not zero inflated so I do not have to run a zero inflated negative binomial regression.

TABLE 9 MEAN AND VARIANCE FOR THE DEPENDENT VARIABLES

	Mean	Variance
WoS 2010	22.79	296,998.00
PubMed	17.18	1,351.48
PPP	6.28	309.68
PatStat	1.42	17.50
Comp09	55.36	7,519.69
Comp10	3.58	59.41

An example of the regression equation I use in this analysis is given by the following equation:

$$ln(wos2010) = b_0 + b_1*usasales2010 + b_2*bod2010 + b_3*increase + b_4*dop + e$$

Limitations

Even though bibliometric analyses have become standard practice, this research method has limitations. First, journal databases such as WoS and PubMed tend to have more journals in English and from rich countries. This means that I am are more likely to bias the analysis in favor of English speaking, western countries (UNESCO, 2005). Also many of these diseases in this study are regionally confined to developing countries and

so research on these diseases may not be published in broad, globally focused journals that are indexed in WoS and PubMed.

In addition to the limitations of the patent and publication datasets, the burden of disease statistics has limitations. As discussed before, it is difficult to collect accurate disease burden statistics for very poor countries, which means that the disease burden statistics for developing countries may not be as accurate as the data for rich countries (Murray et al., 2012). Also the burden of disease in developing countries could be underestimated because individuals in poor nations do not see doctors at the same rate as rich countries. In a poor country, people may only see the doctor in the most severe life threatening cases and therefore, chronic illnesses such as back pain, and Alzheimer's would be left undiagnosed and not counted in the national disease burden statistics (Murray et al., 2012).

There are also limitations with USA medicine sales data. The medicine market is very opaque and it is hard to track global sales. Companies often do not report drug sales for specific medicines and there are a variety of pricing structures that vary between countries (Frank, 2001; Simoens, 2011). For example, pharmaceutical company may donate the medicine or negotiate special pricing structures for poor nations. The data limits the conclusions I can draw from the results. Another issue with USA medicine sales is that it covers a limited number of diseases. The database used to track medicine sales, Bloomberg Financial L.P., does not track medicine sales for many diseases such as neonatal infections and so my regression analysis with USA medicines sales have fewer observations. The lack of data limits my ability to run regression analyses with that variable.

The second part of the analysis consisted of qualitative data analysis of websites and interviews. I collected website data from 28 different PPP, but I was only able to conduct 14 different phone interviews spanning 10 different PPPs. Like many methods, there is a potential non-response bias. The answers of those that were interviewed may be different than the individuals that chose not to be interviewed. Fortunately, from examining websites, I could triangulate the correct information from a variety of sources.

Conclusion

This chapter summarizes the data and methods that I use for this dissertation. The data sources can be divided into two broad types of data. First I use quantitative data to analyze publication patterns of NM research. I use data from Bloomberg L.P., the WHO, G-FINDER, WoS, PubMed, and PatStat. Then I use negative binomial Poisson regression analyses to determine the relationship of the USA medicine sales, disease burden and PPP R&D investment with NM publications and patents.

The qualitative data was from formal PPP websites and interviews. I conducted 14 semi-structured interviews of different scientists and PPP managers and I analyzed 28 different PPP websites. From this data, I can better understand the purpose of PPPs and their role in R&D for DoP. The next chapters give the results of my analyses.

CHAPTER 4: QUANTITATIVE ANALYSIS RESULTS

Introduction

This chapter summarizes the findings from the quantitative analysis. The chapter begins by summarizing the main research questions and hypotheses. Then, I discuss the descriptive statistics and correlation matrix of the different variables and review the results from the negative binomial regression. Finally, I discuss the finding from the comparison between PPP and NM research.

Research Questions

I have several research questions and hypotheses that I am testing for this dissertation. First, I am investigating how USA medicine sales, disease burden and DoP relate to the number of NM publications and patents. The questions and hypotheses are below:

Q1.1: Do diseases with high USA medicine sales have more NM R&D than diseases with low medicine sales?

H1:1 High USA medicine sales for a disease are associated with more NM publications and patents for that disease.

Q1.2: Does disease burden for a specific disease correlate with the amount of NM research and development for that disease? Do diseases with growing disease burden receive more research attention?

H1.2a: Diseases with high burden of disease have more NM publications and patents.

H1.2b: Diseases that have increasing disease burden have more publications and patents.

Q1.3: Is there less NM research for DoP than other diseases?

H1.3a: There are fewer NM publications and patents on DoP compared to other diseases, controlling for medicine sales and disease burden.

H1.3b: DoP with more PPP funding (hotdop) have more NM publications and patents than other DoP with less PPP funding.

My second research question examines how public private partnerships affect research on disease of poverty in NM. The literature suggests that pharmaceutical companies neglect DoP because the companies cannot recoup their R&D expenses from selling medicines for DoP. As a result, medicines are not developed for many diseases that have large disease burdens (Kremer, 2002).

Many scientists propose that public private partnerships (PPPs) could fix this gap because these organizations have different motivations and incentives than pharmaceutical companies. PPPs bring together government, private, and non-profits in order to tackle a specific problem. Over the past few decades, PPPs rose in prominence, and more recently, health PPPs and product development partnerships (PDPs) have become more important in this area.

Given the importance of PPP in DoP medical research, I assumed that PPPs would play a prominent role in NM PPP research. My original hypothesis was:

H2.1: NM DoP research is more likely to be conducted by formalized PPPs than other organizations, controlling for variables such as drug sales, disease burden and whether the illness is a disease of poverty.

However, this hypothesis is not supported by the data. There are very few PPPs publishing or patenting NM research even though there is significant research on DoP with NM. In WoS less than 100 out of 81,200 articles were funded or authored by scientists at PPPs. But, if PPPs are not doing DoP NM research, then who is conducting this research? What organizations and research labs are studying NM for DoP? Moreover, what type of research are formal PPPs doing and is it different than NM researchers? Are they working in the same field? Are they drawing upon the same sources of knowledge (integration)? Are they publishing in the same journals (specialization)? I analyzed PPP and NM research articles from WoS in order to understand the similarities and differences between these two populations.

H2.2: PPPs' publications focus on different diseases than NM publications.

H2.3: PPPs' publications focus on different fields and sub disciplines than NM publications.

H2.4: PPPs partner with different organizations than NM researchers.

H2.5: PPP publications have lower integration scores than NM publications.

H2.6: PPP publications have higher specialization scores than NM publications.

Descriptive Statistics

For this analysis, there are six dependent variables. The first three dependent variables are the number of 2010 NM publications in WoS (*wos2010*), the number of 2010 NM publications in PubMed (*pubmed2010*) and the number of 2009 NM patents in PatStat (*patstat2009*)[3]. The fourth dependent variable is the number of 2010 articles

[3] The last complete year of patent data is 2009 and as a result I have to use 2009 data for this analysis

written or funded by PPPs in WoS *(ppp2010)*. Finally, the last two dependent variables are the number of medical articles in the 2009 and 2010 comparison groups (*comp09* and *comp10*).

There are five independent variables for this study: *bod2010, increase, usasales2010, dop,* and *hotdop*. Table 10 lists all the variables and Chapter 3 gives more details about each of the variables.

TABLE 10 LIST OF VARIABLES

wos2010	Number of NM publications in Web of Science in 2010
pubmed2010	Number of NM publications in PubMed in 2010
patstat2009	Number of NM patents in PatStat in 2009
ppp2010	Number of research articles in Web of Science by public private partnerships in 2010
comp09	Number of medical articles in 2009 comparison group
comp10	Number of medical articles in 2010 comparison group
bod2010	2010 disability adjusted life years of disease x (in millions of DALY)
increase	Difference in DALY between 2010 and 2005
usasales2010	USA medicine sales for a particular disease in 2010 (in $million)
dop	Is the research about a disease of poverty? 0=no, 1=yes
hotdop	Amount of Funding from PPPs in 2010 (in $million)

Table 11 shows the descriptive statistics of the variables and it reports the number of observations, the mean, standard deviation and range of the variables. Each observation represents a different disease. The third column reports the mean number of publications and patents per disease area. On average there are more disease-specific WoS NM articles (22.79) than PubMed articles (17.18). PatStat has the fewest disease-specific articles per disease area with an average of only 1.42. The range articles/patents for each dependent variable is also varied. WoS has a large range, 0 to 443, while the range for the PatStat data is only 0 to 42 patents.

Another interesting observation about that data is that the WoS and PubMed databases have more nanotechnology publications associated with the a disease than PatStat; 4.5% of nanotechnology articles in WoS and 9.6% of nanotechnology articles in PubMed publications are disease specific while only 1.2% of NM patents are disease specific (see Table 12). This is unexpected considering that patents are more closely associated with an end product while publications are more associated with basic research.

The patent database is much smaller than the WoS and PubMed databases. In 2010 there were 91,000 nanotechnology articles in WoS and only 23,000 nanotechnology patents. Despite the differences in size, about the same proportion of articles or patents (12%), are NM. In PubMed about 27% of the articles are NM (See Table 12).

TABLE 11 SUMMARY STATISTICS OF DEPENDENT AND INDEPENDENT VARIABLES

Dependent Variables	# Observation	Mean	Std. Dev.	Min	Max
Number of NM publications in PubMed in 2010 (pubmed2010)	130	17.18	36.76	0	249
Number of NM publications in Web of Science in 2010 (wos2010)	130	22.79	54.50	0	443
Number of NM patents in PatStat in 2009 (patstat2009)	130	1.42	4.18	0	42
Number of articles in Web of Science by public private partnerships in 2010 (ppp2010)	130	6.37	17.56	0	127

Independent Variables	# Observation	Mean	Std. Dev.	Min	Max
2010 disability adjusted life years of disease x (in millions of DALY) (*bod2010)*	98	63.17	93.46	0.02	519
Difference in DALY between 2010 and 2005 (*increase*)	98	-2.09	13.38	-75	27
USA medicine sales for a particular disease in 2010 (in $million) (*usasales2010)*	63	3475.64	4764.64	0.06	19,525
Is the research about a disease of poverty? 0=no, 1=yes (*dop*)	130	0.23	0.42	0	1
Amount of Funding from PPPs in 2010 (in $million) (*hotdop)*	30	93	234	0	1,070

The independent variable 2010 burden of disease (*bod2010*) has a large range (see Table 11). The illness with the highest disease burden in the world is ischemic heart disease. It caused 519 million DALYs in 2010 and it is growing in severity (Murray et al., 2012). The average burden of disease in 2010 is 63.17 million DALYs. This is lower than the 2005 burden of disease by 2.09 million DALYs. This means that the average severity of the diseases in the dataset decreased from 2005 until 2010.

Another independent variable, *USAsales2010,* also has a large range. That data was collected from Bloomberg Finance L.P. and it represents the 2010 USA medicine sales for different diseases. The disease with the highest 2010 USA medicine sales is

unipolar depression disorders with $19.5 billion and the average 2010 USA medicine for a particular disease in the dataset sales is $3.5 billion. However, as stated before, there are only sales data for 63 disease areas. Finally, the last variable, *hotdop*, tracks the amount of PPP funding for DoP in 2010. This data comes from Policy Cure's G-FINDER database and it only measures funding for DoP. Each of the 30 DoP received an average of $93 million worth of funding from PPPs.

Table 12 compares WoS nanotechnology articles to the comparison groups. The comparison groups have higher percentages of health articles, disease specific articles and DoP related R&D than the nanotechnology database. For example in 2009, 33.1% of the articles in the comparison group are related to health while only 12.7% of the nanotechnology articles in WoS are related to health. Moreover in 2009, 2.1% of articles in the comparison group relate to DoP while only 0.3% of WoS nanotechnology articles relate to DoP. I was not able to run a statistical test on these results, but it appears that nanotechnology is less focused on medical issues and DoP than overall scientific research.

TABLE 12 COMPARISON OF INDEPENDENT VARIABLES

	wos2010	pubmed2010	patstat2009	ppp2010	Comp09	Comp10
total publications	91,301	29,853	22,837	734	40,000	1,376
total health	11,625	7,998	2,645	614	13,247	677
total disease	4,099	2,853	285	540	6,546	418
total DoP	301	248	14	452	850	28
% health	12.7%	26.8%	11.6%	83.7%	33.1%	49.2%
% disease specific	4.5%	9.6%	1.2%	73.6%	16.4%	30.4%
% DoP R&D	0.3%	0.8%	0.1%	61.6%	2.1%	2.0%

Table 13 is an illustrative list of diseases and some of their statistics. This chart gives a small snapshot of the dataset. For example, ischemic heart has a very high disease burden, but it does not have as many publications as cancer and periodontal disease. The research gap is even more apparent when comparing breast cancer and meningitis. The disease burden for both these diseases is about 50 million DALYs, but breast cancer has 50 times more publications than meningitis.

TABLE 13 STATISTICS FOR PROMINENT DISEASES

Disease	2010 Burden of Disease (*Bod2010*)	2010 NM publications in WoS (*Wos2010*)	2010 NM publications in PubMed (*PubMed2010*)	2009 NM patents in PatStat (*Patstat09*)	2010 USA medicine sales (*USAsales2010*)	2010 Bod minus 2005 BoD (*increase*)	Do P
Ischemic heart dis.	519.28	82	44	0	6117.28	12.27	
Malaria	330.74	39	38	0	194.54	-74.75	x
HIV/AIDS	326.19	93	99	5	6753.76	-59.14	x
tuberculosis	197.58	51	33	3	0.06	4.32	x
Asthma	89.84	32	21	2	15165.83	2.93	
Diarrheal diseases	87.66	48	27	2	233.09	-13.46	x
Meningitis	52.75	8	4	0	78.06	-0.55	x
Breast cancer	48.07	443	249	6	13857.14	2.94	
Alzheimer and other dementias	45.40	150	118	9	5462.21	7.09	
Periodontal disease	21.64	212	153	42	564.78	2.19	
Tetanus	18.65	8	3	0	1219.76	-9.33	x
Prostate cancer	15.15	160	80	4	2120.74	1.69	

Table 14 shows the correlation matrices of the dependent and independent variables. In this table there is a high correlation (0.96) between WoS (*wos2010)* and PubMed (*pubmed2010*) NM publications. The high correlation shows that both WoS and

PubMed have similar information. WoS and PubMed should have similar patterns because there is a large overlap between the biomedical journals in PubMed and WoS (Falagas et al., 2006).

TABLE 14 CORRELATION MATRIX OF VARIABLES

	Wos2010	Pubmed2010	patstat09	Ppp2010	comp09	comp10	daly10	dop	usasales2010	increase	hotdop
Wos2010	1.00										
Pubmed2010	0.96	1.00									
patstat09	0.58	0.64	1.00								
ppp2010	0.10	0.13	0.04	1.00							
comp09	0.79	0.78	0.34	0.16	1.00						
comp10	0.88	0.84	0.61	0.02	0.84	1.00					
daly10	0.07	0.10	-0.02	0.39	0.31	0.14	1.00				
dop	-0.12	-0.14	-0.13	0.37	-0.19	-0.19	-0.07	1.00			
usasales2010	0.16	0.11	-0.07	-0.11	0.36	0.21	0.18	-0.20	1.00		
increase	0.03	0.00	0.04	-0.69	0.05	0.13	-0.26	-0.25	0.19	1.00	
hotdop	0.12	0.18	0.05	0.81	0.17	0.02	0.40	0.33	-0.02	-0.67	1.00

Another important observation from Table 14 is that there is a lower correlation between patent and publication databases. The correlation between PatStat (*patstat09)* and WoS (*wos2010)* publications is only 0.58 and the correlation between PatStat and PubMed is 0.64. The lower correlations between the databases is not surprising since publication and patents measure different aspects of the R&D process. In general, publications are associated with basic research while patents represent R&D that has a market potential (Moed et al., 2005). Finally, there is very little correlation between articles published by PPPs in 2010 (*ppp2010*) and the other datasets. This is expected since the articles published by PPPs in WoS focus almost exclusively on DoP.

Table 14 also shows the correlations for the independent variables. Overall, the independent variables are not highly correlated. The variables with the highest correlation (0.92) are the 2010 burden of disease (*bod2010)* and 2010 PPP funding (*hotdop)*. This

shows that a high burden of disease is associated with more PPP funding. Another set of variables that are highly correlated are 2010 PPP funding (*hotdop*) and the difference in disease burden from 2005 until 2010 (*increase)*. These variables have a large negative correlation (-0.88) which means that PPPs tended to fund research on diseases with decreasing disease burden. Finally, the large positive correlation (0.8) between 2010 USA medicine sales (*usasales2010*) and 2010 PPP funding (*hotdop*) shows that PPPs tend to fund research on disease areas that have high USA medicine sales.

Question 1: Regression Model

Figure 3 summarizes the research questions. The first research question investigates the relationship between USA medicine sales and R&D for NM. USA medicine sales are a good proxy for near-term market for originator firms. Originator firms are primarily responsible for developing new, patented protected medicines (Blume-Kohout, 2012). By examining USA sales I can determine whether the market for originator firms has any impact on NM R&D. Hypothesis 1 tests if higher medicine sales in the USA (*usasales2010*) are associated with more NM publications (*wos2010*) and patents (*patstat2009*).

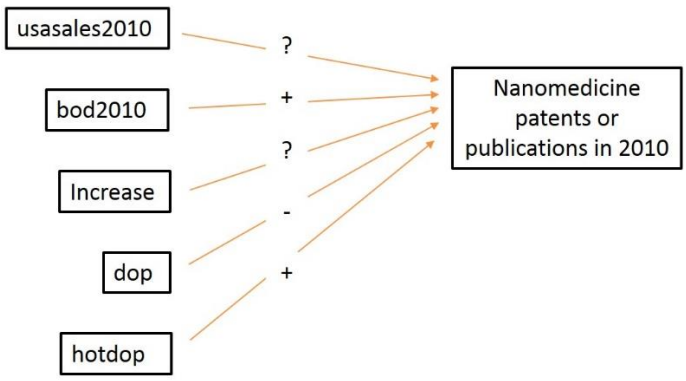

FIGURE 3 REGRESSION MODEL

The next two hypotheses test the relationship between burden of disease and NM R&D. I hypothesize that diseases with higher burden of disease (*bod2010)* have more NM publications (*wos2010* and *pubmed2010*) and patents (*patstat2009)* and that diseases that had increasing disease burden from 2005 until 2010 (*increase*) have more NM publications and patents. The relationship between the increasing disease burden and publications/ patents is less clear because there are not studies that examine the change in disease burden with patents and publications.

Finally, I tested if there is more R&D for DoP than non-DoP. I included a dummy variable, *dop,* in the model that tests whether there is more DoP NM R&D than non-DoP NM R&D.

I ran five negative binomial Poisson regressions models on each of the three dependent variables. I started the analysis by simply comparing the dependent variables with disease burden (*bod2010*) and the dummy variable for DoP (*dop*).

Model 1: $ln(Y) = b_0 + b_1*bod2010 + e$

Model 2: $ln(Y) = b_0 + b_1*dop + e$

Model 3: $ln(Y) = b_0 + b_1*bod2010 + b2*dop + e$

I then ran regression models with USA medicine sales (*usasales2010*) and the amount disease burden increases (*increase*).

Model 4: $ln(Y) = b_0 + b_1*bod2010 + b2*dop + b3*increase + e$

Model 5: $ln(Y) = b_0 + b_1*bod2010 + b2*dop + b3*increase + b4*usasales2010 + e$

After I ran the regression on NM patents and publications, I repeated the analysis with public private partnerships publications (*ppp2010*) and comparison group publications (*comp09* and *comp10*). I am testing whether PPP publications and the comparison groups have the same relationship with 2010 USA medicine sales and burden of disease as NM R&D

Table 15 gives the results of the Poisson regression analysis of NM publication and patents. All the coefficients in the table have been transformed, so that they represent a multiplicative effect of a 1-unit change in the independent variable. For example, a DoP is predicted to have 0.41 times the number of WoS NM articles than a non-DoP.

From Model 1, I find that disease burden (*dop2010)* is not related to research output. The variable *dop2010* is only significant for PPP R&D and the 2009 comparison group and in those models the multiplicative effect of disease burden is almost 1. Models 2 and 3, on the other hand, have very different results than Model 1. In Models 2 and 3, I find that DoP have fewer publications that non-DoP and when I control for disease burden (*dop2010*), the effect becomes stronger. For example, among NM WoS articles, DoP have about 0.41 times the number of publications compared to non-DoP. The results hold across most of the dependent variable. However; there is one exception; PPP articles are 6.68 times more likely to be about DoP than non-DoP. This is expected since most of the PPP were created to focus DoP.

In Model 4, I examine the impact of the variable *increase. Increase* represents the difference in disease burden between 2005 and 2010. In general the change in disease burden has very little impact on R&D and the variable is insignificant for most of the regression equations.

Finally, in the last regression model I test the relationship of USA medicine sales (*usasales2010*) with R&D. In these regressions, USA medicine sales have a multiplicative impact close to one and the variable is insignificant in all the regressions. From this analysis, I cannot determine if USA medicine sales has any relationship with

NM R&D. One reason that the results could be inconclusive is that there is not enough USA medicine sales data to test the model. In Model 5 there are only 55 observations while the other models have at least 98 observations.

Table 15 Negative binomial regression results

	Model 1			Model 2			Model 3			Model 4			Model 5		
WoS	coef.	z	sig	coef.	z	sig	coef.	z	sig	coef.	z	sig	coef.	z	sig
bod2010	1.00	0.70					1.00	1.56		1.00	0.96		1.00	-0.13	
DoP				0.41	-2.10	*	0.28	-2.77	**	0.24	-2.71	**	0.61	-0.51	
Increase										0.99	-0.52		0.99	-0.40	
usasales2010													1.00	0.98	
constant	26.61	14.57	***	26.39	16.07	***	28.27	14.69	***	30.33	12.95	***	42.71	12.86	***
n=	98			130			98			98			55		
PubMed															
bod2010	1.00	0.88					1.01	2.31	*	1.00	1.13		1.00	0.15	
DoP				0.38	-2.09	*	0.18	-3.52	***	0.13	-3.66	***	0.44	-0.90	
Increase										0.98	-1.03		0.99	-0.77	
usasales2010													1.00	0.50	
constant	19.22	12.31	***	20.00	13.67	***	19.51	12.82	***	22.86	11.23	***	33.90	12.30	***
n=	98.00			130.00			98.00			98.00			55.00		
PatStat															
bod2010	1.00	-0.35					1.00	0.79		1.00	0.00		1.00	-0.72	
DoP				0.23	-2.79	**	0.19	-2.80	**	0.14	-2.92	**	0.26	-1.08	
Increase										0.98	-0.93		0.97	-0.99	
usasales2010													1.00	-0.91	
constant	1.91	2.44	*	1.73	2.48	*	1.98	2.67	**	2.28	2.77	**	3.92	3.82	***
n=	98			130			98			98			55		
PPP															
bod2010	1.01	3.37	**				1.01	3.14	**	1.00	1.61		1.00	1.76	.
DoP				6.68	4.24	***	7.32	5.03	***	5.65	4.34	***	7.59	3.76	***
Increase										0.96	-2.10	*	0.97	-2.13	*
usasales2010													1.00	0.08	
constant	3.18	4.59	***	2.72	4.54	***	1.37	1.30		1.54	1.71	.	1.62	1.74	.
n=	98.00			130.00			98.00			98.00			55.00		

Table 15 cont.

comp09															
bod2010	1.00	2.06	*				1.006	2.91	**	1.0054	2.37	*	1.0018	1.16	
DoP				0.40	-2.59	0.01	0.263	-3.86	***	0.2536	-3.48	**	0.8858	-0.19	
Increase										0.9974	-0.18		1.0035	0.27	
usasales2010													1	1.77	
constant	50.80	20.65	***	64.33	24.29	***	55.80	21.43	***	56.75	19.29	***	71.47	19.26	.
n=	98.00			130.00			98.00			98.00			55.00		
Comp10															
bod2010	1.00	1.19					1.00	1.84	.	1.0042	1.63		1.0011	0.55	
DoP				0.21	-3.61	***	0.17	-3.98	***	0.1726	-3.29	**	0.5836	-0.63	
Increase										1.0025	0.15		1.0093	0.54	
usasales2010													1	1.01	
constant	3.75	5.75	***	4.39	7.63	***	4.30	6.50	***	4.23	5.78	***	5.9616	6.49	***
n=	98.00			130.00			98.00			98.00			55.00		
Significance level: <0.1=. , <0.05=*,<0.01=**,<0.001=***															

After running the regression on the full model, I did a smaller regression with just DoP. In this regression, I test if high-profile DoP (such as malaria and tuberculosis) receive more research than low-profile DoP. I cannot regress the variable *hotdop* on the full dataset because there is only *hotdop* data for DoP[4].

For diseases of poverty:

$ln(Y) = b_0 + b_1 * hotdop + e$

The analysis shows that high-profile DoP have slightly more NM publications and patents. For every $1 million increase in DoP funding from PPPs, the number of NM publications in WoS increases by 1.004 times. This is a very small increase in research output. These results hold across all the different databases.

[4] I also ran this regression analysis including variables like *bod2010, usasales2010*, and *increase* and I got similar results.

TABLE 16 REGRESSION MODEL WITH "HOTDOP"

WoS	Coef	z	sig
hotdop	1.004	2.49	*
constant	3.796	3.89	***
PubMed	Coef	z	sig
hotdop	1.007	2.29	*
constant	1.190	0.36	
PatStat	Coef	z	sig
hotdop	1.004	2.5	*
constant	0.122	-0.346	**
PPP	Coef	z	sig
hotdop	1.005	2.6	**
constant	6.130	5.87	***
comp09	Coef	z	sig
hotdop	1.004	2.61	**
constant	8.760	6.83	***
comp10	Coef	z	sig
hotdop	1.003	2.01	*
constant	0.3867	-2.15	*

n=30

Question 2: PPP and NM comparison

Over the past 10 years, there has been exponential growth in the number of NM and PPP articles. In 2000 there were only 16 PPP and 1,217 NM articles in WoS, but by 2010 there were 744 PPP and 11,625 NM articles.

Table 17 summarizes statistics about PPP research. The most notable statistic from the table is that about 59% of PPP research deals with DoP while only 0.2% of nanotechnology articles deal with DoP.

TABLE 17 PPP AND NANOTECHNOLOGY RESEARCH OVERVIEW

	PPP 2000-2012	Nanotechnology 2000-2012
total publications	4,166	769,761
total health	3,537	81,812
total disease	3,076	41,368
total DoP	2,457	1,694
% health	84.9%	10.6%
% disease specific	73.8%	5.4%
% DoP R&D	59.0%	0.2%

Figure 4 and Figure 5 show the subject categories of NM articles and formal PPPs articles. NM involves the fields of nanotechnology and biomedicine and as a result it has a lot of subject categories in materials science and biomedicine. PPP articles, on the other hand, are more specialized in biomedicine.

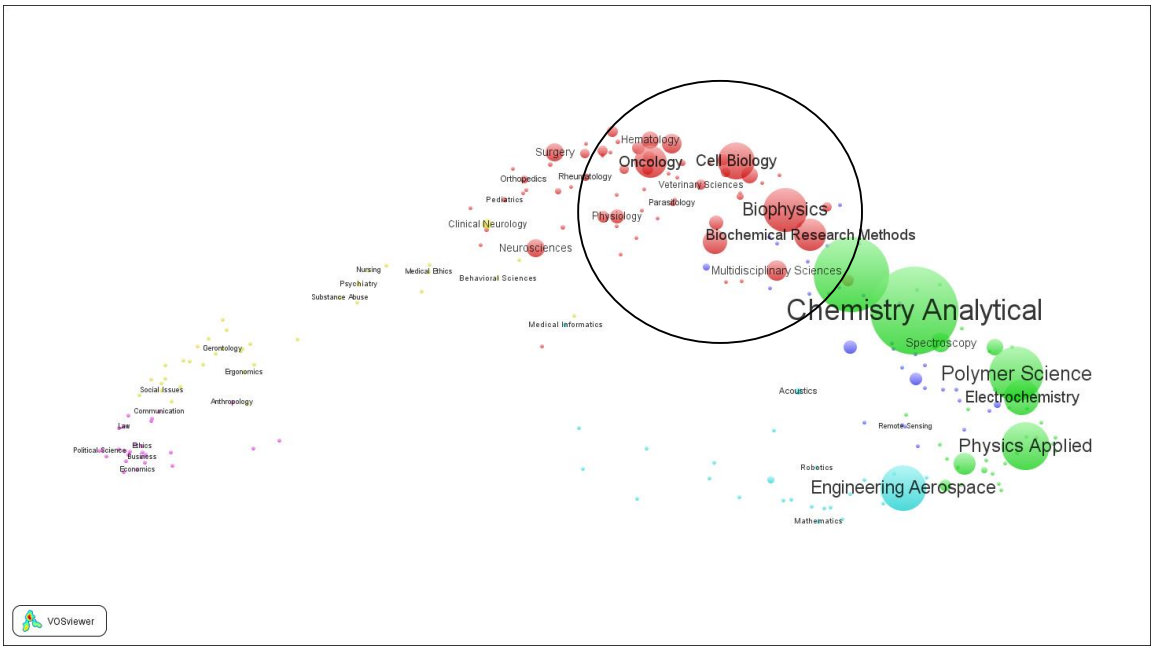

FIGURE 4 SUBJECT CATEGORIES FOR WOS NM ARTICLES

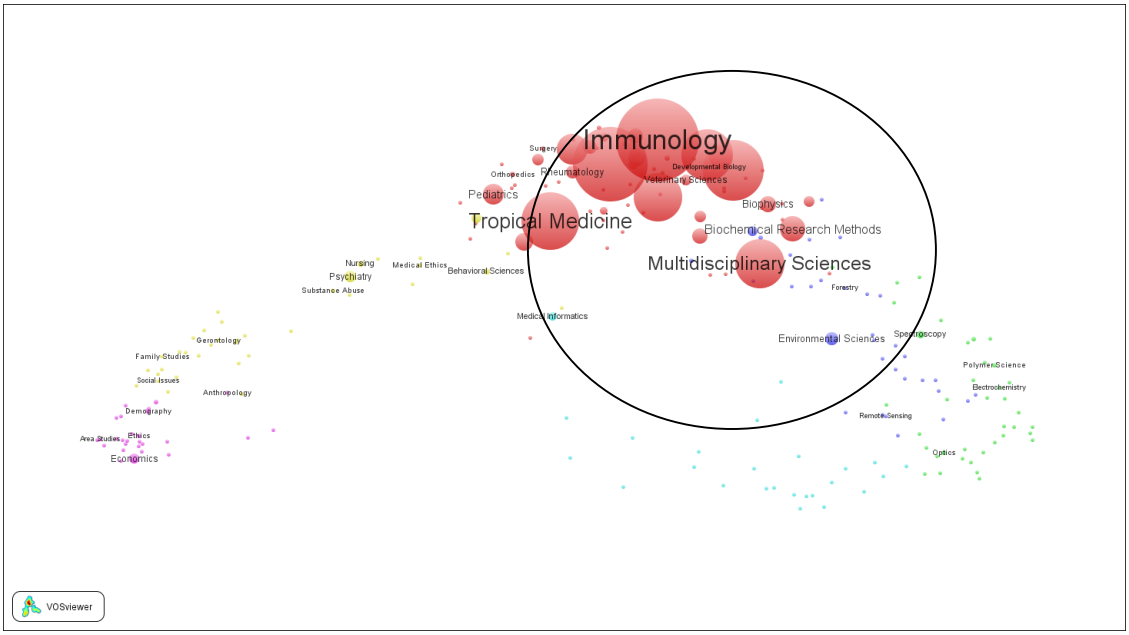

FIGURE 5 SUBJECT CATEGORIES FOR PPP ARTICLES IN WOS

Table 18 lists the top subject categories of NM and PPP articles. I restricted this table to only list biomedical subject categories (the subject categories that are circled and colored red) so that it would be easier to compare the two sets of articles. NM articles have a lot of subject categories related to oncology, dentistry and biophysics while PPP articles relate more with tropical diseases, immunology and infectious diseases. This shows that NM and public-private partnerships conduct research distinctive areas within the biomedical field. I also conducted a difference of means test between PPP and NM subject categories. The test confirms that there is a statistical difference between PPP and NM subject categories (see Table 20 for more details about the difference of means test).

TABLE 18 TOP BIOMEDICAL SUBJECT CATEGORIES OF PPPS AND NM

	Subject Category	PPP	Subject Category	NM
1	IMMUNOLOGY	967	PHARMACOLOGY & PHARMACY	10968
2	INFECTIOUS DISEASES	792	BIOCHEM. & MOLEC. BIOLOGY	7770
3	PHARMACOL. & PHARM.	551	BIOTECH. & APPLIED MICROBIO	4102
4	MICROBIOLOGY	521	BIOPHYSICS	3495
5	Tropical Medicine	468	MATERIALS SCIENCE, BIOMATERIALS	3159
6	PUBLIC, ENVIR. & OCCUPATNL HLTH	437	ENGINEERING, BIOMEDICAL	3110
7	VIROLOGY	371	CELL BIOLOGY	2452
8	Science & Tech - Other Topics	344	ONCOLOGY	1911
9	Research & Experimental Medicine	336	BIOCHEMICAL RESEARCH METHODS	1857
10	PARASITOLOGY	329	RADIOLGY, NUC. MEDICN., MED. IMAGING	1571
11	BIOCHEM. & MOLEC. BIOLOGY	294	Research & Experimental Medicine	1347
12	General & Internal Medicine	197	TOXICOLOGY	1101
13	Chemistry	178	CHEMISTRY, MEDICINAL	880
14	RESPIRATORY SYSTEM	137	DENTISTRY, ORAL SURGERY & MEDICINE	839
15	BIOTECH. & APPLIED MICROBIO	129	IMMUNOLOGY	721
16	CELL BIOLOGY	79	Life Sciences & Biomedicine - Other Topics	640
17	OBSTETRICS & GYNECOLOGY	61	GENETICS & HEREDITY	636
18	PEDIATRICS	61	SURGERY	626
19	Neurosciences & Neurology	53	NEUROSCIENCES	604
20	GENETICS & HEREDITY	50	FOOD SCIENCE & TECHNOLOGY	603

Table 19 gives further evidence that PPP and NM scientists study different areas by showing the diseases that the scientists are investigating. The top diseases in NM articles are breast cancer, neuropsychiatric disorders and periodontal diseases. PPP articles, on the other hand, focus on malaria, tuberculosis and HIV/AIDS and other DoP. The only disease that is heavily researched by both NM and PPP scientists is HIV/AIDS. I also conducted a difference of mean between the two groups and the test shows that

there is a significant difference in NM and PPP disease topics (See Table 20 for more details).

TABLE 19 TOP DISEASES FOR PPP AND NM ARTICLES

	PPP	# Articles	NM	# Articles
1	Malaria	715	Breast cancer	2636
2	Tuberculosis	537	periodontal disease	1549
3	HIV/AIDS	421	Oral diseases	1430
4	Diarrheal diseases	361	skin diseases	1198
5	Dengue	179	Alzheimer/ dementias	1122
6	cholera	152	Prostate cancer	961
7	Respiratory infection	146	Cardiovascular diseases	957
8	Pneumonia	142	Trachea/bronchus/lung cancers	835
9	rotavirus	142	Leukemia	763
10	Leishmaniasis	132	Melanoma/ skin cancers	729
11	Salmonella Infection	111	Ischemic heart disease	520
12	Meningitis	97	HIV/AIDS	508
13	STDs excluding HIV	95	Colon/rectum cancer	482
14	typhoid fever	86	Ovary cancer	481
15	Intestinal Nematode infections	82	Parkinson disease	428

Next I analyzed the integration and specialization scores of NM and PPP articles. This analysis was primarily exploratory. If PPP and NM articles have different integration and specialization scores, then the populations use and disseminate knowledge differently. The integration score measures the range of knowledge that is used to write an article. If the article cites papers from a diverse set of fields, the article will have a higher integration score than if it only cites articles from one field. The integration score for PPP and NM articles are both higher than the average field. Porter and Rafols calculated the integration scores from six disciplines and the integration scores ranged from the 0.20 in math to 0.65 in medicine research (A. L. Porter & Rafols, 2009). In this data, the average integration score for NM and PPP articles is about 0.78, which is much higher than the scores in other fields. The integration scores for NM and

PPP publications are very similar and there is no statistical difference between the scores (see Table 20). This shows that PPP and NM are both integrating knowledge from other fields more than other science disciplines although there is not a significant difference between PPP and NM research.

Specialization measures the extent that a group of papers is narrowly focused in one field. For this study I examined the specialization of NM and PPP articles in the different disease areas. The mean specialization for NM articles is 0.272, while the specialization for PPP articles is 0.351. The difference between these specialization scores is statistical significant. In general, PPP research has a higher specialization than NM research. This means that PPP researchers are publishing articles in fewer areas than NM researchers.

Moreover, the average specialization for science in general is 0.67 (A. L. Porter, Roessner, & Heberger, 2008). This specialization is significantly higher than the specializations for NM and PPP articles. Therefore, even though PPP researchers tend to be more specialized than NM researchers, both types of researchers publish more broadly than scientists as a whole.

Table 20 summarizes the disease, subject category, integration score and specialization score results. For this analysis, I conducted a simple difference of means test comparing NM to PPP research in four different areas: disease topic, subject category, integration score, and specialization score. The mean number of disease specific article in WoS is 0.0025 while the mean for PPP is 0.012. When I do a difference of mean test between these two variables I find that there is a statistical difference between the datasets. There is also a statistical difference in the specialization

scores of NM and PPP articles. However, I could not find a statistical difference in the subject categories or integration scores between WoS and PPP articles.

TABLE 20 STATISTICAL ANALYSIS OF PPP AND NM ARTICLES

	Mean for NM	Mean for PPP	Difference between NM and PPP	Pr(|T| > |t|)
Disease	0.0025	0.012	-0.0093	0.0003
Subject Category	0.008	0.017	-0.009	.03
Integration	0.784	0.788	-0.004	.51
Specialization	0.272	0.351	-0.078	0.001

Third, I analyzed the organizations working with PPPs and doing NM research. Again this analysis gives insight into the differences between PPPs and NM scholars. The organizations working with PPPs and the main organizations doing NM research are very different. First, many of the top organizations doing NM research are from Asia. Of the top 20 NM organizations, 12 of them are from Asia. I suspect that this is because Asian governments have invested a lot of money in nanotechnology research (Guan & Ma, 2007; Hullmann & Meyer, 2003). When I further examine the top organizations conducting NM research, very few of them collaborate with formal PPPs. For example, the Chinese Academy of Sciences has 1,188 nanotechnology articles, but only collaborates with formal PPPs on 12 publications. Again this is further evidence that NM and PPPs are operating in different spaces.

The top organizations partnering with formal PPPs are mostly in Europe and the USA. There are only two Asian or African organizations that are ranked as top organizations that partnered with PPPs. Table 21 summarizes these results.

TABLE 21 TOP ORGANIZATIONS WORKING WITH PPPS AND DOING NM RESEARCH

	Partners with PPP	# Articles	NM Organization	# Articles
1	London Sch Hyg&Trop Med	193	Chinese Acad Sci	1188

2	Univ Oxford	190	Harvard Univ	436
3	Univ Utrecht	183	Nat'l Univ Singapore	400
4	Univ Cape Town	168	Fudan Univ	378
5	Harvard Univ	156	Seoul Nat'l Univ	371
6	Leiden Univ	140	MIT	368
7	Johns Hopkins Univ	133	Sichuan Univ	355
8	Univ Washington	133	Shanghai Jiao Tong Univ	354
9	Univ London Imperial Coll	113	Zhejiang Univ	353
10	Univ Amsterdam	107	Nanyang Technol Univ	296
11	Univ Groningen	101	Peking Univ	270
12	George Washington Univ	96	Nanjing Univ	268
13	Univ Liverpool	87	Univ Michigan	268
14	Radboud Univ Nijmegen	85	CNRS	259
15	Seoul Nat'l Univ	84	Nat'l Taiwan Univ	250
16	Emory Univ	80	Stanford Univ	238
17	Karolinska Inst	76	Univ N Carolina	237
18	Vrije Univ Amsterdam	72	Southeast Univ	230
19	Univ N Carolina	64	Univ Illinois	227
20	Mahidol Univ	59	Univ Calif San Diego	224

Conclusion

In the quantitative analysis, I investigated two aspects of NM and public private partnerships. First, I analyzed the effect of medicine sales and disease burden on research output and I had three hypotheses. The first hypothesis was that medicine sales would be positively correlated with R&D for that disease area

H1.1: High medicine sales in the USA for a certain disease are associated with more NM publications and patents for that disease area

I find that this hypothesis was not supported. Medicine sales do not relate to NM publications or patents.

The next hypothesis predicted that disease burden would drive more NM research. The literature suggests that disease burden has some relationship with research funding and research publications (Vanderelst & Speybroeck, 2013).

H1.2a: Diseases with high burden of disease have more NM publications and patents

H1.2b: Diseases that have increasing disease burden have more publications and patents

These hypotheses are also not supported. There appears to be no relationship between disease burden and NM publications and patents. Therefore, even though other studies show that there is a relationship between disease burden and publications (Vanderelst & Speybroeck, 2013), this relationship does not hold in this analysis.

The third hypothesis tests whether DoP receive less attention than diseases that affect mostly rich countries.

H1.3a: There are fewer NM publications and patents on DoP compared to non-DoP controlling for medicine sales and disease burden

H1.3b: DoP with more PPP funding (hotdop) have more NM publications and patents than other DoP with less PPP funding

These hypotheses are verified. From this set of data, I determine that DoP are less likely to have NM publications and patents than non-DoP. The only database that did not follow this pattern was PPP research. For this population, their research is more likely to be about DoP. Given that the missions of most the PPPs in the dataset relate to creating medicines and vaccines for DoP, these results make empirical sense.

The second part of my quantitative analysis examines the publication patterns of public private partnerships. My initial hypotheses that PPPs are more active in NM than other organizations were found to be false. PPPs are not doing much work in

nanotechnology. In light of this conclusion, I compared the research of PPPs and other organizations. Did they have different foci?

I find that PPPs and NM articles in WoS are different. NM and PPP articles focus on a different set of diseases, publish in journals with distinctive subject categories and operate in two different regions of the world. NM articles tend to focus on diseases that receive a lot of attention in western countries such as cancer and periodontal disease while PPPs specialize in DoP research. Another difference between PPP and NM articles is that different organizations and regions of the world were involved in PPP and NM research. PPP researchers are centered in Europe and the USA while NM researchers span the globe with a major presence in Asia.

The next chapter will discuss some of the qualitative results of the analysis.

CHAPTER 5: QUALITATIVE ANALYSIS RESULTS

Introduction

This chapter gives the results of website content analysis and interviews of public private partnerships. There were several goals of the qualitative analysis. First, I wanted to understand the role of PPPs and how they are better suited than the government or companies for doing R&D for DoP. Second, I wanted to verify the quantitative data. The quantitative data shows that PPPs are not active in NM research and that they have different research foci than NM scholars. Do the interviews and website analyses confirm that PPPs are not doing NM research? Finally, do the qualitative data show unknown links between the actors and research?

To my knowledge, there are 28 formal PPPs that do health R&D and I studied all of them in this analysis. Each of the PPPs have detailed websites that clearly state their goals and funding sources. Moreover, some of the websites feature reports about their progress, financial statements and the advantages of the PPP model for drug development. In addition to reviewing the websites, I conducted 14 semi-structured phone interviews of scientists and managers within PPPs or with NM. The interviews lasted about 30 minutes and after I collected all the website information and interviews, I transcribed the interviews and coded the data in Nvivo. Chapter 3 gives more details about the methods I used for the qualitative data.

This chapter begins by discussing PPPs' self-ascribed definition and purpose. PPPs are aware that they need to be clear about their mission and why they are an improvement on other drug delivery models. Then I describe how PPPs were founded

and the effects their funding has on R&D. Third, I analyze the partnerships' publication strategies, intellectual property policies and their research in NM. Finally, close the chapter by discussing the globalization of PPPs.

History of Health PPPs

The current form of health R&D public private partnerships (which are often called product development partnerships) began around 2000. Before 2000 there were only a few health PPPs, but after 2000, dozens of them sprung up (Cohen, 2006). At that time, several factors arose that created a public buzz to address DoP. In 2000, there was a lot of public outrage directed at pharmaceutical companies because they refused to provide low-cost HIV medicines to victims in poor countries. In response to the negative publicity, many of the big pharmaceutical companies changed their policies on medicines for DoP. The pharmaceutical companies began conducting DoP R&D and they gave away their technology to researchers working on projects targeted for poor communities (The Economist, 2013). Moreover, in 2000, the United Nations launched the Millennium Development Goals (MDGs) and put global health issues for the poor on the world's political agenda. This made people more responsive to the needs of the poor and it put public pressure on countries to find solutions for DoP. Similarly, celebrity activists, such as Bono and Angelina Jolie, emphasized global health issues and they encouraged the popular media to cover their efforts.

Finally, a significant factor that launched PPPs around 2000 is that several large-profile organizations, such as the Bill and Melinda Gates Foundation, began to fund various projects on DoP. But unlike previous efforts, the foundations wanted to change the traditional model of development to be more streamlined and use bottom up processes

(Cohen, 2006). PPPs were seen as a vehicle to leverage the advantages of the private sector to address poverty issues.

There was not an official launch date of health PPPs and one PPP manager recalls that his partnership was formed very informally. He says,

> *"We were founded by a group of global health organizations, sort of informally. In 2000 in a meeting in Cape Town, there were a lot of global health groups in the topic of TB and the resurgence of TB sort of came up. And from that meeting the concept of [PPP_A] was conceived. And then it took a couple of months or years to sort of get off the ground in terms of operation."*

Another way that PPPs began was that large non-profit/government organizations got together to form PPPs. One organization that started about four PPPs in the early 2000's was the WHO-TDR. The WHO-TDR website explains that they made a concerted effort to create several PPPs because they believed that DoP research was getting too complicated for one organization to manage. The WHO-TDR director, Carlos Morel, explained the importance of PPPs by saying,

> *"Some people asked: 'Why are you creating these PPPs? It is going to create more competition for TDR.' Our response was we wanted new products as quickly as possible, and in some cases it [PPP] was more efficient."*

Types of PPPs

PPPs can be divided into two broad groups. The first types of partnerships conduct biomedical research and develop new medicines. Two prominent PPPs that focus on biomedical research are The Program for Appropriate Technology in Health (PATH) and Foundation for Innovative New Diagnostics (FIND). For example, FIND

website says their goal is to "drive the development and early implementation of innovative diagnostic tests that have a high impact on patient care and disease control in low-resource settings"

The other types of partnerships focus on advocacy, education and medicine pricing partnerships. Rather than developing new medicines, these PPPs find solutions to get current medicines to individuals in poorer nations. Though I categorize the PPPs into these two distinct groups, some PPPs, especially the large ones, do both biomedical R&D and downstream health advocacy.

The biomedical R&D PPPs, which is the main focus of this dissertation, can be further divided into in-house R&D PPPs and R&D project managers. The in-house R&D PPPs function like academic research labs by getting research grants from large foundations and government agencies for particular project and they often partner with universities. In fact, many in-house PPPs were started by academics.

A good example of an in-house PPP that works closely with a university is the Sabin Vaccine Institute. Peter Hoetz, who currently holds an academic post at the Baylor College of Medicine, founded Sabin and most of Sabin's vaccine development in housed within Baylor. Moreover, Sabin accesses many of Baylor's resources such as grant services and the IRB process, to decrease costs. A manager at Sabin says,

> *"We leverage the fact that we maximize the resources because we are imbedded in institutions that already have a lot of resources. For instance I don't have to worry about ethic reviews because we utilize the IRB of our institutions … therefore the funding we receive is much better utilized because we don't have to*

recreate the bureaucratic and administrative system….It's like having a biotechnology company embedded within an academic institution."

The other type of R&D PPP is a knowledge facilitator. Rather than doing all the research in-house, these PPPs contract the work to other scientists. A typical scenario for these partnerships is that they receive a research grant and then they redistribute the money to other research labs to do the work. For example, in an interview a person from one PPP says

"Well for each project we have to write a proposal to a donor and get funding for a specific scope of work. PPP_X doesn't just get money to do whatever they please. We write grant applications to do specific activities and often those applications are joint applications between PPP_X and some of our partners. And then depending on the role of PPP_X it might be managing the project or grant out the money to the collaborators."

Another manager from a knowledge facilitator PPP explains that

"PPP_B's R&D expenditure is generally not direct expenditure, but is in the form of grants and contracts with external parties who perform certain tasks at its request."

In the interviews I asked PPPs about their choice to outsource R&D projects instead of using in-house R&D labs. Most of the knowledge facilitator PPPs responded that outsourcing R&D allows them to better manage the projects and it saves them money because they do not have to maintain expensive facilities.

Another difference between PPPs is that some focus on specific diseases while other PPPs research platform technologies or act as advocates for many diseases. In this

study, 8 out of 28 PPPs are disease-specific PPPs. The most common diseases that PPPs' are targeting are HIV/AIDS and tuberculosis (TB). Often the disease-specific PPPs address multiple aspects of that DoP. For example, Aeras wants to advance TB R&D and it works with researchers, helps with clinical trials and does policy/advocacy work.

Other PPPs focus on specific methods and techniques. In general, these PPPs work on platform technologies that can be used on several disease areas. For example, The Foundation for Innovative New Diagnostics (FIND) specializes in developing diagnostic tools and they are working on diagnostics for malaria, Human African Trypanosomiasis and TB. Method-specific PPPs believe that they are better able to produce a product by working on one aspect of the health system. Once they completed their task, method-specific PPPs partner with another organization to bring a product to market.

As mentioned before many PPPs do more than just R&D. Several PPPs concentrate on other aspects of the health care system such as changing the price structure of necessary medicines, improving logistics in order to get medicine to their final destination, and ensuring that health clinics are stocked with the necessary drugs. For example the Global Alliance Vaccine Initiative's (GAVI) mission centers on immunizing the world's poor. GAVI does not conduct research but rather it does a variety of things such as shaping the vaccine market and strengthening the health delivery systems. GAVI believes that one of the main problems of healthcare in developing countries is that medicine prices are too high so they are working on unique market and pricing initiatives, such as advance purchase commitments, in order to make DoP medicines more affordable.

Importance of PPPs

PPPs are keenly aware that they need to describe their purpose and how they are different than traditional pharmaceutical companies. Most PPPs dedicate several pages of their website to describing PPPs, why they exist and the value they bring to R&D. For example, Medicines for Malaria Ventures (MMV) devotes sections of their webpage to describing PPP and product development partnerships (PDPs). They say that PPPs (which are also called PDPs)

> *"Act as a facilitator, bringing dedicated sources of funding and know-how to committed researchers so they can collaborate on the right projects to fulfill the objectives of the PDP's mission. The specific objectives of individual PDPs vary, but the basic mission is the same: to develop pharmaceutical products for use as a public good to address the health needs of vulnerable populations in the developing world."*

PPPs view themselves as changing the traditional model of pharmaceutical drug manufacturers in order to provide medicines for the poor and underserved populations. They employ terms such as "uniquely positioned" or "bridges" to show how crucial they are for DoP R&D. PPPs highlight the realization that one organization cannot fully bring a drug to market efficiently and that they are uniquely positioned to fill that gap. One manager at a PPP explains that,

> *"…if you go back 50 years ago you had one chemist and a doctor who would try a medicine out on patients. Now you have a whole range of skills from chemists to biologists to toxicologists (who make sure things are safe). It's become much more of a team effort."*

Not only do PPPs view themselves as bridging a skill gap between different sectors, but also they think they are bringing together actors with different incentives. Industry and academia have different reward systems and structures. Industry is concerned with generating a profit, while academics are more concerned with generating top research. As one manager says,

> *"Academic cultures and industrial cultures are by definition different... Which means the goal needs to be a concrete goal for the industry which is not the same for the academic environment who can have a lot of benefit from excellent publications but will never lead to a concrete drug that will be brought to the market."*

However, PPPs can bridge the two cultures and make it easier to work together. A partnership is not motivated by profit or publication counts. Rather they care about producing the best medicine for the lowest cost and as a result, PPPs feel they fill a void left by pharmaceutical companies and academics.

A second factor that PPPs use to justify their competitive advantage is that they believe they are the best organizations at picking technologies that have the greatest potential to create medicines. PPPs maintain that academia and industry have incentives that prevent them from choosing a viable research path. PPPs on the other hand, can be impartial and better judges of research lines. One PPP manager compares PPPs to venture capital firms. He says that

> *"The venture capital industry is all about putting the right projects together, picking the right things together, and funding them for as long as they need and giving them all the money they need up to key decision points and then stopping.*

It's a very different funding model than say an academic crowd where you write a proposal and get money for 5 years. And at the end of 5 years you have to explain what you've did with it. So I think when you look at the big consortia [PPP] model it's better suited to the venture capital model. Let pay be based on rewards and stop if it's not working."

The PPPs manage and "prune" research portfolios in order to maximize the potential of the research. If a certain research path is a dead-end, PPPs feel that they can quickly end them.

Finally, PPPs repeatedly say that they change the lack of commercial interest for DoP. Most of the literature on DoP discusses the market failure associated with R&D for these diseases (Kremer, 2002). They reason that pharmaceutical companies do not have an incentive to develop medicines for these diseases because companies could not make a profit from all of their work (Kremer, 2002). One PPP website says that

"*PDPs address the lack of commercial incentive to undertake R&D for vaccines, diagnostics, and drugs for neglected diseases of the developing world. They use public and philanthropic funds to engage the pharmaceutical industry and academic research institutions in undertaking R&D for diseases of the developing world that they would normally be unable or unwilling to pursue independently…"*

This PPP discusses how they use funds from several different sources in order to get different participants to pursue the same project. A manager at a PPP explains that partnerships lower the risk to companies. If an individual company tries to develop a novel drug treatment, then they could lose a lot of money if the research fails. However,

by partnering with a PPP, the company is less exposed to non-productive research portfolios because their R&D expenses are pooled with other investors. The manager explains that

> *"In order for a company to make an investment in developing a technology and providing it…the technology has to make sense financially for them and PPP_B fills in the gap is by helping to de-risk the process."*

Nanotechnology and PPPs

A key goal of this dissertation is to understand the role that PPPs play in NM research. At the outset of this dissertation, there was some hope that PPPs would be heavily involved in NM research for DoP. Much of the nanotechnology literature stated that nanotechnology could be used to address disease of poverty and much of the research on DoP was done by PPPs. As a result, I expected partnerships to do significant amounts of DoP NM research. However, there was very little bibliometric evidence of PPPs authoring or funding NM research. During the interviews, I asked the PPP managers and scientists whether they used nanotechnology for DoP R&D and the managers and scientists gave a wide range of answers about whether they use nanotechnology for DoP research. Several PPPs are actively engaged with nanotechnology and believe that it is a smart research path, while other partnerships think NM is not good for DoP. The sample can be loosely divided into pro-nanotechnology and anti-nanotechnology organizations.

The pro-nanotechnology organizations are conducting NM research and many of them are working on novel drug delivery systems such as encapsulating medicine inside nanoparticles or creating nanoneedle patches that deliver medicines. Some of the pro-NM scientists are very positive about the potential of NM. One of the scientists says that

"Nanoparticles are not only [good] for delivery drug, but you can imagine many things. There is no limit to how you imagine nanoparticles… [there] are so many applications of nanotechnology because you can make smart nanoparticles.…You can track down your drug, do diagnostics… you can do many things."

Most of the other pro-NM interviewees are less optimistic about NM, but they think it should be investigated. They believe that nanotechnology could be helpful for DoP because the current medicines for DoP are not effective. New NMs could shorten treatment times, have fewer side effects and simplify the treatment regimen.

"The challenge is they [nanomedicines] are all novel…But hey if someone doesn't start, then the data is never compiled. So even though we don't know if any of these things in our hands will become licensed, but we're evaluating them because we need to ensure that we have different alternatives."

Another pro-NM interviewee thought nanotechnology had potential, but the initial optimism of the technology has waned. Her organization partners with nanotechnology scientists for drug delivery systems, but nanotechnology is a small part of her R&D portfolio. The manager says that,

"I think with every new technology there's always a spike of initial excitement and enthusiasm where people get excited about it and think this is the next big thing and everything is going to be nano in the future or everything will be needle free in the future. And then with more work and knowledge it becomes more tempered. People realize nano may be good for certain things but it's not going to make sense for other things"

This pro-NM manager believed that nanotechnology could be useful for developing medicines for DoP, but NM will be one piece of a multi-faceted approach. Interestingly, the scientists and managers most excited about nanotechnology were more closely related to academia while those managers that worked on DoP advocacy and price controls were less likely to think NM is useful for DoP.

The anti-NM PPPs do not pursue nanotechnology and they do not think it is useful for DoP. Most of the scientists thought NM would be useful for other medical areas, but not for DoP. The main criticism of the anti-NM scientists focused on the cost and regulatory constraints of the technology. They worried that NMs would be too expensive to manufacture for drugs that require a very low price point. A manager at an HIV PPP says that

> *"We have to be pennies on the dollar for what our products are and governments to buy them and have them a part of their public health programs. Any technology that requires sophisticated manufacturing or high cost manufacturing is… though probably viable from a medical perspective, not viable from a cost perspective. So we had to shy away from a lot of the more unique devices simply from cost."*

This manager recognizes that NM could be a potential solution for DoP but her organization is not pursuing NM for HIV because she believes that the high costs of fabricating nanoparticles would be too expensive for low cost HIV/AIDS medicine.

Another criticism of NM is that it will take too long for it to get through clinical trial and therefore, anti-nanotechnology PPPs believe they should use traditional technologies in order to develop DoP medicines. One manager says that

"*The regulatory pathway to get these things through the approval processes are a little complicated than if you want to use a protein bounded to a di-hydrogen."*

Funding

The formal PPPs in this study received their funding from a variety of sources but the most prominent funders of PPPs are large foundations, particularly the Bill and Melinda Gates Foundation. Almost all the PPPs in this study have funding from the Bill and Melinda Gates Foundation and in most instances the Foundation provided the initial seed funding. Similarly, other studies found that the Bill and Melinda Gates foundation heavily dominated PPP funding. Moran et al. estimate that the Bill and Melinda Gates Foundation provided about 50% of formal PPP funding in 2007 (Moran et al., 2010) and in general, only a few organizations provide the bulk of PPP funding. The data mention the same donors such as the Bill and Melinda Gates, NIH, and USAID. PPPs reliance on a limited number of organizations makes them beholden to a few organizations and their agendas. If the Bill and Melinda Gates Foundation moves away from DoP R&D, formal PPPs could not survive.

The PPPs approach corporate funding very differently. Some PPPs receive lots of funding from big pharmaceutical companies (big pharma) such as Merck or Johnson & Johnson while others tend to stay away from big pharma. One PPP says that big pharma is not interested in their organization because

"There is not a lot of commercial interest of the vaccines that we have in our portfolio versus something like malaria that may have multiuse."

As a consequence this PPP has not been successful in getting corporate funding.

Another challenge for PPPs is that there was a lack of overall funding for R&D. During the recession in the late 2000s there was less money and all the donors, including large government agencies, had to slow down their outlays. One scientists says that

> *"It seems to me that it's getting harder to do the work because of the funding environment. It's probably getting harder for everyone to work."*

The same scientist goes on to say that finding research money for DoP R&D is

> *"…a struggle because you look around and there are cancer grants from the university and things such as that and it's harder to find opportunities other than the NIH to keep your research going."*

As a consequence, several PPPs mentioned that they are targeting new sources of funding. One PPP in this study received funding from Fundación Carlos Slim, a foundation that has not traditionally supported biomedicine research. In addition, this same PPP targeted high net worth individuals for support on specific projects. In one case, the PPP was able to convince a wealthy donor to recruit other high net worth individuals to donate to the PPP.

Another funding diversification strategy is to find organizations that will match research money from large foundations. By soliciting matching donations, PPPs can get more research money and the donors have more confidence that their investment is going to a reputable cause because someone already vetted the project. In addition, giving matching donations prevents the donor from spending resources sorting and choosing the best project since soliciting scientific proposals can be very technical and expensive. Often smaller governments, such as Denmark, will give matching funds. One PPP describes their strategy to use matching funds as

"We can't rely on a single funding mechanism and you certainly can't rely on just federal NIH type of mechanism. So we have a very diverse portfolio. Certainly we have the Bill and Melinda Gates Foundation …However, in the latest 4-5 years we've gathered funders that co-fund the Gates Foundation."

A source of non-monetary support is to use another organization's lab and equipment. In this strategy, money may not exchange hands, but PPPs can save money by sharing resources. A PPP manager explains that

"the NIH will give us money, where we don't directly get the money, but we'll say we need to have this tested and they'll do it without charging us and without giving us money."

Also PPPs can get compounds and formulas from companies without being charged licensing fees. Again this is a non-traditional form of funding.

"So what we can do is go to a pharmaceutical company and ask them for compounds they are developing for HIV treatment and get licenses to them. We have done that for 6-8 compounds. So we go to big pharma like J&J and Pfizer and Merck. They have all given us compounds and we can develop them using donor funds and collaboration with universities."

Finally, a major challenge expressed by PPPs is that donor organizations put strict restrictions on their research money, which hinders the PPP's ability to transfer money to different projects. For example, the donor may require that funds only be spent on a particular HIV project and the funding cannot transfer to another experiment. In addition many donors have onerous reporting requirements. A director at a PPP_C says that

"So reporting back to donors is extremely time consuming. Each donor is very specific about what their money can be spent on and we have to report back. That's an incredibly involved effort."

In addition to funding restrictions, some donors specify the partners of PPPs. For example Fundación Carlos Slim Foundation requires that recipient organizations partner with Mexican institutes. To comply with all the requirements of donors, PPPs must hire full time staff members to handle the grant logistics.

Patents and Publications

The quantitative analysis uses publication and patents as the main dependent variables and therefore I needed to verify that PPPs publish and patent their research. I found that PPPs are very active in publishing. On their websites PPPs often cite their high publication rates as measures of success. For example, a Sabin Vaccine Institute report they highlight that one of their main accomplishments in 2012 was that they had over 25 peer-reviewed journal articles for that year.

PPPs publish for a variety of reasons. First, unlike companies that want some information to remain a secret in order to have a competitive advantage, PPPs broadly share information with other organizations. A manager at a large PPP says that,

"Publishing and disseminating information is a key part of what we do. We have principals of global access that we work with. Global access means that the technology we work on should be accessible as well as the information that we generate should be accessible. So we typically strive to publish our work as much as possible and build that into our agreements with our partners that the information will be made published."

This manager expresses that sharing information is a key part of her organization's strategy and that publishing is a major part of that effort.

Another factor that pushes PPPs to publish is that many PPPs have academic cultures. As discussed before, some PPPs were founded by academics and many of them are closely associated with universities. The academic focus on publishing carries over to PPPs.

Patenting is more complicated for PPPs than publishing. Each PPP approaches patenting slightly differently; however, one major theme across the organizations is that they use patents to protect themselves. Several PPPs expressed concern that other organizations could prevent them from working on certain projects or steal their IP if they do not proactively patent their technology. One manager gives a hypothetical situation in which a research partner sees that a technology has market potential and in order to make money, the partner patents the technology. Once the technology is patented, the partner could block the PPP from developing a low cost medicine and instead the partner would create an expensive drug.

> *"We approach the patenting aspect mostly to protect not because we foresee having some royalties generated. We protect mostly so that we can make sure no one interferes with us advancing this program."*

Another way PPPs deal with intellectual property is by working closely with industry to have more access to the necessary intellectual property for their work. PPPs and pharmaceutical companies will develop special agreements that allow non-profit organizations to develop medicines for DoP without paying licensing fees. The pharmaceutical company retains the rights to use the technology in wealthy nations, but

the PPP can use the technology for humanitarian purposes. The PPP FIND has a long discussion about their use of patents on their website. FIND says that

> *"Industry partners assign all rights to FIND for royalty-free use of their technology in the public and private non-profit sectors in high endemic countries, while the industry partner retains distribution rights for developed countries and the private sector in developing countries. This enables the partner to recover R&D costs and to create the returns needed to develop new technologies."*

FIND goes on to explain that having different patent protection for different markets has allowed it to work with more companies.

> *"Our IP model has been successfully validated with industry partners and has contributed to an important and increasing number of contracts signed with large and small-sized companies."*

Globalization of PPPs

In the quantitative analysis, a major finding is that PPPs and their partners tend to be based in Europe and the USA while organizations doing NM research have a large presence in Asia. During the interviews, I asked respondents about their R&D partners. From the interviews and websites I gathered two underlying trends among formal PPPs. First, 26 out of the 28 formal PPPs are headquartered in the USA or Europe. This evidence supports the bibliometric data that shows that formal health PPPs are mainly creations of the West. Even rich Asian countries, such as Japan, have not been active in DoP R&D and only within the past year has Japan started a started a PPP called the Global Health Innovative Technology Fund (GHIT). Japan's late entry into PPPs is noted on GHIT's website

"From a global perspective, countries in Europe and North America often see the issue of global health as a component of their diplomatic or growth strategy. Although Japan is one of the largest donors of overseas development assistance and also one of the leaders in health technologies innovations, its efforts toward global health have lagged somewhat."

Even though many formal PPPs are headquartered in Europe and the USA, it is not true that these organizations have no presence in Asia and Africa. Most of the PPPs have African and Asians partners and many of the PPPs have brick and mortar office on these continents. Unfortunately, the partnerships are unequal. Most of the developing countries do not have R&D facilities, but rather those countries only host clinical trials. Hosting clinical trials are important, but the host nation does not build significant R&D capacity. However, this trend is changing. The Brazilian, Mexican, Indian and South African governments funded PPPs and are doing more fundamental R&D for DoP.

Conclusion

The interviews and website analysis confirmed that health PPPs are important for DoP research, but they are not major players in NM research. Some PPPs explore nanotechnology for DoP medicines, but many believe that these medicines are too expensive and it will take too long for regulators to approve these drugs. As a result, some PPPs stay away from nanotechnology in favor of more traditional technologies. Moreover, the analysis shows that PPPs are global entities, but their headquarters, donors, and main laboratories are located in the USA and Europe. This confirms the bibliometric data that PPPs are located mostly in Western nations while NM research has become a global endeavor with a large presence in Asia.

The next chapter reviews the major findings and discussion policy implications of this study.

CHAPTER 6: CONCLUSION

Introduction

The previous two chapters discuss the findings from the quantitative and qualitative data analyses. This chapter summarizes the findings and gives implications and policy recommendations. The recommendations focus on increasing R&D and improving the effectiveness of PPPs for DoP research. I suggest a variety of policies such as simplifying the regulation process for new medicines and diversifying research funding.

Summary of Conclusions/Implications

My first research question investigates inequality in NM on three dimensions: USA Medicine sales, disease burden, and DoP. The analysis showed several interesting relationships between NM R&D and disease burden, medicine sales, and DoP. First, the WoS and PubMed data are highly correlated (0.96), while WoS and PatStat data are not as highly correlated (0.64). This is evidence that the patent and publication databases measure two different phenomena. Publications are more likely to relate to basic research, while patents are more likely to relate to development.

Despite the observations from the correlation matrix, I am limited in my interpretations because only one of the variables in the analysis, *dop*, has any significant relationship with NM R&D. I found that DoP have significantly less R&D than non-DoP. In WoS, DoP have 0.24 times the number of publications as non-DoP. From this analysis, I could not determine if the other variables in the model, USA medicine sales and disease burden, have any relationship with NM R&D. These findings are important because many funding agencies, such as the National Institutes of Health, use disease burden as a

component of their criteria to fund research and I showed that the relationship between disease burden and NM research is unclear.

Next, I examined a subset of publications that contain only DoP articles to determine if DoP research increases as PPP funding increases. I found that there is a small relationship between PPP funding and DoP research. If PPP funding for a disease of poverty increases by $1 million dollars, then the expected number of NM publications increases by 1.003 times. Therefore, donors must $1 billion to see an increase of one journal publication. Given the weak financial climate and the difficulty that PPPs have finding donors, it is likely that DoP R&D will increase because there is not enough money to support the research.

I also compared PPP research to NM research and I found that PPP and NM scientists focused on different diseases, published on different topics, and worked in different regions of the world. First, when I compared the types of diseases that PPP and NM scholars study, I found that PPP publications mainly focus on DoP while the majority of NM articles are about cancers, periodontal disease, and Alzheimer's disease. In addition, PPPs published in journals that focused on immunology and infectious diseases while NM scholars published in journals with subject categories such as biophysics, biomaterials, and oncology. These results align with my regression analyses, and they show that PPPs and NM scientists study different areas of science. Scientists originally hoped that nanotechnology would be used to make medicines for DoP, but PPPs, who are the main actors in DoP medicine development, have different research agendas than NM researchers. Unless PPPs and NM scientists align their interests, it is unlikely that NM will be used for DoP medicine research in the near future.

An unexpected difference between NM and PPP publications is that they operate in very different regions of the world. Asian and American institutions are very dominate in nanotechnology R&D while European and American institutes mostly work with PPPs. This is further evidence that there is a mismatch between PPP and NM scholars. Nanotechnology research is much more globalized while PPP research is still concentrated in Europe and North America. Other studies also find that Asian countries and other emerging markets have prioritized nanotechnology research (Liu et al., 2009; Maclurcan, 2005). In many emerging economies, there is a government push to do nanotechnology R&D and as a result emerging economies are becoming hubs of nanotechnology R&D. However, innovation for DoP has not received as much attention in emerging economies. None of the PPPs are headquartered in emerging markets and only two are based outside of Europe or American. Moreover, even rich Asian countries, such as Japan, are not heavily involved with global health initiatives and PPPs. An implication of this finding is that R&D for DoP is only done in the West even though science and technology research is globalizing and moving eastward. If other parts of the world do not invest in DoP research, then it is likely that this type of research will remain under funded and lag behind other research areas.

Despite the differences between PPP and NM research, they both have higher integration and lower specialization scores than science a whole. This means that PPP and NM scientists integrate knowledge from a diverse range of subject categories and they publish their work in a variety of journals. The literature suggests that high integration scores and low specialization scores lead to more innovative science because the research draws upon knowledge from different fields (Hollingsworth, 2008; Moed et

al., 2005). From the evidence, NM and PPP publications both appear to be more innovative than science as a whole.

My next set of questions examined PPPs in order to understand their mission, the benefits of that organizational structure and their relationship with nanotechnology. I collected data from PPP's websites and conducted interviews with PPP managers and scientists. First, I found that most PPPs started around 2000 due to a tremendous global pressure to address DoP. A variety of actors, such as the United Nations, pharmaceutical companies, and celebrities rallied around improving global health and they invested billions of dollars starting PPPs. The window of opportunity that opened in 2000 for DoP research was crucial for PPPs to receive funding and develop DoP medicines. An implication of this finding is that future PPPs may need a similar window of opportunity to raise funds. Without a global emphasis on issues, it may be difficult launch a global PPP to target other areas related to poverty.

Another finding is that there are both pro and anti-nanotechnology PPPs. The pro-nanotechnology PPPs believe that nanotechnology could offer solutions for DoP and scientists should explore this new area for DoP medicines, while the anti-nanotechnology PPPs, believe that nanotechnology is too expensive for low cost DoP drugs and that the regulatory process for NMs will be too cumbersome. Instead of doing NM DoP R&D, anti-nanotechnology firms believe that PPPs should use standard techniques to create cheaper DoP medicines with shorter regulatory timelines. The anti-nanotechnology position has implications for emerging technologies. If governments do not develop processes to promote R&D for poverty related areas with emerging technologies, then the

technology will only be used to solve rich world problems and as a result the technology will increase inequality.

The evidence suggests that DoP NM research will not become a major stream of research and that NM has not progressed as fast as scientists initially hoped. Even though the pro-nanotechnology PPPs conduct NM R&D, it is a small part of their overall R&D portfolio. Until NM becomes a standard medical technology, it will not be heavily used by PPPs for disease of poverty R&D. As a result, nanotechnology could increase health inequality rather than decrease it. The technology will first be used on diseases that affect the rich, such as cancer and Alzheimer's and after it is adopted in high-income markets, then DoP scientists will use the technology.

Another conclusion from the qualitative analysis is that PPPs are only funded by a few organizations. Most of the PPP funding comes from the Bill and Melinda Gates Foundation and large government organizations such as the National Institutes of Health or British aid agencies. At one point the Bill and Melinda Gates Foundation supplied over half the formal PPPs fundeing (Moran et al., 2010). An implication of this finding is that a small donor base makes PPPs more vulnerable. If the Bill and Melinda Gates Foundation stops supporting DoP research then these partnerships could shut down. PPPs recognize their predicament and they are seeking new sources of funding. Unfortunately, fundraising draws resources and personnel away from R&D, which slows down drug development.

Overall, PPPs work well with each other, and they often collaborate on projects. In the interviews, the PPP managers mentioned that they want to partner with organizations, and that they do not worry about competition from other PPPs. Rather,

PPPs want other non-profit drug developers to succeed, so that they can use the results to find medicines and vaccines for their particular disease. Moreover, PPPs informally coordinate with each so that they do not replicate the same research. These collaborations have led to a global network of health PPPs and it is a major strength of the model. The networks facilitate knowledge transfer between the organizations, which causes them to develop DoP medicines quicker.

Finally, PPPs are active in publishing and patenting their research, and many of them cite their publication counts as one of their top accomplishments. However, an unintended consequence of focusing on publishing is that PPPs could turn into research institutions that are more concerned with academic achievement and not producing medicines.

PPPs approach patenting very differently than publishing. They are more strategic with patents and use them as shields so that other organizations cannot block them from doing R&D. PPPs are very clear that they do not patent to make money, but rather they patent an invention and allow others to use the technology for free. A downside to PPPs' patent policy is that they spend a lot of time and resources developing defensive patents. If the patents rules were changed to help PPPs, then they would have more time and money for research. Given the current set of laws, patenting will remain a major a priority for PPPs in order to protect themselves.

Policy Recommendations

Below are several policy recommendations from this study.

Encourage the formation of more PPPs for DoP research

Overall PPPs are at the forefront of DoP research and it is expected that they will develop more DoP medicines. Moreover, other studies conclude that PPPs are more successful than traditional public research institutions and technology transfer strategies for DoP medicine development (Moran et al., 2010; Moran, 2005). If governments want to promote DoP research, then they should fund more PPPs.

Cheaper nanotechnology materials

In this study, I examined NM as an example of an emerging technology and I found there are pro and anti-nanotechnology PPPs. In order for PPPs to use emerging technologies, policy makers must adopt special incentive programs to encourage DoP research with emerging technologies. Several PPPs mentioned that they avoid using nanotechnology because it is costly. They believe that medicines for DoP have to be cheap and that using nanotechnology as a part of the drug delivery system would make the medicine prohibitively expensive. Therefore, in order to push PPPs to do NM research, governments and private organizations should ensure that nanomaterials are cheap. For example, if the USA wants to promote nanotechnology DoP research, then it could subsidize the cost of nanomaterials in DoP medicines, which would bring down their costs and encourage scientists to uses these materials for drug development. Another way to foster R&D is that private companies who are interested in social outreach could establish more partnerships with PPPs and provide them with cheap R&D materials. This allows the company to get involved with a social project and later the company could use the knowledge generated by the PPP to develop other technologies.

Quicker screening for medicine approval

One reason that PPPs are hesitant to develop DoP NMs is that they fear the new medicines will have long approval processes compared to medicines using standard techniques. Therefore, to make emerging technologies more appealing for DoP R&D, government agencies, such as the U.S. Food and Drug Administration, could offer fast track approval processes for them. This will ensure that lifesaving drugs can reach the market as fast as possible. However, regulatory agencies must ensure that the fast approval processes do not allow sub-standard medicines to be used in poor countries.

Strengthen foreign partnerships

PPPs are largely headquartered in Europe and the USA and middle and low-income countries have small roles in DoP research. Organizations in low-income countries mostly assist with medicine trials, medicine distribution, and manufacturing. Other studies also observed unequal partnership in PPPs, which led to asymmetric power relationships, poor R&D and diminished economic development (McQuaid, 2000; Miraftab, 2004).

By being on the periphery, organizations in low-income countries do not develop high-skill R&D knowledge because they are not involved in fundamental research (Miraftab, 2004). In order to decrease these asymmetries, PPPs should develop more R&D facilities in developing countries to increase capacity building. Some donors, such as Fundación Carlos Slim, require that scientists partner with low-income countries. If the donor community adopts more policies that build global R&D capacity, then there will be an increase in R&D on emerging technologies from developing countries.

Public Private Partnerships should diversify funding

Most of the PPP funding comes from a few large donors, such as the Bill and Melinda Gates Foundation and USAID. If the donors change their objectives, then PPPs could lose the majority of their support and the scientific progress on DoP would be severely curtailed. To make PPPs more resilient, they should find donors from a wider range of foundations, governments, companies, and private individuals. Many of the PPPs in this study are broadening their funding base but the economic depression hampered their fundraising capability. Funding is a major issue that prevents PPPs from doing more research on emerging technologies such as NM.

Simplify reporting standards

PPPs spend a lot of time tracking and reporting their donations. One PPP manager suggests that donors should develop one reporting standard that is used by all the donors, so that PPPs could have more time and money to be spent on R&D. However, conforming to one standard weakens each donor's control over their donation and how it is spent and reported.

Change patent protections to help PPPs

PPPs are concerned that companies can patent their innovations and prevent them from developing technologies and as a result they spend a lot of money and time developing defensive patents. PPPs mentioned that the current patent system limits their ability to develop medicines for DoP. However, reforming intellectual property rights for DoP is very complicated. There are numerous papers on this issue and often scholars give competing advice based on their intellectual traditions (Feachem & Sachs, 2002; Global Forum for Health Research, 2007; Kremer, 2002). Webber and Kremer write that "Patent legislation represents a careful balance … Proposals to alter the existing balance should

be regarded with caution. Undermining patent protection could discourage innovative activity on the part of industry, while strengthening patent protection could come at the expense of reduced access" (Webber & Kremer, 2001). Despite the complexity, one common suggestion is to change the patent laws for low-income countries and medicines that target DoP (Kremer, 2002). This strategy would allow PPPs to access the necessary intellectual property to develop novel medicines without going through as many hurdles. In lieu of such reforms, PPPs make special deals with pharmaceutical companies in order to have access to compounds for medicine and vaccine development. Though this strategy has worked in the past, it is highly dependent on the largess of big pharmaceutical companies. Changing the patent system would allow PPPs to be more effective.

Develop PPPs for other poverty alleviating technologies

PPPs are successfully developing medicines for the poor and without their efforts many DoP medicines would not exist. Given the accomplishments of PPPs for DoP R&D, it may be possible to use the PPP model to address other development problems. For example, PPPs could create new seeds and pesticides for subsistence farmers or they could build innovative water filtration systems that are specifically designed for low-income countries. However, the main hurdle that prevents the PPP model from being used in other fields is that scientists and community workers need to find money to invest in more innovations for the poor.

Conclusion

Improving global health is one of the major global public goods and many believe that technology will have a role in poverty alleviation. This study shows that emerging

technologies will not automatically decrease poverty and income inequality. Rather, it is necessary to implement a variety of reforms such as strengthening research collaborations with developing countries and changing the patent system in order to help emerging technologies be used for poverty alleviation.

APPENDIX A

Below is the thesaurus used to find diseases in the bibliometric databases.
*=Sub-category of disease
Abortion
Alcohol use disorders
Alzheimer/ dementias
Appendicitis
Ascariasis
Asthma
Benign prostatic hypertrophy
Bipolar affective disorder
Birth asphyxia and birth trauma
Bladder cancer
Breast cancer
Cardiovascular diseases
Cataracts
Cerebrovascular disease
Cervix uteri cancer
Chagas disease
Childhood diseases
 *Pertussis
 *Diphtheria
* Poliomyelitis
 *Measles
* Tetanus
Chlamydia
Chronic obstructive pulmonary disease
Cirrhosis of the liver
Colon/rectum cancer
Congenital abnormalities
Corpus uteri cancer
Dengue
Dental caries
Diabetes mellitus
Diarrheal diseases
Digestive diseases
Diphtheria
Diseases of the genitourinary system
Drug use disorders
Edentulism
Epilepsy
Glaucoma
Gonorrhea
Hearing loss, adult onset
Hepatitis B
Hepatitis C

HIV/AIDS
Hookworm disease
Hypertensive heart disease
Inflammatory heart disease
Insomnia
Intestinal nematode infections
*Trichuriasis
*nematode[a-z]
*Hookworm disease
*Ascariasis
Iodine deficiency
Iron-deficiency anemia
Ischemic heart disease
Japanese encephalitis
Leishmaniasis
Leprosy
Leukemia
Liver cancer
Lower respiratory infections
Lymphatic filariasis
Lymphomas/multiple myeloma
Macular degeneration
Malaria
Maternal conditions
*Obstructed labor
*Abortion
*Hypertensive disorders
*Maternal sepsis
*Maternal conditions
Maternal hemorrhage
Maternal sepsis
Measles
Melanoma/ skin cancers
Meningitis
Migraine
Mouth/ oropharynx cancers
Multiple sclerosis
Musculoskeletal diseases
Neonatal infections and other conditions (f)
Nephritis/nephrosis
Nutritional deficiencies
Nutritional/endocrine disorders
Obsessive-compulsive disorder
Obstructed labor
Oesophagus cancer
Onchocerciasis
Oral diseases
*Oral diseases
*dental[a-z]
*peridon[a-z]

Otitis media
Ovary cancer
Pancreas cancer
Panic disorder
Parkinson disease
Peptic ulcer disease
Perinatal conditions (e)
Pertussis
Poliomyelitis
Post-traumatic stress disorder
Prematurity and low birth weight
Prostate cancer
Protein-energy malnutrition
Refractive errors
Respiratory diseases
Respiratory infections
*Respiratory infection[a-z]
*Otitis media
Rheumatic heart disease
Rheumatoid arthritis
Schistosomiasis
Schizophrenia
Sense organ disorders
*Glaucoma
*cataract[a-z]
*deaf[a-z]
*Macular-degeneration
Skin diseases
STDs excluding HIV
Stomach cancer
Syphilis
Tetanus
Trachea/bronchus/lung cancers
Trachoma
Trichuriasis
Tropical diseases
*Schistosomiasis
*Chagas disease
*Leishmaniasis
*Tropical disease [a-z]
*Onchocerciasis
*Lymphatic filariasis
*Trypanosomiasis
Trypanosomiasis
Tuberculosis
Unipolar depressive disorders
Upper respiratory infections
Vitamin A deficiency

APPENDIX B

Below is a sample email I sent to participants asking them to participate in the study.

Mrs. XXX,

My name is Thomas Woodson and I am a PhD Student in Public Policy at the Georgia Institute of Technology (Georgia Tech) in Atlanta GA. For my dissertation I'm studying medicines and public private partnerships who do research for neglected diseases.

As a part of my study, I would like to interview you about PPP_X. Would you or someone from PPP_X be available for a quick 30min phone/Skype interview about the organization? PPP_X is doing some fantastic work on _____ and I've love your insight about the future of drug development for diseases of poverty. Please let me know of any questions or concerns that you may have. Thank you for your consideration, and I look forward to hearing from you soon.

Below is the Institutionally Review Board (IRB) approval

Nanomedicine and Public-Private Partnership Research for Diseases of Poverty

Thank you very much for agreeing to speak with me today. As I explained in my e-mail, I am doing research on medical applications of nanotechnology (nanomedicine) for diseases of poverty. I am also studying how public-private partnerships and other organizations are getting involved in the research on diseases of poverty.

I am inviting your participation, which will involve a conversation of 30 minutes to 1 hour about nanomedicine, diseases of poverty and public private partnerships. In this conversation I will ask you to generalize your current work, the applications you see for it, and the motivations behind it. You have the right not to answer any question, and to stop the interview at any time.

Your participation in this study is voluntary. If you choose not to participate or to withdraw from the study at any time, there will be no penalty.

I would like to audio-record this interview. The interview will not be recorded without your permission. Please let me know if you do not want the interview to be taped; you can also change your mind after the interview starts.

I will take notes on our talk in order to use the information in my publications. But I will not use your name in my publications, and I will store the recordings and the notes in a secure place with a code number so that you could not be identified even if someone got access to them.

There may not be any direct benefit to you from this research although my final report may provide insights into research on diseases of poverty. I do not know of any risks to you from participating in this study, and you can withdraw at any time.

If you have any questions about the study, you may contact me, Thomas Woodson, (1-404-894-1039). If you have any questions about your rights as a research participant, you may contact Ms. Melanie Clark, Georgia Institute of Technology Office of Research Compliance, at 1-404-894-6942. Thank you for your time and interest in our project.

Thomas Woodson
School of Public Policy
Georgia Institute of Technology

Your rights as a research participant

- Your participation in this study is voluntary. You do not have to be in this study if you do not want to be.
- You have the right to change your mind and leave the study at any time without giving any reason and without penalty.
- If you decide not to finish the study, you have the right to withdraw any data collected about you. We will destroy any notes or recordings done before that time.
- Any new information that may make you change your mind about being in this study will be given to you.
- You will be given a copy of this consent form to keep.
- You do not waive any of your legal rights by participating in this research project.

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