Neat, Plausible, and Wrong

Why the focus on intellectual property fails to address the complexities of medicinal access in India

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There is always a well-known solution to every human problem — neat, plausible, and wrong.
– H. L. Mencken

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Glossary and Acronyms

ARVs	Antiretrovirals
AYUSH	Department of Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homoeopathy
EML	Essential Medicines List
FDA	Food and Drug Administration
GATT	General Agreement on Tariffs and Trade
GAVI	Global Alliance for Vaccines and Immunization
GMP	Good Manufacturing Practices
INN	International nonproprietary name
LDC	Least Developed Countries
MNC	Multinational Corporations
NACO	National AIDS Control Organization
NGO	Non-governmental organization
NCD	Non-communicable diseases
NTD	Neglected Tropical Diseases
NELM	National Essential Medicines List
OECD	Organisation for Economic Co-operation and Development
PEPFAR	President's Emergency Plan for AIDS Relief
PHC	Primary health care
RUD	Rational Use of Drugs
TRIPS	Trade-Related Aspects of Intellectual Property Rights
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

1.0 Executive Summary

The form and content of this report in no way resembles the original intent behind it. As originally conceived, the authors were commissioned to test a hypothesis that prevailing Indian patent law inhibited rather than enhanced the development and introduction of medicines into India on an equitable basis, and furthermore that it hurts rather than advances the domestic pharmaceutical industry. In performing that analysis through a literature search, the authors quickly discovered that the relationship of patenting to the problem of medicinal access in India was a side-story to a much greater and more important inquiry. That alternative inquiry was nothing less than a derivation of the manifold challenges to medicinal access and an in-depth search and review of academic, peer-reviewed literature that addressed the various dimensions. The research led the authors to conclude that there are eight factors that are the basis for the access to medicines problem, and that these must be addressed on a global basis by a concerted collaboration by stakeholders as diverse as the biopharmaceutical industry, governments, multilateral organizations, care providers, NGOs and, of course, patients themselves.

The authors' method started with a search of the literature as it related to patents and medicinal access. There is a body of such literature and a substantial history of the controversy surrounding the positions of the parties. That literature and history is described in depth in this report. The authors observed in the course of searching, however, that the range of inquiries in the literature went far beyond the issues of patenting. The inquiries fell into eight categories, each of which the authors believe is part of a composite problem. These are:

- **Accessibility of care milieu:** Remoteness; density; percentage of residents living with accessible radius time to health facility for consultation, diagnosis and medicinal intervention

- **Affordability and Health Systems Financing:** Public and private means for payment on national and trade levels; appropriate pricing in proportion to income and national financial resources

- **Availability of care:** Scarcity of care and technology resources allowing appropriate diagnosis and treatment

- **Awareness of the opportunity for care:** Knowledge of available resources and options for care, and the implications for medicinal intervention

- **Essential medicines procurement:** Disconnect between national polices, formulary and sources of supply

- **Regulation:**Ambiguous medicinal approval regime or application of government mandated pricing requirements

- **Socio-cultural obstacles:** nonfinancial obstacles to care such as culture, language, race, and ethnicity, and the related medicinal implications

- **Supply chain management:** Mal-functioning national, local or provider systems for managing flow of necessary products.

This report is centered on India as the case study for medicinal access because the issues for the country are acute, but ironically, India has the most developed capacity for the production of medicines in the world, and actively exports its products globally. Each of the above categories was searched generally, and then specifically for its relationship to India. Nearly 170 articles are reviewed and summarized in this report. They paint a picture that demands a re-thinking of the problem of medicinal access well beyond patenting. The solutions to the composite of issues confronting medicinal access are each elusive in their own right, but addressing any one factor without addressing the other will not result in a solution at any level. An imbalance in the way these eight categories are addressed may well exacerbate the problems.

The relationship of patenting and the related pricing of medicines will continue to be studied. Based on the search and reading of the literature, however, it is clear to the authors that that if the patent system were suddenly abolished there would be virtually no change in medicinal availability over the next 20 years. Then, 20 years from now there would be few, if any, new medicines, and the availability of legacy medicines, (all medicines would be old generics) would soon diminish and the quality of legacy medicines would decline because there would be a collapse across the innovation spectrum. Medicines that are off patent still require

invention and innovation in their production and clinical use. The science of medicinal intervention would not only stall, it would regress.

In order to orchestrate a unified and determined effort to address the milieu of problems that shape the challenge of medicinal access, the authors of this report recommend to the Biotechnology Innovation Organization that steps be taken with all stakeholders to formulate and enter a ***Global Public-Private Partnership for Medicinal Access*** that will seek mutual respect, collaboration, and determination by all stakeholders in addressing and solving the eight factors in a comprehensive and simultaneous fashion.

The goal of the Public-Private Partnership should align with the Sustainability Development Goals such that by 2030 all people have access to the medicines they need through their national or local health systems, and that those medicines be prescribed and managed in such a way as to assure safety and a beneficial outcome as defined by each nation. Another goal of the Public-Private Partnership would be to secure the global innovation system and encourage its development throughout the world. The authors propose an approach for the formation of the ***Global Public-Private Partnership for Medicinal Access*** in the final section**.**

The report concludes with a list of challenges and charges to each stakeholder group so that they may prepare to engage in the Partnership.

2.0 Introduction to the Nature of the Problem

While there have been perennial concerns about the role of patenting in restricting medicinal access, the global AIDS crisis magnified the frustrations, particularly when the first antiretroviral therapies (ARVs) were introduced nearly 20 years ago. During those years, the multinational corporations in the pharmaceutical industry (MNCs) did take a stand in asserting patent rights in the developing world that in many cases did delay proliferation of antiretroviral therapies through the supply chain, and ultimately at the clinic where pricing was significantly higher than patients in these countries could afford. There was a vocal response by advocacy groups through demonstrations and films that inflamed passions. Numerous competitive initiatives by local companies based in these countries challenged the patents on these drugs, and ultimately forced a re-thinking of pricing and availability by MNCs. The MNCs objectively outlined the importance of patents to the process of innovation, but these arguments were rejected out of hand by NGOs and other organizations. Believing that legal adjudication would shed light on the controversy, the industry filed suit against South Africa for patent infringement, naming Nelson Mandela as one of the defendants and further aggravating the negative perception of the industry and the role of patents in limiting access to needed medicines. Both sides of the debate took positions that lead to polarization and the road to the conflation of patents as an obstacle to medicinal access was paved.

In the midst of the controversy, the U.S. government put into effect the President's Emergency Plan for AIDS Relief, or PEPFAR initiative, which increased the availability of antiretroviral therapies. This was accompanied by a loosening of U.S. government regulation, which allowed funds to be spent on antiretrovirals that were not approved for sale in the United States. This did not completely resolve the availability of these needed medicines, but helped improve the situation. The increase in availability demonstrated that the health care systems of the emerging market countries could indeed respond to HIV given the availability of medicines, and that patients competently complied with physicians' orders in the administration of the medicines. Nevertheless, significant gaps remained.

The damage to the standing and role of patenting, however, was done and the efforts of the MNCs to explain the importance of patenting, adjust prices and offer special access programs were not acknowledged to the degree that they should have been. On the contrary, it seemed that every benign action reinforced the perception that patents function as a barrier to medicinal access. During the intervening years, policy makers, international organizations, and activists appear to be drawing lessons from those experiences and applying them to the broader issue of medicinal accessibility, even though the issue of patent protection does not affect the vast majority of products that make up the World Health Organization's list of essential medicines or similar lists instituted by various nations according to Attaran, 2004 and WIPO, 2016. These reports, particularly the latter were the focus of immediate critical response by groups generally opposed to medicinal patenting. Constructive discussion seems elusive.

This past fall, the Secretary-General of the United Nations charged the UN Special Commission with issuing a policy statement that presumes that the international patent system is the root cause of the inaccessibility of medicines. The policy statement is expected to be issued in June 2016. Public documents suggest that the deliberations of the Special Commission are not expected to consider any of the other manifold issues that contribute to the problem of medicinal access for the emerging markets and the developing world.

The basis for the patent system and its role in medicinal innovation has been presented in many forums and is well articulated. Indeed, the World Trade Organization's Trade-Related Aspects of Intellectual Property Rights (TRIPS) was enacted in 1995 with confidence that—as TRIPS related to health care—the pipeline of life-saving therapies would be protected and that incentives for discovery and development for neglected tropical diseases (NTDs) would improve. While this point is argued passionately by those for and against, there has been an increase in discovery and development programs for NTDs but the biological challenges have resisted fulfillment of expectations despite significant basic research at the academies and investment by the MNCs and the biotechnology industry.

This paper does not seek to argue the benefits of the international patent system to innovation or justify the pricing policies of pharmaceutical companies. Instead, it is a literature review that seeks to examine the scope of scholarship that has studied the problems associated with medicinal access in a broad way. The purpose of this review is to expand the global dialog on medicinal access in the hope that

by doing so, it will lead to new efforts to address the universe of issues affecting access in an integrated and rigorous manner, including the role of patenting. The hope is that a more comprehensive range of policies will emerge from a new wave of scholarship that will address the nexus of issues. The role of patenting will still need to be addressed, but ideally in a way that preserves the incentives for investing in innovation while at the same time protecting the needs of the global population for medicinal access.

In reviewing the literature surrounding the complex issue of access to medicines, the authors found that the preponderance of articles by scholars and other advocates for access focused on patents as the central barrier in limiting access by permitting monopolistic pricing practices. In many cases, other factors were ignored. While intellectual property plays a role in the pricing of medicines, it is an incomplete part of the story in terms of national and international policies and programs. Until that issue is put into the context of the problems of access to medicine through an objective appraisal of all of the interrelated factors that drive pricing and availability of drugs, comprehensive solutions to improve access to medicines will go wanting.

The authors of this paper, and their research assistants, reviewed more nearly 170 academic journal articles and various other reports going back more than 20 years that address the issue of access to medicines in the developing world generally, as well as those with a specific focus on India. In addition to the articles discussed herein, the authors reviewed other articles that cited those in the References section. Generally speaking, the articles cited by other later publications fell into the mainstream of criticism about patenting; virtually no scholarly response took exception to conclusions drawn in the literature.

India is a special case in this inquiry because it is a leading producer of medicines—mostly off-patent generic products—that are often priced too high for general access. The review of the literature on access to medicines was conducted in order to develop a comprehensive research agenda for further study by health economists, public health researchers, policy makers and others concerned with these issues.

The existing literature has identified several significant factors that contribute to rising costs and limited access to medicines in India, most of which can be applied to emerging economies. In broad terms, these include:

- Accessibility to care that exists but not in a way that is attainable across societies
- Affordability of care and associated products through either national health insurance, private risk-pooling, and pricing appropriate to the relevant economic environments
- Availability of care in suitably scaled and equipped health care systems
- Awareness of the opportunity to attain care
- Essential medicines procurement
- Pharmaceutical regulation
- Supply chain management
- Socio-cultural obstacles to care

It is our hope that this review will stimulate a deeper conversation about barriers to access to medicines and begin to foster an international dialogue on meaningful strategies to address the problems that undermine the health and wellness of hundreds of millions of people throughout the world. A wide range of creative solutions are needed, whether that be new commercial strategies, public-private partnership models, novel approaches to financing, or the building of indigenous industrial capacity to address various aspects of the problem. The first step to doing that, though, is to develop a common understanding of the complex issues that erect barriers to access.

3.0 History of the Patent and Medicinal Access Controversy

Tracing the lineage of the controversies surrounding the role that patents play in medicinal access is a challenging task for a variety of reasons. These reasons include:

- Writings in the general press or trade publications characteristically conflate non-access related to pricing, production, supply-chain issues, health systems failures and inadequate funding with the existence of patent rights; such literature is polemical, typically not supported empirically and not concerned with sorting out the complexities.

- The history as it appears in scholarly, peer-reviewed literature is non-linear and is punctuated by periods of concentrated attention, e.g. 2000 – 2003 (the HIV-antiretroviral launch) and 2010 to 2013 (review of patent office decisions, primarily in India, surrounding TRIPS or issues emerging from trade negotiations). Consequently, there has been no coherent or sustained objective treatment of the issues.

- Periods of publication dormancy on medicinal access where scholarly attention or focus is on the more generic issues of the role of patents in economic development and innovation without attention to medicines.

- The asymmetry in the role of patenting in medicinal development versus its role in other industrial endeavors has caused inter-industry disagreements and influenced patent policy in ways that satisfy the differing interests of industrial sectors. This situation requires that different industries have different strategies for intellectual property management.

- Complications owing to the influence of global or regional economic instability, civil strife, governmental discontinuity, or catastrophic infectious disease outbreaks on medicinal availability, also add to the challenges.

Nevertheless, there are understandable objections and concerns by groups such as *Médecins Sans Frontières* and other NGOs dedicated to intervention in health needs throughout the developing world, often in the face of unspeakable catastrophe. The mission of these organizations is often frustrated by the lack of access to medicines still under patent sometimes owing to pricing which these groups assume is a function of patenting. The conflation of pricing and patenting, however imprecise, leads to an understandable frustration that has resulted in strong positions challenging the moral basis for patenting medicines. The literature representing that position is generally designed for policy makers and the public. This study does not catalog or comment on that literature as such. The point of view of these organizations has found its way into scholarly studies and some of that is captured and discussed herein. The authors of this report searched for scholarly articles that countered this position, but did not identify publications in peer-reviewed literature.

For the sake of organization, this section of the literature review categorizes the body of literature into three groups: The first group is built around articles analyzing the economic and innovation impact of patenting. The second group is built around the body of literature that confronts whether the patenting of medicines raises human rights issues. The third group is comprised of articles focused on the practical administration of patent regimes vis-à-vis the availability of medicines in the emerging and frontier markets, including India and African countries.

Articles analyzing the economic and innovation impact of patenting

A large body of scholarly economic literature on the role of patenting in economic development and innovation on a general basis is rooted in two separate debates. The first of these was U.S.-centric during the period when U.S. competitiveness was under assault by Japanese and European companies. The analysis at that time and the focused debate resulted in formation during the 1980s of the US Court of Appeals for the Federal Circuit, which included judges with patent expertise. In addition, there was a strengthening of the administration of U.S. patent law and reversal of a trend towards weaker patents that emerged in the 1970s. The second set of debates was in an international context surrounding the Uruguay Rounds of trade negotiations in the General Agreement on Tariffs and

Trade (GATT), the precursor to the World Trade Organization (WTO). Economists and scholars developed positions either supporting or opposing stronger international patent treaties, but ultimately the scales tipped in favor of a stronger system that we know today at Trade-Related Aspects of Intellectual Property Rights, or TRIPS, which was ratified in 1995 and became one of the requirements—with a grace period—for a nation's accession to the WTO. This grace period extends requirements for accession to TRIPS until 2033 for the Least Developed Countries (LDCs)

After the constitution of the WTO, a new round of negotiations began in Doha, Qatar in November 2001. Technically, the Doha Rounds are still in progress, but unlike the Uruguay Rounds of GAAT, the developing nations have demanded and exerted greater influence on the global economy. In the Doha Rounds, with a specific focus on medicinal availability, the emerging economies succeeded in clarifying the concept of compulsory licensing. There are many misconceptions about the history of compulsory licensing and these misconceptions contribute to the ambiguity or misinformation found in public, professional, and scholarly literature. Indeed, the notion of compulsory licensing is not a modern phenomenon. It was anticipated in the formation of American patent law in the 18th century, as well as British and German patent law during the 19th century.

In simple terms, compulsory licensing is the right of a government to allow a party other than the patent holder to produce the patented product or process without the consent of the patent owner, but with the requirement that the patent owner be compensated. It is one of the flexibilities on patent protection that was included in the original TRIPS Agreement of January 1995. The November 2001 Doha "Ministerial Declaration on TRIPS and Public Health" did not create compulsory licensing per se, but better defined and refined the concept. There are two provisions that address the least-developed countries and countries that do not have production capacity. The Declaration clarified the TRIPS Agreement's flexibilities and assured governments that they can use the flexibilities. Until that time, some governments were unsure about how the flexibilities would be interpreted.

This literature review does not study the body of literature leading up to TRIPS and the Doha Declaration that clarified compulsory licensing. Instead, the focus is on carefully selected scholarly works that retrospectively examine, and mostly challenge, the intellectual property principles as they relate to human health and medicinal availability. There is also a body of literature addressing the impact of the existence of compulsory licensing on innovation. A representative piece will be cited below.

An observing reader will notice that most of the articles cited are not recent. This was not a deliberate choice--it represents the body of literature. A great deal of research is yet to be done. By the community of scholars. Moreover, the majority of the articles take a position critical of patent rights. Again, this was not a deliberate selection. Scholarly literature generally has not made a case for patent rights vis-à-vis medicinal access. The articles cited herein are summarized but deliberately not treated critically by the authors of this report. The authors do not necessarily agree with or endorse the premises or conclusions of the articles, but offer them as landmarks in the history of the dispute.

Scholarly literature analyzing the economic and innovation impact of patenting

Boldrin & Levine (2013) take a strong position on the case against patents. They state "there is no empirical evidence that patents serve to increase innovation and productivity, unless productivity is identified with the number of patents awarded—which, as evidence shows, has no correlation with measured productivity." They argue that "this disconnect is at the root of what is called the 'patent puzzle': in spite of the enormous increase in the number of patents and in the strength of their legal protection, the U.S. economy has seen neither a dramatic acceleration in the rate of technological progress nor a major increase in the levels of research and development expenditure." A critical view might challenge this approach to measurement of innovative output and the causal relationships with R&D funding. The authors, however, assert that "both theory and evidence suggest that while patents can have a partial equilibrium effect of improving incentives to invent, the general equilibrium effect on innovation can be negative. The historical and international evidence suggests that while weak patent systems may mildly increase innovation with limited side effects, strong patent systems retard innovation with many negative side effects. It is only after the initial stage of rampant growth ends," they claim, "that mature industries turn toward the legal protection of patents, usually because their internal growth potential diminishes and they become more

concentrated." Their assessment, they believe, can be supported historically across several industries, but seems inconsistent with the genesis and development of biotechnology innovation and biotechnology patents. Their proposed solution, however, is to abolish the patent system and replace it with other legislative instruments.

Chien (2003) posits that the patent system is built on the premise that patents provide an incentive for innovation by offering a limited monopoly to patentees. The inverse assumption that removing patent protection will hurt innovation has largely prevented the widespread use of compulsory licensing. In this article, Chien empirically tests this assumption. The article compares rates of patenting and other measures of inventive activity before and after six compulsory licenses over drug patents issued in the 1980s and 1990s. Chien observed no uniform decline in innovation by companies affected by compulsory licenses and found little evidence of a negative impact, which Chien reports is consistent with earlier empirical work. According to Chien, while anecdotal, these findings suggest that the assertion that licensing harms innovation is probably wrong. Chien comments on the use of compulsory licensing to reduce the price of AIDS and other drugs for developing countries suggesting that compulsory licenses need not result in a decline in innovation and that this policy option for increasing access to medicines deserves greater exploration.

Eisenberg (2001) asserts that patents are often portrayed as the necessary reward to compensate pharmaceutical firms for the huge costs and risks associated with U.S. Food and Drug Administration (FDA)–mandated clinical trials of new drugs. Eisenberg observes that the relationship between the patent system and other regulation of drugs, however, is more complex than this simple formulation suggests. Drug regulation operates in tandem with patents to make proprietary products profitable, and patents themselves threaten to limit profitability by diverting profits elsewhere. At the same time, according to Eisenberg, resistance to high drug prices is prompting new state and federal regulatory initiatives that threaten to reduce the value of drug patents. Eisenberg concludes that "the distinctive intertwining of patents with other regulatory regimes and the shifting role of patents in the biopharmaceutical sector call into question how this singular success story for innovation policy will play out in the future.

Moser (2013) is an example of the inherent difficulty in the analysis of patent policy across industries. Moser argues that in the most basic theoretical models, patents pose a tradeoff between social benefits from incentives for invention and losses in consumer welfare as a result of monopoly pricing. Moser adds that providing stronger patents for early generations of inventors may also weaken incentives to invest in research and development for later generations making the overall effects of stronger patents on innovation difficult to predict. Negative incentive effects, she asserts, are particularly severe if the boundaries of intellectual property are poorly defined so that later generations of inventors place themselves at risk of ruinous litigation. Litigation risks are exacerbated when incumbents build "thickets" of strategic patents that cover little innovative progress and instead serve as a legal weapon to protect incumbents' profits. Moser observes that recent patent wars over smartphones and tablet computers have moved these issues to the forefront of policy debates. Analyses of historical data have emphasized the role of patent laws in creating incentives to invent, promoting innovation, and encouraging economic growth. Patent data may, however, fail to capture innovation that occurs outside of the patent system, for example, in countries without patent laws or in industries in which inventors rely on alternative mechanisms to protect their intellectual property. Moser concludes that survey data for the late 20th century indicate that commercial research and development labs in most industries deem alternative mechanisms, such as trade secrets and lead-time to be more effective than patents. This approach to intellectual property protection, however, is not characteristic of the biopharma industry [Author's observation].

According to Ouellette (2010) the pharmaceutical industry is the poster child for a strong patent system. Medicines companies bear the high costs of obtaining approval from the FDA only because they can then charge high prices for patented drugs without fear of generic competition. As described by Burk and Lemley (2009), drugs are also special because of the low number of patents per product. "In some industries, such as chemistry and pharmaceuticals, a single patent normally covers a single product," they write. "Much conventional wisdom is built on the unstated assumption of such a one-to-one correspondence." Although many have repeated this one-patent, one-drug assumption, Oullette states, there has been little empirical analysis of how many patents actually protect each drug. Most small-molecule drugs are protected by multiple

patents. The average was nearly 3.5 patents per drug in 2005**,** with more than five patents per drug for the best-selling pharmaceuticals. These numbers have increased over time. Oullette makes an important observation with respect to follow-on patents that has important implications for the growing number of universities and other public-sector research institutions that want to make their patented medical technologies accessible in developing countries. For example, if a university chooses not to patent a new drug molecule in India but subsequently licenses its U.S. patent on that molecule to a pharmaceutical company that files a follow-on method-of-treatment patent in India, then Indian generic manufacturers will be unable to produce the drug. These results are important for the ongoing debate about public-sector patenting. The widespread prevalence of follow-on patents also has implications beyond the university context.

Rangnekar (2006) writes that the January, 2005 amendment to the Indian Patent Act of 1970 brought India into full compliance with its obligations under TRIPS. The amendment allowed for medicinal product patents. This amendment was characterized, he says, "by a relatively muted rhetoric and a remarkable level of shared consensus amongst campaigners and critics." The paper suggests that the limits to implementing TRIPS are equally on account of ambivalence within the government with respect to intellectual property and the changing self-interest of sections of the Indian pharmaceutical industry. Thus, despite a favorable international climate in the area of intellectual property, patent reform in India has been doubly constrained by the narrow agenda and domestic factors. This article is somewhat difficult to interpret. The title suggests that there will be an argument that the patent policy changes in India will deny needed medicines to the population. The argument, however, seems to be that in addressing competing concerns among Indian stakeholders that the Parliament produced a law that does not serve national ambitions to build innovative companies or those entities in India focused on medicinal innovation.

Scholarly literature that confronts whether the patenting of medicines raises human rights issues

Attaran and Gillespie-White (2001) offer a balanced view when asking the question "Do patents for antiretroviral drugs constrain access to AIDS treatment in Africa?" Although this report focuses on India, their reasoning on the African situation anticipates the review of the literature offered in Section 6 of this paper. Attaran and Gillespie-White observe that public attention and debate have focused on access to treatment of AIDS in poor, severely infected countries. Whether patents on antiretroviral drugs are impeding access, Attaran and Gillespie-White state, is unknown. The authors of this report have not identified studies since 2001 that answer that question. Attaran and Gillespie-White studied the patent status of 15 antiretroviral drugs in 53 African countries. Using a survey method, they found that these antiretrovirals were patented in few African countries (median, 3; mode 0) and that in countries where antiretroviral patents do exist, only a small subset were patented (median 4; mode, 4). At the time, the observed scarcity of patents cannot be simply explained by a lack of patent laws because most African countries offered patent protection for pharmaceuticals for many years. Furthermore, in the case at hand, geographical patent coverage did not correlate with access to antiretroviral therapies in Africa suggesting that patents and patent law are not a major barrier to treatment access in and of themselves. The authors conclude that a variety of de facto barriers are more responsible for impeding access to ARV therapies including but not limited to the poverty of African countries, the high cost of antiretroviral treatment, national regulatory requirements for medicines, tariffs and sales taxes, and above all, a lack of sufficient international financial aid. Subsequent to publication of the Attaran and Gillespie-White in 2001, some of these issues have been addressed through the emergence of the Global Fund and PEPFAR, but the overall circumstances have not been entirely relieved.

Cullett (2003) declares that patenting and inaccessibility to medicines have become conflated in the view of many people because there have been circumstances where the relationship of pricing allowed by a patent position and lack of access became somewhat stark. Cullett points out that that the link between medical patents and the human right to health care became a subject of central concern at the international level, as exemplified by the debates at the 2001 World Trade Organization ministerial conference. International attention to the issue was focused in large part on the HIV/AIDS crisis and the question of access to drugs for patients in developing countries, which are the most severely affected by the epidemic. He extends the concern to the broader issue of access to medicines identifying two main areas of law as relevant in the patent-human rights debate. First, he declares that the question of access to medicines is a central issue in any consideration of the human right to health care as codified in the

Covenant on Economic, Social and Cultural Rights. Second, debates on access to drugs became linked to a fundamental question of whether medicines should be patentable. Cullet goes on to explain that the increasing scope of patentability in the health sector, codified in TRIPS, constitutes one of the most significant changes in law for developing countries that are WTO members. Intellectual property law and human rights law, he believes, have largely evolved independently. "While human rights documents have given some consideration to the position of intellectual property in relation to human rights," writes Cullet, "there has been no similar effort in the field of intellectual property."

Hestermeyer (2008) discusses the facts that called attention to the conflict between the TRIPS Agreement and access to medicine. The public discussion was initially triggered by the pricing decision of the patent holder of the first AIDS medicine, AZT. It took on global proportions when the pharmaceutical industry sued the South African government that wanted to impose compulsory licenses for patents on pharmaceuticals to provide its population with cheap AIDS medication. Hestermeyer also recounts the events surrounding the anthrax attacks in the United States, when the Canadian and U.S. governments threatened to break Bayer's patent on Cipro®.

Lanjouw (1997) offers a provocative title: "The introduction of pharmaceutical product patents in India: heartless exploitation of the poor and suffering?" She writes that the decision to require that countries grant product patents for pharmaceutical innovations as a condition of membership in the WTO was very contentious. Almost fifty developing countries were not granting patent monopolies for drugs during the period the Uruguay round of GATT was being debated and these countries fiercely resisted the inclusion of this requirement, claiming that vastly higher drug prices would be associated with such patents. On the other side, business interests in the West urged them to consider the beneficial effects such protection might bring both in terms of focusing more research on tropical diseases and encouraging greater domestic and foreign investment in local research activities. The paper discusses the various theoretical implications for a developing country of introducing product patents for pharmaceuticals. Using India as an example, it then brings together information gathered from both published sources and personal interviews to examine the potential magnitude of these effects. While not arriving at a conclusive answer to the question posed in the title, there are some suggestions about the way events might unfold as the policy is implemented.

Sampat (2009) notes that there is a widespread and growing concern that patents hinder access to life-saving drugs in developing countries. Sampat observes that student movements and legislative initiatives emphasized the potential role that research universities in developed countries could have in ameliorating this "access gap." These efforts are based on the assumption that universities own patents on a substantial number of drugs and that patents on these drugs are currently filed in developing countries. Sampat provides empirical evidence regarding these issues and explores the feasibility and desirability of proposals to change university patenting and licensing practices to promote access to medicines in the developing world.

't Hoen (2002) explores the issues of essential medicines access. She offers that the reasons for the lack of access to essential medicines are manifold, but in many cases the high prices of drugs are a barrier to needed treatments. Prohibitive drug prices are often the result of strong intellectual property protection. [Note: as previously cited there are articles and reports cited that dispute the assertion that the essential medicines list is populated by patented products.] Governments in developing countries that attempt to bring the price of medicines down have come under pressure from industrialized countries and the multinational pharmaceutical industry. Public health advocates welcomed the aforementioned Doha Declaration as an important achievement because it gave primacy to public health over private intellectual property, and clarified WTO Members' rights to use TRIPS safeguards. But the Doha Declaration did not solve all of the problems associated with intellectual property protection and public health. The recent failure at the WTO to resolve the outstanding issue to ensure production and export of generic medicines to countries that do not produce may even indicate that the optimism felt at Doha was premature. While this article is nearly 15 years old, the sentiments that it expresses are still widely felt.

Scholarly articles focused on the practical administration of patent regimes vis-à-vis the availability of medicines in the emerging and frontier markets, including India and African countries

Lanjouw (2003) observed that, at the time of publication, there continued to be widespread criticism of the extension of patent rights on pharmaceuticals in the developing world as required by WTO membership. This book chapter examined arguments in favor and against this strengthening of worldwide patent protection. It emphasized that these new pharmaceutical patents promised benefits and costs that differ according to the characteristics of diseases. Some diseases primarily affect poor countries. For these diseases, patents will not be sufficient to attract substantial private investment, because purchasing power is low. However, globally available and well-defined patent rights could increase the benefits derived from greater public financing of research on pharmaceutical products for the developing world. For major global diseases the justification for extending patents in poorer countries is less clear. Thus the optimal global framework for pharmaceutical patents might require differentiating the protection given to products in accordance with their extremely different global markets. The chapter considers standard intellectual property and regulatory mechanisms that could be used to differentiate protection. All have serious drawbacks. It then describes a new mechanism that would make differentiating protection a more feasible policy option.

Lanjouw (2005) considers how patent rights and price regulation affect whether new drugs are marketed in a country, and how quickly. The analysis covers a large sample of 68 countries at all income levels and includes all drug launches over the period 1982-2002. It uses originally compiled information on legal and regulatory policy, and is the first systematic analysis of the determinants of medicinal launch in poor countries. Price control tends to discourage rapid product entry, while the results for patents are mixed. There is evidence that local capacity to innovate matters and that international pricing externalities may play a role.

Ngoasong (2009) offers constructive thinking on approaches to addressing the problems of medicinal access. During the first decade of the new millennium global health partnerships had been formed to provide a better policy response to Africa's health problems. This paper uses narrative policy analysis to explain the historical processes and challenges facing national and global health policy in facilitating access to medication in African countries. An overview of the historical context of events leading to the creation of global health partnerships is followed by a content and context analysis of two such efforts—the Roll Back Malaria partnership and the Accelerating Access Initiative. The historical narratives implicitly reflect the context in which policy decisions are produced and implemented. The deployment of global health partnerships in Africa reflects a convergence of the competing and conflicting narratives, in relating to strategies previously promoted by various multilateral and bilateral development agencies, international civil society organizations, and the private commercial industry to facilitate access to medication. The importance of this article will be emphasized in the recommendations section of this report.

Scherer & Watal (2002) explore the tension between granting patent protection under TRIPs and the availability of medicines at affordable prices to developing countries. A crucial consideration under the TRIPS compulsory licensing option is the "adequate remuneration" paid. Their analysis shows that the royalties set under past compulsory licenses have been much lower than those that would be established under the "forgone profits" standard of U.S. Patent law. To respect comparative advantage in the supply of licensed drugs, the TRIPS language requiring that compulsory licensing be predominantly for domestic supply needed clarification at the time of writing. The multinational drug pricing strategy that best combines equity with coverage of research and development costs is a variant pricing method under which prices are much lower in nations with an inability to afford medicines and/or high price elasticities in wealthy nations. This is sometimes referred to as tiered pricing methodology. Donations can also enhance the supply of medicines to low-income nations. An analysis shows that when the marginal cost of production is low relative to inventoriable average cost, donations can actually enhance a drug producer's after-tax profits under U.S. tax laws. Minor tax law changes to enhance donation incentives are suggested.

Sell (2007) offers an argumentative piece challenging TRIPS and TRIPS-Plus. Sell states that the battle over access to essential medicines revolves around the rights to issue compulsory licenses and to manufacture and export generic versions of brand name drugs to expand access. Global brand name pharmaceutical firms have sought to ration access to medicines and have used their economic and political clout to shape United States trade policy. They have succeeded in getting extremely restrictive TRIPS-Plus, and even U.S-Plus, intellectual property provisions into regional and bilateral free trade agreements. Asymmetrical power relations continue

to shape intellectual property policy, reducing the amount of leeway that poorer and/ or weaker states have in devising regulatory approaches that are most suitable for their individual needs and stages of development. While the overall trend is disturbing to these nations, some recent activities in the World Health Organization and evidence of greater unity behind health-based TRIPs flexibilities provide some grounds for cautious optimism for them.

Waning, et al. (2010) offer that Indian manufacturers of generic antiretroviral medicines facilitated the rapid scale up of HIV/AIDS treatment in developing countries though provision of low-priced, quality-assured medicines. The legal framework in India that facilitated such production appeared to be changing with implementation of the TRIPS, and intellectual property measures being discussed in regional and bilateral free trade agreement negotiations. Indian generic producers supply the majority of antiretrovirals (ARVs) in developing countries. Future scale up using newly recommended ARVs will likely be hampered until Indian generic producers can provide the dramatic price reductions and improved formulations observed in the past. Rather than agreeing to inappropriate intellectual property obligations through free trade agreements, India and its trade partners—plus international organizations, donors, civil society and pharmaceutical manufacturers—should ensure that there is sufficient policy space for Indian pharmaceutical manufacturers to continue their central role in supplying developing countries with low priced, quality-assured generic medicines.

Conclusion on the History of the Patent and Medicinal Access Controversy

The above survey of the literature over the last 15 years identifies a preponderance of articles critical of the patent regime generally and TRIPS in particular. This report refrains from making a critical assessment of each article. While the authors of this report have reservations regarding the hypotheses and methods of many of the articles, the papers merit detailed response through scholarly channels and the courtesy of treatment in kind. Following a study of articles published later that cite the above, the authors of this report conclude that the academic community, thus far, has not responded with research and publication that either contradicts the findings of the cited articles or establishes an alternative interpretation of the role of patenting on medicinal innovation and access. This will be addressed further in the Recommendations section.

4.0 India and Medicinal Access

Why the focus on India?

One of the tragic ironies of India's health care continuum is that even though the nation is one of the world's major manufacturers of pharmaceuticals, and it is able to supply medicines at lower prices than most other low- and middle-income countries, the Indian people have limited access to medicines at affordable prices. Spending on medicines represents the largest component of out-of-pocket spending on health care for its citizens. For the nation's poorest people, it accounts for about three-fourths of all out-of-pocket spending on health care (Joumard et al. 2015). Health care in India, as measured by a variety of indicators, continues to lag most other large, middle-income countries despite the nation's significant gains in life expectancy during the past 40 years (Joumard et al. 2015).

The situation is exacerbated in India by the size of the population, the pervasiveness of poverty, and the rise of non-communicable diseases. With a population of approximately 1.3 billion people, nearly 40 percent of India's population lives on less than US $1 per day (Bhargava and Kalantri 2013). In fact, according to the World Health Organization, an estimated 649 million people in India are without regular access to essential medicines. Because public health facilities are often out of stock of most essential medicines, people in need of these medicines often are forced to purchase them in the private sector, "a compulsion that often spells calamity for those who can ill afford the twin burdens of sickness and health care costs" (Bhargava and Kalantri 2013).

As a nation, India continues to underinvest in health care relative to other nations. Overall, India's spending on health care in 2012 accounted for just 4 percent of GDP, half of the level of spending seen in Brazil and South Africa, and significantly less than seen in China, according to data from the Organisation for Economic Co-operation and Development. In fact, India ranks 184 out of 191 countries in terms of public spending on health with government at various levels accounting for about one-third of that spending (Joumard et al. 2015).

The Trade-Related Aspects of Intellectual Property Rights agreement, or TRIPS. the international agreement administered by the World Trade Organization that established minimum standards for intellectual property in an effort to harmonize regulation among its members, has been an ongoing source of controversy in India and elsewhere because of provisions that address patents on medicines. Critics of the agreement blame patents for limiting access to medicines by making medicines too expensive in the developing world.

Critics of TRIPS argue that by allowing patent holders to maintain a monopoly on a medicine they are able to charge more for it than they would be able to in the face of robust competition from generic drugs. The public benefit of granting a period of market exclusivity through patent protection is meant to serve as an inducement for innovators to make high-risk investments in the research and development of innovative medicines, but these critics argue that in developing nations there has not been the promised payoff of the availability and access to new medicines. Moreover, the granting of pharmaceutical patents, they contend, has not resulted in significant investment by drug developers in efforts to develop drugs for neglected diseases that represent a substantial unmet medical need in these nations. The industry responds to these arguments thought the implementation of access systems, on-going research on neglected diseases and tiered-pricing systems. In many instances, local low-cost producers are issued licenses by the MNCs so that lower cost products can be made available. These policies and actions are generally not acknowledged.

India's accession to TRIPS in 2005 was preceded by heated debate within the Indian Parliament about how intensely to push back on the WTO intellectual property provisions related to medicines. Policy makers expressed concern over the public health effects by arguing that pharmaceutical patents would inhibit access to medicines because the population would be forced to pay higher prices. The Indian pharmaceutical industry also expressed objections because of the economic impacts of the agreement under the belief that the adoption of TRIPS would challenge the business model of the Indian industry and ultimately lead to the failure of indigenous pharmaceutical producers, drive unemployment in the industry, and increase prices of medicines by reducing competition.

In anticipation of India's accession to TRIPS, the country passed the Patent (Amendments) Act, 2005. Section 3(d) of the act, for the first time, extended patents to include pharmaceutical products. The provision, however, carefully proscribes what is and what is not patentable. For example, Section 3(d) does not allow for the patenting of discoveries of new forms of medicines when they do not increase

therapeutic (or clinical) efficacy. Moreover, Section 3(d) does not grant patent rights for new uses of an existing medicine, a reflection of concern that pharmaceutical companies might seek to extend patents by modifying them in ways that do not provide real benefits. This latter justification of Section 3(d) is built around a dubiously premise. The concern embedded in the law is that pharmaceutical companies employ insignificant changes to "evergreen" the product's patent position. This is rarely the case. Most research and development on existing pharmaceuticals is for the purpose of increasing the safety profile, improving efficacy or promoting more efficient use or bioavailability – all socially beneficial aims which are still subject ot regulatory review and approval.

More than 10 years after India's accession to TRIPS, concern about the negative impact of patents on access to medicines has not diminished. As efforts to weaken patent protections on pharmaceuticals continues, there is growing anxiety among the pharmaceutical industry outside of India that Indian patent law is problematic. Innovation-oriented Indian pharmaceutical and biotechnology companies also express concerns that Indian patent law might actually restrict the growth of domestic firms, even as they advance their own innovation agendas.

5.0 Comprehensive analysis of the components of medicinal access: a literature review

5.1 Accessibility to care that does exist but is not attainable

The dimensions of accessibility to care relate to: remoteness; density; percentage of residents living with accessible radius time to health facility for consultation, diagnostics, therapeutics and other intervention. Accessibility to care can be defined as having "the timely use of personal health services to achieve the best health outcomes."

Nature of the problem

The literature points to a prominent theme of people choosing a doubly expensive path for care: treatment over preventive care and private doctors over public doctors. The literature also observes a general lack of essential medicines provided in public facilities for a plethora of reasons described in the Essential Medicines section below. As a practical matter, public health facilities are often closed during day time with doctors and nurses absent during scheduled hours. This is also the case for the public generic pharmaceutical outlets that provide essentially free medicines. While these are relative frequent circumstances in India, the literature suggests that there are similar problems throughout the emerging markets.

Review of scholarly literature

Some 50 to 80 percent of the Indian population has limited access to essential medicines. This may be due to facilities not having essential medicines, or to the fact that the Indian population chooses not to purchase essential medicines in public facilities, but often opt to when financial means permit them to purchase these medicines from private retailers. The literature is inconclusive on the reasons for this phenomenon. There is a frequent lack of medicines from the public sector providers. This compels patients to purchase from private suppliers at an average cost that is six times higher. The WHO Essential Medicines has been adopted in different ways by different countries. The widest variations among countries have to do with the administration of national essential medicines programs.

Sengupta (2005) observed that Indians frequently choose to seek private sector medical services. The Government, until the time of that publication, subsidized the private sector by providing building land at low rates, exemptions from taxes and duties for importing drugs and medical equipment, and through concession to doctors setting up private practices and nursing homes. Health professionals trained in public institutions typically move to private sector providers as soon as soon as their careers permit because of better compensation and superior care infrastructures.

As of the time of publication, the private sector had made significant strides at the expense of the public sector. At first, people at the base of the pyramid could not afford to access private care, but today national and state insurance programs directed at the base of the pyramid allow access to private care, but arguably this dilutes resources for the public providers.

In a more recent publication, Kotwani (2010) probes the question "Will generic drug stores improve access to essential medicines for the poor in India?" The framework for answering this question starts with consumer perceptions and preferences. There is an important distinction between "Branded versus Branded-generic" products. Branded medicines are manufactured by a multinational or an Indian manufacturer of good repute. Branded medicines sell at higher prices. All medicines carry trade names and are available in private retail outlets. Kotwani found that median availability of any given basket of essential medicines to be 0 to 30 percent in the public sector outlets. The paper observes that lack of availability drives low-income patients to buy more expensive medicines from private sources or simply go without treatment. The paper observed that consumers have less confidence in the quality of generic medicines available at public facilities. On the one hand, if patients can afford them, they buy from private retail pharmacies. On the other hand, when they visit a public facility, they want free medicines. "Are new stores being opened for the benefit of low-income populations or for the sustenance of government-owned drug companies?" writes Kotwani, who asks shouldn't essential drugs at generic drug stores reflect the national list of essential medicines or the state essential medicine list?

Singhal et al (2011) report on the Jan Aushadhi Stores in India and the quality of the medicines they distribute. The Government of India has initiated the scheme of Jan Aushadhi Stores, planned in each district in the country, to provide for cheaper generic medicines as a way of addressing concerns about the

availability of such products in public sector hospitals. However, several surveys had focused on poor quality image of generics, both in the mindsets of prescribers, as well as patients. Singhal tested these perceptions and compared the quality of four commonly used drugs: Alprazolam, Cetrizine, Ciprofloxacin, Fluoxitine, available as generics from Jan Aushadhi Stores, with that of the respective leading brands, known as, Restyl®, Alerid®, Ciprobid® and Fludac® respectively, from the market. The researchers tested the medicines as per the Indian pharmacopoeial guidelines. They found that all the four pairs of generics vs. popular branded medicines passed the relevant pharmacopoeial tests, thereby underlining that generics are of as good quality as branded medicines. The study highlighted the importance of spreading awareness on quality of generics, amongst the prescribers and the public as well. These stores are slowly proliferating and by July 2014, 166 stores had been opened, but 76 of them were non-functional. As of this writing, they remain closed. None of the stores in Andhra Pradesh, West Bengal, and Uttarakhand is operational. The Bureau of Pharma PSUs is determined, however, to launch as many as 3,000 Jan Aushadhi Stores by 2017 and will subsidize the establishment of the facilities.

Open areas of investigation on accessibility to care

Accessibility to care is a bedrock issue that must be addressed as a prerequisite to the problem of medicinal access. There are many areas of open investigation such as:

- What is the relationship of the geographic concentration of healthcare facilities to the concentration of access to medicines?
- What are the sources for the dispensing of medicines in rural regions or inner cities?
- What is the reliability of the products dispensed to people in rural areas?
- Are the staffs of remote primary care facilities able to dispense and monitor medicines?

5.2 Affordability

The question of affordability centers on the ability of patients to be able to pay for the medicines they need. More broadly, the issue of affordability encompasses payment mechanisms, such as public and private insurance, the market dynamics that enhance or minimize competition, taxes and tariffs that increase costs to patients, and the use of price controls. A variety of issues affect affordability. This includes such things as the cost of medicines in proportion to incomes and government financing, pricing policies, the impact of tariff or other obstacles to trade, as well as related issues, such as currency conversion and the balance of trade.

It is not possible to separate the pervasive poverty in India with the challenge of access to medicines. Despite the fact that India is now home, in U.S. dollar terms, to more than 1 million millionaires—more than any other nation other than the United States, Russia, Turkey, and Germany—there is growing poverty as well. A 2007 report by the National Commission for Enterprises in the Unorganized Sector found that 836 million Indians or 77 percent of India's population, earn less than 50 cents (Rs. 20) a day, a threshold that qualified them for the official designation of "poor and vulnerable" (Satyanarayana and Srivastava 2007). In 2014, the Indian government recalculated what it means to be below the poverty line to include people earning less than 52 cents (Rs. 32) a day in rural areas and less than 78 cents (Rs. 47) a day in urban areas.

How big a portion of India's population lives in poverty depends on how poverty is defined. In 2011, the gross national income per capita in India reached US $1,420, or US $3.89 a day, according to the World Bank. Some 42 percent of the population earns less than US $1.25 a day, meeting the World Bank's definition for poverty (Kotwani 2013).

While India's planning commission in 2007 put the number of people below the poverty line at 27.5 percent of the population, some 315 million people, others have suggested it is much higher. Duggal (2007) says the estimate is based on a "ridiculous" monthly per capita consumption rate of Rs. 356.30 for rural areas and Rs. 538.60 for urban areas, far less than the "globally accepted figure under Millennium Development Goals of $1 per day for absolute poverty, or Rs. 1,200 monthly per capita expenditure. Duggal (2007) notes that using this definition, two-thirds to three-fourths of the population would be in absolute poverty.

Some 50 to 80 percent of the Indian population is not able to access all of the medicines they need (Maiti et al. 2015). In fact, 39 percent of the world's population without access to medicines lives in India. A central reason for that is their inability to afford the drugs they need. As Satyanarayana and Srivastava

(2007) write, "the likelihood of an individual having access to essential medicines is still greatly affected by income level."

Though many people have made the argument that patents, by preventing competition, allow drugmakers to demand more for their products than they otherwise would be able to charge, almost all of the drugs on Essential Medicines List are off-patent. A 2004 *Health Affairs* study authored by Amir Attaran, then a fellow in the Royal Institute of International Affairs in London, found that more than 98 percent of the drugs on the list at that time were drugs that were not protected by patents. Though there's reason to believe there has been a slight increase in the number of drugs under patent protection that have been added to the list since then, the indication is that the vast preponderance of medicines on the list continue to be ones that are without patent protection today. "Briefly," he wrote, "I find that patents for essential medicines are uncommon in poor countries and cannot readily explain why access to those medicines is often lacking, suggesting that poverty, not patents, imposes the greater limitation on access" (Attaran 2004). The World Intellectual Property Organization (WIPO) recently published a similar study that revealed that no medicines on the Essential Medicine List were currently covered by patents.

Poverty and illness are closely bound together. Each drives the other. And, combating one is a powerful way to combat the other. As Satyanarayana and Srivastava (2007) note, the two create a "vicious cycle." "The poor are especially vulnerable to major health risks as inadequate and improper nutrition, unsafe water supply, poor sanitation and hygiene, toxic indoor smoke, and extremely limited access to health education and services, all of which contribute to huge disease burden in the poor countries," they write. "Illness keeps poor wage earners away from work, children away from the school depriving them of education they need."

The situation in India is exacerbated by the lack of public spending on health care and the resultant financial burden individuals must bear to pay for care. The government of India spends around 1 percent of GDP on health, among the lowest levels of public spending in the world (Kumar et al. 2011). (That figure has not changed significantly with government spending on health care rising to 1.3 percent of GDP according to the Economic Survey of India 2015-16.) In the absence of robust public spending, individuals have had to fill the gap with private expenditures accounting for some 78 percent of health spending (Kumar et al. 2011). The availability of public health services is limited and falls far short of the need. "As a result, most Indians access private health care that is expensive, unaffordable, unreliable, and impoverishing," write Kumar et al. (2011). Nevertheless, it can be difficult for people to find quality care in the private sector, particularly in rural and remote areas. Practitioners often lack appropriate training and facilities are often substandard, he adds. One consequence of the lack of public spending is the high portion of health care funded by out-of-pocket spending, with the majority of that—some 70 percent—going to pay for the purchase of medicines (Garg et al. 2009).

Price surveys have shown a wide disparity in prices of particular medicines and found that people who are poor cannot afford the costs. Roy et al. (2012) found that there was not only a great variance between different brands of the same drug (25 to 3400 percent), but even among retail stores selling the same brand (32.7 percent). Difference in wholesale prices, retail mark-ups, and taxes all contributed to the variability in prices of medicines (Roy et al. 2012). Since that study the government of India has expanded the range of medicines subject to price controls and that action would have likely caused a narrowing of the price range for some essential medicines.

In addition, studies have found that markups from the various players in the supply chain, as well as taxes, play a significant role in increasing the cost of drugs. Kotwani et al. (2007) examined the prices of six common drugs at six sites in India and found that the prices of medicines in the private sector were about three to five times the procurement price in the public sector. The study characterized those margins as high and said it indicates that there is a lot of margin for manufacturers, wholesalers, and retailers (Kotwani et al. 2007).

The literature indicates an ongoing debate in India as to whether free market competition or price controls are the most effective way to contain the cost of medicines. Both approaches have had problems for various reasons. In order for free market forces to produce adequate pressures to contain prices requires vibrant competition. Even though the overwhelming majority of medicines that make up the essential medicines list are off patent, the peculiarities of the India marketplace has undermined the competition from unbranded (or INN) generic alternatives. That is because in India the market is essentially made up of

so-called "branded medicines," generic drugs that use the power of a well-known global name global or Indian manufacturer that is marketed to doctors, and branded generics, which are more like traditional generic drugs and left to retailers to push to consumers.

Many doctors in India do not trust unbranded generic drugs, even though the same manufacturer may produce an equivalent branded generic in the same plant that they produce its unbranded equivalent. Doctors may also have economic incentives from the manufacturer or others in the pharmaceutical supply chain to prescribe a specific branded version of the drug. A commonly voiced concern is that doctors are unaware of an unbranded generic's chemical name and only familiar with the branded names. An added barrier to the use of less expensive unbranded generics is a legal prohibition in India for a pharmacist to provide a substitution of a generic equivalent (whether branded or unbranded) when a branded medicine is prescribed (Singal et al. 2011). "Hence," writes Singal et al (2011), "consumer awareness for the generics, variety of trade names available in the market, and price variation is very limited." This prohibition also leads to pharmacies to focus on stocking branded medicines since doctors are more likely to prescribe them and they cannot provide substitution. As a result, patients are often left without choice but purchase more expensive branded products (Kotwani 2013).

The sheer volume of medicines available in India and the challenge doctors face staying informed about what is available complicates matters and adds to the difficulties of expanding the use of generic medicines. Roy et al. (2012) notes there are more than 20,000 formulations on the market in India. "Many are formulations of unproven efficacy," they write. "It is not humanly possible for even a well-informed, health care provider, to be informed about all these formulations. Due to this lack of information, it is the poor patient who has to bear the medical and economic consequent of these formulations." Bhargava and Kalantri (2013) argue that brand name medicines in India not only cause the cost of treatment to spiral, but are also a "frequent but under-reported cause of medication errors." He notes that there are more than 60,000 brands in the Indian market, but there is no registry of these drugs. "As a result," he writes, "brand names of medicines with dissimilar therapeutic effects (look-alike or sound-alike drugs), result in serious medication errors." The problem is further exacerbated by the fact that the government does not regulate brand names, allowing such problems to occur.

Contributing to a bias against the use of unbranded generics both among doctors and patients is a perception that these drugs are of inferior quality. Several studies noted the need for doctor and patient education about unbranded generic drugs and the need for studies to demonstrate their equivalency and raise awareness that they are identical formulations that can provide the same benefits as branded medicines to patients at lower prices. The problem of counterfeit and substandard drugs undermines their adoption and fuels distrust of their value. The Partnership for Safe Medicines India has said that India is a hub for fake medicines, a global $90 billion industry. It notes the Indian government says that 0.4 percent of the country's drugs are counterfeit and that substandard drugs account for about 8 percent, but it argues that independent estimates put the figure at between 12 and 25 percent (http://www.safemedicinesindia.in/patients1.php).

In India, most prescribers do not know that there is no difference, in pharmaceutical terms, between unbranded and branded medicines, or between brands, write Bhargava and Kalantri (2013). They say the drug regulatory authorities make no effort to educate them. Doctors and patients, concerned about the quality of medicines, prefer brand name drugs over generic drugs because of the widespread belief that generic medicines are low quality, subpotent, and substandard—if not counterfeit. Patients prefer to spend on brands they can trust, and consider a company's visibility and corporate image as a proxy for authenticity and quality control. "If the government were to provide quality assurance of all medicines available in the market," write Bhargava and Kalantri (2013), "then a truly competitive market for generics competing on the basis of price could emerge in India which would immensely benefit the consumer."

One effort the government has made to increase the use and availability of generic drugs to patients is the establishment of so-called Jan Aushadhi stores through India's Department of Pharmaceuticals. There were 22 of these stores as of March 2016, according to a government website. [http://janaushadhi.gov.in/jan_aushadhi_stores.html] with plans to increase the number of stores to 3,000 by the completion of the fiscal year ending March 31, 2017. Anita Kotwani, associate professor in the Department of Pharmacology at the V. P. Chest Institute at the University of Delhi, argued in a 2010

commentary in the India in the *Journal of Public Health Policy* that these stores needed to stock the medicines on the national Essential Medicines List or the State Medicines List, but instead the inventory until recently was determined by the public sector drug companies that supply the stores. Kotwani also notes that these stores are located in urban areas, but not in the small villages and towns that need them as well. As such, she warns that the Jan Aushadhi campaign will "increase the affordability of very few medicines for a very small population" (Kotwani 2010). Recently, under new guidelines issued by the Indian Government, the agency overseeing Jan Aushadhi is now seeking tenders for supply of generic medicines from private sector sources.

In the absence of the free market working to contain the price of medicines through competition, some have called for government intervention in the form of increased use of price controls. This is an issue of some debate as to whether India should rely on the free market to contain the price of medicines, or whether price controls are the solution. Studies have offered contradictory findings as to whether price controls are an effective way to contain cost and increase the affordability of drugs.

Balarajan et al. (2011) note that spending on medicines has increased over time and that it represents a growing portion of out-of-pocket expenditures for people who are poor compared to those who are not. They write that the percent of medicines subject to price control has fallen dramatically from approximately 90 percent in the 1970s to around 10 percent today. An analysis of drug prices between 1996 and 2006 found that a select basket of medicines rose by 40 percent. That compared to an increase of just 15 percent for medicines on the Essential Medicines List and 137 percent for medicines not on the essential drug list and not under price controls (Balarajan et al. 2011).

Matti et al (2015) notes that pharmaceutical companies have objected to efforts by the government to increase the use of price controls because of the erosion to their top and bottom lines. He suggests that if medicines with price caps become unprofitable for manufacturers, they may discontinue production of the medicine. He points to what took place prior to the introduction of the National Pharmaceuticals Pricing Policy of 2011 when 27 of the 74 drugs under price control were discontinued. "Such a scenario," they write, "would render these price control efforts counter-productive." At the same time, they suggest that generic drug makers may be tempted to raise prices of low-cost medicines to move closer to the price cap, actions that would increase the average price of a medicine. Regulations, however, have since been put in place to prevent such beavhior.

A 2015 study from IMS Health on the impact of price control measures on access to medicines in India found that they appeared to subsidize the cost of medicines for high- and middle-income segments of the population that can already afford the cost of medicines while the efforts did nothing to improve the ability of low-income households to purchase medicines. "Reduction in generic prices only weakens the ability of players to make inroads in rural markets and creates a commercially non-sustainable environment," Goel (2015) wrote. "Given that prices are already low compared to elsewhere in the world; further reduction has a potential impact on availability and quality of generic medicines."

In that same study, Goel (2015) notes the role that taxes and tariffs play in worsening the problem of lack of affordability. India charges import duties on medicines, including vaccines and antibiotics. Domestic taxes, he reports, often constitute the third largest component in the final price of a medicine after the manufacturers' suggested price and markups. He says these taxes and tariffs increase the price of a drug by 8 to 10 percent. Countries poorer than India have abolished tariffs on medicines, and credit doing so with contributing to broader improvements in health. India generated revenue of only 0.0094 percent of its GDP in 2001 from tariffs on medicines, even though the tariffs then were between 30 percent and 35 percent. "The tariffs therefore provide increasing price to patients," writes Goel (2015), "[and] provide very little revenue for the government."

As noted, the Indian government's investment in public health represents about 1 percent of GDP, far below the level made by comparable nations. There has been an effort to increase spending on health care, but it's been slow to materialize. One reason spending on health care is so low is that the government spends little on health insurance. In fact, spending on insurance represented around 1 percent of total health spending in 2004-2005 (Kumar 2011).

There have been both public and private efforts to introduce medical insurance in India. Kumar et al. (2011) attributes the slow increase in medical insurance in India to several factors. Chief among them is the fact that 93 percent of India's workforce is within what is referred to as the "unorganized

sector." The unorganized sectors include people who are working in private enterprises in work that is labor intensive, in enterprises that consist of ten people or less, and may be unincorporated. This can include agricultural laborers, fisherman, artisans, and other workers who do not have a regular source of income. "Contribution to regular medical insurance premiums is difficult and not easily affordable," writes Kumar et al. (2011), "and the high cost of collecting small amounts of premium every month from such families adds to this difficulty."

The benefits of insurance coverage accrue only to a few privileged individuals. For example, the Central Government Health Scheme, introduced in 1954, which offers comprehensive medical care for outpatient and hospital admission, benefits only the employees of central government (those in service or retired) and their families, members of parliament, and judges in the supreme and high courts. Similarly, the Employees' State Insurance Scheme, established in 1948, provides cash and medical benefits only to a select category of employees in factories in which at least ten people are employed. (Kumar et al. 2011) And, with nearly three quarters of out-of-pocket payments for health going to pay for medicines, one problem with national insurance schemes is that they cover only hospital expenses, but not outpatient costs such as pharmaceuticals. Such plans, says Shahrawat and Rao (2012), "will fail to adequately protect the poor against impoverishment due to spending on health."

Balarajan et al. (2011) reports that private insurance entered the Indian market after passage of the Insurance Regulatory and Development Authority Bill in 1999, and private insurance companies account for 6.1 percent of health expenditures on insurance. Community-based health insurance schemes and schemes for workers in the informal sector, which encourage risk pooling, cover less than 1 percent of the population. As such, these plans have done little to address the problem of inequity faced by the majority of India's population.

The National Family Health Survey 2005–2006 found that 10 percent of households in India had at least one member covered by medical insurance. "India's medical insurance sector," writes Kumar et al. (2011), "remains weak and fragmented despite several medical insurance schemes operated by the central and state governments, public and private insurance companies, and several community-based organizations."

Affordability is an obvious but complex component of the factors that affect access to medicines. Open research questions relating to role of affordability in regards to access to medicines include:

- Does the elimination of tariffs and taxes improve the affordability and access to medicines?
- What are the elements for vibrant competitions for a specific type of medicine and what is the impact of robust price competition on affordability and access to medicines?
- What distinguishes successful efforts to implement health insurance and what affect do they have on affordability and access to medicines?

5.3 Availability of care in suitably scaled and equipped health care systems

"Availability of care" has many interpretations in the literature and in public health. Here we are writing in terms of scarcity of care and technology resources allowing appropriate diagnosis and prescription, and other approaches to intervention in the face of disease or promotion of wellness. Availability can refer to either insufficient capacity in a locale, or whole non-existence of practitioners or facilities. In India, "Practitioner" does not necessarily refer to a qualified physician. India has institutionalized the professionalization and use of alternative providers under the Department of Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homoeopathy, abbreviated as AYUSH. This governmental body in India is charged with developing education and research in Ayurveda (Indian traditional medicine), yoga, naturopathy, unani, siddha, and homoeopathy, and other alternative medicine systems. Despite this extension of human resources, there is still scarcity and insufficient capacity across India for primary and secondary care. This paper focuses on "availability" in the context of medicines.

Nature of the problem as described in the literature

Prinja et al (2015), investigated the availability of medicines in public sector health facilities of two North Indian states, Punjab and Haryana, both of

which are attempting to provide essential medicines for free. These states have similar size populations (Punjab 28 million and Haryana 25 million). Focusing data collection on June to July 2013 they found availability in Punjab at 45.2 percent and in Haryana at 51.1 percent. Of the medicines that were not available, 60 percent of these were out of stock for a period of three to six months. With respect to specific categories of medicines, availability of anti-hypertensives was about 60 percent, and availability of anti-diabetics was 40 to 50 percent. The medicines that were particularly inaccessible were thrombolytics, anti-cancer medicines, and endocrine medicines. They had a typical availability of less than 30 percent.

Beyond India, Babar et al. (2013) studied the availability, pricing and affordability of three essential asthma medicines in 52 low- and middle-income countries and made several observations. In particular, the study focused on the three medicines on the WHO Essential Medicines List used to treat asthma—salbutamol, beclometasone, and budesonide. In each country, data collection occurred in the capital or main provincial city at two private retail pharmacies, the national procurement center, and a public hospital. Across all countries, the study found low availability for corticosteroids, especially in national procurement centers and hospitals. Inhaled corticosteroids are not on the essential medicines lists of many countries because they have not been updated. This is an issue because medicines are important for patients with moderate to severe asthma. Salbutamol (a bronchodilator) was available in the highest number of countries, which correlated with its presence on the highest number of essential medicines lists. However, some medicines not on the Essential Medicines List were nonetheless available.

Open areas for additional investigation in availability of care

"Availability of care" has many interpretations in the literature and in public health. Here we are writing in terms of scarcity of care and technology resources allowing appropriate diagnosis and prescription, and other approaches to intervention in the face of disease or promotion of wellness. Availability can refer to either insufficient capacity in a locale, or whole non-existence of practitioners or facilities. Therefore, the open areas of investigation include:

- What is the profile of staffing and equipment at different levels of care facilities and do these provide a suitable basis for care sought by patients?
- What resources are provided for patient education and information in regards to the use of medicines and how are these implemented and monitored for compliance?
- Do resources in specific settings align with the epidemiologic needs?

5.4 Awareness of opportunities to obtain care

"Awareness" is suggestive of multiple issues, education being one of them. Specifically, awareness pivots around knowledge of available resources and options for care, and the implications for diagnostics, therapeutics or other approaches to intervention. It is also a function of health literacy. For the purpose of this study we considered the issue of awareness broadly. This includes not only patients' awareness of the availability of medical resources, options for care, and when to access them, but also understanding the proper use of medicines. We also considered awareness as an issue that can hinder access to medicines in the context of medical professionals' training, as well as the training of pharmacists.

Education has been shown to be the most important correlate of good health (Grossman and Kaestner 1997). Education provides the consumer with the basis for evaluating whether they or a dependent require treatment. Information on the best places to seek care is additionally required. Both education and information are interconnected since the ability to assimilate health information is likely to be determined in part by the level of general education. The impact of information on treatment options and health seeking behavior is also an important determiner of demand (Okumura et al. 2002).

The lack of awareness and understanding about the availability of health care and when to seek it in India has been noted in studies. Two notable examples of this occur around access to free treatments. O'Donnell (2007) notes that two in five children in India are not fully immunized, despite the fact that immunizations are available for free. He writes that almost a third of mothers that had not immunized their children because they were unaware of the benefits. An additional 30 percent said they did not know where to go to get their child vaccinated. He pointed to a separate study of a North Indian

village that illustrated the role poor knowledge had on demand for effective interventions. "Households are typically passive users of vaccines, accepting them when presented with them at doorstep but with little or no active demand," writes O'Donnell. "There is very poor knowledge of the link between vaccines and disease and the pace of learning of the relationship is slow."

A similar example of the role awareness plays in access to medicines is found in Baru et al.'s (2010) study of female sex workers and their access of free antiretroviral therapies. They found that there was inadequate understanding about these therapies, their benefits and side effects, and when use of these medicines should be initiated. People living with HIV infections with CD4 counts of less than 200 cells per microliter are eligible for the free medicines from government centers, but the study found that some HIV-positive female sex workers were unaware of their CD4 counts. There were some of these women who might have initiated the therapy had they known their CD4 counts, but the study found they tend to seek medical care only when they have severe opportunistic infections.

In addition to patients' lack of awareness, shortcomings of the professionals in the healthcare system and the lack of training, particularly for doctors and pharmacists, create barriers for patients. In relation to access to medicines, this is most pronounced in the area of generic alternatives to more expensive branded versions of the same drugs. As previously mentioned, there are a number of reasons for a preference of brands. This includes reliance on brands as a proxy for quality and the inability of pharmacists to legally provide substitution of generic equivalents when a doctor prescribes a branded medicine. Bhargava and Kalantri (2013) report that "in India, most prescribers do not know there is no difference, in pharmaceutical terms, between unbranded and branded medicines, or between brands, and the drug regulatory authorities make no effort to educate them."

Basak et al. (2009) write that other important barriers to access to medicines exist, including the lack of proper education and training of pharmacists. They say that most drugs are dispensed illegally without prescription by drug sellers with little or no knowledge of laws governing the sale of medicines. While they call community pharmacists the "most accessible of all health care workers" in many countries including India and that they should play a role in ensuring affordable access to quality essential medicines, dissemination of appropriate information to patients, the general public and other health professionals, their review found little evidence of their playing this role in India. They pointed to a survey of health care professionals in an Indian state that found that 99 percent of the patients and doctors do not trust community pharmacists on health and prescription related issues. This suggests not only the need to improve the training of community pharmacists, but the need to create awareness among patients and doctors about the role they could play.

Open areas for additional investigation on availability of health resources

Awareness of the availability of health resources, knowledge of when to seek medical care, and compliance with treatments affect the demand side of health care. Awareness also affects the use of generics and consequently affects access to care because of the reliance on more expensive branded medicines. Open research questions relating to role of awareness in regards to access to medicines include:

- Does providing education and information to specific populations about health issues improve access, compliance, and outcomes?
- Does providing education and information to people with a specific disease on how to care for themselves improve access, compliance, and outcomes?
- Does educating doctors, pharmacists, and patients about the equivalency of generic medicines to branded medicines improve access, compliance, and outcomes?

5.5 Essential medicines procurement

Definition

Essential medicines procurement assumes that, in addition to a country's development and maintenance of an Essential Medicines List, an infrastructure has been put in place to source, aggregate, warehouse, distribute, support, and pay for the products identified. The issue of procurement is raised when there is a disconnect between national policies, formulary management, and sources of domestic or off-shore supply, as well as lack of funds to purchase such products owing to national economic limitations or inability to obtain donor support.

Nature of the Problem

Countries, especially India, take their Essential Medicines List with the utmost seriousness and focus. India maintains a list of about 350 medicines that are reviewed by a national panel of nearly 100 experts every few years. There is a turnover of about 40 to 50 medicines per review cycle. The magnitude of these numbers, the frequency of review, and the demographic and social complexity of India should provide an immediate indication of the logistical complexity in procurement, warehousing, national distribution, payment, and tracking of such a large inventory. Under the circumstances, it is not surprising that at any given time about half of the medicines are not available in any given locale. It is actually remarkable that half the medicines are available as needed. The problem then is obvious: essential medicine procurement is as much about the system in place to obtain and manage the inventory as it is the availability and cost of the medicines themselves. The systems' infrastructure, not surprisingly, can be equal to or exceed the cost of the medicines. This paper discusses the problem of supply chain management below, but essential medicines brings additional challenges, many of which are described in the literature.

Review of the scholarly literature

In addition to the asthma medicines study of Babar et al. (2013) as cited above, Bansal et al. (2013) provide a literature review that studies the accessibility and use of essential medicines in health care with a focus on current progress and challenges in India. According to the article, India put forth its first list of essential medicines in 1996. In December 2015, the Health Ministry issued a new National List of Essential Medicines 2015, adding 106 mostly new medicines and deleting 76 others deemed redundant or otherwise non-essential, with a net increase of 30 medicines. Having a standardized list is helpful in encouraging rational use of drugs, because there are fewer drugs from which to choose when making a prescribing decision. When prescribers do, however, have a valid reason for prescribing a drug not on this list, it can be a hindrance. Delhi's decision to create an essential medicines list in 1994 led to a decrease in procurement costs, and overall availability of essential medicines is higher than 80 percent across the board. Having said that, there are constraints in access to essential medicines for 50 to 80 percent of people in India. Bansal observes that worldwide, generic medicines obtained through private sector distribution and sales networks are six times more than the international reference price for the consumer. This suggests that national programs might represent a greater economy at the point of use depending on the efficiency of the system put in place and whether the cost of that system is amortized over each and every prescription or acquisition. Costs of drug procurement differ significantly by state in India. The authors speculate that the legal system could be used to enforce essential medicines access and provide some uniformity to access and distribution. Other variables in essential medicine access include inadequate numbers of health workers and facilities, or a lack of convenient outlets for access.

Bhargava et al. (2013), in an ethically proscriptive piece, examine the crisis in access to essential medicines in India and the key issues that call for action. They identify three obstacles to essential medicines: the first is that access is often unclear due to misconceptions about brand-name or branded generic products vis-a-vis generic medicines; the second is related to high prices because price regulation had been growing more lax at the time of the study; and, third, a flawed drug approval process that was not transparent. In recent years, India has been aggressively addressing its drug approval process and has improved the oversight of clinical trials, although some critics feel not quickly enough. As was observed above, the confusion is a result of marketing wherein domestic pharmaceutical companies support the notion that brand name drugs (either branded generics or proprietary) are better than unbranded generic drugs. The authors recommended strengthening public provisioning systems, regulating prices, and approving drugs through a revamped process that champions hard evidence.

Danawala and Zhang (2013) report on the implications of TRIPS flexibilities for access to non-communicable disease medicines in low- and middle-income countries. Their article investigates how to address barriers to essential medicines access specifically for non-communicable diseases. These barriers include factors such as not having an adequate budget to procure medicines, imperfect predictions of demand, and inefficient distribution. They further cite TRIPS as an obstacle, but rather than dismissing it, propose a modification in the way that it is administered. The least-income countries that enter the WTO, have until 2033 to meet accession criteria of TRIPS. India joined the WTO in 1995 but had until 2005 to accede to TRIPS.

Danawala and Zhang recommend that least-developed countries and middle-income countries receive an extension from 2016 to 2025 to incorporate TRIPS flexibilities, but in the case of lease developed countries, this is already 2033. In addition, differential pricing (in which price is determined based on a country's income and poverty level), they recommend, could be used by middle-income countries as well as least-developed countries. MNCs have instituted policies and practices for tiered pricing for LMICs, but do not accept that the full range of flexibilities uniformly apply to middle-income Countries (MICs) Finally, trade agreements should be leveraged to expand access to essential medicines. The authors are assuming that patents play a role in essential medicine access. While there is literature suggesting that there is a weak linkage in this regard, further study by objective scholars employing acceptable methodology is still needed.

Goyal and Gilhotra (2015) take a close look at the pharmaco-economics of selected essential medicines for common ailments in Sonipat District, Haryana, India, an example of a precise study with carefully considered methodology. The study focused on prices for 18 essential medicines, intended for palliative care, gastrointestinal conditions, and others. Data were collected at retail pharmacies scattered across Sonipat District in Haryana, India. The study found large variations in price for antibacterials (from 0.30 to 40 percent). They observed that analgesics, antiulcers, and antiemetics saw smaller price differentials. It is not clear why this is the case.

Publishing in the *Lancet*, Hogerzeil et al. (2013) describe promotion of access to essential medicines for non-communicable diseases and the practical implications of the UN political declaration. In the UN political declaration, many governments pledged to expand essential medicines access. In this carefully researched study, the authors state that even with the same level of spending, it is possible to procure more essential medicines if generic medicines are selected and procured. They point to some aspects of HIV treatment programs that have been implemented could be adapted to NCDs. They also observe that health insurance is effective and a few different models are possible (mandatory or through taxes). They provide a particular example with the stark differences in the level of access to opioid analgesics globally, speculating causes related to public perceptions of opioid safety and addiction, under-prescription, and unnecessarily tight monitoring of opioid distribution. The authors provide sweeping recommendations including the view that governments should institute equitable policies regarding intellectual property and make note of conflicts of interest among parties.

Kotwani (2013) asks a pointed question: "Where are we now: assessing the price, availability and affordability of essential medicines in Delhi as India plans free medicine for all?" The author examined 50 essential medicines in both public and private sector facilities in Delhi finding that generic medicines were more readily available in the private sector. He observed that there are large differences in procurement prices depending on which procurement agency is involved. Many medicines are not affordable for the general public, one example being that a mainstream antibiotic cost 2.3 days' worth of wages for public sector workers at the bottom of the payscale.

Levison (2012) explored policy and programming options for reducing the procurement costs of essential medicines in developing countries. The article reports that governments face large essential medicines procurement costs, which the author argues are the biggest impediment to availability (more so than inefficiencies in distribution and logistics). The costs go beyond the base price set by the manufacturer. They encompass markups, administrative costs, stock losses, and tariffs, all of which accumulate and compound. The article proposes four potential ways in which governments can reduce these costs:

- Create a list of essential medicines
- Eliminate tariffs and taxes on essential medicines
- Ensure that markups are reasonable
- Promote public understanding and procurement of generic drugs

Levison further proposes five potential ways in which the procurement division can reduce these costs:

- Focus on suppliers that have been prescreened
- Monitor suppliers periodically to ensure high performance

- Allow and encourage procurement staff to look up drug price data online
- Promote the adoption of practices to ensure greater transparency
- Implement a quality assurance program

Roy (2013) looks at a way to procure low-cost, quality medicines through refinement in implementation of an essential medicines policy in public health facilities in Delhi. The article observes that essential medicines are not easily accessible in India. As described elsewhere in this paper, in 1994, the Government of Delhi put in place a rule that published a list of essential medicines and codified quality and procurement standards. This study focused on medicines that the Government of Delhi procured in the 15 years after this rule, looking at costs and quality. During this time period (1995-2009), the data show a 33.3 percent drop in the costs of essential medicines and a drop of 1.3 percentage points in the proportion of samples that did not adhere to quality standards. Overall, the rule had a positive effect—it has led to higher quality and lower procurement costs. Procurement costs could be reduced even further if various agencies pool their purchasing.

Singh et al. (2013) go into a deep study of comparative public drug procurement in India by performing a qualitative study of five Indian states: Tamil Nadu, Kerala, Odisha, Punjab, and Maharashtra. Procurement model types include pooled, mixed, and decentralized. Each of these types is on a spectrum from completely autonomous to government-owned. The study showed that autonomous procurement is correlated with low prices and efficiency within the process itself. However, the study did not examine essential medicines availability.

Open areas for additional investigation on essential medicines procurement

Essential medicines procurement assumes that, in addition to a country's development and maintenance of an Essential Medicines List, that an infrastructure has been put in place to source, aggregate, warehouse, distribute, support and pay for the products identified. The issue of procurement is raised when there is a disconnect between national policies, formulary management and sources of domestic or off-shore supply, as well as lack of funds to purchase such products owing to national economic limitations or inability to obtain donor support. There are significant gaps in the literature that can be addressed. These include:

- What is the relationship of patenting to medicines on the list? What portion are under any active patent? Is the medicine supplied by the original producer? Is the medicine provided by more than one producer?
- For essential medicines still under patent, what is are the pricing parameters from factory to patient
- What is the pricing by medicine, by region, by outlet?
- [Related to supply chain management below] What are the steps between the factory and the patient and what are the economics associated with each step?
- What safeguards are put in place to assure quality products in the essential medicines list?
- What is the infrastructure associated with the procurement, inventory control and dispensing of essential medicines and how is that manifest in overall costs?

5.6 Regulation

Regulation includes government mechanisms for oversight of the manufacturing, distribution, pricing, and other related issues concerning medicines. In many instances, the literature suggests the biggest concerns about needed regulatory reforms to improve access to medicines lies largely in its implementation.

The problem of counterfeit and adulterated medicines, corruption, a misalignment of the patients' interests with that of doctors and pharmacists, and a lack of transparency in pricing all work to undermine patients' trust in the Indian health care system, the use of medicines, and access to them. These ailments of the health care system can conspire to increase costs, harm patients, or cause patients to avoid Western medicines altogether. "Regulatory approaches are often neglected as ways to improve access to health services, but they many

also hold potential," write Peters et al (2008). "It is important to recognize the degree to which poor people in many countries seek health care, purchase drugs, and find health-related information in markets that are mostly unregulated."

Peters and Muraleedharan (2008), in a separate article, noted that India has well established regulations, but suffers from a legal system that provides minimum protections to the public, relies on administrative and bureaucratic controls to enforce regulation, and a regulatory system that doesn't address the realities of India today. "The main problem is not with the law as it exists on paper, but with the law as it is practiced," they write. They note the ability to enforce civil and criminal laws in India is limited by an overburdened court system that makes it difficult to prosecute cases. The study references reports that there are about 25 million civil court cases pending in India, which at current rates, would take 324 years to clear (Peters and Muraleedharan 2008).

Legal standards have long been in place in India that make it punishable by fines and imprisonment to trade in adulterated and counterfeit medicines. As Chaudhuri (2007) notes, the Drugs & Cosmetics Act, 1945 and other rules prohibit the importation, sale, manufacturing, stocking or distribution of drugs that fail to meet quality and other standards. He warns that while regulation of manufacturing and distribution of medicines is an important part of health policy in India, progress in manufacturing has not been matched by progress in drug regulation. "The issue of quality is integral to accessibility: a medicine is not "accessible" if it is of poor quality and unable to effectively tackle the diseases for which it is taken" (Chaudhuri 2007). The problem of substandard drugs can have serious consequences for public health as drugs without adequate active ingredients can lead to death or fuel drug resistance. "Resistance at the population level renders legitimate drugs and even entire classes of drugs less effective," notes Bate et al. (2009), "even for patients who did not previously take poor-quality drugs."

The problem of counterfeit, adulterated, and substandard drugs continues to undermine trust in medicines in India, although how significant a problems it represents remains an issue of some debate. As mentioned earlier, the government has put the figure of substandard drugs at around 8 percent, although independent estimates suggest it is more likely between 12 and 25 percent (Partnership for Safe Medicines India 2016). While the government places the percent of drugs sold that are counterfeit at less than 1 percent, India has been identified as a major exporter of counterfeit medicines. For instance, a 2008 study that analyzed anti-malarial drugs sold in six major African cities found that 31 percent of the samples purportedly of Indian origin were found to be substandard (Bate et al. 2009).

Compounding the problem is India's decentralized approach to regulation and enforcement turning over responsibility for parts of these efforts to state authorities. The result is that standards of enforcement are not consistent from state to state. A study by Bate et al. (2009) sought to determine how big a problem substandard drugs were in Delhi and Chennai. The researchers used field-deployable techniques to conduct their analysis. These techniques are less sensitive than advanced laboratory techniques. While their findings were in accordance with the Indian government's estimates for the prevalence of substandard drugs, it did find the problem varied by location and manufacturer. That, the researchers said, suggests "India's substandard drug problem is not ubiquitous, but driven by a subset of manufacturers and pharmacies which thrive in an inadequately regulated environment."

The Indian government has taken some steps to address the problem. At the end of 2001, India raised standards on drug manufacturers by requiring they comply with WHO standards for good manufacturing practices (GMP), but Chaudhuri (2007) said the government did not effectively implement those provisions. Out of 6,000 drug manufacturing units in the country, less than 1,000 received WHO GMP certification at the time of the 2007 study.

In 2003, the Indian government commissioned a report from an expert committee under the direction of Dr. R.A. Mashelkar to examine the problem of counterfeit drugs and to recommend reforms to India's regulatory system. The resulting Mashelkar report found that the regulatory problems were "primarily due to inadequate or weak drug control infrastructure at the state and central level, inadequate testing facilities, shortage of drug inspectors, non-uniformity of enforcement, lack of specially trained cadres of specific regulatory areas, non-existence of data bank and non-availability of accurate information" (Bate et al. 2009). The committee also found discrepancies in the level of enforcement from state to state. For instance, the committee found that of the 17 of 31 states and united territories that responded to its inquiry had

functional drug testing laboratories, only seven of which had adequate staff and equipment.

The decentralized approach to drug regulation within India that places authority at the state level for licensing and monitoring domestic drug manufacturers for quality, writes Bates et al. (2009), has the effect of leaving India without national norms for drug quality as policing is performed at the state level and there is no uniformity to oversight or enforcement. This leaves open the potential that a producer of substandard drugs in a state with weak oversight could then sell those drugs anywhere within India (Bate et al. 2009).

The committee called for the creation of a National Drug Authority as part of its recommendations, something India has on occasion taken steps toward establishing, but has yet to implement. It should be noted that the Indian government has called upon committees in the past to review the regulatory system and make recommendations for its improvement. Though some steps have been taken to address the regulatory weaknesses in India, Bate et al. (2009) note that other committees have issued recommendations without bringing about needed changes. "These recommendations have been implemented by the Government to some extent," they write, "but the core issues have remained unresolved." In August 2015, the Indian government said it would invest $292 million over three years to strengthen its drug and medical device regulatory system.

One effect of the weak oversight and enforcement in India is that it has the effect of giving a market advantage to medicines from reputable brands, even though these brands can be significantly more expensive, according to Chaudhuri (2007). Even though less expensive generic alternatives may be available, doctors may not make the effort to find them, and instead rely on the branded product marketed by large, well known firms. "In India, brands are used effectively to signal quality. Brands of reputed companies sell at substantially higher prices because the products are considered reliable. This is in contrast to the situation in the U.S., where strict drug regulation ensures that any generic product is equally safe and effective and prices crash after generic entry with hardly any price differential between generic products" (Chaudhuri 2007).

That advantage to brands is intensified by a lack of transparency that leaves prescribers and purchasers in a vacuum of information that serves to weaken the market demand for lower cost generic drugs. Roy et al. (2012) identified the availability of "unbiased information on the quality and comparative prices of all medicines available in the country" as one way that would allow physicians provide better services and reduce the costs of medicines. Bideli et al. (2012) discuss the lack of transparency in low- and middle-income countries as a barrier to access. This includes transparency not only on price, but on the source and quality of medicines. But creating mechanisms for transparency and enforcing them becomes complicated since, as they note, responsibility is "often beyond the scope of the health sector alone." It would cut across sectors at a national level and involved trade, customs, law enforcement agencies and others.

The regulatory review and approval of new medicines is also an area of concern. Bhargava and Kalantri (2013) argue that India's drug regulatory agency need not only be evidence-based in their review and approval of new medicines, but given the nation's widespread poverty and reliance on out-of-pocket expenditures to pay for medicines, must also ensure medicines they approve serve the public health needs of the country and are cost effective. They criticize India's drug regulatory agencies for a lack of "rigorous, impartial review of the scientific evidence, public health relevance, transparency and public disclosure before approving a drug." They point to a 2012 parliamentary committee report that found an "overwhelming majority" of recommendations were based on "personal perception without giving any hard scientific evidence of data." That report went on to say that there was adequate evidence to conclude that many opinions were "actually written by the invisible hands of drug manufacturers and experts merely obliged by putting their signatures" (Bhargava and Kalantri 2013).

The Indian government has made some effort to expand oversight and establish standards of traditional medicine in India. At the end of 2014, the Indian government established The Ministry of AYUSH (http://www.indianmedicine.nic.in/). This had previously been the Department of Indian Medicine and Homeopathy. The Ministry of AYUSH oversees Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homoeopathy, and is charged with upgrading educational standards for practitioners of these disciplines, and evolve pharmacopoeial standards for these systems. It has issued guidelines for good clinical practices, but its works is relatively new and its impact unclear.

Corruption also remains a persistent problem that erodes patient trust in the healthcare system and results in physicians sometimes failing to act in the best interest of patients and undermines access to and affordability of medicines. Berger (2014) writes of the problem of widespread corruption in the pharmaceutical industry, saying that doctors are bribed to prescribe particular drugs. He also writes of tales of hospital directors given luxury cars and other inducements when their hospitals enter into contracts to prescribe certain medicines preferentially. "Lack of trust in doctors, and the costs associated with going to see them, mean many patients rely on pharmacists, who seem to have a similar lack of ethics, selling inappropriate drugs over the counter at exorbitant prices to people who often have to borrow the money to pay for them" (Berger 2014).

The use of essential medicines lists can be a powerful tool by governments for improving access and affordability, particularly when married to standards. In 1994, the Government of Delhi put in place a rule that published a list of essential medicines and codified quality and procurement standards. As previously mentioned, a study by Roy (2013) focused on medicines that the Government of Delhi found the rule led to higher quality and lower procurement costs. A separate study by Bansal and Purohit (2013) found Delhi's decision to create an Essential Medicines List not only led to a decrease in procurement costs, but also resulted in the availability of essential medicines to be greater than 80 percent.

Rao et al. (2011) describe India's shortage of human resources in the health sector as "severe." They note that not only is there a shortage of qualified health workers, but that the workforce is concentrated in urban areas and that it is difficult to attract qualified health workers to rural, remote, and underserved areas. The authors call for a comprehensive national policy for human resources to achieve universal health care in India, new training for institutions for nurses, the creation of incentives to draw qualified health works to underserved areas, a reorientation of training of doctors and nurses to the public health needs of the country, and the establishment of a database for accurate and comprehensive information about health workers in the country and the services they provide.

As policy makers seek regulatory approaches to improving access to medicines, some have suggested that solutions that might work well in strong states or civil society regulatory arrangements have different results in other situations. As such, many poor countries have sought to rely on other means of creating accountability, such as crafting ways for governments and citizen groups share responsibility for regulating public services. "It has been posited that rather than the typical regulatory role played by the Ministries of Health in India, facilitating the participation of civil society, the media, and the providers could be more effective in improving access to health care," writes Peters et al. (2008).

Open areas for additional investigation on the role of regulation and medicinal access

The decentralized approach to regulation in India, while a contributor to the problems of access to medicines, also presents opportunities to determine the most effective approaches from a regulatory and enforcement perspective to determine what works and what does not. Open research questions relating to role of regulation in regards to access to medicines include:

- Does transparency on drug prices and their components help contain or reduce the price of medicines to patients?
- Do policies to emphasize the use of generic drugs reduce costs and improve access to medicines?
- Does enforcement of regulations and standards improve access to medicines?

5.7 Supply-chain management

Definition

Shah (2004) defines a supply chain as the sequence of organizations—their facilities, functions, and activities—that are involved in producing and delivering a product or service. A typical pharmaceutical supply chain consists of the following members: primary manufacturing, secondary manufacturing, market warehouse/distribution centers, wholesalers, retails/hospitals and patients.

Supply chain management is more complex in healthcare vis-à-vis other industries because of the impact on people's health adequate and accurate supply of medicines have medical supply according to the patient's needs (Beier, 1995). This section explores malfunctioning national, local, or provider

systems for managing flow of necessary products, their storage and distribution, and dispensing.

Nature of the problem

Privett and Gonsalvez (2014), through a series of interviews and surveys identified the top 10 global health supply chain issues.

1. Lack of coordination: The current system of health delivery is siloed, fragmented, and ultimately uncoordinated; this lack of coordination was cited as critical by more than half of survey respondents. In fact, 100 percent of respondents rated it between important and critical.
2. Inventory management
3. Absent demand information
4. Human resource dependency
5. Order management
6. Shortage avoidance
7. Expiration
8. Warehouse management
9. Temperature control
10. Shipment visibility

McKinsey & Company (2013) identified several benefits that a strong supply chain can provide. This includes lower costs, improved access to care, and enhanced security of the supply of medicines through the reduction of counterfeits, theft, and fake medicines. The benefits are tied to direct economic benefits as well as improvements that translate into greater profits for hospitals and retailers, and reduce costs driven by shortages of medicines. They conclude that ineffective and poorly designed supply chains for purchasing and distributing the medicines, vaccines, and health technologies are one of the most important barriers to increasing access. Every year, around 10 million children under the age of 5 die due to lack of access to simple and affordable interventions (WHO 2008).

Caldwell (1986, 1990), Halstead et al. (1985), and Kim and Moody (1992) explain why supply chain is as important as affordability. Evidence from such varied places as Costa Rica, Sri Lanka, Kerala State in India, and Mongolia has shown that income improvement is not a prerequisite for better health outcomes. In fact, health can be improved before income increases, as improved health appears to contribute to economic growth (implying a reverse sign of causality is also in play).

Review of scholarly literature on supply chain management

Mendis et al. (2007) studied the availability and affordability of chronic disease essential medicines in Bangladesh, Brazil, Nepal, Malawi, Pakistan, Sri Lanka and found significantly better availability of drugs in private sector than public. Less than 7.5 percent of essential medicines were available in public sector.

Although cited previously, Prinja et al. (2015) offer supply chain management issues in their study if medicinal availability in public health facilities in Haryana (the Indian state with the third highest per capital GDP) and Punjab. The availability in Punjab (45.2 percent) and in Haryana (51.1 percent) was well below the WHO standards of 80 percent (Cameron et al., 2009). Of the drugs that were not available, 60 percent of drugs were out of stock for three to six months. In primary health care, medicines took 25 days to reach facility after placing the order in Punjab. In Haryana, it took seven days. In terms of storage, in Punjab 95 percent of the facilities had dedicated temperature controlled storage space for drugs. In Haryana, 89 percent of the facilities had temperature control. Vermin were a problem in 10 percent of the facilities.

Prinja et al. (2015) further found that most medicines for acute conditions were available, such as anti-spasmodics, anti-parasitics, anti-emetics. Availability of medicines for chronic conditions, such as diabetes mediciations, antidepressants, and antipsychotics, were in shorter supply. This is a troubling because non-communicable diseases require long-term compliance to treatment, sometimes even for a lifetime. With the rising burden of non-communicable diseases, poor availability of medicines to treat chronic conditions, such as high blood pressure, diabetes, asthma, and depression, as reported in the study, forces patients to purchase medicines from the private sector or forego treatment if they cannot afford it.

Along these lines, Saxena et al. (2010) in their article asking whether the drivers of expenditures in

catastrophic circumstances are associated more with outpatient services, hospitalization, or medicines observe that the availability of free essential medicines is critical to delivering universal health care. Lack of access to medicines causes households to face financial catastrophe through increased out-of-pocket expenditure.

Kotwani (2013) reported poor availability of essential medicines for chronic diseases in six low- and middle-income countries in the public sector, but better availability in the private sector. It is estimated that the average service level of drugs at public health facilities is less than 25 percent, and even at private outlets, where products are often unaffordable to most of the population, availability is less than 65 percent (Cameron et al. 2009).

Questionable medicines and the supply chain

It is also a documented fact that spurious and substandard medicines enter the supply chain. Khan and Khar (2015), in a systematic review of such medicines in India, observed that every country is the victim of substandard or spurious drugs that result in life threatening issues, financial loss to consumers and manufacturers, and loss in trust in the health system. Gentry et al. (2001) write that people accept, prefer, and buy counterfeit or substandard products over genuine or branded products due their cheap price, easy accessibility, and availability in the market.

Shepherd reported in 2004 that Russia, China, India, Brazil, Mexico, Pakistan, Southeast Asian, and Middle Eastern countries are considered as the chief operators in distribution and manufacturing of counterfeit drugs. Newton et al (2010) observe that ignorance of poor quality, unregistered medicines, lenient penalties, and inadequate enforcement of laws are some of the significant causes which provoke the situation.

While we were unable to identify reliable data on counterfeit or substandard medicines in India, Morris (2006) reports on China, providing a reference point or at least a basis for concern. He writes that 200,000 to 300,000 people die every year in China just because of counterfeit and substandard drug products. According to a report revealed by International Policy Network (2013), globally 700,000 deaths were reported for malaria and tuberculosis because of counterfeit drugs. This data reveals the gaps in the regulatory system and the damages of poor quality medicines.

India is widely viewed as the main originator and distributor of substandard and counterfeit drugs. This may be spurious speculation because no authentic evidences exist against the country according the data provided by the government and non-government agencies of India. Many researchers have investigated only individual drugs or narrow range of drug preparations and formulations. Currently, no large randomized studies of drugs quality have been performed in India (Seear, 2012). Rumors, however, can affect patient and purchase behavior and give rise to concern.

Supply-chain issues

Sridhar and Batniji (2008) state, ‘‘the pluralism of global health institutions and the informal alliances on which power in global health rests make a unified and fully coordinated health system unlikely.” On the matter of inventory, the WHO reports that there is most often no information or data generated on consumption at any level of the supply chain.

As to the issue of personnel in the supply chain, logistics-specific positions are rare. Instead, medical personnel are often responsible for making supply chain calculations and decisions. The few qualified staff must bear heavy workloads due to the lack of qualified personnel and the reliance on unqualified staff. The result is that they often make poor decisions although with the best intent.

Product expiration is generally less an issue in India because it is a large producer of medicines. Elsewhere in the emerging markets, it is an issue. By way of example, Nakayanzi et al. (2010) report that in the Uganda National Medical Stores, ‘‘at least U.S. $550,000 worth of antiretrovirals and 10 million antimalarial doses recently expired.” A WHO study (2010) found that in Nigeria noncompliance with conventional inventory management practices was a main cause of expiry.

Systems of any kind are expensive to create and maintain, and supply chain management is no exception. Within the healthcare industry, the supply chain associated with pharmaceutical products is critical in ensuring a high standard of care for patients and providing adequate supplies of medication for pharmacies. In terms of cost, it is estimated that supply accounts for 25 to 30 percent of operational costs for hospitals (Roark, 2005).

For normal orders, there is a delivery lead time of five days, increasing the risk of a seller being out

of stock. Unlike consumer products, where the customer can either defer their purchase or acquire an alternative, this can be critical in providing patient care as there may be no alternative treatment for the patient. Therefore, urgent orders need to be delivered immediately. Just a few products are delivered in each urgent shipment and, due to the scattered locations of clinics, vehicle capacity is lower with increased transportation costs. (Mustaffa and Potter (2009)

A method known as Vendor Managed Inventory is believed to be the solution that represents the best course of action for a company or provider. According to Brennan (1998), centralized logistics is a key toward enhancing health care supply chain operating efficiencies. As detailed earlier, this kind of approach has gained popularity in the health care sector since it also can reduce the time and effort needed to manage the inventory.

Open areas for additional investigation into supply chain management

- What role can novel IT systems play in reducing cost and improving last-mile availability in public sector facilities?
- There is a need for randomized control studies of drug quality in India.
- An analysis of the impact of having multiple distributors vs. a few with subsidy?
- Conduct organization-level case studies in supply chain management throughout the emerging markets to determine best practices.
- What is the relationship between price and the administration of the supply chain?

5.6 Socio-Cultural Barriers

Issue of culture, language, race, and other related matters often are overlooked for the impact they can have in erecting barriers to access of medicines. These factors can have significant effects on demand as patients, for a variety of reasons, may not seek to address their health needs. While policy interventions intended to address access to healthcare have tended to focus on reducing supply barriers, Barkat et al. (1995) argue that as important are the physical and financial barriers patients in low-income countries face, the accessibility of services, knowledge of what providers offer, education about how to best utilize services, and the cultural norms of treatment.

In India, the size and diversity of the nation, in addition to its sharp divisions of caste and ethnicity, creates a variety of barriers to access. As Basak et al. (2009) note, India is a multicultural society and consists of 28 states and seven union territories and is home to nearly 17 percent of the world's population. There are 22 national languages which have been recognized by the constitution of India, with more than 400 mother tongues and approximately 844 dialects. Language and literacy pose challenges not only for access to medicines, but compliance with their proper use. In addition, the pluralistic nature of Indian society has also fostered a pluralist medical system where patients may not only use practitioners of allopathic medicine, but more traditional and alternative Indian medicine as well, including Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homoeopathy.

Peters et al. (2008) said patients will seek out not only people who are formally trained in Western medicine, but others, such as shopkeepers or informally trained providers, for consultation. "Village doctors in particular have been found to have convenient hours and locations and available drug stocks, but they also have fewer social barriers with their fellow villagers and have helpful attitudes and longstanding relationships with them," they write. "Gender inequities in health services are also common, particularly for poor women, and manifest as health services that are not available or acceptable to women."

The complexity of supply chain management as it relates to health

Education has been shown to be the most important correlate of good health (Grossman and Kaestner 1997). For instance, one study in Pakistan found that maternal schooling was the most important factor in determining child survival (Agha 2000). Education provides the consumer with the basis for evaluating whether they or a dependent require treatment. Information on the best places to seek care is additionally required. Both education and information may be interlinked since the ability to assimilate health messages is likely to be determined in part by the level of general education. The impact of information on treatment options and desirable health seeking behavior is also important in determining demand.

While there has been progress made in improving the health of India's population as a

whole, Balajan et al. (2011) note that inequity persists due to socioeconomic status, geography, and gender. Increases in such areas as longevity and decreases in others, such as infant mortality, has belied the uneven distribution of the benefits of greater access to health care. Despite improvements in health outcomes, Balajan et al. (2011) find that they continue to be "strongly patterned along dimensions such as gender, caste, wealth, education, and geography." "The inverse care law, whereby those with the greatest need for health care have the greatest difficulty in accessing health services and least likely to have their health needs met, is highly applicable in India," they write.

For instance, while India has seen an overall improvement in longevity, life expectancy has great variation depending on where in India someone lives. In the south Indian state Kerala, life expectancy averages 74 years, but in the central Indian state Madhya Pradesh, life expectancy is just 56 years, an 18-year difference. Balajan et al. (2011) report that that difference is more dramatic than the difference in life expectancy seen between provinces in China or states in the United States. He attributes many of the inequalities in health to "a broad set of social, economic, and political conditions which influence the level and distribution of health within a population."

Consider that in 2004-2005, 29.2 percent of public expenditures made at both the central and state level government levels went to pay for allopathic services in urban areas. That compares to just 11.8 percent for allopathic services in rural areas during the same period. Balajan et al. (2011) says that imbalance is amplified by the private sector's bias toward higher level curative services, which as a result of market forces, tend to be centered in wealthier urban areas.

The physical distance to health services represents a significant barriers to care with the concentration of services in urban areas despite the fact that 68 percent of India's population being in rural area, according to data from The World Bank [http://data.worldbank.org/indicator/SP.RUR.TOTL.ZS]. Though the concentration of services in urban areas provides economies of scale, Balajan et al. (2011) notes that vulnerable groups tend to be clustered in areas where services are scarce. As a reflection of that uneven distribution of healthcare services, they point to the regional variation of the distribution of the nation's beds in government hospitals. In 2008, the northeastern state of Arunachal Pradesh boasted 533 people per government hospital beds. That compared to 5,494 people per government hospital bed in the eastern state of Jharkhand.

Deogaonkar (2004) reports that the distance of a given population from primary healthcare centers has a direct effect on childhood mortality rates. It also has been shown that while the distance to private hospitals does not affect health parameters, the distance from public health center does. "Those who live in remote areas with poor transportation facilities are often removed from the reach of health systems," Deoganonkar (2004) writes.

Ensor and Cooper (2004) found that demand-side barriers, such as geography, were important factors in preventing people from obtaining care, but often overlooked by policy makers and researchers, who instead tend to focus on supply side factors that pose barriers to access. He notes distance to a facility can impose significant costs on individuals and that they can work to reduce demand. This is not limited to the cost of transportation, but also the lost ability to earn money by needing to give up work to seek care. This can be particularly costly during period of peak economic activity, such as harvest time. Peters et al. (2008) argue that geographic access is an important part of accessing health care in low- and middle-income countries. They note that there is an inverse relationship between the distance or travel time to health facilities and the use of health services. "Good roads, often a rarity in the poor areas of developing countries, are required not only for people to go to health facilities but also for the easy distribution of drugs and other supplies to health facilities, for timely referrals in emergencies, and for better supervision of health workers," they write. "Lack of adequate communication services also limits access to health care. This obstacle becomes more pertinent in remote areas where communication gets cut off during adverse weather conditions. Remote health centers mean that more time and money is spent on travel-related expenditures, all of which act as obstacles to obtaining care, especially for the poor."

For women, cultural issues can worsen geographic barriers. Distance, one study found, represented a greater barrier to women than men of similar incomes because it was considered culturally unacceptable for women to be away from home for long periods. They might also have less access to household resources to pay for needed transportation to obtain care (Ensor and Cooper 2004).

Gender discrimination makes women in India more vulnerable to various diseases and associated morbidity and mortality, according to Deogaonkar (2004). Women from both a cultural and economic perspective are in a subordinate position to men and dependent upon them. They are often excluded from making decisions, have limited access to and control over resources, and are restricted in their mobility. "In general, an Indian woman is less likely to seek appropriate and early care for disease, whatever the socioeconomic status of family might be," writes Deogaonkar 2004. "This gender discrimination in healthcare access becomes more obvious when the women are illiterate, unemployed, widowed or dependent on others. The combination of perceived ill health and lack of support mechanisms contributes to a poor quality of life."

As an example of the social and cultural barriers to care, consider India's National AIDS Control Organization (NACO), which in 2004 began providing free first-line anti-retroviral therapy to people with HIV who needed it. NACO estimated that in 2006, nearly 2.4 million adult in India were infected with HIV and 25 percent of them required anti-retroviral therapy. Even though the therapy was free and accessible, Chakrapani et al. (2009) found that only about 20 percent of those who required the therapy got it. In examining why so many infected female sex workers chose not to take advantage of the free therapy available to them, the reasons were many. They included fear or adverse consequences of disclosure of their illness because of stigma and discrimination associate with HIV and sex work, lack of family support, negative experiences with health care providers, and lack of adequate knowledge about antiretroviral therapy, among other reasons (Chakrapani et al. 2009).

In many cases husbands and other family members may not know their wives are sex workers. These women fear that if they are discovered, they may be thrown out of their home, ostracized by their family, and prevented from getting any kind of work.

The routine of taking antiretroviral therapies also provided additional obstacles. Some women chose not to use the medicines because they required being taken with "proper food." One woman in the study explained she did not have regular access to proper food and therefore decided not to use the medicines. Others said because they have to take the medicines at regular intervals it would require them to take it while working. That could lead to be discovery by others that they are infected and that could cause them to lose clients and income (Chakrapani et al. 2009).

The way socio-cultural barriers play out in India is exemplified in Dutta-Bergman (2004) study focused on the Santal, a tribal population in west Bengal without access to many of the resources available to the rest of the Indian population. Though Santal see the power and benefit of allopathic medicine, going to the hospital can mean long waits in long lines and the loss of a day's wages. Making the trip to the state hospital can mean being at risk of not only losing a day's wages, but employment for a longer period. Such a loss could mean going hungry. "Because food and hunger are central to the Santali experience," writes Dutta-Bergman, "most Santalis are not willing to go to the hospital." Homeopathic medicine is cheaper and more accessible in the villages where the Santali live. The Ojha, a spiritual healer viewed as imbued with supernatural powers, lives in the community, and unlike allopathic doctors, is viewed as member of the community, speaks the language, and is viewed as accountable" (Dutta-Bergman 2004).

The World Health Organization has launched its Traditional Medicine Strategy 2014-2023. It aims to support member states efforts to develop policies and to strengthen the role of traditional medicine in keeping populations healthy. Health activists have argued that a more patient centered approach to healthcare is needed if universal healthcare in India is to become a reality. "Allopathic treatments have provided longevity, and Ayurveda can add quality to this prolonged life," Shailaja Chandra, former AYUSH secretary in the health ministry, told The BMJ. "The government needs to implement a policy framework whereby integration of traditional medicine systems with allopathy is validated." Studies have suggested that Ayurvedic approaches can have benefits compared to allopathic treatments. For instance, a 2011 double blind, randomized, placebo controlled pilot study of 43 patients found that an Ayurvedic herbal compound was just as effective at treating rheumatoid arthritis symptoms as methotrexate but with fewer adverse events Furst et al. (2011); Chopra et al (2013).

Additional areas for investigation in the role of socio-cultural issues in medicinal access

Socio-cultural issues are often overlooked in their role of hindering access to medicines because they affect the demand side of health care and are difficult to measure and quantify. Open research questions relating to socio-cultural issues include:

- Do efforts to customize care to specific populations (race, gender, ethnicity) improve access, compliance, and outcomes?

- Does the integration of traditional medicines with allopathic approaches improve access, compliance, and outcomes?

- Does delivery of care to remote and rural areas through telemedicine or the physical location of clinics or mobile services improves access, compliance and outcomes?

6.0 Discussion, conclusions and recommendations

This final section is divided into the following parts:

- The need for a comprehensive approach for building access to medicines
- A recap of the Indian case study
- Summary of open areas for additional investigation
- Recommendations to the Biopharmaceutical Industry, Governments, Multilateral Organizations and Providers of Care: A Global Public-Private Partnership
- Challenges and charges to specific stakeholders and the academic research community

6.1 Discussion and design of a comprehensive approach to building access

After testing the hypothesis through a survey of scholarly literature that the obstacles to providing just and equitable access to medicines for all global citizens cut across manifold problems, the authors of this report conclude that attention to no one element will address global needs in a comprehensive and sustainable way. In fact, unless the following factors are addressed in a coordinated and carefully orchestrated way, the problems of medicinal access may be exacerbated. To review, these factors are:

- **Accessibility of care milieu:** Remoteness; density; percentage of residents living with accessible radius time to health facility for consultation, diagnosis and medicinal intervention
- **Affordability and Health Systems Financing:** Public and private means for payment on national and trade levels; appropriate pricing in proportion to income and national financial resources
- **Availability of care:** Scarcity of care and technology resources allowing appropriate diagnosis and treatment
- **Awareness of the opportunity for care:** Knowledge of available resources and options for care, and the implications for medicinal intervention
- **Essential medicines procurement:** Disconnect between national polices, formulary and sources of supply
- **Regulation:** Ambiguous medicinal approval regime or application of government mandated pricing requirements
- **Socio-cultural obstacles:** nonfinancial obstacles to care such as culture, language, race, and ethnicity, and the related medicinal implications
- **Supply chain management:** Mal-functioning national, local or provider systems for managing flow of necessary products.

This list is silent on another factor: the existence of medicines in the first place, especially for maladies not yet addressed, diseases that have been hitherto neglected (especially tropical diseases) or the modification or development of new medicines better suited for particular populations based on genetic factors. This report was originally intended to make the case that a strong and consistent patent systems, as embodied in TRIPS, was essential to fostering the innovation necessary to address the creation and modification of new medicines. In surveying the literature, the authors concluded that the existence of patents is not the root cause of lack of access. Nor would its dissolution address any of the above eight factors that are addressed in the literature. Based on these preliminary conclusions, the authors proposed to the sponsoring organizations (BIO and ABLE) that the report's emphasis shift to a comprehensive analysis of medicinal access. Advocacy for the creation and execution of a comprehensive strategy for addressing all eight factors of medicinal access is now the objective of this report.

The global medicinal armamentarium is still generations away from providing treatments for those diseases ultimately destined to be treated by medicines. For better or for worse, capitalist approaches in combination with public funding of basic biological research, have produced an impressive array of effective medicines over the last 50 years, and that has been mere prolog to what is yet

to come. If based on the presumption that it is an obstacle to health equity when there are other unaddressed factors in medicinal access, dismissal of the patent system would result in incalculable lost opportunities to prevent and treat diseases in the future.

Again, the challenge is building a viable and sustainable global system that assures that once a medicine is available to treat a disease—communicable or non-communicable—that it makes its way to the people who need it. Pricing of medicines can have a relationship to patenting, but it is not the patent itself that dictates price. Pricing is a function of a multiplicity of factors that are generally not under control of the seller of products in any industry. This is especially true in health care.

Patents are a mechanism through which the risks and costs of innovation can be compensated. They provide a series of options for the holder of patent rights to address market needs wherever and however they occur. Exercising patent rights, when done within a global milieu that accommodates the diversity of cultures, national economies and health systems, can assure the existence of new medicines and enhance their availability across borders. It is the authors' view that if the patent system were suddenly abolished there would be virtually no change in medicinal availability over the next 20 years. Then, 20 years from now there would be few if any new medicines, and the availability of legacy medicines, (all medicines would be old generics) would soon diminish and the quality of legacy medicines would decline because there would be a collapse across the innovation spectrum. Medicines that are off patent still require invention and innovation in their production and clinical use.

Again, patents are a tool within the system of global innovation. The task is to globalize the innovation system so that all nations can participate in value-creation. The discovery and development of new medicines will have to globalize through either new innovative companies indigenous to Africa, Asia, South America, or through research outposts in these regions created and funded by historical MNCs. The new biology enables this migration of knowledge and capacity, and data demonstrates that national and private funding of research is steadily equilibrating throughout the world (Chakma et al, 2014).

The challenge is building a global capacity of care that can absorb and best use the innovation in hand and the promising new medicines in current and future pipelines. The authors propose a strategy for addressing this challenge below.

6.2 Recap of the Indian case study

If there is an emerging economy on the planet positioned to address its own needs in meeting its population's medicinal needs, it is India with its enormous capacity for medicinal development and production. And yet, it is one of the countries where the problem remains acute. The problems underlying barriers to access of medicines in India are complex. The review of the academic literature shows that there are many factors at play in limiting access and suggests the need for comprehensive, multi-pronged solutions that must involve the many stakeholders in the Indian health care continuum if solutions are to be effective.

India represents a unique opportunity because of its size, diversity, and acute nature of the problem of access to medicines. With the cooperation of participants in various sectors it could serve as a fertile ground for experimentation with solutions. The academic sector, in partnership with government, payers, providers, pharmaceutical companies (both innovators and generic), NGOs, pharmacies, and other entities can play a critical role in monitoring, analyzing, and evaluating pilot programs to see if they provide measurable improvement to access and better health outcomes.

To do this will require credible leadership driven by no agenda other than the goal of seeking means of addressing India's crisis in healthcare in providing access to medicines. This leadership could be an international foundation or organization focused on public health issues, or it could be a coalition of stakeholders who come together to work cooperatively to design, test, evaluate, and apply solutions that work. What is clear is that there is an urgent and humanitarian health crisis. Because this crisis is not in the form of an outbreak of an infectious disease, it is easy to dismiss as the status quo. But to do so ignores the pervasive suffering, premature loss of life, and wasted productive potential that results.

This project was reconstituted as an effort to identify the nexus of issues underlying barriers to access of medicines in India through a review of the existing literature. It showed that the barriers to access of medicines are many. Some have to do with the underlying nature of Indian society including widespread poverty, a diversity of languages and cultures, and the dispersal of about 70 percent of the

population throughout rural areas. These represent issues that demand a set of solutions that are not intended to address them directly, but take into account their effects and seek means of countering the impediments they create. Others problems, such as the need for better health information, the underutilization of generic drugs, and lack of transparency of costs in the supply chain can be addressed more directly.

The final task, though, will rest largely with policy makers. Once solutions are designed, tested, and proven to work, they will need to be implemented. It will not be enough to identify solutions that work. They will only provide long-term benefit if they are put into practice. What we propose below will require a long-term process and ongoing commitment of stakeholders to address the many problems underlying barriers to access to medicines. There is no easy fix and solutions will require a concerted effort to combat the problem.

6.3 Summary of open areas for additional investigation

Accessibility to care

Accessibility to care is a bedrock issue that must be addressed as a prerequisite to the problem of medicinal access. There are many areas of open investigation such as:

- What is the relationship of the geographic concentration of healthcare facilities to the concentration of access to medicines?
- What are the sources for the dispensing of medicines in rural regions or inner cities?
- What is the reliability of the products dispensed to people in rural areas?
- Are the staffs of remote primary care facilities able to dispense and monitor medicines?

Affordability of care

Affordability is an obvious but complex component of the factors that affect access to medicines. Open areas of investigation relating to role of affordability in regards to access to medicines include:

- Does the elimination of tariffs and taxes improve the affordability and access to medicines?
- What are the elements for vibrant competition for a specific type of medicine and what is the impact of robust price competition on affordability and access to medicines?
- What distinguishes successful efforts to implement health insurance and what affect do they have on affordability and access to medicines?

Availability of care

Availability of care has many interpretations in the literature and in public health. Here we are writing in terms of scarcity of care and technology resources allowing appropriate diagnosis and prescription, and other approaches to intervention in the face of disease or promotion of wellness. Availability can refer to either insufficient capacity in a locale, or whole non-existence of practitioners or facilities. Therefore, the open areas of investigation include:

What is the profile of staffing and equipment at different levels of care facilities and do these provide a suitable basis for care sought by patients?

- What resources are provided for patient education and information in regards to the use of medicines and how are these implemented and monitored for compliance?
- Do resources in specific settings align with the epidemiologic needs?

Awareness of opportunities to obtain care

Awareness of the availability of health resources, when to seek medical care, and compliance with treatments affect the demand side of health care. Awareness also affects the use of generics and consequently affects access to care because of the reliance on more expensive branded medicines. Open areas of investigation relating to role of awareness in regards to access to medicines include:

- Does providing education and information to specific populations about health issues improve access, compliance, and outcomes?

- Does providing education and information to people with a specific disease on how to care for themselves improve access, compliance, and outcomes?
- Does educating doctors, pharmacists, and patients about the equivalency of generic medicines to branded medicines improve access, compliance, and outcomes?

Essential medicines procurement

Essential medicines procurement assumes that, in addition to a country's development and maintenance of an Essential Medicines List, an infrastructure has been put in place to source, aggregate, warehouse, distribute, support and pay for the products identified. The issue of procurement is raised when there is a disconnect between national policies, formulary management and sources of domestic or off-shore supply, as well as lack of funds to purchase such products owing to national economic limitations or inability to obtain donor support. There are significant gaps in the literature that can be addressed. These include:

- What is the relationship of patenting to medicines on the list? What portion are under any active patent? Is the medicine supplied by the original producer? Is the medicine provided by more than one producer?

- For essential medicines still under patent, what is are the pricing parameters from factory to patient?

- What is the pricing of medicine by medicine, by region, and by outlet?

- What are the steps along the supply chain between the factory and the patient, and what are the economics associated with each step?

- What safeguards are place to assure quality products in the Essential Medicines List and where do gaps exist?

- What is the infrastructure associated with the procurement, inventory control, and dispensing of essential medicines and how is that manifest in overall costs?

Regulation

The decentralized approach to regulation in India, while a contributor to the problems of access to medicines, also presents opportunities to determine the most effective approaches from a regulatory and enforcement perspective to determine what works and what does not. Open areas of investigation relating to the role of regulation in regards to access to medicines include:

- Does transparency on drug prices and their components help contain or reduce the price of medicines to patients?

- Do policies to emphasize the use of generic drugs reduce costs and improve access to medicines?

- Does enforcement of regulations and standards improve access to medicines?

Supply Chain Management

Supply chain management is more complex in healthcare vis-à-vis other industries because of the impact on people's health requiring adequate and accurate medical supply according to the patient's needs (Beier, 1995). Areas for further exploration include:

- What role can novel IT systems play in reducing cost and improving last-mile availability in public sector facilities?

- There is a need for randomized control studies of drug quality in India.

- An analysis of the impact of having multiple distributors vs. a few with subsidy

- Development of organization level case studies in supply chain management throughout the emerging markets to determine best practices.

- What is the relationship between price and the administration of the supply chain?

Socio-cultural Barriers

Socio-cultural issues are often overlooked in their role of hindering access to medicines because they affect the demand side of health care and are difficult to measure and quantify. Open areas of investigation relating to socio-cultural issues include:

- Do efforts to customize care to specific populations (race, gender, ethnicity) improve access, compliance, and outcomes?
- Does the integration of traditional medicines with allopathic approaches improve access, compliance, and outcomes?
- Does delivery of care to remote and rural areas through telemedicine or the physical location of clinics or mobile services improves access, compliance and outcomes?

6.4 Recommendations to the Biopharmaceutical Industry, Governments, Multilateral Organizations and Providers of Care: A Global Public-Private Partnership

A unique opportunity exists for humanity to address the problem of medicinal accessibility and, at the same time, meet the needs of all stakeholders. The opportunity exists only if the biopharmaceutical industry (innovators and generic manufacturers alike) shares its knowledge and experience in solving problems across the health care value chain with governments, multilateral organizations and providers of care. These latter stakeholders should contribute their expertise and knowledge of cultural, economic and political complexity.

The goal of the Public-Private Partnership should align with the Sustainability Development Goals such that by 2030 all people have access to the medicines they need through their national or local health systems, and that those medicines be prescribed and managed in such a way as to assure safety and a beneficial outcome as defined by each nation. Another goal of the Public-Private Partnership would be to secure the global innovation system and encourage its development throughout the world. Medicinal discovery and development must be local in order to meet the specific biological needs of populations within the context of the local health system, culture of health and economic context. Put simply: Local capacity in medicinal discovery and development must be actively promoted.

6.5 Epilog: challenges and charges to stakeholders

There are a diverse group of stakeholders involved in India's health care ecosystem any one of which can begin the process of moving towards more equitable access to medicines. Sometimes these various entities collaborate and other times they may find themselves at odds with each other. What should unite them is a shared concern in improving the quality and availability of health care in India and easing access to it. With the shared goal in mind, the list below suggests areas of opportunity for different stakeholders in this effort.

Health Care Providers

Healthcare providers, including hospitals, public clinics, and private clinics, can serve as important points of education for both patients and doctors. For patients, they can help improve understanding of when to seek care and how to properly use medications. For doctors, they can provide education on the use of generic drugs to drive greater competition. They can also work with doctors and help train them on how to best work with patients from diverse social and cultural backgrounds. Providers can also experiment with telemedicine, mobile, and satellite facilities to improve access to care and medicines.

Physicians

As the primary point of contact with patients, physicians can play a critical role in educating patients on disease management and prevention, when to seek care, and how to properly use medication. Physicians also need to be aware of the financial constraint on patients who may not be able to afford medicines and learn about lower cost generic alternatives. Physicians in India are often working with diverse populations and must become aware of social and cultural issues that can impede their patients' access to medicines.

Indian pharmaceutical producers

Indian generic pharmaceutical producers can work with government to conduct testing to establish the equivalency of generic drugs to their branded counterparts. They can also work with regulators to assure compliance with quality standards and play a role in educating both physicians and consumers. They can work with government and pharmacies to improve the supply chain and institute means using information technology to avoid shortages of essential medicines. They can also work with

government and pharmacies to institute transparency in the added cost of medicines as a result of the various players within the supply chain.

Global pharmaceutical producers

Global pharmaceutical makers can work with the government of India to ensure essential medicines are available at affordable prices or licensed for use in India in a way that protects their economic interests while advancing the health of India's population. They can also provide expertise in addressing supply chain issues that limit the availability of essential medicines or increase their costs.

Government of India

The government of India's investment in healthcare remains low relative to investments made by comparable countries. One area for targeted and expanded investment where the government can improve access to medicines is through health insurance and efforts to make essential medicines available and affordable. The government could also end tariffs and taxes on essential medicines to improve affordability. It can increase competition through scientific review to determine when a generic is equivalent to a branded product and give pharmacies the freedom to substitute a less expensive equivalent of a drug that is prescribed. It can also take steps to work with Indian pharmaceutical makers and pharmacies to ensure adequate supply of essential medicines. To address unreasonable markups of drugs throughout the supply chain, it can use information technology to create transparency and publicly report markups. It can also take steps to prevent unreasonable markup of pharmaceuticals. To increase trust in generic drugs and increase competition, the government should take steps to perform regular testing of drugs and consistently apply penalties for people who sell adulterated or counterfeit medicines.

G-8 nations

Currently the advanced economies are under economic duress, but nevertheless retain significant foreign aid programs. The major donor countries can serve the needs of medicinal access by collaborating with one another and grantee countries in the most efficient means of production, transfer, inventory control and clinical use of donated medicines, or by seeking greater transparency in the planning and use of donated funds. Despite generous intentions, the literature suggests gross inefficiencies in the use of donated funds and medicines.

Multilateral Organizations

Multilateral Organizations such as the UN, WHO, WIPO, the World Bank Group have issued directives and recommendations that are aligned with one another. There is still, however, a pervasive disconnect between these organizations and the private sector. There is an opportunity for far greater Public-Private Partnering to address all aspects of medicinal availability beyond merely providing pills. The knowledge resources, financial strength, and insights acquired by the private sector—pharmaceutical, biotechnology and device producers—in their activity within health systems globally can be used a guide and partner in health system strengthening across the entire value chain of healthcare. As non-communicable diseases become the predominant disease burden in the developing world, the capacity of the private sector to deal with chronic needs on a sustainable basis can assist in addressing health needs generally and medicinal access in particular.

NGOs

NGOs can play a role in improving access to medicines through education on when to seek care and how to properly use medicines. They can also improve access by expanded care to remote areas through telemedicine, mobile, and satellite facilities. They can help address cultural barriers to care by establishing programs that target specific populations that may face particular challenges in gaining access to care.

Pharmacies

Pharmacies can play a critical role in helping create competition through helping educate patients and encouraging the use of generic equivalents. They can also take steps to improve the availability of essential medicines, which are often unavailable.

Academics

Academic researchers can play a critical role in formulating, testing, monitoring, and reporting solutions to the various problems underlying access

to medicines in India by working with various stakeholders. Furthermore, the global academy is in a position to hold health systems and medicinal access accountable by rigorous research, intellectual honesty and objective assessment of programs and outcomes. Finally, it is the view of the authors of this report that for the most part the scholarly research community has not yet discovered that the complexity of medicinal access opens huge vistas for research that can be approached quantitatively or qualitatively and from specialized disciplines as well as interdisciplinary perspectives. In short, there is every opportunity to pursue what Andrew van de Ven refers to as engaged scholarship. The authors of this report have attempted to provide a few suggestions for investigation into each aspect of medicinal access. There are of course numerous others that the community will find inviting. Time and thought invested in this arena will be rewarded with the satisfaction that the research will have an immediate impact on human welfare and progress.

References

The Access to Medicine Index 2014; Access to Medicines Foundation; http://www.accesstomedicineindex.org/sites/2015.atmindex.org/files/2014_accesstomedicineindex_fullreport_clickablepdf.pdf

Agha S. 2000. The determinants of infant mortality in Pakistan. *Social Science and Medicine* **51**: 199–208.

Aitken, M. (2015). Understanding the role and use of essential medicines lists: IMS institute for healthcare informatics. April 2015

Amin, T. (2007). Voluntary licensing practices in the pharmaceutical sector: an acceptable solution to improving access to affordable medicines? World Health Organization. February 8, 2007. http://apps.who.int/medicinedocs/documents/s19793en/s19793en.pdf accessed March 30, 2016

Amooti-Kaguna, B., & Nuwaha, F. (2000). Factors influencing choice of delivery sites in Rakai district of Uganda. *Social Science and Medicine*. **50**: 203–13.

Atre, S., Kudale, A., Morankar S., Rangan, S. and Weiss, M. (2004). Cultural concepts of tuberculosis and gender among the general population without tuberculosis in rural Maharashtra, India. *Tropical Medicine and International Health*. **9**:11, pp 1228–1238.

Attaran, A. (2004). How do patents and economic policies affect access to essential medicines in developing countries? *Health Affairs.* **23**, 3 pp. 155-166 doi: 10.1377/hlthaff.23.3.155

Attaran, A. & Gillespie-White, L. (2001). Do patents for antiretroviral drugs constrain access to AIDS treatment in Africa? *JAMA*, 286:15, 1886 – 1892.

Babar, Z., Lessing, C., Mace, C., & Bissell, K. (2013) The availability, pricing and affordability of three essential asthma medicines in 52 low- and middle-income countries; *Pharmacoeconomics.* **1**: 11, pp. 1063-82.doi: 10.1007/s40273-013-0095-9

Balarajaran, Y., Selvaraj, S. & Subramanian, S. (2011). Health care and equity in India. *Lancet*. **377** (9764), pp. 505–515. Published online 2011 Jan 10. doi: 10.1016/S01406736(10)618946

Bhandari, N. (2015). Is ayurveda the key to universal healthcare in India? *British Medical Journal*. 350:2879. doi: 10.1136/bmj.h2879

Bansal, D. & Purohit, V. (2013) Accessibility and use of essential medicines in health care: current progress and challenges in India. *Journal of Pharmacology & Pharmacotherapeutics*. **4**:1, pp. 13–18. doi: 10.4103/0976500X. 107642

Barkat A., Helali J., Rahman M., Majid M. & Bose, ML. (1995). Knowledge, attitude, perception and practices relevant to the utilization of emergency obstetric care services in Bangladesh: a formative study. Dhaka: University Research Corporation. 13:89, pp. 115.

Baru, R., Acharya, A., Acharya, S., Kumar AKS & Nagaraj, K. (2010). Inequities in access to health services in India: caste, class and region. *Economic and Political Weekly*. **45**: 38, pp. 49-58

Basak, S., Foppe van Mil, J. & Sathyanarayana, D. (2009). The changing roles of pharmacists in community pharmacies: perception of reality in India; Pharmacy World Science. **31**:612–618.

Bate, R., Tren, R., Mooney, L., Hess, K., Attaran A. (2009). Pilot study of essential drug quality in two major cities in India; PLoS One. **4:**6.

Bazargani, Y., Ewen, M., de Boer,A., Leufkens, H. & Mantel-Teeuwisse, A. (2014). Essential medicines are more available than other medicines around the globe; PLoS One. **9**:2. Published online 2014 Feb 12. doi: 10.1371/journal.pone.0087576

Beier, F.J. (1995). The management of the supply chain for the hospital pharmacies: a focus on inventory management practices. *Journal of Business Logistics*. **16**:2, pp. 153 - 73.

Berger, D. (2014. Corruption ruins the doctor patient relationship in India. *BMJ*. **348**:g3169. doi: http://dx.doi.org/10.1136/bmj.g3169 (Published 08 May 2014)

Bhargava, A.& Kalantri, S. (2013). The crisis in access to essential medicines in India: key issues which call for action. *Indian Journal of Medical Ethics.* **10**:2
.

Bigdeli, M., Jacobs, B., Tomson, G.… and Van Damme, W. (2012). Access to medicines from a health system perspective. *Health Policy and Planning*. Advance Access published November 22, 2012; 1-13 doi:10.1093/heapol/czs108

Bigelowa, J., Singh, V. & Singh, M. (2013). Medication adherence in patients with epilepsy after a single neurologist visit in rural India. *Epilepsy & Behavior*. **29**: pp. 412–415.

Bodeker, G. (2001). Lessons on integration from the developing world's experience. *BMJ*. **322:**7279, pp. 164–167.

Boldrin, M. & Levine, D. (2013). The case against patents. *The Journal of Economic Perspectives*. 27:1, pp. 3-22.

Brennan, C.D. (1998). Integrating the healthcare supply chain. *Healthcare Financial Management*, **52**: 1, pp. 31 - 34.

Burk, D. & Lemley, M. (2009). The patent crisis and how the courts can fix it. University of Chicago Press.

Cameron, A., Ewen, M., Ross-Degnan, D., Ball, D. & Laing R. (2009). Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. The Lancet. **373**:9659, pp. 240 – 9.

Chakma, J., Sun, G., Steinberg, J., Sammut, S. & Jagsi, R. (2014). Asia's ascent — global trends in biomedical R&D expenditures. *New England Journal of Medicine.* **370**:1, pp. 3 – 6.

Chakrapani, V., Newman, P., Shunmugam, M., Kurian, A. & Dubrow, R. (2009). Barriers to free antiretroviral treatment access for female sex workers in Chennai, India. *AIDS Patient Care and STDS*. 23:11, pp. 973–980.

Chatterjee, C. & Sheoran, G. (2007). Vulnerable groups in India. Centre for Enquiry into Health and Allied Themes. Retrieved from: http://www.cehat.org/humanrights/vulnerable.pdf

Chaudhuri, S. (2007). The gap between successful innovation and access to its benefits: Indian pharmaceuticals. *European Journal of Development Research*. **19**:1, pp.49–65. DOI: 0.1080/09578810601144293

Chesney, M. (2000). Factors affecting adherence to antiretroviral therapy. *Clinical Infectious Diseases.* **30**(Suppl 2): S171–6.

Chien, C. (2003). Cheap drugs at what price to innovation: does the compulsory licensing of pharmaceuticals hurt innovation? *Berkeley Technology Law Journal*. 18:3, pp. 853 – 907.

Chokshi, N. & Hasan M. (2015). A comparative review of the list of essential medicines of three Indian states: findings and implications. *International Journal of Medicine & Public Health*. **5:**716.

Creese, A., Gasman, N. & Mariko, M. (2004); Chapter 7: "Access to essential medicines." As published in *The World Medicines Situation*. World Health Organization. http://apps.who.int/medicinedocs/en/d/Js6160e/9.html

Cullet, P. (2003). Patents and medicines: the relationship between TRIPS and the human right to health. *International Affairs*. 79:1, pp. 139 -160.

Danawala, S. & Zhang, Z. (2013). Implications of TRIPS flexibilities for access to non-communicable disease medicines in lower and middle income countries. *GSTF International Journal of Nursing and Health Care (JNHC)*. **1**:1.DOI: 10.5176/2345-718X_1.1.1

Dang, A., Mendon, S. & Desireddy, P. (2016). Improving Access to New Treatments with value based pricing: an Indian perspective. *PTB Reports*,**2**:1.

Das, S., Mandal, M. & Mandal, S. (2007). A critical study on availability and price variation between different brands: Impact on access to medicines. *Indian Journal of Pharmaceutical Sciences*. **69**:1.

Dell'Arciprete (2014). Cultural barriers to effective communication between Indigenous communities and health care providers in Northern Argentina: an anthropological contribution to Chagas disease prevention and control. *International Journal for Equity in* Health. 13:6 DOI: 10.1186/1475-9276-13-6

Deodhar, N. (1982). Primary health care in India. *Journal of Public Health Policy*. **3**:1, pp. 76 –99

Deogaonkar, M. (2004) Socioeconomic inequality and its effect on healthcare delivery in India: Inequality and healthcare. *Electronic Journal of Sociology*.

Dhawan, A. (2015). Health care outlook India. Deloitte. https://www2.deloitte.com/content/dam/Deloitte/global/Documents/Life-Sciences-Health-Care/gx-lshc-2015-health-care-outlook-india.pdf

Dong, H., Bogg, L., Wang, K., Rehnberg, C. & Diwan, V. (1999). A description of outpatient drug use in rural China: evidence of differences due to insurance coverage. *The International Journal of Health Planning and Management*. **14**: pp. 41–56.

Duggal, R. (2007). Poverty & health: criticality of public financing. *Indian Journal of Medical Research.* 126: pp. 309-317.

Duggan, M., Garthwaite, C. & Goyal, A. (2014) The market impacts of pharmaceutical product patents in developing countries: evidence from India, Working Paper 20548 http://www.nber.org/papers/w20548 National Bureau of Economic Research

Dutta-Bergman, M. (2004). Poverty, structural barriers, and health: A Santali narrative of health Communication. *Qualitative Health Research*. 14:8, pp. 1107-1122 DOI: 10.1177/1049732304267763

Ebel, T., George, K., Larsen, E., Shah,K. & Ungerman, D. (2013) Building new strengths in the healthcare supply chain. McKinsey & Company. January 2013. https://www.mckinsey.com/~/media/mckinsey/dotcom/client_service/Pharma%20and%20Medical%20Products/PMP%20NEW/PDFs/McKinsey%20white%20paper%20%20building%20new%20strenghts%20in%20healthcare%20supply%20chain%20VF.ashx

Edwards, D., Coppens, D., Prasad, T., Rook, L. & Iyer, J. (2015). Access to hepatitis C medicines. *Bulletin of the World Health Organization*. **93**:11, pp. 799–805. doi: 10.2471/BLT.15.157784

Eisenberg, R. (2001). The shifting functional balance of patents and drug regulation. *Health Affairs.* 20:5, pp. 119 – 135.

Ensor, T., & Cooper, S. (2004). Overcoming barriers to health service access: influencing the demand side. *Health Policy and Planning*. 19:2, pp. 69–79. doi:10.1093/heapol/czh009

Ford, N. (2004). Patents, access to medicines and the role of non-governmental organizations. *Journal of Generic Medicines*. **1**:2, pp. 137-145.

Frew, E., Wolstenholme, JL., Atkin, W. & Whynes, DK. (1999). Estimating time and travel costs incurred in clinic based screening: flexible sigmoidoscopy screening for colorectal cancer. *Journal of Medical Screening*. **6**: 119–23.

Friedman, M., den Besten, H. & Attaran, (2003). A. Viewpoint: out-licensing: a practical approach for improvement of access to medicines in poor countries. *The Lancet*, 361; 9345, pp. 341 - 344.

Galvao, J. (2002). Access to antiretroviral drugs in Brazil. *Lancet*. 360: 1862 – 65.

Garg, C. & Karan, A. (2009); Reducing out-of-pocket expenditures to reduce poverty: a disaggregated analysis at rural-urban and state level in India. *Health Policy and Planning*. **24**:116–128. doi:10.1093/heapol/czn046

van der Geest, S. & Hardon, A. (2006). Social and cultural efficacies of medicines: complications for antiretroviral therapy. *Journal of Ethnobiology and Ethnomedicine*. **2**:48. doi:10.1186/1746-4269-2-48

Goel, N. (2015). Assessing the impact of price control measures on access to medicines in India; IMS Health; July 2015. http://freepdfhosting.com/65888ecb0d.pdf

Goyal, A. and Gilhotra, N. (2015). Pharmacoeconomics of selected essential medicines for common ailments in Sonipat district, Haryana, India. *Journal of Applied Pharmaceutical Science* **5**:6, pp. 083-087 DOI: 10.7324/JAPS.2015.50614

Grace, C. (2004). The effect of changing intellectual property on pharmaceutical industry prospects in India and China: considerations for access to medicines. *DFID Health Resource Centre. www.who.int/hiv/amds/Grace2**China**.pdf*

Grace, C. (2005). A briefing paper for DFID: update on China and India access to medicines; *DFID Health Resource Centre.* https://www.google.com/?gws_rd=ssl#q=A+briefing+paper+for+DFID:+update+on+China+and+India+access+to+medicines

Grossman, M. & Kaestner, R. (1997). Effects of education on health. In: Behrman, JR & Stacey, N. (eds). *The social benefits of education*. Ann Arbor, MI: University of Michigan Press.

Grover, A. & Citro, B. (2011) Comment: India: access to affordable drugs and the right to health; *The Lancet.* **377**: 9770, pp. 976–977. DOI:10.1016/S0140-6736(10)62042-9

Gudwani, A., Mitra, P., Puri, A. & Vaidya, M. (2012) India healthcare: inspiring possibilities, challenging journey. McKinsey & Company, http://www.mckinsey.com/~/media/mckinsey%20offices/india/pdfs/india_healthcare_inspiring_possibilities_and_challenging_journey_executive_summary.ashx

Hale, V., Woo, W. & and Levens Lipton, H. (2005). Oxymoron no more: the potential of nonprofit drug companies to deliver on the promise of medicines for the developing world. *Health Affairs*. **24**:4, pp. 1057-1063 doi: 10.1377/hlthaff.24.4.1057

Hsiao, WC. (2007). The political economy of Chinese health system reform. *Health Economics, Policy and Law*. **2**: pp 241 –249.

Hestermeyer, H. (2008). *Human rights and the WTO: the case of patents and access to medicines.* Oxford University Press.

Heywood, M. (2002). Drug access, patents and global health: 'chaffed and waxed sufficient'; *Third World Quarterly*. 23:2, pp. 217 – 231.

Hogerzeil, H., Liberman, J., Wirtz, V., Kishore, S., Selvaraj, S., Kiddell-Monroe, R., Mwangi-Powell, F. & von Schoen-Angerer, T. (2005). Promotion of access to essential medicines for non-communicable diseases: practical implications of the UN political declaration. *The Lancet*. **19**:3423. DOI: 10.1016/S0140-6736(12)62128-X

John, TJ., Dandona, L., Sharma, V. & Kakkar, M. (2011). Continuing challenge of infectious diseases in India. The Lancet. *377*(9761), pp. *252 - 269.*DOI:10.1016/S0140-6736(10)61265-2

Joumard, I. & Kumar, A. (2015). Improving health outcomes and health care in India. Organisation for Economic Co-operation and Development; Economics Department Working Papers No. 1184; January 8, 2015

Kaplan, W. & Laing, R. (2005). Local production of pharmaceuticals: industrial policy and access to medicines: an overview of key concepts, issues and opportunities for future research. HNP Discussion Paper; Human Development Network, The World Bank; January 2005

Khan, AN., & Khar, R. (2015). Current scenario of spurious and substandard medicines in India: a systematic review. *Indian Journal of Pharmaceutical Sciences.* **77**:1, pp. 2 – 7.

Khan, AY & Ghilzai, NMK. (2007). Counterfeit and substandard quality of drugs: the need for an effective and stringent regulatory control in India and other developing countries. *Indian Journal of Pharmacology*. 39:4, pp. 206 – 207.DOI: 10.4103/0253-7613.36541

Knox, P. (1980). Measures of accessibility as social indicators: a note. *Social Indicators Research*. 7:1/4, pp. 367 – 377.

Kotwani, A. & Levison, L. (2007). Price components and access to medicines in Delhi, India; Department for International Development, http://apps.who.int/medicinedocs/documents/s19208en/s19208en.pdf

Kotwani, A., Ewen, M., Dey, D., Iyer, S., Lakshmi, P. . . . Laing, R. (2007). Prices & availability of common medicines at six sites in India using a standard methodology. *Indian Journal of Medical Research*. **125**:5, pp. 645-54.

Kotwani, A., Gurbani, N., Sharma, S. & Chaudhury, R. (2009). Insights for policymakers from a medicine price survey in Rajasthan. *Indian Journal of Medical Research*. 129:4.

Kotwani, A. (2010). Access to essential medicines and standard treatment for chronic diseases. *Indian Journal of Pharmacology*. **42**:3, pp. 127–128.

Kotwani, A. (2010). Commentary: will generic drug stores improve access to essential medicines for the poor in India? *Journal of Public Health Policy*. 31:2, pp. 178-184.

Kotwani, A. (2009). Availability, price and affordability of asthma medicines in five Indian states. *The International Journal of Tuberculosis and Lung Disease.* 13:5, pp. 574 – 579.

Kotwani, A. (2013). Where are we now: assessing the price, availability and affordability of essential medicines in Delhi as India plans free medicine for all. *BMC Health Services Research* DOI: 10.1186/1472696313285

Kraiselburd, S. & Yadav, P. (2013). Supply chains and global health: an imperative for bringing operations management scholarship into action. *Production and Operations Management*. **22**:2.

Lanjouw, J. (2005). Patents, price controls and access to new drugs: how policy affects global market entry. Working paper for Commission on Intellectual Property Rights, Innovation, and Public Health of the WHO.

Lanjouw, J. Intellectual property and the availability of pharmaceuticals in poor countries. Chapter 4 in Jaffe, A., Lerner, J. & Stern, S. eds., (2003). *Innovation Policy and the Economy*, Volume 3. MIT Press.

Lanjouw, J. (1997). The introduction of pharmaceutical product patents in India: heartless exploitation of the poor and suffering. Leibniz Information Centre for Economics. Working Paper No. 775.

Levison, L. (2012). Policy and programming options for reducing the procurement costs of essential medicines in developing countries. Boston University School of Public Health Department of International Health. http://apps.who.int/medicinedocs/documents/s21609en/s21609en.pdf

Malhotra, C. & Do, YK.(2012). Socio-economic disparities in health system responsiveness in *Indian Health Policy Planning*. 28:2 pp.197-205. doi: 10.1093/heapol/czs051

Maiti, R., Bhatia, V., Padhy, BM & Hota, D. (2015). Essential medicines: an Indian perspective; Indian Journal of Community Medicine. **40**:4, 223–232. doi: 10.4103/09700218.164382

McKinsey & Company. Building new strengths in the healthcare supply chain. Jan 2013

Manikandan, S. & Gitanjali, B. (2012). National list of essential medicines of India: The way forward. *Journal of Postgraduate Medicine*. **58:**1.

Mehrotra S. (2000). Integrating economic and social policy: good practices from high-achieving countries. Working Paper. Florence: Innocenti Research Centre, UNICEF.

Mendis, M., Fukino, K., Cameron, A., Laing, R., Filipe A., Khatib, O., Leowski, J. & Ewene, M. (2007). The availability and affordability of selected essential medicines for chronic diseases in six low- and middle-income countries. *Bulletin of the World Health Organization*. 85:4.

Mercurio, B. (2006). Resolving the public health crisis in the developing world: problems and barriers of access to essential medicines. *Northwestern Journal of International Human Rights*. 5:1.

Moon, S., Jambert, E., Childs, M. & von SchoenAngerer, T. (2011). A win-win solution?: A critical analysis of tiered pricing to improve access to medicines in developing countries; *Globalization and Health*, 7:39 http://www.globalizationandhealth.com/content/7/1/39 doi: 10.1186/17448603739

Moser, P. (2013). Patents and innovation: evidence from economic history. *The Journal of Economic Perspectives.* 27:1, pp. 23 – 44.

Morris, J., & Philip, S. (2006). Counterfeit medicines in less developed countries: problems and solutions. International Policy Network, London

Mustaffa , NH. & Potter, A. (2009). Healthcare supply chain management in Malaysia: a case study, *Supply Chain Management: An International Journal*. **14**: 3 pp. 234 – 243.

Musungu, S. & Oh, C. (2006). The use of flexibilities in TRIPS by developing countries: can they promote access to medicines? Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH); http://www.who.int/intellectualproperty/studies/TRIPSFLEXI.pdf?ua=1

Mwangangi, F. (2011); Accessibility to Health Care in Urban Environments. From *Women's Health and the World's Cities*. University of Pennsylvania Press. (2011)

Nakayanzi, J., Kitutu, F., Oria, H. & Kamba, P. (2010) Expiry of medicines in supply outlets in Uganda, *World Health Organization. Bulletin*. Pp.154–158.

Nayar, K. & Razum, O. (2003). Cooperatising Medical Care: A Leap in the Dark. *Economic and Political Weekly*, 38: 22, pp. 2121 – 2122.

Newton, PN., Green, MD. & Fernendez, FM. (2010) Impact of poor-quality medicines in the "developing" world. Tredns in Pharmacologic Science. **31**: pp. 99 – 101.

Newton, P., Amin, A., Bird, C., Passmore, P., Dukes, G. . . . White, N. (2011). The primacy of public health considerations in defining poor quality medicines. PLoS Medicine. **8**:12.

Ng, E. & Kohler, J. (2008). Finding flaws: the limitations of compulsory licensing for improving access to medicines–an international comparison. *Health Law Journal*. **16**, pp 143 - 172.

Ngoasong, M. Z. (2009). The emergence of global health partnerships as facilitators of access to medication in Africa: a narrative policy analysis. *Social Science & Medicine*. 68; 949 – 956.

O'Donnell, O. (2007). Access to health care in developing countries: breaking down demand side barriers. *Cad. Saúde Pública*. **23**:12, pp. 2820-2834.7

OECD Health Statistics (2014). How does India compare? http://www.oecd.org/els/health-systems/Briefing-Note-INDIA-2014.pdf

Okumura, J., Wakai, S., & Umenai T. (2002). Drug utilisation and selfmedication in rural communities in Vietnam. *Social Science and Medicine*. **54**: 1875–86.

Ouellette, L. (2010). How many patents does it take to make a drug – follow-on pharmaceutical patents and university licensing. *Michigan Telecommunications and Technology Law Review*. 17:1, pp. 299-336.

Panikar, PGK. (1992). High Cost of Medical Care in Kerala: Tentative Hypothesis; Economic and Political Weekly. **27**:23 pp. 1179 - 1181.

Peters, D., Garg, A., Bloom, G., Walker, D., Brieger, W. & Rahman, MH. (2008). Poverty and Access to Health Care in Developing Countries. *Annals of the New York Academy of Sciences*. DOI: 10.1196/annals.1425.011

Peters, D., Muraleedharan, VR. (2008). Regulating India's health services: To what end. *Social Science & Medicine*. 66: 2133 – 2144.

Pogge, T (2008). Access to medicines. *Public Health Ethics*. **1**:2, pp. 73 - 82.

Prinja, S., Bahuguna, P., Tripathy JP & Kumar, R. (2015). Availability of medicines in public sector health facilities of two North Indian States. *BMC Pharmacology and Toxicology*. **16**:43. DOI 10.1186/s40360-015-0043-8

Prinja, S., Kanavos, P. & Kumar, R. (2012). Health care inequities in north India: role of public sector in universalizing health care. *Indian Journal of Medical Research*. **136**:3: pp. 368-369.

Privett, Natalie. Gonsalvez, David. (2014) The top ten global health supply chain issues: perspectives from the field. *Operations Research for Health Care*. 3:4 pp. 226-230.

PSM. Counterfeit Drug Incident Encyclopedia. Partnership for Safe Medicines. 2013.

Quick, J. (2003). Essential medicines twenty-five years on: closing the access gap. Health Policy and Planning. 18:1, pp. 1–3.

Quick. J., Boohene, NA., Rankin, J. & Mbwasi, RJ. (2005). Medicines supply in Africa: should improve through regional collaborations and accredited drug shops. *British Medical Journal*. **331**:pp. 709–710.

Rangnekar, D. (2006). No pills for poor people? Understanding the disembowelment of India's patent regime. *Economic and Political Weekly*. 41:5, pp. 409 – 417.

Report of the Commission on Intellectual Property Rights, Innovation and Public Health; Public health, innovation and intellectual property rights. (2006) World Health Organization. http://www.who.int/intellectualproperty/documents/thereport/ENPublicHealthReport.pdf?ua=1

Report of the Core-Committee for Revision of National List of Essential Medicines. (2015) http://cdsco.nic.in/WriteReadData/NLEM-2015/Recommendations.pdf

Ridley, D., Grabowski, H. & Moe, J. (2006). Developing drugs for developing countries. *Health Affairs*, **25**: 2, pp. 313-324 doi: 10.1377/hlthaff.25.2.313

Roark, D.C. (2005). Managing the healthcare supply chain. *Nursing Management*. 36:2, pp. 36-40.

Roy, V. (2003). A way to low cost, quality medicines: implementation of an essential medicines policy in public health facilities in Delhi. *International Journal of Research in Pharmaceutical Sciences*. **4**:3, pp. 397 – 410.

Roy, V., Gupta, U. & Agarwal, AK (2012). Cost of medicines & their affordability in private pharmacies in Delhi. *The Indian Journal of Medical Research;* **136**:5 pp. 827 – 835.

Roy, V. (2013). A way to low cost, quality medicines: implementation of an essential medicines policy in public health facilities in Delhi (India). *International Journal of Research in Pharmaceutical Sciences*. 4:3, pp. 397-410.

Sabot, O., Yadav, P. & Zaffran, M. (2011). Maximizing every dose and dollar: the imperative of efficiency in vaccine delivery, The National Bureau of Asian Research, Seattle.

Saksena, P., Ke Xu, K., & Durairaj, V. (2010). The drivers of catastrophic expenditure: outpatient services, hospitalization or medicines? World Health Report 2010 Background Paper, No 21. Geneva: World Health Organization.

Sampat, B. (2009). Academic patents and access to medicines in developing countries. *American Journal of Public Health*. 99:1, pp. 9 – 17.

Sampath, PG. (2005). Economic Aspects of Access to Medicines after 2005: Product Patent Protection and Emerging Firm Strategies in the Indian Pharmaceutical Industry. United Nations University-Institute for New Technologies. http://www.who.int/intellectualproperty/studies/PadmashreeSampathFinal.pdf

Satyanarayana, K. & Srivastava, S. (2007). Poverty, health & intellectual property rights with special reference to India. *Indian Journal of Medical Research*. **126**: pp 390 – 406.

Sauerborn, R., Bodart, C., & Essomba, R. (1995). Recovery of recurrent health services costs through provincial health funds in Cameroon. *Social Science and Medicine*. **40**: 1731–9.

Scherer, F & Watal, J. (2002). Post-TRIPS options for access to patented medicines in developing nations. *Journal of International Economic Law*. 5:4, 913 – 939.

Seear, M. (2012). Pharmaceutical quality: an urgent and unresolved issue. Lancet Infectious Disease.**12**: pp. 428 - 9.

Sell, S. (2007) TRIPS-plus free trade agreements and access to medicines. *Liverpool Law Review*. 28: 41 - 75.

Selvaraj, S. & Karan, AK. (2009). Deepening Health Insecurity in India: Evidence from National Sample Surveys since 1980s. *Economic & Political Weekly*. **44**: 40.

Shah, N. (2004). Pharmaceutical supply chains: key issues and strategies for optimization. *Computers & Chemical Engineering*. **28**: pp. 929 – 41.

Shahrawat, R. & Rao, KD. (2012). Insured yet vulnerable: out-of-pocket payments and India's poor. *Health Policy and Planning*. **27**:213–221. doi:10.1093/heapol/czr029

Shaikh, N. (2015). Indian Pharmaceutical Trade. *International Research Journal of Multidisciplinary Studies*. **1**:2.

Shepherd, M. (2004). Vulnerable points in the U.S. drug-distribution system. *Managed Care* **13**(Suppl 3): pp. 25-9.

Shobhana, R., Begum, R., Snehalatha, C., Vijay, V. & Ramachandran, A. (1999). Patients' adherence to diabetes treatment. *Journal of the Association of Physicians India*. **47**:pp. 1173-1175.

Shukla, N. & Sangal, T. (2009). Generic drug industry in India: the counterfeit spin. *Journal of Intellectual Property Rights*. **14**: pp. 236-240

Simonetti, R., Archambault, E., Côté, G. & Kale, D. (2007). The dynamics of pharmaceutical patenting in India: evidence from USPTO Data. *Technology Analysis & Strategic Management*. 19: 5, pp. 625 – 642.

Singal, GL., Nanda, A. & Kotwani, A. (2011). A comparative evaluation of price and quality of some branded versus branded–generic medicines of the same manufacturer in India. *Indian Journal of Pharmacology*. **43**:2, pp. 131 – 136. doi: 10.4103/02537613.77344

Singhal G.L., Kotwani, A. & Nanda, A. (2011). Jan Aushadhi Stores in India and Quality of Medicines Therein. International Journal of Pharmacy and Pharmaceutical Sciences. 3:1.

Steinbrook, R. (2007). Closing the affordability gap for drugs in low-income countries. *The New England Journal of Medicine*. **357**:1996-1999.

Singh, PV., Tatambhotla, A., Kalvakuntla, R. & Chokshi, M (2013). Understanding public drug procurement in India: a comparative qualitative study of five Indian states; *BMJ Open*. doi:10.1136/bmjopen-2012-001987

Sridhar, D. & Batniji, R.(2008). Misfinancing global health: a case for transparency in disbursements and decision making. *The Lancet* **372**: pp. 1185 – 1191.

Sultana, G., Kapur, P., Aqil, M., Alam, MS. & Pillai, KK. (2010). Drug utilization of oral hypoglycemic agents in a university teaching hospital in India. *Journal of Clinical Pharmacology and Therapeutics*. **35**: pp. pp.267-277.

Taylor, D., Mrazek, M, & Mossialos, E. (2004). Regulating pharmaceutical distribution and retail pharmacy in Europe. In: Mossialos, E., Mrazek, M., Walley, T, eds. *Regulating Pharmaceuticals in Europe: Striving for Efficiency, Equity and Quality*. Maidenhead: OpenUniversity Press. Pp. 196–212.

Tetteh, E. (2009). Creating reliable pharmaceutical distribution networks and supply chains in African countries: Implications for access to medicines. *Research in Social and Administrative Pharmacy*. 5: 286–297.

Terra de Souza, AC., Peterson, KE., Andrade, FM., Gardner, J. & Ascherio, A. (2000). Circumstances of post-neonatal deaths in Ceara, Northeast Brazil: mothers' health care-seeking behaviors during their infants' fatal illness. *Social Science and Medicine*. **51**: 1675–93.

't Hoen, E., Berger, J., Calmy, A. & Moon, S. (2001). Driving a decade of change: HIV/AIDS, patents and access to medicines for all. *Journal of the International AIDS Society*. **14**:15.

't Hoen, E. (2002). TRIPS, pharmaceutical patents and access to essential medicines: a long way from Seattle to Doha. *Chicago Journal of International Law*. 3:1, 27 – 46.

Uba, L. (1992). Cultural barriers to health care for Southeast Asian refugees. Public Health Reports. 107:5, pp. 544 – 548

Vidyarthi, A., Soumya, A., Choudhary, S. & Sinha, BK. (2013). Barriers to breast cancer screening in young Indian women: A tale of two cities. *Asian Journal of Experimental Sciencei*. **27**: pp. 29-35.

Waning, B., Diedrichsen, E. and Moon, S. (2010). A lifeline to treatment: the role of Indian generic manufacturers in supplying antiretroviral medicines to developing countries; *Journal of the International AIDS Society*. **13**:35. doi: 10.1186/1758-2652-13-35

van Wassenhove, LN. (2006) Blackett Memorial Lecture - Humanitarian aid logistics: supply chain management in high gear. *Journal of the Operational Research Society*. **57**, pp. 475–489.

Watal, J. (2000). Access to Essential Medicines in Developing Countries: Does the WTO TRIPS Agreement Hinder It? Science, Technology and Innovation Discussion Paper No. 8, Center for International Development, Harvard University. http://www.iatp.org/files/Access_to_Essential_Medicines_in_Developing_Co.pdf

Westerhaus, M. & Castro, A. (2006). How Do Intellectual Property Law and International Trade Agreements Affect Access to Antiretroviral Therapy? *PLoS Medicine*. **3**:8.

World Health Organization (2008). 10 Facts on the Global Burden of Disease

World Health Organization. (2010). Mapping of partners' procurement and supply management systems for medical products, Federal Ministries of Health, Nigeria, 2010.

World Health Organization. (2013). WHO traditional medicine strategy: 2014-23. www.who.int/medicines/publications/traditional/trm_strategy14_23/en/

World Intellectual Property Organization: Beall, R. & Attaran. (2016). Patent-based analysis of the World Health Organization's 2013 model list of essential medicines. http://www.wipo.int/policy/en/global_health/documents.html

Xuan Yua, B, Cheng Li, A., Shib, Y. & Yua, M. (2010) Pharmaceutical supply chain in China: Current issues and implications for health system reform. *Health Policy*. **97**: pp. 8–15.

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Daniel S. Levine is an award-winning business journalist who has reported on the life sciences, economic development, and business policy issues throughout his 25-year career. He founded Levine Media Group in 2013 to provide strategic communications to life sciences companies. He is host of *The Bio Report* and *RARECast* podcasts, a senior fellow at the Center for Medicine in the Public Interest, and a member of the advisory board of the BioCalifornia. Most recently he served as managing director of publications for Burrill & Company, a global financial services and media firm focused on the life sciences. From 2011 to 2014, he served as the lead editor and writer of Burrill's acclaimed annual book on the biotech industry. He also served as editor for *The Burrill Report*, which tracked trends, clinical developments, and financing activity within the life sciences. His work has appeared in *The New York Times*, *The Industry Standard*, *TheStreet.com*, and other national publications. Before entering journalism, Levine spent five years in the investment banking industry and served as a vice president and general principal of Herbert Young Securities. He holds a bachelor's in English from Vassar College and a master's in journalism from the University of California, Berkeley.

Appendix

Call for Papers

THIS IS A DRAFT OF AN ANNOUNCEMENT

Special Issue of *XXXXXXX*
on "The Complexities of Medicinal Access: Problems and Systematic Solutions"
Target Date for Submissions, XXX
Target Date for Publication, XXX

This special issue is a joint effort of *XXXX*, *XXXX*, the Biotechnology Innovation Organization (BIO - Washington, DC) and . . . .

Background

Access to Essential and Special Medicines has been problematic for decades and cited throughout health sciences literature, although over the last decade there has been limited scholarly attention to this critical issue in global health and health equity. The last burst of activity was in the first few years of the new millennium and the focus was largely on the pricing and accessibility of ARVs for HIV, and the role that patenting was believed to play in limiting accessibility. The Editors believe that the time has come for a renewed comprehensive dialog on a global basis to discuss the full range of issues that are the basis for medicinal inaccessibility by at least half of the world's population. While there is significant concern about the impact of the international patent system in this regard among several Multi-lateral organizations and NGOs in the global health community, there is also evidence that addressing the problem without an assessment and set of solutions for the full range of causes will not create broader access in any meaningful way, and at the same time might compromise the medicinal innovation urgently needed for neglected tropical diseases and the growing role of non-communicable diseases.

The literature often concludes that the biggest obstacle to access is the high pricing of medicines and that that pricing is a function of the patent positions held by pharmaceutical companies, particularly those multi-national pharmaceutical companies that are categorized as discovery-driven in their research enterprises. While there is little doubt that pricing and patenting are linked and that the combination of these factors often permits aggressive pricing of medicines beyond the range of affordability for many countries and their citizens, it has also been demonstrated that in sixty-five low- and middle-income countries, where four billion people live, patenting is rare for 319 products on the World Health Organization's Model List of Essential Medicines. Less than 2 percent are actually patentable and these are concentrated in larger markets (Attaran, 2004; WIPO, 2016). The majority of medicines on the list are manufactured by generics producers, many of which operate out of India and China where labor cost advantages are reflected in pricing. Moreover, some pharmaceutical manufacturers, through creative commercial arrangements and public-private partnerships, have found successful approaches to making medicines available where needed.

These and other phenomena question the state of the current policy dialogue that is often based on premises about how patents affect corporate revenues or the health of the world's poorest and that the solution to medicinal access is abandonment of the international patent system. At a time when the principles of patenting and its role on innovation in medicinal discovery and development are being debated in international trade discussion, the dialog about the root causes and solutions to the problems of medicinal access must be expanded to include the manifold reasons and their interrelationships.

These categories include but are not limited to:

- **Accessibility of care milieu:** Remoteness; density; percentage of residents living with accessible radius time to health facility for consultation, diagnosis and medicinal intervention
- **Affordability:** Pricing in proportion to income / government finance

- **Availability:** Scarcity of care and technology resources allowing appropriate Dx and Rx
- **Awareness:** Knowledge of available resources and options for care, and the implications for medicinal intervention
- **Essential medicines procurement:** Disconnect between national polices, formulary and sources of supply
- **Health Systems Financing:** Public and private means for payment on national and trade levels (another dimension of Affordability)
- **Regulation:** Ambiguous medicinal approval regime or application of government mandated pricing requirements.
- **Socio-cultural:** nonfinancial obstacles to care such as culture, language, race, and ethnicity, and the related medicinal implications
- **Supply chain management:** Mal-functioning national, local or provider systems for managing flow of necessary products.

For a thorough discussion of the full range of issues that the Editors wish to vet in this special issue, please visit:

The Challenge

The Editors are inviting quantitative or qualitative analyses on each of these topics. Preference will be given to interdisciplinary approaches that provide insight into the complex milieu of causes and a set of actionable recommendations for international and national polices for addressing discontinuities in the medicinal access. The timeline for proposals and submissions is:

By XXXXX, a proposal identifying the authors, affiliation, topic of interest and an abstract. The Editors will respond with guiding comments.

By XXXXX, submission of final paper. An early submission will get preference in the review and publication process.

Publication: XXXX. Each article will be sent to two or three independent reviewers, with the intent that each paper will be examined by experts in the topic area. *The Editors* also invite the curriculum vitae of those interested in serving as referees.

Send your proposal and manuscript to:

For more information, visit the official website of the journal: www.xxxxx.xxx