

Rethinking Trade Treaties & Access to Medicines:

Toward a Policy-Oriented
Research Agenda



Report by the Working Group
on Trade, Investment Treaties
& Access to Medicines





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By the Working Group on Trade, Investment Treaties, and Access to Medicines

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The **Global Development Policy (GDP) Center** is a University-wide center at Boston University in partnership with the Frederick S. Pardee School for Global Studies and the Vice President and Associate Provost for Research. The GDP Center conducts interdisciplinary research to advance policy-oriented research for financial stability, human well-being, and environmental sustainability across the globe.

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EXECUTIVE SUMMARY

Since the establishment of the World Trade Organization (WTO) in 1994 that brought intellectual property rules into the global trading regime via the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), there has been a concern that the trading regime would globalize the monopolies created by patent rights and therefore make it more difficult for low- and middle-income countries (LMIC) to ensure access to essential medicines for all those in need. Despite the landmark decision in Doha, there continue to be concerns about the extent to which the trading system is compatible with Sustainable Development Goal (SDG) 3, in particular access to medicines. Trading partners from high-income countries continue to pursue bilateral and regional trade agreements that seek intellectual property and investment protections beyond what is required by the TRIPS Agreement (TRIPS-plus). Those same partners also tend to limit the adoption and use of public health flexibilities in the TRIPS Agreement (TRIPS-flexibilities). The trade and investment policy is entering a new era of debate and (re)negotiation shaped by the graduation of many least developed countries (LDCs) who will need to adhere to TRIPS, and the review of multilateral and bilateral agreements in the US.

Many important knowledge gaps remain about the processes and factors that influence the implementation of trade treaties, which can explain the variation in implementation between countries and their effects on access to medicines. Furthermore, rigorous evaluation of the effects of trade treaties on access to medicines is restricted by the limited availability of data, and a lack of uniformity in indicators and weak study methods.

Boston University's Global Development Policy (GDP) Center convened a working group of 13 global experts with the goal to develop a policy-oriented research agenda to strengthen the ability of nation-states to implement policies for universal access to medicines at the national level and help stakeholders calibrate the trade regime toward meeting SDG 3. The working group met at Boston University's Washington, DC offices in March 2019 to review key evidence on the implementation and evaluation of trade treaties on access to medicines, collaborate on identifying knowledge gaps, and propose a research agenda.

This Report of the Working Group on Trade Treaties and Access to Medicines synthesizes the results of the expert group's work.

The Working Group identified three broad categories of research gaps:

1. **Analysis of treaty provisions and language**, including their adoption and implementation in domestic law and their subsequent use in domestic and international litigation, to understand how such provisions and language constrain domestic access to medicine policy.
2. **Rigorous empirical studies** to quantify the effects of treaties on access to medicine for people residing in LMIC countries.
3. **Analysis of political economy factors** which influence the processes and effects of LMIC governments in signing and implementing treaties and related policies.

Our analysis of treaty provisions found that, while there is an overwhelming amount of legal and policy literature discussing the flexibilities and constraints in trade and investment treaties for access to medicines, the research is not sufficiently systematized. As a result, we lack an understanding of each treaty as a whole document, attempting to consider all the provisions that might impact policy-making for access to medicine. We also lack a birds-eye view of the global treaty regime more broadly, both in its homogeneity and diversity, which would allow us to understand what treaty commitments impact access to essential medicine globally. Moreover, researchers lack access to specific information about the timing and implementation of domestic legal and regulatory reforms. The small number of international disputes involving pharmaceuticals, and the lack of public records from domestic court systems are another obstacle for researchers seeking to understand how pharmaceutical companies employ litigation to defend their intellectual property rights.

Our analysis of ex ante and ex post empirical studies suggests that both approaches can result in inaccuracies and limitations in our ability to estimate the impact of trade treaties on access to medicines. Estimating medicines access requires the measurement of multiple dimensions (affordability, availability, acceptability, accessibility); much empirical work is focusing on one dimension only. Assessments of the impact of trade agreements ex ante by proving a correlation between the dependent and independent variables often neglect the fact that each provision affects different pharmaceuticals at different points in time. Ex post econometric analyses suffer from challenges of unreliable data, improper framing of an empirical question and statistical or econometric errors. Studies have also failed to account for exogenous factors that significantly impact access to medicines such as the macroeconomic restraints imposed externally or domestically that limit or even reduce governments' health budgets and procurement of medicines.

Our analysis of the political economy factors reveals a gap in our understanding of how LMICs can mobilize domestic constituencies to implement policies promoting access to essential medicines. In addition to the negotiating histories of key trade treaties, and accurate records of domestic legal changes, we also need to be able to read that data in the context of the verified use of TRIPS flexibilities, as well as information on the policy actors who have implemented those changes. Moreover, we need a better understanding of the influence and political strategies of stakeholders and how policy implementation is managed. This evidence would complement databases on (1) the use of compulsory licenses and government use orders issued, as well as voluntary licenses, (2) the catalysts and obstacles permitting parallel imports, and (3) the cross-country variability of patentability standards and opposition procedures.

In light of the research gaps in each category, we recommend the following research agenda to begin to fill in the gaps and better empower LMICs to implement public health policies for access to essential medicines.

Related to treaty provisions and language:

- Create a comprehensive list of relevant treaty provisions and code these treaties at an acceptably granular level.
- Create a database identifying domestic implementation of treaty commitments.
- Establish a system of tracking new international and domestic disputes dealing with intellectual property rights relevant to pharmaceuticals.

Related to ex ante and ex post studies:

- Create a map of the different empirical study methods and designs used to study the question of treaties and access to medicines.
- Isolate, if possible, the specific impacts on access to medicines of various IP protection vehicles, such as data exclusivity, patent term extensions, patent exhaustion rules and registration linkage provisions.
- Conduct medicine-specific and patent-specific studies to understand outcomes unique to certain contexts.
- Prioritize empirical studies on countries that had implemented pharmaceutical patenting prior to TRIPS.
- Consider the differential impacts of various trade treaty provisions on different income quartiles in specific countries.

Related to political economy factors:

- Study the political and financial pressure exercised by interest groups and external, non-trade state pressure to shape trade treaties and their access to medicines provisions and the responses by in-country interest groups.
- Conduct country-specific studies to identify background political conditions which prevail when a country decides to use (or threaten) compulsory licensing.
- Explore associations between World Intellectual Property Organization advice on TRIPS compliance and the flexibilities adopted in domestic law under in new trade treaties.
- Conduct country-specific studies along the medicine value-chain from procurement/customs to end user (i.e., consumer).
- Catalogue those policy levers that would improve access to medicines apart from TRIPS flexibilities but that are related to trade treaties.

Given the interconnectedness of these issues, two broader proposals undergird the specific research tasks we choose to tackle. First, we propose to create a best practice research guide including identifying a list of empirical indicators for access to medicine research, relevant treaty provisions and the impacts they may have, as well as common pitfalls in trade and access to medicine research. Second, in support of the first proposal, we propose to create a “global access data commons”, akin to “national patent data”. This database would link individual sets of standardized data including medicine registration information, patents (including information about whether they are primary or secondary patents), treaty codification and trade flow, so they would be able to “speak” to each other and so that researchers could more easily draw associations between indicators.

Given the current research gaps with respect to the effects of trade treaties on access to medicines there is an urgent need to generate evidence that can guide countries in their negotiations, implementation and evaluation of these trade treaties. To carry out the research necessary to address the current knowledge gaps requires multi-disciplinary research in areas such as health economics, law, political science and public health. It also benefits from the co-creation of the research with those involved in the negotiation and implementation of trade treaties. Finally, the policy-orientated research agenda could be strengthened by further feedback from civil society, government officials, industry representatives and those advising governments and industry.

ACRONYMS AND ABBREVIATIONS

ARV: Anti-retroviral medicine

AUSFTA: Australia- US Free Trade Agreement

BIT: Bilateral Investment Treaty

BNDES: National Bank for Economic and Social Development (Brazil)

COMESA: Community of Eastern and Southern Africa

COMTRADE: Common Format for Transient Data Exchange for Power Systems

CPTPP: Comprehensive and Progressive Trans-Pacific Partnership

EAC: East African Community

FTA: Free Trade Agreement

HIV: Human Immunodeficiency Viruses

IP: Intellectual Property

IPR: Intellectual Property Right

ISDS: Investor-State Dispute Settlement

LDC: Least Developed Country

LMIC: Low or middle income country

NAFTA: North American Free Trade Agreement

PDP: Productive Development Partnerships

R&D: Research and Development

SADC: Southern African Development Community

SCTIE: Secretariat of Health, Science, Technology and Strategic Inputs (Brazil)

SDG: Sustainable Development Goal

TPP: Trans-Pacific Partnership

TRIPS: Agreement on Trade-Related Aspects of Intellectual Property

UN: United Nations

WTO: World Trade Organization

WIPO: World Intellectual Property Organization

BACKGROUND

The United Nations Sustainable Development Goals (SDGs) put global health at the center of the global development agenda. SDG number 3 seeks to “Ensure healthy lives and promote well-being for all at all ages.” Under that rubric, the SDGs outline an important pathway to achieve that goal, aiming to “achieve universal health coverage, including access to safe, effective, quality and affordable essential medicines and vaccines for all.” This requirement is consistent with existing human rights norms establishing equitable and affordable access to medicines of assured quality and access to the results of scientific advancement as essential to the right to health (See, e.g., Moon et al. 2012, Vawda & Baker 2013).

Since the establishment of the World Trade Organization (WTO) in 1995 that brought intellectual property rules into the global trading regime via the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), there has been a concern that the trading regime would globalize the monopolies created by patent and other intellectual property rights and therefore make it more difficult for low- and middle-income countries to ensure access to essential medicines for all those in need.¹ Some of those concerns were addressed in the 2001 Doha Declaration on the TRIPS Agreement and Public Health, which led to an important clarification of the existing policy flexibility inherent in TRIPS. In the aftermath of the Doha Declaration, parties crafted the so-called “Paragraph 6 solution” which allows compulsory licenses to be granted for pharmaceuticals produced for export to least developed countries, especially those that lack their own manufacturing capacity.

“ There is concern that, despite the flexibilities in multilateral arrangements, trade and investment treaties can pose threats to access to some essential medicines.”

Despite these decisions at Doha (and post-Doha) there continue to be concerns about the extent to which the trading system is compatible with SDG 3. Trading partners from high-income countries continue to pursue bilateral and regional trade agreements that seek intellectual property and investment protections beyond what is required by the TRIPS Agreement (TRIPS-plus). Those same partners also tend to limit the adoption and use of public health flexibilities in the TRIPS Agreement (TRIPS-flexibilities), including those clarified and extended by the

Doha Declaration and its aftermath. As a result, since 2001, the WTO has waned in importance with regards to the regulation of intellectual property rights, while a proliferation of new regional and bilateral trade and investment treaties have increased in prominence in the global trade policy landscape. Moreover, investment provisions in these treaties have the potential to expose governments looking to increase access to medicines to costly investor-state disputes (Baker & Geddes 2017). Overall, there is concern that, despite the flexibilities in multilateral arrangements, trade and investment treaties can pose threats to access to some essential medicines.

Trade and investment policy is entering a new era of debate and (re)negotiation. The most recent proposed US trade agreement, the USMCA, has further raised the access bar by including new intellectual property protections exceeding those found in prior agreements. Furthermore, many least

¹ “Essential medicines” is the term found in SDG 3.8. It is a term of art employed by the World Health Organization (WHO) for those medicines which satisfy the specific priority health needs of a country’s population, recognizing that resources are limited in any context, even an affluent country such as the US. Over 130 countries have adopted this process of setting priorities for government medicines reimbursement and it is up to each nation to define its national priorities. Some activists, academics, and civil society organizations view this list as under-inclusive from the perspective of access to medicines, because many medicines are excluded because of cost, health system incapacity, and delayed government action. Indeed the UN High Level Panel (UN 2016) suggested a broader concept of “access to medicines for all conditions for all people.” In order to maintain our connection between access to medicines and SDG 3, we are using the term “essential medicines” as defined by the WHO, while acknowledging that other views exist.

developed countries (LDCs) with current rights to exempt themselves from TRIPS will graduate and will have to adhere to the agreement when their transition periods end.

Over the last two decades many organizations and expert groups have issued policy recommendations to increase policy alignment between trade treaties and access to medicines in low- and middle-income countries. Two recent global landmark reports were published by The United Nations High Level Panel on Access to Medicines (UN 2016) and The Lancet Commission on Essential Medicines Policies (Wirtz et al. 2017). However, despite the large number of policy recommendations, including those that encourage countries to adopt TRIPS flexibilities into national legislation and avoid TRIPS-plus provisions, there are large variations in their implementation between countries. Many important knowledge gaps remain about the processes and factors that influenced both the outcome and the implementation of trade treaties, which can explain the variation between countries. Furthermore, rigorous evaluation of the effects of trade treaties on access to medicines is restricted by limited availability of data, and a lack of uniformity in indicators and methods.

Boston University's GDP Center held a workshop titled "Rethinking Trade Treaties and Access to Medicines: Toward a Policy Oriented Research Agenda for the Sustainable Development Goals" at Boston University's Washington, DC offices in March 2019. The goal of the workshop was to develop a policy-oriented research agenda for SDG 3. Thirteen experts² attended the meeting, gave presentations on key evidence on the implementation and evaluation of trade treaties on access to medicines, collaborated to identify knowledge gaps, and proposed a research agenda. Evidence generated from this new research should strengthen the ability of nation-states to implement policies for universal access to medicines at the national level and help stakeholders calibrate the trade regime toward meeting SDG 3.

This report summarizes the identified knowledge gaps and presents the proposed research agenda, which should be improved and expanded on as research and critical analysis continue and in consultation with other experts.

Thematic areas of evidence and knowledge gaps:

As mentioned above, despite almost three decades of research on this topic, there remain many gaps in the data and unanswered questions in the research about the relationship between trade and investment agreements and access to medicines, in particular in low- and middle-income countries (LMICs).

The workshop uncovered three broad categories of research gaps that leave room for a new policy-oriented research agenda:

1. **Analysis of treaty language**, including their adoption and implementation in domestic law and their subsequent use in domestic and international litigation, to understand how such provisions constrain domestic access to medicine policy.
2. **Rigorous empirical studies** to understand how treaties impact actual access to medicine for constituents in LMIC countries.
3. **Analysis of political economy factors** which influence LMIC governments in signing treaties and putting in place public health policy.

2 The experts attending the meeting can be found in the Annex.

In the following section we outline some key evidence with respect to each of these categories and identify corresponding data and research gaps. The final section lays out a proposed research agenda.

THEMATIC AREA 1:

TRADE AND INVESTMENT TREATY LANGUAGE

The TRIPS agreement marked a new era of globalized minimum standards of intellectual property protection for access to medicines. Before TRIPS, many developing countries did not grant patents for pharmaceutical products, often because they viewed the costs of granting patents on medicines as exceeding the benefits. Policy was informed by a sense that any individual LMIC's medicine patent protection would have a limited impact on global research and development of new pharmaceutical products (Shadlen et al. 2019). In the late 1970s and early 1980s, pharmaceutical patenting began to proliferate as innovators and their host states recognized the benefits of increased patent protection. There was no universally accepted standard of pharmaceutical patent protection, however, and countries had different rules regarding patent terms, patent requirements for different types of pharmaceutical products (e.g. active ingredients, compositions and formulations, medical uses), and data protection, among others (Shadlen et al. 2019). TRIPS changes this, reducing this space for cross-national diversity, as it requires all countries to allow patents on pharmaceutical products. Furthermore, the IP provisions in bilateral and regional trade agreements that have followed TRIPS require countries to introduce further measures. This section is divided in two parts. The first part focuses on key evidence of policy flexibilities and constraints in trade and investment treaties that affect access to medicines. The information presented is based on several literature reviews on the topic. In the second part, drawing from the results of these literature reviews, we identify current research gaps.

“ Although TRIPS set new minimum standards, it left member states some degree of policy space on how to achieve these standards.”

Evidence: As TRIPS entered into force in 1995, WTO members that had previously declined to patent medicines were required by 2005 to begin offering patents (lasting for 20 years from the date of application) for pharmaceuticals, and to create a process by which they maintained priority for all patent applications filed after 1995 (mailbox rule). Although TRIPS set new minimum standards, it left member states some degree of policy space on how to achieve these standards (Shadlen et al. 2019). The provisions allowing for discretion in their implementation have come to be known as “flexibilities” (Table 1). Countries could use those flexibilities to facilitate access to medicine under the new regime.

Table 1. Recognizing TRIPS “flexibilities” in specific TRIPS provisions

Flexibility	Definition
Exclusions from patentability (Art. 27.3)	Countries permitted to exclude “mere discoveries”, surgical, diagnostic and therapeutic methods, genes or extractions from naturally occurring matter, new uses and methods of use of known substances, among others.
Standards of patentability (Art. 27)	High/strict standards of patentability, especially concerning combinations of prior art, novelty, inventive step and industrial applicability
Disclosure (Art. 29)	Applicant must disclose all known practical methods of carrying out the invention, and the best-known mode, as well as corresponding applications in other jurisdictions.
Patent Revocation and Opposition (Arts. 32 and 62.4)	Allows both pre- and post-grant opposition procedures with broad standing rights and easy-to-use administrative procedures. Also includes broad grounds for revoking patents, including inequitable conduct, fraud, non-payment of patent maintenance fees, failure to make required disclosures, and failure to satisfy requirements/standards of patentability
Bolar/Early working (Limited Exceptions (Art. 30))	Generic manufacturers allowed to use the patented invention for the purpose of seeking regulatory approval before the patent expires. Includes both commercial and non-commercial research rights, for domestic use and for export, and for pharmacy formulation and individual use.
Compulsory Licensing and government use (Arts. 31 and 44.1)	Broad grounds for issuing a government authorization for use of an invention without the consent of the patent holder, including excessive pricing, refusal to license, denial of access to an essential facility, and failure to supply sufficient quantities of a drug, among others. Licenses in the case of national security or public health crises allowed without prior negotiation. Public, non-commercial-use or government-use licenses without prior negotiation. Production for export licenses pursuant to Art. 31bis or, possibly, by an Art. 30 limited exception (although such an interpretation is not established in WTO jurisprudence). Judicial licenses also allowed with clear, efficient and easy-to-use administrative procedures and remuneration guidelines.
Parallel Imports (Art. 6)	Countries may choose whichever domestic rule of exhaustion they like. Under the adoption of an international exhaustion rule, for example, products marketed by the patent owner or with the patent owner’s permission in one country may be imported into another country without the approval of the patent owner. Furthermore, practices related to parallel importation cannot be challenged under the WTO dispute settlement system.
Data Protection (Art. 39)	Countries must protect undisclosed test data from unfair commercial use and other disclosure unless “necessary to protect the public or unless steps are taken to” protect against unfair commercial use.
LDC Waiver (Art. 66.1)	LDCs are not required to recognize patents on pharmaceuticals, as well as data rights, mailbox obligations and market exclusivity, currently extended by the TRIPS Council to the year 2033.
Competition Policies (Arts. 8.2 and 40)	Prevents abuse of IPRs by right holders, practices that unreasonably restrain trade or adversely affect international transfer of technology. Also prevents licensing practices or other IPR conditions that restrain competition, adversely affect trade and impede transfer of technology.
Enforcement Flexibilities (various)	No border measures required for suspected patent infringement of goods in transit (Art. 51). No requirement of criminal penalties for patent violations (Art. 61). Although injunctions must be an available remedy, it is also permissible to limit remedies to adequate remuneration like that provided for compulsory and government use licenses (Art. 44). Although provisional measures must be possible, their use is not mandatory (Art. 50). Although compensatory damages must be an available remedy for infringement, alternative measures damages based on market value, selling price, or deterrence are not required (Art. 45).

Source: Baker 2018.

One of the most basic flexibilities is rooted in the way TRIPS laid out its patent requirements. Article 27 maintained relatively common standards of patentability, novelty, inventive step and industrial applicability. However, countries have implementation flexibility with respect to the stringency or leniency of such standards. For example, more stringent standards and permission exclusions from patentable subject matter, such as abstract ideas, laws of nature and isolates of biological substances, are particularly important in eliminating unwarranted patents and patent “evergreening” – the extension of patent exclusivities by minor tweaks to known chemical entities, dosages, formulations, and combinations. The most prominent examples of countries incorporating this flexibility are found in Argentina, Brazil and India (Shadlen 2017). Under India’s Section 3(d), for instance, new forms of existing drugs are not eligible for a patent unless they demonstrate improvements in efficacy. Section 3(d) came under attack when the India’s patent office refused to patent Novartis’ key cancer treatment, Glivec®. As a modification of an existing substance, it was not patentable under Indian law. Although Novartis sued in Indian courts, the Supreme Court upheld the decision and secured India’s right to maintain high domestic patentability standards (Gabble & Kohler 2014).

WTO Members were likewise explicitly permitted (but not required) to exclude “mere discoveries”, diagnostic and therapeutic methods, as well as new uses and methods of use of known substances, among others (TRIPS Art. 27.3). This provision is important for purposes of access to essential medicine because it gives member states the discretion, for example, to decide whether to grant patents on certain biotechnological inventions or new uses for an existing medicine (Correa 2002). TRIPS also required a certain amount of disclosure in the application of a patent which identified all known practical methods of carrying out the invention, as well as the best-known mode and any additional patent applications in other jurisdictions (Art. 29).

Once a patent application has been filed, TRIPS permits pre- and post-grant opposition procedures whereby interested parties can help screen applications for the requisite patent criteria and disclosure inadequacies (Art. 32). Limited exceptions to patent rights, recognized in Article 30, allow WTO members to adopt important exceptions in their domestic laws aimed at enabling access to essential medicines. The “Bolar” or early-working exception is especially important to enable generic medicine producers to begin working on developing a generic for a medicine and submitting it for regulatory approval while the patent is still active (Gleeson et al. 2017).

“ TRIPS affirms the rights of the parties to balance the interests of intellectual property rights holders and the public’s need for essential medicines.”

One of the most widely discussed flexibilities preserved by the TRIPS Agreement is the right of states to grant compulsory licenses in order to gain access for their constituents to an essential medicine that would otherwise not be available. Clarified by the Doha Declaration, TRIPS affirms the rights of the parties to balance the interests of intellectual property

rights holders and the public’s need for essential medicines by confirming countries’ broad discretion to define the grounds for compulsory licenses, including identification of what constitutes an “emergency” which would permit expedited licensing. Countries may grant compulsory licenses in the case of a national emergency or public health crisis without prior negotiation with the patent holder, as well as for drug production for public, non-commercial or government use. Later revisions to Article 31 (Article 31bis) permit members to also produce licensed medicines for export and import if the importing countries lacks manufacturing capacity to make use of compulsory licensing (Baker 2008, Abbott & Reichman 2007). This temporary waiver was approved as an amendment to the TRIPS Agreement in December 2005. Only in 2017, however, did the required two-thirds of WTO membership officially ratify Article 31bis, fully allowing countries that produce generic

medicines under a compulsory license to export those medicines to countries that lack their own manufacturing capacity (New 2017).

Another widely discussed flexibility, is the ability of member states to choose their own patent exhaustion regime (national, regional, or international). Through the principle of exhaustion, once a patent owner has sold a patented product for the first time, they “exhaust” their right to control further exploitation and the buyer can use, sell (or export), license or destroy the product as they wish. Choosing international exhaustion allows pharmaceutical products, whose patent rights are exhausted in one country, to be imported into another without the patent owner’s permission (Krikorian & Szymkowiak 2007). This is known as parallel importation. For some LMICs, parallel importation theoretically provides the opportunity for increased access. Yet, employing an international exhaustion regime could potentially harm both an LMIC importer and an exporter of those parallel imports by discouraging the patent holder from making the drug available in the exporting market.³

A few “flexibilities” are derived from the absence, rather than the presence of treaty language. TRIPS lacks any specific mention of patent term extensions, for example, which would allow patent holders to receive longer patent periods for regulatory or patenting delays. Data protection in TRIPS Article 39 only requires countries to protect undisclosed test data from “unfair commercial use” unless “necessary to protect the public or unless steps are taken to” protect against unfair commercial use – a much narrower standard of protection than so-called “data exclusivity” (discussed below).

Some flexibilities go far beyond rights limited to patent holders. Competition rules in TRIPS (Articles 8.2 and 40) prevent holders of IPRs from abusing their rights in ways that “unreasonably restrain trade and adversely affect the international transfer of technology” as well as impeding competition. TRIPS also includes various rules on enforcement which allow member countries to protect IPRs in various ways. It does not require that states impose criminal penalties for patent violations, for example, and gives broad discretion in enforcing remedies for IPR infringement (Articles 44, 45, and 61). Finally, although this is not directly related to a specific policy choice, LDCs benefit from the adoption and subsequent extension of a transition period for providing patent and data protections for pharmaceuticals until 2033 which gives them additional time to develop pharmaceutical patenting rules (WTO 2015).

The language of TRIPS and its subsequent legal interpretation is fairly well-understood and discussed. The newer regime of free trade agreements (FTAs) and bilateral investment treaties (BITs), however, has further expanded IPRs to effectively undermine the flexibilities available in TRIPS. The provisions that restrict flexibilities in FTAs and BITs are thus called “TRIPS-plus” provisions (Table 2). It is important to note that since FTAs and BITs are not homogeneous, the following provisions are not universally included in each agreement. Indeed, in some cases these TRIPS-plus measures have been proposed but not ultimately included in certain agreements.⁴

“ The newer regime of [FTAs and BITs] ... has further expanded IPRs to effectively undermine the flexibilities available in TRIPS.”

³ If Pfizer (for example) has a patent on a drug in a Lower Income Country (LIC) and a Middle Income Country (MIC) and it makes the price lower in the LIC, parallel importation allows the MIC to import the drug, and this should get Pfizer to lower the price in the MIC too. While that seems a boon to access, unless the LIC is an important market (which almost by definition of being low-income it’s not), then the actual impact of parallel importation might be that Pfizer stops making the drug available in the LIC, in which case everyone loses – the LIC and the MIC.

⁴ As an example, during the TPP negotiations, the US proposed provisions including patents for new forms as well as for diagnostic, therapeutic & surgical methods. Both provisions were ultimately rejected by the rest of the parties and not included in the final agreement.

Table 2. TRIPS-plus measures with implications for access to medicines⁵

MEASURES	MECHANISM OF IMPACTING ACCESS
Old provisions; New standards	
Eased standards of patentability and secondary patents	Requires patents on: (1) new uses or methods of use of known medicines, and (2) new forms for known substances regardless of therapeutic efficacy. Lowers standards on novelty, inventive step (changed to “obviousness”) and industrial applicability (changed to “usefulness”- both terms as used in the US). Secondary patents (additional, defensive patents) available on a broader range of inventions.
Limitations on Patent revocation/opposition	No or limited allowance of pre- or post-grant opposition procedures. Limited grounds for patent opposition/revocation by government.
Compulsory Licensing limitations	Limiting a country’s ability to authorize a party (other than the patent holder) to use, manufacture, sell, etc. that invention without the consent of the patent holder by allowing license language to restrict the grounds on which a license may be granted
Limitations on Exhaustion rules	International exhaustion regime not permitted
Lower requirements for disclosure in patent applications	Less stringent disclosure requirements or prevention of allowable disclosure requirements
Weakened limited exceptions for patent use	Restriction on the use by non-patent holder of early working/Bolar provisions in obtaining third-market registration. No exception or weak exception for non-commercial and commercial research and educational use of patented technology. No exception permitted for prior use of patented technology.
New provisions	
Patent term extension	Extensions for delays in processing patent applications, medicines registration and marketing and other regulatory delays.
Elimination of patent exceptions	Requires patents on diagnostic, therapeutic and surgical methods for treatment of humans
Patent registration linkage	Restricts the medicine regulatory authority’s ability to register a generic medicine whenever an originator merely claims that a patent would be infringed
Data exclusivity	Gives exclusive rights to regulatory data to the patent holder and prohibits medicine regulator’s reliance on, or reference to, innovator’s submission data in reviewing registration applications of generics. Includes the possibility of extending data exclusivity upon submission of additional clinical data not available at the time of the original submission.
Enforcement measures	
Mandatory injunctions	Requires the availability of injunctions (and prohibits collecting royalties as a remedy for patent infringement)
Increased civil and border measures remedies	Deterrent civil remedies, such as damages based on average retail price. Requires seizure of goods in transit, mandatory destruction and allows third-party enforcement.
Broadened criminal remedies	Criminal sanctions for patent violations (beyond TRIPS requirement for criminal trademark counterfeiting and copyright piracy only)
Investor-state dispute settlement provisions	Inclusion of IPRs as covered investment, which permits ISDS claims based on patent decisions.

Source: Baker 2018, Gleeson et al. 2019.

⁵ Although this table is quite comprehensive in terms of the IP and investment provisions that directly impact access to medicines, it lacks additional IP rules that might affect delivery of medicines including trade secrets and in some cases trademark. It also does not include a much broader set of treaty provisions that have potential impacts on core pharmaceutical policy objectives, which include such provisions as procedural requirements for national pharmaceutical pricing and reimbursement, government procurement rules, rules on state-owned enterprises and designated monopolies, among others. For a detailed discussion of these aspects of trade agreements, see Gleeson et al. 2019.

TRIPS-plus provisions impact access to medicines in three key ways: (1) by increasing IP protection available to the patent holder under old TRIPS provisions, (2) by introducing new standards of IP rules and IP protection, and (3) by ramping up the enforcement requirements for intellectual property infringement. Traditional standards of patentability, disclosure in patent applications, revocation and opposition, and limited exceptions now contain new standards which provide increased protection for intellectual property holders. Rather than allow flexibility in patenting rules, these treaties tend to require patents on new uses and new methods of use on known substances. They set lower standards for “novelty” and “industrial applicability”, as well as disclosure in patent applications. They also limit the grounds for patent opposition or revocation, and weaken the limited exceptions (TRIPS Art. 30) to decrease access to early-working and government use exceptions (TRIPS Art. 31). Finally, many FTAs restrict the grounds on which a compulsory license may be granted, and some prohibit international exhaustion standards.

New provisions likewise limit the policy options available to member states. These treaties introduce patent term extensions, which require countries to grant extensions for patent processing and regulatory delays. They contain patent registration linkage provisions which effectively halt a generic medicine’s registration in the event of any claim by the originator (however substantiated) that it would infringe on a patent. The treaties also demand that member states recognize patents on diagnostic, therapeutic and surgical methods for treatment.

One of the most commonly discussed new provisions in trade agreements is the protection of data exclusivity. Unlike “data protection” (TRIPS Article 39.3) which relates to “unfair commercial use”, data exclusivity provisions require that a country’s medicine regulatory authority protect the test data (i.e., typically a product’s clinical trial data) of a company wishing to be first on the market exclusively for a certain number of years (e.g. 5 to 12 years in most trade agreements). This could delay the launch of generic competition if those generic companies must either generate their own data or wait until the data exclusivity period ends (Shadlen et al. 2019). Data exclusivity provisions have become more prevalent as the United States and the EU have pushed for these heightened standards in their agreements. China has proposed to include the most stringent data exclusivity rules in their domestic law – 6 years for innovative drugs and 12 for biologics (Wang 2018).

“Data exclusivity provisions have become more prevalent as the United States and the EU have pushed for these heightened standards in their agreements”

Enforcement mechanisms give additional teeth to the heightened IPR standards in these agreements. New FTAs can increase the required remedies for IP infringement – demanding the availability of injunctions in lieu of a royalties remedy, requiring seizure of goods in transit and mandatory destruction of counterfeit goods. They also often broaden the requirement for criminal remedies for patent violations.

FTAs with investment provisions and BITs also expand enforcement of IPRs by including them as a covered investment. Moreover, regulations that interfere with patent and data-protection rights might also run afoul of investor protections under the agreement and make countries subject to investor-state disputes for their public health policies. These challenges can prove very expensive, especially for LMICs, even if the investor-claimant is unsuccessful (Gleeson et al. 2017). Non-IPR provisions like these are not often mentioned in the debate surrounding access to medicine but can have a direct effect on medicine pricing and availability.

At the time of this writing, three different countries have faced ISDS challenges initiated by

pharmaceutical companies. Gilead (US) brought a claim against the Ukraine after failing in domestic courts to secure exclusivity in the country for Sovaldi® (for hepatitis C). In Colombia, Novartis threatened an ISDS claim when Colombia prepared to issue a compulsory license on its prized cancer medication, Gleevec® (Glivec). Eli Lilly sued Canada based on the Canadian domestic court's application of the "promise doctrine" whereby patents must live up to their (medicinal) promises in order to maintain patent protection (Baker and Geddes 2017). Only the latter of those three resulted in a decision, but all three highlight the susceptibility of countries' IP laws when covered by BITs and FTAs.

Ukraine and Colombia both settled with the pharmaceutical companies, deciding to negotiate for lower prices rather than pursue the domestic policies they had originally implemented (Baker and Geddes 2017). In Canada's case, the arbitration tribunal decided in favor of the State, that Canada's revocation of Eli Lilly's patents was not a violation of the investment treaty's "fair and equitable treatment" standard because it was rooted in established Canadian law. Countries without the "promise doctrine" on the books, however, might find themselves liable for voiding a pharmaceutical patent - even if that patent did not live up to its promised utility (Baker and Geddes 2017).

Knowledge gaps: Although there is an overwhelming amount of legal and policy literature discussing the flexibilities and constraints in trade and investment treaties for access to medicines, the research is not systematized. It often identifies the provisions of one or two treaties of interest and highlights some but not all of the relevant text. In addition, the research and subsequent

literature seems to focus unduly on only a few key treaty provisions - discussing in depth the treaty language on biologics, compulsory licensing, parallel importation, or data exclusivity. As a result, we lack an understanding of each treaty as a whole document, attempting to consider all the provisions that might impact policy making for access to medicine. We also lack a birds-eye view of the treaty regime more broadly, in an attempt to understand what the IPR commitments are across the globe.

"We lack an understanding of each treaty as a whole document, attempting to consider all the provisions that might impact policy making for access to medicine."

Furthermore, there is significant language variation in different trade agreements, in particular in the different approaches to the framing of data exclusivity or patent linkage. We need to understand better how these variations in treaty language shape what kinds of policies parties may adopt. Indeed, in certain instances, constructive ambiguities in FTAs and BITs are intentionally negotiated which allow parties to mitigate the effects of provisions that might otherwise have a greater impact on access to medicines.⁶

Due to the small sample size of international disputes, we also do not have a complete view of how pharmaceutical companies employ litigation to defend their intellectual property rights. Many of those cases take place within domestic court systems, or are settled out-of-court with no "paper trail", and as a result the full scope of the role of litigation is unknown. Finally, the timing and process of implementation of these agreements into domestic law is not well-known. Specific information about domestic legal and regulatory reforms and domestic litigation is difficult to access compared with international legal texts and jurisprudence.

⁶ In the AUSFTA and TPP/CPTPP, for example, the patent linkage provisions allow room for countries to implement a 'soft' form of linkage like Australia's as an alternative to the 'hard' US form (Son et al. 2018).

THEMATIC AREA 2:

EMPIRICAL STUDIES OF ACCESS TO MEDICINES

Although the global intellectual property rights landscape for medicines has been in the making for 25 years, it is still in the process of evolving. Despite the large amount of descriptive legal and policy literature on trade agreements and access to medicines, there is little empirical research that measures the effects of trade treaties on access to medicines in LMICs. Most of the literature presents *ex ante* predictive analyses of the effects of intellectual property provisions on access to medicine, while *ex post* analyses tend to be burdened by serious methodological challenges.⁷

Evidence: *Ex ante* empirical models are *predictive studies* based on theoretical assumptions about the relationships between a trade treaty (or treaties) as the independent variable and supply, demand, prices and expenditure as dependent variables among others. *Ex post studies*, which are far less prevalent, describe what has happened to the supply, demand, prices of or expenditure on medicines in a particular place and time.

Ex ante studies use a variety of methods to predict outcomes. Econometric analyses rely on historical correlative relationships between dependent and independent variables (e.g., indicators of access to medicines and the presence of a treaty or new IPR legislation, respectively), and predicts the future based on these correlative trends (e.g., Chauduri et al. 2006). These analyses can estimate variations in medicine prices and volume based on mathematical models and often take the form of predicted impact assessments of a relevant treaty or treaty provision. More common among international relations scholars, scenario modeling relies on narratives to “map a set of causes and trends in future time” (Bernstein et al. 2000). This approach, while less precise than econometric analyses, can more ably consider many different possible outcomes and offer predictions that respond in real time the progression of events. A scenario model might lay out a whole series of scenarios with logical chains beginning with a country’s accession to a new treaty or adoption of new legislation (e.g., Kessomboon et al. 2010, Chaves et al. 2017, Moir et al. 2018). Some of these studies (both econometric and scenario modeling) focus on a specific flexibility or policy constraint (e.g. data exclusivity or patent linkage) present in many treaties. Others focus on a specific treaty, like the TPP, to predict the potential effects of proposed provisions allowing patent term extensions and increasing data exclusivity to indicate the impact on access to medicine (Shadlen et al. 2019, Gleeson et al. 2017).

Despite the differences in methodology, modeling, and scope, *ex ante* empirical studies tend to predict that proposed trade policy changes will result in higher medicine prices, increased medicine expenditures and lower availability of necessary medicine (Trachtenberg et al. 2019). These studies make several assumptions about causal relationships between factors and must simplify the state of the market and global trading regime. For example, the studies assume that the introduction of generic medication results in lower medicine prices due to competition (e.g., Akaleephan et al.

⁷ In addition to the literature reviewed here, there’s a much bigger literature that examines specific intellectual property settings outside of the context of trade agreements. In the interests of keeping our scope narrow and focused on trade treaties and access to medicines, we have elected to omit that literature.

2009). The studies reason that patents, by prohibiting the sale of generics, decrease the options available and result in higher prices paid for treatments (Trachtenberg et al. 2019).

Ex ante studies suffer from a number of limitations inherent to the predictive approach. As described above, each treaty contains not only the well-known provisions on pharmaceutical patenting, and data and market exclusivity, but also investment rules and other constraints on domestic regulation.

“ The impact of those domestic policies is not easily calculated and leads to a mismatch between the pessimistic *ex ante* study predictions and the more mixed results of *ex post* research.”

Each researcher has to make strategic decisions about what to include, which may have significant impacts on the results. Moreover, in some cases, countries have exploited TRIPS “flexibilities” by maintaining strict patentability criteria, permitting opposition procedures, and issuing or threatening compulsory licensing, as well as employing domestic price control measures not prohibited under most agreements, to mitigate what might otherwise be huge barriers to access (see Thematic Area 1, Table 1

“Recognizing TRIPS ‘flexibilities’”). The impact of those domestic policies is not easily calculated and leads to a mismatch between the pessimistic *ex ante* study predictions and the more mixed results of *ex post* research (see below). Furthermore, many of these studies fail to distinguish between proposed treaty texts, the signing of those treaties and their actual implementation and enforcement in domestic law, which limits the accuracy in predicting how a new treaty might impact access to medicine (Akalephan et al. 2009).

Innovators and generic companies also influence domestic access to medicines by deciding whether and where to register their medicines. These decisions may be quite independent of what *ex ante* analysis would predict. For example, despite the presence of certain flexibilities allowing their theoretical market entry, generic companies are slow in entering smaller and poorer markets and even if they do, the number of competing companies might not be enough to lower prices significantly.

In addition to failing to account for domestic variations and contextual influences, the *ex ante* literature also tends to ignore certain international developments. For example, the Medicines Patent Pool has promoted generic competition for anti-retroviral medicines (ARVs) used to treat HIV, with license terms allowing generic provision to 90% of adult patients and 99% of pediatric patients in LMICs (MPP 2019). Moreover, as a result of civil society pressure, some pharmaceutical companies have committed to avoid pharmaceutical patenting in low-income countries and to systematically offer price discounts in those same countries (Pagliarulo 2019, Merck 2016, Novartis 2019).⁸

As indicated above, the *ex post* studies differ substantially from their *ex ante* counterparts in their results. Unfortunately, the *ex post* literature is much sparser and suffers from some of the same problems. *Ex post* studies, generally, do not vary much in methodology but vary substantially in scope. Methodologically speaking, they assess the effects of treaties using medicine prices, medicines as a share of health expenditures and other related measures, as outcome (dependent) variables in econometric analysis (Shadlen et al. 2019). The time and geographical scope of the studies varies widely, however. The majority of these studies examine impacts in a specific country once a treaty has been signed or entered into effect, such as the effects of the US-Jordan FTA on the pharmaceutical market in Jordan (Alawi and Alabbadi 2015). Other studies focus on a larger sample of countries and examine a wider set of provisions (Bollyky 2016). Additionally, a handful of studies

8 We should note that these sources note the policy of non-patenting or non-enforcement of patents but do not credit civil society for those policies.

examine the impact of limiting a TRIPS flexibility like data exclusivity on medicine volume and pricing (e.g, Alawi and Alabaddi 2015, Palmedo 2018).

The results of the *ex post* studies are more mixed, and less negative than the *ex ante* studies (Trachtenberg, et al. 2019). Three *ex post* studies found that the implementation of an FTA with TRIPs-plus provisions in Jordan had a harmful impact on access to medicine (Abbott et al. 2012, Alawi and Alabaddi 2015, OXFAM 2007). Trachtenberg et al. (2018) find that TRIPs-plus provisions in the US-Chile FTA resulted in both an increased volume of medicines (which could indicate *increased* access) and increased price of imported medicines. As consequence of the latter, patients pay more out-of-pocket, governments have to increase their medicines budget or they cannot afford the purchase, and access decreases.

Kyle and Qian (2014) found that TRIPS had neutral effects on medicine pricing, led to earlier product launch and higher sales. Results may also vary by the income level of the country implementing IPR policies. In a cross-country analysis, Kyle and McGahan (2012) show that patent protection as a result of TRIPS implementation increases research and development (measured by volume of new clinical trials) in high income countries but lowers R&D or has no effect in LMICs. Finally, some *ex post* analyses have examined countries implementing domestic pricing interventions alongside TRIPS implementation and found a positive correlation between low prices and the pricing intervention (e.g., Duggan 2016; Kyle and Qian 2014).

However, it is hard to conclusively review the results of *ex post* studies due to the small sample size and the fact that most are looking exclusively at the impact of data exclusivity rather than trade treaties more generally. As discussed below, some researchers assert that it is too early to measure the steady state effects of treaties on access to medicine in most countries and suggest that scholars should be much more precise and cautious when it comes to undertaking and interpreting *ex post* studies (Shadlen et al. 2019).

Knowledge Gaps: There are many challenges to *ex ante* and *ex post* studies that could result in inaccuracies. First, authors must decide which outcomes best represent access to medicine. As most studies rely on medicine prices or volume, either alone is insufficient to measure access because it is a multi-dimensional concept. Imported volumes may be high but if prices are unaffordable to the majority of the population there is still lack of access. If the volume imported is lower than the demand, access to imported medicines cannot be ensured. Measuring access requires the measurement of multiple dimensions (affordability, availability, acceptability, accessibility). Assessing the impact of trade agreements by proving a correlation between the dependent and independent variables is further complicated by the fact that “different provisions in [trade] agreements will affect different medicines at different points in time” (Shadlen et al. 2019, 12). As a result, identifying the correct “pre” treaty time period for each set of medicines is complicated, to say the least.

“Some researchers assert that it is too early to measure the steady state effects of treaties on access to medicine in most countries.”

Ex post econometric analyses can be subject to issues of “unreliable data, statistical or econometric errors and improper framing of an empirical question” (Trachtenberg et al. 2019). As with *ex ante* studies, *ex post* studies can also fail to account for exogenous factors that significantly impact access to medicines. For example, domestic spending on medicines is often impacted by macroeconomic restraints imposed by international financial institutions or adopted pursuant to neoliberal orthodoxy that limit or even reduce governments’ health budgets and procurement of medicines.

Furthermore, some suggest that *ex post* studies may be irrelevant at this stage because it is too soon to tell what the effects of trade agreements are on access to medicines (Shadlen et al. 2019). First, the relevant year after which medicines were patentable matters substantially. Countries that first implemented a medicine patent system after signing TRIPS (“later-patenting”) only had to consider applications filed from 1995 onwards. Since patents expire 20 years from filing, the earliest that patents in these post TRIPS systems would expire is in 2015. The expiration of patents becomes important because several of the TRIPS-plus provisions in trade agreements would “plausibly affect competition and prices at (or near) the end of patent terms” (Shadlen et al. 2019).

In particular, patent term extensions will only begin to have an effect at the tail end of the 20-year patent terms. Secondary patents, in some situations, will extend terms after the drug’s primary patent (if granted) has expired. For “later-patenting” countries, those on the right-hand side of Table 3, the effects of extending patent terms (e.g., for new uses, regulatory term extensions and various secondary patents) will begin to be seen only after the post-1995 patents expire (after 2015). As a result, only a small number of medicine molecules will have been affected in this subset of countries as of the time of this writing, and broad analyses relying on overall medicine prices or pharmaceutical expenditures as a share of country health budgets would not yet capture those impacts (Shadlen et al. 2019).

Data exclusivity provisions can also have delayed effects depending on the age of the patent system. Data exclusivity granted during a patent period will not have visible effects until the patent expires and generics are delayed or made more expensive because generic companies did not have access to the original data and have had to create it from scratch. Given that data exclusivity provisions in trade agreements are a recent development, the majority of patents covered by data exclusivity policies have not expired, we will not be able to see the effects of data exclusivity provisions in trade agreements on generic market introduction and pricing until much later. However, for medicine without patents, data exclusivity can create more immediate barriers to generic entry.

Table 3. Introduction of Pharmaceutical Patent Protection in Countries with US Trade Agreements

Prior to TRIPS		Following TRIPS	
Australia	1990	Bahrain	2004
Canada	1983	Colombia	2000
Chile	1991	Costa Rica	2000
Mexico	1991	Dominican Republic	2000
Singapore	1994	El Salvador	2000
South Korea	1986	Guatemala	2000
		Honduras	2000
		Jordan	1999
		Morocco	2000
		Nicaragua	2000
		Oman	2000
		Panama	1996
		Peru	2000

Source: Shadlen et al. 2019.

THEMATIC AREA 3:

POLITICAL ECONOMY IN TRADE & ACCESS TO

MEDICINES

Analysis of treaty language illuminates what sorts of policies countries are permitted (or not permitted) to deploy. Empirical studies uncover associations between the presence of certain treaties or specific provisions, and effects on other indicators such as household health expenditures, medicine pricing and medicine volume sold.

The lens of political economy, by contrast, offers insight into *how* and *why* trade and investment treaties might – or do – impact domestic public health and the implementation of intellectual property laws. In trying to understand the extent to which trade treaties affect access to medicines, studies in political economy help to understand the mechanisms through which this effect occurs.

“*The lens of political economy, by contrast, offers insight into how and why trade and investment treaties might – or do – impact domestic public health and the implementation of intellectual property laws.*”

Much political economy research on trade treaties and access to medicines has taken the form of country studies (Sweet 2013, Hassali et al. 2013, Gray & Vawda 2013, Shadlen 2017). Some of these involve comparative historical analysis over time (Shadlen 2017), while others look carefully at one specific country experience (Sweet 2013, Gray & Vawda, 2013).

Unlike our coverage of treaty language analysis and *ex post* and *ex ante* empirical research, which are supported by extensive literature reviews, this section on political economy does not benefit from such an exhaustive background, although there have been several attempts to review and synthesize the state of political economy research, which we do not attempt here (Shadlen 2017, Lofgren & Williams 2013).

Instead, this section offers some illustrations of the topic through a political economy lens, highlighting the limited country and regional experiences represented in our workshop. We rely principally on the experience of two key economies (South Africa and Brazil) as examples of how politics has influenced implementation of TRIPS measures. We pay particular attention to the ways in which the political and institutional responses have minimized (in some cases) and exacerbated (in others) some of the potentially negative impacts of the global IP regime.

Evidence:

It is well established that the TRIPS agreement was the result of a campaign of lobbying by large pharmaceutical and information technology corporations, first in the United States and later in the EU and Japan (Braithewaite and Drahos 2000; Sell 2003). The story of the fight over the patenting of anti-retroviral medicines in South Africa illustrates how this pressure came to a head. The United States and a coordinated private pharmaceutical sector found itself faced with a public political fight against a wide range of international and civil society organizations. The result was a clarification and, ultimately a modification of the TRIPS Agreement ('t Hoen 2009). In Brazil, civil society waged a similar battle, defending the economic sustainability of Brazil's policy of universal access to HIV/AIDS medicines through compulsory licensing (Chaves et al. 2008). In the aftermath of these events, global access to anti-retrovirals has improved (as measured in increased volume and lower prices), although many believe the fight to be on-going (Chaves et al. 2008, Chaves et al. 2017).

Furthermore, these countries and others have faced challenges in providing access to other essential medicines, including those for malaria and Hepatitis C. Each country has its own institutions with

different power and influence, and therefore different ways of delimiting their policy space and implementing stricter IP rules due to TRIPS and TRIPS-plus treaty commitments.

Brazil, soon after adopting pharmaceutical patenting under TRIPS, established a new institution called the Secretariat of Health, Science, Technology and Strategic Inputs (SCTIE) which is a specialized agency within the Ministry of Health that supports government health policy goals (Fonseca, Shadlen & Bastos 2019b). Due to the effects that pharmaceutical patents would have on the price of drugs, particularly in light of guarantees of universal access for many key medications, the Ministry of Health became particularly concerned with implementing TRIPS in a way that did not bankrupt the public health system. As a result, Brazil has been active in negotiating prices with manufacturers, increasing local production, creating mechanisms to evaluate pharmaceutical patent applications, using threats of compulsory licenses, and in one case issuing a compulsory license, to secure a price reduction on patented medicines (Shadlen 2017).

Another, more recent policy response in Brazil has been the establishment of a government and industry coalition through public-private partnerships – named “productive development partnerships” (PDPs). With a primary goal of encouraging technology transfer in local pharmaceutical production, the process involves strategic government purchases of medicines produced in Brazil by these partnerships and voluntary licenses issued from the multinational pharmaceutical corporation to the local private producers (Fonseca 2018). A study on the political economy of these partnerships found that in order to implement this, as well as follow-through on its promise of universal access to essential medicines, Brazil had to centralize public procurement of certain high-cost medicines, and alter laws that required the government to procure only the lowest cost goods (Shadlen & Fonseca 2013). Concerned with the sustainability of local supply, the Brazilian Ministry of Health decided that in some cases it would rather pay higher prices for domestically produced medicines than import lower-priced Indian generic medicines. PDPs have led to successful local production of ARVs and (to a more limited extent) hepatitis C medicines. Access to the state of the art hepatitis C treatment, sofosbuvir (made by Gilead), is still uncertain as patent protection for the medicine is controversial and currently being litigated in Brazilian courts (Fonseca, Shadlen & Bastos 2019a).⁹

In addition to PDPs, new health regulations have provided incentives for large-scale public investment (through Brazil's National Bank for Economic and Social Development (BNDES)) to support the domestic health industry. Their public pharmaceutical investment program, Profarma, provided loans to local producers so that they could comply with new laws regulating generic medicines, as well as support new biotechnology and medicine research and development. BNDES employs joint venture requirements to increase collaboration among firms and reduce risk (Shadlen & Fonseca 2013).

Unlike Brazil, nations in eastern and southern Africa do not have a large domestic pharmaceutical industry. Instead – as several political economy studies show – they have deployed a variety of other approaches to respond to the global shift in IPRs and encourage access to essential medicines (Malleche & Rutter 2019, Ahonkhai et al. 2016, SAIIA 2014). These countries are attempting to build cross-border coalitions of like-minded countries in order to wield more power at an international level. Some larger countries are able to make more decisive changes to domestic policy, while others are setting priorities at a regional level.

“ *These countries are attempting to build cross-border coalitions of like-minded countries in order to wield more power at an international level.*”

⁹ The Brazilian Ministry of Health ran into serious problems procuring the medicine from the local consortium producing it, on account of Gilead's patent and on-going litigation. For more discussion, see Fonseca, Shadlen & Bastos (2019a).

South Africa, for example, has issued a new Intellectual Policy Phase I, which has a particular focus on public health (aligned with SDG 3), and which insists on including no TRIPS-plus measures in trade agreements (IPPSA Art. 7.2.2). Regionally, the East African Community (EAC) drafted an Intellectual Property Policy on the use of TRIPS Flexibilities (EAC 2013). This policy encourages its members to use LDC transition flexibility, enforce strict patentability criteria, permit parallel importation, omit data exclusivity and linkage provisions, as well as pre- and post-grant administrative opposition, determine specific grounds for compulsory licenses and encourage the use of all applicable exceptions.

Several policy studies show that new domestic implementation of the IP Flexibilities Policy in the EAC has been slow, but at least initially successful in promoting the use of flexibilities. Kenya's Industrial Property Act, for example, has aided in the negotiation of at least two voluntary licenses for domestic production (Avafia et al. 2006). Elsewhere in sub-Saharan Africa, similar attempts to promote the use of flexibilities are underway, including in Rwanda (Spoor & Fisher 2011), Uganda (Issa 2019), Zambia (Alves 2018), and Botswana (Parliament of Botswana 2010). The creation of the Tripartite Free Trade Area, comprised of the countries in the Community of Eastern and Southern Africa (COMESA), the Southern African Development community (SADC), and the EAC, could provide an opportunity for regional harmonization of a policy in favor of greater access to medicines (Juma & Mangeni 2015). Likewise, the African Union might work as a forum for administering and harmonizing IPRs across Africa through the Pan African Intellectual Property Organization (AU 2016). The alignment of continental and regional instruments for coherent and uniform overarching policy program that is pro-access, in favor of harmonized regulation, and prioritizes local manufacturing capacity could successfully promote access to affordable medicines.

“*International politics can impact domestic political processes by empowering some groups (activating otherwise indifferent actors through linked incentives, creating new constituencies like new industry groups), and destabilizing others”*

Not all changes are aimed at increasing access to medicine, however. Certain members of the East African Community have passed anti-counterfeiting legislation, and other countries (Guinea, Morocco, Burkina Faso) have adopted the European MediCrime Convention in 2016 (MediCrime Convention 2016, Vawda & Baker 2013). Both of these lend strength to the enforcement of existing intellectual property laws. As political economists have pointed out, international politics can impact domestic political processes by empowering some groups (activating otherwise indifferent actors through linked incentives, creating new constituencies like new industry groups), and destabilizing others. Meanwhile, domestic policy decisions can “alter subsequent trajectories” limiting the future policy options available (Shadlen 2017). These mechanisms produce a feedback loop which amplify the impact on access to medicines in individual countries. This could help to explain how a country that once vehemently defended its right to a more flexible IP regime, now has changed its priorities and adopted aggressive IP rules even without the requirements of an international treaty.¹⁰

The results of the studies are not conclusive of causes and effects of trade treaty impacts on access to medicines. These examples simply illustrate how some countries have responded to the modern IP regime and provide a glimpse as to why they may have done so. The clearest finding from our discussions was that there are a myriad of important questions which need to be addressed using these methods, and much more work is left to be done.

Knowledge gaps:

In order for LMICs to know how to mobilize domestic constituencies to implement policies that promote access to affordable medicines, much more evidence on the political economy of IP rules

10 This has been particularly apparent in the case of China in recent years (Wang 2018).

implementation is needed. In addition to the negotiating histories of key trade treaties, and accurate records of domestic legal changes, we also need to be able to read that data in the context of the verified use of TRIPS flexibilities, as catalogued by 't Hoen et al. (2018), as well as information on the policy actors who have implemented those changes.

Moreover, we need a better understanding of the different stakeholders, their influence, their political strategies and how policy implementation is managed (Reich 2019). This evidence would complement databases on (1) the use of compulsory licenses and government use orders issued, as well as voluntary licenses (partially available in MPP (2017)), (2) the catalysts and obstacles permitting parallel imports, and (3) the cross-country variability of patentability standards and opposition procedures.¹¹ Furthermore, additional case studies are needed, especially those which

illustrate ways to better integrate SDG 3 with SDG 9 (industry, innovation) in ways that are politically palatable and feasible in LMICs.

“ We need a better understanding of the different stakeholders, their influence, their political strategies and how policy implementation is managed.”

Toward a policy-oriented research agenda:

As we have illustrated, our three broad categories of research offer some positive evidence, while uncovering many research gaps. In the following section of our report, we lay out our proposed policy-oriented research agenda aimed at filling those knowledge gaps and crafting policies that preserve access to medicine while encouraging innovation.

Toward more effective treaty language analysis:

We identified four key knowledge gaps in our understanding of how treaty provisions constrain policy space for improving access to medicines. These are: (1) undue focus on only a few key treaty provisions rather than looking at the whole treaty in context; (2) the relationship between the treaty language and what national law may adopt, including how the often vague language in trade treaties is used to negotiate national law; (3) a lack of knowledge about domestic timing, and implementation of, treaty commitments into domestic law, and (4) a lack of knowledge about how domestic case law has –or has not- evolved to defend IPRs. In order to gain a more complete understanding, we suggest the following:

- **Create a comprehensive list of treaty provisions** that might have an impact on access to medicines in all aspects of pharmaceutical management and code these treaties at an acceptably granular level in order to capture those provisions. Some such language binds or enables government policy-making, while other text mitigates the potential effects of provisions or provides flexibility in their implementation. This must include not only the rules governing intellectual property, but also tangentially related provisions like research and development, investment protection, investor-state dispute settlement, regulatory restrictions and harmonization, and government procurement (Gleeson et al. 2019)
- **Create a database identifying domestic implementation of treaty commitments.** By identifying and categorizing domestic IP laws, we may better understand the factors that determine how treaties impact domestic legislation.
- **Create a system of tracking new international and domestic disputes dealing with intellectual property rights relevant to pharmaceuticals.** This would enable us to understand how

¹¹ Some relevant data is already available, such as patent opposition procedures captured by the Medecins Sans Frontieres' Patent Opposition Database. <https://www.msf.org/patent-opposition-database>.

pharmaceutical companies are using domestic lawsuits to assert their rights under treaties or domestic law. This will, however, be challenging, as the large majority of these disputes are either settled out of court or otherwise leave no easily available public record (WIPO 2018). Incentives would need to be created to report on these disputes.

Toward more accurate and precise empirical studies:

Key gaps in the empirical literature on the impact of trade treaties on medicines access are: (1) comparative effects of certain trade treaties on a variety of outcome measures of access to medicines including the affordability on health systems and individual households (e.g. does the Central America Free Trade Agreement have more effect on affordability of medicines or geographic accessibility of medicines?); (2) differentiating between the impacts of various treaty provisions by type of intellectual property protection (e.g., does data exclusivity have a large effect on affordability than patent protection?); and (3) a lack of understanding of the differential timing and impact of certain provisions (i.e., Which provisions impact access as soon as they go into effect and which provisions have later impacts?). In light of these gaps and others, we recommend the following research agenda:

- **Create a map of the different methods including study designs and choice of outcome used to study the question of treaties and access to medicines.** This collaborative tool would allow researchers to learn from each other, identify best practice and build from previous research without reinventing the wheel.
- **Isolate, if possible, the specific impacts on access to medicines of various IP protection vehicles, such as data exclusivity, patent term extensions, patent exhaustion rules and registration linkage provisions.**
- **Conduct medicine-specific and patent-specific studies to understand outcomes unique to certain contexts.** By undertaking a critical mass of specific studies in a variety of countries, we may gain a better overall view of the impact of pharmaceutical patenting as a whole. In this we should pay particular attention to the special context of biologic medicines (including vaccines), diagnostics and the role of data exclusivity for medicines (like biologics) that are very expensive to develop. As part of this effort, attention should be paid to trying to link patent classification data (typically available from WIPO) to trade data such as information found in the COMTRADE database. The variety of contexts envisioned in this research should also focus on medical devices and diagnostics, not just pharmaceuticals.
- **Conduct empirical studies first on countries that had implemented pharmaceutical patenting prior to TRIPS** (e.g. Chile, Mexico, South Korea).
- **Consider the differential impacts.** Include in any empirical study, if possible, an analysis of any differential impacts on affordability and access to medicines as between different income quartiles (e.g., differences between the poor and elite).

Toward a better understanding of the political economy factors:

The key knowledge gaps we identified in our understanding of the factors which influence LMIC governments in signing treaties and putting in place public health policy are: (1) a lack of knowledge about the political economy of IP rules implementation including a lack of knowledge of the different

stakeholders and their influence and political strategies through compulsory and voluntary licensing, parallel imports, and variations in patentability standards and opposition procedures, and (2) an incomplete set of case studies which demonstrate how to better integrate SDG 3 with SDG 9 (industry, innovation) in ways that are politically palatable and feasible in LMICs. In order to expand our understanding, we recommend the following:

- **Study the political and financial pressure exercised by interest groups and external, non-trade state pressure to shape trade treaties and their access to medicines provisions and the responses by in-country interest groups.** We would be able to see, through political funding and lobbying records in the US, how much pressure is exerted by pharmaceutical MNCs. We could also try to document foreign policy pressure put on countries through US Special 301 and other means. Moreover, we could document pro-access advocacy and other efforts by civil society groups and other stakeholders.
- **Conduct country-specific studies to identify background political conditions which prevail when a country decides to use (or threaten) compulsory licensing.** In that same vein, we may be able to determine how much bargaining power a country exerts by threatening a compulsory license in those cases. As part of this effort, qualitative survey data should be obtained from generic medicine companies with a view towards understanding how they respond to these treaty-based IP rules.
- **Explore associations between World Intellectual Property Organization advice on TRIPS compliance and the factors that influence whether or not new trade treaties contain flexibilities adopted in their domestic legislation.**
- **Conduct country-specific studies along the medicine value-chain from procurement/customs to end user (i.e., consumer).** These studies would enable us to understand the in-country experience, especially the effects on prices at different points in the supply chain. This would allow researchers to examine the gap between the trade agreement commitments and the actual domestic policy implementation and enforcement which takes place in country.
- **Catalogue policy levers that would improve access to medicines apart from TRIPS flexibilities but related to trade treaties.**

Given the interconnectedness of each of these issues,¹² we will need to integrate the work of economists, political scientists, and public health and legal experts in order to round out our understanding of trade and investment treaties and their impact on access to medicines. With this in mind, two broader proposals undergird the specific research tasks we will chose to tackle.

First, we propose to create a best practice research guide which identifies a list of empirical indicators for access to medicine research, relevant treaty provisions and the impacts they may have, as well as common pitfalls in trade and access to medicine research. Our second proposal, which supports the first, is to create a “global access data commons”, akin to “national patent data”. This database would link individual sets of standardized data, so they would be able to “speak” to each other and so that researchers could more easily draw associations between indicators. This would include data at the medicine-level, medicine registration, patents (including information about whether they are primary or secondary patents), treaty codification and trade flow.

¹² In addition to the topics discussed above, our experts brought up other overlapping issues that related to SDG 3, such as impacts on diagnostics and devices, vaccines, medicine pricing transparency, the role of the General Agreement in Trade in Services in access to health care services, and competition rules on health care monopolies. In the interest of maintaining our narrow scope, we declined to expand our coverage to these issues, however, we acknowledge their importance and hope that future research will attempt to understand these pieces of SDG 3 alongside access to essential medicines.

Existing efforts to centralize knowledge about access to medicines could inform and support this project, which will require curating and quality control at some central point (Knowledge Portal 2019). However, a global access data commons combined with a best practice research guide would hopefully lead to research breakthroughs, and a trade regime better crafted to reach our development goals.

“ Given the interconnectedness of each of these issues, we will need to integrate the work of economists, political scientists, and public health and legal experts in order to round out our understanding of trade and investment treaties and their impact on access to medicines. ”

Conclusion

Given the current research gaps with respect to the effects of trade treaties on access to medicines there is an urgent need to generate evidence that can guide countries in their negotiations, implementation, and evaluation of trade treaties To carry out the research necessary to address the current knowledge gaps requires multi-disciplinary research spanning health economics, law, political science and public health. It also benefits from the co-creation of research with those involved in the negotiation and implementation of trade treaties. Finally, the policy-oriented research agenda could be strengthened by further feedback from civil society, government official, industry representatives and those advising governments and industry.

ANNEX

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