Pharmaceuticals : Reimbursement, Utilization, and Contribution To Improved Health

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Pharmaceuticals: Reimbursement, Utilization, and Contribution to Improved Health

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Summary

The list of "essential" medicines, created by the World Health Organization in 1977 and maintained to this day, as well as the promotion of access to affordable medicines while avoiding financial hardships in both the Millennium and the Sustainable Development Goals set by the United Nations in 2000 and 2015, respectively, are international policies that reflect the crucial role pharmaceuticals play in population health. At the national level, affordability is ensured through national health coverage. In the case where medicines are included in the health benefit package, setting the list of reimbursable pharmaceuticals goes through significant scrutiny. This thesis takes a humble shot at addressing the following trilogy: How does a Ministry of Health decide which medicines to include in the benefit package of its national health insurance? Does this subsidy translate into better access, in other words, more utilization? And finally, does more utilization mean improved health? Using the Moroccan health system as a case study for the first two questions, and a sample of MENA region countries for the last one, we show that: first, reimbursement probability is positively driven by disease burden, generic availability (a proxy for affordability), and national manufacturing concentration. Second, using the variation in a drug's reimbursement status, we find that utilization increases after the expansion of health insurance, but only as an aggregate effect. The rise in the use of reimbursed drugs is primarily attributed to structural differences between reimbursed and unreimbursed medicines. Finally, in the countries examined in our study, more use of pharmaceuticals caused a decline in Disability-Adjusted Life Years (DALYs), with an implied elasticity of around 6%. The cost per DALY gained varies across countries and causes, but on average the estimates suggest that pharmaceuticals are cost-effective.

Résumé

La liste des médicaments "essentiels", créée par l'Organisation mondiale de la santé en 1977 et maintenue à ce jour, ainsi que la promotion de l'accès à des médicaments abordables tout en évitant les difficultés financières, sont des politiques internationales inscrites dans les objectifs du Millénaire pour le développement (OMD) en 2000 et les objectifs de développement durable (ODD) en 2015, fixés par les Nations unies. Ces politiques reflètent le rôle crucial que jouent les produits pharmaceutiques dans la santé de la population. Au niveau national, l'accessibilité financière est assurée par la couverture nationale des soins de santé. Lorsque les médicaments sont inclus dans l'ensemble des prestations de santé, l'établissement de la liste des produits pharmaceutiques remboursables fait l'objet d'un examen minutieux. Cette thèse tente humblement de répondre à la trilogie suivante : comment un ministère de la santé décide-t-il des médicaments à inclure dans la liste des médicaments remboursables dabs le cadre des prestations couverts par l'assurance maladie nationale ? Cette subvention se traduit-elle par un meilleur accès, en d'autres termes, par une plus grande utilisation ? Et enfin, une plus grande utilisation signifie-t-elle une amélioration de la santé ? En utilisant le système de santé marocain comme étude de cas pour les deux premières questions, et un échantillon de pays de la région MENA pour la dernière, nous démontrons que : premièrement, la probabilité de remboursement est positivement influencée par la charge de morbidité, la disponibilité des génériques (une approximation de l'accessibilité financière) et la concentration nationale de la fabrication. Deuxièmement, en utilisant la variation

du statut de remboursement d'un médicament, nous constatons une augmentation de l'utilisation après l'expansion de l'assurance maladie, mais seulement en tant qu'effet global. L'augmentation de l'utilisation des médicaments remboursés est principalement attribuée aux différences structurelles entre les médicaments remboursés et non remboursés. Enfin, dans les pays examinés dans notre étude, une plus grande utilisation de produits pharmaceutiques a entraîné une diminution des années de vie corrigées de l'incapacité (DALYs), avec une élasticité implicite d'environ 6%. Le coût par DALY gagnée varie selon les pays et les causes, mais en moyenne, les estimations suggèrent que les produits pharmaceutiques sont rentables.

Contents

List of Figures

List of Tables

General introduction

Life expectancy at birth has significantly increased since World War II. The determinants of improved health, specifically mortality reduction, have been extensively studied to identify the key contributors to this improvement. For a long period, it was widely accepted that income played a dominant role in enhancing the longevity of populations, with lower per capita income associated with lower life expectancy. However, in 1975, Preston's work (Preston (1975)) demonstrated the inadequacy of the argument centered around income. The apparent positive association between income per capita and life expectancy alone did not provide a sufficient explanation for why life expectancy continued to increase even in the absence of rising income levels. Despite the emergence of new arguments about what made mortality decline so rapidly – mainly nutrition, defended extensively by Fogel (1997), these explanations fell short for the same reason as income.[1]

The attempt to provide a general theory of mortality reduction would always suffer from inadequacy given its heterogeneity by age group and cause of death. In their work on the US population, Cutler & Meara (2001) studied the change in mortality over the twentieth century and concluded that, given the age distribution and cause of mortality, the determinants of improved health depend on where you position yourself in the century. During the first four decades, mortality reduction was attributed to public health and better nutrition (filtering water, sanitation systems, etc.); during the mid-century, the first medical advances allowed further elimination of mortality from infectious diseases (penicillin and sulfa drugs); mortality reduction during the last decades of the century was mainly attributed to further medical advances that tackled chronic diseases and in-

[1] We refer you to Cutler et al. (2006) and Soares (2007) for a more detailed discussion.

fant mortality. Conclusions drawn from examining a single country or a homogeneous group of countries (high income, for instance) are hardly restrictive, as they can be applied to examine determinants in other countries, as long as mortality reduction is studied in terms of underlying causes of death and by age group, and by the technologies available at a given point in time (Soares (2007)).

The role that medical advances have played in reducing mortality during the last century has put pharmaceuticals at the center of economic debates. This is due, on one hand, to the cost of their development (DiMasi et al. (2003)), and on the other hand, to their effectiveness and widely spread use. Both features become relevant through price, which is the second barrier to access to treatment after availability. The financial burden of pharmaceuticals is a global issue, affecting both developed and developing countries. In order to alleviate the cost on patients, governments mandate national health insurance including pharmaceuticals in the health benefit package. However, that only shifts the cost from direct out-of-pocket payments towards government expenditures, which usually include some sort of cost-sharing to limit the consequences of eventual moral hazard. The financial burden on government accounts is dealt with differently. Given the need of the population and the cost of treatment, coverage by national health insurance can be limited. Therefore, it was necessary to introduce some sort of evaluation of medicines before coverage, in order to increase the optimality of the choices made by the government.

What makes a drug fit for reimbursement differs from one country to another, taking into account population need and budget limitations as first-order conditions, and industrial and bureaucratic consequences in the second order. This is translated by the divergence of decisions made by different countries regarding the coverage of the same set of treatments. The fact that the same drug can be judged differently by different health agencies gives relevance to the first question that we are addressing in this thesis. Taking Morocco as a case study for developing countries—for which the literature is highly scarce—we attempt to fill in the gap left by academics on the one hand, and the insufficient official (ministerial) communication on the other hand, and provide an answer to how medicines are chosen to be included in the benefit package of a national health insurance. What we find is not far from what other countries' experiences would suggest: pharmaceuticals that are clinically important; that treat burdensome diseases, and that allow for a local industrial development are the attributes that were associated with higher probability of reimbursement in

the case of the Moroccan national health insurance.

The second immediate question that comes after studying what makes some treatments reimbursable and other not is whether subsidizing pharmaceuticals translate into better access and higher utilization, which is the subject of the second chapter of this thesis. Our setting is different than that usually found in the literature given the nature of the data that we exploit in order to address this question. Studying the impact of coverage on utilization requires patient-level data in order to use the variation in insurance affiliation and link it to healthcare consumption, which allows to estimate the causal effect of benefiting from drug subsidy on utilization. However, market-level data does not provide the researcher with the same luxury. Having to rely only on whether a drug is reimbursed or not does not restrict consumption of covered treatments to insured patients only, which, if it was the case, would converge to having individual data. The conclusions that can be drawn from such a study is at the aggregate market level: did consumption increase, as a whole, after coverage expansion? and whether there was a market difference between the utilization of reimbursed as opposed to unreimbursed drugs? Our results suggest that, without controlling for structural differences between the two sets of treatments, utilization have increased after the expansion of subsidizing healthcare; and after controlling for attributes that potentially explain the choice of reimbursement (taken from the first chapter), we could not find significant difference between the utilization of both drugs that were subsidized and others that were not.

If pharmaceutical utilization has increased, does that mean better health? This is the subject of the last chapter of our thesis. Linking medicines to diseases that they treat or prevent in a sample of MENA countries allowed us to address this question. The contribution of pharmaceuticals to improved health is well-established, both in the literature and in the findings of our study. Using expenditures and gains from pharmaceuticals implied that the cost per DALY gained varies across countries and causes, but on average, the estimates suggest that pharmaceuticals are cost-effective.

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CHAPTER 1

Who Makes the Cut?

Evidence from the Moroccan Mandatory Health Insurance (AMO)

1.1 Résumé

Étant donné que les budgets sont limités et que les besoins de la population sont hétérogènes, les politiques de remboursement font l'objet d'un examen minutieux. Les ministères de la santé du monde entier utilisent diverses méthodes pour évaluer les produits pharmaceutiques en vue de leur remboursement, ce qui se traduit par des critères et des listes de remboursement différents. Cet article étudie les déterminants du remboursement pris en compte par le ministère marocain de la santé à la suite de l'extension de l'assurance maladie en 2005. En testant trois hypothèses susceptibles de refléter les préférences non observées du ministère - l'importance de la maladie, l'importance du médicament et la politique industrielle - les résultats suggèrent que l'organisme marocain ne s'est pas écarté des normes internationales. La charge de morbidité, l'importance du médicament (exprimée par le critère d'évaluation français, le SMR) et la fabrication locale ont été identifiées comme des déterminants du remboursement. En outre, nous notons quelques particularités. Tout d'abord, la majorité des médicaments sans évaluation SMR ne sont pas remboursés, ce qui peut être attribué au fait que le ministère marocain de la santé s'appuie fortement

sur la classification SMR fournie par la HAS. Deuxièmement, le coefficient positif significatif sur le nombre de fabricants locaux implique une double explication : soit une politique industrielle locale qui encourage la fabrication nationale (souveraineté, suffisance locale, etc.), soit une corrélation entre l'entrée des entreprises locales et la variable omise "importance du médicament" pour le gouvernement.

1.2 Introduction

Promoting better access to healthcare and improving health outcomes have long been an important part of the agenda of the United Nations (UN) and national governments. In 2000, the Millennium Development Goals (MDGs) established health-related targets, aiming to achieve improvements in primary health problems, from nutritional deficiencies and infectious diseases to maternal health and child mortality. However, despite improvements (such as a decline in the share of the global population impoverished by out-of-pocket health spending from 22.2% to 15.6% between 2000 and 2015,[1]) Target 3.8 of the 2015 Sustainable Development Goals (SDGs) established even more ambitious targets, including "universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all." Delivery of such targets usually rests with national governments, many with limited resources and experience.

Even prior to the UN declaration of the MDGs, in 1998, the Moroccan government announced its intention to reform health financing given the multitude of problems encountered both in the financing and the access to treatment aspects.[2] A draft law was proposed in 2000 as part of the economic and social development plan for 2000-2004, which consisted of promoting a compulsory medical coverage policy.[3] Approved in 2002, the new law (to be known as Law n°65-00) consisted of introducing two health insurance regimes: "Assurance Maladie Obligatoire (AMO)", and "Régime d'Assistance Médicale (RAMed).[4] Moreover, it has changed many features of health insurance in Morocco. First, from optional to compulsory, health coverage was decided to be

[1] Tracking universal health coverage: 2023 global monitoring report. Geneva: World Health Organization and International Bank for Reconstruction and Development / The World Bank; 2023.
[2] See Daoud (1998).
[3] The reform's report is available at the Haut Comissariat au Plan (HCP) website. See chapter 2 "Le développement sectoriel: La valorisation des ressources humaines et le développement social" for the precise reference.
[4] See Section 1.3.1 for more details.

mandatory for a large fraction of the population and to be phased in gradually. In the medium term (which corresponds to the implementation date of the law in 2005), coverage included salaried employees and pensioners from the public and private sectors. Later on, coverage would expand to include beneficiaries of the economically disadvantaged medical assistance scheme (RAMed) in 2012, students not eligible as dependents in 2015, and self-employed, professionals, and unwaged persons in 2021. The second feature of health insurance in the new law is inclusivity. In fact, multiple options were discussed with regards to the benefit package to be considered and whether coverage would be standardized or allowed to vary by insurer. Scenarios varied between catastrophic coverage (coverage only for catastrophic risks and services such as surgery and chronic illnesses); catastrophic and ambulatory coverage; and coverage for hospitalization, ambulatory care, and pharmaceuticals. In the end, it was recommended that the benefit package be standardized and include hospitalization, ambulatory care, and pharmaceuticals (Ruger & Kress (2007)).[5]

The share of pharmaceutical spending in total health expenditures in Morocco has persistently been the most significant, placing the pharmaceutical industry at the center of debates and policy reforms. Between 1997/98 and 2010, more than third (34.7%, on average) of health spending was on pharmaceuticals, half of which was direct payments from households. While a high share of medical treatment could imply better access and use of drugs, it was not not the case in Morocco during that period. First, even though procurement of pharmaceuticals by the public sector is centralized and has led to lower prices than the private sector, comparisons with international prices show that public prices are as high as 2.82 times the international reference prices (measured as the local price divided by the international reference price) for generics, and 5.14 times for originator brands (Dubois et al. (2021) show that price reductions depend on the concentration of the supply side, which could explain the pattern displayed in Morocco).[6] In addition, public procurement inefficiency is also translated in the fact that more pharmaceuticals were procured as originator brands than as generic equivalents. Knowing that they are more expensive than generics, the burden on the already limited budget results in poor availability of drugs in public health facilities, exposing households to the private sector.

Second, relatively to the income level, the average cost of a medical prescription in the retail

[5]This benefit package is specific to AMO only. See Section 1.3.1 for differences between AMO and RAMed and why restriction to only AMO is made.

[6]World Health Organization. Regional Office for the Eastern Mediterranean. (2008). Morocco: medicine prices, availability, affordability and price components.

market in 1997/98 was the equivalent of four days of work at the minimum wage, or 2% of per capita GDP.[7] To illustrate, in 2004, the cost of one month's hypertension treatment with atenolol (a beta-blocking agent) required more than two days' wages for a low-income family, and the cost of a course of treatment for a viral infection using aciclovir was as high as four days of work at minimum wage. Furthermore, the burden of high medicine prices in the private market primarily stems from doctors' prescribing behavior, as they tend to prescribe more originator brands than the more affordable generic versions.[8] Therefore, the high share of pharmaceutical spending in total health expenditures is driven more by price than by utilization.

Before Law n°65-00 was enacted, health insurance in Morocco was optional, covering only 16.3% of the population by the year 2001. More than two-thirds of those covered were state employees or comparable categories and their dependents. Moreover, the burden of pharmaceutical spending has also weighed heavily on the budgets of different insurance entities in Morocco. In fact, 35% of insurance spending was on pharmaceuticals in 2001—a share that is even higher (42%) for the mutual insurance companies that covered public and private sector employees. The high burden of pharmaceutical spending has led stakeholders to recommend that drugs covered by national heath insurance (AMO) be reimbursed in reference to the price of their generic version, when it exists. Evidently, national health accounts suggest that the share of spending on medicines has been steadily declining, going from 36.4% in 2001 to 26.2% in 2013.

The primary objective of the newly decided national insurance scheme then became determining which drugs to reimburse. Right before its implementation, the Ministry of Health published all the official documents that regulate the AMO regime, including the levels of contributions, healthcare services that are included and those that are excluded from the benefit package, as well as the rates at which they are reimbursed or covered. Specifically, pharmaceuticals reimbursement procedure was specified in Decree n°2-05-733, article 8. Very vaguely, the Decree states that the choice of drugs included in the reimbursement list would be based on their 'service médical rendu (SMR).' However, it does not provide any definition or a list of the SMR for each drug, which represents a significant caveat to the implementation of an ambitious and important policy.

In this paper, we investigate how the Moroccan Ministry of Health has determined which phar-

[7] See the 1997/98 National Health Accounts (NHA) report.
[8] National Health Accounts, Morocco (2001).

maceuticals to reimburse as part of the health benefit package included in the newly established national insurance scheme, AMO. Given the unclear and somewhat absent official guidelines, we proceed by assuming that the ministry is maximizing an unobserved utility function, revealing its preferences. We test several hypotheses that could have motivated the ministry's choice. The first set of assumptions we explore is related to the ministry's behavior. Accordingly, either the entire list of reimbursable drugs was decided at the implementation date and set to be published in several waves over time, or drugs were evaluated before each wave of reimbursement, resulting in a different list for each wave. We also investigate whether there was a specific order of reimbursement, i.e., prioritized drugs were reimbursed before others. The second set of assumptions are related to the ministry's preferences. For that, we test three assumptions: the first assumption tests whether the Ministry of Health has chosen treatments that treat or prevent diseases with a severe burden on the population; the second assumption investigates whether the ministry has chosen the best drugs of a therapeutic class; the last assumption examines whether an industrial policy (or bureaucratic) preference was part of the ministry's rationale.

The results suggest that drugs treating or preventing diseases with a high burden, possessing better quality, holding a higher market share within their therapeutic class, and being manufactured by multiple local manufacturers and important firms in the market, have a higher probability of being included in the national reimbursement list. Other attributes indicate dynamic reimbursement patterns over time. In fact, more treatments with available generic versions and measures of innovation were reimbursed during the first wave of reimbursement.

The remainder of the paper is organized as follows: the second section gives some more detailed information on the institutional setting of the national health insurance in Morocco. The third section briefly reviews the literature on how drugs attributes play an important role in various relevant questions related to pharmaceuticals, development and reimbursement as an example. The fourth section discusses the hypotheses tested in our analysis. The fifth section introduces the data and defines the variables used to test the hypotheses. The following section presents our estimation results. The seventh section discusses the results and presents a robustness analysis. In conclusion, the final section provides a summary of the main results along with a discussion of potential caveats that limit our study.

1.3 Context and Institutional setting

1.3.1 Overview

As a step towards universal healthcare (UHC), the Moroccan government introduced a new law (known as Law n°65-00) concerning basic medical coverage in 2002. Law n°65-00 established two regimes of health coverage: "Assurance Maladie Obligatoire (AMO)", and "Régime d'Assistance Médicale (RAMed)."[9] The former is an insurance-based regime whose target population includes employees of both the public and private sectors and their families (insured person's partner, children, and parents with additional contribution), as well as pensioners.[10] Before Law n°65-00 was implemented, health insurance for both sectors' employees was optional, and was guaranteed by various insurance and mutual insurance companies. The current regime is mandatory and requires monthly contributions[11] that are equally shared between the insured and the employer (the State for public employees). In contrast, RAMed is an assistance-based regime that targets the poor population.[12] Annual contributions to RAMed are fixed at a low level, as it is mostly financed by the state, whose contributions are reported annually in the Budget Law.

Law n°65-00 came into effect in 2005, and the newly created "Agence National de l'Assurance Maladie (ANAM)" responsible for technical, regulatory and financial supervision. Additionally, AMO's management was delegated to two already existing national funds: "La Caisse nationale de sécurité sociale (CNSS)" for private sector beneficiaries, and "La Caisse Nationale des Organismes de Prévoyance Sociale (CNOPS)" for the public sector.[13] Both funds operated under the general supervision of ANAM. RAMed's management was assigned directly to ANAM.

Figure 2.3.1 provides an overview of the evolution of health coverage rate in Morocco between 2001 and 2018, in total and by type of insurance organization. The percentage of insured people has more than doubled between 2001 and 2018, going from 16% to 41% of the Moroccan population. AMO's share of this coverage is relatively high (67% by 2018) compared to insurance companies and internal regimes, at a value of 27.2% of total population. RAMed, on the

[9] AMO: Compulsory Health Insurance. RAMed: Medical Assistance Regime.
[10] Other categories also benefit from AMO, but since their legislation is specific, we do not report them in this paper. See Law n°65-00 for details.
[11] 5% of public sector employees' monthly salary, and 4% of that of private sector employees. See Decree n°2-05-735, Decree n°2-05-734, and Law n°65-00 for more details.
[12] See Decree n°2-08-177 for definitions and details.
[13] ANAM: National Agency of Health Insurance. CNSS: National Social Security Fund. CNOPS: National Provident Organizations Fund.

other hand, was not implemented until 2008, and only as a pilot study (during which it targeted around 1.3% of total population) before generalizing it in 2012. By 2018, 35.6% (22.5%) of total population was (effectively) benefiting from RAMed (CNS, 2018).

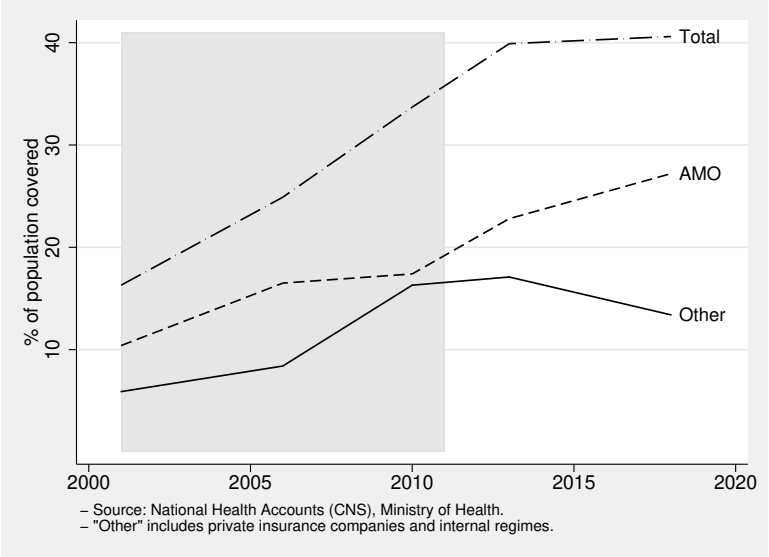

Figure (1.1) Evolution of Coverage Rate in Morocco

The shaded area corresponds to our period of analysis, which goes from the adoption date of Law n°65-00 to the last quarter of 2011. We restrict our study to 2011 for several reasons. First, ANAM's sub-entity, the Transparency Committee (CT), whose duties include the evaluation of drugs for reimbursement, came into effect shortly after 2010 (in 2012). In addition, a major change in price regulation policy was introduced in 2013. Consequently, for this paper, we focus on the period between 2005 and 2011, when the Ministry's reimbursement decisions were most salient and before other changes to the pharmaceutical market in Morocco occurred.

Healthcare services covered by the two regimes (AMO and RAMed) are seemingly similar, as they include surgeries, medical tests, dental care, etc. However, RAMed covers treatments received at public hospitals only. In contrast, AMO's beneficiaries are free to choose where and by whom to be treated. Another substantial difference between the two regimes, and the most relevant to our study, is the fact that RAMed does not provide health coverage for pharmaceuticals dispensed at pharmacies: it is restricted to pharmaceuticals that are administered during treatment at a public hospital. Because we are interested in the retail market for drugs, we focus for the rest of the paper only on AMO, and specifically on pharmaceuticals' reimbursement status.

1.3.2 Pharmaceutical Reimbursement

AMO partially reimburses healthcare costs, including spending on pharmaceuticals. Pharmaceuticals' reimbursement is uniformly set at 70% of the "Prix Public Maroc[14] (PPM)" for all drugs, and can be increased to at least 90% if the drug(s) in question falls into an exemption list that includes severe, chronic, or expensive diseases.[15] The reference price of reimbursement is set by the Ministry at the public price of the generic version of a drug, when it exists.[17] However, out of all pharmaceuticals that are on the market, only a subset are eligible for reimbursement, thus give right to coverage. Therefore, determining a list of reimbursed drugs was necessary.

All information related to the implementation of Law n°65-00 was specified in Decree n°2-05-733. With respect to pharmaceutical reimbursement, this Decree states:

– *The list of reimbursable pharmaceuticals is set by the Ministry of Health, based on the* ***"Service Médical Rendu (SMR)"****. It is established by International Non-proprietary Name (INN), therapeutic class, concentration of the active ingredient, and route of administration.*

The first list of drugs eligible for reimbursement was published shortly after the publication of this Decree, and four subsequent lists were published between 2005 and 2010.[18] However, the Decree does not precisely explain the Ministry's criteria for reimbursement. For example, the SMR is not defined, nor was an ex-post list of each drug's SMR value(s) published.[19] Spending on pharmaceuticals represents an important budgetary burden for both households and all insurance regimes (though decreasing over time, a trend we do not try to explain in this paper), as it accounted for an average of 49.5% and 37% of total spending, respectively (table 1.1).

Because public authorities provided only limited information about the selection of pharmaceuticals for reimbursement, and because this selection has significant financial consequences for households, this paper investigates the determinants of reimbursement status.

[14] Public Price [in] Morocco.

[15] These diseases, called "Affections de Longue Durée (ALD)", are fixed by the Ministry of Health[16], and require filing a request for prior authorization that can be approved or denied by the governing entity's (ANAM) expert doctors.

[17] If there are multiple generic versions available, it is not specified which generic's price is taken, whether it is the cheapest or the closest to the branded version's price.

[18] A subset of the list of reimbursable drugs that includes treatments for diseases that are considered ALD is also published in the same Order. Since we only look at the reimbursement decision and not the rates at which different treatments are reimbursed, we focus on the broader list for the rest of the paper.

[19] We could not find any public record of such information.

Table (1.1) Pharmaceutical Spending [2001,2011]

Year	Household Spending	Insurance Spending		
	% OOP	% AMO	% Other*	% Total
2001	57.4	41.9**	28.2	34.9
2006	47	45.2	35.6	40
2010	44.1	38.4	32.4	35.8
Average	49.5	41.8	32.1	36.9

National Health Accounts (CNS), MoH. (2001, 2006, and 2010 reports).
All values are percentages of total spending (all healthcare services).
* Insurance Companies and Internal regimes.
** This values corresponds to CNOPS and the dominating mutual insurance company (CMIM) in the private sector, we report it under AMO for presentation only.

1.4 Literature

The relevant literature to our study would normally cover studies that look into decisions made by health agencies regarding pharmaceuticals' reimbursement. Health agencies publish official documents that outline the criteria that they take into account while deciding drugs reimbursement. Whether those criteria are met or not is then the subject of empirical studies. For example, the French health authority (HAS) states that for a drug to be reimbursed, it has to be evaluated based on the following criteria: efficacy-security, severity of the disease, place in the therapeutic strategy (existence of therapeutic alternatives), and public health value[20]. Moreover, Le Pen et al. (2003) show that only two of the aforementioned criteria – efficacy and disease severity – explain sufficiently the evaluation. Furthermore, a series of papers have studied reimbursement decisions made by several health agencies. In a systematic review, Angelis et al. (2018) studied the value-assessment for new pharmaceuticals across eight European countries – France, Germany, England, the Netherlands, Spain, Italy, Sweden, and Poland – and concluded that all countries assess similar types of evidence (in different ways however. Analysing those differences falls outside the scope of this paper). First, 'Burden of disease', which includes severity, availability of alternative treatments, and Prevalence. Second, 'therapeutic and safety impact', which involves clinical efficacy and safety, as well as the consideration of surrogate endpoints. Third, 'innovation level' includes clinical innovation, patient ease of use and nature of treatment (symptomatic, preventive or curative). Finally, 'economic evaluation', either via cost-effectiveness or cost-benefit/budget-impact analysis.

[20] See the HAS website for more detailed information. Furthermore, based on these criteria, the HAS constructs an indicator, service médical rendu (SMR). We come back to this measure in Section 1.6.2.

Additionally, since reimbursing a drug implies evaluating its attributes, studies that are based on drugs' attributes would also be included. Their relevance comes from the fact that they highlight some drug characteristics that are related to a specific, other than reimbursement, question and that could explain reimbursement decisions when official guidelines are absent. In a study that looks at whether 'important' drugs enter the market sooner, Dranove & Meltzer (1994) define a measure of drug importance that is based on drug's clinical importance (citations in medical textbooks, medical journals and subsequent patent applications), worldwide introductions, and sales. More formally, the Food and Drug Administration (FDA) has published in 2014 a procedural guide to its expedited program for serious conditions, which is intended to facilitate and accelerate development and review of new drugs. According to the FDA, expedited review and approval would consider the seriousness of the condition a drug is intended for, the availability of other therapies, and the eventual unmet medical need both where therapy is available and where it is not (FDA, 2014). More fundamentally, both the availability (through approval) and affordability (through coverage) of treatments serve to improve patients health, we therefore argue that it would be reasonable to apply the former's guidelines as criteria that health agencies might consider when deciding reimbursement.

Furthermore, because of the public (as opposed to private) feature of AMO, studies on the allocation of public funds on research (biomedical research specifically) could provide insight into government's choice of target diseases (thus drugs). Lichtenberg (2001) has looked at how the NIH (National Institutes of Health) allocate public biomedical research funds across diseases. He shows that public R&D expenditures are strongly positively related to both total life years lost and prevalence of an-activity limiting disease. Moreover, studies on commercial health plans could also be informative. Chambers et al. (2018) studied the restrictiveness of drug coverage decisions issued by the largest US commercial health plans compared to the FDA-labeled indication. They show that less restrictive coverage included indications for orphan (rare) diseases or pediatric populations, absence of safety warnings, time on the market, lack of alternatives, and expedited FDA review.

1.5 Model and Hypotheses

To explain how the Moroccan Ministry of Health has chosen which drugs to reimburse and which drugs to leave out, we assume that the Ministry is maximizing an unobservable utility function, and that the underlying preferences are revealed by the choice of drugs to reimburse. The rationale of the approach is similar to that used in Kyle et al. (2017), Lichtenberg (2001), and Thomas (1988). In fact, if the ministry is benevolent and its interests are completely aligned with the needs of the population, then variables that capture population health needs (drug quality, and eventual expenses for instance) should explain the decision. If instead the ministry is maximizing some other utility function (industrial, bureaucratic or political agendas), then a different set of variables should explain the decision.

Furthermore, given the setting of the Ministry's decision (multiple lists of drug reimbursement), we begin, first, by explaining how Ministry officials might have carried out the decision, to which we refer as 'behavioral assumptions' (subsection 1.5.1), and second, we present the hypotheses that could reveal the Ministry's underlying preferences (subsection 1.5.2).

1.5.1 Behavioral Assumptions

Assumption one

The first assumption suggests that the Ministry of Health has performed an evaluation analysis between AMO's decision and implementation dates, based on which the full list of reimbursable drugs was decided, but that will be divided into multiple lists published (thus take effect) at multiple periods. This assumption enables us to set the initial conditions of all drugs' attributes to their values before the first wave of reimbursement (or to an average between the decision and implementation dates). Moreover, we are able to derive two sub-specifications: in the first one, we are interested only in the reimbursement status, i.e. if a given drug will ever be reimbursed, or will never be reimbursed (the wave of its reimbursement is not important). In the second one, we take into account the order of reimbursement, in other words, we investigate whether some drugs were prioritized over others.

Furthermore, the choice set of drugs that the Ministry can choose from is also affected by the assumption. In fact, if the full list of reimbursable drugs was decided before the first wave, then,

for both sub-specifications, the comparison group includes the "never reimbursed" drugs, while the "reimbursed" group includes drugs that are reimbursed at any given time.

Assumption two

The second assumption suggests that the Ministry's evaluation analysis (we assume that the Ministry has conducted an evaluation) has preceded each published list of reimbursable drugs, meaning that the decision was taken between waves of reimbursement. Therefore, we estimate our model independently for each wave. Consequently, the initial conditions of drugs' attributes are set to their values before the period of their admission into reimbursement (or to an average between two subsequent waves).

Similar to the first assumption, the choice set of drugs available to the Ministry at each time is also impacted. In fact, before the first wave, the choice for reimbursement was possible among all drugs available on the market, however, for later waves, the choice set is restricted to the "not yet" and "never" reimbursed. For example, the comparison group for drugs that are reimbursed during the second wave are drugs that will never be reimbursed, in addition to drugs that will be reimbursed in later waves, minus drugs that were reimbursed during the first wave.

The implications that each assumption have on the economic interpretation are worth mentioning. On the one hand, for the first assumption, one could argue that if the list of reimbursable drugs was decided at once before the first wave, then the sample of drugs that should be included in the model are only drugs that existed in the market prior to later waves, because drugs that will be reimbursed later and also entered the market after the first wave were not available to the Ministry at that point. However, we argue that we are interested in drugs' attributes that make them eligible for reimbursement, not the treatments per se. Therefore, even if a drug was not on the market at the moment of the Ministry's decision, our assumption would imply that had it been on the market, the Ministry would have chosen these attributes (thus treatment) to reimburse. Additionally, in order to fully investigate whether an order of reimbursement has taken place, not only we would want to estimate the model including all modalities of reimbursement (never reimbursed, first wave, second wave, ...), but also a model using only reimbursed drugs, thus capturing what attributes made some drugs be reimbursed before others.

On the other hand, the second assumption has the appeal of disentangling period heterogeneous effects, if they are present. In fact, some attributes might have different weights during different reimbursement periods, in a way that the Ministry might have prioritized some attributes in the first waves, and that the same attributes were not considered (or at least not with the same importance) in later waves, and vice versa. Moreover, since drugs that are decided to be reimbursed do not get delisted (removed from the reimbursement list), the possibility of variables' endogeneity after reimbursement is irrelevant.

1.5.2 Determinants of Reimbursement: Hypotheses

In addition to the assumptions that outline the behavior of the Ministry of Health during decision making, the choice of drugs to reimburse is determined by some hypotheses on the Ministry's preferences (given its behavior). Accordingly, we divide the determinants that might explain the Ministry's decision regarding pharmaceuticals' reimbursement into three main blocs, each bloc tests a specific hypothesis that reveals the Ministry's underlying preferences:

1. The first hypothesis that we test is whether the Ministry of Health has chosen treatments that treat or prevent diseases with severe burden on the population (1.6.2).

2. The second hypothesis investigates the choice of treatments within a given disease, testing whether the Ministry of Health has chosen the best drugs of a therapeutic class (1.6.2).

3. The last hypothesis is an industrial policy (bureaucratic) hypothesis. It examines whether the Ministry of Health has favored national over foreign firms, with the objective of stimulating local economy and therefore satisfying local demand with local production (1.6.2).

Each one of these hypotheses is tested using a variety of explanatory variables from various databases that we will present in details in the next section.

1.5.3 Model

Before we present our model, we define some terms to avoid confusion. We use "drug" whenever we refer to "molecule" or "active ingredient". We call "presentations" the different forms that a drug can take, which are differentiated by strength and route of administration. For example, 500mg tablet (oral) and 1000mg injectable (parenteral) of Amoxicillin are considered **two**

different presentations of **the same drug** Amoxicillin.

Formally, Let k index diseases, j index drugs, and i index presentation forms of a drug.

Simple Logit

When the dependent variable (reimbursement status) takes only one of the two values: "reimbursed" or "Not Reimbursed", a simple Logit is considered for estimation. This is the case for the first specification of the first assumption, and the specifications that are derived from the second assumption and estimated at each wave.

Therefore, for the first specification of the first assumption, the probability that the ministry of Health decides to reimburse presentation i of drug j that treats or prevents disease k can be written as:

$$P(Reimbursement_{ijk} = 1) = P_{ijk} = Z_k\alpha + W_{jk}\beta + X_{ijk}\gamma + \varepsilon_{ijk} \tag{1.1}$$

whereas for the second assumption's specifications, let superscript $\omega = \{1, ..., \Omega\}$ index waves:

$$P^{\omega}(Reimbursement_{ijk} = 1) = P^{\omega}_{ijk} = Z^{\omega}_{k}\alpha + W^{\omega}_{jk}\beta + X^{\omega}_{ijk}\gamma + \varepsilon^{\omega}_{ijk} \tag{1.2}$$

where Z is a vector of disease characteristics, W is a vector of drug characteristics, and X is a vector of presentation characteristics. The error term ε reflects cross-sectional heterogeneity or specification error.

Ordered Logit

This model is specific to the second specification of the first assumption, where we investigate whether an order of drugs' reimbursement was set by the Ministry of Health. Therefore, our dependent variable is no longer binary, as it takes ordinal values accounting for the number of waves.

Using the same variables as the simple Logit, let y^* be the latent variable that relates the observable characteristics to the observable ordered dependent variable:

$$y^*_{ijk} = Z_k\alpha + W_{jk}\beta + X_{ijk}\gamma + \varepsilon_{ijk} \tag{1.3}$$

the ordered Logit implies:

$$P(Reimbursement_{ijk} = l) = P^l_{ijk} \text{ if } \tau^l_{ijk} < y^*_{ijk} \leq \tau^{l+1}_{ijk} \tag{1.4}$$

where $l = 1, ..., L$ indicates reimbursement waves, and τ represents model's thresholds.

1.6 Data and Variables

1.6.1 Data

Our study data set is constructed using multiple data sources. Reimbursement status (whether a drug is ever reimbursed, or during which wave it was reimbursed) is defined based on the lists that were published by the Ministry of Health in the official Orders. We identified six lists (official Orders) between the implementation date of AMO (third quarter of 2005) and 2010[21]. We recall that, according to Article 8 of Decree n°2-05-733, reimbursement lists were established by international non-proprietary name (INN), therapeutic class, concentration of the active ingredient, and route of administration. Therefore, our unit of observation in this study is the presentation level of a drug.

It is worth mentioning that the published lists contain all medicines that are approved and are eligible for reimbursement, whether they are dispensed at a pharmacy or they are restricted to hospital use only. Since our study is focused on the retail market, we drop pharmaceuticals that are administered only in hospitals.

Identifying hospital-only pharmaceuticals can be challenging and requires specific official data that is not at our disposal. However, we make use of the second data source available to us to make that distinction, the MIDAS database provided by IQVIA. This database gathers all drugs transactions (quantities and revenues) in a given market, the Moroccan retail market for instance, as well as a variety of drugs' characteristics. Merging the reimbursement data set and MIDAS would leave us with only drugs that are dispensed at pharmacies, hospital-only drugs are the unmatched drugs. Furthermore, MIDAS database does not serve only as an identifier of the retail market, it also provides us with extensive information on drugs and the market that we will use as

[21] Orders n°2517-05, n°1687-06, n°929-06, n°601-08, n°477-09, and n°1653-10.

attributes that could explain the Ministry's decision.

The third data source that we use in our study is relevant to disease burden: the Global Burden of Disease (GBD) dataset created by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington.[22]. It reports annual country specific health outcome measures linked to their corresponding diseases. However, the GBD database does not provide these measures for a disease matched to that disease's treatments, and since our analysis is at the drug level, matching drugs to burden measures is necessary. In order to link drugs to diseases, we exploit tools provided by the Unified Medical Language System (UMLS) from the National Library of Medicine in the US. We determine the list of pharmaceuticals that, according to the Medication Reference Terminology within the UMLS, may treat or prevent each cause from the GBD (see Appendix of the third paper of this thesis for details).

Finally, the previous databases do not include the SMR information used by the Moroccan Ministry of Health, and as we mentioned above, we could not find any record of a document that reports these values, either as a database, or as an official publication. Moreover, because it was the only criterion that was officially stated as a determinant of reimbursement, its availability is primary. SMR is a measure constructed and used by the French reimbursement agency (Haute Autorité de Santé (HAS)), the Transparency Committee (Comité de Transparence (CT)) in particular, to evaluate drugs for reimbursement. Therefore, for our study, we consider HAS's SMR as a proxy of the SMR used by the Moroccan Ministry of Health. In addition, we also use Amelioration du service médical rendu (ASMR) (added therapeutic value of a drug relative to other treatments available) as a measure of innovation.

Merging all databases gives us the necessary information to carry out the analysis. Evidently, we retain a variety of variables that would enable us to test the hypotheses considered in Section 1.5. We next define these variables with respect to the hypothesis they test, as well as their expected effects as determinants of reimbursement.

[22] See the IHME website for more detailed information on this dataset.

1.6.2 Variables

Hypothesis one: Disease importance

The first hypothesis states that the Ministry of Health decided which drugs to reimburse based on the burden of the diseases they treat or prevent. Accordingly, the severe the disease, the higher the probability that its treatments would be reimbursed. To test this, we retain several health outcome measures from the GBD database to reflect disease burden: disease prevalence, years of life lost (YLLs) (measure of premature mortality, it takes into account both the frequency of deaths and the age at which it occurs), mortality, and disability-adjusted life years (DALYs) (the sum of the years of life lost to due to premature mortality and the years lived with a disability). We recall that all measures are defined annually at the drug level. We note that not all drugs are matched to measures from the GBD database, therefore, to account for the possible selection bias we run an additional estimation where we do not include health outcomes.

Furthermore, reimbursement probability is expected to vary with the anatomical system as well (cardiovascular system, nervous system, ...), in a way that drugs that treat diseases relevant to specific systems could have been prioritized over others given their urgency or/and fatality (one could argue that cardiovascular diseases are more urgent/fatal than dermatological ones, for example). Therefore, since MIDAS reports the anatomical classification of drugs[23], we use level one – ATC1, anatomical main group – of that classification as the corresponding explanatory variable[24].

Hypothesis two: Drug importance

Assuming that the Ministry of Health has decided which diseases are important to be prioritized, the second step would be to decide which drug of the various drugs that treat that disease is the best. This hypothesis implies a measure of drug quality.

It is in this step that the official criterion (SMR) would take effect. The "service médical rendu (SMR)" is the first measure of drug quality that we include in our estimation. As it is defined by the HAS, it includes the following criteria: level of efficacy relative to adverse effects, disease severity, treatment properties (preventive, curative, symptomatic), the treatment's position in therapeutic

[23] The MIDAS database uses the EPHMRA Anatomical Classification of Pharmaceutical Products. See the EPHMRA website for more details.
[24] See Appendix A for the details of this level.

strategy (availability of alternatives), and public health benefit. Based on these criteria, three levels of SMR are defined: "major or important", "moderate or low", and "insufficient". The more important a drug is, the highest its reimbursement probability. In practice, one drug can have multiple SMR values depending on the indication it was intended for, or on the evaluation date[25]. In this paper, we assign the best SMR score as the true value that was considered in the decision. Drugs with no SMR value are drugs that were not evaluated by the French HAS, either because they are not marketed in France, or because they were not submitted by their producers to be reimbursed. We also add a dummy variable that indicates weather a treatment has the highest SMR score in its disease class. Moreover, we include the "amélioration du service médical rendu (ASMR)" – as a measure of innovation – in the same manner. According to its definition, the ASMR has five levels: ASMR I (Major), ASMR II (Important), ASMR III (Moderate), ASMR IV (Minor), and ASMR V (Non-existent).

The second variable is the popularity (or success) of a drug, measured by its market share. The drug with the highest market share might have been prioritized by the ministry, either because it reflects its superior efficacy (through the market) in comparison to other drugs, or it reflects doctors prescribing preferences. Therefore, we define two measures of market share: the first one is defined at the market level (sales of drug divided by total sales of all drugs); and the second one is at the disease level[26] (sales of drug divided by total sales of all drugs within a disease). While it is the latter definition that seems to be more relevant, we include the former to relax the strong assumption that substitution between drugs occurs only within the same therapeutic class (see Kyle (2007) for a brief discussion).

The third variable is the number of alternative treatments of a drug that treats or prevents a specific disease. Theoretically, drugs with several alternatives could have been prioritized in reimbursement because they can be substituted in case of specific circumstances (shortages, intolerance, lack of improvement, ...), therefore if assuring security for patients is what the government is aiming for, a higher reimbursement probability would be assigned to drugs with several alternatives. On the other hand, however, having less (or no) alternatives can also be a signal of importance (orphan drugs for example), in this case, acting on securing access to treatment would

[25] Multiple evaluations were carried out for the same treatment at different dates. The first evaluation usually corresponds to 'inscription', and the following ones either to a 'renouvellement' or 'extension'.

[26] We define a disease at the third level of an ATC.

be the government's aim, thus favoring one-drug (or no-alternatives) treatments. In our estimation, we exploit the anatomical classification used in MIDAS and calculate the number of different treatments that treat or prevent each disease (third level of ATC). This measure could also reflect disease importance in the sense of rarity. For example, the Orphan Drug Act is a law passed by US Congress in 1983 that incentivizes the development of drugs to treat rare diseases, which are defined as diseases or conditions that affect less than 200,000 people in the United States. If drug development is encouraged because of rarity, we argue that reimbursement could also be.

The number of different alternatives should not be confused with the availability of generics of a drug. In fact, alternatives of a treatment are different molecules acting in different mechanisms. On the contrary, the generic version of a molecule is the same as the branded one (clinically-wise). In this paper, we exploit treatment's licensing status (reported in MIDAS) and we define a brand-name as treatments that are either coded "branded" or "licensed". The rest is considered a generic. Moreover, the existence of generics could affect reimbursement as well. In fact, on the one hand, generics enter the market after patent expiration with a cheaper price, and the more the entrants, the cheaper the drug gets (Grabowski & Vernon (1992) and Frank & Salkever (1997)). On the other hand, having several manufacturers of the same drug assures market availability at any moment, thus less likelihood of shortages to occur. From the government's perspective, drug's importance with regards to this attribute is two-folded. First, if drugs are available at a cheaper price, and since reimbursement is based on the generic's price (Article 8 of decree n°2-05-733), drugs with multiple generics would be favored. Second, securing access to treatment at any moment is a priority of Health Ministries worldwide, the Moroccan one for instance, therefore, it would make sense to prioritize molecules with multiple generics. In our model, this attribute is measured by the number of manufacturers of a molecule and a dummy variable indicating whether the treatment has a generic version or not.

Reimbursing pharmaceuticals can weigh heavily on the budget, as a consequence, Health Ministries tend to introduce various policies to reduce that burden (cost sharing, reference pricing, deductibles, ...). To measure the burden that a drug might have on the budget, reimbursement agencies either require (from pharmaceutical companies) or carry out (internally) an economic evaluation. In our case, we are not aware of the application on any economic evaluation while deciding which drug to reimburse. Therefore, as a proxy for cost, we use drug sales (spending),

since reimbursement is based on and proportionate to drugs' public price, and eventually their demand (thus quantity multiplied by price).

Hypothesis three: Industrial Policy and Firm Importance

Since AMO is a national insurance policy, rent seeking from pharmaceutical firms is highly possible. Rent seeking in our context is any form of lobbying the government for reimbursement, however, data on this matter is unavailable, even, we do not know which (if any) type of negotiation has taken place between companies and the government. Moreover, not only that companies would lobby to seek reimbursement approval, but it is also likely that the Ministry of Health would have been biased towards locally produced drugs as part of a governmental industrial policy to develop the local economy. However, analysing the possible channels through which bias could have occurred is out of the scope of this paper, as we are interested in the outcome only. In fact, since we observe what drugs are reimbursed, and we know form MIDAS to which corporations they belong (or by which manufacturer they are produced), investigating this issue is possible in two ways.

First, to test the origin effect, we define a dummy variable that indicates whether a treatment has local manufacturers or not. We use this measure rather than the origin per se because even if reimbursement was decided at the presentation level of a treatment, it did not cover presentations that were manufactured by local firms only. Therefore, we argue that having a local manufacturer is a better measure since it includes the origin information on the one hand, and it avoids the possible underestimation in the case where a reimbursed presentation is manufactured by more of foreign firms than local ones. We also calculate the number of local manufacturers within a presentation to account for local presence in the market. Second, lobbying is usually a practice of big firms, and a firm's importance in a market can be reflected by its revenues. Accordingly, firms that possess the highest market share could leverage their weight in exchange for reimbursement, and not necessarily for one drug (that might have higher market share because of its proven efficacy), but also for the rest of their treatment portfolio. Therefore, we calculate corporation's and manufacturer's market shares from MIDAS and use them in our estimation to test this hypothesis.

1.7 Results

1.7.1 Summary statistics

Figure 1.2 plots the share of reimbursed drugs of total drugs marketed in Morocco between 2000 and 2010, both in terms of the numbers of presentations and their sales. After the implementation of AMO, the first wave of reimbursement consisted on including 14% of treatments, accounting for roughly 25% of total sales. By the end of the period, and after five waves of reimbursement, the percentage of reimbursed drugs reached 42%, equivalent to 66% in revenues. In absolute terms, 271 presentations were added to the reimbursement list in the first wave, 31 in the second, 189 in the third, 292 in the fourth, and finally, 116 in the fifth wave.

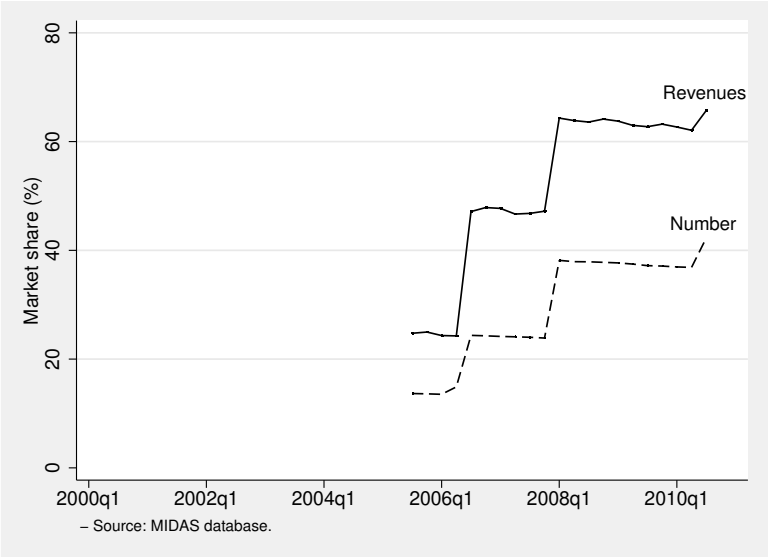

Figure (1.2) Evolution of reimbursement in Morocco

The profile of reimbursement by ATC1 (main anatomical group) and wave of reimbursement is shown in Figure B1 (Appendix B). Figure B1a shows the heterogeneity across anatomical groups within reimbursed treatments. It shows some groups were prioritized in all waves (Cardiovascular (C), Anti-Infectives (J), and Nervous (N)), other groups had their share of reimbursement vary, in a way that they were prioritized in some specific waves (Alimentary (A), Musculo-Skeletal (M) and Respiratory (R) for example) and marginalized in the rest. Descriptively, it is safe to say that pharmaceuticals reimbursement depended on the system they were intended for. Figure B1b provides the same heterogeneity but in the total market.

Table 1.2 presents summary statistics for data used in estimation, as well as some other variables

that describe the market. It covers the period between the second quarter of the year 2000 and the third quarter of the year 2010. The sample used in estimation contains 2127 unique presentations (1080 drugs) treating a total of 214 different diseases, out of which 127 had at least one reimbursed treatment to be treated with. Moreover, 23% of presentations in the market were produced by more than one manufacturer, and at the drug level, 45% of drugs are multi-source. In addition, 75% of available presentations were manufactured by a Moroccan firm. The total number of manufacturers in the market is 240, the majority of which are local firms. While it seems to be high, it reflects several licensing agreements between foreign and local firms[27]. The average market share of a corporation is about 10% of revenues, with Sanofi as the leader of the market at a share of 23% of total revenues, followed by Laprophan as the local leader firm, holding 8.5% of the market. Regarding alternative treatments, a disease could be treated with one of 10 possible alternative drugs (9 presentations) on average, a third of which is in the reimbursement list. Not to be confounded with the availability of generic versions of a molecule, this latter suggests that 70% of treatments have their unbranded versions on the market.

As mentioned above, not all drugs were evaluated by HAS. Evidently, only half of treatments marketed in Morocco have an SMR value: 75% were considered Important, 16% Low, and 8% had Insufficient SMR. Since one disease can be treated with multiple drugs, having a value of SMR that is equal to the maximum of SMR values with that disease class could reflect drug's superiority, in that regard, 76% of drugs that were evaluated had the maximum SMR values within the disease they treat or prevent. Even modestly, only 30% of pharmaceuticals that are in the market had an ASMR evaluation, the majority of which (83%) have an ASMR of 4 or 5, meaning minor to non-existent innovation.

Disease burden variables are measured in number of cases. We focus on disability-adjusted life years (DALYs), and present results using other health outcome measures in Appendix **??**. In addition, since all measures are at the molecule level, and knowing that drugs could treat multiple diseases, their interpretations vary with how we aggregate to the molecule level. In fact, the first way we could aggregate health outcomes is by taking the average across all diseases, and is interpreted as the average burden that a molecule is possibly treating. The second way is to take

[27] For example, Sanofi and Pfizer are foreign firms, and Laprophan is a local firm. Sanofi-Laprophan and Pfizer-Laprophan would be considered two different manufacturers, and would also be considered local since they involve at least one local firm.

the max, and it corresponds to the disease with the highest burden of all diseases that the molecule is treating, thus, one could assume that it is the main disease that the drug is intended for. The last aggregation is the sum of the burden of all possible diseases that the drug could treat or prevent. We use the last aggregation in our main estimation, average and max are used as robustness checks.

1.7.2 Reimbursed VS Not-Reimbursed

In the previous subsection, we described our variables regardless of pharmaceuticals' reimbursement status, i.e. whether they are reimbursed or not. In this section, we take reimbursement into account and calculate differences in drug attributes, as well as the corresponding t-test. Results are shown in Table 1.3. Differences between the two groups' (ever-reimbursed and never-reimbursed) attributes are all statistically significant at 1% (except for market share within disease).

First, all measures of burden of disease are higher for the reimbursed group, meaning that it is likely that the drugs that the Ministry of Health has prioritized for reimbursement treated burdensome diseases. Furthermore, it seems that the Ministry has decided to reimburse more of drugs with higher number of alternative treatments and number of manufacturers (multi-source), indicating a tendency to favor both drugs that are substitutable and are cheaper.

Second, more of reimbursed drugs have important SMR and high ASMR value than unreimbursed drugs. Moreover, the majority of drugs with no SMR/ASMR evaluation were not reimbursed. However, having an SMR value that is equal to the maximum value within a disease does not seem to be a feature of reimbursed treatments only, as it is slightly higher for treatments that are never reimbursed. This pattern could be explained by other attributes other than the SMR value, since multiple treatments could have the highest score but differ in other characteristics that would change their probability of reimbursement. Regarding market outcomes, pharmaceuticals that were reimbursed had more sales, higher total market share, and although insignificant, higher market share within the diseases that they treat or prevent. Furthermore, treatments that were reimbursed were largely produced by more than one manufacturer, specifically more local manufacturers (whether the measure is simply having a local manufacturer or not, or the number of local manufacturers). However, having more than one manufacturer does not necessarily mean having multiple generics, as this latter shows that reimbursed drugs had less generic versions. This is possibly because of our definition of non-generic pharmaceuticals, which included brand-names

Table (1.2) Descriptive statistics

	N	Mean	SD	Min	Max
Market Level Variables:					
Number of drugs	42	1004.81	54.35	895	1080
Number of presentations	42	1918.86	136.93	1666	2127
Number of reimbursed presentations	42	21.40	104.78	0	684
Number of diseases (ATC3)	42	208.40	5.01	199	214
Number of corporations	42	41.26	1.82	39	47
Number of manufacturers	42	227.38	6.04	218	240
Number of local manufacturers	42	200.21	5.75	191	209
Disease Level Variables:					
Number of presentations within disease	8753	9.21	11.05	1	91
Number of reimbursed presentations within disease	8753	3.89	7.02	0	52
Diseases with at least one reimbursed drug	8753	0.59	0.49	0	1
Number of manufacturers within disease	8753	6.60	7.00	1	43
Number of local manufacturers within disease	8753	5.16	6.00	0	36
Drug Level Variables:					
Log(DALYs)	23015	13.85	1.22	9	16
Log(Mortality)	22622	9.14	1.74	2	13
Log(YLLs)	22622	12.85	1.71	4	16
Log(Prevalence)	23015	16.56	1.26	9	19
Important SMR	42202	0.39	0.49	0	1
Low SMR	42202	0.08	0.28	0	1
Insufficient SMR	42202	0.04	0.20	0	1
No SMR	42202	0.48	0.50	0	1
Equals to max(SMR) within disease	21865	0.76	0.43	0	1
ASMR 1-3	42202	0.05	0.23	0	1
ASMR 4-5	42202	0.24	0.42	0	1
No ASMR	42202	0.71	0.45	0	1
If has generic version	42202	0.69	0.46	0	1
Drug age (1 = New)	42202	0.40	0.49	0	1
Presentation Level Variables:					
Sales at public price (Spending)	80592	1012.90	2722.18	0	83591
Market share (of total spendind)	80592	0.05	0.13	0	3
Market share (of spending within disease)	80005	10.59	20.91	0	100
Corporation's market share	80592	9.85	8.15	0	28
Manufacturer's market share	80592	2.66	3.38	0	14
Number of manufacturers within presentation	80592	1.61	1.61	1	18
Number of local manufacturers within presentation	80592	1.18	1.49	0	14
If multi-source	80592	0.23	0.42	0	1
If has local manufacturer	80592	0.75	0.43	0	1
Presentation age (1 = New)	80592	0.60	0.49	0	1

Source: Author's calculations.
Sales are in 1000MAD (local currency). Diseases are defined at ATC level 3.

and treatments under licensing agreements.

Finally, the position of a corporation in terms of total market share suggests that treatments that were not reimbursed were owned by firms with higher share of sales. In contrast, a manufacturer's total market share indicates the opposite. This could be explained by the fact that multiple corporations could have the same manufacturer, which happens to manufacture treatments that are reimbursed. Therefore, that manufacturer would end up with a larger market share, which would be divided by the firms that own the treatments, resulting in lower market share.

We note that Table 1.3 shows the differences between treatments attributes over the entire period 2000-2011. Therefore, one could argue that it is possible that reimbursement would impact some of the variables, resulting in biased differences. To address this issue, we constructed the same table restricting the analysis to the period prior to the implementation of reimbursement (first wave). Results did not change and are consistent with those reported above[28].

1.7.3 Regression Results

Table 1.4 provides estimation results from the models specified in Section 1.5.3. Results are reported in odds ratios. The first part of the table (columns (1) to (5)) analyse reimbursement status at each time regardless of the order (meaning that the dependant variable is binary in each specification, reimbursed or not-reimbursed). The second part (columns (6) and (7)) investigate the order of reimbursement (meaning that the dependant variable takes ordinal values depending on the wave of reimbursement).

Full list of reimbursement before the 1^{st} wave

Column (1) corresponds to the first specification of the first assumption, i.e. the Ministry of Health decided the entire list of reimbursed drugs before the first wave, and additionally, we only look at whether a drug will ever be reimbursed. The results suggest that the higher the burden of diseases that a drug could treat or prevent is a significant determinant of reimbursement. Using Mortality[29], on the one hand, as a measure of health outcome does not seem to significantly affect reimbursement, on the other hand, prevalence suggests that higher probability of reimbursement is assigned

[28] Table of results is available upon request.
[29] Results using diffrent health outcomes are in Appendix D.

Table (1.3) Reimbursed VS Not-Reimbursed

	Ever Reimbursed		Never Reimbursed		Difference	
	Mean	SD	Mean	SD	t-statistic	p-value
Disease attributes						
Log(DALYs)	14.31	1.11	13.65	1.32	-61.843	0.000***
Log(Mortality)	9.75	1.70	8.82	1.80	-60.084	0.000***
Log(YLLs)	13.44	1.62	12.59	1.88	-55.323	0.000***
Log(Prevalence)	16.91	0.98	16.44	1.49	-43.282	0.000***
Number of presentations within disease	26.23	23.15	19.70	19.76	-43.021	0.000***
Drug attributes						
Important SMR	0.81	0.39	0.28	0.45	-173.575	0.000***
Low SMR	0.06	0.23	0.12	0.33	31.281	0.000***
Insufficient SMR	0.02	0.12	0.05	0.23	28.519	0.000***
No SMR	0.12	0.32	0.54	0.50	137.596	0.000***
Equals to max(SMR) within disease	0.71	0.45	0.74	0.44	7.032	0.000***
ASMR 1-3	0.12	0.33	0.03	0.17	-52.751	0.000***
ASMR 4-5	0.46	0.50	0.19	0.40	-84.654	0.000***
No ASMR	0.42	0.49	0.78	0.42	112.084	0.000***
Sales at public price (Spending)	1567.04	3756.22	607.81	1457.63	-50.176	0.000***
Market share (of total spendind)	0.08	0.18	0.03	0.07	-52.350	0.000***
Market share (of spending within disease)	10.73	19.33	10.49	22.01	-1.585	0.113
If multi-source	0.40	0.49	0.11	0.32	-99.992	0.000***
If has generic version	0.72	0.45	0.77	0.42	16.140	0.000***
Firm attributes						
Corporation's market share	9.47	7.62	10.12	8.51	11.159	0.000***
Manufacturer's market share	3.00	3.25	2.40	3.45	-24.915	0.000***
If has local manufacturer	0.76	0.43	0.74	0.44	-5.678	0.000***
Number of local manufacturers within presentation	1.58	1.99	0.89	0.87	-66.283	0.000***
Observations	34035		46557		80592	

Source: Author's calculations.
Prevalence and YLL are in 1000. sales are in 1000 local currency (MAD). Diseases are defined at ATC level 3.
*** p<0.01, ** p<0.05, * p<0.10.

to more prevalent disease. Since DALYs is a measure that combines premature mortality and years lived with disability, it seems that disability is more of a determinant to reimbursement than mortality. Moreover, given that it was the only criterion that was specified explicitly in the official document, the SMR value determines significantly whether a drug will ever be reimbursed or not. Moreover, having an "Insufficient" SMR implies less probability of reimbursement, even less than not having an SMR value at all. Having a higher ASMR (innovation) score is linked with higher probability of reimbursement. Relative to treatments that have no ASMR score, even drugs with insufficient or non-existent innovation score compared to already existing treatments have higher probability of reimbursement. The coefficient on market share within disease favors reimbursement for drugs with higher sales in their therapeutic class. Including market share in total market does not change the results, indicating that popular treatments (spending-wise) were prioritized. A treatment that has more alternatives, manufactured by more than one firm, and specifically local firms had more probability of being included in the reimbursement list. Surprisingly, the coefficient on generic availability suggests that treatments without generic versions on the market were favored compared to treatments that have at least one generic. In contrast to the coefficient suggested by multi-source drugs and multiple local manufacturers, this could be partly due to our definition of a non-generic drug, which included also drugs that are produced by local firms under licensing agreements. Lastly, treatments that are manufactured by firms that have higher shares of the market have higher probability of reimbursement. Using corporation's market share yields the same result (lower in magnitude however), suggesting that the place of the firm owning or producing the treatment is important regarding reimbursement. Furthermore, treatments that are associated with specific anatomical groups had higher probability of being reimbursed than others. In fact, cardiovascular drugs, anti-infectives, drugs that treat cancer, drugs that are related to the nervous system, and blood drugs and hormones, were all prioritized over treatments of other anatomical systems. We note that these results should be interpreted in relative terms to the class "A", which is an important class in terms of added treatment into reimbursement (B1). Therefore, a lower probability associated with any other anatomical group could only suggest that its treatments were less important than those of the alimentary system.

Table (1.4) Ever/Never Reimbursed and Reimbursement Order regressions

	Ever Reimbursed VS Never Reimbursed					Reimbursement Order	
	All waves	First wave	Second/Third waves	Fourth wave	Fifth wave	All sample	Only reimbursed
Log(DALYs)	1.148**	1.425***	1.050	1.147	1.012	1.009	0.790***
	(0.076)	(0.115)	(0.091)	(0.104)	(0.096)	(0.054)	(0.053)
Number of Alternatives	1.797***	0.804	1.386*	2.646***	1.172	1.606***	1.389**
	(0.224)	(0.110)	(0.264)	(0.481)	(0.227)	(0.159)	(0.191)
Market share within disease	1.390***	1.229***	1.483***	1.396***	1.120	1.156***	0.821**
	(0.092)	(0.087)	(0.138)	(0.128)	(0.120)	(0.057)	(0.063)
If multi-source	1.620*	1.193	1.150	1.101	2.364*	1.672***	1.364
	(0.411)	(0.313)	(0.425)	(0.368)	(1.125)	(0.293)	(0.338)
If has local manufacturer	0.720	1.010	0.662	0.742	1.306	1.234	0.875
	(0.226)	(0.324)	(0.277)	(0.311)	(0.855)	(0.262)	(0.262)
Number of local manufacturers	2.386**	1.345	2.962***	3.388***	0.462	0.901	0.683*
	(0.817)	(0.355)	(1.214)	(1.601)	(0.410)	(0.150)	(0.155)
Important SMR	3.405***	1.499	2.554***	3.153***	3.053***	3.492***	1.629*
	(0.650)	(0.409)	(0.894)	(0.973)	(1.148)	(0.652)	(0.450)
Low SMR	0.710	0.471*	0.417*	0.709	1.412	1.063	2.944**
	(0.203)	(0.210)	(0.219)	(0.298)	(0.680)	(0.310)	(1.369)
Insufficient SMR	0.405**	1.001	1	0.463	0.381	0.646	1.660
	(0.183)	(0.575)	(.)	(0.338)	(0.434)	(0.274)	(1.416)
ASMR I-III	1.969**	0.678	1.473	1.977**	0.938	1.839***	1.679***
	(0.554)	(0.197)	(0.474)	(0.649)	(0.396)	(0.322)	(0.335)
ASMR VI-V	1.765***	1.337	0.848	1.327	1.807**	1.529***	1.224
	(0.283)	(0.252)	(0.194)	(0.288)	(0.505)	(0.184)	(0.205)
If has generic version	0.603***	2.376***	0.485***	0.710	0.344***	0.510***	0.371***
	(0.106)	(0.567)	(0.119)	(0.166)	(0.092)	(0.077)	(0.074)
Manufacturer's market share	1.412***	1.352**	1.235	1.451**	1.158	1.219*	0.782*
	(0.180)	(0.198)	(0.246)	(0.239)	(0.234)	(0.126)	(0.112)
Observations	1246	1239	978	882	685	1246	710
Pseudo R^2	0.281	0.178	0.229	0.256	0.138	0.095	0.083

Source: Author's calculations.
Prevalence and YLL are in 1000. sales are in 1000 local currency (MAD). Diseases are defined at ATC level 3.
*** p<0.01, ** p<0.05, * p<0.10. Robust standard errors are between parentheses.

Reimbursement decision between waves

Columns (2) to (5) provide results based on the assumption that the Ministry of Health evaluated and decided drugs' reimbursement between waves. Each column corresponds to a wave of reimbursement. We combine the 2^{nd} and 3^{rd} waves because of the low number of reimbursed drugs in the 2^{nd} wave, and because the two lists were published in subsequent quarters.

The interpretation of results from these specifications differ from the previous section by the addition of an implicit dynamic dimension, in a way that if a variable is significant in a wave and is no longer significant in another, that does not mean it was not taken into account while deciding reimbursement (at all), but it implies a prioritizing behavior of attributes.

Accordingly, the first set of reimbursed drugs was characterized by higher burden of disease (all measures of health outcomes: DALYs, mortality and prevalence), higher sales within a disease class, availability of generic versions, and importance of manufacturer. The rationale behind this result could be formulated as: "reimburse drugs that treat more people and burdensome diseases, that have higher sales within their therapeutic class, that have a generic version (cheaper version), and that are manufactured by a firm that has a solid place in the market"[30].

From what is left after the first wave, the Ministry of Health seemed to have switched to some precise drugs. None of health outcome measures have an effect on the probability of reimbursement during this wave. In addition, drugs that are reimbursed have important SMR (validated with a negative (effect) reimbursement probability associated with having a low SMR value), higher market share both within their disease classes, more alternatives to treat the same condition, less generics, and manufactured by more than one local firm. It could be formulated as: "Reimburse drugs that are important (clinical-wise and market-wise), that have more substitutes and less generics, and that are largely produced locally.".

The fourth and fifth waves did not show any notable change in reimbursement determinants. Higher probability was linked with better drug quality, number of alternatives, local manufacturers, and less generic versions. Moreover, the innovation measure suggests that more innovative treatments were included in the reimbursement list in the fourth wave, a pattern that will switch towards less innovative drugs. However, these results are computed relatively to treatments that

[30] An imaginary government statement.

were not evaluated by the French HAS. additionally, ASMR scores are only available starting 2004, with few retroactive evaluations of old drugs. Therefore, after reimbursing treatments that show clear innovation in the fourth wave, it is possible that the ministry has switched to treatment with low innovation score, but were new in comparison to the rest of the treatments.

The most notable change in subsequent waves is the significance of all SMR values relative to not having an SMR. In fact, quality of drug (measured by the SMR) appears to have become less important as a drug attribute in determining whether it will be reimbursed or not. Furthermore, the significance of the positive impact of sales and the negative effect of market share within disease, as well as the inconsistency of other attributes suggest that the Ministry started reimbursing what is left of drugs without necessarily having a rationale that could be formulated in a clear manner.

Order of Reimbursement

To investigate whether pharmaceuticals' reimbursement implied an implicit order set by the Ministry of Health, the last two columns provide results from the Ordered Logit. We recall that these results should be interpreted relative to the values of drugs' attributes before the first wave.

Column (6) suggests that drugs that have important SMR and ASMR scores, higher market share within their disease class, more alternatives, manufactured by more than one firm, less generics were likely to be reimbursed in later waves. Moreover, we argue that these results are mainly driven by the fact that the dependent variable includes both the not-reimbursed modality (zero) and the reimbursed modalities (one to four), therefore, it is likely that the shift from zero to other values is weighing more, thus impacting the results. To avoid this issue, we run the same specification but only on reimbursed drugs (column (7)).

Results are different and arguably reasonable. Drugs that were likely to be prioritized are drugs that treat burdensome diseases, have higher market shares within their therapeutic class, and that are manufactured by important firms and more than one local firm. The coefficients that caused confusion are still indicating that those attributes are associated with late reimbursement. However, the decrease in magnitude of the coefficients indicates a shift towards early reimbursement.

1.8 Discussion

Ideally, we would want clear answers to the following questions: What are the determinants of the Ministry's decision? Are these determinants consistent with the various hypotheses on the government's unobserved preferences?

Results from all models serve the purpose of specifying what makes a drug admitted into reimbursement, and if there was an order of reimbursement, what does make a drug prioritized over another? The change in results between models from our assumptions provides more insight on reimbursement decision mechanisms rather than being seen as contradictory.

All our variables determine reimbursement decision in a way or another, since they impact the decision either in a positive way (higher probability) or in a negative way (lower probability). Moreover, some of these variables had consistent effect on reimbursement across specifications. In fact, treating burdensome diseases, having important SMR and ASMR scores (as measures of quality and innovation, respectively), having higher market share within a disease, being manufactured by more than one local firm and well placed firms in the market, had a consistent positive effect on the probability of being reimbursed. This finding implies reasonable decision making by the Moroccan Ministry of Health.

The inconsistency (insignificance or change of sign) of other variables makes their interpretation less validating. However, given the nature of our study, even the insignificance and the change in effect could be considered results. In fact, having generic versions is the attribute that displayed a change in effect between waves of reimbursement. It implied that, during the first wave, the ministry of Health has decided to reimburse more of drugs with at least one generic version. A pattern that will change completely during the following waves, thus favoring treatments with less generics. Knowing that generics are mostly associated with lower costs and multiple manufacturers, we could say that the ministry included as much as treatments with generic versions in the first wave, in a way that the majority of what is left to reimburse later are drugs without generics. Furthermore, since reimbursement is based on the generics price, it is fairly reasonable to suggest that the ministry started with reimbursement the reference first, then the rest of the drugs. As a result, consequences on the budget wouldn't be as high as if non-generic drugs were reimbursed first. Additionally, not all drugs have generics, and each drug is necessary in its therapeutic class,

therefore, even if the Ministry would prioritize drugs with generics, sooner or later it would be necessary to switch to drugs with no generics.

Additionally, the number of alternatives of a drug within its disease class could be interpreted with the same duality as above. In fact, the Ministry finds itself between favoring drugs that could be substituted and drugs that are scarce, and to each its relevance and importance. Picking drugs that are easily substituted (in the sense of availability of alternatives) shows, in fact, a bias towards diseases that can be treated easily (again, in terms of availability, we do not refer to the fatality of diseases), and a lower preference for diseases that present difficulty of access to treatment, and vice versa. It is not unreasonable for the Ministry to transition from a rationale to the other however, it only implies a specific priority. In our case, the Moroccan Ministry of Health could have favored diseases with less treatments first (1^{st} wave, almost significant at 10%), then it shifted to the other set of diseases (later waves).

Results related to the industrial policy and lobbying section of our study should be interpreted with caution. The measures that we included in our analysis are the number of local manufacturers and the manufacturer's market share of revenue. Both variables indicate that drugs that are manufactured by several local manufacturers and by important firms (market-wise) were favored in comparison to other treatments. The first measure, along with the insignificance of the variable that simply measure whether a treatment has at least one local manufacturer, suggests that not only the presence local manufacturer within a treatment is preferred, but rather the concentration in number. Disregarding the number of local manufacturers could be problematic from the government's point of view, in a way that if a drug is manufactured by several foreign firms and only one local firm, the market for that drug is fragile as it depends heavily on foreign production. The second measure is a proxy for the importance of a firm in the total market. Firms with large shares of the market are better positioned to apply pressure on the government in order to include their treatments in the reimbursement list. Manufacturers with high market shares have also high number of treatments in their portfolios, therefore, even without lobbying, it is possible that the government would choose their treatments over others because of the fact that they secure continuous availability of treatments in the market, and also because of their success from doctors' prescriptions point of view. This latter point could be driven by the practice of detailing in the Moroccan market, however, we do not have data on marketing to investigate it.

1.9 Robustness analysis

In the previous sections, we analyzed the Ministry's reimbursement decision under the assumption that all attributes were considered simultaneously, in other words, diseases, drugs, and firms were evaluated at the same time. However, it is likely that the Ministry began by targeting diseases first, then choosing between potential drugs, and finally adding other restrictions that translate specific preferences. Therefore, in this section, we use the same approach as before but we divide into three levels.

The first level corresponds to the choice of diseases to target, and the variables that we use are diseases' attributes. The dependent variable for this level is also binary, with $(Y = 1)$ indicating whether a disease has at least one reimbursed treatment, and $(Y = 0)$ indicating no reimbursed drug in that disease class. The second level is similar to our main analysis, the only difference is the sample used for estimation. Because we want to investigate what would make a drug reimbursed and another excluded knowing that their disease class is targeted by the Ministry, the sample is restricted to only diseases with at least one reimbursed drug. Variables that we use are drugs' attributes. The last level corresponds to the additional preference that the Ministry might have imposed (industrial policy or firm preference as in our third hypothesis of the main model). For this level, we use firms' attributes as explanatory variables for this potential preference, and similar to the second level, the sample is restricted to molecules with at least one reimbursed presentation.

1.10 Conclusion

Understanding the rationale behind pharmaceuticals' reimbursement in an ex-post exercise is not straightforward. In fact, not knowing, for certain, how the Ministry of Health has decided which drugs to reimburse leaves the researcher with multiple hypotheses to test, which are not mutually exclusive, i.e. the realization of one does not necessarily mean the non-validity of the other. Also, even if one could specify the determinants that the Ministry has possibly considered, the sense in which they impact reimbursement is still up for discussion.

In our analysis, we divided these determinants into three main blocks. The first one is related to diseases that the available drugs treat or prevent; the second block is specific to drugs themselves; and the third covers firm importance and probable industrial policy effects. In addition, since it is

an ex-post analysis, assumptions on the Ministry's behavior were also necessary. Accordingly, we assumed that the Ministry either decided which drugs to reimburse prior to each list's publication, or that it decided the entire list before the first wave and divided it into multiple lists.

The starting point of this kind of studies would generally stem from official documents that shed light into how public policies are being implemented. However, the lack of this starting point is exactly what motivated our paper. In fact, for such an ambitious and important public policy, the absence of clear guidelines to how pharmaceuticals would be reimbursed constitutes a big gap in the understanding of the policy on the one hand, and any attempt to evaluate its progress and evolution on the other hand. Scrutiny in the choice of drugs that would be included in the national reimbursement list in no less important than the policy itself. The official determinant of drug reimbursement that was published by the Ministry of Health is the "service médical rendu (SMR)", a measure of drug quality that is used by the French health agency for the same purpose, to evaluate drugs for reimbursement. However, the indicators that are used to construct the measure include attributes that are population-specific. Therefore, the inadequacy is two-folded. First, if the Moroccan Ministry of Health has borrowed the SMR scores as they were produced by the French agency, given the fact that the two countries' populations are largely different from each other, at least from an epidemiological point of view, the scores would be deficient, counter productive even, since reimbursing treatments based on a wrong measure implies leaving out treatments that should be included in the reimbursement list and that are based on a true, unperformed, measure.

Secondly, if the Ministry of Health has merely adopted the definition of what an SMR is and subsequently assessed treatments locally, then the inadequacy would arise from a lack of communication, leading to market inefficiencies. If firms could understand the criteria determining a drug's eligibility for reimbursement, this knowledge could incentivize them to align their preferences with those of the government, potentially resulting in higher surplus. Similarly, if doctors are better informed about why some drugs are reimbursed and others are not, their prescribing behavior could be more efficient and less costly for patients. Patients, in general, do not know whether a drug is reimbursed until they visit the pharmacist, who does not have substitution rights and is legally obliged to dispense a drug by its commercial name, or until they receive the reimbursement of fees several weeks later.

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Appendices

A ATC level One

A : ALIMENTARY TRACT AND METABOLISM

B : BLOOD AND BLOOD FORMING ORGANS

C : CARDIOVASCULAR SYSTEM

D : DERMATOLOGICALS

G : GENITO-URINARY SYSTEM AND SEX HORMONES

H : SYSTEMIC HORMONAL PREPARATIONS (EXCL. SEX HORMONES)

J : GENERAL ANTI-INFECTIVES SYSTEMIC

K : HOSPITAL SOLUTIONS

L : ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS

M : MUSCULO-SKELETAL SYSTEM

N : NERVOUS SYSTEM

P : PARASITOLOGY

R : RESPIRATORY SYSTEM

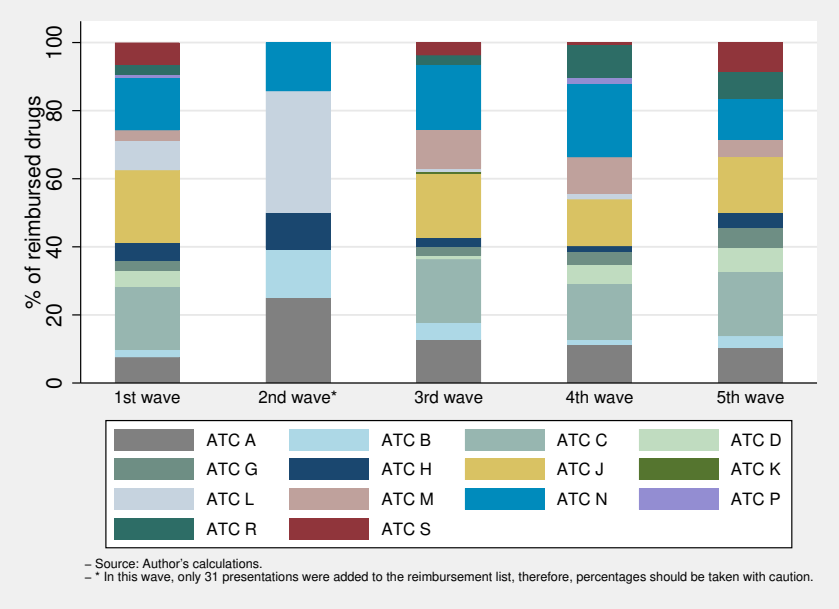
S : SENSORY ORGANS

T : DIAGNOSTIC AGENTS

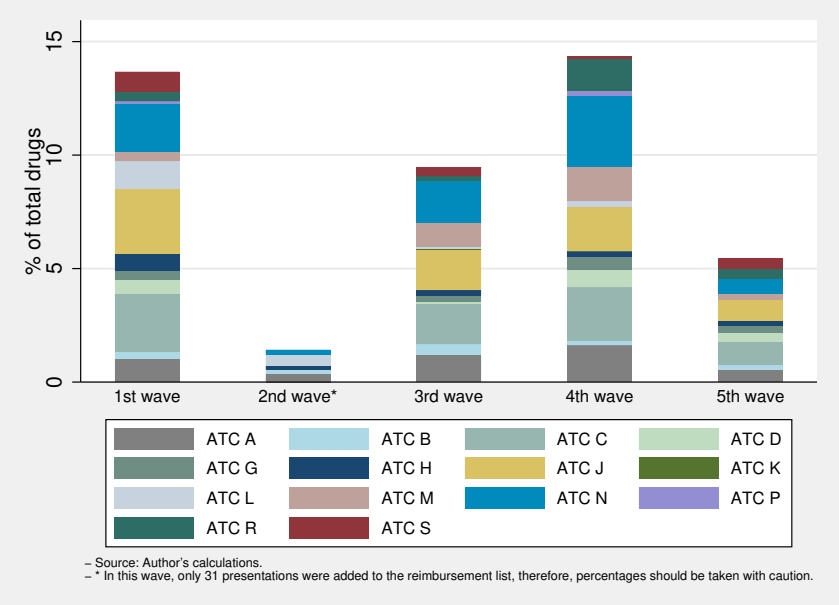
V : VARIOUS

B Reimbursement by ATC1 and wave of reimbursement

Figure (B1) Reimbursement by ATC1 and wave of reimbursement



(a) Within reimbursed treatments



(b) Within the market

C Main regression: ATC1 estimates

Table (C1) Ever/Never Reimbursed and Reimbursement Order regressions: ATC1 estimates

	Ever Reimbursed VS Never Reimbursed					Reimbursement Order	
	All waves	First wave	Second/Third waves	Fourth wave	Fifth wave	All sample	Only reimbursed
A	1	1	1	1	1	1	1
	(.)	(.)	(.)	(.)	(.)	(.)	(.)
B	7.644***	1.313	6.791***	1.006	2.928	2.926**	0.927
	(5.036)	(0.866)	(3.679)	(1.490)	(2.557)	(1.287)	(0.505)
C	5.587***	4.797***	1.983*	2.783**	2.448*	1.710**	0.379***
	(1.852)	(1.763)	(0.713)	(1.140)	(1.147)	(0.366)	(0.111)
D	0.639	1.457	0.112***	0.796	0.885	0.604	1.404
	(0.191)	(0.625)	(0.091)	(0.372)	(0.460)	(0.186)	(0.706)
G	0.551*	0.796	0.285**	0.578	0.626	0.523**	1.528
	(0.193)	(0.385)	(0.162)	(0.294)	(0.353)	(0.172)	(0.769)
H	3.444**	2.990**	2.745*	1.266	5.302**	1.644	0.623
	(1.778)	(1.522)	(1.620)	(0.866)	(3.893)	(0.546)	(0.315)
J	2.220***	2.219**	1.324	1.346	2.152*	1.572*	0.767
	(0.602)	(0.780)	(0.455)	(0.507)	(0.990)	(0.364)	(0.242)
K	0.377	1	1.282	1	1	0.421	1.546
	(0.507)	(.)	(1.585)	(.)	(.)	(0.513)	(0.758)
L	7.408***	8.519***	4.950***	6.663***	1	1.608**	0.219***
	(3.337)	(3.700)	(2.476)	(4.224)	(.)	(0.374)	(0.079)
M	1.040	1.022	0.769	0.885	0.558	1.098	0.789
	(0.380)	(0.521)	(0.382)	(0.412)	(0.381)	(0.315)	(0.264)
N	1.863**	2.862***	0.564	1.581	0.839	1.417	0.703
	(0.492)	(1.049)	(0.241)	(0.590)	(0.389)	(0.322)	(0.221)
P	2.357	1.120	1	10.11***	1	2.430	3.004
	(1.872)	(0.912)	(.)	(8.592)	(.)	(1.931)	(2.041)
R	0.846	1.078	0.115***	1.320	1.149	1.042	1.778
	(0.256)	(0.514)	(0.089)	(0.539)	(0.568)	(0.334)	(0.676)
S	1.021	4.441***	0.518	0.196**	1.012	0.615*	0.176***
	(0.314)	(1.887)	(0.243)	(0.143)	(0.521)	(0.169)	(0.096)
Observations	1246	1239	978	882	685	1246	710
Pseudo R^2	0.281	0.178	0.229	0.256	0.138	0.095	0.083

Source: Author's calculations.
Prevalence and YLL are in 1000. sales are in 1000 local currency (MAD). Diseases are defined at ATC level 3.
*** p<0.01, ** p<0.05, * p<0.10.Robust standard errors are between parentheses.

D Regression: alternative definitions

D.1 Using Mortality:

Table (D1) Ever/Never Reimbursed and Reimbursement Order regressions

	Ever Reimbursed VS Never Reimbursed					Reimbursement Order	
	All waves	First wave	Second/Third waves	Fourth wave	Fifth wave	All sample	Only reimbursed
Log(Mortality)	1.086	1.180***	1.035	1.062	1.050	0.999	0.904**
	(0.057)	(0.067)	(0.065)	(0.072)	(0.076)	(0.039)	(0.045)
Number of Alternatives	1.774***	0.831	1.345	2.562***	1.124	1.586***	1.368**
	(0.222)	(0.113)	(0.255)	(0.455)	(0.218)	(0.158)	(0.189)
Market share within disease	1.375***	1.214***	1.453***	1.376***	1.130	1.146***	0.830**
	(0.091)	(0.086)	(0.135)	(0.128)	(0.121)	(0.058)	(0.066)
If multi-source	1.684**	1.198	1.174	1.144	2.472*	1.735***	1.392
	(0.428)	(0.315)	(0.436)	(0.383)	(1.188)	(0.305)	(0.343)
If has local manufacturer	0.684	1.039	0.630	0.687	1.178	1.166	0.842
	(0.216)	(0.338)	(0.267)	(0.288)	(0.783)	(0.250)	(0.253)
Number of local manufacturers	2.377**	1.376	3.024***	3.428***	0.450	0.905	0.656*
	(0.810)	(0.360)	(1.236)	(1.630)	(0.403)	(0.151)	(0.149)
Important SMR	3.439***	1.607*	2.598***	3.243***	2.935***	3.516***	1.547
	(0.659)	(0.436)	(0.905)	(1.015)	(1.091)	(0.659)	(0.428)
Low SMR	0.749	0.509	0.434	0.753	1.496	1.139	2.888**
	(0.216)	(0.224)	(0.227)	(0.320)	(0.723)	(0.336)	(1.349)
Insufficient SMR	0.418*	1.110	1	0.467	0.384	0.643	1.542
	(0.187)	(0.630)	(.)	(0.345)	(0.436)	(0.274)	(1.326)
ASMR I-III	1.874**	0.681	1.318	1.930**	0.975	1.817***	1.781***
	(0.529)	(0.199)	(0.435)	(0.626)	(0.414)	(0.326)	(0.358)
ASMR VI-V	1.728***	1.342	0.842	1.289	1.737*	1.497***	1.242
	(0.278)	(0.251)	(0.195)	(0.277)	(0.492)	(0.182)	(0.208)
If has generic version	0.621***	2.397***	0.489***	0.754	0.357***	0.518***	0.374***
	(0.109)	(0.583)	(0.122)	(0.175)	(0.096)	(0.079)	(0.075)
Manufacturer's market share	1.373**	1.345**	1.223	1.402**	1.091	1.190*	0.767*
	(0.178)	(0.199)	(0.248)	(0.232)	(0.232)	(0.124)	(0.108)
Observations	1232	1225	965	871	675	1232	702
Pseudo R^2	0.279	0.170	0.227	0.254	0.138	0.096	0.082

Source: Author's calculations.
Prevalence and YLL are in 1000. sales are in 1000 local currency (MAD). Diseases are defined at ATC level 3.
*** p<0.01, ** p<0.05, * p<0.10. Robust standard errors are between parentheses.

D.2 Using Prevalence:

D.3 Using the average DALYs:

D.4 Using the maximum DALYs:

D.5 Using corporation's market share:

Table (D2) Ever/Never Reimbursed and Reimbursement Order regressions

	Ever Reimbursed VS Never Reimbursed					Reimbursement Order	
	All waves	First wave	Second/Third waves	Fourth wave	Fifth wave	All sample	Only reimbursed
Log(Prevalence)	1.172***	1.449***	1.107	1.136*	1.105	1.061	0.716***
	(0.070)	(0.119)	(0.076)	(0.087)	(0.096)	(0.065)	(0.063)
Number of Alternatives	1.795***	0.852	1.392*	2.675***	1.158	1.605***	1.348**
	(0.225)	(0.115)	(0.264)	(0.491)	(0.224)	(0.159)	(0.187)
Market share within disease	1.387***	1.228***	1.490***	1.394***	1.125	1.157***	0.815***
	(0.092)	(0.088)	(0.139)	(0.129)	(0.122)	(0.058)	(0.062)
If multi-source	1.622*	1.193	1.173	1.116	2.398*	1.662***	1.368
	(0.411)	(0.312)	(0.435)	(0.371)	(1.159)	(0.291)	(0.339)
If has local manufacturer	0.727	1.018	0.685	0.753	1.320	1.245	0.844
	(0.230)	(0.322)	(0.286)	(0.317)	(0.879)	(0.264)	(0.249)
Number of local manufacturers	2.372**	1.325	2.831**	3.292**	0.448	0.895	0.701
	(0.822)	(0.347)	(1.166)	(1.567)	(0.403)	(0.149)	(0.159)
Important SMR	3.405***	1.487	2.472***	3.234***	2.929***	3.418***	1.790**
	(0.649)	(0.403)	(0.858)	(0.990)	(1.091)	(0.636)	(0.501)
Low SMR	0.683	0.379**	0.391*	0.688	1.367	1.046	3.541***
	(0.197)	(0.181)	(0.210)	(0.289)	(0.651)	(0.304)	(1.656)
Insufficient SMR	0.398**	0.969	1	0.461	0.367	0.643	1.587
	(0.182)	(0.572)	(.)	(0.341)	(0.423)	(0.273)	(1.312)
ASMR I-III	1.955**	0.696	1.463	1.958**	0.926	1.834***	1.675***
	(0.552)	(0.199)	(0.472)	(0.643)	(0.392)	(0.322)	(0.335)
ASMR VI-V	1.744***	1.331	0.830	1.320	1.751**	1.509***	1.274
	(0.282)	(0.250)	(0.190)	(0.288)	(0.485)	(0.183)	(0.214)
If has generic version	0.601***	2.462***	0.483***	0.726	0.333***	0.504***	0.362***
	(0.105)	(0.588)	(0.118)	(0.167)	(0.087)	(0.076)	(0.073)
Manufacturer's market share	1.391***	1.288*	1.226	1.428**	1.159	1.217*	0.807
	(0.176)	(0.187)	(0.243)	(0.232)	(0.236)	(0.126)	(0.115)
Observations	1246	1239	978	882	685	1246	710
Pseudo R^2	0.283	0.178	0.230	0.257	0.140	0.096	0.086

Source: Author's calculations.
Prevalence and YLL are in 1000. sales are in 1000 local currency (MAD). Diseases are defined at ATC level 3.
*** p<0.01, ** p<0.05, * p<0.10. Robust standard errors are between parentheses.

Table (D3) Ever/Never Reimbursed and Reimbursement Order regressions

	Ever Reimbursed VS Never Reimbursed					Reimbursement Order	
	All waves	First wave	Second/Third waves	Fourth wave	Fifth wave	All sample	Only reimbursed
Number of Alternatives	1.797***	0.858	1.396*	2.619***	1.183	1.609***	1.371**
	(0.224)	(0.116)	(0.266)	(0.468)	(0.228)	(0.159)	(0.189)
Market share within disease	1.390***	1.209***	1.477***	1.378***	1.120	1.156***	0.832**
	(0.092)	(0.085)	(0.137)	(0.125)	(0.120)	(0.057)	(0.064)
If multi-source	1.620*	1.240	1.160	1.127	2.377*	1.675***	1.322
	(0.411)	(0.323)	(0.429)	(0.375)	(1.130)	(0.293)	(0.323)
If has local manufacturer	0.720	0.969	0.659	0.707	1.315	1.236	0.892
	(0.226)	(0.307)	(0.273)	(0.297)	(0.859)	(0.262)	(0.266)
Number of local manufacturers	2.386**	1.404	2.983***	3.430***	0.456	0.901	0.647*
	(0.817)	(0.368)	(1.220)	(1.640)	(0.403)	(0.150)	(0.146)
Important SMR	3.405***	1.703**	2.576***	3.422***	3.108***	3.489***	1.525
	(0.650)	(0.452)	(0.889)	(1.081)	(1.162)	(0.644)	(0.427)
Low SMR	0.710	0.466*	0.419*	0.713	1.404	1.063	2.934**
	(0.203)	(0.210)	(0.221)	(0.304)	(0.679)	(0.310)	(1.352)
Insufficient SMR	0.405**	1.053	1	0.472	0.380	0.644	1.526
	(0.183)	(0.599)	(.)	(0.355)	(0.429)	(0.273)	(1.310)
ASMR I-III	1.969**	0.701	1.458	1.994**	0.951	1.832***	1.664**
	(0.554)	(0.207)	(0.469)	(0.652)	(0.403)	(0.321)	(0.336)
ASMR VI-V	1.765***	1.421*	0.851	1.395	1.851**	1.525***	1.197
	(0.283)	(0.259)	(0.193)	(0.301)	(0.519)	(0.184)	(0.200)
If has generic version	0.603***	2.622***	0.484***	0.764	0.346***	0.508***	0.353***
	(0.106)	(0.614)	(0.117)	(0.174)	(0.091)	(0.077)	(0.071)
Manufacturer's market share	1.412***	1.322*	1.238	1.409**	1.147	1.223*	0.779*
	(0.180)	(0.189)	(0.247)	(0.231)	(0.233)	(0.127)	(0.110)
mean_DALYs		1.181	1.142	0.985	0.934	1.048	0.984
		(0.127)	(0.139)	(0.121)	(0.132)	(0.082)	(0.098)
Observations	1246	1239	978	882	685	1246	710
Pseudo R^2	0.281	0.166	0.230	0.254	0.138	0.095	0.077

Source: Author's calculations.
Prevalence and YLL are in 1000. sales are in 1000 local currency (MAD). Diseases are defined at ATC level 3.
*** p<0.01, ** p<0.05, * p<0.10. Robust standard errors are between parentheses.

Table (D4) Ever/Never Reimbursed and Reimbursement Order regressions

	Ever Reimbursed VS Never Reimbursed					Reimbursement Order	
	All waves	First wave	Second/Third waves	Fourth wave	Fifth wave	All sample	Only reimbursed
max_DALYs	1.101	1.294***	1.099	1.081	0.914	0.992	0.837***
	(0.079)	(0.105)	(0.098)	(0.102)	(0.093)	(0.057)	(0.057)
Number of Alternatives	1.797***	0.816	1.379*	2.626***	1.199	1.609***	1.390**
	(0.224)	(0.111)	(0.262)	(0.471)	(0.233)	(0.160)	(0.191)
Market share within disease	1.383***	1.216***	1.481***	1.385***	1.119	1.155***	0.827**
	(0.091)	(0.086)	(0.137)	(0.126)	(0.120)	(0.057)	(0.063)
If multi-source	1.643*	1.213	1.149	1.114	2.388*	1.676***	1.330
	(0.417)	(0.318)	(0.426)	(0.372)	(1.134)	(0.293)	(0.328)
If has local manufacturer	0.718	0.995	0.666	0.726	1.309	1.230	0.891
	(0.225)	(0.318)	(0.277)	(0.305)	(0.854)	(0.260)	(0.266)
Number of local manufacturers	2.385**	1.370	2.947***	3.404***	0.456	0.904	0.673*
	(0.817)	(0.361)	(1.203)	(1.618)	(0.402)	(0.150)	(0.153)
Important SMR	3.523***	1.626*	2.551***	3.288***	3.196***	3.516***	1.562
	(0.670)	(0.437)	(0.884)	(1.019)	(1.199)	(0.655)	(0.436)
Low SMR	0.710	0.467*	0.421	0.710	1.406	1.064	2.933**
	(0.203)	(0.209)	(0.222)	(0.299)	(0.682)	(0.311)	(1.355)
Insufficient SMR	0.406**	1.038	1	0.462	0.383	0.646	1.619
	(0.183)	(0.584)	(.)	(0.343)	(0.433)	(0.275)	(1.373)
ASMR I-III	1.964**	0.687	1.456	1.976**	0.947	1.844***	1.685***
	(0.552)	(0.202)	(0.468)	(0.647)	(0.404)	(0.323)	(0.338)
ASMR VI-V	1.783***	1.382*	0.840	1.358	1.886**	1.534***	1.206
	(0.286)	(0.256)	(0.191)	(0.294)	(0.534)	(0.185)	(0.201)
If has generic version	0.614***	2.477***	0.479***	0.736	0.355***	0.512***	0.368***
	(0.107)	(0.587)	(0.117)	(0.172)	(0.094)	(0.077)	(0.074)
Manufacturer's market share	1.406***	1.342**	1.238	1.432**	1.142	1.217*	0.784*
	(0.179)	(0.195)	(0.248)	(0.235)	(0.230)	(0.126)	(0.111)
Observations	1246	1239	978	882	685	1246	710
Pseudo R^2	0.280	0.171	0.230	0.255	0.139	0.095	0.080

Source: Author's calculations.
Prevalence and YLL are in 1000. sales are in 1000 local currency (MAD). Diseases are defined at ATC level 3.
*** p<0.01, ** p<0.05, * p<0.10. Robust standard errors are between parentheses.

Table (D5) Ever/Never Reimbursed and Reimbursement Order regressions

	Ever Reimbursed VS Never Reimbursed					Reimbursement Order	
	All waves	First wave	Second/Third waves	Fourth wave	Fifth wave	All sample	Only reimbursed
Log(DALYs)	1.139**	1.409***	1.055	1.165*	1.007	1.004	0.791***
	(0.074)	(0.113)	(0.091)	(0.108)	(0.095)	(0.054)	(0.054)
Number of Alternatives	1.810***	0.822	1.404*	2.695***	1.176	1.617***	1.361**
	(0.225)	(0.111)	(0.265)	(0.504)	(0.228)	(0.159)	(0.186)
Market share within disease	1.397***	1.239***	1.482***	1.406***	1.124	1.161***	0.814***
	(0.092)	(0.088)	(0.137)	(0.134)	(0.119)	(0.057)	(0.062)
If multi-source	2.122***	1.464	1.348	1.509	2.617**	1.932***	1.161
	(0.512)	(0.358)	(0.471)	(0.472)	(1.182)	(0.312)	(0.274)
If has local manufacturer	0.529**	0.757	0.525*	0.486*	1.179	1.006	1.122
	(0.151)	(0.210)	(0.191)	(0.192)	(0.768)	(0.193)	(0.297)
Number of local manufacturers	2.135**	1.238	2.906***	3.349***	0.432	0.865	0.730
	(0.707)	(0.324)	(1.189)	(1.552)	(0.384)	(0.141)	(0.164)
Important SMR	3.474***	1.505	2.510***	3.176***	3.084***	3.513***	1.595*
	(0.658)	(0.412)	(0.871)	(0.997)	(1.167)	(0.655)	(0.449)
Low SMR	0.706	0.476*	0.411*	0.630	1.445	1.051	2.810**
	(0.204)	(0.211)	(0.219)	(0.268)	(0.701)	(0.309)	(1.311)
Insufficient SMR	0.419*	1.042	1	0.452	0.386	0.648	1.535
	(0.188)	(0.598)	(.)	(0.337)	(0.437)	(0.276)	(1.308)
ASMR I-III	2.063***	0.682	1.552	2.479***	0.957	1.863***	1.652**
	(0.575)	(0.198)	(0.506)	(0.814)	(0.402)	(0.327)	(0.328)
ASMR VI-V	1.828***	1.359	0.846	1.432*	1.817**	1.560***	1.191
	(0.297)	(0.255)	(0.194)	(0.310)	(0.504)	(0.189)	(0.201)
If has generic version	0.598***	2.352***	0.486***	0.688	0.349***	0.505***	0.372***
	(0.105)	(0.558)	(0.119)	(0.162)	(0.093)	(0.076)	(0.074)
Corporation's market share	1.271**	1.088	1.246	1.853***	1.043	1.132*	0.922
	(0.125)	(0.120)	(0.180)	(0.239)	(0.150)	(0.084)	(0.090)
Observations	1246	1239	978	882	685	1246	710
Pseudo R^2	0.281	0.175	0.230	0.274	0.137	0.095	0.081

Source: Author's calculations.
Prevalence and YLL are in 1000. sales are in 1000 local currency (MAD). Diseases are defined at ATC level 3.
*** p<0.01, ** p<0.05, * p<0.10. Robust standard errors are between parentheses.

CHAPTER 2

The Impact of Health Insurance on Drug Utilization: Aggregate Market Effects

2.1 Résumé

L'impact de l'assurance maladie sur l'utilisation des médicaments est largement documenté dans la littérature. Cependant, la majorité des études se sont principalement concentrées sur les pays développés. Des facteurs tels que le prix comme barrière à l'accès, l'insuffisance des informations fournies aux médecins et aux patients, l'infrastructure des soins de santé et la transition épidémiologique contribuent aux différences entre les pays développés et les pays en voie de développement. Dans cet article, nous examinons l'impact de l'extension de la couverture médicale sur l'utilisation des médicaments dans un pays en développement, le Maroc. En utilisant des données au niveau du marché sur les ventes de médicaments et la variation du statut de remboursement d'un médicament (remboursé ou non), les résultats du modèle de base, contrôlant uniquement le traitement, suggèrent une augmentation de l'utilisation après l'expansion de l'assurance maladie. Cependant, lorsque l'on contrôle les déterminants du remboursement, il n'y a pas de différence significative entre l'utilisation des médicaments remboursés et non remboursés. Cela pourrait être attribué à des habitudes de prescription et d'utilisation rigides, à un manque d'information sur ce

qui est remboursé et ce qui ne l'est pas, ou à des insuffisances dans le système de remboursement.

2.2 Introduction

Access to treatment has been a longstanding concern for countries around the world, as reflected in the importance assigned to healthcare in both the Millennium Development Goals (MDGs) and Sustainable Development Goals (SDGs). The role that pharmaceuticals have played since the introduction of the world's first synthetic pharmaceutical, Aspirin, in 1897 and the significant advances in drugs for a wide range of health concerns during the twentieth century, has motivated the implementation of the WHO's list of essential medicines (LEM) in 1977. As defined by the WHO, essential medicines "are those that satisfy the priority health care needs of a population" and "are intended to be available in functioning health systems at all times" and "at prices individuals and health systems can afford." In that regard, targets 8.E and 3.8 of the MDGs and SDGs, respectively, aimed to realize these objectives by promoting access to affordable essential drugs and ensuring financial risk protection in the process.

Spending on pharmaceuticals as a share of overall health care expenditures indicates the weight that medicines have on the budget. In the OECD countries for example, pharmaceuticals accounted for one-sixth of overall health spending in 2019, ranging from as low as 8.6% in Switzerland to around 31% in Greece. France sits close to the average at around 16.4%, and the United States at 13%[1]. In developing countries, lower-middle income countries for example, medicines account for 20% to 60% of health spending[2]. In Morocco, the latest national health accounts report (NHA, 2018) indicates that pharmaceuticals are in third place after hospital care and ambulatory care, constituting 23.4% of total health spending. Still exceeding the OECD average, spending on pharmaceuticals in Morocco has undergone significant changes over the last two decades.

In 1997/98, approximately 40% of health spending was allocated to pharmaceuticals. The shift between 1998 and 2018 began around 2006, shortly after the expansion of national health insurance in 2002, which came into effect later in 2005. The observed decrease in the share of pharmaceuticals, however, does not signify a decrease in their utilization. In fact, in 1997/98, 60% of the spending was financed by households – a share that decreased to 40% in 2013 and further

[1] OECD Health Statistics.
[2] World Health Organization. (2017). Access to medicines: making market forces serve the poor.

to 34% by the end of 2018.[3] Access to medicines significantly improved after 2005, partly due to subsidizing a portion of the cost, the promotion of the use of generics rather than brand-names, and also because of the procurement of drugs at public health facilities for a specific fraction of the population. In this paper, we attempt to provide evidence for an increase in utilization.

The impact of health insurance on healthcare utilization, pharmaceuticals in particular, has been well established by numerous studies (Finkelstein & McKnight (2008), Card et al. (2008), Card et al. (2009), Duggan & Scott Morton (2010), Anderson et al. (2012)), Finkelstein et al. (2012)). However, little is known about access to pharmaceuticals as a response to health insurance in developing countries (Maurer (2008) as an example). Health insurance acts on access to drugs by reducing the out-of-pocket (OOP) costs that patients must pay. The magnitude of the change depends on the importance of subsidies brought by insurance – cost-sharing – (Newhouse (1993), Chandra et al. (2014), Einav et al. (2018) and Ghosh et al. (2019)). Estimating the elasticity of demand for drugs is straightforward when one has access to patients' medicine purchases and the level of cost-sharing they had to bear as an out-of-pocket (OOP) cost. However, in cases where only market-level data is available, as is the case in this study, linking an increase in utilization to a decrease in OOP cost becomes ambiguous. Market-level data provides the total consumption of a product, such as pharmaceuticals, without specifying who purchased what. Consumption could be driven by prescriptions to insured patients, uninsured patients, or even self-medication. knowing the particularities of the market then becomes a necessity to deduce the reasons behind the change in utilization. The source of variation when only market-level data is available is the change in a product's attribute that is relevant to the question. For example, increasing the VAT on only some products and not others is sufficient variation to quantify the effect of taxes on certain market outcomes. In our paper, we exploit the fact that after the expansion of health insurance, some drugs were eligible for reimbursement, while others were not.

Linking the change in pharmaceutical utilization to health insurance while relying only on drugs' reimbursement status is challenging.[4] However, at this stage, we only provide the aggregate effect of coverage on utilization. Further work is still necessary to disentangle the direct effect of insurance – by reducing the OOP (demand) – from the indirect effect – by affecting the

[3] In 2013, the Moroccan government introduced a significant policy change regarding pharmaceutical pricing, transitioning from a cost-based pricing system to a system based on external references. We only interpret results up to 2013 to focus on the expansion of insurance.

[4] We go into greater detail in section 2.4.

pharmaceutical industry (supply) –, and also from what we could call a 'false effect' that is coming from a change in utilization but that is not linked to a change in cost-sharing (the uninsured part of the population).

The expansion of health insurance in Morocco was mandated in 2002 and implemented later in 2005. It consisted of generalizing coverage to the working population of both public and private sectors (called AMO) and establishing a medical assistance regime for the poor (called RAMed).[5] After 2005, health insurance in Morocco became mandatory for the eligible populations. Moreover, only the first regime provided access to subsidized pharmaceuticals purchased in the retail market. The second regime, although implemented only later in 2012, involved access to free medicines procured in public health facilities. Since our analysis is limited to 2011, RAMed falls outside the scope of this paper. However, this only pertains to the direct effect of RAMed, which would not be captured in our selected period. In fact, increased access to public hospitals and the inadequacy of public procurement of medicines could drive most RAMed beneficiaries to the retail market, thereby increasing overall utilization without benefiting from cost-sharing. Moreover, during our period of analysis, we cannot rule out the indirect effect that might result from the impact of insurance (immediate or anticipatory) on the pharmaceutical market, benefiting RAMed enrollees as well.

The effect we are estimating is an aggregate effect of the expansion of national health insurance on drug utilization, exploiting only the variation in a drug's reimbursement status. If, as a result of insurance, the supply side of the pharmaceutical industry has reacted in the same manner for both reimbursed and unreimbursed drugs, doctors prescribed medicines they judged to be necessary regardless of their reimbursement status,[6] and adding the possibility that the practice of detailing of unreimbursed drugs has increased, thus persuading doctors to prescribe reimbursed drugs to covered patients and left-out medicines to uninsured patients, we argue that there is no reason to expect an increase in the utilization of reimbursed pharmaceuticals.

Our results from the baseline model (no covariates) suggest that drug utilization increased after the expansion of national health insurance in 2005. The more a drug was exposed to treatment

[5] See section 2.3 for more details.

[6] Either due to a lack of knowledge about which drugs are included in the reimbursement list or because they are superior drugs that happen to be reimbursed. Although the latter point wouldn't make a difference when we control for attributes that could explain the selection process.

(insurance), the more its utilization increased. Moreover, patterns of utilization before the actual treatment date, as shown in 2.7.1, are validated by the magnitude of pretrends both right before the implementation of the expansion and for large periods preceding treatment (specifically for late-treated groups). In addition, the impact is increasing with calendar time, because utilization did not respond to the sudden change in reimbursement status immediately; both patients and doctors had to learn about the new changes brought about by the expansion of insurance.

On the other hand, preliminary results from the model with covariates show that, taking into account drug attributes that were likely considered in the selection of treatments to include in the reimbursement list, there was no significant increase in the utilization of reimbursed drugs. This shows that the increase in utilization estimated in the baseline model is due to differences between drugs that are both making them consumed more, and being selected for reimbursement. While it is possible that reimbursement status affected the consumption decisions of individual patients, at an aggregate level, the reimbursement status of a drug did not introduce a significant shift from unreimbursed drugs to reimbursed ones, other than the structural differences between drugs that are in the two groups. The coverage rate of the national health insurance (only 40% insured by 2013) may limit what can be observed at the aggregate level. It is also possible that manufacturers of non-reimbursed drugs changed their pricing or advertising strategies to offset any loss of demand.

The rest of the paper is structured as follows. Section 2 provides background on the institutional setting of the expansion of national health insurance in Morocco. In section 3, we relate the institutional setting to our research question and discuss the different outcomes to expect. Section 4 presents our empirical design and model and section 5 describes the primary data sources. Section 6 presents our main results. Section VI discusses interpretation of our estimates and concludes.

2.3 Institutional Setting

2.3.1 National Insurance: AMO

Before 2005, health insurance in Morocco was optional and was restricted to a small fraction of the population, almost all of which were employees[7]. In fact, only 16% of the Moroccan population was covered during that period, the majority of which are public sector's employees (67%) and private insurance beneficiaries (26.4%) (Figure 2.3.1). Health insurance of public sector employees was guaranteed by CNOPS and the mutual companies that are federated into it; that of private sector employees was guaranteed by mutual companies and private insurance contracts (individual or group), and finally, employees of some institutions benefited from internal health insurance regimes (only 1.6% of the population in 2001). According to National Health Accounts (CNS) reports, healthcare services that were covered by all types of insurance institutions included inpatient and outpatient care services, with differences in reimbursement rates and annual spending limits (specific to private insurance contracts).

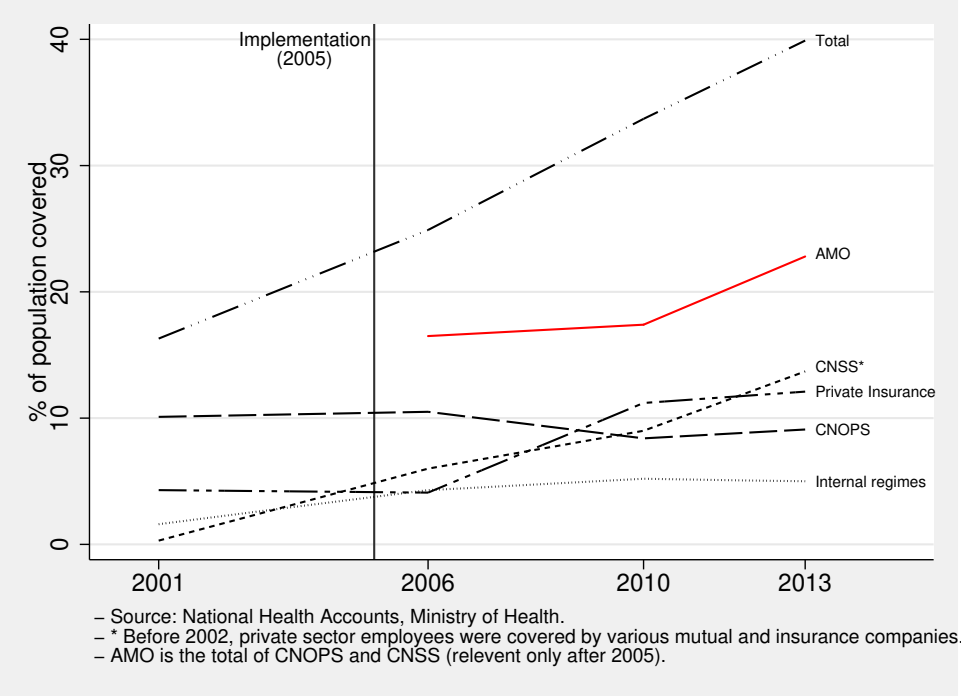


Figure (2.3.1) Evolution of Coverage Rate in Morocco

Regarding pharmaceuticals coverage, CNOPS's mutual companies were managing outpatient

[7] At that time, the poor population could benefit from free (or subsidized) healthcare at public hospitals using an authority-issued certificate called "Certificate of indigence". Unfortunately, we do not have statistics on that fraction of the population. Moreover, it stands out of the scope of our analysis since it did not offer drugs coverage.

care reimbursement (drugs for instance) at a 70% coverage rate as part of a common health insurance plan, the rest of the OOP could also be reimbursed as part of a complementary plan (an additional 16% rate). Drugs' reimbursement for private sector employees varied depending on the insurance plan that they were enrolled in. In fact, employees who were enrolled in mutual companies insurance plans (CMIM in particular) benefited from at least an 80% coverage rate (to 85% or 100% depending on the plan) without any limit on reimbursement spending. However, private insurance contracts varied from one beneficiary to another and from one firm's group-contract to another, in addition, they included a limit on annual reimbursement spending.

In 2002, the national insurance law (known as Law n°65-00) was announced and obliged employees of both sectors to enroll in the so-called "Assurance Maladie Obligatoire (AMO)"[8] by the time of its implementation (in 2005)[9]. The newly set law was restricted to the working population and differentiated between the two sectors' employees. The novelty of the new law was for private sector employees, who would benefit from a national insurance scheme, as opposed to the previous setting where, first, employers were not obliged to offer health insurance, and second, contributions for private contracts were high and constrained (medical history before affiliation and spending limits after enrollment). In terms of management, public sector employees' health insurance continued to be managed by CNOPS and its federated mutual companies, and that of private sector employees was delegated to CNSS. Consequently, after one year of its implementation, the percentage of the Moroccan population with any health insurance increased to 25% (in 2006), to reach 40% by the end of 2013, with AMO accounting for more than half of the coverage rate (22.8%) (Figure 2.3.1).

Healthcare services that were included in the national insurance scheme were heterogeneous. Public sector employees benefited from a generous insurance plan in terms of services, as it included inpatient and outpatient care[10]. For instance, pharmaceuticals are covered at a 70% rate[11] (increased to 90% or 100% if the corresponding disease is either severe, chronic, or expensive) with the possibility of enrollment in an optional complementary scheme (guaranteed by mutual companies) that covers a fraction of the rest of the OOP.

[8] AMO: Mandatory Health Insurance.

[9] A five year transitory phase was allowed for employers/employees who chose to keep their previous health insurance plans, with the condition that they provide CNOPS/CNSS with proof of insurance at the end of each year. However, employees that we recruited after 2005 were obliged to abide by the new law.

[10] See Article 7 of Law n°65-00 for all services included.

[11] See Decree n°2-05-736 for coverage rates of all healthcare services.

On the other hand, health insurance offered to private sector employees as part of the national scheme was restrictive. In fact, it covered inpatient and outpatient-care only for expensive, severe, or chronic diseases, maternal care, and child care under the age of 12[12]. Pharmaceuticals that fall into those categories are covered at a 70% rate (increased to 90% if disease is either severe, chronic, or expensive, and treated at a public hospital). It is only later, in 2010, that CNSS expanded its benefit basket to include outpatient-care services for any type of care with coverage rates remaining unchanged[13]. In addition, private sector employees were allowed to enroll in complementary health insurance of their choice (private contracts).

We note that AMO, as it was mandated, served as a baseline for health benefits that should be guaranteed to the working population. Thus, if employees were already enrolled in a plan that was generous than AMO, switching to the latter would be optional. However, employees who were not enrolled in any health insurance, or were in a less generous one, were obliged to switch to the national insurance scheme.

2.3.2 Price Regulation

Pharmaceuticals' prices in Morocco are regulated[14], i.e. all margins (manufacturer, wholesaler, and pharmacist) are fixed by regulation. For drugs that are manufactured locally, manufacturer's margin is inversely proportional to the "cost price" of one drug unit (to which an 8% VAT rate is applied), wholesaler's margin is fixed at 10%, and pharmacist's margin is equal to 30%. Imported drugs are priced differently, as calculation is based on the FOB price (Free on Board), which is the price of a drug in its country of origin, converted to local currency (MAD), and to which are added: approach expenses, tariffs, and importer's commission (fixed by regulation). Wholesaler and pharmacist's margins are similar to those of drugs that are manufactured in Morocco. In addition, as of 1998, if an imported drug has similars that are manufactured locally, its price is equal to the average of their prices.

Furthermore, when price is regulated in a market, changing that price is also subject to specific rules. In the case of imported drugs, the initially listed price could be changed upon request if the variables that were considered in its calculation vary (FOB, tariffs, exchange rate). However,

[12] See Decree n°2-05-737.
[13] Official source?
[14] See Ministerial Orders n°465-69, n°2365-93, and n°1577-98.

it should remain fixed for at least three months before the importer requests its change. Also, an increase in price that is greater than 5% is subject to prior approval by the Ministry of Health. For drugs that are manufactured locally, we could not find specific rules regarding price revision in the Ministry's documents. Nevertheless, since firms have to secure at least three months supply of each drug that they manufacture (at a given reported cost), we assume that prices should be fixed for that duration (therefore similar to imported drugs).

2.4 Institutional Setting and Research Question

Our study investigates the impact of the newly set national insurance scheme (AMO) on drugs utilization. The expected effect is directly linked to the way both pharmaceuticals' coverage and their price setting are regulated. In this section, we discuss how the institutional settings described in subsections 2.3.1 and 2.3.2 are related to our research question.

2.4.1 AMO Setting

Given the profile of health insurance in Morocco before and after the enactment of AMO, drug utilization outcome that is due to AMO must be interpreted based on the relative change in health benefit. Therefore, the question boils down to the impact of, first, eventual expansion of health insurance in terms of population covered; second, whether pharmaceuticals are included in the benefit basket, if so, their reimbursement rate; and finally, healthcare services that are either substitutes or complements to pharmaceuticals and are covered by health insurance, as well as their reimbursement rates. Tables 2.4.1 and 2.4.2 summarize the changes brought by the new national health insurance in Morocco, in other words, changes in the above-mentioned points.

On the one hand, the percentage of population covered with any health insurance has significantly increased after the implementation of AMO (from 25% to 40%). Moreover, despite the fact that drugs could be reimbursed before 2005 for that specific target population, the expansion of coverage alone would increase the likelihood of prescriptions being filled, thus increasing drug utilization. On the other hand, the impact that insurance would have on the utilization of a particular service depends also on whether complementary and/or substitute services are covered or

not[15]. Consequently, the effect of insurance on drug utilization should be interpreted with caution, since it is not the pure effect of subsidizing drugs only, but also that of subsidizing other services that are related to drugs. For example, since pharmaceuticals and doctor visits are complementary services (the latter is required for a drug to be reimbursed), drug consumption would shift solely because consultations are included in the health plan, regardless of drugs being reimbursed or not. These aforementioned channels translate the indirect effects of insurance on drug utilization.

Table (2.4.1) Insurance profile in Morocco before and after Law n°65-00

	2001 (Before)	2006 (After)	2010 (After)	2013 (After)
Optional/Mandatory	Optional	Mandatory	Mandatory	Mandatory
Population covered	16.3%	24.9%	33.7%	39.9%
Pharmaceuticals coverage	Yes	Yes	Yes	Yes
↪ Reimbursement rate	[70%,100%]	[70%,100%]	[70%,100%]	[70%,100%]
Other services coverage	Yes	Yes	Yes	Yes
↪ Reimbursement rate	[70%,100%]	[70%,100%]	[70%,100%]	[70%,100%]

- Source: National Health Accounts (2001, 2006, 2010, and 2015 reports).

The direct effect of insurance on drug utilization comes from the changes related to drug reimbursement per se. In fact, identifying that effect relies on the passage from a situation where drug coverage is weak, i,e,. higher out-of-pocket (OOP) price, to a situation where it is stronger, i,e,. lower OOP price (or vice versa). Therefore, the difference between the before and after periods (OOP-wise) should be analyzed carefully in order to assess which causal effect is estimated. In fact, a passage from having no insurance at all to being insured differs strictly from a passage from a level of insurance to another level. Confounding the two situations would lead to over- or under-state the expected results. Regarding our setting, we could identify six categories of OOP price variations. The most relevant (policy- and study-wise) one is the never-insured part of the population that will acquire health insurance after the passage of AMO, whose, as a consequence, OOP drug price would dramatically decrease from 100% to 30% (category (2)). Other categories show little to no variation in their OOP medication cost (categories (4) and (6) for the former, and categories (1), (3) and (5) for the latter). The magnitude of the impact related to each category is proportional to the variation in the size of its population. In fact, categories that do not change affiliation have no reason to show any variation in drug utilization (assuming that other services are held unchanged).

[15] Services that are reimbursed by AMO encompass nearly all healthcare services, such as doctor visits, pharmaceuticals, medical tests and surgeries, etc. Procedures like cosmetic surgeries and thermal treatments are excluded.

Table (2.4.2) The possible variations in the OOP due to AMO

Change in OOP (ΔOOP)	Category of population
$100\% \rightarrow 100\%$	(1) Never insured $\rightarrow$ Never insured
$100\% \rightarrow 30\%$	(2) Never insured $\rightarrow$ AMO
$30\% \rightarrow 30\%$	(3) CNOPS $\rightarrow$ AMO
$\leq^{*} 30\% \rightarrow 30\%$	(4) CMIM/Other insurance $\rightarrow$ AMO
$\leq 30\% \rightarrow \leq 30\%$	(5) CMIM/Other insurance $\rightarrow$ CMIM/Other insurance
$?^{**}\% \rightarrow 30\%$	(6) Private insurance $\rightarrow$ AMO

* The passage from generous insurance to AMO (less generous).
** Reimbursement rates guaranteed by private insurance contracts are unknown to us.

We must note that we do not have the necessary data to investigate the heterogeneous variation of the OOP price and its subsequent impact on drug utilization for each of the categories mentioned in table 2.4.2. Therefore, it would only serve as a clarifying tool while discussing empirical results.

2.4.2 Price Setting

Regulation of pharmaceuticals' price setting is relevant because it reflects the supply side of the market. Moreover, before we jump to the specific price setting in Morocco, we outline how the supply side, in general, is linked to health insurance.

First, as a strategic response, it is plausible to assume, on the one hand, that firms could position themselves for reimbursement by lowering the prices of their drugs, assuming that the government would choose cheaper drugs to put in the reimbursement list. On the other hand, eventual moral-hazard could motivate firms to increase their prices since the OOP would be lower for the patient after the law, therefore benefit from the pre-period's high prices. Second, the change in prices could be an imposition (in the form of re-negotiation) by the government on firms as a requirement for their drugs to be included in the reimbursement list. In that case, the government might enforce that reduction by forbidding firms to change their prices in the future (when the law is enacted). Third, national drug coverage often stipulates that the reference price for reimbursement is the generic's price (when it is available, it could be the cheaper generic in the class or the closest to the brand-name's price), therefore prices could converge to the reference price. Finally, since drug reimbursement would decrease prices faced by patients (in general), firms could consider entering the market because of the potential increase in demand, as a consequence to entry, competition could drive prices down. These potential changes in price are relevant to both the covered and the non-covered populations, since they affect the listed price directly. Furthermore, these changes

before the law could persist during the post period, therefore be accounted for as an impact of national insurance.

Given price regulation in Morocco, it is hard to link, with certainty, the different assumptions outlined above to the specifics of the local setting. However, since every upward revision of price requires prior authorization from the government, it is plausible to assume that manufacturers' attempt to increase prices due to future moral hazard is less likely to occur, unless it is justifiable through the nature of price setting (cost reporting), or it is agreed upon by both parties for other reasons. Positioning for reimbursement (usually in the form of decreasing price) is most likely to take place given that revising price downward does not fall into any regulatory restrictions, other than the three months fixed-price period. Furthermore, whatever the change in price would be, it adds up to the direct effect of insurance on drug utilization through the OOP cost that patients face. In fact, regardless of their reimbursement rate, if drug prices shift as a response to insurance, spillovers would reach the entire population (covered and non-covered), as well as all drugs marketed (reimbursed or non-reimbursed), therefore affecting their utilization in an indirect way.

2.5 Treatment Design and Empirical Approach

Analyzing the impact of health insurance on pharmaceuticals utilization using market data (i.e. drug sales in a market over a time period) is not straightforward. In fact, when individual data is available, insurance status of patients helps identify the shift in utilization that is due to being insured. For example, studies that investigate the impact of Medicare or Medicaid on drug utilization in the US exploit the individual variation in coverage to estimate the causal effect of insurance. However, when only market data is available, knowing the origin of utilization is not possible, as we only observe the market outcome, in other words, total demand by both the covered and the non-covered populations. Nevertheless, the source of variation when only market data is available is whether a drug is reimbursed or not. Furthermore, we cannot argue that reimbursed drugs are only demanded by covered patients, as those drugs might be prescribed to the rest of the population as well. Consequently, the impact of insurance on drug utilization is twofold. On the one hand, the shift in demand that comes directly from the decrease in the out-of-pocket (OOP) price due to insurance, which is specific to the covered population only. On the other hand, the shift in

demand that is due the impact of health insurance on the pharmaceutical industry market (supply), as it is the only way that the spillover would reach the non-covered population (not exclusively however), therefore affect their demand.

Given the specificity of the data we possess, we analyze the impact of health insurance on drug utilization by taking a drug as unit of observation, and drug's reimbursement status as treatment. For this study, our market is the Moroccan pharmaceutical market between 2000 and 2012, and our treatment is the national health insurance scheme (AMO).

The national health insurance law was announced in 2002, guaranteeing partial or total reimbursement of pharmaceuticals that are eligible for reimbursement. In 2005, the Ministry of Health published Decree (n°2-05-733) that outlined the modalities of implementation of the law, specifically, which pharmaceuticals and at what rate would they be reimbursed. Accordingly, the first list of drugs eligible for reimbursement was published later in 2005, and five subsequent lists were published between 2006 and 2012[16]. A list of reimbursable drugs at a given period contains the international non-proprietary name (INN) of drugs; their therapeutic classes; their strengths; and the routes of their administration; that would be reimbursed starting from that period. In addition, once a drug is included in the reimbursement list, it stays in the list[17]. Therefore, our treatment design is a staggered design, where each treatment group contains drugs included in each published list, and its treatment period is the corresponding date of publication.

In light of recent advances in the econometric literature when dealing with staggered design studies (Borusyak & Jaravel (2018), De Chaisemartin & d'Haultfoeuille (2020), Goodman-Bacon (2021), Sun & Abraham (2021), and Callaway & Sant'Anna (2021)), the standard two-way fixed effects (TWFE) estimator is no longer the ideal go-to specification, solely because of the strong assumption of homogeneous treatment effects. Instead, a body of alternative estimators were proposed by the aforementioned authors (except that of Goodman-Bacon (2021), as it outlines TWFE's blind spot only), out of which we choose to work with the Callaway and Sant'Anna estimator (referred to as SC in the rest of the paper). The reason why SC is preferable to other estimators in our setting is its flexibility regarding the parallel trends assumption, as it offers the possibility to include covariates to account for a 'conditional parallel trends'. In fact, since our

[16] See Section 3.5, Subsection 2.6.1, for details.

[17] Delisiting of drugs did not occur during our period of analysis. In addition, official documents did not refer to delisting as a possible act by the Ministry of Health.

treatment is the choice of drugs to include in the reimbursement list, the parallel trends assumption is guaranteed to fail because governments do not assign reimbursement randomly, on the contrary, a lot of scrutiny precedes such national schemes. Therefore, it is safe to say that drugs with some specific attributes were prioritized over others, thus, failing the parallel trend assumption required for the identification of the causal effect. In addition, the richness of the SC estimator comes also from the possibility to use either to 'never treated' or the 'not-yet treated' drugs as a control groups at a particular time period. The latter group gives more identification power (more observations), however, it dictates that pre-trends should be restricted.

As for the reason why the standard TWFE is not ideal in our case, not all staggered designs are (or could be) forgiving. In fact, choosing some drugs to treat first and others to treat later differs from choosing to treat some States with a program first and others later. The dynamic effects in the latter design are likely to be independent between states, whereas those in the former are correlated, because a drug that is reimbursed later could impact the outcome of an early-treated drug.

Another specificity of our design is the gap between the announcement and the implementation dates of the new law. Alpert (2016) show that accounting for patients' anticipatory response (demand side) significantly reduced the estimated total effect of Medicare Part D (prescription drug benefit). Though the paper focuses only on the demand side, we suspect that the anticipation is relevant to the supply side as well, which is, to our knowledge, scarce in the literature[18] (see Subsection 2.4.2).

Our design consists of a treatment where the Ministry of Health chooses which drugs to reimburse after the implementation of AMO, a treatment that only the target population (the working population) would benefit from. Since we only observe the market outcome (sales), we cannot disentangle, with certainty, whether the target population would be acting in anticipation to the law. However, all we can observe is the total drug utilization, and at best, utilization by reimbursement status at each period (i.e, reimbursed and non-reimbursed drugs). Furthermore, for anticipation to make sense, both groups' utilization should shift in the same direction before the implementation, since future-reimbursed drugs list is not known to any agent in the market (manufacturers, doc-

[18] Duggan & Scott Morton (2010) and Duggan & Scott Morton (2006) offer, in part, insight on the impact of drug coverage on the supply side of the pharmaceutical market. They do not address the anticipatory effects however.

tors, pharmacists, or patients), otherwise, either the market could anticipate which drugs are going to be selected for reimbursement (doctors recommendations or/and strategic positioning by manufacturers), or the government chose drugs based on their outcomes between the announcement and implementation dates of the law (doctors prescriptions or/and manufacturers response). To test whether such trends took place in our setting, we will present (see subsection 2.7.1) graphical evidence on trend breaks in the market outcomes time series, sales and prices (similar approach to that used by Jayachandran et al. (2010)).

Formally, the first step of estimating the parameter of interest that would capture the impact of the Moroccan national health insurance (AMO) on drug utilization is to estimate the individual average treatment effects (ATT's) for each of the groups of drugs first treated at each time period g (i.e., reimbursement list), in calendar time t:

$$ATT(g,t) = \mathbb{E}[Y_t(g) - Y_t(0) | G_g = 1], \text{ for } t \geq g \tag{2.5.1}$$

where Y_t is drug utilization at time t and G_g is a binary variable that is equal to one if a drug is first treated in period g.

After recovering all the $ATT(g,t)$'s, which are simply all the possible 2×2 differences-in-differences that could be derived from the treatment design, Callaway & Sant'Anna (2021) propose a number of ways to aggregate group-time average treatment effects. The most relevant aggregations would be the total average, across groups and time, of the individual $ATT(g,t)$'s (which would give the unbiased version of the TWFE's estimator); the group-specific average effect, to highlight treatment effect heterogeneity with respect to treatment adoption period; and treatment time-specific average effect, to highlight treatment effect dynamics (event-study).

2.6 Data

We briefly describe each data source here. Additional details can be found in the appendix.

2.6.1 Reimbursement Data

Data on drugs' reimbursement status (whether a drug is ever reimbursed, or in which period it was reimbursed) is constructed based on the lists that were published by the Ministry of Health in the official Orders. We identified six lists (official Orders) between the implementation date of AMO (third quarter of 2005) and 2012[19]. According to Article 8 of Decree n°2-05-733, reimbursement lists were established by international non-proprietary name (INN), therapeutic class, concentration of the active ingredient, and route of administration. Table 2.6.1 summarizes the number of drugs included in each reimbursement list (by date of publication).

Table (2.6.1) Drug Reimbursement by AMO

	Molecule Level			Presentation Level		
	Matched count	Not Matched count	Total count	Matched count	Not Matched count	Total count
05Sep2005	133	29	162	324	47	371
15May2006	17	21	38	43	44	87
04Aug2006	86	5	91	228	13	241
19Mar2008	122	14	136	312	30	342
02Jul2010	64	15	79	146	31	177
20Feb2009		1	1		3	3
N	422	85	507	1053	168	1221

- Ministerial Orders. Author's rearrangement.

Between 2005 and 2012, 507 drugs (in 1221 presentation froms) were decided to be reimbursed by the new national health insurance (AMO). 'Molecule Level' counts the number of drugs by their INN, and 'Presentation Level' takes into account their dosage forms (i.e., strength and route of administration). The 'Matched' and 'Not Matched' differentiation refers to an ex-post merge with market data (see Subsection 2.6.2), in other words, 'Not Matched' drugs are drugs that were included by the Ministry of Health but that we could not find in the utilization data during that period of time. One possible explanation is that the published lists contain all medicines that are approved and are eligible for reimbursement, whether they are dispensed at a pharmacy or they are restricted to hospital use only, whereas utilization data is restricted to the retail market only. As a consequence, 'Not Matched' drugs are dropped from our analysis, leaving us with 422 (1053) reimbursed drugs (presentations)[20].

[19] Orders n°2517-05 (2005q3), n°1687-06 (2006q2), n°929-06 (2006q3), n°601-08 (2008q1), n°477-09 (2009q3), and n°1653-10 (2010q3).

[20] In appendix **??**, we outline how the final dataset was constructed, starting from the raw Ministry files. We also report all the drugs that fall into the 'Not Matched' category.

Our main study is at the molecule level. Accordingly, the reimbursement date of a drug is the date of the earliest reimbursement list that includes at least one of its presentation forms. The consequences of aggregating to molecule level are not unknown to us, however. First, assigning the earliest reimbursement date to all presentation forms of a molecule alters the treatment period of drugs, in other words, we would not capture the true reaction to reimbursement at the right time. Moreover, it would problematic only if the impact of drug coverage reaches the presentation level of the supply side, i.e., manufacturers adjust their supply (drugs or prices), thus affecting market outcomes. Second, reimbursing only one presentation of a drug would probably push doctors (assuming perfect information) to switch their prescriptions to the only reimbursed presentation within that drug. In that case, we assume that the gain in sales of the reimbursed presentation(s) is equal to the loss in sales of other non-reimbursed presentations of the same molecule, such that if all presentations were to be reimbursed, gains would be attributed uniformly. However, it would not be equal if substitution occurs between (similar) reimbursed molecules, but even in that case, it would not impact the (general) results since it is within reimbursed drugs. Finally, to address all this issues, future estimation will be at the presentation level.

2.6.2 Drug Utilization Data

Utilization data is provided by IQVIA, the MIDAS database. It gathers all drugs transactions (quantities and revenues) in a given market, the Moroccan retail market for instance, as well as a variety of drug characteristics. The unit of observation in MIDAS is the pack level of a drug, i,e,. its different presentation forms, its origin (corporation and manufacturer), its licensing status (brand-name, licensed, ...), as well as its launch dates (globally and locally, it would serve to calculate drug age). Utilization data are reported quarterly using different measures. For sales in quantities, measurement units that are included are the number of Units, the number of Counting Units, and the number of Standard Units[21]. Revenues are reported at the three levels of a market's supply chain: manufacturers, wholesalers, and retail pharmacies. Prices are deduced by dividing revenues by sales in quantities. Since our analysis is at the molecule level, the MIDAS database is also aggregated accordingly by taking the sum of all sales variables. For Morocco, only retail

[21] Units are the number of packs sold. Counting Units are the number of tablets, millilitres of liquid, grams of ointment sold. Standard Units are the number of standard 'dose' units sold (the number of counting units sold divided by the smallest common dose of a product form as defined by IQVIA).

market is available, therefore, merging with reimbursement data restrict the latter to only drugs that are sold at a pharmacy.

MIDAS variables that are included in the main specification are drug utilization in Units, price per unit, and drug age (based on its global launch date, since the analysis is at the molecule level). Various robustness checks using other variables are estimated and reported in the appendix.

2.6.3 Other Data

The other sources of data that we are using in this study are the global burden of disease (GBD) database and the French HAS's ASMR evaluation data.

The first database reports annual country specific health outcome measures linked to their corresponding diseases. However, the GBD database does not provide these measures for a disease matched to that disease's treatments, and since our analysis is at the drug level, matching drugs to burden measures is necessary. To do so, we use NIH's UMLS (Unified Medical Language System) Terminology Services (UTS) and Medical Subject Headings (MeSH) services[22] to link MIDAS drugs to the diseases that they treat or prevent, and eventually to the burden of those diseases from GBD (See Appendix of the third paper of this thesis for details on the mapping). The variables that we retain as health outcome measures are Mortality, Prevalence, and DALYs (disability-adjusted life years).

The second additional source of data concerns how the French government (via the HAS) evaluates drugs for reimbursement. In fact, prior to pricing and reimbursement negotiations in France, the HAS provides two assessments of a drug: Service médical rendu (SMR) (is a drug important to be reimbursed); and Amelioration du service médical rendu (ASMR) (added therapeutic value of a drug relative to other treatments available). We use SMR as a measure of importance, and ASMR as a measure of innovation. As they are defined, the SMR has three levels: Important, Moderate or Low, and Insufficient; the ASMR has five levels: ASMR I (Major), ASMR II (Important), ASMR III (Moderate), ASMR IV (Minor), and ASMR V (Non-existant). However, this evaluation is only available beginning 2004 onward, with retroactive evaluations products for the late 1990s. Moreover, we expect the majority of drugs not to be matched to an SMR/ASMR value,

[22] See https://www.nlm.nih.gov for more details about UTS and Mesh.

since not all drugs that are marketed in France are necessarily marketed in Morocco. For robustness purposes, we will estimate some specifications using only drugs with SMR/ASMR values, and others replacing missing values with either zero or a higher value (since a higher value means a worse rating, and assuming that drugs with no SMR/ASMR values are old and presumably less efficient than new drugs).

Merging all databases gives us the necessary information to carry out the analysis. Evidently, the final data set contains, for each quarter of the calendar time between 2000 and 2012, a drug, whether it is reimbursed or not, when was it reimbursed if so (treatment group), its utilization (outcome variable), its price, the severity of diseases that it treats or prevents, its age, and finally its SMR/ASMR evaluation score. Price, severity, age, and SMR/ASMR score are the covariates that we will use for the conditional parallel trends assumption, i.e., identification.

2.6.4 Descriptive Statistics

Table 2.6.2 provides summary statistics for the Moroccan pharmaceutical market between 2000 and 2012. The main summary statistics that we present here differentiate only between the group of drugs that are never reimbursed and the group of drugs that will ever be reimbursed (regardless of their treatment group), during both the pre- and post-treatment periods (the post-treatment period for drug that are ever treated is the date of the implementation of the law). In the appendix, the same statistics are reported by group of treatment. Utilization and price variables provided in the table measure the variation in each variable relative to the first quarter of our period of analysis (or the drug's first quarter of sales in the market).

On average, over the entire period, drugs that will ever be reimbursed increase utilization more and price less than drugs that will remain out of the reimbursement list. In addition, they are more important drugs, more innovative, have less substitutes within their disease class (defined at the third level of the ATC), and treat more burdensome diseases (in all health outcome measures). Furthermore, variations in utilization and price are more pronounced in the post-treatment period. In fact, after the implementation of AMO, both groups reacted positively and increased utilization. Moreover, ever-reimbursed drugs had a significantly higher increase than never-reimbursed drugs. The slight increase in utilization in the pre-treatment period would suggest possible violation of the parallel trends assumption before treatment. Regarding price, despite the overall modest up-

ward shift, ever-reimbursed drugs had, on average, stable prices, whereas never-reimbursed drugs continued to raise prices. More importantly, the table only highlights the differences between ever- and never-reimbursed drugs, concealing, as a results, heterogeneities across treatment groups. Differences in utilization and price across groups is graphically analysed in the next section.

Differences in the other variables suggest that, in the absence of treatment, ever-reimbursed drugs are systematically different than never-reimbursed drugs, which would result in higher utilization. Controlling for these covariates is necessary to disentangle treatment effects from other drug characteristics effects.

Table (2.6.2) Descriptive Statistics

	Pre-Treatment Period 2000-2005					Post-Treatment Period 2005-2012					Overall Period 2000-2012				
	N	Mean	SD	Min	Max	N	Mean	SD	Min	Max	N	Mean	SD	Min	Max
Never Reimbursed Drugs															
Drug utilization (units), indexed	17262	1.31	6.92	0	243	23350	4.59	74.19	0	4161	40612	3.19	56.46	0	4161
Price (per unit), indexed	12058	1.02	0.20	0	7	13526	1.06	0.46	0	12	25584	1.04	0.36	0	12
Log(DALYs)	2327	12.02	1.99	0	15	3320	12.23	1.93	0	15	5647	12.15	1.96	0	15
Log(Mortality)	1693	7.28	2.61	1	12	2415	7.55	2.63	2	12	4108	7.44	2.63	1	12
Log(Prevalence)	2327	15.28	2.20	0	18	3320	15.42	2.10	0	18	5647	15.36	2.14	0	18
Drug age in years	17262	16.76	11.82	0	64	23350	21.39	12.25	0	70	40612	19.42	12.29	0	70
SMR score	17262	3.48	1.03	1	4	23350	3.45	1.06	1	4	40612	3.47	1.05	1	4
ASMR score	17262	5.88	0.52	1	6	23350	5.85	0.59	1	6	40612	5.86	0.56	1	6
Number of substitues	17262	11.01	8.36	0	32	23350	11.77	8.83	0	34	40612	11.45	8.64	0	34
Number of local manufacturers	17262	0.90	0.75	0	10	23350	0.93	0.86	0	10	40612	0.92	0.82	0	10
Number of generics	17262	0.82	0.42	0	2	23350	0.81	0.42	0	2	40612	0.81	0.42	0	2
Ever Reimbursed Drugs															
Drug utilization (units), indexed	7856	1.54	3.20	0	120	10930	5.39	16.26	0	262	18786	3.78	12.71	0	262
Price (per unit), indexed	7264	1.02	0.23	0	5	9786	1.02	0.31	0	5	17050	1.02	0.28	0	5
Log(DALYs)	5462	12.68	2.05	7	16	7490	12.82	2.03	7	16	12952	12.76	2.03	7	16
Log(Mortality)	4702	7.94	2.99	0	13	6416	8.19	2.94	0	13	11118	8.08	2.96	0	13
Log(Prevalence)	5462	15.48	1.63	9	18	7490	15.59	1.60	10	18	12952	15.54	1.62	9	18
Drug age in years	7856	17.66	10.27	0	64	10930	21.94	10.86	0	70	18786	20.15	10.83	0	70
SMR score	7856	1.56	1.10	1	4	10930	1.57	1.11	1	4	18786	1.57	1.11	1	4
ASMR score	7856	5.15	1.16	1	6	10930	5.10	1.19	1	6	18786	5.12	1.18	1	6
Number of substitues	7856	8.04	6.67	0	32	10930	8.96	7.45	0	34	18786	8.57	7.15	0	34
Number of local manufacturers	7856	1.28	1.70	0	14	10930	1.67	2.18	0	15	18786	1.51	2.00	0	15
Number of generics	7856	0.56	0.59	0	2	10930	0.61	0.61	0	2	18786	0.59	0.60	0	2

2.7 Results

2.7.1 Trend Breaks in Utilization and Price Time Series

Drug Utilization

Figure 2.7.1 plots drug utilization between 2000 and 2012 by treatment group. All graphs show drug utilization on a normalized log scale (solid black curve), and on a deseasonalized normalized log scale (dashed red curve). The vertical solid line indicates the 'Treatment' date for each treatment group, and for the 'Never Reimbursed' group, it indicates the date of the beginning of the treatment (implementation of AMO). The vertical dashed line refers to the 'Announcement' date of the national health insurance. All groups show increasing utilization over time, but with heterogeneous trends.

The first group of drugs (Figure 2.7.1b) showed steeper increase in utilization right after the publication of the first list of reimbursed drugs. Moreover, a slight reaction to the announcement of the law is noticed, however, its magnitude seems to be marginal to assume that an anticipation has taken place. The second and the third groups of reimbursed drugs (both treated in the same year, 2006) displayed less noticeable breaks of utilization trends in reaction to both the announcement and the treatment. In fact, the second group (Figure 2.7.1c), while comprising a small set of drugs (17 drugs), had continuous increase in utilization with a slightly slope increase around 2008, two years after being treated. Similarly, the third group (Figure 2.7.1d), which is significantly large, also displayed continuous increase in utilization with a hardly visible positive change in trend around its treatment period. The fourth and fifth lists of reimbursed drugs has resulted also in increased utilization of the drugs that they included, in a different manner, however. On the one hand, drugs that were treated in the fourth wave (Figure 2.7.1e) showed pronounced positive reaction during the period of treatment of the first group than to its treatment, which, on the contrary, led to flatten the curve right after the publication of the list. On the other hand, the last group of reimbursed drugs (Figure 2.7.1f) is the only group that shifted from a downward slope to an upward one as a reaction the national health insurance, not around the treatment period however, but right after the announcement by the end on 2002. In addition, a marginal change in the upward trend could be picked up around 2006, which is also far from the effective reimbursement date. For this last group, the short window of post-treatment periods is limiting us from, before all, having

visuals of the mid- to long-term effects of the treatment. Finally, the immediate change in the curve of utilization of drugs that were never reimbursed (Figure 2.7.1a) after the implementation of AMO (i.e., the publication of the first list of reimbursement) indicates that the newly set national health insurance did not affect drugs that were treated only, but had spillovers that reached drugs that are kept out of the benefit plan as well.

Furthermore, It is important to keep in mind that the graphs show an average trend by treatment group, in other words, heterogeneity that is coming from the different therapeutic classes that are in the market (Cardiovascular Drugs vs Dermatologicals, for example) is hidden. Drug utilization by treatment group and therapeutic class are reported in the online appendix.

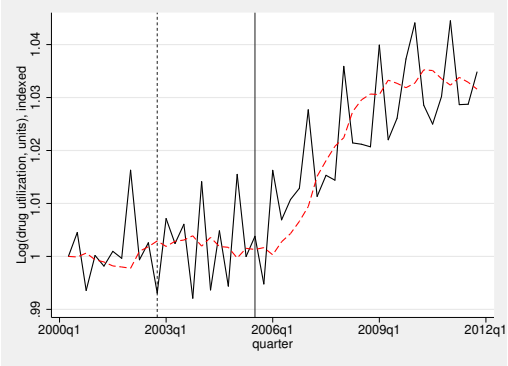
Trying to explain the different observed trends from only the graphical visualization is complex and somewhat premature. In fact, it is only after running a robust analysis that we can refer back to the graphs and offer clarity. Controlling for covariates that affect utilization is necessary, as well as disentangling those that might be an outcome to the treatment per se. Utilization responds to a variety of demographics even in the absence of insurance. Its increase could be a sign of increasing demand from a disease burden point of view. It could also respond to changes in the pharmaceutical market through price or/and entry (since they are correlated). However, as we argued in subsection 2.4.2, price is endogenous to reimbursement, in both directions. Reimbursement could be favored because of price, and price could be impacted by reimbursement. Dealing with this endogeneity in a proper manner requires that we model the supply side of the market as well, which would lead to a structural analysis. However, it currently falls out of the scope of this paper, but remains the immediate extension to this study in future work. As a remedy, we investigate price trends in the same manner as drug utilization.

Price

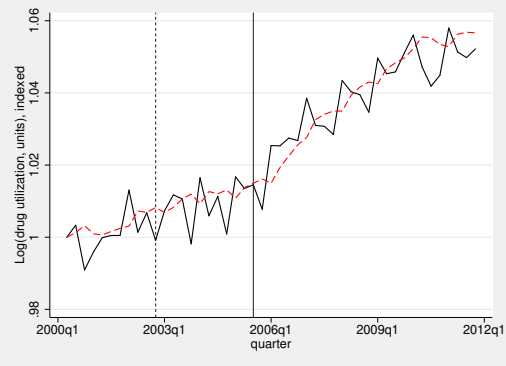
Overall, prices seem to have increased between 2000 and 2012 (Figure 2.7.2). Whether it is a response to the national health insurance, an anticipation, or a general market trend depend on each group of drugs. While the average prices increase for all groups have not exceeded 10% relative to 2000's price, analyzing their evolution is important as it reveals potential market mechanisms.

Three features of price evolution are displayed. First, reimbursement increases prices and sta-

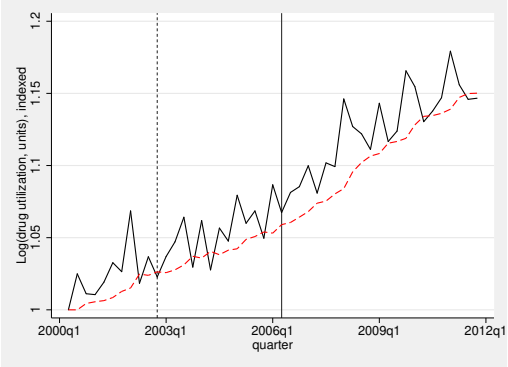
Figure (2.7.1) Drug Utilization (in logs, indexed) by Treatment Group, 2000-2012



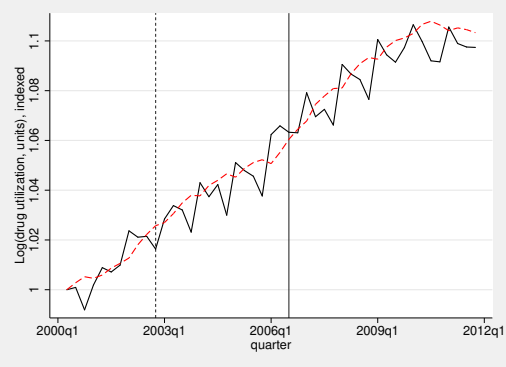
(a) Log drug utilization, indexed.
Never Reimbursed



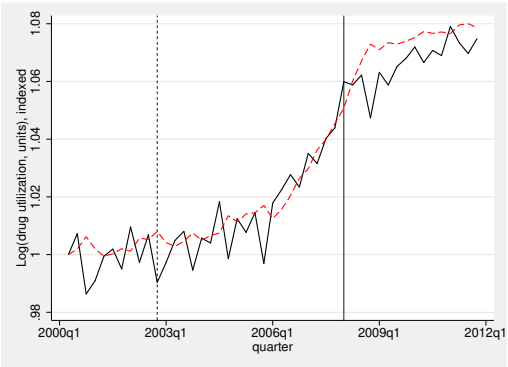
(b) Log drug utilization, indexed.
Reimbursed, 1^{st} group



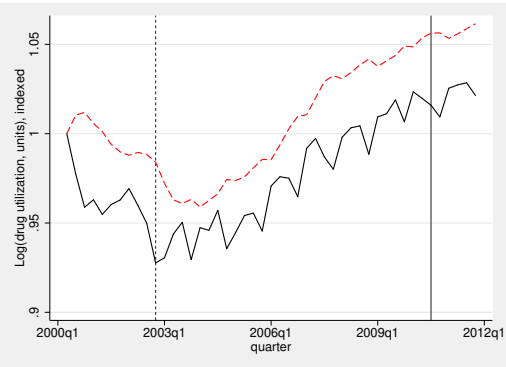
(c) Log drug utilization, indexed.
Reimbursed, 2^{nd} group



(d) Log drug utilization, indexed.
Reimbursed, 3^{rd} group



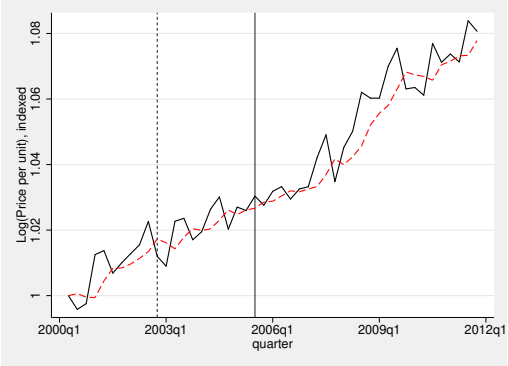
(e) Log drug utilization, indexed.
Reimbursed, 4^{th} group



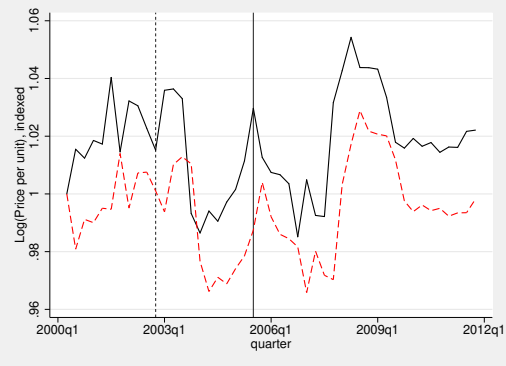
(f) Log drug utilization, indexed.
Reimbursed, 5^{th} group

Notes: The solid vertical line refers to the 'Treatment' date for each treatment group. The dashed vertical line refers to the 'Announcement' date. The black curve refers to normalized log drug utilization. The red curve (when present) refers to normalized deseasonalized log drug utilization.

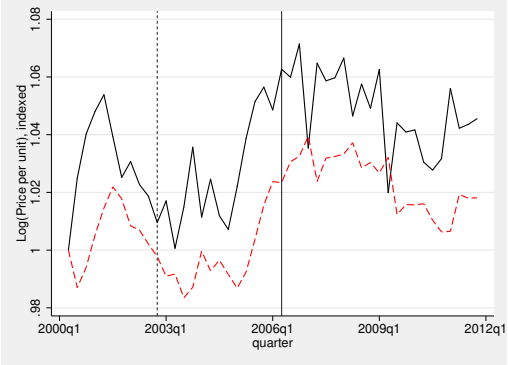
Figure (2.7.2) Price per unit (in logs, indexed) by Treatment Group, 2000-2012



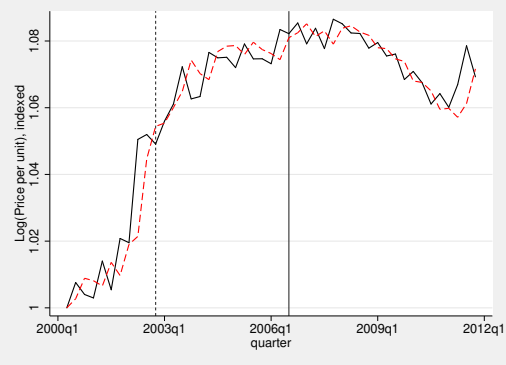
(a) Log price per unit, indexed.
Never Reimbursed



(b) Log price per unit, indexed.
Reimbursed, 1^{st} group

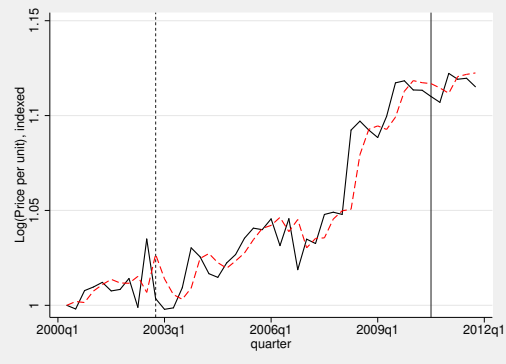


(c) Log price per unit, indexed.
Reimbursed, 2^{nd} group



(d) Log price per unit, indexed.
Reimbursed, 3^{rd} group

(e) Log price per unit, indexed.
Reimbursed, 4^{th} group



(f) Log price per unit, indexed.
Reimbursed, 5^{th} group

Notes: The solid vertical line refers to the 'Treatment' date for each treatment group. The dashed vertical line refers to the 'Announcement' date. The black curve refers to normalized log price. The red curve (when present) refers to normalized deseasonalized log price.

bilizes them. In fact, this feature is shown in figures 2.7.2d, 2.7.2e, and 2.7.2f. Two possible explanations could be argued: on the one hand, because data is left censored in the first two cases, we could assume that, in general, prices were in an upward slope (that we do not observe), and that trend was halted by reimbursement, either the government has imposed (or negotiated) that prices should be stable once they are reimbursed, or manufacturers have stabilized their prices in order to be fit for reimbursement. However, we could not say if the prior increase in price is an anticipation to future moral hazard or just a market trend. The last figure, on the other hand, sheds light on this and suggests that manufacturers react to insurance and increase their prices before they get stabilized. Moreover, it also indicates that the government possibly constrains manufacturers after reimbursement. Second, figures 2.7.2b and 2.7.2c do not show any noticeable trend, high variation could imply high heterogeneity within those groups. Finally, the last feature is displayed by the never-reimbursed group. Figure 2.7.2a shows that drugs that are never reimbursed continued to raise price over the entire period (a positive change in slop is observed around 2008), suggesting in part that reimbursement stabilizes prices.

The increase in utilization of never-reimbursed drugs, in addition to the continuous increase in their prices could be explained by various mechanisms. While it is only a part of the population (40% in 2013) that is benefiting from drug coverage, 60% of a population left without reimbursement is reasonable incentive for manufacturers to increase prices. However, for that explanation to hold exclusively, we have to assume that reimbursed drugs are only consumed by covered patients (or at least in a significant proportion), which is not possible, as reimbursed drugs are prescribed to non-covered patients as well. Therefore, it is plausible that the increase in price of never-reimbursed drugs is meant for the treated population as well. In fact, reimbursing part of a given household's medical bill leaves room for unmet medical needs (in this example, we only refer to pharmaceuticals), which probably is in the form of additional withheld treatments that has no reimbursed substitute. In that case, both demand and price would increase as a result to health insurance. Finally, another possible explanation is previously suggested by Duggan & Scott Morton (2010), where they find that uninsured patients are less price-sensitive than insured patients, which they explained by the group purchasing power of Medicare Part D insurance. Similarly to our case, the government is the only buyer of AMO insurance, giving it the necessary purchasing power to negotiate lower prices or lower increases in price.

2.7.2 Regressions

Table 2.7.1 and figures 2.7.3 and 2.7.4 show results from the model specified in Section 3.4. The baseline model includes only the treatment variable (reimbursed or not), whereas the second model controls for covariates that characterize drugs. These covariates include drugs and their disease class characteristics. Results indicate that, aggregating across all groups and periods, national health insurance (AMO) had a significant positive effect on drug utilization only when no covariates are included in the model. Evidently, controlling for attributes that could have explained the selection into reimbursement captures much of the increase in utilization. This indicates that reimbursed and unreimbursed drugs differ structurally from each other, and that difference explains their utilization. However, we emphasize the fact that even if the baseline model does not show an increase in the use of covered drugs relative to those that were excluded controlling for their attributes, it does indicate that the overall use of drugs has increased after the expansion of health insurance. It possibly reflects the increase in the utilization of healthcare as a whole, with pharmaceuticals as a consequence.

Table (2.7.1) Average Treatment Effect, Utilization in Units

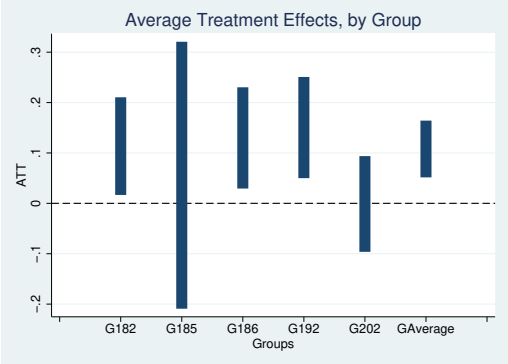
	Control Group: Never Treated		Control Group: Not-Yet Treated	
	Basline	Covariates	Baseline	Covariates
ATT	0.118^{***}	0.0566	0.112^{***}	0.0452
	(0.025)	(0.073)	(0.024)	(0.056)
Observations				

Standard errors in parentheses

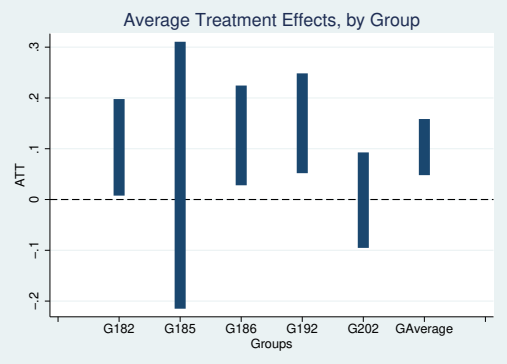
* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$

Moreover, aggregating by treatment cohorts, figures 2.7.3a and 2.7.3b suggest that groups (G182, first group), (G186, third group), and (G192, fourth group) contribute the most to the identification of the treatment effect (baseline). The absence of statistical significance for both the second (G185, second group) and last (G202, fifth group) groups is due to the small number of drugs and short window of post-treatment periods, respectively. Furthermore, event-study plots show that the more a drug is exposed to reimbursement, the higher its utilization increases (figures 2.7.3c and 2.7.3d). However, they also indicate pre-treatment trends that are more pronounced for larger periods until treatment. In fact, from graphical evidence in figure 2.7.1, almost all treated groups have reacted to reimbursement well before their effective treatment date, therefore, even

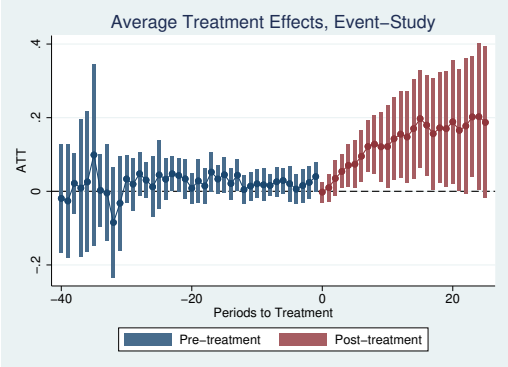
Figure (2.7.3) Impact of AMO on Drug Utilization (in Units), Baseline



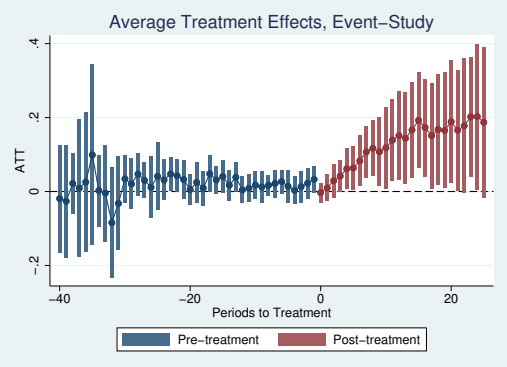
(a) **ATE, by Group**. Never.



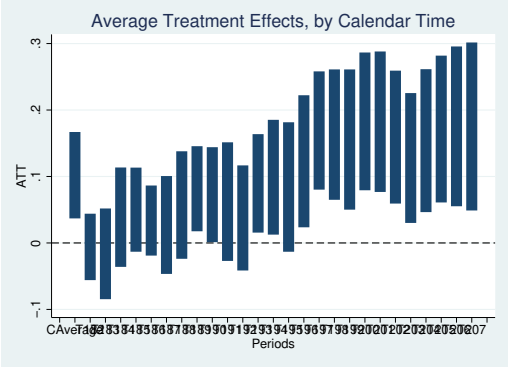
(b) **ATE, by Group**. Not-Yet.



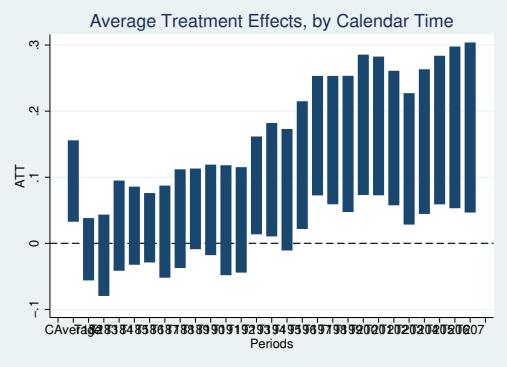
(c) **ATE, Event-Study**. Never.



(d) **ATE, Event-Study**. Not-Yet.

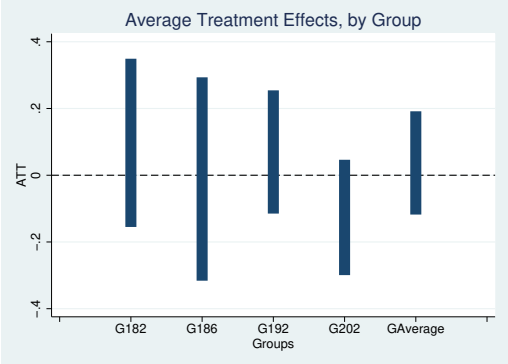


(e) **ATE, by Calendar time**. Never.

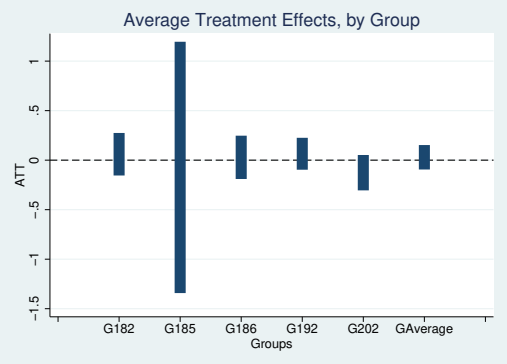


(f) **ATE, by Calendar time**. Not-Yet.

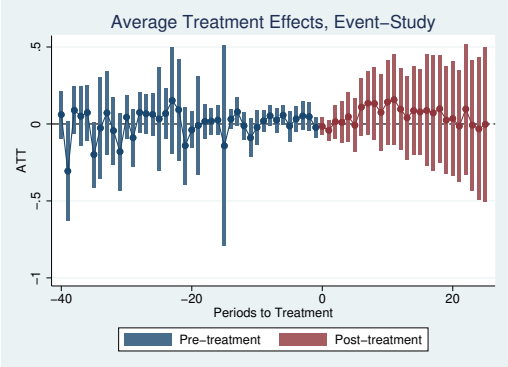
Figure (2.7.4) Impact of AMO on Drug Utilization (in Units), Covariates



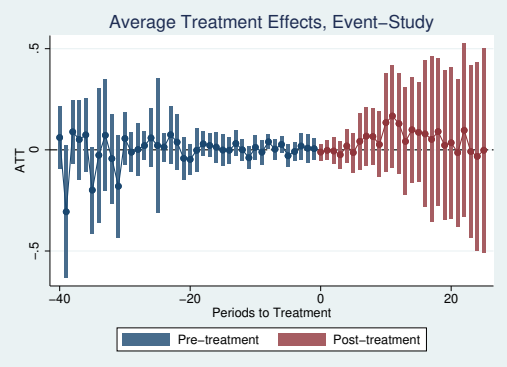
(a) **ATE, by Group**. Never.



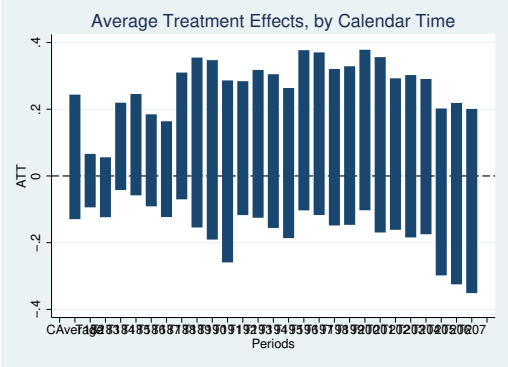
(b) **ATE, by Group**. Not-Yet.



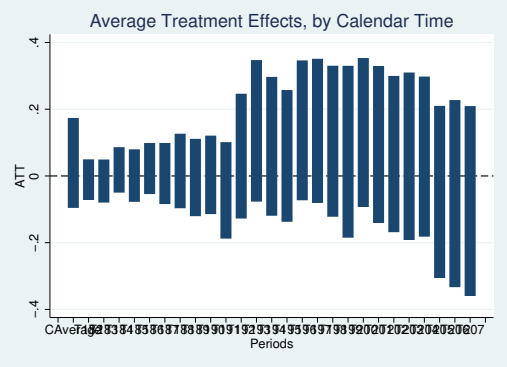
(c) **ATE, Event-Study**. Never.



(d) **ATE, Event-Study**. Not-Yet.



(e) **ATE, by Calendar time**. Never.



(f) **ATE, by Calendar time**. Not-Yet.

when drugs that belong to those groups were waiting for their reimbursement period, their utilization has already been increasing. This result could also be backed by the higher magnitude of pre-trends when we use 'not-yet treated' as control units rather than 'never treated'. The last figures (2.7.3e and 2.7.3f) are obtained by aggregating across all groups by calendar time, indicating that drug reimbursement, first, has been increasing over time in the post-treatment periods, and, second, is more pronounced by the end of our period of study. It refers to the possibly sudden reaction of all groups to the implementation of AMO, and as the time passes by, reimbursement has taken a larger share of drug utilization.

The inclusion of covariates in the model changes the story entirely. In fact, the variables included in the model are attributes that characterize drugs and their therapeutic classes. Consequently, controlling for those differences seems to have captured almost all of the increase in the utilization of drugs reimbursed by national health insurance, suggesting that what makes those drugs consumed more is nearly equal to what led the Ministry of Health to choose them for reimbursement. Moreover, although insignificant, a slight increase in utilization could be observed in periods after the expansion of insurance. This might be explained by a shift towards reimbursed drugs due to their subsidy. The subsequent attenuation could be attributed to several reasons, including insufficient procurement of those treatments in pharmacies or a preference towards unreimbursed drugs, unobserved to us and thus not included in the model.

Heterogeneity across treatment periods is shown to have a significant impact on the results. Table E1 presents the results from a TWFE specification. The baseline coefficient of the TWFE model implies that the increase in utilization due to reimbursement is about three times that from the SC estimation. Adding covariates, the impact is still positive and significant. This validates the literature on the under-performance of TWFE when the design includes treatment with multiple time periods.

2.8 Conclusion

The objective of health insurance is to promote better access to healthcare while ensuring financial protection. To quantify the impact of health insurance on utilization, empirical studies require individual data. 'Individual' is not necessarily 'patient' level data; it could also be prescription

data where each drug is linked to its consumption, but that could be linked to an individual under an insurance affiliation. The change in utilization is then the difference in consumption before and after the expansion of health insurance. If using individual data, it represents the change in a patient's use of healthcare, specifically drugs. If using prescription data, it signifies the change in the number of prescriptions issued to a group of patients under an insurance scheme.

Our paper attempts to quantify a change in drug utilization relying entirely on market-level data. The only relevant source of variation related to insurance that we could use is the reimbursement status of a drug. However, this setting presents numerous caveats that we will try to address in upcoming versions of this study. Firstly, we cannot directly link drug consumption to insurance, as the utilization measured in this study is the aggregate market outcome of a drug. Therefore, the impact that we quantify includes both the effects due to cost-sharing (which is typically what we aim to estimate) and the effects due to changes in the supply of the pharmaceutical industry. Secondly, price is a crucial determinant of utilization, and not including it in the model is not without reason. In fact, it is highly likely that insurance would also impact the price, making it endogenous—both a regressor and an outcome. Although the rate of reimbursement is uniform across reimbursed drugs (with the exception of a subset related to chronic and severe diseases), the fact that reimbursement is based on the generic version's price introduces variation, in addition to the obvious difference between reimbursed and unreimbursed drugs. We would normally include a "net price," equal to the listed price minus the subsidy shared with insurance. If consumers are price-sensitive, even if the net price is lower than the listed price, it would still be unattractive if it is higher than the listed price of a drug that is not reimbursed, affecting utilization as a result.

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Appendices

E TWFE Specification Results

Table (E1) TWFE Specification Results

	Baseline		Covariates	
ATT	0.3416***	0.3463***	0.2051***	0.2089***
	(0.041)	(0.041)	(0.049)	(0.049)
Log(DALYs)			0.5382***	0.4407***
			(0.203)	(0.150)
Has generic version=1			0.7306***	0.7360***
			(0.091)	(0.090)
Number of substitues			-0.2399	-0.2222
			(0.211)	(0.211)
Number of local manufacturers, within ATC3			0.5461***	0.5419***
			(0.160)	(0.161)
Number of generics, within ATC3			-0.1618	-0.1624
			(0.122)	(0.124)
New drug (1990)				0.2762
				(0.207)
Important SMR				0.8608***
				(0.270)
Low SMR				0.5289
				(0.409)
Insufficient SMR				-0.3430
				(1.345)
ASMR I-III				0.0062
				(0.282)
ASMR VI-V				0.1597
				(0.206)
Observations	59398	59398	18599	18599
Drug fixed effects	Yes	No	Yes	No
Disease fixed effects	No	Yes	No	Yes
Time fixed effects	Yes	Yes	Yes	Yes

*** p<0.01, ** p<0.05, * p<0.10. Bootstrap standard errors are between parentheses.

CHAPTER 3

The Contribution of Pharmaceuticals to Improved Health: Evidence from the MENA Region

This is a joint work with Margaret Kyle.[1]

3.1 Résumé

Le lien positif entre la disponibilité des produits pharmaceutiques et l'amélioration des résultats en matière de santé est solidement étayé par des données empiriques. Néanmoins, la relation entre l'utilisation des produits pharmaceutiques et les résultats sanitaires dans les pays en développement et émergents peut différer de celle observée dans les pays développés, principalement en raison de plusieurs facteurs, parmi lesquels l'automédication joue un rôle important. Cet article examine si l'augmentation de l'utilisation des traitements pharmaceutiques est associée à des améliorations significatives de la santé dans neuf pays du Moyen-Orient et d'Afrique du Nord (MENA). En utilisant les différences entre les maladies, les pays et le temps, et en employant des variables instrumentales pour traiter l'endogénéité de l'utilisation des médicaments, nous consta-

[1] Access to the IQVIA MIDAS data is provided through a Third-Party Agreement with Pfizer, Inc. We thank Ekaterina Efimova for sharing some of her code.

tons qu'une utilisation accrue de produits pharmaceutiques a conduit à une diminution des années de vie corrigées de l'incapacité (AVCI), avec une élasticité implicite d'environ 6%. Le coût par AVCI gagnée varie selon les pays et les causes, mais en moyenne, les estimations suggèrent que les produits pharmaceutiques sont rentables

3.2 Introduction

Life expectancy at birth has risen by more than 25 years since 1950, according to the United Nations Population Division. This increase reflects many factors, including fewer or less deadly armed conflicts; improvements in nutrition; public health interventions; expansion of health insurance; and innovations in health care. Pharmaceutical treatments, which are relatively inexpensive to manufacture, easy to distribute, and similarly effective across geographies, represent much of this innovation. The World Health Organization maintains a list of "essential" medicines, consistent with the important role that drugs have in population health.

However, while it has increased at a faster rate than in the developed world, life expectancy developing countries (and particularly in Africa) continues to lag behind that of richer countries. Access to new health technologies is generally slower, and the price of pharmaceuticals may make them unaffordable to most of the population in many developing countries due in part to limited health insurance. In recent decades, some countries have increased the provision of public health insurance that includes (at least partial) reimbursement of drugs.

This paper examines whether increased use of pharmaceutical treatments is associated with significant improvements in health in eight Middle Eastern and North African (MENA) countries. Self-medication, or use of treatments without a prescription or physician supervision, is more common in these markets.[2] If consumers have limited information about what treatments are appropriate and available, their choices may not be optimal or lead to health improvements. In such environments , the relationship between pharmaceutical use and health outcomes may differ from that seen in developed countries. Given the result from the second paper of this thesis – that consumption increased following reimbursement – it is natural to study whether that increased consumption improves health. Finally, even if a positive relationship is established, the treatments

[2] In a systematic review, Alhomoud et al. (2017) and Khalifeh et al. (2017) show that the prevalence of self-medication misuse (over the counter use and antibiotic non-compliance) in Eastern Mediterranean countries is very high.

may be so expensive that they provide little "value for money." This work provides evidence on this point.

We find that more use of pharmaceuticals caused a decline in DALYs, with an implied elasticity of around 6%. The cost per DALY gained varies across countries and causes, but on average the estimates suggest that pharmaceuticals are cost-effective.

3.3 Literature Review

The positive link between the availability of pharmaceuticals and improvement in health outcomes has strong empirical support. A series of studies by Lichtenberg has analyzed the effect of launches of new drugs on longevity in multiple disease areas, countries and time periods. In a sample of 50 upper-middle-income developing and developed countries, Lichtenberg (2005) shows that the launch of new drugs between 1986 and 2000 were responsible for 40% of the gains in life expectancy observed in the sample during the period. Between 2000 and 2009, Lichtenberg (2014*c*) estimates that consumption of drugs introduced after 1990 contributed 73% of the gains in life expectancy. Subsequent studies that are country specific or disease specific have validated the positive effect of new pharmaceuticals on health improvement.[3] Other authors have studied the the relationship between pharmaceuticals and health outcomes in different contexts. Jayachandran et al. (2010) argue that sulfa drugs, a groundbreaking medical innovation in the 1930s, reduced US mortality by 2-3% and increased life expectancy by 0.4 to 0.7 years. Howard et al. (2016) show that new anticancer drugs were associated with an increase in life expectancy, though modest to justify the increase in costs (for example, they show that among patients with breast cancer who received physician-administered drugs, life expectancy increased by 13 months, for an increase in lifetime costs by $72,000). Moreover, in an attempt to explain why medical spending has been declining around 2005, Cutler et al. (2019) conclude that half of the spending slowdown was attributable to slower growth in spending for cardiovascular diseases, half of which was attributable

[3]To cite a few, Lichtenberg (2007) in the US, Lichtenberg (2009) on cancer in the US, Lichtenberg (2003) on HIV in the US, Lichtenberg (2013*b*) on orphan drugs in the US and France, Lichtenberg (2014*b*) in France, Lichtenberg & Pettersson (2014) in Sweden, Lichtenberg (2017*c*) in Australia, Lichtenberg et al. (2014) and Lichtenberg et al. (2017) in Turkey, Lichtenberg (2015*b*) in Slovenia, Lichtenberg (2018*a*) on Cancer, Lichtenberg (2015*a*) on cancer in Canada, Lichtenberg (2016*b*) on cancer in Switzerland, Lichtenberg (2017*a*) on cardiovascular diseases in Switzerland, Lichtenberg (2016*a*) on cancer in Belgium, Lichtenberg (2017*b*) on cancer in Mexico, Lichtenberg (2021) on cancer in New Zealand, Lichtenberg (2020) in Korea, Lichtenberg (2023) in Thailand, Cutler et al. (2007) on hypertension.

to medications controlling cardiovascular risk factors.

Some authors have investigated the contribution of pharmaceuticals on health improvement relative to other health interventions such as imaging and surgery. Lichtenberg (2012) previously showed that pharmaceuticals contributed to about one-third (32%) of the increase in life expectancy in Germany during the period 2001–7, whereas non-pharmaceutical medical innovation (diagnostic imaging innovation) contributed to only 3.6% of health improvement. Buxbaum et al. (2020) show that pharmaceuticals are second only to public health interventions in contribution to improved life expectancy in the US between 1990 and 2015, with 35% of total improvement.[4] Their paper highlights that pharmaceuticals could also result in harm as well as in improvement: their calculated contribution of 35% is the net of a positive effect of 44% and a negative effect of -9%, which they attribute to increases in fatal prescription and nonprescription drug use, particularly opioids.

The afore-mentioned papers use a variety of definitions of pharmaceutical innovation, the most common being the launch of new drugs after a specific year (1990 for example), and of health outcomes, the most common being mortality before a specific age (75 years for example). Almost all of the papers assessing the impact of pharmaceuticals on health improvement use market-level data, a market being a country-year in some, and disease-country-year in others.[5] Because availability of drugs does not necessarily translate into utilization, using the availability of pharmaceuticals to assess their impact on improved health could lead to biased results. Under-use of healthcare services in general, and medication in particular, is a well documented issue. Schafheutle et al. (2002) show that patients' medical management decision (prescription-wise) was influenced by factors such as symptom or disease severity, effectiveness, or necessity of treatment. Although cost was not the overriding influence, it was reflected in the various strategies used by patients to reduce medication cost, such as not having some prescribed items dispensed, taking a smaller dose or buying a cheaper over-the-counter product. Kemp et al. (2010) claim that under-use of medication because of cost was less of an issue in countries with the lowest out-of-pocket costs. Although affordability of drugs is not the focus of our study, we argue that using drug utilization

[4] Public health was broadly defined as reductions in identifiable risk factors for injury or disease not classified in the three following categories: pharmaceuticals; other (non-pharmaceutical) medical care; and a residual category for other/unknown factors.

[5] Lichtenberg (2013*a*) and Howard et al. (2016) are two of the few papers that use patient level data, finding that use of relatively new drugs increases life expectancy.

even at the aggregate level rather than only their availability should yield more accurate results.

While there is an abundance of evidence on the relationship between pharmaceuticals and health outcomes in rich countries, little work has been done on developing countries and the Middle East and North Africa (MENA) region in particular. The most relevant paper to our study is Lichtenberg (2018*b*), in which the impact of new drug launches on longevity growth was assessed in nine Middle Eastern and African Countries (eight of which are included in our study). Results suggest a highly significant inverse relationship between cumulative new chemical entity (NCE) launches and years of potential life lost before age 75 (YPLL75). According to the estimates, an 8-year (2007-2015) increase in the number of post-1992 NCEs ever launched reduced YPLL75 in 2015 by 9.5%, in other words, 2.80 million additional YPLL before age 75 would have been lost in the absence of eight previous years of NCE launches. Disease-specific studies have proven the efficacy of pharmaceuticals in tackling burdensome diseases in developing countries. For example, through the availability and affordability of sofosbuvir (SOF) in 2014 (and other direct acting anti-viral agents after that), Egypt (highest burden of hepatitis C virus (HCV) infection in 2008) has been able to cure more than 4 million patients chronically infected with HCV, reducing its prevalence in the country from 6% in 2015 to an estimated 0.4% in 2021[6] (Waked (2022)). Another example is the expansion of antiretroviral therapy (ART) is sub-Saharan Africa, where ART has proven to reduce HIV/AIDS mortality (Reniers et al. (2014) in Kenya, Malawi, South Africa, Tanzania, Uganda, and Zimbabwe) and morbidity (Lucas & Wilson (2018) in Zambia).

3.4 Empirical Model

3.4.1 Evaluating the Benefits of Increased Access to Pharmaceuticals

The most straightforward approach to estimating the benefits of particular pharmaceutical intervention is, of course, to run a controlled clinical trial. Indeed, evidence of this type is typically required in order for to market a medicine in most countries. This information is also expensive to generate. For example, the National Institutes of Health spent more than $6 billion on clinical studies in the US in 2022,[7] and represents only about 10% of industry spending on clinical trials

[6] The success of SOF-based treatments was in part due to the national screening program implemented in 2018. Its aim was to screen all adults and teenagers in the country who had not been treated for HCV previously, and to treat all those who proved viremic in the shortest time possible (Waked et al. (2020)).

[7] "Clinical Trials and Supportive Activities" from NIH Research Portfolio Online Reporting Tools (RePORT).

(Zhou et al. 2023).

In addition, such studies have limitations in reaching conclusions about the benefits of a new drug in a larger population. Outside of the controlled conditions of a clinical trial, the use of a drug may vary in important ways. The population treated, the expertise of medical practitioners in selecting the appropriate treatment and dosage, and patient compliance can all affect the benefits realized from "real-world" use of the drug. These may be of particular concern when extrapolating the results of clinical trial conducted on patients in relatively rich countries to a developing country context.

Our study instead relies on aggregate (at the country and disease level) measures of health outcomes and the use of pharmaceuticals. Our reasons for choosing this approach are pragmatic: we do not have access to patient-level information on medical care (including drugs) or health outcomes. As noted in our review of the literature, a large body of research in health economics has similarly relied on aggregate data.

The key challenge we face is linking specific pharmaceuticals to a health outcome for which they are expected to have an effect and that we can observe. We describe the process of linking drugs to diseases and health outcomes in Appendix F.

3.4.2 Estimation

We estimate the following equation:

$$\ln y_{idt} = \alpha_{id} + \delta_t + \gamma \mathbf{x}_{idt} + \beta m_{idt} + \varepsilon_{idt} \tag{3.4.1}$$

where y_{idt} is the health outcome in disease d for country i at year t, α_{id} is a country-disease fixed effect, δ_t is a year effect, $\mathbf{x}_{idt}$ are variables such as the prevalence of disease d in country i in year t, and m_{idt} captures the intensity of use of medications in year t for disease d in country i.

An advantage of measuring intensity of use of medications is that this varies over time, due to information about the suitability of these treatments, increases in insurance coverage, changes in price, or new product introductions/withdrawals.[8] In many specifications, we distinguish be-

[8] In contrast, using a count of available medications requires the inclusion of several lags in order to capture this

tween "new" and "old" treatments, allowing for the possibility that more recent products are more innovative and have larger effects on health.

This is essentially a triple-difference estimation using variation across countries, diseases, and time. Fixed effects control for many changes over time and differences across countries and diseases, as does prevalence measured at the country-disease-year level. It is an extension of Jayachandran et al. (2010), who estimate the causal effect of sulfa drugs (a class of antibiotics) on mortality in the US using a differences-in-differences approach. We broaden both the number of countries and diseases considered. It is also similar to many studies by Lichtenberg, except that we measure the intensity of use of medications rather than availability. If the error term ε_{idt} is not correlated with m_{idt}, β can be interpreted as the causal effect of medications on a health outcome.

3.4.3 Identification

While using variation across countries, diseases, and over time allows us to control for many confounding factors driving health outcomes, it is also likely that the use of medications is endogenous. The existence of therapeutically effective pharmaceuticals is the result of research and development (R&D) investments, which are driven by variables such as market size and disease severity. The adoption of medications is also a function of demand or need, or even "taste" for pharmaceutical interventions. Finally, more effective medications may be used more intensively than those with little therapeutic value. If unobserved to the econometrician or omitted from the regression, the $\hat{\beta}$ is a biased estimate of the causal effect of the use of medications on health outcomes.

The literature cited above largely ignores the potential endogeneity. In most papers, authors argue that the use of two-way fixed effects addresses omitted variable bias. In some cases, such as Jayachandran et al. (2010), the discovery of novel treatments is described as exogenous, and diffusion instantaneous. While these conditions may be true for some pharmaceuticals, such as penicillins, innovative effort is generally considered to be an endogenous response to market size, and the adoption of new technologies is a function of (often unobserved) product and consumer characteristics. Lichtenberg (2014*a*) and Lichtenberg (2014*c*) discuss both the endogeneity that might come from the market size effect and endogeneity that might come from omit-

diffusion (e.g., **?**).

ted non-pharmaceutical medical innovation. The former uses exogenous demographic changes as an instrument for market size (similar to Acemoglu & Linn (2004) and Costinot et al. (2019)). Lichtenberg (2014*c*) and Lichtenberg (2014*b*)) present evidence that pharmaceutical and non-pharmaceutical innovation are not correlated across countries or diseases, suggesting that failure to control for non-pharmaceutical innovation is likely to bias estimates.

This paper extends the literature by using instrumental variables in addition to a rich set of controls. We propose three instruments. The first is a measure of global demand for treating a disease, which we proxy for using prevalence in all countries except country i. This should be correlated with the development and introduction of new treatments, but have no direct effect on the health outcome in country i. Second, we use the intensity of use of medications for other diseases within the same country. This should be correlated with the use of medications for disease d in country i, due to a taste for drugs versus other health interventions for example, but have no direct effect on the health outcomes associated with disease d. Finally, we use the intensity of use of medications treating disease d in other countries. This should be correlated with the quality of those treatments, but again have no direct effect on the health outcome in country i.

3.5 Data

3.5.1 Health outcomes

Our measures of health outcomes come from the Global Burden of Disease (GBD) dataset created by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington.[9] We focus on disability-adjusted life years (DALYs), and present results using mortality in Appendix G. DALYs are relevant for diseases that reduce quality of life, but that are not necessarily fatal. The GBD provides annual estimates for more than 300 causes at the country level, at different levels of aggregation. For example, the non-communicable disease category (level 1) includes cardiovascular disease (level 2), which includes stroke (level 3). We exclude causes that are not typically addressed by pharmaceuticals, such as injuries, and we focus on level 3 causes.

[9] See the IHME website for more detailed information on this dataset.

3.5.2 Pharmaceutical consumption

To construct measures of pharmaceutical consumption, we use the MIDAS dataset from IQVIA. This provides information on retail units sold and revenues at the presentation level (e.g., a package of 30 acetaminophen tablets of 300mg) for each manufacturer of a pharmaceutical. We have this information for nine MENA countries (Algeria, Egypt, Jordan, Kuwait, Lebanon, Morocco, Saudi Arabia, Tunisia, and the United Arab Emirates) for the period 2000-2019.

Each pharmaceutical must be matched to a specific disease or cause, in order to create a measure of the intensity of pharmaceutical use at the cause level. In order to link drugs to diseases, we exploit tools provided by the Unified Medical Language System (UMLS) from the National Library of Medicine in the US. We determine the list of pharmaceuticals that, according to the Medication Reference Terminology within the UMLS, may treat or prevent each cause from the GBD (see Appendix F for details).

With a list of all treatments for each disease, we construct a measure of intensity of use as follows. We determine the number of packages sold in a country-year across all presentations and manufacturers of drugs that treat or prevent a specific disease, and index this to the year 2000. This intensity measure captures both increased use of existing drugs and the introduction of new treatments over time.

While we believe this measure is an improvement on the approach in much of the literature, it has a number of limitations. The first concern is that most drugs are available in multiple strengths and package sizes. We are assuming that a package corresponds to a prescription, usually a monthly supply for a chronic condition or a course of therapy for an acute condition. We are therefore treating 30 pills of 25 milligrams as "equivalent" to 30 pills of 50 milligrams of the same molecule, under the assumption that each pack is consumed by patients with different clinical needs. Switching a patient from 25mg to 50mg would not change our measure of intensity of use under this assumption. An alternative would be to use the total weight of active ingredients, or the sum of the strengths. However, molecules can differ significantly in the amount of active ingredient necessary.

Though many drugs may treat multiple conditions, we only have total consumption of a given drug. We therefore assume the consumption of that drug for a particular disease is a function

of the disease prevalence. To illustrate, atenolol is a beta-blocking agent normally used for the treatment of hypertension. Our mapping procedure matched it to four cardiovascular conditions: hypertensive heart disease, atrial fibrillation and flutter, ischemic heart disease, and non-rheumatic valvular heart disease. Therefore, we assign units of atenolol to ischemic heart disease as total consumption multiplied by the share of ischemic heart disease prevalence in total prevalence of the four matched conditions. Appendix G includes specifications that allocate sales under two different assumptions. In one case, we assign 100% of consumption to each condition, which clearly overstates the use of a drug for a particular condition. In the second case, we assign all units to the condition with the highest prevalence associated with that treatment.

Finally, we have data only on retail sales, not hospital sales, in this set of countries. Treatments that are likely to be administered in a hospital setting, such as many cancer therapies, are therefore missing from our measure of intensity of use. Future versions will include specifications that exclude diseases for which hospital-administered drugs dominate.

3.5.3 Other controls

Countries differ from each other by their healthcare systems. Country fixed-effects deal with time-invariant characteristics of each country, including their health systems if they do not vary over time. However, in order to improve access to treatment, countries may adopt policies that change healthcare access and delivery over time. The Global Health Expenditure Database (GHED) provides comparable data on health expenditure for more than 190 WHO Member States, including our sample of countries, since 2000.[10] How much countries spend on health, how much of the health spending comes from government, from households out-of-pocket, and how much is covered by any form of health insurance, are all indicators that vary over time and determine health outcomes, and therefore would be included in our analysis as country-specific healthcare covariates, in addition to general economic indicators (GDP per capita, government expenditures, ...).

3.5.4 Descriptive statistics

Tables 3.5.1 provides descriptive statistics of the main variables that are included in our analysis. Health outcome measures – DALYs, mortality, YLLs and prevalence – are rates (per 100,000

[10] See the WHO website for more detailed information on this dataset.

population). Utilization variables are reported in two way: consumption in levels, they are interpreted as thousands of packs consumed; and intensity of consumption, indexed to the year 2000 (or the first year of sales when 2000 is not available). Overall, old treatments (launched in the global market[11] before 1990) are consumed more than new treatments (– after 1990). This is true across all countries and diseases in our data. However, availability and utilization patterns differ. More than 70,000 treatments were available somewhere in the global market by 2019 (all causes combined), but in the sample of MENA countries that are included in this study, only one fifth of total treatments were available locally. Newer pharmaceuticals are not more likely to be available: only 17% of total new pharmaceuticals were marketed in the local market. In fact, despite the fact that more of new pharmaceuticals have entered the MENA market than old treatments, on average, we should note that not all countries displayed the same pattern. For example, the number of old pharmaceuticals in Morocco and Tunisia was about double that of new ones, in contrast to UAE where pharmaceuticals that were launched anywhere after 1990 were double in number of those that were launched before.

Heterogeneity across countries regarding their healthcare systems is provided in Table 3.5.2. The countries included in our sample fall into different income categories – four countries are lower-middle income countries (Algeria, Egypt, Morocco, and Tunisia), two are upper-middle income (Jordan and Lebanon), and three are high income (Kuwait, Saudi Arabia, and United Arab Emirates (UAE)). Healthcare spending increases with income level. These countries differ in how they finance healthcare, which affects access to treatment. While Kuwait, Saudi Arabia, and UAE spend an average of around $2000, the fraction that patients bear as an out-of-pocket (OOP) cost comes down to an average of $395, or 18% of spending. For comparison, France – whose health expenditure is nearly double ($3935) – has a lower OOP cost, at $357. Lebanon's OOP is higher despite the fact that their health expenditure is about half that of rich countries. Moreover, north-African countries (with the exception of Algeria) have the highest OOP spending with the lowest health expenditure per capita.

Furthermore, general government expenditures reflect different levels of government involvement in financing public services, and healthcare in particular. Government expenditures on healthcare in countries included in our analysis vary between a minimum of 5% of general ex-

[11] We define the global launch date as the date of the first registered sales in any country, which is recorded in the MIDAS database.

Table (3.5.1) Descriptive statistics, main variables

	N	Mean	SD	Min	Max
DALYs	18900	173.10	425.42	0	5098
Mortality	12960	4.57	17.64	0	252
YLLs	12960	142.32	462.61	0	4890
Prevalence	18900	3048.32	7617.60	0	51223
Prevalence in other countries	18900	3179.93	7609.77	0	49642
Number of new treatments (1990)	722	4.36	11.68	0	158
Number of old treatments (1990)	945	8.66	13.43	0	109
Treatment use	18900	1457.97	6684.39	0	193615
New treatments (1990) use	18900	73.31	465.24	0	15222
Old treatments (1990) use	18900	1384.71	6485.91	0	192225
Treatment use, unmatched	180	174066.67	256861.97	0	1440157
Treatment use, other countries	18900	11663.19	29652.92	0	297586
New treatments (1990) use, other countries	18900	586.08	2150.05	0	29486
Old treatments (1990) use, other countries	18900	11077.14	28609.24	0	296041
Treatment use, other diseases	18900	151707.95	226082.32	0	1296387
New treatments (1990) use, other diseases	18900	7665.16	13895.02	0	102734
Old treatments (1990) use, other diseases	18900	144042.79	213571.33	0	1193653
Intensity of treatment use	18165	2.77	12.81	0	897
Intensity of use, new treatments (1990)	18165	11.01	107.56	0	6901
Intensity of use, old treatments (1990)	18165	2.41	10.98	0	897
Intensity of treatment use, unmatched	173	2.56	1.59	1	9
Intensity of treatment use, other countries	18165	3.69	8.17	0	188
Intensity of use, new treatments (1990), other countries	18165	54.76	375.26	0	22804
Intensity of use, old treatments (1990), other countries	18165	3.51	8.53	0	188
Intensity of treatment use, other diseases	18165	2.80	1.90	1	11
Intensity of use, new treatments (1990), other diseases	18165	17.40	19.81	1	96
Intensity of use, old treatments (1990), other diseases	18165	2.64	1.69	1	10

Unit of Observation: Disease*Country*Year (Except: Use of unmatched treatments, Country*Year level. Number of treatments, Country*Cause level). Countries: Algeria, Egypt, Jordan, Kuwait, Lebanon, Morocco, Saudi Arabia, Tunisia and United Arab Emirates. Health outcome variables are in rates (per 100,000). Treatment use variables are in thousand units (x1000 packs). Intensity of use variables are indexed to the year 2000, or the first year of sales.

penditures in Egypt and a maximum of 13% in Jordan. Moreover, the share of government's expenditures on healthcare in total health spending is as modest as 32% and 35% in Egypt and Morocco, respectively, and as generous as 80% and 70% in Kuwait, Algeria and Saudi Arabia, respectively.

However, these figures should be interpreted in the context of the cost of healthcare services in general, and pharmaceuticals in particular, as well as the monthly wage in a country. A higher OOP share in a country where treatments are less costly, on average, than treatments in another country where the OOP share is lower may be less of a financial burden to patients. The final OOP cost that patients must pay should be compared to their monthly wage to assess the true burden of healthcare costs. Table 3.5.3 summarizes the different inputs enabling the comparison between the set of countries regarding cost and its burden on patients. To illustrate, on the one hand, the share of OOP cost in Egypt (61.2%) is about three times that of the UAE (20.6%). However, the average price of a pack of treatment in the UAE ($198) is more than five times that of the average price in Egypt ($39). Applying the OOP share of health expenditures, the average cost of a treatment in Egypt comes down to $24, compared to an average of $42 in the UAE. Moreover, taking into account wages in a country, the average cost of a treatment in Egypt represents 5% of the average monthly wage, whereas in the UAE, it is barely 0.6%. Interestingly, Morocco leads the countries included in our study in the overall average OOP costs as a share of monthly wages. In fact, for a family with the average monthly wage of $544, the cost of a one-pack new treatment would necessitate 16% of their income. In terms of the number of days of work, it would require them roughly 5 days' wages.

3.6 Results

We focus on specifications that use DALYs as the outcome measure. In the regressions, we do not use age-adjusted values for DALYs or prevalence, as we have no way of similarly adjusting consumption. We also the intensity of treatment use in two ways. First, we consider all treatments associated with a disease or cause. We then distinguish between treatments first introduced before 1990, which we call "old," and "new" drugs brought to market after 1990.

Tables 3.6.1 and 3.6.2 present OLS results for these two measurement approaches. In the first

Table (3.5.2) National Health Accounts

	Algeria	Egypt	Jordan	Kuwait	Lebanon	Morocco	Saudi Arabia	Tunisia	UAE
Overall Economy:									
Income Category	1.00	1.00	2.00	3.00	2.00	1.00	3.00	1.00	3.00
	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)
GDP per Capita	11563.01	9625.66	11027.24	64195.78	15882.05	6533.34	45695.70	10500.09	80703.83
	(1020.15)	(1270.28)	(1114.87)	(9403.20)	(2048.43)	(1089.81)	(3147.84)	(1276.31)	(16363.67)
GGE per Capita	4235.28	3023.16	3727.09	26142.58	5110.10	1969.43	15416.61	2735.26	20185.09
	(904.86)	(501.95)	(576.41)	(2602.48)	(404.16)	(453.36)	(2300.22)	(562.77)	(2895.44)
Health Ependitures:									
CHE per Capita	585.31	472.48	905.47	1870.43	1279.91	343.47	2024.76	595.07	2516.96
	(195.72)	(72.45)	(108.34)	(449.25)	(109.42)	(87.89)	(578.66)	(122.52)	(304.97)
OOP per Capita	165.00	288.21	283.53	308.45	546.59	180.43	326.27	243.73	511.08
	(67.97)	(37.87)	(73.29)	(58.75)	(105.69)	(39.08)	(65.31)	(48.75)	(147.53)
GGHE as % of GGE	9.51	5.09	13.18	5.83	10.21	6.22	9.10	11.75	8.06
	(1.29)	(0.71)	(1.96)	(1.45)	(1.68)	(1.44)	(1.72)	(0.95)	(0.45)
CHE as % of GDP	4.97	4.91	8.23	3.05	8.16	5.18	4.40	5.62	3.23
	(1.32)	(0.41)	(0.77)	(1.14)	(1.05)	(0.61)	(1.01)	(0.57)	(0.69)
GGHE as % of CHE	70.65	32.27	54.13	81.16	40.61	35.62	69.68	53.92	64.83
	(3.20)	(2.52)	(8.78)	(4.67)	(5.24)	(7.15)	(3.23)	(2.40)	(8.15)
OOP as % of CHE	27.52	61.23	31.44	17.13	42.83	53.17	16.50	41.00	20.64
	(3.35)	(2.74)	(7.64)	(4.33)	(7.94)	(4.02)	(1.93)	(1.54)	(6.46)
Health Insurance:									
CHI as % of CHE	25.69	6.96	9.57	0.00	17.56	15.24	11.95	26.36	20.67
	(1.16)	(1.93)	(5.81)	(0.00)	(4.98)	(10.95)	(0.17)	(5.40)	(13.79)
SHI as % of CHE	25.69	6.96	9.57	0.00	17.56	9.00	0.00	26.36	.
	(1.16)	(1.93)	(5.81)	(0.00)	(4.98)	(6.81)	(0.00)	(5.40)	(.)
PvHI as % of CHE	0.00	0.00	0.00	0.00	0.00	6.24	11.95	0.00	3.70
	(0.00)	(0.00)	(0.00)	(0.00)	(0.00)	(4.28)	(0.17)	(0.00)	(9.07)
VHI as % of CHE	0.93	3.13	7.46	1.71	16.21	5.24	5.95	3.24	6.56
	(0.21)	(3.25)	(5.23)	(0.39)	(2.30)	(6.68)	(4.42)	(1.72)	(1.39)

Source: Global Health Expenditures Database (GHED), WHO.
Values reported are averages over the period [2000:2019]. Standard Errors between parentheses. Monetary values are in one unit constant (2020) international $(PPP). Percentage values are in %. Income Category (WHO, 2022): 1: Lower-middle income. 2: Upper-middle income. 3: High income. **GDP:** Gross Domestic Product. **GGE:** General Government Expenditure. **CHE:** Current Health Expenditures. **OOP:** Out-of-pocket. **GGHE:** General Government Health Expenditure. **CHI:** Compulsory Health Insurance. **SHI:** Social Health Insurance. **PvHI:** Private Health Insurance. **VHI:** Voluntary Health Insurance.

Table (3.5.3) Cost per treatment across countries

	Algeria	Egypt	Jordan	Kuwait	Lebanon	Morocco	Saudi Arabia	Tunisia	UAE
Monthly wage (in $(PPP))	964	802	919	5350	1323	544	3808	875	6725
OOP % of CHE	28%	61%	31%	17%	43%	53%	16%	41%	21%
Average treatment price (in $(PPP))	28	39	27	50	34	47	291	59	198
Average new treatment price (in $(PPP))	59	75	44	94	57	163	875	224	360
Average old treatment price (in $(PPP))	18	8	20	28	12	22	54	21	47
OOP per treatment (in $(PPP))	7.84	23.8	8.4	8.5	14.6	24.9	46.6	24.2	41.6
OOP per new treatment (in $(PPP))	16.5	45.8	13.6	16	24.5	86.4	140	91.8	75.6
OOP per old treatment (in $(PPP))	5	4.9	6.2	4.8	5.16	11.7	8.6	8.6	9.9
OOP per treatment as % of wage	0.8%	4.1%	0.9%	0.2%	1.1%	4.5%	1.2%	2.8%	0.6%
OOP per new treatment as % of wage	1.7%	5.7%	1.5%	0.3%	1.9%	15.9%	3.7%	10.5%	1.1%
OOP per old treatment as % of wage	0.5%	0.6%	0.7%	0.1%	0.4%	2.2%	0.2%	1%	0.1%

Source: MIDAS (IQVIA) and GHED (WHO). Author's calculations. All monetary values are in one unit constant (2020) international $(PPP).

Table (3.6.1) OLS Regressions, total use of pharmaceuticals

	Log(DALYs)			
	(1)	(2)	(3)	(4)
Log(Intensity of treatment use)	0.4506***	0.0089	-0.0164**	-0.0158***
	(0.014)	(0.007)	(0.007)	(0.004)
Log(Prevalence)	0.4452***	0.4686***	0.4380***	0.8783***
	(0.003)	(0.013)	(0.013)	(0.030)
Log(Intensity of treatment use), unmatched	-0.3439***	-0.1184***	0.0446**	0.0468***
	(0.038)	(0.012)	(0.021)	(0.008)
Constant	1.2610***	-0.0497	0.2002	-4.0929***
	(0.061)	(0.148)	(0.144)	(0.275)
Observations	18165	18165	18165	18165
Adj. R-squared	0.6012	0.9642	0.9680	0.9963
F-statistic	1458.47	48947.18	16248.07	72992.96
Time fixed effects	Yes	Yes	Yes	Yes
Cause fixed effects	No	Yes	Yes	No
Country fixed effects	No	No	Yes	No
Cause*Country fixed effects	No	No	No	Yes

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

column, only year fixed effects are included. In the next two columns, cause and country fixed effects are added. The last column includes cause*country fixed effects, which absorb any disease-country specific factors that do not vary over time. All specifications control for prevalence of the disease in country i in year t.

Our main variable of interest is the intensity of use of pharmaceutical treatments. When including only year fixed effects, the coefficient on intensity of use is positive and very large. This is not surprising given the endogeneity mentioned previously. Adding cause and country fixed effects reduces the estimated coefficient, which is negative and statistically significant. Because the coefficient is relatively close to zero, the implied elasticity of DALYs to use of pharmaceutical treatments is very low. In contrast to much of the literature, when we separate relatively new treatments from older ones, we find that it is use of the older treatments that is associated with improvements in health.

We next present results from estimating two-stage least squares using the three instruments described in section 3.4.3 in Tables 3.6.3 and 3.6.2. The first stage results, in the first column, show that the instruments have significant explanatory power for intensity of use. Standard tests

Table (3.6.2) OLS Regressions, use of pharmaceuticals by age of treatment

	Log(DALYs)			
	(1)	(2)	(3)	(4)
Log(Intensity of use, new treatments (1990))	0.1891***	0.0186***	0.0004	0.0267***
	(0.010)	(0.003)	(0.003)	(0.002)
Log(Intensity of use, old treatments (1990))	0.3691***	-0.0008	-0.0202***	-0.0359***
	(0.016)	(0.007)	(0.007)	(0.005)
Log(Prevalence)	0.4276***	0.4687***	0.4384***	0.8723***
	(0.003)	(0.013)	(0.013)	(0.030)
Log(Intensity of treatment use), unmatched	-0.3684***	-0.1207***	0.0461**	0.0495***
	(0.038)	(0.012)	(0.021)	(0.008)
Constant	1.3787***	-0.0400	0.1987	-4.0671***
	(0.061)	(0.148)	(0.144)	(0.274)
Observations	18165	18165	18165	18165
Adj. R-squared	0.6092	0.9643	0.9680	0.9963
F-statistic	1474.77	47687.87	16145.24	55852.80
Time fixed effects	Yes	Yes	Yes	Yes
Cause fixed effects	No	Yes	Yes	No
Country fixed effects	No	No	Yes	No
Cause*Country fixed effects	No	No	No	Yes

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (3.6.3) IV Regressions, total use of pharmaceuticals

	Log(DALYs)	
	First Stage	IV Regression
Log(Intensity of treatment use)		-0.0592**
		(0.024)
Log(Prevalence)	0.1797***	0.8967***
	(0.016)	(0.062)
Log(Intensity of treatment use), unmatched	-0.2805***	0.0690***
	(0.071)	(0.023)
Log(Intensity of treatment use in other countries)	0.5085***	
	(0.014)	
Log(Intensity of treatment use, other diseases)	0.7986***	
	(0.068)	
Log(Prevalence in other countries)	0.0737***	
	(0.012)	
Observations	18165	18165
R-squared	0.8648	0.4744
F-Stat	889.65	17.93
Effective F-Stat		1126.621
5% TSLS Critical Value		30.221

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

for weak instruments confirm that they are valid. The coefficient on intensity of use in the second stage is negative in Table 3.6.3), and larger in magnitude than the OLS estimate in Table 3.6.1: the IV results imply an elasticity of around 5%, versus less than 2% for OLS. Failing to account for endogeneity of availability and use may bias the estimates of the effect of pharmaceuticals on health outcomes. The estimated coefficients for intensity of use of novel treatments and older treatments are both larger in magnitude than the OLS estimates, but again of the opposite sign. If the two are substitutes, the fact that they have opposite signs is not surprising, though it is puzzling that newer treatments are not associated with improved outcomes. However, we have not attempted to model the demand for old vs. new treatments or to estimate the elasticity of substitution.

The specifications above relate short-term changes in pharmaceutical use to short-term changes in health outcomes. While this may be appropriate for certain diseases, in some cases, it is likely that the benefits of a health intervention are realized slowly, or the result of years of consistent

Table (3.6.4) IV Regressions, use of pharmaceuticals by age of treatment

	Log(DALYs)	
	First Stage	IV Regression
Log(Intensity of use, new treatments (1990))		0.0570***
		(0.010)
Log(Intensity of use, old treatments (1990))		-0.0471***
		(0.014)
Log(Prevalence)	0.0441**	0.8617***
	(0.021)	(0.060)
Log(Intensity of treatment use), unmatched	0.1704***	0.0472**
	(0.033)	(0.021)
Log(Intensity of use, new treatments (1990) in other countries)	0.4205***	
	(0.010)	
Log(Intensity of use, new treatments (1990) of other diseases)	0.1579***	
	(0.017)	
Log(Prevalence in other countries)	0.1676***	
	(0.014)	
Observations	18165	18165
Adj. R-squared	0.8580	0.4802
F-Stat	254.16	18.70
Effective F-Stat		1352.372
5% TSLS Critical Value		32.462

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (3.6.5) IV Regressions (long differences), total use of pharmaceuticals

	Log(DALYs)	
	First Stage	IV Regression
Log(Intensity of treatment use)		-0.0925***
		(0.026)
Log(Prevalence)	0.2468***	1.0438***
	(0.059)	(0.078)
Log(Intensity of treatment use), unmatched	-0.0872	0.1085***
	(0.231)	(0.030)
Log(Intensity of treatment use in other countries)	0.5305***	
	(0.034)	
Log(Intensity of treatment use, other diseases)	0.5657***	
	(0.200)	
Log(Prevalence in other countries)	0.0131	
	(0.033)	
Observations	1890	1890
Adj. R-squared	0.6650	0.5313
F-Stat	2498.93	60.37
Effective F-Stat		368.080
5% TSLS Critical Value		30.163

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

treatments. As an alternative, we also estimate "long-difference" regressions that consider changes over the entire 20 year time period.

Tables 3.6.5 and 3.6.6 present the results from this specification. The estimated coefficient on total use of pharmaceuticals is even larger in magnitude, around 9%. We continue, however, to estimate coefficients with opposite signs for the use of new and old pharmaceuticals.

It is also likely that there is important heterogeneity across diseases. The effects of novel treatments for HIV and Hepatitis C have been documented in numerous studies, for example, but other diseases may have seen less dramatic changes. Our preliminary estimates confirm large differences across broad disease categories, but are nevertheless inconsistent with the literature concerning specific diseases.

Relatedly, our mapping of drugs to diseases certainly introduces measurement error, as does our allocation of units of a drug to different diseases when a drug is mapped to multiple diseases. We are currently comparing the set of drugs mapped to specific diseases by our algorithm with those

Table (3.6.6) IV Regressions (long difference), use of pharmaceuticals by age of treatment

	Log(DALYs)	
	First Stage	IV Regression
Log(Intensity of use, new treatments (1990))		0.0585***
		(0.010)
Log(Intensity of use, old treatments (1990))	0.2122***	-0.0713***
	(0.049)	(0.019)
Log(Prevalence)	-0.0412	0.9823***
	(0.088)	(0.076)
Log(Intensity of treatment use), unmatched	0.2408**	0.0664**
	(0.110)	(0.027)
Log(Intensity of use, new treatments (1990) in other countries)	0.4712***	
	(0.026)	
Log(Intensity of use, new treatments (1990) of other diseases)	0.0879	
	(0.056)	
Log(Prevalence in other countries)	0.0628	
	(0.045)	
Observations	1890	1890
Adj. R-squared	0.6369	0.5466
F-Stat	4330.70	57.31
Effective F-Stat		461.848
5% TSLS Critical Value		31.214

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

in other papers.

Appendix G includes the results of regressions that use mortality as the outcome measure; a mapping of treatments to narrowly-defined diseases; different assignments of units to diseases for drugs that treat multiple conditions; post-2000 launches as the definition of "new"; and excluding cancer drugs (because these are generally administered in hospitals, which are not in our dataset). These robustness checks yield similar results.

In order to put these estimates into context, we consider the contribution of pharmaceuticals to changes in DALYs since 2000 in our sample of countries. These calculations are summarized in Table 3.6.7 for total pharmaceutical use, using estimates from Table 3.6.3. The first row presents the net change in DALYs per 100,000 for each country. While most countries realized a net improvement, DALYs increased slightly in the UAE. The use of pharmaceuticals increased in every country, although to different extents, and prevalence increased everywhere except Egypt on average.

To estimate the contribution, we multiply the estimated coefficients by the change in prevalence or pharmaceutical use between 2000 and 2019. For example, Morocco experienced an improvement in average DALYs per 100,000 of approximately 0.18. This compares to an average increase in prevalence per 100,000 of about 0.03, while the intensity of pharmaceutical use increased by more than 50%. Over the 20 year period, this implies that prevalence increased DALY/100,000 in Morocco by 2.5%, while pharmaceuticals are responsible for a decrease of 3%. Across all the countries we study, pharmaceuticals are responsible for almost zero (Jordan) to as much as almost 60% (Tunisia) of the net gain in DALYs. For comparison, Buxbaum et al. (2020) attribute 35% of the net gain in US life expectancy between 1990 and 2015 to pharmaceuticals.

The cost of treatments – whether borne by patients or subsidized by governments or private insurers – is important to consider, both as a driver of pharmaceutical use as well as for evaluating whether this is money well spent. We do not attempt a cost-effectiveness evaluation of every product here, but provide an aggregate assessment. First, we calculate how many DALYs were gained due to pharmaceuticals in each country-cause-year. We compare the total DALYs gained to total spending on pharmaceuticals over the 2000-2019 period to arrive at a cost per DALY/year. The unweighted average across causes yields a large cost per DALY, but this is apparently driven

by very high costs for some causes. The total cost per DALY ranges between about 3700 USD (Tunisia) to 13,675 USD (Algeria) in PPP terms, or 495 USD (Egypt) to 4,742 USD (Algeria) based on exchange rates without PPP adjustments. These estimates are, not surprisingly, much lower than those for the US although still a large percent of GDP per capita.

Table (3.6.7) Contribution of pharmaceuticals to DALYs (PPP)

	Algeria	Egypt	Jordan	Kuwait	Lebanon	Morocco	Saudi Arabia	Tunisia	UAE
2000-19 change in DALYs	-0.1217	-0.2674	-0.1684	-0.0631	-0.1024	-0.1692	-0.1785	-0.0513	0.0007
2000-19 change in prevalence	0.0891	-0.0600	0.0688	0.0510	0.0474	0.0280	0.0198	0.1050	0.0958
2000-19 change in pharma. use	0.5148	1.0073	0.1091	0.4270	0.5327	0.5431	0.6369	0.5727	0.9320
Prevalence contribution to DALYs	0.0799	-0.0538	0.0617	0.0457	0.0425	0.0251	0.0177	0.0941	0.0859
Pharma. contribution to DALYs	-0.0305	-0.0596	-0.0065	-0.0253	-0.0315	-0.0321	-0.0377	-0.0339	-0.0552
Average across causes:									
2000-19 expenditures (in million $(PPP))	518.8	472.7	42.2	30.8	84.8	244.3	674.1	99.9	194.7
2000-19 expenditures (in million US$)	179.9	115.8	15.7	17.5	41.8	105.6	270.9	37.3	106.4
2000-19 DALYs gained	37940.0	233652.5	7727.6	4258.6	9499.2	54666.4	84352.8	26968.5	33662.7
2000-19 cost per DALY (in $(PPP))	52263.3	11964.0	29989.2	20700.0	-9035.3	18567.1	41712.9	30441.0	232243.7
2000-19 cost per DALY (in US$)	17979.7	2939.1	11206.2	11940.1	-4163.4	8044.7	15582.9	11392.8	141011.7
Total across all causes:									
2000-19 country expenditures (in million $(PPP))	54477.3	49635.2	4430.6	3229.7	8905.8	25655.3	70782.8	10490.6	20445.5
2000-19 country expenditures (in million US$)	18890.8	12161.7	1646.7	1838.0	4385.2	11090.2	28442.5	3921.5	11175.7
2000-19 country DALYs gained	3983696.0	24533508.0	811400.2	447151.0	997411.8	5739972.0	8857045.0	2831693.8	3534587.5
2000-19 country-cost per DALY (in $(PPP))	13675.1	2023.2	5460.4	7222.8	8929.0	4469.6	7991.7	3704.7	5784.4
2000-19 country-cost per DALY (in US$)	4742.0	495.7	2029.4	4110.4	4396.6	1932.1	3211.3	1384.9	3161.8

Finally, we consider how these costs vary by cause within countries. Tables 3.6.8, 3.6.9, and 3.6.10 present these calculations for the diseases with the highest DALYs in 2000 for Algeria, Morocco, and Saudi Arabia. In all countries, there is significant variation in the cost per DALY by cause. Those with low cost per DALY are causes with few pharmaceuticals interventions (and low spending). Despite the arsenal of cardiovascular treatments available, heart disease and stroke are high cost per DALY causes in all three countries.

Table (3.6.8) Algeria

	Neonatal disorders	Ischemic heart disease	Congenital birth defects	Stroke	Lower respiratory infections	Depressive disorders	Headache disorders	Low back pain	Gynecological diseases	Anxiety disorders
2000-rank of burden, DALYs	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0
N° total treatments	3.0	38.0	2.0	26.0	16.0	17.0	9.0	0.0	32.0	24.0
2000-19 DALYs gained	105119.5	85481.9	10941.6	24480.3	3252.8	25144.2	371592.0	0.0	671484.3	47823.9
2000-19 spending (in M.US$)	292.83	2488.05	4.50	384.07	6.72	173.16	268.40	0.00	877.74	338.98
Cost/DALY (in US$)	2785.68	29106.18	411.68	15688.76	2066.09	6886.79	722.31	.	1307.16	7088.17

Table (3.6.9) Morocco

	Neonatal disorders	Ischemic heart disease	Lower respiratory infections	Diarrheal diseases	Stroke	Congenital birth defects	Measles	Depressive disorders	Tuberculosis	Low back pain
2000-rank of burden, DALYs	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0
N° total treatments	4.0	42.0	18.0	4.0	29.0	2.0	0.0	22.0	12.0	1.0
2000-19 DALYs gained	127774.7	127392.5	2377.0	51206.7	39649.9	33033.6	0.0	172576.1	239260.2	873763.3
2000-19 spending (in M.US$)	33.72	1008.23	5.43	102.08	220.68	0.38	0.00	292.27	301.19	8.11
Cost/DALY (in US$)	263.93	7914.33	2285.66	1993.48	5565.71	11.48	.	1693.56	1258.84	9.29

Table (3.6.10) Saudi Arabia

	Neonatal disorders	Ischemic heart disease	Congenital birth defects	Stroke	Depressive disorders	Headache disorders	Low back pain	Chronic kidney disease	Lower respiratory infections	Diabetes mellitus
2000-rank of burden, DALYs	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0
N° total treatments	4.0	56.0	2.0	41.0	34.0	10.0	1.0	4.0	22.0	51.0
2000-19 DALYs gained	93954.3	105907.2	57929.3	46319.4	158553.6	469210.4	529697.6	322045.2	5932.4	282858.1
2000-19 spending (in M.US$)	320.50	2770.48	4.17	541.60	739.56	217.55	39.53	79.49	30.13	2641.72
Cost/DALY (in US$)	3411.28	26159.54	71.91	11692.67	4664.43	463.65	74.62	246.83	5078.81	9339.39

3.7 Conclusion

Many studies have credited pharmaceuticals with significant gains in health outcomes. For this reason, increased access to pharmaceuticals is a priority of many international organizations. The World Health Organization maintains a list of essential medicines that should be available in every country. Compared to many interventions, pharmaceutical treatments are relatively easy to deliver, particularly in the retail setting. Most can be manufactured at low cost. In the countries examined in this study, use of pharmaceuticals increased substantially. We find that more use of pharmaceuticals caused a decline in DALYs, with an implied elasticity of around 6%. The cost per DALY gained varies across countries and causes, but on average the estimates suggest that pharmaceuticals are cost-effective.

While additional work is necessary to confirm these results, our findings on the use of new pharmaceuticals are inconsistent with most of the literature. One explanation is that pharmaceuticals are only one tool in healthcare, and it is important to consider whether the healthcare systems in this set of countries provide the complementary tools necessary to realize their full benefits. Even when a drug is established as effective in clinical trials, its use in practice may not yield the same results. There are many diseases for which physician expertise is important in diagnosing and selecting the appropriate treatment. If patients instead choose their own treatments (because a prescription is not required, as is the case in many countries), some treatments may be used unwisely. Antibiotics are an obvious example. Often accessible without a prescription, they may be used for flu or other viral diseases for which they are not clinically effective. This "mismatch" may be more important for newer drugs, for which both physicians and patients have less information or experience.

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Appendices

F Linking treatments to diseases

To determine the use of treatments for a disease, we must first have list of drugs known to treat or prevent it. The Medication Reference Terminology (MED-RT), one of the vocabularies included in the UMLS and the RxNAV APIs from the National Library of Medicine, provides this mapping. We must also link the disease or cause name from the GBD database to the disease identifier in MED-RT, and the drug identifiers in MED-RT to the molecule names in the MIDAS data.

An advantage of using these APIs is that the search functions include the normalized word search option that "removes lexical variations such as plural and upper case text, and compares search terms to the Metathesaurus normalized word index to retrieve relevant concepts." The vocabularies are also linked by concepts. A disease name has associated broader or narrower disease names, and molecules are linked to similar drugs (such as salts or hydrochlorides, or combinations that include that molecule).

We begin with a list of GBD cause names and their associated ICD-10 codes. We first search for each GBD cause for a list of synonyms for that cause. For example, "Peripheral artery disease" from GBD has 25 synonyms or associated terms in UMLS. For each of these terms, we use UMLS APIs to get a list of drug names and identifiers that "may treat" or "may prevent" it. For peripheral artery disease, this yields 49 unique drug names and identifiers.

Some disease identifiers have no drugs mapped to them. In these cases, we search for a broader disease term. In our main specifications, we use this "broad" definition of disease-to-drug mapping. For example, "hypertensive heart disease" does not have any drugs mapped to its disease identifier, so we use the broader concept (as defined by UMLS) "hypertension," which does. We also search using each of the ICD-10 codes that GBD assigns to a cause, instead of beginning with the cause name. As a robustness check, we also include results restricted to the narrow disease definition.

To link to the MIDAS data, we first search for each molecule name to get a list of associated drug identifiers. In the case of combination products, we attempt to find a drug identifier in UMLS that corresponds to the exact combination. In some cases, combinations in MIDAS include a long list of ingredients, many of which are not pharmaceuticals (such as saline or garlic oil). For these observations, we select the drug identifier from UMLS that corresponds as closely as possible to

Table (F1) Mapping MIDAS drugs to GBD causes

MIDAS Drugs ($N = 8445$)	Drug-ID ($N = 1147$)	Narrow match ($N = 1139$)	In sample ($N = 1138$)	GBD Causes ($N = 107$)
		Broad match ($N = 597$)	In sample ($N = 479$)	GBD Causes ($N = 20$)
	Disease-ID ($N = 6018$)	Narrow match ($N = 5790$)	In sample ($N = 5752$)	GBD Causes ($N = 88$)
		Broad match ($N = 228$)	In sample ($N = 216$)	GBD Causes ($N = 18$)
	Any-ID ($N = 6238$)	Narrow match ($N = 6004$)	In sample ($N = 6002$)	GBD Causes ($N = 127$)
		Broad match ($N = 825$)	In sample ($N = 695$)	GBD Causes ($N = 35$)

the list from MIDAS.

Table F1 summarizes the mapping of MIDAS drugs to GBD conditions. The first column reports the total number of unique treatments – from MIDAS – marketed in our sample of countries between 2000 and 2019. UMLS APIs provide us with both drugs and diseases identifiers, 'Drug-ID' and 'Disease-ID', respectively. Column 2 shows the number of treatments that were mapped to at least one condition by type of identifier. 'Any-ID' is the union of both -ID sets, and corresponds to the mapping that we use in our analysis. Next, we differentiate between 'Narrow' and 'Broad' match as discussed above (column 3). Furthermore, the GBD dataset includes a hierarchy of disease levels that goes from level 0 (general) to level 4 (specific). For example, diabetes mellitus type 1 is a level 4 condition; its level 3 is diabetes mellitus, whose parent condition is diabetes and kidney diseases at level 2. These are non-communicable diseases (level 1), a subset of all causes (level 0). Ideally, we would want to map treatments to the most specific condition whenever possible. However, we focus on level 3, which results in a more complete drug mapping. Column 4 reports the number of drugs mapped to at least a level 3 disease. Level 4 matches were identified and mapped back to their level 3 parent. The last column provides the number of GBD diseases that we were left with using each type of mapping approach.

G Additional regressions

G.1 Mortality as outcome

Table (G1) OLS Regressions, total use of pharmaceuticals

	Log(Mortality)			
	(1)	(2)	(3)	(4)
Log(Intensity of treatment use)	0.2722***	-0.0068	-0.0322***	-0.0301***
	(0.012)	(0.006)	(0.006)	(0.004)
Log(Prevalence)	0.1147***	0.1123***	0.0880***	0.2883***
	(0.003)	(0.007)	(0.007)	(0.020)
Log(Intensity of treatment use), unmatched	-0.3129***	-0.1778***	-0.0019	0.0007
	(0.028)	(0.012)	(0.021)	(0.008)
Constant	0.3652***	0.2157**	0.3671***	-1.7632***
	(0.047)	(0.085)	(0.083)	(0.184)
Observations	12456	12456	12456	12456
Adj. R-squared	0.2367	0.9162	0.9269	0.9925
F-statistic	171.40	1321.50	1490.53	11512.49
Time fixed effects	Yes	Yes	Yes	Yes
Cause fixed effects	No	Yes	Yes	No
Country fixed effects	No	No	Yes	No
Cause*Country fixed effects	No	No	No	Yes

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G2) OLS Regressions, use of pharmaceuticals by age of treatment

	Log(Mortality)			
	(1)	(2)	(3)	(4)
Log(Intensity of use, new treatments (1990))	0.2100***	0.0339***	0.0215***	0.0185***
	(0.013)	(0.005)	(0.004)	(0.002)
Log(Intensity of use, old treatments (1990))	0.2082***	-0.0288***	-0.0504***	-0.0457***
	(0.012)	(0.007)	(0.007)	(0.005)
Log(Prevalence)	0.0909***	0.1136***	0.0896***	0.2819***
	(0.003)	(0.007)	(0.007)	(0.020)
Log(Intensity of treatment use), unmatched	-0.3465***	-0.1774***	0.0029	0.0047
	(0.028)	(0.012)	(0.021)	(0.008)
Constant	0.4987***	0.2206***	0.3611***	-1.7260***
	(0.047)	(0.085)	(0.083)	(0.183)
Observations	12456	12456	12456	12456
Adj. R-squared	0.2816	0.9168	0.9273	0.9926
F-statistic	167.44	1314.21	1478.67	11750.81
Time fixed effects	Yes	Yes	Yes	Yes
Cause fixed effects	No	Yes	Yes	No
Country fixed effects	No	No	Yes	No
Cause*Country fixed effects	No	No	No	Yes

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G3) IV Regressions, total use of pharmaceuticals

	Log(Mortality)	
	First Stage	IV Regression
Log(Intensity of treatment use)		-0.0610**
		(0.025)
Log(Prevalence)	0.1797***	0.3009***
	(0.016)	(0.064)
Log(Intensity of treatment use), unmatched	-0.2805***	0.0162
	(0.071)	(0.023)
Log(Intensity of treatment use in other countries)	0.5085***	
	(0.014)	
Log(Intensity of treatment use, other diseases)	0.7986***	
	(0.068)	
Log(Prevalence in other countries)	0.0737***	
	(0.012)	
Observations	18165	12456
R-squared	0.8648	0.2079
F-Stat	889.65	7.06
Effective F-Stat		882.988
5% TSLS Critical Value		29.763

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G4) IV Regressions, use of pharmaceuticals by age of treatment

	Log(Mortality)	
	First Stage	IV Regression
Log(Intensity of use, new treatments (1990))		0.0373***
		(0.010)
Log(Intensity of use, old treatments (1990))		-0.0523***
		(0.016)
Log(Prevalence)	0.0441**	0.2737***
	(0.021)	(0.063)
Log(Intensity of treatment use), unmatched	0.1704***	0.0045
	(0.033)	(0.022)
Log(Intensity of use, new treatments (1990) in other countries)	0.4205***	
	(0.010)	
Log(Intensity of use, new treatments (1990) of other diseases)	0.1579***	
	(0.017)	
Log(Prevalence in other countries)	0.1676***	
	(0.014)	
Observations	18165	12456
Adj. R-squared	0.8580	0.2252
F-Stat	254.16	7.73
Effective F-Stat		967.932
5% TSLS Critical Value		32.278

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G5) OLS Regressions, total use of pharmaceuticals

	Log(DALYs)			
	(1)	(2)	(3)	(4)
Log(Intensity of treatment use)	0.3434***	-0.0013	-0.0170***	-0.0277***
	(0.015)	(0.007)	(0.006)	(0.004)
Log(Prevalence)	0.4701***	0.4696***	0.4369***	0.8771***
	(0.003)	(0.013)	(0.013)	(0.029)
Log(Intensity of treatment use), unmatched	-0.3608***	-0.1128***	0.0476**	0.0572***
	(0.039)	(0.013)	(0.021)	(0.009)
Constant	1.1903***	-0.0547	0.2087	-4.0793***
	(0.061)	(0.147)	(0.144)	(0.273)
Observations	18165	18165	18165	18165
Adj. R-squared	0.5929	0.9642	0.9680	0.9963
F-statistic	1453.49	50128.58	16285.96	72215.19
Time fixed effects	Yes	Yes	Yes	Yes
Cause fixed effects	No	Yes	Yes	No
Country fixed effects	No	No	Yes	No
Cause*Country fixed effects	No	No	No	Yes

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

G.2 Assigning all units of a drug to each matched disease

Table (G6) OLS Regressions, use of pharmaceuticals by age of treatment

	Log(DALYs)			
	(1)	(2)	(3)	(4)
Log(Intensity of use, new treatments (1990))	0.1816***	0.0166***	-0.0005	0.0232***
	(0.009)	(0.003)	(0.003)	(0.001)
Log(Intensity of use, old treatments (1990))	0.2802***	-0.0112*	-0.0206***	-0.0417***
	(0.016)	(0.007)	(0.006)	(0.004)
Log(Prevalence)	0.4490***	0.4692***	0.4370***	0.8680***
	(0.003)	(0.013)	(0.013)	(0.029)
Log(Intensity of treatment use), unmatched	-0.4039***	-0.1158***	0.0492**	0.0555***
	(0.039)	(0.013)	(0.021)	(0.008)
Constant	1.3325***	-0.0377	0.2103	-4.0187***
	(0.061)	(0.148)	(0.144)	(0.273)
Observations	18165	18165	18165	18165
Adj. R-squared	0.6030	0.9643	0.9680	0.9964
F-statistic	1479.84	48761.62	16150.64	54019.53
Time fixed effects	Yes	Yes	Yes	Yes
Cause fixed effects	No	Yes	Yes	No
Country fixed effects	No	No	Yes	No
Cause*Country fixed effects	No	No	No	Yes

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G7) IV Regressions, total use of pharmaceuticals

	Log(DALYs)	
	First Stage	IV Regression
Log(Intensity of treatment use)		-0.0773**
		(0.032)
Log(Prevalence)	0.0698***	0.8869***
	(0.013)	(0.061)
Log(Intensity of treatment use), unmatched	-0.0561	0.0904***
	(0.074)	(0.029)
Log(Intensity of treatment use in other countries)	0.3875***	
	(0.016)	
Log(Intensity of treatment use, other diseases)	0.7199***	
	(0.072)	
Log(Prevalence in other countries)	0.1042***	
	(0.010)	
Observations	18165	18165
R-squared	0.8431	0.4747
F-Stat	744.66	17.12
Effective F-Stat		491.410
5% TSLS Critical Value		31.310

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G8) IV Regressions, use of pharmaceuticals by age of treatment

	Log(DALYs)	
	First Stage	IV Regression
Log(Intensity of use, new treatments (1990))		0.0488***
		(0.010)
Log(Intensity of use, old treatments (1990))		-0.0486***
		(0.013)
Log(Prevalence)	0.0950***	0.8568***
	(0.023)	(0.061)
Log(Intensity of treatment use), unmatched	0.2715***	0.0497**
	(0.035)	(0.021)
Log(Intensity of use, new treatments (1990) in other countries)	0.4267***	
	(0.010)	
Log(Intensity of use, new treatments (1990) of other diseases)	0.2759***	
	(0.018)	
Log(Prevalence in other countries)	0.1995***	
	(0.016)	
Observations	18165	18165
Adj. R-squared	0.8482	0.4824
F-Stat	295.94	17.56
Effective F-Stat		1456.408
5% TSLS Critical Value		30.439

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G9) OLS Regressions, total use of pharmaceuticals

	Log(DALYs)			
	(1)	(2)	(3)	(4)
Log(Intensity of treatment use)	0.2210***	0.0338***	0.0188***	0.0006
	(0.014)	(0.006)	(0.006)	(0.003)
Log(Prevalence)	0.4677***	0.4676***	0.4357***	0.8714***
	(0.003)	(0.013)	(0.013)	(0.029)
Log(Intensity of treatment use), unmatched	-0.2051***	-0.1280***	0.0281	0.0385***
	(0.039)	(0.012)	(0.021)	(0.008)
Constant	1.1972***	-0.0559	0.2040	-4.0301***
	(0.061)	(0.147)	(0.144)	(0.274)
Observations	18165	18165	18165	18165
Adj. R-squared	0.5873	0.9643	0.9680	0.9963
F-statistic	1395.78	46613.94	16140.64	67879.99
Time fixed effects	Yes	Yes	Yes	Yes
Cause fixed effects	No	Yes	Yes	No
Country fixed effects	No	No	Yes	No
Cause*Country fixed effects	No	No	No	Yes

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

G.3 Assigning all units of a drug to disease with the highest prevalence among matches

Table (G10) OLS Regressions, use of pharmaceuticals by age of treatment

	Log(DALYs)			
	(1)	(2)	(3)	(4)
Log(Intensity of use, new treatments (1990))	0.2012***	0.0262***	0.0098***	0.0224***
	(0.010)	(0.003)	(0.003)	(0.001)
Log(Intensity of use, old treatments (1990))	0.0958***	0.0114**	0.0021	-0.0150***
	(0.016)	(0.006)	(0.006)	(0.003)
Log(Prevalence)	0.4569***	0.4682***	0.4364***	0.8667***
	(0.003)	(0.013)	(0.013)	(0.029)
Log(Intensity of treatment use), unmatched	-0.2315***	-0.1286***	0.0324	0.0374***
	(0.039)	(0.012)	(0.021)	(0.008)
Constant	1.2966***	-0.0423	0.2092	-4.0153***
	(0.061)	(0.147)	(0.144)	(0.273)
Observations	18165	18165	18165	18165
Adj. R-squared	0.5944	0.9643	0.9680	0.9963
F-statistic	1433.09	45931.28	16007.24	53798.71
Time fixed effects	Yes	Yes	Yes	Yes
Cause fixed effects	No	Yes	Yes	No
Country fixed effects	No	No	Yes	No
Cause*Country fixed effects	No	No	No	Yes

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G11) IV Regressions, total use of pharmaceuticals

	Log(DALYs)	
	First Stage	IV Regression
Log(Intensity of treatment use)		0.0022
		(0.018)
Log(Prevalence)	0.1375***	0.8708***
	(0.017)	(0.062)
Log(Intensity of treatment use), unmatched	-0.3322***	0.0377*
	(0.087)	(0.021)
Log(Intensity of treatment use in other countries)	0.3346***	
	(0.013)	
Log(Intensity of treatment use, other diseases)	0.7677***	
	(0.083)	
Log(Prevalence in other countries)	0.1217***	
	(0.012)	
Observations	18165	18165
R-squared	0.8115	0.4801
F-Stat	580.69	19.68
Effective F-Stat		649.211
5% TSLS Critical Value		32.942

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G12) IV Regressions, use of pharmaceuticals by age of treatment

	Log(DALYs)	
	First Stage	IV Regression
Log(Intensity of use, new treatments (1990))		0.0498***
		(0.009)
Log(Intensity of use, old treatments (1990))		-0.0224**
		(0.010)
Log(Prevalence)	0.0656***	0.8574***
	(0.020)	(0.061)
Log(Intensity of treatment use), unmatched	0.2559***	0.0315
	(0.033)	(0.021)
Log(Intensity of use, new treatments (1990) in other countries)	0.3792***	
	(0.009)	
Log(Intensity of use, new treatments (1990) of other diseases)	0.1300***	
	(0.017)	
Log(Prevalence in other countries)	0.1224***	
	(0.013)	
Observations	18165	18165
Adj. R-squared	0.8310	0.4779
F-Stat	147.39	18.08
Effective F-Stat		1474.249
5% TSLS Critical Value		32.252

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G13) OLS Regressions, use of pharmaceuticals by age of treatment (launch date, 2000)

	Log(DALYs)			
	(1)	(2)	(3)	(4)
Log(Intensity of use, new treatments (2000))	0.1213***	0.0252***	0.0241***	0.0151***
	(0.012)	(0.003)	(0.003)	(0.001)
Log(Intensity of use, old treatments (2000))	0.4358***	-0.0015	-0.0274***	-0.0209***
	(0.014)	(0.007)	(0.007)	(0.004)
Log(Prevalence)	0.4382***	0.4690***	0.4385***	0.8745***
	(0.003)	(0.013)	(0.013)	(0.030)
Log(Intensity of treatment use), unmatched	-0.3767***	-0.1221***	0.0406*	0.0432***
	(0.038)	(0.012)	(0.021)	(0.008)
Constant	1.3255***	-0.0339	0.2148	-4.0489***
	(0.061)	(0.148)	(0.144)	(0.276)
Observations	18165	18165	18165	18165
Adj. R-squared	0.6037	0.9643	0.9681	0.9963
F-statistic	1459.99	47332.67	16054.46	67729.47
Time fixed effects	Yes	Yes	Yes	Yes
Cause fixed effects	No	Yes	Yes	No
Country fixed effects	No	No	Yes	No
Cause*Country fixed effects	No	No	No	Yes

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

G.4 Using post-2000 launch as the definition of "new"

Table (G14) IV Regressions, use of pharmaceuticals by age of treatment (launch date, 2000)

	Log(DALYs)	
	First Stage	IV Regression
Log(Intensity of use, new treatments (2000))		0.0375***
		(0.008)
Log(Intensity of use, old treatments (2000))		-0.0256**
		(0.012)
Log(Prevalence)	0.0123	0.8677***
	(0.020)	(0.061)
Log(Intensity of treatment use), unmatched	0.4083***	0.0369*
	(0.028)	(0.021)
Log(Intensity of use, new treatments (2000) in other countries)	0.3548***	
	(0.007)	
Log(Intensity of use, new treatments (2000) of other diseases)	-0.0059	
	(0.005)	
Log(Prevalence in other countries)	0.1164***	
	(0.014)	
Observations	18165	18165
Adj. R-squared	0.7533	0.4786
F-Stat	34.87	18.37
Effective F-Stat		1991.614
5% TSLS Critical Value		31.377

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G15) IV Regressions, total use of pharmaceuticals (long difference)

	Log(DALYs)	
	First Stage	IV Regression
Log(Intensity of treatment use)		-0.0925***
		(0.026)
Log(Prevalence)	0.2468***	1.0438***
	(0.059)	(0.078)
Log(Intensity of treatment use), unmatched	-0.0872	0.1085***
	(0.231)	(0.030)
Log(Intensity of treatment use in other countries)	0.5305***	
	(0.034)	
Log(Intensity of treatment use, other diseases)	0.5657***	
	(0.200)	
Log(Prevalence in other countries)	0.0131	
	(0.033)	
Observations	1890	1890
Adj. R-squared	0.6650	0.5313
F-Stat	2498.93	60.37
Effective F-Stat		368.080
5% TSLS Critical Value		30.163

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G16) IV Regressions, use of pharmaceuticals by age of treatment (long difference)

	Log(DALYs)	
	First Stage	IV Regression
Log(Intensity of use, new treatments (1990))		0.0585***
		(0.010)
Log(Intensity of use, old treatments (1990))	0.2122***	-0.0713***
	(0.049)	(0.019)
Log(Prevalence)	-0.0412	0.9823***
	(0.088)	(0.076)
Log(Intensity of treatment use), unmatched	0.2408**	0.0664**
	(0.110)	(0.027)
Log(Intensity of use, new treatments (1990) in other countries)	0.4712***	
	(0.026)	
Log(Intensity of use, new treatments (1990) of other diseases)	0.0879	
	(0.056)	
Log(Prevalence in other countries)	0.0628	
	(0.045)	
Observations	1890	1890
Adj. R-squared	0.6369	0.5466
F-Stat	4330.70	57.31
Effective F-Stat		461.848
5% TSLS Critical Value		31.214

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses.

Table (G17) IV Regressions, total use of pharmaceuticals (by Level 2 causes)

	Log(DALYs)								
	Id344	Id386	Id491	Id508	Id526	Id542	Id558	Id626	Id640
Log(Intensity of treatment use)	-0.2349***	0.1167	-0.0063	-0.2111**	0.1070**	-0.0278	-0.0043	-0.0101**	-0.3366
	(0.075)	(0.084)	(0.063)	(0.082)	(0.049)	(0.019)	(0.006)	(0.004)	(0.216)
Log(Prevalence)	0.6497***	0.3245**	0.8824***	0.9667***	0.5398***	1.0541***	0.9717***	0.9385***	1.5877***
	(0.098)	(0.157)	(0.122)	(0.134)	(0.158)	(0.073)	(0.009)	(0.018)	(0.318)
Log(Intensity of treatment use), unmatched	0.0456	0.0623	0.0381	0.2053***	0.0725	0.0289	0.0059	0.0094**	0.3826
	(0.034)	(0.054)	(0.057)	(0.075)	(0.044)	(0.056)	(0.005)	(0.005)	(0.258)
Observations	3287	692	1557	692	1557	865	1384	865	865
Adj. R-squared	0.3802	0.8258	0.3569	0.5504	0.1543	0.8324	0.9946	0.9972	0.3863
F-Stat	28.00	16.11	11.28	10.76	5.13	57.25	2079.35	2455.70	8.73
Effective F-Stat	136.135	111.639	57.429	37.867	61.663	120.627	90.921	14.136	11.038
5% TSLS Critical Value	29.423	19.137	29.038	18.264	24.903	23.096	22.294	31.272	22.407

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses. Id344: Neglected tropical diseases and malaria. Id386: Nutritional deficiencies. Id491: Cardiovascular diseases. Id508: Chronic respiratory diseases. Id526: Digestive diseases. Id542: Neurological disorders. Id558: Mental disorders. Id626: Musculoskeletal disorders. Id640: Other non-communicable diseases.

Table (G18) Continued from previous table

	Log(DALYs)								
	Id653	Id669	Id955	Id956	Id957	Id961	Id962	Id973	Id974
Log(Intensity of treatment use)	-0.0006	0.0662*	0.0155	-0.2317	0.0712	-0.0491	-0.1438	-0.2866	-0.1021**
	(0.009)	(0.039)	(0.100)	(0.415)	(0.356)	(0.393)	(0.090)	(0.257)	(0.043)
Log(Prevalence)	0.8112***	0.9178***	1.0571***	1.8910***	3.6375***	1.0240***	0.1106	1.1145***	1.0392***
	(0.062)	(0.114)	(0.239)	(0.322)	(0.879)	(0.061)	(0.167)	(0.279)	(0.134)
Log(Intensity of treatment use), unmatched	-0.0075	-0.0513*	0.1747	0.3279	0.0811	0.0627	0.0423	0.5518	0.0986
	(0.019)	(0.029)	(0.119)	(0.489)	(0.156)	(0.180)	(0.104)	(0.451)	(0.060)
Observations	1903	346	346	692	519	1384	346	346	519
Adj. R-squared	0.6415	0.8913	0.4845	0.7370	0.8658	0.7399	0.8253	0.2920	0.7205
F-Stat	85.12	574.34	137.82	52.65	107.33	173.29	123.90	79.24	49.59
Effective F-Stat	168.147	19.447	17.138	16.329	18.297	6.933	12.168	2.550	127.045
5% TSLS Critical Value	18.734	21.813	24.957	15.791	30.238	24.918	24.138	23.186	17.601

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses. Id653: Skin and subcutaneous diseases. Id669: Sense organ diseases. Id955: HIV/AIDS and sexually transmitted infections. Id956: Respiratory infections and tuberculosis. Id957: Enteric infections. Id961: Other infectious diseases. Id962: Maternal and neonatal disorders. Id973: Substance use disorders. Id974: Diabetes and kidney diseases

Table (G19) IV Regressions, use of pharmaceuticals by age of treatment (by Level 2 causes)

	Log(DALYs)								
	Id344	Id386	Id491	Id508	Id526	Id542	Id558	Id626	Id640
Log(Intensity of use, new treatments (1990))	-0.3043	-0.0378	0.0248*	-0.0331**	-0.0258	0.0270	-0.0024	-0.0082***	0.0214
	(0.618)	(0.050)	(0.013)	(0.015)	(0.028)	(0.024)	(0.003)	(0.002)	(0.026)
Log(Intensity of use, old treatments (1990))	-0.0510	0.0806	-0.0222	-0.0337	0.0467***	-0.0023	-0.0016*	0.0002	-0.0883
	(0.148)	(0.052)	(0.025)	(0.037)	(0.012)	(0.009)	(0.001)	(0.001)	(0.062)
Log(Prevalence)	0.6154***	0.4031***	0.8663***	0.8204***	0.5905***	0.9978***	0.9744***	0.9564***	1.5563***
	(0.081)	(0.127)	(0.116)	(0.106)	(0.140)	(0.056)	(0.009)	(0.014)	(0.359)
Log(Intensity of treatment use), unmatched	0.0447	0.0969	0.0408	0.0866	0.0941**	0.0056	0.0040	0.0090***	0.1035
	(0.031)	(0.065)	(0.048)	(0.058)	(0.038)	(0.041)	(0.003)	(0.003)	(0.124)
Observations	3287	692	1557	692	1557	865	1384	865	865
Adj. R-squared	0.3463	0.8204	0.3669	0.6705	0.2274	0.8645	0.9946	0.9972	0.5393
F-Stat	44.37	22.22	9.73	23.82	9.24	48.95	2113.52	5603.21	3.96
Effective F-Stat	6.551	20.898	536.055	109.689	67.738	17.080	204.830	69.170	213.375
5% TSLS Critical Value	27.817	26.778	26.005	21.122	28.481	16.607	17.092	27.736	19.000

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses. Id344: Neglected tropical diseases and malaria. Id386: Nutritional deficiencies. Id491: Cardiovascular diseases. Id508: Chronic respiratory diseases. Id526: Digestive diseases. Id542: Neurological disorders. Id558: Mental disorders. Id626: Musculoskeletal disorders. Id640: Other non-communicable diseases.

Table (G20) Continued from previous table

	Log(DALYs)							
	Id653	Id669	Id955	Id956	Id957	Id961	Id962	Id973
Log(Intensity of use, new treatments (1990))	-0.0150	0.0164*	-0.0731	0.0056	0.1436	0.0000	0.0054	-0.0412
	(0.011)	(0.009)	(0.083)	(0.099)	(0.122)	(.)	(0.029)	(0.042)
Log(Intensity of use, old treatments (1990))	0.0231*	-0.0019	-0.0533	-0.0955	-0.0572	-0.0283	-0.0028	-0.0688***
	(0.012)	(0.008)	(0.078)	(0.127)	(0.052)	(0.043)	(0.026)	(0.020)
Log(Prevalence)	0.7886***	0.9834***	1.1622***	1.8505***	1.0291***	-0.1114	1.1245***	1.1380***
	(0.065)	(0.057)	(0.215)	(0.375)	(0.064)	(0.171)	(0.169)	(0.197)
Log(Intensity of treatment use), unmatched	-0.0096	-0.0218	0.2410*	0.1777	0.0531	-0.0521	0.0717	0.0809
	(0.019)	(0.017)	(0.124)	(0.164)	(0.101)	(0.115)	(0.115)	(0.058)
Observations	1903	346	346	692	1384	346	346	519
Adj. R-squared	0.6064	0.9462	0.5274	0.7302	0.7323	0.8503	0.8842	0.7084
F-Stat	45.46	645.75	19.68	64.79	104.38	267.54	398.57	43.24
Effective F-Stat	50.386	197.636	2.974	10.337	21.177		50.713	4.844
5% TSLS Critical Value	19.102	24.310	23.627	18.608	30.455		21.140	17.673

*, ** and *** indicate significance at the 10%, 5% and 1% levels, respectively. Robust standard errors are shown in parentheses. Id653: Skin and subcutaneous diseases. Id669: Sense organ diseases. Id955: HIV/AIDS and sexually transmitted infections. Id956: Respiratory infections and tuberculosis. Id961: Other infectious diseases. Id962: Maternal and neonatal disorders. Id973: Substance use disorders. Id974: Diabetes and kidney diseases

General conclusion

Access to treatment has been a longstanding concern for countries around the world, as reflected in the importance assigned to healthcare in both the Millennium Development Goals (MDGs) and Sustainable Development Goals (SDGs). The role that pharmaceuticals have played since the introduction of the world's first synthetic pharmaceutical, Aspirin, in 1897 and the significant advances in drugs for a wide range of health concerns during the twentieth century, has motivated the implementation of the WHO's list of essential medicines (LEM) in 1977. As defined by the WHO, essential medicines "are those that satisfy the priority health care needs of a population" and "are intended to be available in functioning health systems at all times" and "at prices individuals and health systems can afford." In that regard, targets 8.E and 3.8 of the MDGs and SDGs, respectively, aimed to realize these objectives by promoting access to affordable essential drugs and ensuring financial risk protection in the process. In line with their role, scrutiny that is required in their development, pricing, and subsidizing is of high relevance around the world.

This thesis is a work in reverse gear. The starting point is the importance of pharmaceuticals in every healthcare system. Next comes the issue of whether patients can easily access pharmaceuticals without having to deal with eventual financial hardships. The last question, which became the first in our work, addresses the optimality of the choice made by governments on which treatments to subsidize, constituting a cost-opportunity situation—subsidizing a bad treatment is worse than not subsidizing treatments at all. While additional work is necessary to refine the results suggested by our work, we argue that it is necessary for studies based on real-world data to be promoted during discussions involving healthcare policies, whether they are national or international. The

scarcity of studies in the developing world is no longer as forgiving as before. Therefore, we hope that this work helps shed light on the specificities of developing countries and the need to produce tailored studies that take that into account for better understanding and adequate policy decision-making.

Bibliography

RÉSUMÉ

L'amélioration de la santé a toujours été une préoccupation des organisations internationales et des pays du monde entier. Pour atteindre cet objectif, l'accès à des soins de santé de meilleure qualité a été jugé nécessaire. Les produits pharmaceutiques jouent un rôle crucial dans les services de santé, s'avérant efficaces pour réduire la morbidité et la mortalité. De plus, afin d'atténuer les difficultés financières pendant le traitement, l'assurance maladie nationale couvre une partie des coûts supportés par les patients. Dans cette thèse, nous examinons d'abord comment un ministère de la santé choisit les produits pharmaceutiques à subventionner dans le cadre des prestations de santé de l'assurance maladie nationale. Nous cherchons ensuite à déterminer si la prise en charge de certains traitements se traduit par une augmentation de leur utilisation. Enfin, dans un échantillon de pays, nous étudions la contribution des produits pharmaceutiques à l'amélioration de la santé au cours des deux dernières décennies.

MOTS CLÉS

Industrie pharmaceutique, Produits pharmaceutiques, Remboursement, Utilisation, Santé, Assurance maladie.

ABSTRACT

Improving health has always been a concern for international organizations and countries around the world. In pursuit of this goal, access to better healthcare has been deemed necessary. Pharmaceuticals play a crucial role in healthcare services, proving to be efficacious in reducing morbidity and mortality. Furthermore, to mitigate financial hardships during treatment, national health insurance covers a portion of the costs faced by patients. In this thesis, we first examine how a ministry of health chooses which pharmaceuticals to subsidize as part of the health benefit of the national health insurance. We then investigate whether covering certain treatments translates into increased utilization. Finally, in a sample of countries, we study the contribution of pharmaceuticals to improved health over the last two decades.

KEYWORDS

Pharmaceutical industry, Pharmaceuticals, Reimbursement, Utilization, Health, Health insurance.