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MEDICINES IN INDIA:

PRACHI SINGH, SHAMIKA RAVI AND DAVID DAM

Accessibility, Affordability and Quality

MARCH 2020

Recommended citation:

Singh, Prachi; Ravi, Shamika & Dam, David: "Medicines in India: Accessibility, Affordability and Quality," Brookings India Research Paper No. 032020-01

ISBN 978-81-941963-6-5

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Acronyms	
AMRIT	Affordable Medicines and Reliable Implants for Treatment
API	Active Pharmaceutical Ingredient
ATC	Anatomical Therapeutic Chemical
BPPI	Bureau of Pharma Public Sector Undertakings of India
CDSCO	Central Drugs Standard Control Organisation
DPCO	Drug Price Control Order
FDA	Food and Drug Administrations
FS	Fake/Spurious and Substandard
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
ICMR	Indian Council of Medical Research
JA	Jan Aushadhi Pariyojna
MIC	Minimum Inhibitory Concentration
MNC	Multinational Corporations
MRP	Maximum Retail Price
NABL	National Accreditation Board for Testing and Calibration Laboratories
NDPS	Narcotic Drugs and Psychotropic Substances
NGO	Non-Governmental Organisation
NHA	National Health Authority
NIB	National Institute of Biologicals
NLEM	National List of Essential Medicines
NPPA	National Pharmaceutical Pricing Authority
NSQ	Not of Standard Quality
OOPE	Out-of-Pocket Expenditure
PMBJP	Pradhan Mantri Bhartiya Janaushadhi Pariyojana
PMJAY	Pradhan Mantri Jan Arogya Yojana
SCST	Schedule Castes/Schedule Tribes
SNCM	Standard National Committee on Medicines
THE	Total Health Expenditure
TNMSC	Tamil Nadu Medical Services Corporation
UT	Union Territory
WHO	World Health Organization
WHO-GMO	WHO's Good Manufacturing Practices
WTO	World Trade Organization

Acknowledgments

The authors would like to thank many people for their contributions to this study. We thank Dr. Deepika Saraf (Indian Council of Medical Research), Dinesh Thakur and an anonymous reviewer for their extensive comments and suggestions on the original draft. In addition, we would like to thank Sachin Singh (CEO of Bureau of Pharma PSUs of India) and Asif Khan (Bureau of Pharma PSUs of India) for extending their help to us by sharing data on Pradhan Mantri Bharatiya Janaushadhi Pariyojana. We would also like to thank Zehra Kazmi and Rohan Laik for editing this report, Mukesh Rawat for his work on designing the report and Aradhika Menokee for her research support. The conclusions and recommendations of any Brookings India publication are solely those of its authors, and do not reflect the views of the Institution, its management, or its other scholars. Brookings India does not hold an institutional view on any subject.

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Executive summary

Pharmaceuticals contribute 43.16% to the total out-of-pocket expenditure (OOPE) on health. This makes it the single largest category under OOPE, followed by expenditure incurred in private hospitals, medical diagnostics, government hospitals, and general medical practitioners, in that order.

The Pradhan Mantri Bhartiya Jan-Aushadhi Pariyojna (PMBJP) scheme, aimed at providing cheap, high-quality generic medicines, now has 5,294 stores in India. This scheme was launched in 2008 but initially suffered setbacks due to supply chain management issues. The revamped scheme provides financial incentives to store owners and boasts an expanded product basket with over 1000 medicines and 154 surgical items.

The JA scheme saw maximum expansion in urban districts, areas of high literacy and high level of development. The establishment of JA stores is driven by considerations of potential market size and resulting profits. Most districts in 2019 had at least one JA store but few Northeastern and Central districts have no JA stores.

E-pharmacies form 0.5% of the Indian pharmaceutical market. At present, the maximum number of e-pharmacy sales take place in Delhi. The e-pharmacy market segment is primed to take off due to increasing internet reach; the untapped rural market can fuel future growth. Prescription verification, safe transportation, and ethical disbursement of medicines are important issues in this domain.

Between 3-4% of drugs are found to be substandard, or fake or spurious (FS) in India. The level of FS drugs is especially high when sourced from government outlets as against retail outlets. Northeastern states are outliers when it comes to low-quality drugs. The proportion of sub-quality drugs found from both retail outlets and government sources in Northeastern states is very high when compared to the national average.

FS drugs originate from manufacturing sites that may lie outside a state legislative boundary. Data analysis from six states reveal that drugs manufactured in Himachal Pradesh and Uttarakhand are of low-quality. States are powerless when it comes to de-licensing firms that produce bad quality medicines but lie outside the state boundary. Almost all states face an acute shortage of drug inspectors required for drug-testing and inspections.

Multiple firms are responsible for notifications regarding FS drugs. The problem of low-quality drugs is not because of a handful of manufacturing firms, multiple firms routinely flout the norms.

Price control has been chosen as the policy instrument to keep costs of drugs low in the country. The Drug Price Control Order (DPCO) of 2013 has put 347 drugs on the National List of Essential Medicines (2011) under price control. The number of drugs that fall under price regulation have increased under all therapeutic classes.

The disease burden of the country has shifted away from communicable to non-communicable diseases. The latest DPCO has witnessed an increase in drugs put under regulation from key therapeutic classes which include cardiovascular, alimentary tract, and metabolism (related to diabetes) and respiratory therapeutic class.

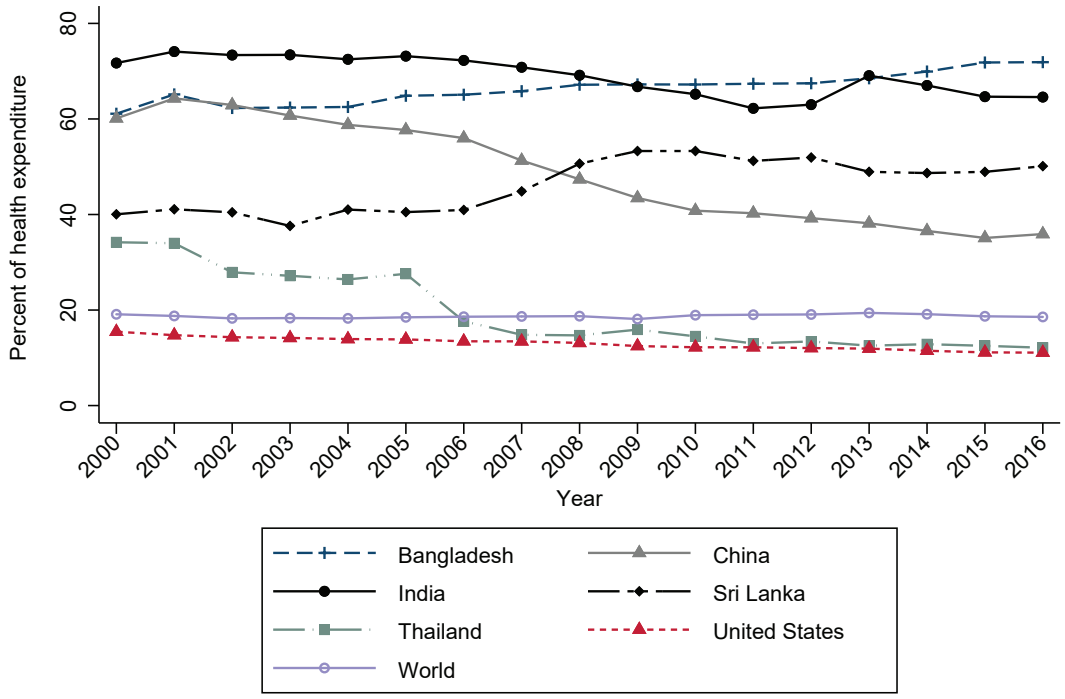
Introduction

Healthcare expenditure is financed through various sources in a country. It can be financed by the government (state or union), insurance schemes (public or private) or borne by households directly in the form of out-of-pocket expenditures (OOPE). More financing by the government implies less financial burden on households in the form of huge out-of-pocket expenses. The World Health Organisation's (WHO) data on global health expenditures, graphically presented below in Figure 1, reveals that when it comes to out-of-pocket expenditure as a proportion of current health expenditure, India does much worse in comparison to the world average (65% for India versus world average of around 20% in 2016). A comparison with other Asian countries also reveals a similar scenario. Thailand and China have reduced the proportion of out-of-pocket expenditure over time, while Sri Lanka and Bangladesh witnessed an increase over time.

The state-level scenario is not very different from the national picture which reveals that the burden of health expenses falls mostly on households. In the state of Bihar, out-of-pocket expenses are a whopping 80% of the total health expenditure. In Uttar Pradesh, India's most populous state, OOPE forms three-fourth of the total health expenditure. Some states do relatively better, such as Karnataka, Himachal Pradesh, and Gujarat, but even in these states, households bear almost half of the total health expenditure as OOPE.[1]

OOPE warrants special attention as it leads to impoverishment, with 7% of the households falling below the poverty line on account of health expenses.[2] OOPE has increased in both rural and urban areas with the expenditure attributable to medicines forming the single largest category. Medicines are an integral part of any medical treatment and the expenditure incurred on them is quite substantial. The share of medicines in OOPE was around 51% in 2013-14, this figure reduced to 43% in 2015-16, but still remained the biggest contributor to the OOPE incurred by households. Lastly, out of the total pharmaceutical expenditure incurred by households, 18% is for in-patient treatment while 82% is for out-patient care. These figures suggest that the cost of pharmaceuticals is an important area for policy intervention.

Figure 1: Out-of-pocket expenditure as a percentage of health expenditure, 2000-2016



Source: Data from World Health Organization - Global Health Expenditure Database.

[1] National Health Accounts 2015-16.
[2] Ravi, Shamika, Rahul Ahluwalia, and Sofi Bergkvist. "Health and Morbidity in India (2004-2014)." Brookings India Report (2016).

In this report, we focus on three important aspects of medicines in India – accessibility, quality, and affordability of drugs. The first part analyses access to drugs from two main perspectives – the accessibility of medicines via Jan Aushadhi (JA) stores and e-pharmacies. With branded generic drugs priced far higher than their unbranded generic counterparts, access to reasonably-priced drugs is limited in India. To address this, the Jan Aushadhi scheme was launched in 2008 to increase access to affordable and quality medicines. The key features of this scheme included setting up pharmaceutical stores with government support and making cheaper drugs available to consumers. Using district-level demographic and economic characteristics, we find that more JA stores are found in districts with larger proportions of urban population, higher literacy rates and a greater level of development. Despite the incentive-based nature of the scheme, which rewards store owners for the volume of business, some districts in the Northeast and Central India failed to attract any JA entrepreneurs. Lastly, with the proliferation of the internet in urban cities, we have witnessed the growth of e-pharmacies. The market share of this segment is currently small but the convenience and price discounts offered by startups in this domain are set to propel the e-pharmacy sector in the coming years. In this relatively new, innovative space, business growth has to be balanced against important regulatory needs. Without an accurate prescription validation mechanism, we could witness a rise in antibiotic resistance over time or overuse and habit formation for opioids.

While access to affordable medicines is important, the quality of medicines is essential to achieve desired curative outcomes. In the second chapter, we look at drug-testing capabilities and bottlenecks such as the shortage of manpower needed for inspections. We draw upon publicly available information from the Central Drugs Standard Control Organisation (CDSCO), Lok Sabha questions, and notifications related to substandard and spurious drugs released by individual state regulatory bodies. Based on CDSCO data, we find that the overall percentage of substandard and spurious drugs in India is around 3-4% for the years 2014-16. Data from six individual states show that most notifications related to substandard drugs originate from manufacturing units within the same state. However, a substantial proportion of these alerts are ascribed to drugs originating from other states such as Himachal Pradesh and Uttarakhand. The state regulatory machinery is powerless when it comes to punitive actions against manufacturing units located outside the state's administrative boundaries.

In the final chapter, we focus on past policies that have struck a balance between providing affordable and reasonably priced medicines to consumers and enabling the pharmaceutical industry to grow with sufficient profit margins. Price regulation of pharmaceutical products is the policy instrument that has been used to address the affordability of medicines in India. It is implemented by the Department of Pharmaceuticals under the Ministry of Chemicals and Fertilisers via Drug Price Control Orders (DPCOs), with the National Pharmaceutical Pricing Authority acting as the executing body.

The recent drug price regulation extended price control to 347 drugs (with over 800 formulations) that are on the National Essential List of Medicines. The ambit of regulation increased from just 74 drugs being regulated between 1995 and 2012 to 347 drugs post-2013. This report aims to examine how drug price regulation has evolved over the last four decades during which three-drug price control orders were executed. We also analyse how this regulation has kept pace with the changing disease burden in the country during the same time period. Though the scale of the regulation has increased over time, there was a brief period of deregulation as a result of DPCO 1995. We observe that recent orders have increased drugs under regulation in all therapeutic classes, especially drugs used to treat cardiovascular and respiratory diseases, which have witnessed an increase in disease burden as well.

It is important to consider all aspects of drug accessibility – affordable medicines will lessen the financial burden on households; easy availability of generics would mean less reliance on expensive alternatives, and good-quality of drugs is the minimum requirement for effective treatment. Through our analyses in each of these three chapters, we put forth recommendations aimed at addressing issues in the quality of medicines, increasing the availability of medicines and the structure of price control in our country.

CHAPTER—**01**

ACCESSIBILITY

1.1 Introduction

India's total health expenditure (THE) amounts to 3.8% of GDP, as of 2015-16. Out-of-pocket expenditures (OOPE) are a major component of THE, constituting 60.5% of all expenditure. Breaking down OOPE by its components reveal that expenditures on pharmaceuticals is quite substantial, amounting to 43% of the OOPE. With greater financial burden of pharmaceutical expenditures falling on households, access to affordable medicines is of paramount importance. While affordability has received policy focus (in the form of price controls on selected drugs), availability of essential medicines has remained an area of grave concern. In 2004, the World Health Organisation estimated that 649 million Indians lacked regular access to essential medicines.[3] Another study of six locations in India revealed a median availability of a basket of essential medicines to be 0-30% in the public sector.[4] With the dual intention of addressing affordability and availability of medicines, the central government launched The Pradhan Mantri Bhartiya Jan-Aushadhi Pariyojna (PMBJP)[5] in 2008 with a mandate to sell quality generic medicines in India. In the following sections, we describe how access to medicines has improved spatially under Jan Aushadhi scheme and how it can be improved further. We also critically assess the new platforms that sell medicines online, and the potential concerns that could arise when medicines are offered on alternate platforms like these. In light of the Sustainable Development Goal of achieving universal health coverage for all by 2030, access to safe, effective, quality, and affordable essential medicines needs to be addressed. New schemes like Jan Aushadhi need to be assessed carefully since they can potentially solve the problem of accessibility for millions of vulnerable patients in our nation.

[3] World Health Organization (2004). *The World Medicines Situation.* Retrieved January 17, 2019 from: http://apps.who.int/medicinedocs/en/d/Js6160e/9.html.

[4] *Indian Journal of Medical Research (2007)* Kotwani, A. et al (2007) Medicine prices & availability of common medicines at six sites in India: Using a standard methodology.

5 We refer to this scheme as Jan Aushadhi or JA Scheme (JA), interchangeably throughout the report.

Jan Aushadhi scheme

Launched in 2008, the main objectives of the Jan Aushadhi (JA) scheme are to sell affordable, generic, and high-quality medicines through dedicated stores. While the Bureau of Pharma Public Sector Undertakings of India (BPPI) monitors the scheme, the government does not directly operate these Jan Aushadhi stores. Instead, anyone can register and open a store if they meet certain requirements.[6]

Government-nominated non-governmental organisations (NGOs) or institutions can operate JA stores located inside government hospitals or within medical college premises; the state government would provide the space free of charge. Other NGOs and organisations with the experience, space, and financial capacity to open a store can also apply online. Individual entrepreneurs, provided that they meet set requirements, can also open their own stores. The medicines sourced in these stores originate from manufacturers who follow the WHO's Good Manufacturing Practices (WHO-GMP) guidelines.[7] Drug-testing laboratories accredited by the National Accreditation Board for Testing and Calibration Laboratories (NABL) provide further quality checks before the medicines reach store outlets for sale.[8]

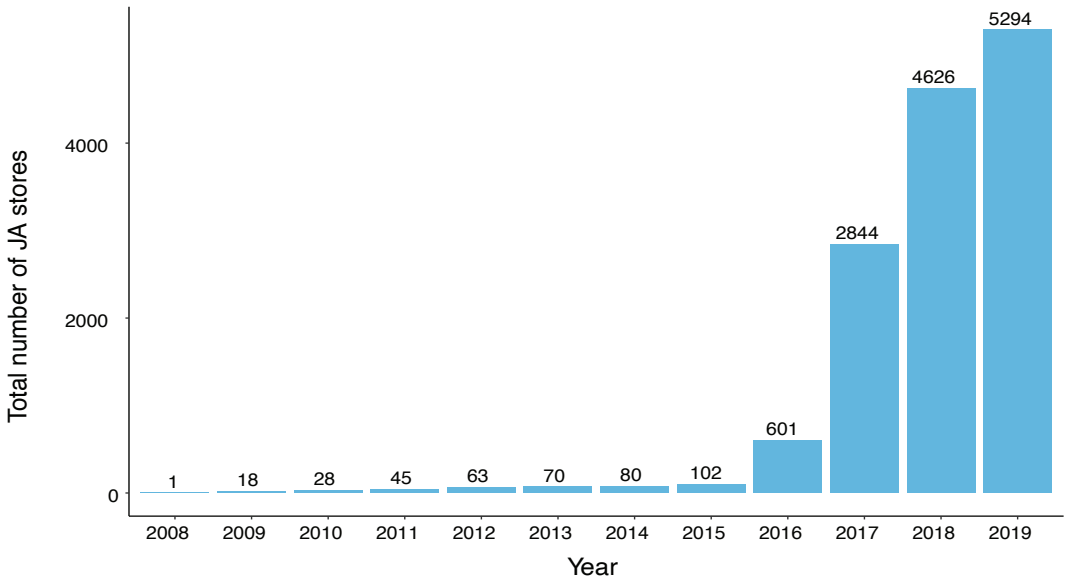
Once an application is accepted, a one-time grant of Rs. 2.50 lakhs is provided to store owners. The break-down of this grant varies based on the applicant. Those opening stores in a government hospital, medical college, or any government-owned building receive up to Rs. 2.50 lakhs,[9] which includes Rs. 1 lakh reimbursement for furniture and fixtures, Rs. 1 lakh worth of medicines at the start of the store's operation, and Rs. 50,000 for computers, internet, printers, scanners, etc.[10] For other stores that are linked with BPPI software, owners are given 15% of the store's monthly sales up to a total limit of Rs. 2.50 lakhs, with a maximum of Rs. 10,000 per month.[11] This monthly ceiling is higher at Rs. 15,000 for stores located in Northeastern states and tribal areas. Applicants belonging to Scheduled Castes, Scheduled Tribes, and those who are differently-abled receive Rs. 50,000 worth of medicines in advance, in addition to 15% of monthly sales up to Rs. 2.50 lakhs, with a maximum of Rs. 10,000 per month. Thus, the early successes of the Jan Aushadhi scheme depended on organisations or individuals finding incentives to open these stores, and then ensuring these stores are well-stocked and functioning.

For the first few years, the programme struggled. Few new stores opened for the first half-decade that the programme was in effect (Figure 2). Additionally, problems plagued those that did open. The Public Health Foundation of India evaluated the scheme and found that the JA stores overly depended on external support, and poor supply chain management resulted in shortages.[12] Individual state governments also had their own policies aimed to increase access to drugs, rendering Jan Aushadhi stores in those specific states extraneous to already-existing programs.

In 2015, the government rebranded the Jan Aushadhi scheme while also waiving the application fee and providing additional financial support. The government also increased trade margins for retailers from 16% to 20%, and from 8% to 10% for distributors.[13] These increased trade margins allowed retailers to gain more of a profit; they can now price the medicines 20% higher than what they bought them for, as opposed to the original 16%. The financial incentive was raised to Rs. 2.50 lakhs, where it currently stands, from the original Rs. 1.50 lakhs. This push, along with an improved supply chain, has allowed the number of JA stores to swell to over 5200 (Figure 2).[14]

[6] http://janaushadhi.gov.in/FAQ.aspx
[7] Bureau of Pharma Public Sector Undertakings of India, Department of Pharmaceuticals.
[8] Ibid.
[9] Department of Pharmaceuticals, Annual Report 2017-2018.
[10] http://janaushadhi.gov.in/pdf/State%20Govt_16012019.pdf
[11] Department of Pharmaceuticals, Annual Report 2017-2018.
[12] http://pib.nic.in/newsite/mbErel.aspx?relid=117031
[13] Department of Pharmaceuticals. Annual Report 2017-2018.
[14] Bureau of Pharma Public Sector Undertakings of India, Department of Pharmaceuticals as of June 2019.

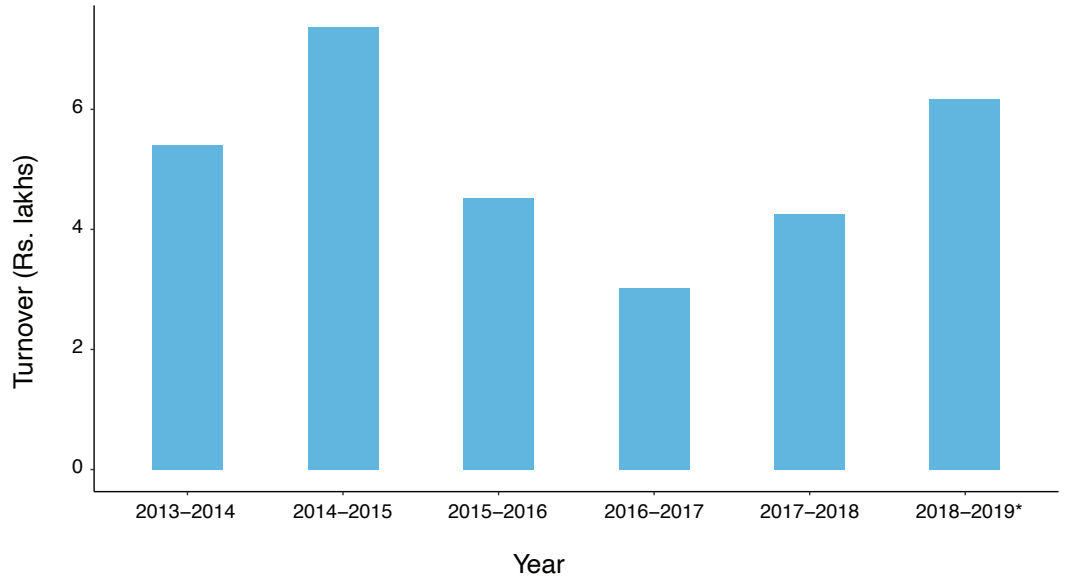
Figure 2: Cumulative number of Jan Aushadhi stores over time



As of June 2019. Data provided by Bureau of Pharma Public Sector Undertakings of India, Department of Pharmaceuticals

Purchases at these stores have also increased since 2014. Unbranded generics are estimated to be about 5% of the Indian domestic pharmaceutical market, according to BPPI. As of March 31, 2019, in the 2018-2019 financial year, the scheme reported Rs. 315 crores in sales. Accounting for the number of functional Jan Aushadhi stores, Figure 3 presents the average turnover for a single Jan Aushadhi store.

Figure 3: Average turnover (Rs. Lakhs) of a Jan Aushadhi store, yearly



*As of March 31, 2019 Data provided by Bureau of Pharma Public Sector Undertakings of India, Department of Pharmaceuticals

The average turnover per store decreased from financial year 2014-2015 to 2016-2017. However, this figure has risen in the past two years, signaling that not only are the number of stores increasing across the country, more people are buying from these stores as well. BPPI estimates that Rs. 315 crores of unbranded generic medicines sold in 2018-19 equates to a value of Rs. 2000 crores in branded alternatives.[15]

[15] Bureau of Pharma Public Sector Undertakings of India, Department of Pharmaceuticals.

1.2 Analysis

1.2.1 Price benefits

The Jan Aushadhi website lists each formulation provided in their stores, the price offered by the JA stores, and the price offered by the top three leading brands. While the price savings for each drug can then be calculated, we instead aggregate such information by their defined therapeutic classes to present average percent savings at Jan Aushadhi stores. More than 900 medicines and 154 surgical items make up the product basket offered by the JA scheme,[16] with major price benefits for all therapeutic class categories.

Table 1 shows the average percent decrease in drug prices (compared to the top three leading brands) by therapeutic class. For example, the 108 formulations covered under the anti-infective drugs therapeutic class had an average 62.66% price decrease compared to the top three leading brands. The therapeutic class with the largest price decreases was drugs acting on urogenital organs (83.39% decrease for six formulations), while the smallest price decrease was for solutions correcting water and electrolyte disturbances (52.35% decrease for two formulations). Currently, all medicines are cheaper by at least 50%, with over 300 medicines seeing their prices reduced by at least 80%.[17]

Table 1: Average price benefits of Jan Aushadhi stores

Therapeutic class	Percent decrease	Formulations covered
Analgesic and antipyretic /Muscle relaxant	-76.20%	51
Antiallergic drugs	-77.37%	17
Anticancer drugs	-74.69%	16
Antiinfective drugs	-62.66%	108
Diuretic drugs	-55.07%	5
Drugs acting on cardio vascular system	-74.47%	82
Drugs acting on central nerve system	-73.12%	54
Drugs acting on endocrine gland including steroids & immunosupressant	-59.19%	17
Drugs acting on eye & ENT	-69.98%	14
Drugs acting on female reproductive organs	-78.12%	6
Drugs acting on gastro-intestinal-tract	-68.87%	53
Drugs acting on respiratory tract	-60.33%	16
Drugs acting on skin (Topical/local Application)	-69.66%	29
Drugs acting on urogenital organs	-83.39%	6
Drugs used in diabetes	-68.18%	32
Local/General anaesthetics drugs	-61.34%	4
Miscelleneous	-79.64%	1
Solutions correcting water & electrolite disturbances	-52.35%	2
Vaccine	-52.38%	1
Vitamins, minerals & food supplement	-75.03%	18

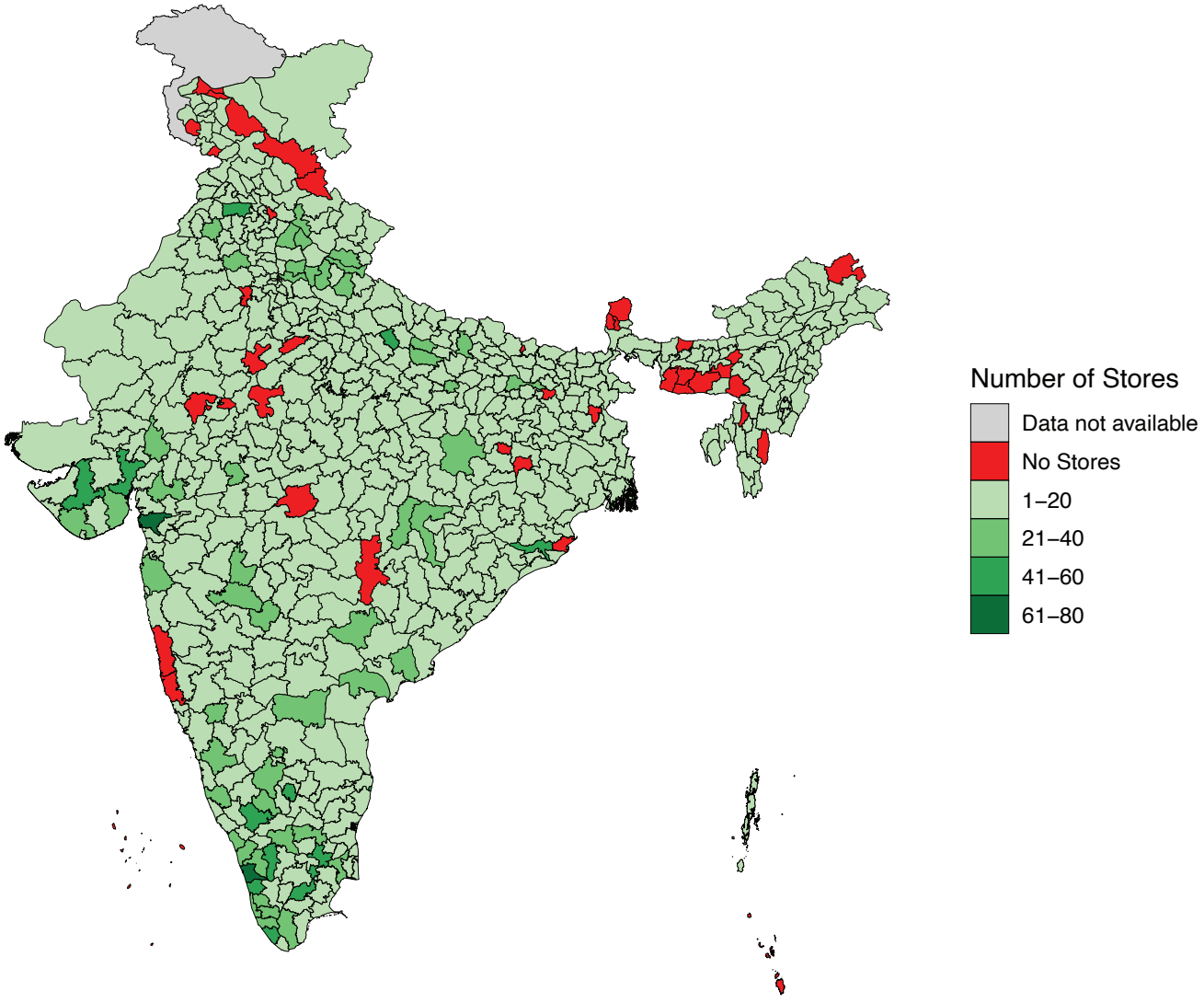
Source: http://janaushadhi.gov.in/Data/pmbjp-book.pdf

[16] Bureau of Pharma Public Sector Undertakings of India, Department of Pharmaceuticals.
[17] Ibid.

1.2.2 Spatial distribution

The increase in the number of JA stores and the reported price differences are both positive signs for increasing accessibility to essential medicines. However, a spatial distribution analysis can provide further insights into whether these JA stores serve all areas of the country. Additionally, the scheme still faces several obstacles that could hinder its full potential to provide essential medicines at affordable prices. To conduct the following analysis, we obtained data of Jan Aushadhi stores from the Bureau of Pharma Public Sector Undertakings of India. We aggregated the stores by their districts, and mapped them to the 2011 district boundaries. For stores located in new districts, we mapped them back to the original 2011 districts from which the new districts were carved out, or looked up the pincode of the store and remapped that location back to its 2011 district.

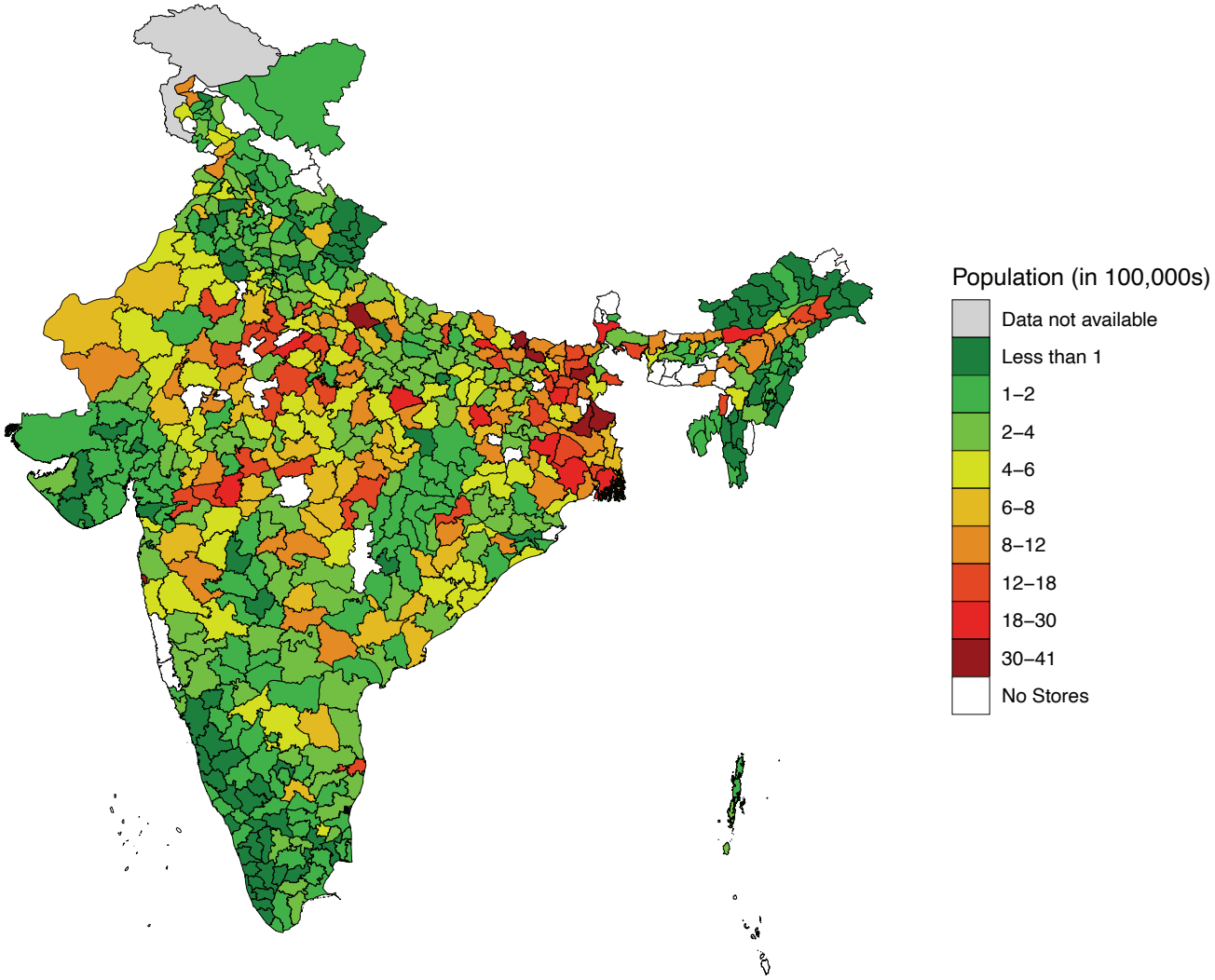
Figure 4: Number of Jan Aushadhi stores by district



As of June 2019. Data provided by Bureau of Pharma Public Sector Undertakings of India, Department of Pharmaceuticals

Figure 4 shows that the rapid expansion of JA stores has allowed most districts to have at least one JA store as of June 2019, but some districts still lack the presence of even a single JA store. Most of these districts are concentrated in East India, where, for example, the state of Meghalaya has only one JA store as of June 2019. Many southern districts enjoy an abundance of JA stores, such as Thrissur in Kerala which has 79 stores. However, district populations vary. Some districts with smaller populations may only need one JA store to serve their needs while denser districts would require a larger number of JA stores. Figure 5 below shows the number of people within a district that are served by a JA store. In other words, we divide the population by the number of JA stores in that district.

Figure 5: Population per Jan Aushadhi store by district



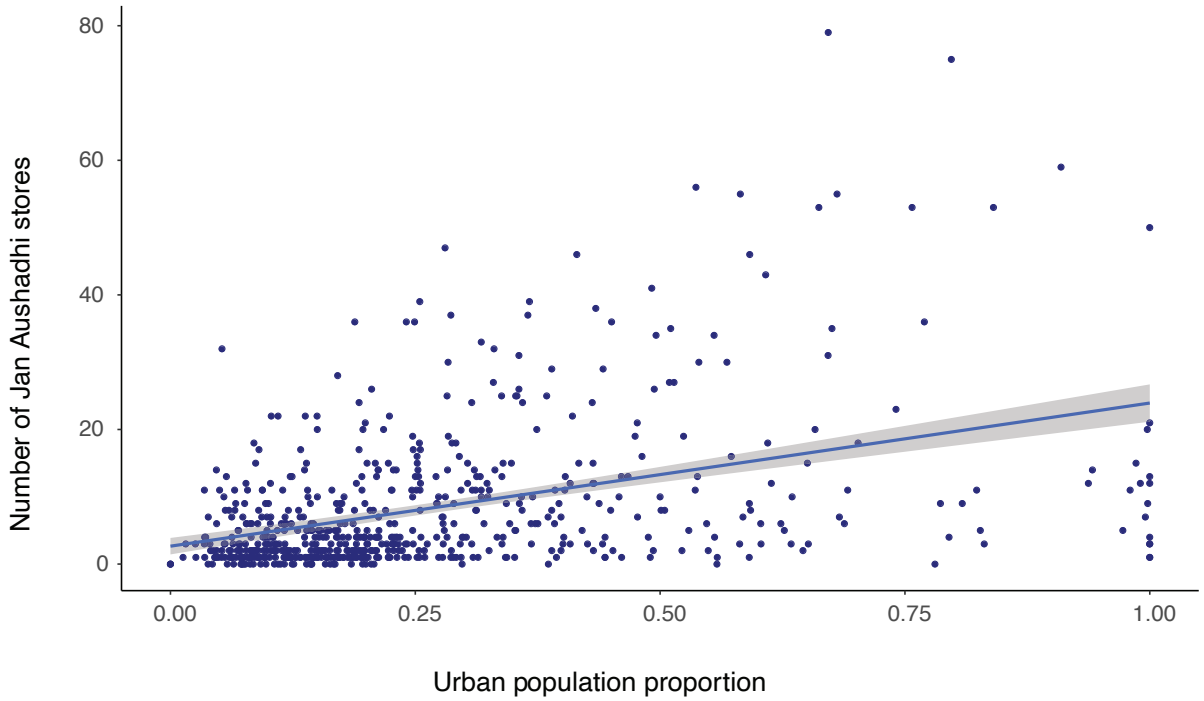
As of June 2019. Data provided by Bureau of Pharma Public Sector Undertakings of India, Department of Pharmaceuticals

The numerous JA stores in the southern districts allow some districts to have fewer than 100,000 people served by a single JA store. Thrissur in Kerala has a JA store for approximately every 40,000 people within the district. However, other districts, most of them lying in the north-central and eastern regions of India, have far too few JA stores to serve their populations. For example, the single JA store in Birbhum, West Bengal, serves the district's entire population of 3.5 million. That many people served per JA store can potentially put immense pressure on drug supplies.

1.2.3 Determinants of JA stores establishment in a district

We observe that variations exist within the country in terms of where these Jan Aushadhi stores open. This observation is not surprising; the establishment of a JA store could be seen as a business decision, where district-level variables factor into the decision on whether a store could generate a profit. Thus, more stores could open in urban areas where there are more people. In Figure 6 below, we provide a scatterplot of each district's urban population proportion and the number of Jan Aushadhi stores it has to better examine this relationship.

Figure 6: Relationship between a district's number of Jan Aushadhi stores and urban population proportion



As of June 2019. Each dot represents one district, data for number of stores from Bureau of Pharma Public Sector Undertakings of India, Department of Pharmaceuticals

The scatterplot (Figure 6) shows that districts with higher proportions of urban populations do tend to have more Jan Aushadhi stores. We fit a regression line to capture the overall pattern of number of JA stores versus proportion of urban population in a district. The positive-sloping line implies that some sort of positive relationship does exist between a district's urban population proportion and number of Jan Aushadhi stores.

We use a few district-level variables to see whether any relationship exists between the number of Jan Aushadhi stores and the district's demographics in Table 2. We use the population density per square kilometer because denser districts could have more stores due to increased footfall, and bigger potential market size. The SC/ST population proportion is used as a signal to see whether more stores open in areas where there are large proportions of historically disadvantaged groups. The literacy rate is another signal that could imply whether a district's population is aware about the scheme, its benefits and the safety of generic drugs. All of these variables come from the 2011 census.

The number of sub-centers, primary health centres, and community health centres are obtained from the 2018 Rural Health Statistics to see whether districts that have more rural healthcare infrastructure in place have more stores as well. Finally, nightlights data from 2013 serves as a proxy for economic well-being of a district, such as how wealthy and how developed it is.

We divide these districts into four quartiles on the basis of the district's urban population proportion (Table 2), based on the assumption that stores are more likely to be opened in urban areas due to larger potential market size or greater ease of access. Within each of these four quartiles, we average the selected variables to analyse if certain patterns exist.

Table 2: Urban population proportion quartiles

	Q1 Less than 11.70%)	Q2 (11.70% to 19.82%)	Q3 (19.83% to 33.85%)	Q4 (33.86% to 100%)
Averages				
Number of Jan Aushadhi stores	3.98	4.68	8.98	15.45
Population density per square kilometer	511.15	393.06	399.44	2441.06
SC/ST population proportion	0.38	0.37	0.30	0.26
Literacy rate	66.98	68.55	72.26	81.45
Subcentres	215.53	252.84	292.58	235.95
Primary health centres	37.54	38.74	48.44	37.24
Community health centres	7.88	8.85	9.88	8.78
Nightlights	2.44	3.84	6.80	15.96
Districts	**160**	**160**	**160**	**160**

Districts that are in the top 25% in terms of urban population proportion have an average of 15.45 stores per district, much higher than the average 3.98 stores for districts in the bottom 25%. Interestingly though, our variable breakdowns show that districts with higher urban population proportions also have higher literacy rates, lower Scheduled Castes/Scheduled Tribes (SCST) population proportions, and more nightlights. These relationships all imply that Jan Aushadhi stores open in more urban, developed districts. However, this pattern works against the government's aims of increasing access to essential medicines for those who need it the most: the more rural districts where the population is more dispersed and less wealthy.

1.3 Discussion

Revamping the programme and increasing incentives for organisations and individuals to open Jan Aushadhi stores has greatly increased the number of stores nationwide. However, the scheme's model could fail to fulfil the programme's goal of making essential medicines accessible to all. Because opening these stores is a business decision, store owners inevitably consider their abilities to generate profits in certain places. Our findings indicate that these places—where more Jan Aushadhi stores are located—tend to be in better-off districts where these districts are more developed, wealthy, and urban. Fewer stores are found in poorer, less developed, and rural districts—the kinds of districts that the JA scheme is supposed to target. The districts that already lack access to essential medicines do not see a strong presence of JA stores. Rural areas are also where pharmaceuticals have the most potential for growth. A PricewaterhouseCoopers report using IMS Health data from 2010 reported that while nearly two-thirds of India's population live in rural areas, rural markets contribute only 17% to the overall domestic pharmaceutical market.[18]

In addition to the JA scheme's main objective of increasing access to medicines, its mission statement attempts to create increased awareness among the general public regarding generic medicines and to create a demand for generic medicines through medical practitioners.[19] The pursuit of these goals become more difficult especially given the high amount of marketing/advertising which is conducted by branded drug companies to target medical practitioners in India.[20] This leads to higher number of prescriptions for branded drugs which are more costly than generic drugs for patients. BPPI is currently testing a mobile-based application that would allow a consumer to find generic substitutes for a prescribed branded drug and

[18] PricewaterhouseCoopers (2011). "India Pharma Inc.: Capitalising on India's Growth Potential," Retrieved from: https://www.pwc.in/assets/pdfs/publications-2011/pwc_cii_pharma_summit_report_22nov.pdf.
[19] http://janaushadhi.gov.in/pmjy.aspx
[20] Vijay Thawani, Abin Mani, and Neeraj Upmanyu (2017), "Why the Jan Aushadhi Scheme Has Lost Its Steam in India?" *Journal of Pharmacology & Pharmacotherapeutics* 8, no. 3: 134-36, Accessed January 17, 2019, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5642129/.

locate nearby stores that stock those medicines.[21] This initiative would help direct consumers toward cost-saving generic medicines, as well as the Jan Aushadhi stores.

However, the JA scheme fails if the public perception of generic drugs does not improve. A descriptive study conducted in northern India found large majorities of people understood the difference between generic and branded drugs, and that generic drugs were cheaper.[22] However, 61% of these people believed that generic medicines have a lower quality than branded medicines, which the study concludes as worrisome for the sustainability of JA scheme. Additionally, another study in southern India assessed perceptions of quality between generic and branded medicines. They found that both patients and health workers perceived branded medicines as better in quality, thus driving them to choose the more expensive medicines.[23] People tend to stick with these branded medicines, which is why some still retain a fair amount of market power (or the ability of a firm to still profit from pricing its products above the market's) even with generic competition.

A Canadian study looked at branded drugs that had no generic competition, and looked at the drugs' prices when generic competitors entered the market. For 81 different products, no change occurred for the branded drugs' prices, and the study found that four or more generic competitors actually increased the price of the branded drug.[24] Danzon et al. (2015) looked at HIV/AIDS, tuberculosis, and malaria drug prices for middle- and low-income countries to examine various effects on prices. They found that a marginal generic retail competitor reduced average generic prices by less than one percent with no impact on the branded incumbent's prices.[25] These studies all suggest that branded drugs retain their market share despite the entrance of generic drugs, and better perception of branded drugs perhaps induces consumers to continue to buy them despite having cheaper options.

Ensuring that high-quality generic medicines are sold in these Jan Aushadhi stores is vital to prevent misinformation. Drugs procured under the Jan Aushadhi scheme already go through quality tests of their own. In a study conducted during the early years of the programme, the authors test the quality of four Jan Aushadhi medicines and their branded counterparts. They find that there was no difference in quality between the two groups of medicines.[26] Thus, the government must do more to promote not only Jan Aushadhi stores, but the public perception of generic medicines as a whole.

Many JA stores already face shortage problems even when the scheme is not at the height of its popularity. News reports of JA stores facing shortages are a norm.[27] Additionally, poor supply chain management has been blamed for the stores not having such essential medicines in stock. Earlier in 2018, the government sought to strengthen the supply chain by establishing five additional regional warehouses, along with a central warehouse in Gurgaon, Haryana.[28] Each store is also connected to a real-time tracking software system to ensure supplies do not run low. Based on the volume of sales of a medicine, different stock level recommendations attempt to provide uninterrupted supplies for fast-moving, average-moving, and slow-moving drugs. As of May 2019, six months' worth of stock was the target for stores to maintain for fast-moving drugs. Four months and two months were the stock maintenance levels for average- and slow-moving drugs.[29] These new improvements are promising for the long-term viability of the Jan Aushadhi programme.

[21] Bureau of Pharma Public Sector Undertakings of India, Department of Pharmaceuticals.

[22] Shailesh Tripathi and Sudip Bhattacharya (2018), "Patient Perception about Generic vs. Branded Medicines Prescribed in a Tertiary Care Hospital in Northern India – A Descriptive Study," *Indian Journal of Pharmacy Practice* 11, no. 2: 91-95. Accessed January 21, 2019. http://dx.doi.org/10.5530/ijopp.11.2.19

[23] Aivalli, P. K., Elias, M. A., Pati, M. K., Bhanuprakash, S., Munegowda, C., Shroff, Z. C., & Srinivas, P. N. (2018). Perceptions of the quality of generic medicines: Implications for trust in public services within the local health system in Tumkur, India. *BMJ Global Health, 2*(Suppl 3). doi:10.1136/bmjgh-2017-000644

[24] Lexchin, J. (2004). The effect of generic competition on the price of brand-name drugs. *Health Policy, 68*(1), 47-54. doi:10.1016/j.healthpol.2003.07.007

[25] Danzon, P. M., Mulcahy, A. W. and Towse, A. K. (2015), Pharmaceutical Pricing in Emerging Markets: Effects of Income, Competition, and Procurement, *Health Econ.*,24, pages 238– 252, doi: 10.1002/hec.3013.

[26] Singhal, G.L. & Anita, K & Nanda, A. (2011). "Jan Aushadhi store in India and quality of medicines therein." *International Journal of Pharmacy and Pharmaceutical Sciences* 3, no. 1. 204-207.

[27] Zubeda Hamid (2018), "Jan Aushadhi Stores Gaining Popularity, but Supplies Low," The Hindu, Accessed January 20, 2019, https://www.thehindu.com/news/cities/chennai/jan-aushadhi-stores-gaining-popularity-but-supplies-low/article22438906.ece.

[28] "Govt to Strengthen Supply Chain of Jan Aushadhi Stores." The Times of India. June 10, 2018. Accessed January 19, 2019. https://timesofindia.indiatimes.com/business/india-business/govt-to-strengthen-supply-chain-of-jan-aushadhi-stores/articleshow/64526716.cms.

[29] Bureau of Pharma Public Sector Undertakings of India, Department of Pharmaceuticals, March 2019.

Lastly, Jan Aushadhi may have to compete with state governments' own programmes that provide essentially the same services, and have product baskets tailored for local needs. Odisha's state government offers over 500 medicines for free under its Niramaya scheme.[30] Other states have programmes in place that have medicine distribution schemes that could impact not only the viability of Jan Aushadhi stores in the area, but dampen the programme's outreach in terms of raising awareness for generic medicines.

For example, Tamil Nadu has its own system to provide essential drugs to its people. The Tamil Nadu Medical Services Corporation (TNMSC) was created in 1994 by the Tamil Nadu government to procure, store, and distribute essential drugs of high-quality throughout the state's healthcare system.[31] A team of medical experts look through lists of drugs and surgical items required by government medical institutions throughout the state to finalise the essential drug list. These drugs are also classified as fast-moving and slow-moving products. Tamil Nadu has 32 warehouses that then deliver medicines to hospitals and medical institutions. Medicines are supplied by manufacturers who submit bids based on postings by the TNMSC. Quality checks of the medicines are conducted at the warehouses.

While the Jan Aushadhi scheme has expanded its partnership to include more public sector undertakings, the scheme today functions in a similar manner to the TNMSC model. However, the scope of Jan Aushadhi means that many of these stores would be less tailored to local needs and disease burden. The product basket of the Jan Aushadhi scheme boasts of nearly 1,000 drugs now. If there was more coordination between state-specific drug schemes and local Jan Aushadhi stores, then this initiative could better serve the local communities.

The JA Scheme is not the only initiative to increase accessibility to cheaper medicines by the Government of India. While PMBJP is run under the Department of Pharmaceuticals, a similar program exists under the Ministry of Health and Family Welfare called the Affordable Medicines and Reliable Implants for Treatment (AMRIT) Retail Pharmacy Stores.[32] HLL Lifecare Limited, a Government of India Enterprise, runs these AMRIT pharmacies, the first of which opened in November 2015. The pharmacy network offers more than 5,200 medicines, devices, and other consumables at large discounts as well. As of February 15th, 2019, AMRIT has saved nearly Rs. 600 crores for patients.

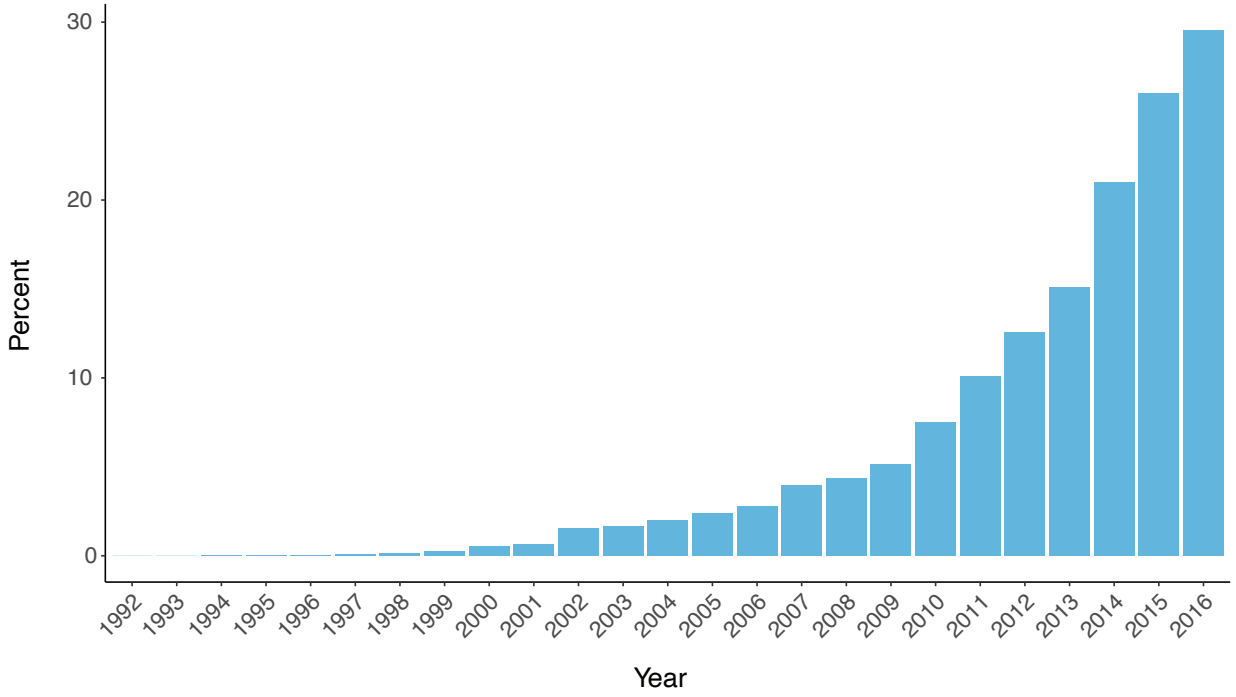
However, there are key differences between AMRIT and JA scheme. There are only 153 AMRIT retail pharmacies operating in 23 States/Union Territories, far below the over 5,000 Jan Aushadhi stores across the country. Retail outlets open in partnership with Central and State Government medical institutions, which hinders its ability to be as widespread as Jan Aushadhi.

[30] Odisha Sun Times Bureau, "After 'Niramaya', Fate of 'Jan Aushadhi' Uncertain in Odisha," Odisha Sun Times, June 13, 2015, Accessed January 20, 2019, https://odishasuntimes.com/after-niramaya-fate-of-jan-aushadhi-uncertain-in-odisha/.
[31] Tamil Nadu Medical Services Corporation, "Drug Procurement Policy."
[32] "Amrit Retail Pharmacy Stores," HLL Lifecare Limited. Available at: http://www.lifecarehll.com/page/render/reference/Amrit_Retail_Pharmacy_Stores_

1.4 Increasing access through e-pharmacies

The proliferation of the internet in modern day lives has revolutionised many industries in economies worldwide. With India's government pushing for digitalisation, the percentage of India's population with access to the internet has grown exponentially in the past two decades (as shown in Figure 7). These numbers have huge ramifications for the sharing economy, where access to goods and services are coordinated through an online community. Thus, many businesses are taking flight through the usage of the internet.

Figure 7: Percent of India's population using the internet



Source: World Bank, from International Telecommunication Union World Telecommunication/ICT Development Report and database

Within the pharmaceutical industry, companies taking advantage of the country's digitalisation have moved into the online pharmacy, or the e-pharmacy, space. Online pharmacies are different from traditional brick-and-mortar pharmacies because they cut out the interactions between the consumer and physical retailers. Some e-pharmacies connect licensed pharmacies to the final consumer, while others dispense directly from their warehouses through online channels.[33] Consumers can access a pharmacy remotely online, purchase medicines based on a prescription, and then have it delivered right to their front door. Data from Health Ministry reveals that around 0.5% of the current pharmaceutical market is catered by e-pharmacies, with sales in Delhi contributing between 10% to 15% of the total e-pharmacy business in India. Analysts predict that the e-pharmacy industry will make up nearly 10% of the pharmaceutical market by 2024.[34]

The business model of e-pharmacies allows them to offer many advantages to consumers. E-pharmacies allow consumers to access a drug marketplace remotely and then have such medications delivered to them. Many e-pharmacies also advertise their much lower costs, mainly through cost-savings of eliminating brick-and-mortar stores and upkeep expenditures. A survey in Delhi suggested that the public is generally aware of online pharmacies, and many desired the accessible services

[33] Priyanka VP, Ashok BK (2016), E-pharmacies Regulation in India: Bringing New Dimensions to Pharma Sector. Pharmaceutical Regulatory Affairs 5, no. 2. doi: 10.4172/2167-7689.1000175

[34] Kuick Research (2018). *India E Pharmacy Market Opportunity Outlook 2024.* https://www.researchandmarkets.com/research/mplbjp/india_e_pharmacy?w=5.

that e-pharmacies provide.[35] However, very few have purchased medicine through these online platforms due to fears of substandard drugs and unlicensed vendors.

Like many aspects of the sharing economy, this lucrative, innovative space presents regulatory challenges. Authorities face difficult questions regarding privacy data, safety concerns, and how the law applies to such entities. Regulators are often slow to act, but regulations should be seen as a way to encourage competition and safety, as opposed to curtailing the industry altogether.[36] Even without the presence of regulations on e-pharmacies, the Federation of Indian Chambers of Commerce and Industry outlined a self-regulation code of conduct to protect consumers, with provisions such as providing only prescription drugs, partnering with the government on public health initiatives, and restricting the sale of habit-forming medicines.[37]

The actual laws which govern pharmacies originate from outdated provisions within many acts such as the Drugs and Cosmetics Act, 1940; the Drugs and Cosmetics Rules, 1945; and the Pharmacy Act, 1948. The emergence of e-pharmacies not only relates directly to these acts but incorporates provisions outlined in the Information Technology Act, 2000 as well. Thus, e-pharmacies can operate within certain rules and regulations. Rule 65 of the Drugs and Cosmetics Rules, 1945, mandates the presence of a registered pharmacist during the sale of the drug and requires detailed recordkeeping of the transaction.[38] Section 42 of The Pharmacy Act, 1948, prevents anyone other than a registered pharmacist from dispensing medicine.[39] During the latter half of 2018, the Ministry of Health and Family Welfare released a draft to amend the Drugs and Cosmetics Rules, 1945, to specifically regulate e-pharmacies. The proposed rules would require the registration of e-pharmacies and data protection to prevent disclosure of information, and the constant monitoring of e-pharmacies.[40]

These regulations are an important step in addressing the legal status of e-pharmacies. However, the distribution of drugs through these e-pharmacies is another concern. The delivery of drugs may need specific transportation methods to maintain an environment that does not hinder the effectiveness of the drug. As drug access becomes easier, the types of drugs offered through these e-pharmacies should be looked at closely.

Narcotics and habit-forming drugs should have stricter restrictions on their dispersal. As early as 1977, an Expert Committee's report directed by the Ministry of Health and Family Welfare, Government of India, laid the groundwork for the regulation of these types of drugs.[41] Since then, the Narcotic Drugs and Psychotropic Substances Act in 1985 (NDPS) has provided the foundation for regulating narcotic drugs and psychotropic substances with the establishment of the Narcotics Control Bureau.[42] This Act was most recently amended in 2014, which recognised the use of essential narcotic drugs for pain relief.[43] The Act requires licenses for manufacturers, those who use such substances in practice, and distributors. Thus, the proliferation of e-pharmacies raises key questions on how—if they even should—dispense substances under NDPS regulation. The overuse and misuse of antibiotics could accelerate antibiotic resistance as bacteria adapt in response to these medicines.

India's antibiotics consumption doubled between 2000 and 2015,[44] and is the world's largest consumer of antibiotics. The country became the largest consumer of oxazolidinones, a last-resort antibiotic, in 2012.[45] Increasing accessibility to medicines, such as antibiotics, can save millions of lives, but this increases the threat of accelerating antibiotic resistance if left unregulated and overused.

[35] Ravinder K. Sah, Rakhamaji D. Chandane, Umesh Suranagi, Sachin Manocha, Ajita Kapur, and Priyanka Hotha (2018). "Awareness and Behavioural Outlook Towards Online Pharmacy Services Among Consumers in Delhi, India: A Pilot Survey," *European Journal of Pharmaceutical and Medical Research* 5, no. 3: 552-557. https://www.ejpmr.com/admin/assets/article_issue/1520135288.pdf

[36] Yaraghi, Niam; Ravi, Shamika (2017). "The Current and Future State of the Sharing Economy," Brookings India IMPACT Series No. 032017. March 2017.

[37] http://ficci.in/pressrelease/2600/ficci-press-nov21-e-pharmacy.pdf

[38] Rule 65, The Drugs and Cosmetics Rules, 1945.

[39] Section 42, The Pharmacy Act, 1948.

[40] Ministry of Health and Family Welfare. NOTIFICATION G.S.R. 817(E). August 28, 2018.

[41] Ajit Avasthi & Abhishek Ghosh, (2019). "Drug misuse in India: Where do we stand & where to go from here?" *Indian Journal of Medical Research, 149*(6), 689. doi: 10.4103/ijmr.ijmr_548_19

[42] The Narcotic Drugs and Psychotropic Substances Act, 1985.

[43] The Narcotic Drugs and Psychotropic Substances (Amendment) Act, 2014.

[44] Eili Y. Klein, Thomas P. Van Boeckel, Elena M. Martinez, Suraj Pant, Sumanth Gandra, Simon A. Levin, Herman Goossens, and Ramanan Laxminarayan (2018). "Global increase and geographic convergence in antibiotic consumption between 2000 and 2015." *Proceedings of the National Academy of Sciences of the United States of America* 115, 15: E3463-E3470. https://doi.org/10.1073/pnas.1717295115

[45] Klein et al. (2018).

Even now, anti-microbial resistance is already a concern. The Indian Council of Medical Research (ICMR) published the first treatment guidelines for antimicrobial use in 2017. The ICMR developed these guidelines in hopes that appropriate antimicrobial selection and use would slow antimicrobial resistance, especially when it is estimated that 50% or more of hospital antimicrobial use was inappropriate.[46] The report also drew on its nationally representative sample of anti-microbial resistance in hospitals across India. They used a variety of common antibiotics on a wide range of common pathogens. For example, *Plasmodium falciparum*, a deadly strain of malaria, was resistant to chloroquine, a common anti-malarial, in at least 25% of the cases nationwide.[47] *Staphylococcus aureus*, a strain of the common staphylococcal bacteria, was resistant over 25% of the time to multiple antibiotics.[48] The ICMR guidelines establish findings on effective treatment methods that are crucial to slowing down the rapid global growth of anti-microbial resistance.

Even within traditional pharmacies, 64% of the antibiotic formulations sold in India had not yet been approved before they reached the market.[49] This lack of regulatory oversight raises genuine concerns on whether such regulations can even be effective in the e-pharmacy space.

The e-pharmacy industry is relatively young, but it shows immense promise. Drug delivery systems and online ordering of medicines can increase access for consumers. While many of these e-pharmacies are based in urban areas, if these companies scale in size, rural area deliveries should not be impossible. The obvious concerns regarding e-pharmacies are illegally operating entities as well as the dispensing of drugs. Stronger efforts should be made to verify legally operating e-pharmacies. Prescription verification, and whether that can be proven online, raises questions on what types of drugs e-pharmacies should dispense. Habit-inducing medications or those that require strict climate controls may not be suitable items for e-pharmacies to dispense. Additionally, as antimicrobial resistance increases, e-pharmacies can play a role in accelerating such resistance if left unregulated. An increase in the ease of access to medications also means an increase in the misuse of medications. These are the challenges that regulators must tackle next.

[46] "Treatment Guidelines for Antimicrobial Use in Common Syndromes" (2017). Indian Council of Medical Research, Department of Health Research. New Delhi, India.
[47] Ibid, 7.
[48] Ibid, 9.
[49] Patricia Mcgettigan, Peter Roderick, Abhay Kadam, and Allyson Pollock (2018), "Threats to Global Antimicrobial Resistance Control: Centrally Approved and Unapproved Antibiotic Formulations Sold in India," *British Journal of Clinical Pharmacology* 85, no. 1 (2018): 59-70. doi:10.1111/bcp.13503.

1.5 Recommendations

BPPI should provide more incentives to open Jan Aushadhi stores in rural, less developed areas: Our analysis finds that while the JA scheme is promising, both in its magnitude and mission, it falls short in terms of an effective incentives-based scheme. Stores are more likely to open in more developed areas. In this regard, additional incentives are already provided to store owners based on their social background, and to stores located in the Northeast and tribal areas. However, the scheme must experiment with spatially-targeted incentives to expand stores located in rural areas, and in districts that are less developed.

The Jan Aushadhi scheme should be flexible and do more beyond providing initial funding for stores: Some states already have strong systems in place to increase access to essential medicines. Instead of forcing more stores into these states, BPPI should look into covering drugs not already covered by the states, or somehow accommodating state provisions with the central government's programme.

Jan Aushadhi supply chain management: The new supply chain methods introduced last year are promising steps to have an end-to-end supply model. The delineation of products into fast, average, and slow-moving volume of sales is also promising. This system should be constantly studied, and a more centralised system should be in place to track potential shortages.

Generic medication - outreach and safety: The success of JA scheme depends on changing public perception of generic drugs. Not only is a massive information campaign needed, the government also needs to ensure all generic medicines, not just those sold in JA stores, are of the highest quality. Quality tests and regular audits for drugs sold in JA stores are essential, but such measures should be taken nation-wide.

Regulation of e-pharmacies: A proper regulatory framework is essential for helping the flourishing e-pharmacy industry while maintaining drug safety and confidentiality of patient information. Ensuring safety standards is vital, but the government should avoid too many regulations that could hinder the growth of the e-pharmacy sector.

Regulation of drugs access: Prescriptions exist because they not only regulate what substances people can have access to, but also who can legally prescribe these substances. The government should bolster efforts to ensure drugs are dispensed ethically, both within traditional pharmacies and e-pharmacies.

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CHAPTER—**02**

QUALITY

2.1 Introduction

India's pharmaceutical industry has grown into a global supplier of medications, manufacturing nearly 20% of the active pharmaceutical ingredients sold in the United States, by far the world's largest importer of medicines.[50] India was a top-ten exporter of pharmaceuticals based on sales alone in 2015, an impressive feat given the country mostly exports generic medicines, which are much cheaper than branded, patent-protected ones.[51] However, increased scrutiny over the quality of India's pharmaceutical exports has accompanied this growth in recent years.

In 2015, 27 different drug companies operating 39 drug manufacturing facilities lost their clearances to make medicines for U.S. consumers. Two years prior, India's once largest drug company paid $500 million in fines for quality failures.[52] An independent study looked at drugs made in India which were sold to low and middle-income countries with less-developed regulatory oversight structures in place. They found that over 10% of these drug samples failed a basic test for active pharmaceutical ingredients, suggesting that on a global scale, more substandard drugs (made in India) were sold in these countries.[53] The Drugs and Cosmetics Act, 1940, uses slightly different terminology for legal purposes, which is what we refer to for the rest of this section. Substandard drugs are legitimately manufactured by the company, but fail quality-of-standards tests, such as assay tests (determining the right amount of the pharmaceutical ingredient) and dissolution tests (the time it takes for the active pharmaceutical ingredient to be released from the dose). Spurious drugs refer to drugs that are counterfeits of existing brands or drugs whose active pharmaceutical ingredients are substituted by another substance. Adulterated drugs are those contaminated by outside substances that compromise the safety and effectiveness of the drug. Misbranded drugs are products which have misleading or false labeling, or do not follow prescribed conventions.

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[52] Amy Kazmin, "Indian Drugs: Not What the Doctor Ordered (2015)," Financial Times. September 09, 2015. Accessed January 26, 2019. https://www.ft.com/content/de0ca3f4-5581-11e5-97e9-7f0bf5e7177b.
[53] Roger Bate, Ginger Zhe Jin, Aparna Mathur, and Amir Attaran (2016), "Poor Quality Drugs and Global Trade: A Pilot Study." American Journal of Health Economics 2, no. 3 (Summer 2016): 373-98. doi:10.3386/w20469.

The quality of India's pharmaceutical products has a wide-ranging impact on not only the country but also the world. While numerous reports and studies on the lack of standard-quality drugs harm the industry's reputation, patients are ultimately harmed by substandard drugs. The World Health Organization commissioned research into the impact of falsified and substandard (FS) drugs on a variety of diseases. While the WHO recognises that its terminology of falsified and substandard medical products differs from that of Member States, including India's, the WHO defines falsified medical products as those that are deliberately misrepresenting their composition. Substandard medical products, according to the WHO, fail to meet quality standards. These two terms are similar to India's substandard and spurious definitions, and will be used to refer to both spurious and substandard drugs later in the report. The report provided numerous estimates of excess deaths based on the prevalence of substandard and falsified products. For childhood pneumonia, between 8,688 and 18,372 children would die if one percent of medicines were FS. At 10% FS drugs, which is still lower than the average of 13.6% FS drugs for low and middle-income countries,[54] an estimated 72,430 to 169,271 deaths would occur depending on the assumed increased case fatality rate.[55] Depending on different malaria estimates, the reduced effectiveness of antimalarial medication due to substandard and falsified drugs can cause upwards of over 100,000 deaths. But even if a drug is not inherently dangerous, substandard drugs still pose huge problems.

Substandard drugs can prolong treatment, adding additional costs to the already high out-of-pocket expenditure on medicines that Indians bear. They also undermine trust in the pharmaceutical industry and the healthcare system. And worryingly, substandard drugs—drugs that do not contain enough of the recommended active pharmaceutical ingredient—can lead to accelerated antibacterial resistance.

Various studies have concluded that low levels of antibiotics—below the minimum inhibitory concentration (MIC), or the threshold that inhibits bacterial growth—foster an environment for antibiotic-resistant bacteria. However, at sub-MIC levels, most bacteria can still grow in the environment and follow the different evolutionary trajectories. A 2018 study exposed the bacteria *Salmonella enterica* to sub-MIC environments (as opposed to MIC environments, which the researchers also tested), and found that it still developed high-level resistance.[56] The results show that sub-MIC environments can foster different mutations that ultimately lead to high-level resistance. Several other papers discuss the connection between low-dosing with the spread of drug-resistant parasites and tuberculosis.[57]

We use publicly available data to assess the quality of India's pharmaceutical industry for the domestic market. We compile information on various metrics like state capacity for drug inspection, quality of drugs, source of origin of substandard drugs, and reasons of drug quality test failures using four main publicly available data sources – Central Drug Standard Control Organisation (CDSCO) reports, National Institute for Biologicals (NIB) 2014 report on drug quality in India, answers submitted to 16th Lok Sabha questions in the parliament and notifications on substandard drugs released by individual state regulatory authorities.

2.2 Quality of drugs in India

Throughout much of the early 1900s, India was dependent on drug imports, exposing the country to fraudulent practices such as exporters dumping substandard drugs into the market and sales malpractices.[58] As a result, the government created the Drugs Enquiry Committee in 1930 to make recommendations, many of which were passed in the Drugs and Cosmetics Act, 1940. This central legislation's main objective is to ensure the safety and quality of drugs and cosmetics for consumer use. Within the legislation are the Drugs and Cosmetics Rules, 1945, which contain

[54] Ozawa, S., Evans, D. R., Bessias, S., Haynie, D. G., Yemeke, T. T., Laing, S. K., & Herrington, J. E. (2018). Prevalence and Estimated Economic Burden of Substandard and Falsified Medicines in Low- and Middle-Income Countries. JAMA Network Open, 1(4). doi:10.1001/jamanetworkopen.2018.1662

[55] WHO, 2017. A Study on the Public Health and Socioeconomic Impact of Substandard and Falsified Medical Products. Geneva, Switzerland: World Health Organization.

[56] Wistrand-Yuen, E., Knopp, M., Hjort, K., Koskiniemi, S., Berg, O. G., & Andersson, D. I. (2018). Evolution of high-level resistance during low-level antibiotic exposure. *Nature Communications, 9*(1), 1599. doi:10.1038/s41467-018-04059-1

[57] Johnston, A., & Holt, D. W. (2014). Substandard drugs: a potential crisis for public health. *British Journal of Clinical Pharmacology, 78*(2), 218–243. doi:10.1111/bcp.12298

[58] Harkishan Singh, "Ram Nath Chopra (1882-1973) – A Visionary in Pharmaceutical Science*," *Indian Journal of History of Science* 43, no. 2 (2008): 231-64, https://www.insa.nic.in/writereaddata/UpLoadedFiles/IJHS/Vol43_2_4_HSingh.pdf.

regulations for the storage, sale, display, and prescription of different drug schedules.[59] The Act also established the Central Drug Standard Control Organisation (CDSCO) as India's central drug regulatory authority. The CDSCO is divided into numerous regional offices and laboratories to carry out its functions, such as licensing inspections, surveilling markets, and testing new drugs.[60]

Data released by CDSCO on drugs sampled over time shows that substandard drug rates were close to 10% from 1995 to 2002, but these rates reduced to be 6% to 7% for the years spanning 2003 to 2007.[61] Spurious drugs peaked in 1997 at 0.47% and formed 0.17% of all drugs available in 2007. We supplement this data for recent years by looking at data compiled by CDSCO on substandard and spurious drugs from questions asked during the 16th Lok Sabha. The CDSCO compiled the data from each state or Union Territory's numbers.[62, 63] We aggregate this information to present the national substandard drug rate in Table 3. For the years 2012 to 2017, each calendar year listed in the table runs from April 1 of the current year to March 31 of the next year. For example, 2017 would refer to drugs sampled between April 1, 2017, to March 31, 2018. For these recent years, the proportion of FS (i.e. both Fake/Spurious and Substandard combined) drugs ranges from 3.66% to 5.27%.

Table 3: Percentage of substandard and spurious drugs, 1995 to 2017

Year	Total Sample	Substandard (%)	Spurious (%)	Source
1995	32770	10.64	0.30	CDSCO, Mashelkar Committee
1996	38936	8.19	0.24	CDSCO, Mashelkar Committee
1997	32936	9.04	0.47	CDSCO, Mashelkar Committee
1998	38936	8.19	0.24	CDSCO, Mashelkar Committee
1999	35570	10.31	0.32	CDSCO, Mashelkar Committee
2000	36947	8.36	0.30	CDSCO, Mashelkar Committee
2001	38824	8.96	0.25	CDSCO, Mashelkar Committee
2002	36314	9.34	0.34	CDSCO, Mashelkar Committee
2003	38313	6.3	0.30	CDSCO, Mashelkar Committee
2004	49287	7.5	0.29	CDSCO
2005	41494	7.3	0.35	CDSCO
2006	42354	6.4	0.16	CDSCO
2007	38313	6.3	0.17	CDSCO
2008	—	—	—	—
2009	**24136**	**4.75**	**0.05**	**CDSCO Nation Wide Survey**
2010-11	—	—	—	—
2012	58537	4.04	0.12	CDSCO Data for Lok Sabha Questions
2013	72712	4.16	0.16	CDSCO Data for Lok Sabha Questions
2014	74199	4.99	0.11	CDSCO Data for Lok Sabha Questions
2015	74586	4.96	0.31	CDSCO Data for Lok Sabha Questions
2016	76721	3.62	0.16	CDSCO Data for Lok Sabha Questions
2014 to 2016	**47954**	**3.16**	**0.02**	**National Institute for Biologicals, Nation Wide Survey**
2017	82599	3.37	0.29	CDSCO Data for Lok Sabha Questions

*Source – CDSCO, National Institute for Biologicals, Lok Sabha Questions

[59] Lily Srivastava, *Law & Medicine*, New Delhi: Universal Law Publishing Pvt., 2010, 216-218.
[60] "Functions," Central Drugs Standard Control Organisation, Accessed December 26, 2018, https://cdsco.gov.in/opencms/opencms/en/About-us/Functions/.
[61] Central Drugs Standard Control Organisation (2009), "Report on Countrywide Survey for Spurious Drugs."
[62] Department of Health and Family Welfare (2015). Lok Sabha Unstarred Question No. 2262 to be Answered on 11th December, 2015.
[63] Department of Health and Family Welfare (2018). Lok Sabha Unstarred Question No. 552 to be Answered on 20th July, 2018.

Two national surveys conducted in the years 2009 & 2014-2016 by CDSCO and National Institute of Biologicals (NIB) respectively, reveal important findings. The data for CDSCO (2009) survey had a sample size of around 24,136 which was close to half of the NIB (2014-2016) survey.[64] The percentage of substandard drugs in the 2009 CDSCO survey was found to be 4.75% while the corresponding figure for the 2014-2016 NIB survey was 3.16%. The percentage of spurious drugs found has been below 0.05% in both the surveys.

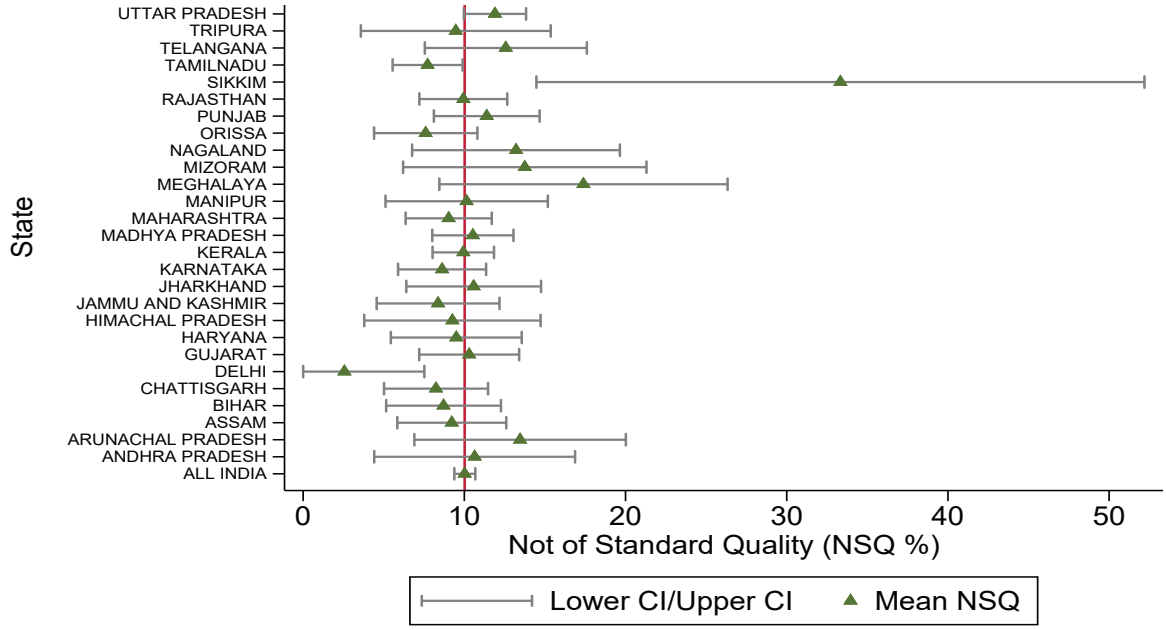
However, other independent studies that look at individual drugs have found even more troubling numbers. A study published in 2015 found that 15.62% of the sampled diclofenac sodium tablets, a common anti-inflammatory, were substandard.[65] A second study in 2015 looked at the popular anti-biotic amoxicillin in northern India and found that 13.04% of the sampled products were substandard.[66] However, questions surround whether these numbers understate the true extent of substandard and spurious drugs in the country. An audit conducted by the Comptroller and Auditor General of India on the medical establishments in the defense services found that samples from the Armed Forces Medical Stores Depot had increasing rates of quality test failures over time.[67] From 2006 to 2007, 15% of samples were rejected due to quality test failures. By 2010 to 2011, 31% of samples were rejected. The lower government-reported numbers raise questions regarding the accuracy of the drug sampling process. Quality regulation requires an accurate, representative sample, but when Dinesh Thakur and Prashant Reddy reached out to several states regarding their budget allocation and methodology for drug sampling, Tamil Nadu and Kerala were able to provide such information while most states and the CDSCO could not.[68] We further explore this issue later on when we discuss the role of inspections within the regulatory framework.

National level figures put the proportion of FS drugs to be 3.18% for 2014-2016 based on the NIB report. However, subsample analysis for samples drawn from government sources and retail outlets shows that, on average, one in 10 drugs sampled from government sources was found to be Not of Standard Quality (NSQ); the corresponding figure for retail outlets is much lower at 0.3 in 10 drugs.

The state-level figures below (Figure 8 and 9) are based on data presented in the NIB report, and they reveal some alarming facts. We notice stark regional differences in terms of proportions of medicines found to be NSQ in individual states. The NSQ percentage for various states varies from 0 to 8.82% for drugs sourced from retail outlets (except Lakshwadeep at 16.67%). In subsamples from both government sources and retail outlets, the Northeastern states (especially Meghalaya, Manipur, Nagaland, Sikkim, and Mizoram) exhibit a distinct pattern: a high proportion of drugs which are found to be NSQ, far above the national average. Other states which show a high prevalence of NSQ drugs (above national average) include Gujarat, Andhra Pradesh, Uttarakhand, and Punjab. One of the possible reasons could be low state regulatory capacity to counter the infiltration of NSQ products in the market. We explore this further in the next section.

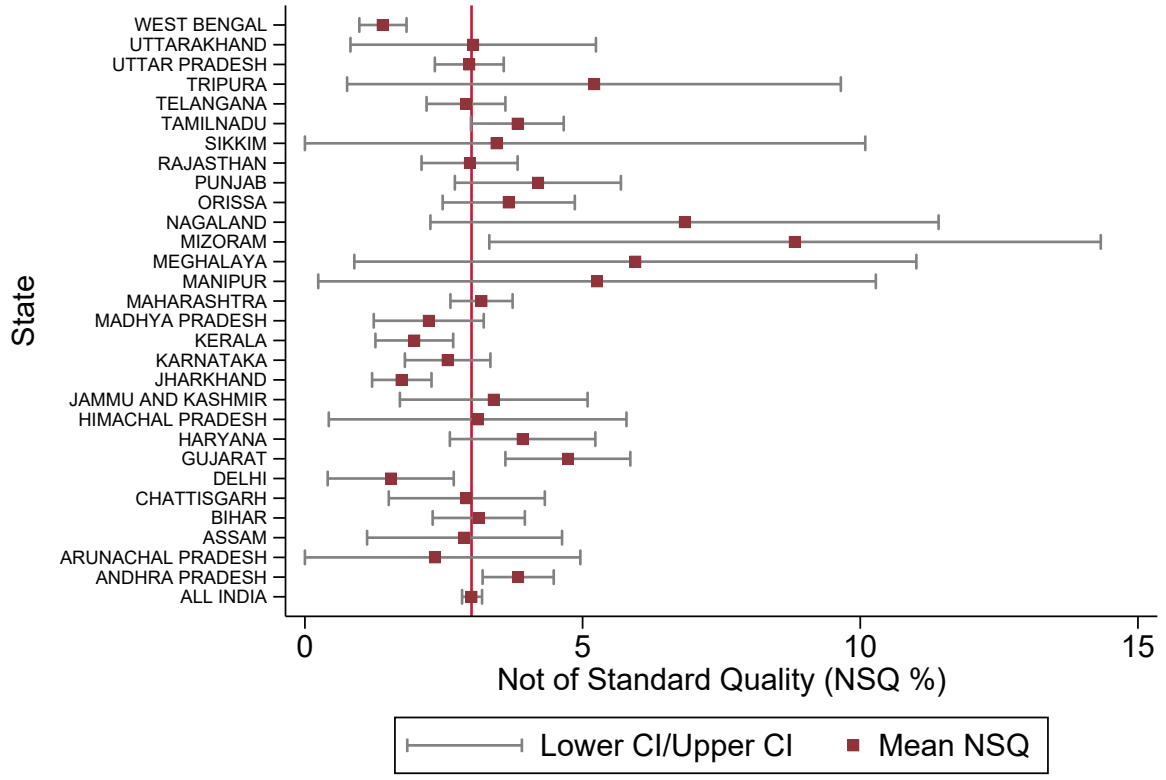
[64] National Institute of Biologicals (2016), "National Drug Survey 2014 – 2016."
[65] Khan, Ahmed, Roop Khar, and Malairaman Udayabanu. "Pilot Study of Quality of Diclofenac Generic Products Using Validated In-House Method: Indian Drug Regulatory Concern." *Journal of Applied Pharmaceutical Science*, July 11, 2015, 147-53. doi:10.7324/japs.2015.501226.
[66] Khan, Ahmed, Roop Khar, and Malairaman Udayabanu. "Quality and Affordability of Amoxicillin Generic Products: A Patient Concern." *International Journal of Pharmacy and Pharmaceutical Sciences* 8, no. 1, December 02, 2015, 386-390.
[67] "Report of the Comptroller and Auditor General of India on Performance of Medical Establishments in Defence Services", (2013). Comptroller and Auditor General of India, Union Government.
[68] Thakur, Dinesh S. and Prashant Reddy (2016). "A report on fixing India's broken drug regulatory framework."

Figure 8: Percentage of NSQ drugs from government sources ESI, CGHS, Civil Hospital, state govt medical stores



Source: Figures from National Institute for Biologicals, 2014-16 National Survey
The red reference line represents national average of percent of NSQ drugs found from government sites.

Figure 9: Percentage of NSQ drugs at retail outlets



Source: Figures from National Institute for Biologicals, 2014-16 National Survey
The red reference line represents national average of percent of NSQ drugs found at retail outlets.

2.3 Regulatory structure

Under the Drugs and Cosmetics Act, 1940, regulation is split between the central government and state authorities (which includes 29 states and seven union territories). The central government approves new drugs, clinical trials, and sets standards for drugs. State authorities, which have their own Food and Drug Administrations (FDAs), issue licenses and monitor the manufacturing, distribution, and sale of drugs.[69] Loopholes exist within this regulatory framework and the decentralisation of regulations has led to pervasive problems in India's drug market.

2.3.1 Inspections

One of the main purposes of the Drugs and Cosmetics Act, 1940 was to ensure standard-quality drugs in India. To do so, Section 21 actually gives both the central and state governments the power to appoint inspectors,[70] though the state is primarily concerned with such affairs. Sections 22 and 23 elaborate on the powers and procedures of inspectors, and Rule 49 of the Drugs and Cosmetics Rules, 1945, specifies the qualifications of such inspectors. However, these guidelines fall short in practice.

There is a nationwide shortage of inspectors; their numbers have not kept pace with the growth of the pharmaceutical industry. As early as 1975, the Hathi Committee Report estimated that 480 drug inspectors were required in all states, as opposed to the 369 inspectors then.[71] The report also admonished the level of enforcement in most states, citing varying standards of inspection, licensing, and lack of qualified supervisors. In 2003, the Mashelkar Committee also found that for the number of sales and manufacturing licenses present, the recommended number of drug inspectors (one drug inspector for every 50 manufacturing units, and one drug inspector for every 200 distribution units) across the country should total around 1720, far more than the 935 then.[72] The 59th Parliamentary Standing Committee Report on the Functioning of the CDSCO in 2012 estimated that the recommended number of drug inspectors had grown to 3,200.[73] The total number of sanctioned drug inspector posts across the county was only at 1,349, and only 846 of those posts were actually filled. Authors from a 2015 field research study found that the states of Tamil Nadu, Gujarat, Kerala, and Maharashtra face acute shortages when it comes to filling positions for the required number of inspectors (as per the Mashelkar Committee Report) to be appointed by state drug regulatory authority.[74]

State authorities are responsible for filling these roles, and their standards on personnel qualifications and numbers also differ. A case study in Maharashtra, which accounts for 29% of India's manufacturing units and 38% of its medicine exports, found that as opposed to the "one drug inspector per 'x' manufacturing/distribution units" recommendation, the Maharashtra State Food and Drug Regulatory Authority's requirements for 2011-2012 was 10 inspections, per drug inspector, per month, for manufacturing units and 21 inspections, per drug inspector, per month, for distribution units.[75] Despite these different calculations in the number of recommended drug inspectors, Maharashtra still had a 78% shortfall in the number of inspectors under their FDA calculations, compared to 83% based on the Mashelkar Committee's calculations between 2009 and 2010.[76]

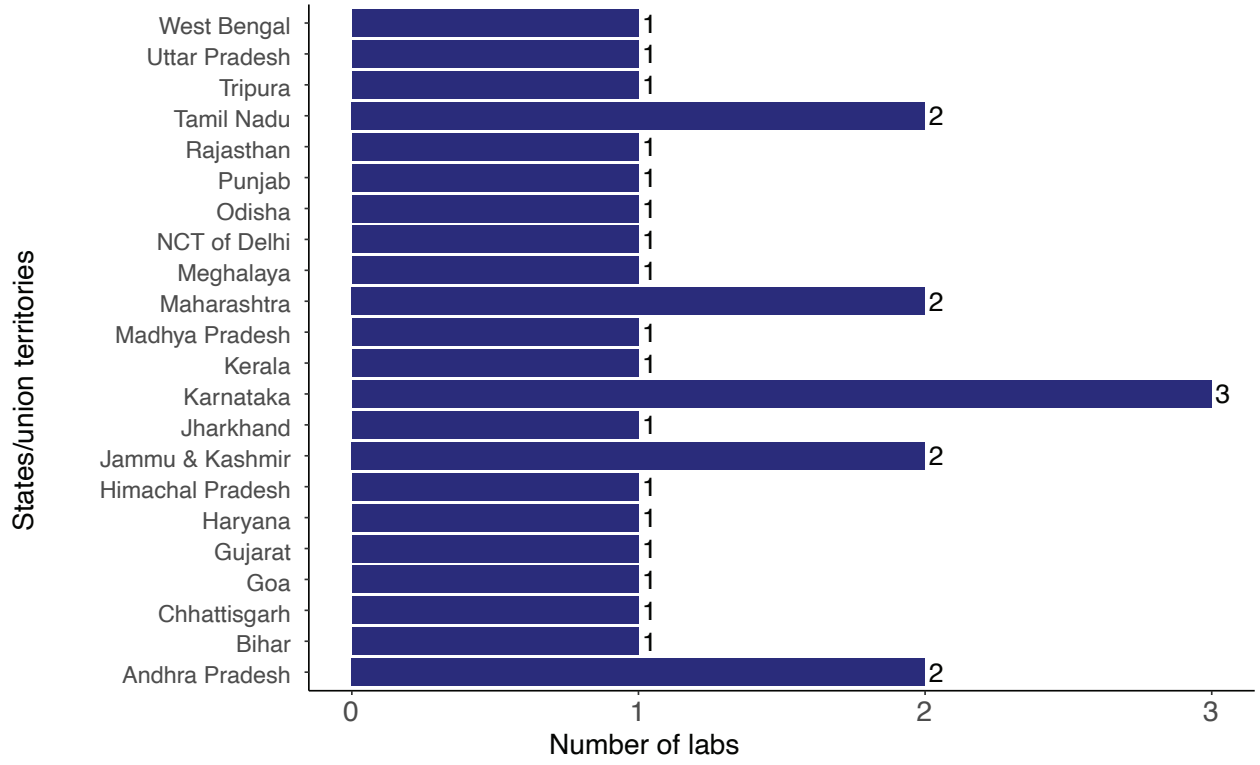
Similar to Maharashtra's standards, Kerala's drug inspectors have to meet a mandatory number of inspections as well.[77] These target-based inspections create an incentive to finish a certain number of inspections, as opposed to strategically targeting

[69] Ibid.
[70] *Section 21,* Drugs & Cosmetics Act 1940.
[71] *Chapter IX, para 8*, Hathi Committee Report, 1975.
[72] *Section 6.3,* Mashelkar Committee Report, 2003.
[73] Section 4.2, Fifty-Ninth Report on the Functioning of the Central Drugs Standard Control Organisation (CDSCO).
[74] Chokshi, Maulik, Rahul Mongia, and Vasudha Wattal (2015). "Drug Quality and Safety Issues in India," *Indian Council for Research on International Economic Relations* Policy Brief #2.
[75] Abhay B. Kadam, Karen Maigetter, Roger Jeffery, Nerges F. Mistry, Mitchell G. Weiss, and Allyson M. Pollock, "Correcting India's Chronic Shortage of Drug Inspectors to Ensure the Production and Distribution of Safe, High-Quality Medicines," *International Journal of Health Policy and Management* 5, no. 9 (September 2016): 535-42, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5010656
[76] Ibid.
[77] Chowdhury, Nupur, Pallavi Joshi, Arpita Patnaik, and Beena Saraswathy (2015). "Administrative Structure and Functions of Drug Regulatory Authorities in India," *Indian Council for Research on International Economic Relations* Working Paper 309 (September 2015).

inspections toward higher-risk facilities, such as manufacturers that have a known history of manufacturing substandard drugs. Additionally, drug inspectors in certain states, such as Kerala, Himachal Pradesh, and Bihar, have to perform other duties in addition to drug inspections. They are often required to serve in the courts as prosecuting authority, and drug inspectors in Bihar perform other administrative tasks.[78] Drug inspections need to cover drugs from both urban and rural areas, with similar inspection focus from all kinds of manufacturers (small, medium, large).[79]

Even with inspection shortfalls, the necessary infrastructure for quality checks is often lacking in certain states. The Ministry of Health and Family Welfare provides a list of government drug-testing laboratories that the states and union territories set up (see Figure 10 below). For analysis in this section, we focus on 29 major states and the National Capital Territory of Delhi (if the data is available). We exclude six union territories due to their small populations and lack of sampling. Many do not even have their own drug-testing laboratories.

Figure 10: Government drug-testing laboratories set up by States/UTs



Source: Ministry of Health & Family Welfare Available at: https://mohfw.gov.in/fooddrugs/list-drug-testing-labs-country

Apart from seven central drug-testing laboratories under CDSCO, most states seem to have a government drug-testing laboratory set up, but only Karnataka stands out with three such labs. As of 2015, the states of Sikkim, Assam, Nagaland, Manipur, Mizoram, and Arunachal Pradesh did not have a drug-testing laboratory. The union territories that did not have a drug-testing laboratory as of 2015 were Andaman and Nicobar, Lakshadweep, Dadra & Nagar Haveli, and Daman & Diu.[80]

In addition to these government drug-testing laboratories, the CDSCO also approves additional private drug-testing laboratories to carry out quality tests on behalf of manufacturing licensees. Pursuant to Form 37 of Schedule A in the Drugs and Cosmetics Act, 1945, these private drug-testing laboratories must follow strict conditions before receiving approval to test drugs, and must report the results of such tests. The CDSCO releases public notices regarding the list of private drugs-testing laboratories on its website (Figure 11 below).

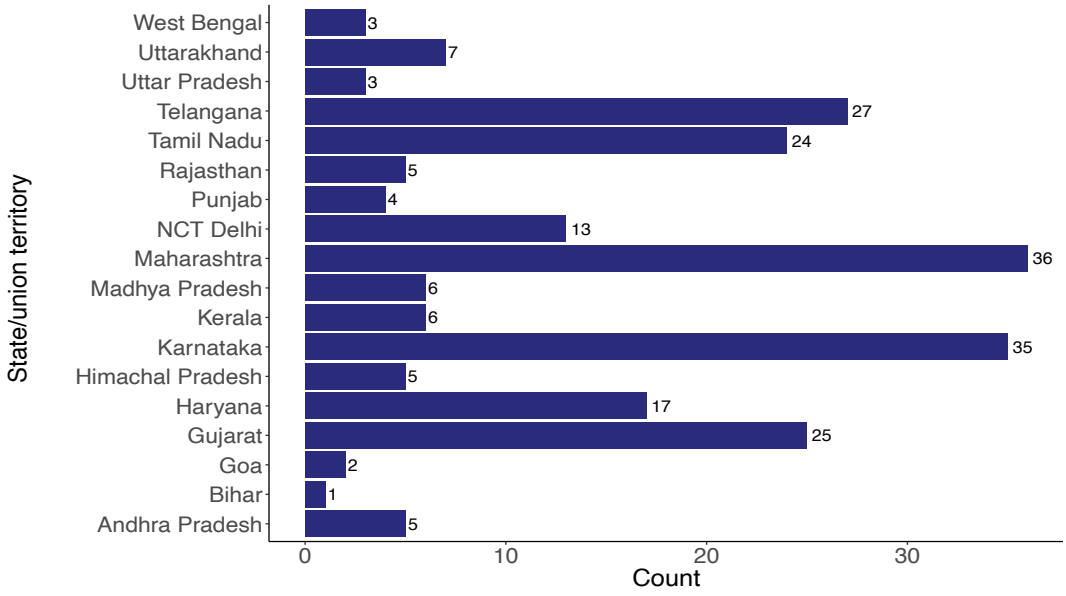
[78] Chowdhury et al. (2015), "Administrative Structure and Function."
[79] Chokshi et al. (2015), "Drug Quality and Safety Issues in India."
[80] Department of Health and Family Welfare (2015). Lok Sabha Unstarred Question No. 2262 to be Answered on 11th December, 2015.

It is worth noting that states which have larger manufacturing capabilities, such as Maharashtra and Gujarat, tend to have more additional approved state drug-testing laboratories. Karnataka, Tamil Nadu, and Telangana also top the list with many such laboratories. Worryingly, populous states such as Uttar Pradesh and Bihar have three and one additional approved state drug-testing labs, respectively.

Labs often differ in the types of tests they can conduct, and in the number of samples they can accept per year to sample. An inadequate number of labs within a state or union territory makes sampling impractical. While drug samples can be forwarded to the Regional or Central Drugs-Testing Laboratories run by the CDSCO, this puts extra pressure on those labs, which also perform their duties. Similar to inspections, laboratories also face their issues regarding staffing. The Composite Testing Laboratory in Kandaghat, Himachal Pradesh had 25 vacant positions out of a total of 54.[81]

These discrepancies mean that individual states or union territories may not be adequately sampling drugs sold in their jurisdictions. Using the same substandard and sampling numbers compiled by the CDSCO and published in the Lok Sabha answers, we provide a breakdown of total sampling and substandard drug numbers by states in Figures 12 and 13, which cover April 1st, 2012 to March 31st, 2018.The states are listed by the population in descending order. Yearly graphs can be found in the appendix of this chapter (Figures 21 to 24).

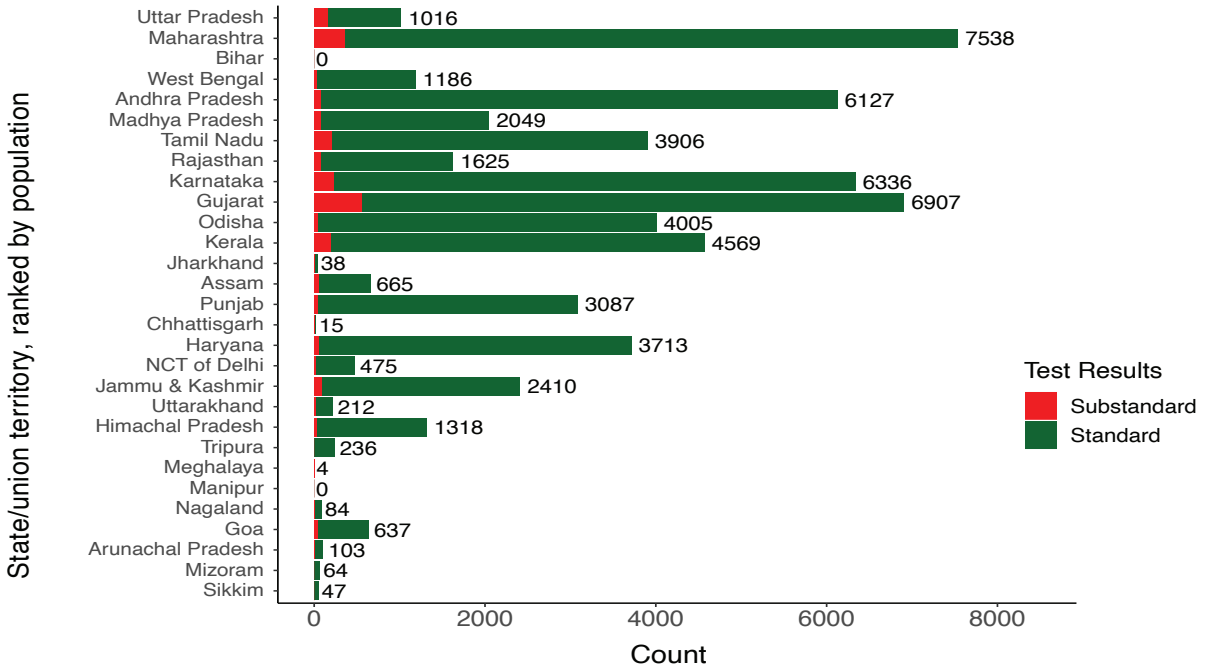
Figure 11: Number of additionally approved state drug-testing laboratories



Source: Central drugs standard control organization. Data as of May 2019.

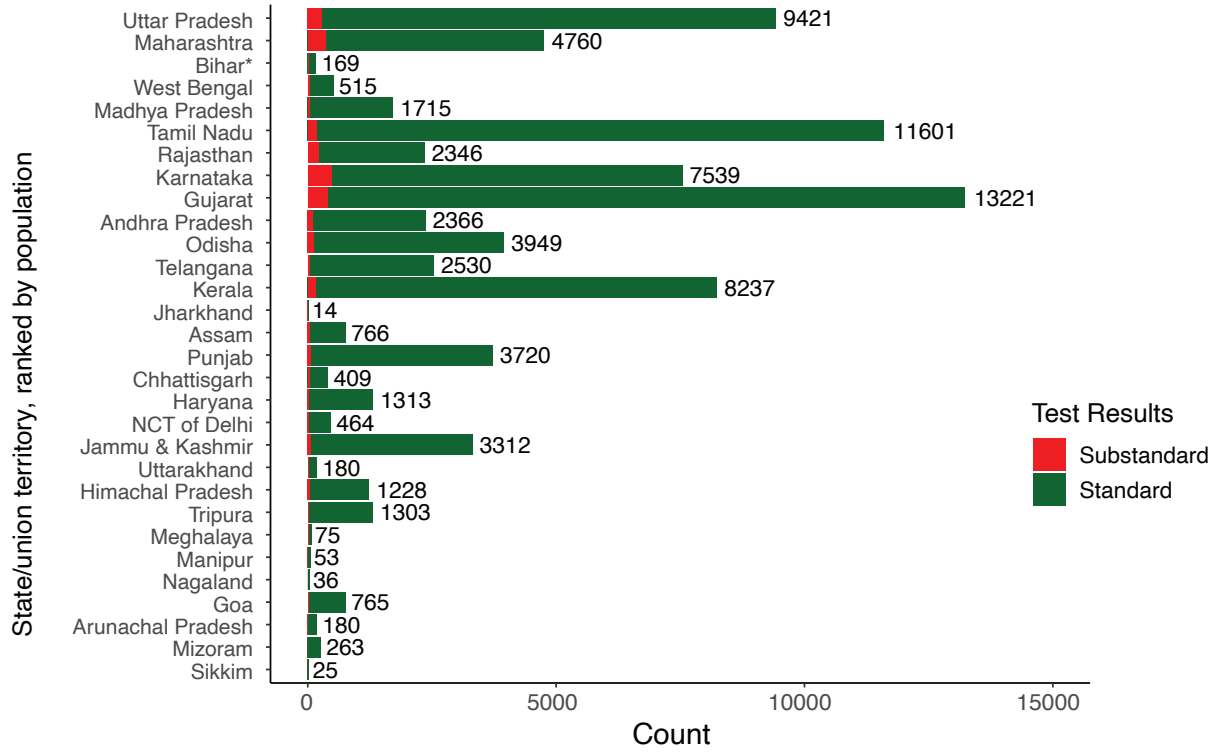
[81] Derived from http://www.hp.gov.in/dhsrhp/CTL%20KANDAGHAT.html.

Figure 12: Number of quality tests conducted by State/UT drug controllers, 2012



Source: Compiled by CDSCO for Lok Sabha Question No. 2262 on 11 December 2015.
Each year is from April 1st of the current year to March 31st of the next year spurious drugs are rare. No SUTs with a large sampling size found more than 0.92% (Rajasthan) of their drug samples as spurious.

Figure 13: Number of quality tests conducted by State/UT drug controllers, 2017



Source: Compiled by CDSCO for Lok Sabha Question No. 552 on 20 July 2018. Each year is from April 1st of the current year to March 31st of the next year * indicates only six months were reported. Spurious drugs are rare. But among SUTs with large sampling sizes, Rajasthan stands out, with 5.24% of its drug samples found as spurious.

These figures tell us the sampling numbers of each state or union territory, and the results of those quality tests. We see that sampling numbers fluctuate year-to-year across all states,[82] but a few states continually sample large numbers of drugs sold in their jurisdictions. For example, Gujarat and Tamil Nadu rank in the top three for most quality test samples conducted dating back to 2013. Karnataka, Kerala, and to a lesser extent Maharashtra, also sample large numbers of drugs since 2012.

If we look back at our drug-testing laboratory analysis, Karnataka set up the highest number of government drug-testing laboratories, with Tamil Nadu and Maharashtra close behind. In terms of states having additional approved drug-testing laboratories, Maharashtra leads the count. Other states with notable numbers of approved drug-testing laboratories include Tamil Nadu, Karnataka, Telangana, and Gujarat. With the data that is available, states with higher drug-testing capabilities are able to sample more drugs. These states also find more substandard drugs due to their larger sample sizes and enhanced testing capabilities.

The impact of the lack of drug-testing laboratories is seen clearly through the state drug control administration's number of quality tests conducted in a year. Populous states such as Bihar and West Bengal, both of which do not have sizable drug-testing capabilities, see a minuscule number of quality tests conducted in a calendar year. Due to the extremely small number of quality tests that are conducted, the true extent of substandard drugs is perhaps not captured accurately in these states. These small number of quality tests fail to pick up on the number of substandard drugs sold in their states. Globally, evidence exists that substandard drugs manufactured in India are sold more in countries with a weaker regulatory structure.[83] Thus, there is some urgency to establish stronger drug-testing capabilities in these states.

Up until this point, we have only looked at sampled drugs sold within a certain jurisdiction. Where these drugs are manufactured poses another policy problem.

2.3.2 Manufacturing licenses

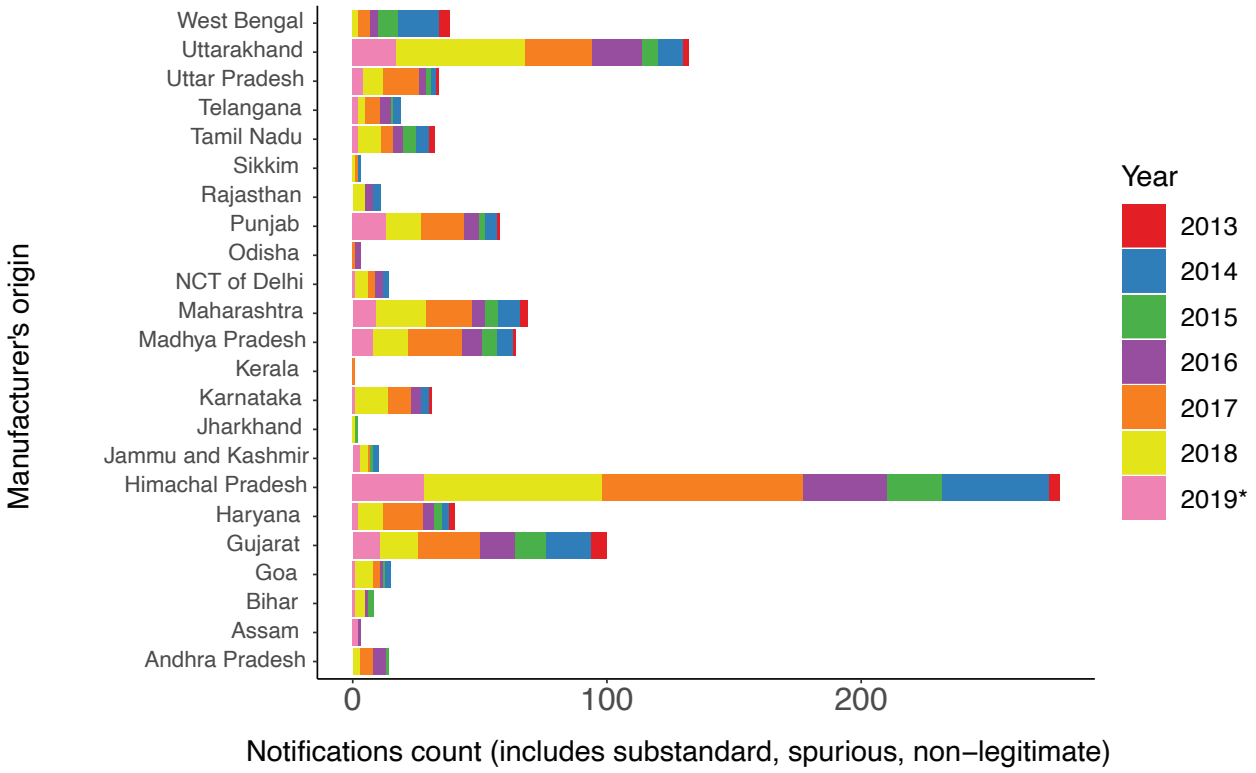
States have the power to issue licenses for the manufacturing and sale of drugs, according to Rules 67 and 68 of the Drugs and Cosmetics Rule, 1945. Thus, even though states follow the Central Government's regulations, a license can only be rescinded by that state's licensing authority.

This decentralisation of drug manufacturing licenses creates problems, such as when a licensed manufacturer from one state produces substandard drugs to sell in another state. Therefore, we are interested in where these non-standard quality (NSQ) drugs are coming from.

No centralised database exists to study where substandard drugs are manufactured, and the most recent, in-depth National Drug Survey makes no comment on this important regulatory aspect. Thus, we looked at circulars issued by the CDSCO every month in Figure 14, which include a drug alert list dating back to 2013. These drug alerts not only include substandard drugs, but also spurious and other non-legitimate drugs. The drug alerts also include medical devices and cosmetics products, which are grouped under "drugs."

[82] We provide the earliest and latest years that these numbers are available to avoid repetition of the same charts. 2013-2016 can be found in the Appendix.
[83] Bate et al. (2016), "Poor-Quality Drugs."

Figure 14: CDSCO's drug alert lists, 2013-2019*



*As of May 2019. Source: Central Drugs Standard Control Organization

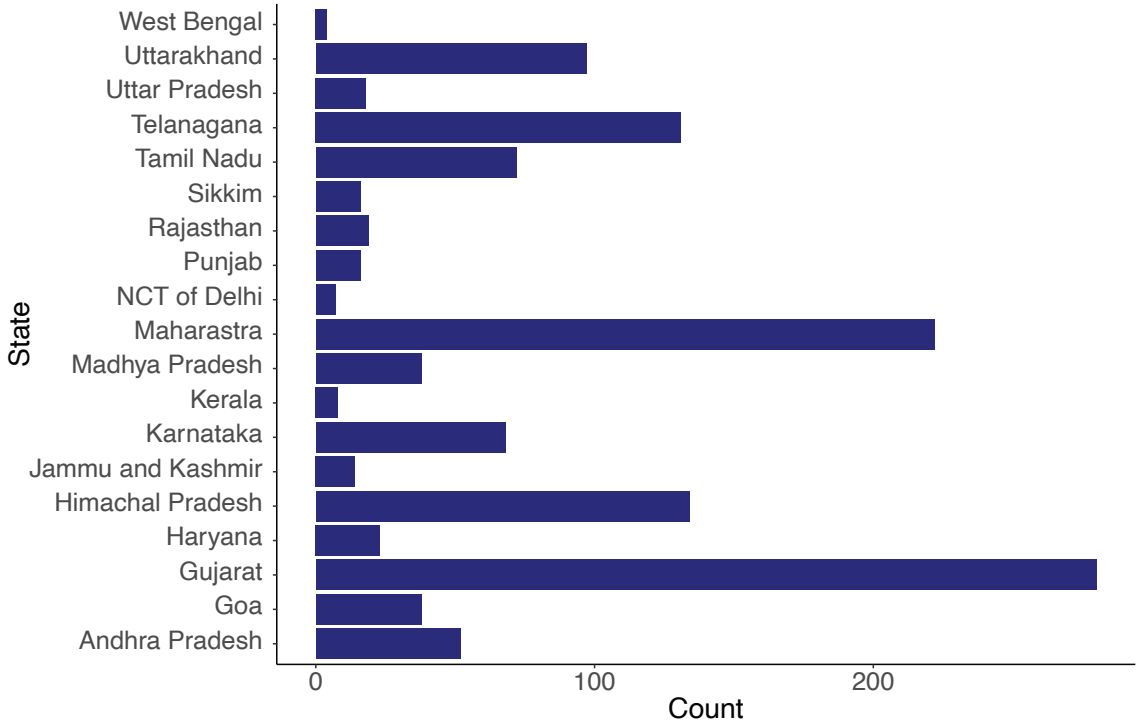
The stacked bar plot shows the number of substandard drugs found in different states each year, as compiled by the CDSCO.[84] The CDSCO started reporting their sampling sizes each month in March 2019. The substandard (includes spurious as well) sample percentages for March, April, and May 2019 were 2.49%, 2.83%, and 4.02%, respectively. Because we do not have access to state sample sizes or total sample sizes for the other circulars, we cannot draw definitive conclusions about the percentage of manufactured substandard drugs out of all drugs sampled in each state.

Interestingly, we see a much greater proportion of substandard drugs manufactured in the states of Himachal Pradesh and Uttarakhand, out of all of the states. Himachal Pradesh consistently leads in the number of notifications from 2013 to May, 2019. Uttarakhand was third behind Gujarat from 2013-2015, before taking second place for most notifications from 2016 onwards. In terms of raw notification counts, Himachal Pradesh has the largest number of notifications, followed by Uttarakhand and Gujarat. This may be due to the sheer number of firms operating within the states. We expect a state with more drug manufacturers to have a larger number of substandard drugs found there.

Data on the number of drug manufacturing units in the country is old and outdated. The most recent data from 2017 is the number of firms designated by the World Health Organization as manufacturers that follow good manufacturing practices (WHO-GMP).[85] We use this as an imperfect measure of which states have the highest number of high-performing manufacturers. A bar chart showing the number of WHO-GMP firms is shown in Figure 15 below.

[84] The months that we cover during the time of download start from February 2013 to December 2018. Notifications for October 2013 and July 2015 are missing.
[85] https://www.who.int/biologicals/vaccines/good_manufacturing_practice/en/

Figure 15: Number of WHO 'good manufacturing practices' firms



Source: Central Drugs Standard Control Organization

Himachal Pradesh is ranked third, but lags far behind Gujarat, ranked first, and Maharashtra, ranked second, the two states with the maximum number of WHO-GMP designated firms. Uttarakhand stands fifth. However, both Himachal Pradesh and Uttarakhand come in first and second in the country for the number of substandard drugs found originating from their manufacturing units. This disparity suggests that the manufacturing standards set by the government are not adhered to by many manufacturing firms in these two states.

Because the CDSCO data lists the manufacturing firm as well, we also look at whether the bulk of the substandard drugs found in each state is a result of a large number of firms failing a few quality tests, or is a result of few firms shirking their responsibilities concerning the maintenance of quality standards. We show this relationship graphically in Figure 16 by using a scatterplot that shows the relationship between the number of notifications and unique firms that received notifications in a state during a certain year. The 45-degree line represents a scenario where the number of notifications on substandard drugs is the same as the number of firms responsible for these notifications. A point farther below the 45-degree line represents that a few firms are the top culprits responsible for multiple notifications for substandard drugs found in a state in a particular year. Each dot represents a state-year pairing (for example, Himachal Pradesh 2017 is in the top right corner). The scatterplot suggests that, on average, a single firm is a culprit for each substandard notification (i.e. many points lie closer to the 45-degree line). Some notable state-years include Punjab's 17 notifications for only five unique firms in 2017, Maharashtra's 18 notifications for nine unique firms in 2017, and Uttarakhand's 51 notifications for 32 unique firms in 2018.

Where these manufactured substandard drugs are eventually sold is of particular interest as well. Data on where substandard drugs are sold and their manufacturing origin is rare. However, we looked at individual state FDA websites to conduct this analysis. Six state websites, those of Maharashtra, Gujarat, Karnataka, Tamil Nadu, Jammu & Kashmir[86] and Andhra Pradesh,[87] provided quality substandard drugs information over a multi-year period. We cannot comment on the percentage of substandard drugs because the data only includes substandard drugs and not the total number of drugs sampled. However, we can extract vital information such as the manufacturing origins of the drug.

[86] At the time of writing of this report Jammu & Kashmir was still state.

[87] Dates are not given for each substandard drug found, but we can tell from the drug's expiration date that some of the data come from before 2014, before Telangana was created. However, our analysis looks at whether substandard drugs are manufactured out-of-state, which is still insightful even if Andhra Pradesh's jurisdiction changed in the data.

Figure 16: Relationship between number of notifications and unique firms featured in notifications (by state-year)

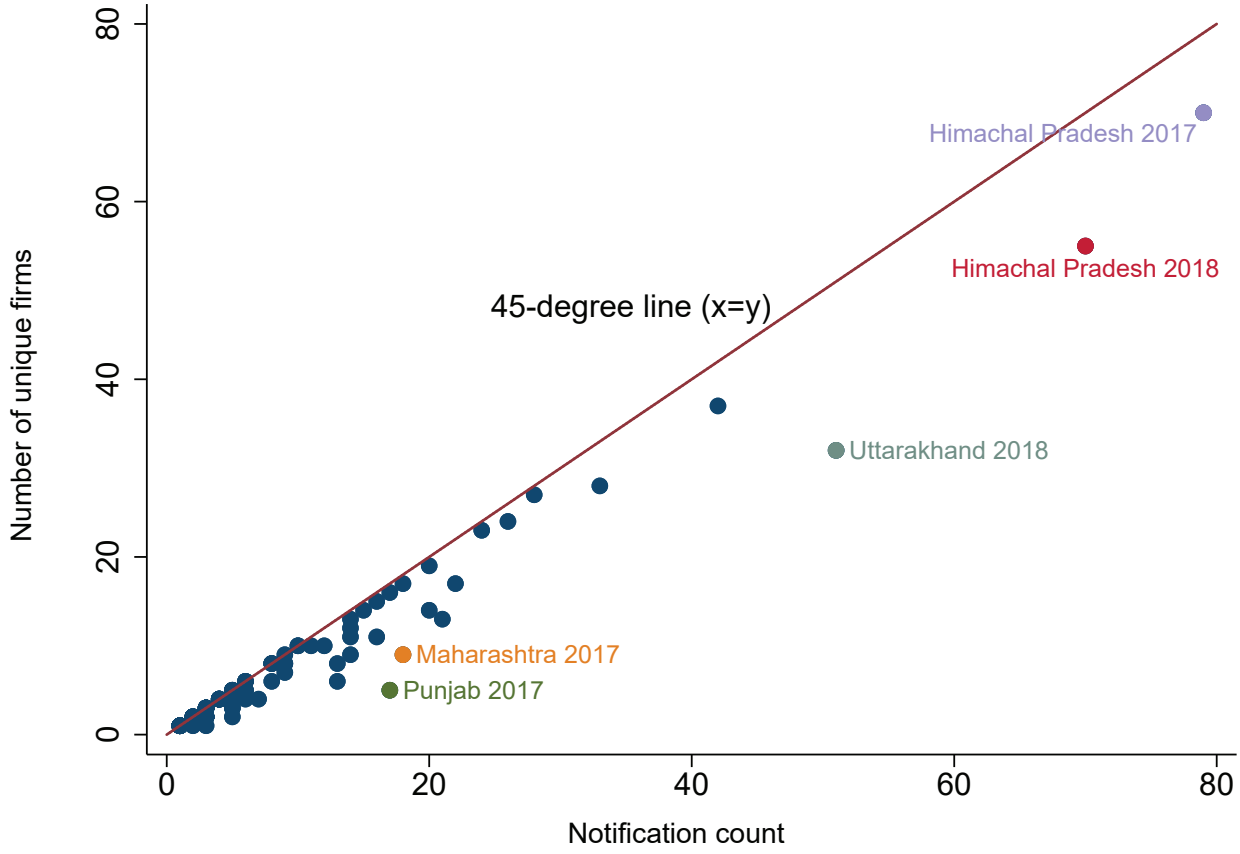
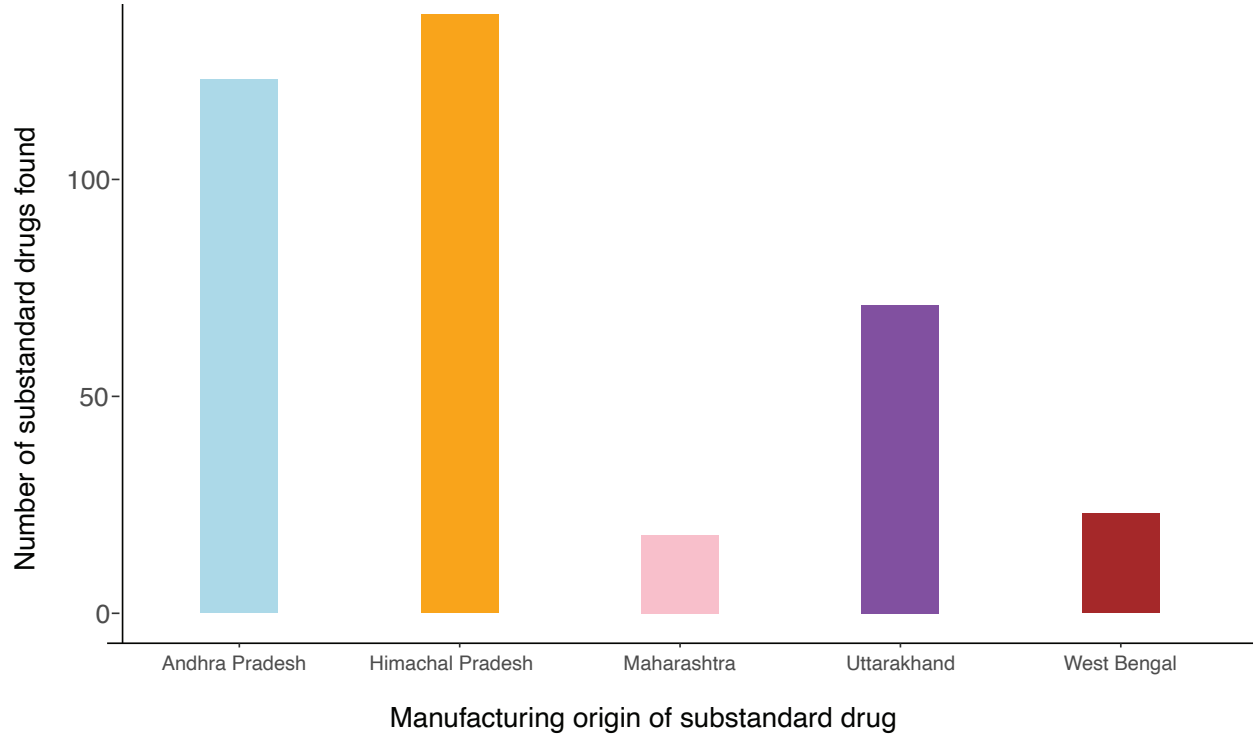


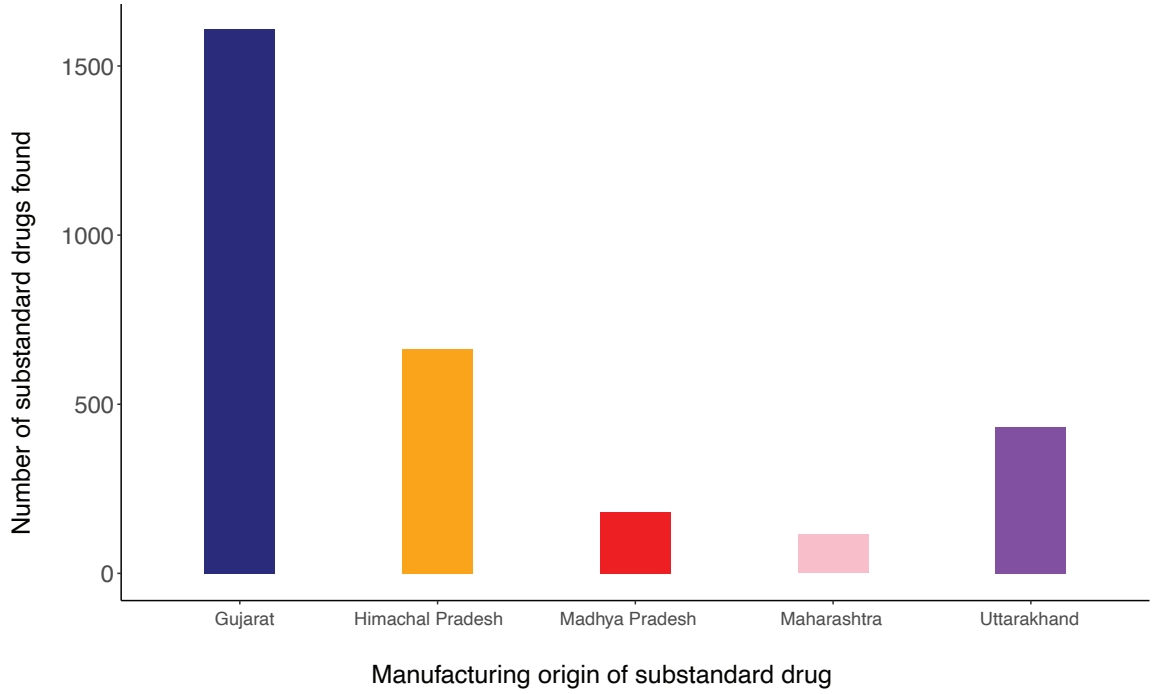
Figure 17: Manufacturing origin of substandard drugs for select states

Figure 17.1: Andhra Pradesh (May 2010 – Jan. 2019)



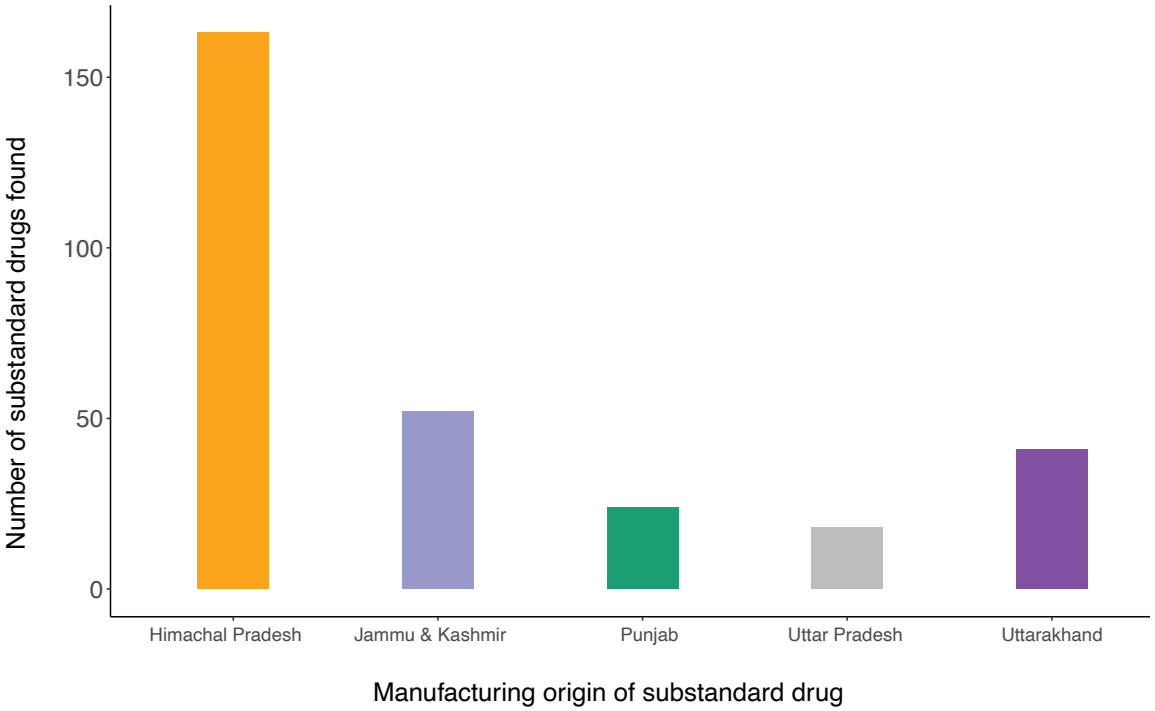
Source: Data from Drugs Control Administration Sales Licensing System, Government of Andhra Pradesh. https://dcadls.nic.in/xln_Nsq_search_frm.aspx?st=AP# Data downloaded as of January 2019

Figure 17.2: Gujarat (Jan. 2007 – Jun. 2019)



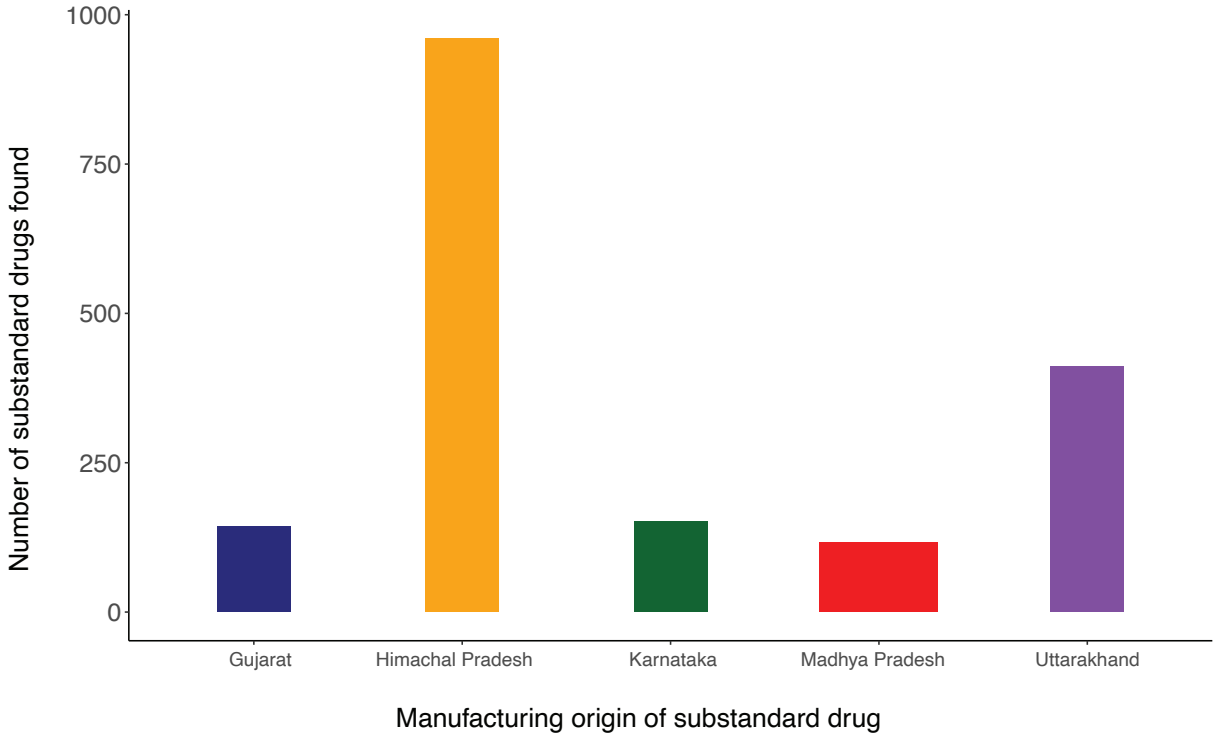
Source: Data from XLN-Xtended Lincensing, Laboratory & Legal Node (Gujarat).
https://xlnindia.gov.in/GP_FailedSample.aspx Data downloaded as of June 2019

Figure 17.3: Jammu & Kashmir (Jan. 2012–Mar. 2019)



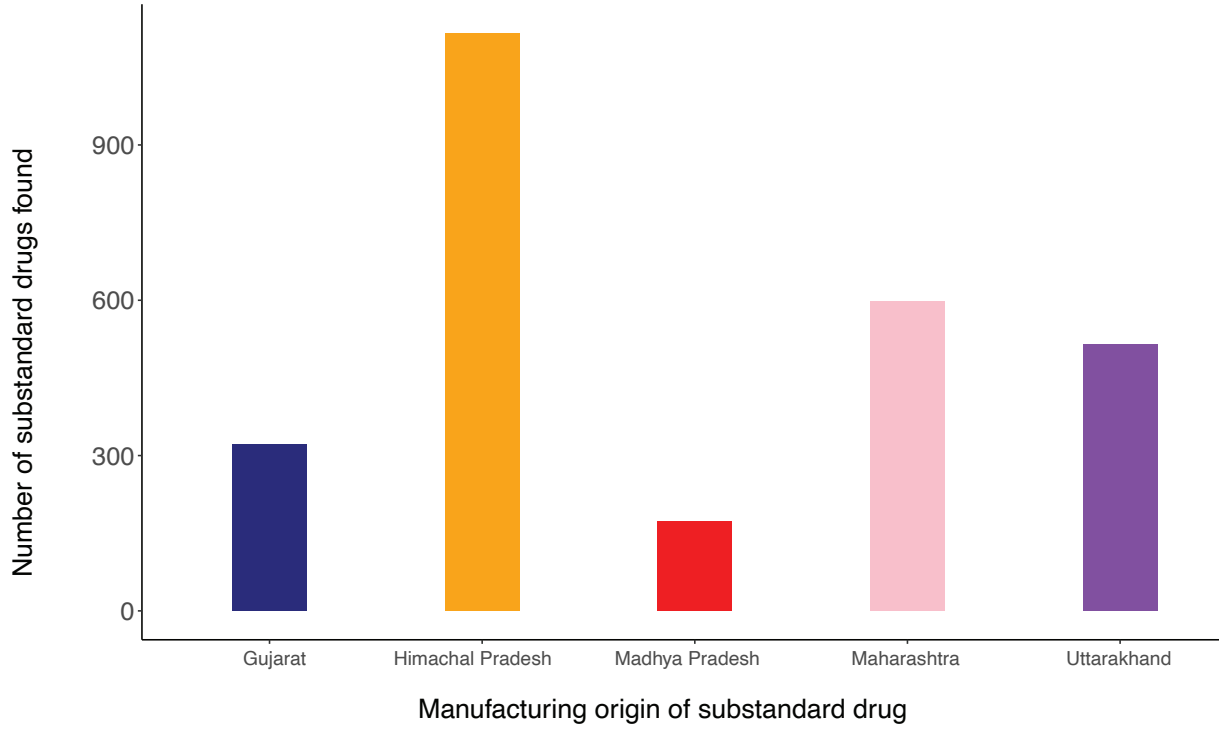
Source: Data from Drugs and Food Control Organization Jammu & Kashmir.
https://dfcojk.org/NSQ_Drugs.php Data downloaded as of June 2019

Figure 17.4: Karnataka (Mar. 2013 – Jun. 2019)



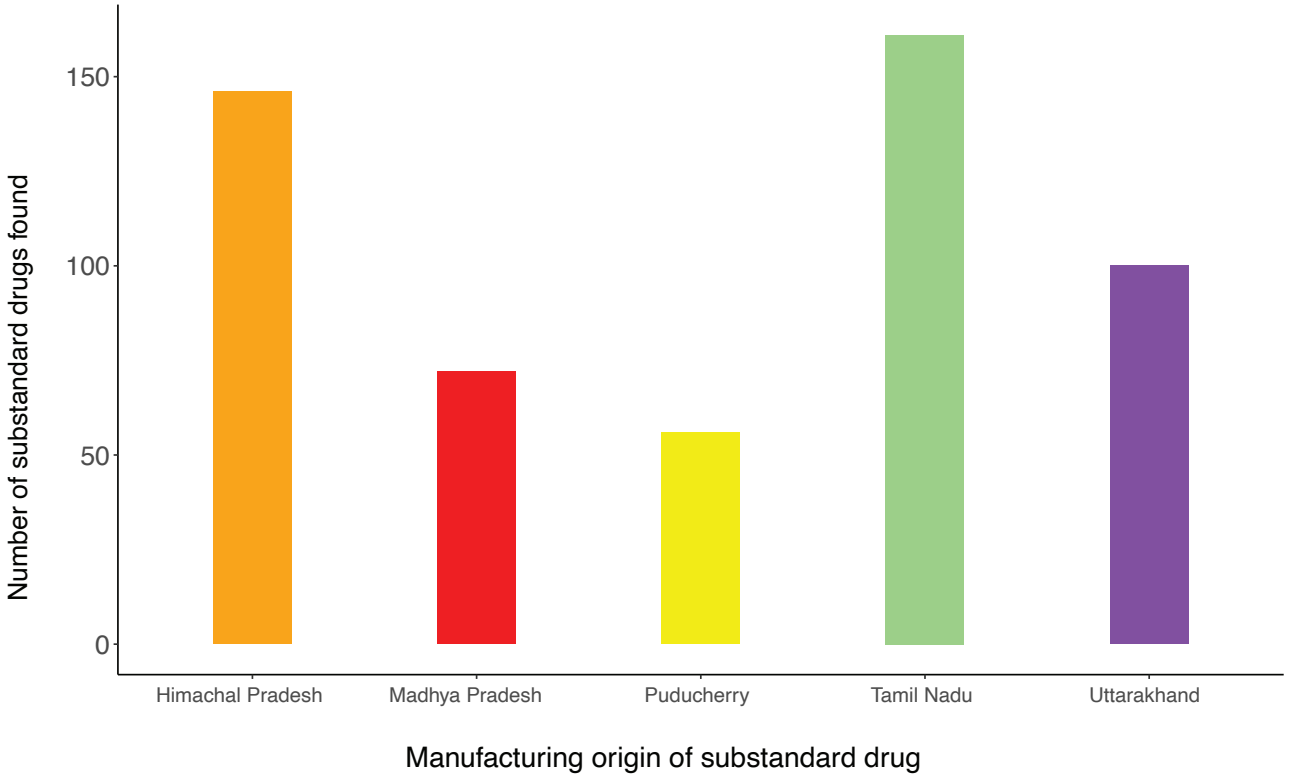
Source: Data from Drugs Control Department, Drugs Testing Laboratory (Karnataka).
https://dcd.kar.nic.in/sampling/NSQCases.aspx?flag=2 Data downloaded as of June 2019

Figure 17.5: Maharashtra (Jan. 2011 – Jun. 2019)



Source: Data from Food & Drugs Administration (Maharashtra).
http://fdamfg.maharashtra.gov.in/GP_FailedSample.aspx Data downloaded as of June 2019

Figure 17.6: Tamil Nadu (Nov. 2016 – Mar. 2019)



Source: Data from Food Sefety and Drug Administration Department (Tamil Nadu)
http://www.drugscontrol.tn.gov.in/nsq_list.html Data downloaded as of June 2019

These six individual charts in Figure 17 show the top five origins of substandard drugs for each of the states. Himachal Pradesh and Uttarakhand are present in all six, meaning that substandard drugs manufactured from these two states are sold in Andhra Pradesh, Maharashtra, Gujarat, Tamil Nadu, Jammu and Kashmir, and Karnataka. Their presence in all six states also suggests that there is some uniformity between the five different drug control administrations since each state is tasked with quality checks. Other than Gujarat and Tamil Nadu, all other states see the highest number of substandard drugs coming from out of state.

There are a number of policy questions that arise from this. Are Gujarat and Tamil Nadu testing their own drugs more rigorously, or are their own manufacturing units and procurement systems just providing more local drugs? How standardised are each state's drug control administrations? Most importantly, how can states such as Karnataka stop culprit manufacturing firms from Himachal Pradesh producing and selling substandard drugs? Since individual states issue manufacturing licenses, a state that finds substandard drugs manufactured by another has little power to suspend the license of the manufacturer, besides contacting the state of origin.

2.3.3 Reasons for quality test failures

Why do drugs fail their quality tests? There are many reasons: it could be due to the actual contents of the drugs, such as whether the correct amount of the active pharmaceutical ingredient is present or whether the active substance is released from its dosage form in an appropriate timeframe; another reason could be misbranding and description errors. We break down the most common reasons for quality test failures to see whether any patterns emerge in Figure 18. While there are many reasons for quality test failures, we use the same categories specified in the NIB report. However, we exclude "others" as those test failures are more on a case-by-case basis.

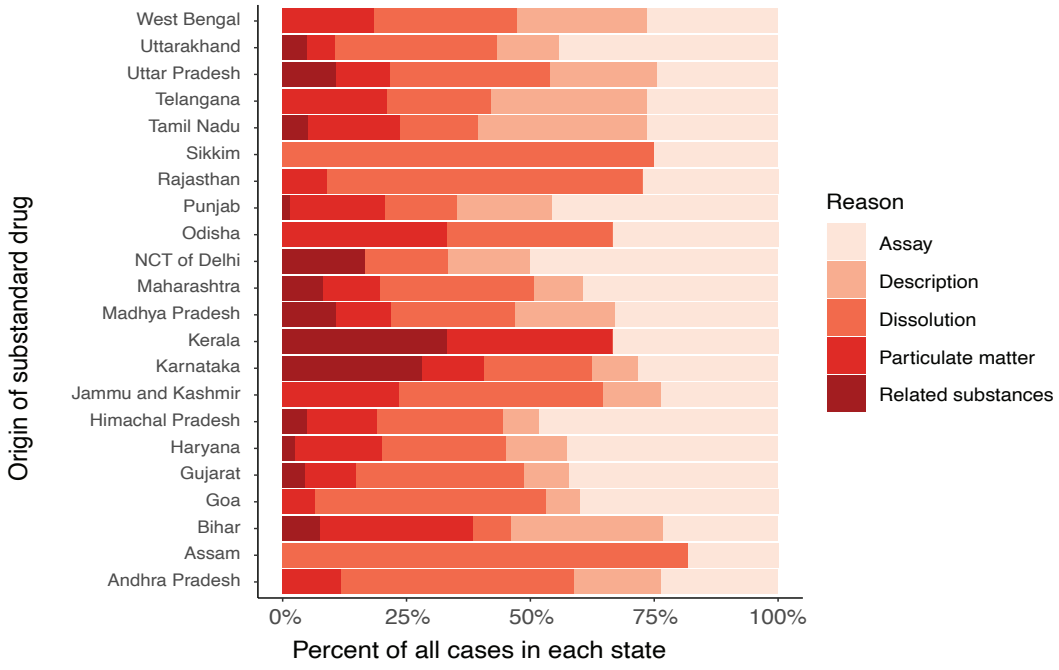
Of all the issued notifications for substandard drugs, "assay" (the correct amount of active pharmaceutical ingredient) or "dissolution" (the time it takes for an active pharmaceutical ingredient to be released) are the main

reasons for quality test failures across the states and union territories. Remember that Himachal Pradesh, and Uttarakhand are states where most substandard drugs originated. Assay and dissolution make up for almost half of the reasons why those drugs failed. Some states or union territories only had a few substandard drugs cases, so, Figure 19 looks at the top five states which had the most substandard drugs. Assay and dissolution dominate as the primary reasons for quality test failures.

However, the dominance of these two reasons could be that they were the two recommended in the CDSCO's guidance document as tests that should at least be done. While the guidance document is not the law, it raises questions on what constitutes the least number of tests necessary to ensure that a drug is safe, especially when sampling targets prioritise the quantity of drugs undergoing simple tests as opposed to the quality of tests conducted on a single drug. Inspections should scrutinise every step of the production process, such as the purity of the water used and even storage conditions of the drug. For example, the U.S. Food and Drug Administration found traces of the carcinogen NDMA in ranitidine in 2019, which increased further scrutiny on Indian drug manufacturers and regulators.

These instances raise questions on whether Indian quality testing guidelines are enough. The 2013 Report of the Prof. Ranjit Roy Choudhary Expert Committee to Formulate Policy and Guidelines for Approval of New Drugs, Clinical Trials, and Banning of Drugs recommended bioequivalence studies or stability testing for all generic medicines sold in India; current Indian guidelines do not require such tests for most generic medicines.[88] However, the Drugs Consultative Committee turned down the bioequivalence recommendation, and its recommendation of mandatory stability testing has yet to receive government action.[89]

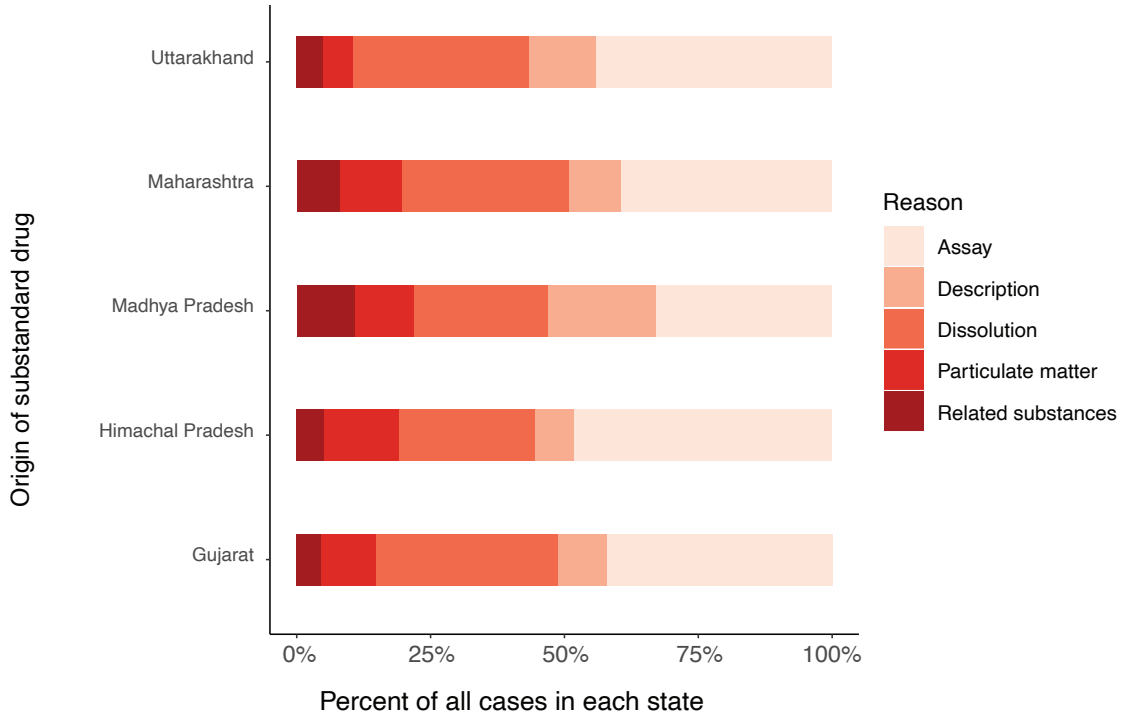
Figure 18: Reason for quality test failure (from CDSCO, 2013-2019)



*Data as of May 2019. Source: Central Drugs Standard Control Organization.

[88] Thakur, Dinesh S. and Prashant Reddy (2016). "A report on fixing India's broken drug regulatory framework."
[89] Ibid.

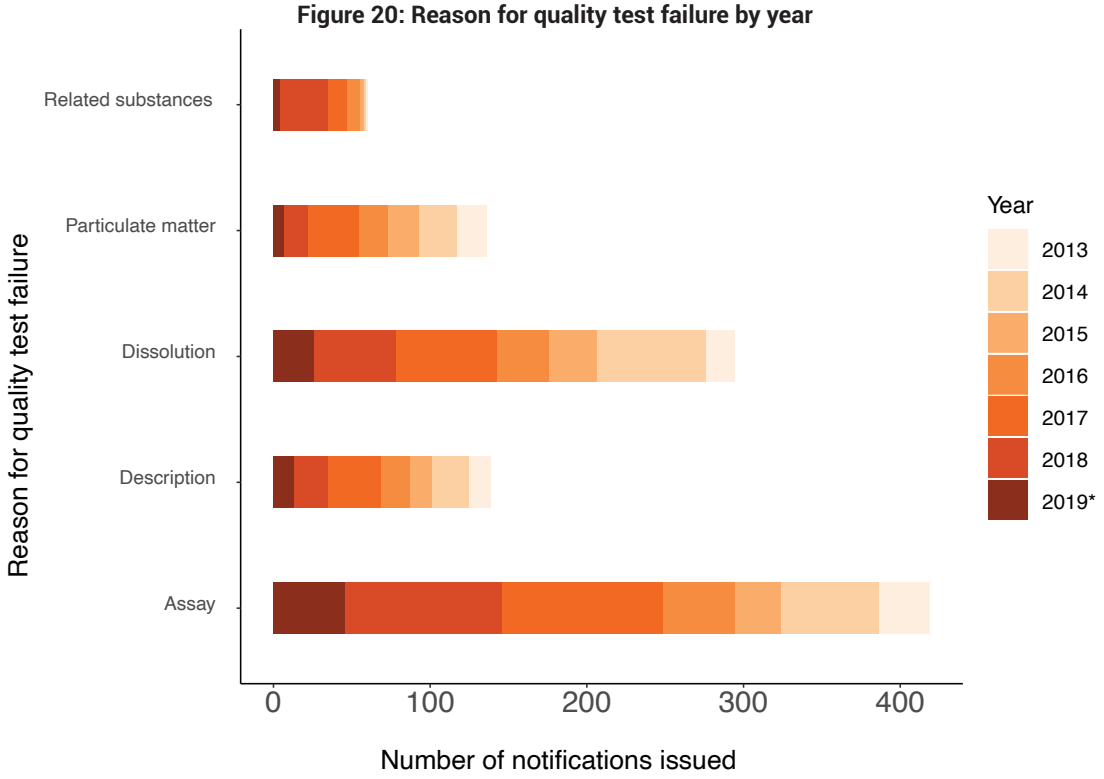
Figure 19: Reason for quality test failure (from CDSCO, 2013–2019*)



*Data as of May 2019. Source: Central Drugs Standard Control Organization.

On a national level, assays remain the top reason for quality failures for most of the time period from 2013 to May 2019 (see Figure 20).

Figure 20: Reason for quality test failure by year



*As of May 2019. Source: Central Drugs Standard Control Organization.

2.3.4 Punitive action

Amendments to the Drugs and Cosmetics Act, 1940, were introduced in 2008 to deter the sale and manufacture of spurious and adulterated drugs, while Section 18 under the same act prohibits the manufacture and sale of drugs and cosmetics that are not of standard quality.[90] Not only is it illegal to manufacture substandard drugs for sale or distribution, but it is also illegal to sell, stock, or exhibit such substandard drugs. Section 19 of the same law governs some of the legal proceedings behind such violations.[91] Defendants cannot claim ignorance when it comes to substandard drugs, though non-manufacturers (retailers) will not be liable under Section 18 provided that they acquired drugs from a licensed manufacturer, had no way of knowing that the drug was substandard, and properly stored the drugs.

Substandard drugs, which include adulterated or spurious drugs, that upon consumption likely cause death or grievous hurt as defined within Section 320 of the Indian Penal Code could result in a prison term of no less than five years to life in prisonment. A monetary fine of at least Rs. 10,000 is also included.[92] Section 30 increases these punishments for subsequent offenders.

For example, between April 1, 2017 to March 31, 2018, Gujarat found a total of 399 substandard, spurious, or adulterated drugs. The value of the drugs seized was Rs. 19.92 lakhs. Based on our analysis, we found that the ratio of notifications on substandard drugs and number of firms responsible for these sub-quality drugs is closer to one. However, only two prosecutions were launched against the manufacturing, sale, and distribution of these drugs, and no one has been arrested thus far. It is unlikely that just two companies were responsible for all 399 substandard drugs. On the other hand, during the same time period, Maharashtra reported that prosecution orders were issued for all cases and five cases have been filed in court, with 19 arrests. These are only the actions recorded for cases that involved the manufacturing, sale and distribution of spurious or adulterated drugs. There is no information available on the punitive actions taken on substandard drugs, if any. While the state can suspend manufacturing licenses, we do not know how long these suspensions last, whether the penalties actually increase for repeat offenders, and whether these manufacturers remove their substandard products from the market. Additionally, important state-level differences exist even when it comes to prosecution of companies which produce (or market) substandard, spurious or adulterated drugs. As documented in Dinesh Thakur's and Prashant Reddy's 2016 report, legal action against wrongdoers is too weak and inconsistent.[93]

Internationally, there are various laws that disincentivise manufacturers and distributors of substandard drugs. In the United States, counterfeit drugs are considered as stolen property, and the trafficking of counterfeit goods or services can result in fines for individuals of no more than $5 million ($15 million for non-individuals), no more than 20 years in prison, or both.[94] Subsequent offenses see these upper limits raised to a $15 million fine and 30 years of imprisonment for individuals, and $30 million for non-individuals. These monetary fines are much higher than those outlined in the Drugs and Cosmetics Act, 1940. Larger prosecution rates and fines in India can potentially be the much-needed deterrent.

2.4 Conclusion

Various sources estimate the proportion of fake/substandard/spurious (FS) drugs in India in recent years to be around 3% to 4%. We have, thus far, outlined two major regulatory issues within the Indian pharmaceutical industry: state-level inspections and manufacturing licensing discrepancies. Research in this domain has found that Indian pharmaceutical firms present a pattern of differentiating drug quality depending on the final destination (internationally).[95] Places with underdeveloped regulatory oversight structures were more likely to receive substandard products. Whether this pattern holds true domestically as well needs additional investigation, but this points to a need for rigorous quality inspections in states where sampling numbers

[90] *Section 18,* The Drugs and Cosmetics Act, 1940.
[91] *Section 19,* The Drugs and Cosmetics Act, 1940.
[92] *Section 27a,* The Drugs and Cosmetics Act, 1940.
[93] Thakur, Dinesh S. and Prashant Reddy (2016). "A report on fixing India's broken drug regulatory framework."
[94] 18 U.S. Code § 2320.Trafficking in counterfeit goods or services
[95] Roger Bate, Ginger Zhe Jin, Aparna Mathur, and Amir Attaran (2016), "Poor Quality Drugs and Global Trade: A Pilot Study." *American Journal of Health Economics* 2, no. 3 (Summer 2016): 373-98. doi:10.3386/w20469.

are low and the proportion of FS drugs is high (such as the Northeastern states). Competition can also play a role in quality determination in local markets, as has been shown using a natural experiment that looked at the entry of retail chains in Hyderabad, India. This study found that in areas where incumbent single-enterprise pharmacies operate, the entry of retail chains ultimately lowered prices by 2% and increased the quality of drugs sold by all pharmacies in the market by 5%.[96] The authors also find that incumbent firms, in order to compete in terms of quality with the chain entrants, became more selective in their procurement sources. Additionally, quality perceptions of generic and branded drugs vary. But in a study,[97] researchers looked at the quality of five commonly used branded and branded-generic medicines made by the same manufacturer in India in 2011. They found that there were no quality differences between the two. Active efforts are needed to debunk these negative perceptions.

The data shows that irregularities exist between states/union territories and their quality tests. Both state-level and federal-level data show that drugs manufactured in certain states are much more likely to be substandard than products sourced from other states. These are pertinent issues that require more attention to ensure the safety of India's pharmaceutical products.

2.5 Recommendations

Centralise manufacturing licensing system: States are powerless to stop substandard drugs manufactured out-of-state. The regulatory structure should be modified to facilitate better cooperation & coordination between state FDAs, for the purpose of closing the investigations regarding sub-standard drugs. Centralising this system can reduce the number of substandard drugs in the market and hold all states accountable for licensing approvals.

Create central databases for substandard and spurious drugs and their manufacturers: There is no current database that can inform consumers which manufacturers have consistently produced drugs that could harm consumers. An accessible database also allows officials to quickly remove such items from stock. State drug control authorities can also monitor risky manufacturers within their domain easily with a central database. We note that there is already a database foundation in place but only a few states have participated in this initiative (called the XLN Xtended Licensing & Laboratory Node).

There is an urgent need to clearly distinguish between cases of NSQ drugs vis-à-vis cases of spurious drug manufacturing (where the NSQ drug is found to be manufactured by a non-legitimate person or company, who is not the licensed manufacturer for the drug in question). In the cases of spurious drugs manufactured by non-legitimate people or companies, the investigation should be completed on an urgent basis against the accused without jeopardising the genuine manufacturer's image and the brand value of genuine drugs.

Standardise hiring and training process of inspectors, but emphasise the importance of local inspectors: There is a need to set standards for inspections, but the bigger problem stems from lack of state resources. The central government should step in to provide resources and training to inspectors on the local level. The staff that operates drug-testing laboratories are essential to the drug inspection process as well.

Quality checks should be boosted at the manufacturing site: While sampling drugs from retailers provide useful information, better quality checks at the manufacturing site, such as those in Himachal Pradesh and Uttarakhand, could stop substandard drugs at their origin.

[96] Bennett, D., & Yin, W. (2019). The Market for High-Quality Medicine: Retail Chain Entry and Drug Quality in India. *The Review of Economics and Statistics, 101*(1), 76-90. doi:10.1162/rest_a_00758

[97] Singal, G. L., Nanda, A., & Kotwani, A. (2011). A comparative evaluation of price and quality of some branded versus branded-generic medicines of the same manufacturer in India. *Indian journal of pharmacology*, 43(2), 131–136. https://doi.org/10.4103/0253-7613.77344

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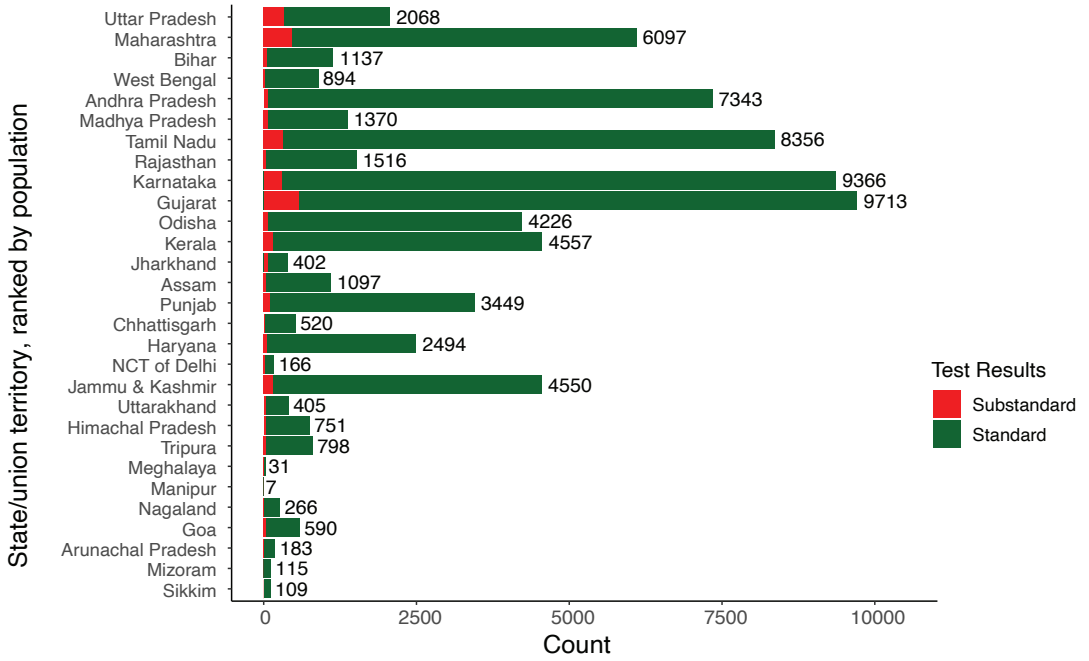
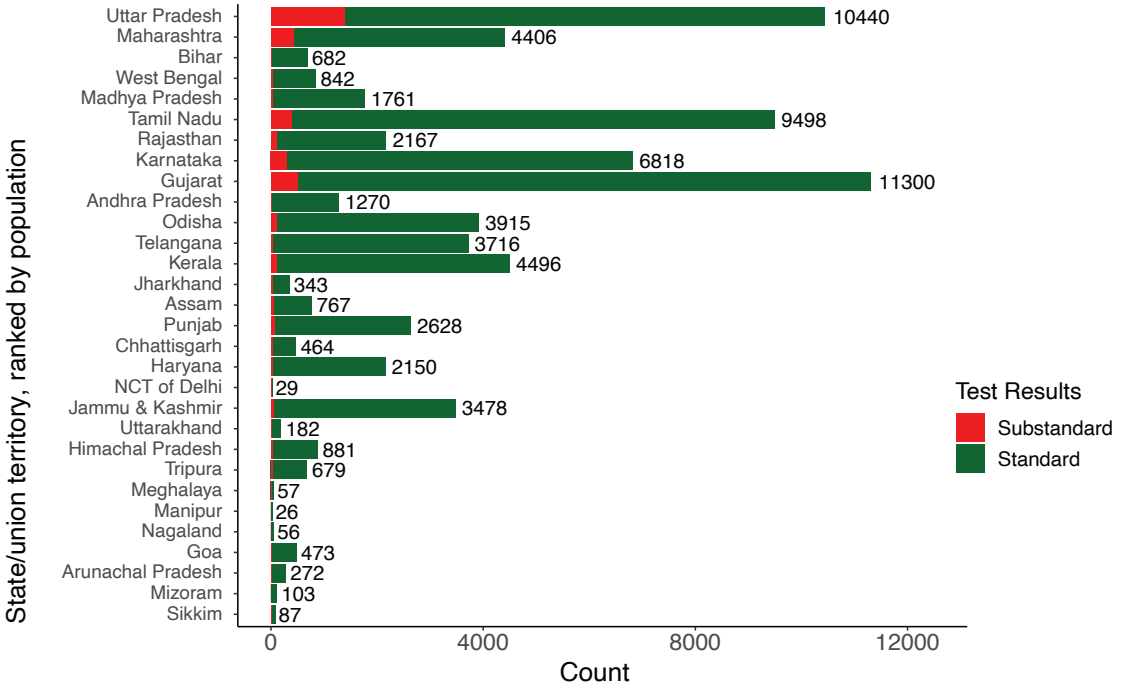
2.7 Appendix

Figure 21: Number of quality tests conducted by State/UT drug controllers, 2013



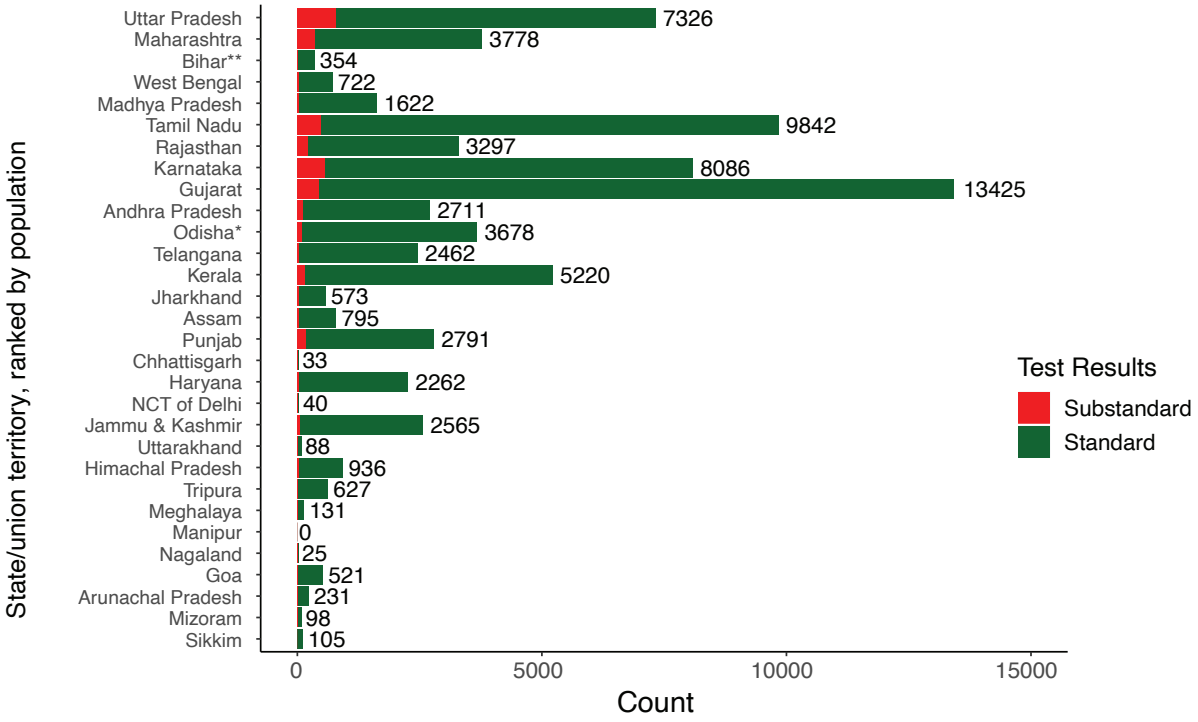
Source: Compiled by CDSCO for Lok Sabha Question No. 2262 on 11 December 2015. Each year is from April 1st of the current year to March 31st of the next year Spurious drugs are rare. No SUTs with a large sampling size found more than 0.46% (Rajasthan) of their drug samples as spurious.

Figure 22: Number of quality tests conducted by State/UT drug controllers, 2014



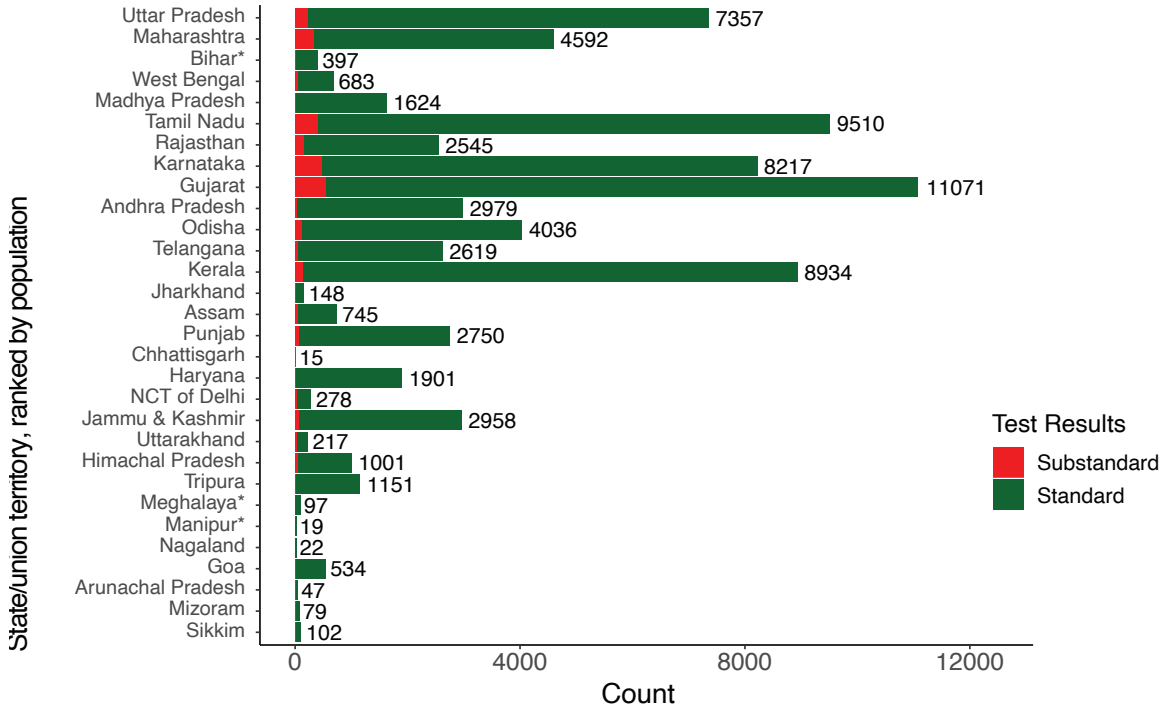
Source: Compiled by CDSCO for Lok Sabha Question No. 2262 on 11 December 2015. Each year is from April 1st of the current year to March 31st of the next year Spurious drugs are rare. No SUTs with a large sampling size found more than 0.56% (Maharashtra) of their drug samples as spurious.

Figure 23: Number of quality tests conducted by State/UT drug controllers, 2015



Source: Compiled by CDSCO for Lok Sabha Question No. 552 on 20 July 2018. Each year is from April 1st of the current year to March 31st of the next year * indicates only 11 months were reported. ** indicates only 6 months were reported. Spurious drugs are rare. But among SUTs with large sampling sizes, Andhra Pradesh stands out, with 3.32% of its drug samples found as spurious. Figure 24: Number of Quality Tests Conducted by State/UT Drug Controllers, 2016

Figure 24: Number of quality tests conducted by State/UT drug controllers, 2016



Source: Compiled by CDSCO for Lok Sabha Question No. 552 on 20 July 2018. Each year is from April 1st of the current year to March 31st of the next year * indicates only 6 months were reported. Spurious drugs are rare. No SUTs with a large sampling size found more than 1.18% (Rajasthan) of their drug samples as spurious.

CHAPTER—**03**

AFFORDABILITY

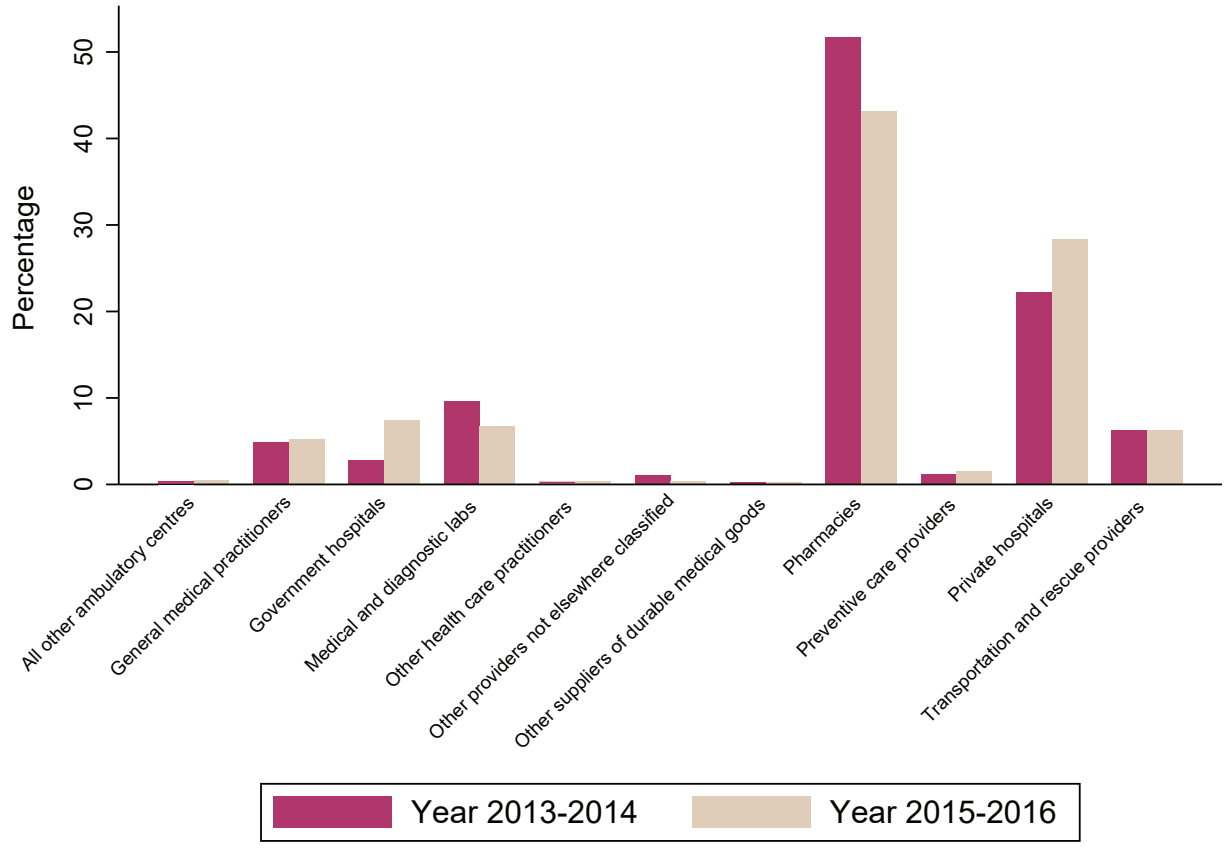
3.1 Introduction

Drug costs pose a significant financial burden to families in India. Rising costs prevent households from buying the medicines that they need, and out-of-pocket expenditure (OOPE) on medicines has pushed millions into poverty.[98] Data from the National Health Accounts (NHA) for 2013-2014, 2014-2015, and 2015-2016, shows that households spend nearly half of their OOP expenditures in pharmacies, far outpacing expenditures in hospitals (Figure 25).[99] In 2013-2014, pharmacies contributed to 51.67% of total healthcare-related out-of-pocket expenditures. In 2015-2016, this declined to 43.12% of all OOPE, according to the latest NHA report, even as spending in both private and government hospitals rose.

[98] Sakthivel Selvaraj, Habib Hasan Farooqui, Anup Karan (2018), "Quantifying the financial burden of households' out-of-pocket payments on medicines in India: a repeated cross-sectional analysis of National Sample Survey data, 1994–2014," *BMJ Open* 8, no. 5. doi: 10.1136/bmjopen-2017-018020.

[99] National Health Accounts (2016). *Household Health Expenditures in India (2013-14).*

Figure 25: Split of OOPE on the basis of type of expenditure



*Source: National Health Accounts 2013-14 & 2015-16.

In terms of absolute numbers of the amount spent out-of-pocket, expenditures in pharmacies decreased by around Rs. 12,000 crores from 2013-2014 to 2015-2016. Thus, the share of expenditures in pharmacies in all healthcare-related out-of-pocket expenditures fell between 2013-2014 and 2015-2016 by about 8%.[100] Expenditures in private hospitals, on the other hand, increased by more than Rs. 25,000 crores in the same time period. While these two NHA reports show that the OOPE in pharmacies is falling, the NHA 2015-2016's numbers are an increase from the NHA 2014-2015 report (data and figures not shown). Between 2014-2015 and 2015-2016, the share of expenditures in pharmacies in all healthcare-related OOPE did not rise much, but in absolute numbers, it meant an increase of Rs. 8,000 crores.[101]

Thus, given the significant costs that households bear due to pharmaceutical needs, policies have been formulated to address this issue. Price control has been chosen as the policy instrument to keep costs of medicines low in the country; we provide details of the structure of drug price control in India.

3.2 History of drug price controls

For years, government policies have attempted to combat rising drug prices with the use of price controls. Price controls occur when the government sets either a maximum price, called the price ceiling, or a minimum price, called the price floor, on products. Sellers are prohibited from pricing the product beyond such boundaries. The government first imposed price ceilings under Section 3 of the Essential Commodities Act, 1955,

[100] National Health Accounts (2018). *National Health Accounts Estimates for India 2015-2016.*
[101] National Health Accounts (2017). *National Health Accounts Estimates for India 2014-2015.*

on a range of defined goods deemed important for the general public.[102] The early drug price controls fell under the Defence of India Act, which froze all final drug prices on the Drugs Order's implementation date in 1963.[103] In 1966's Drug Prices (Display & Control) Order, government approval was required for raising drug prices.

From 1970 onwards, Drug Price Control Orders (DPCO) were issued in accordance with the Essential Commodities Act, 1955, with amendments added over time. The Drug Price Control Order, 1970, specified a maximum selling price of bulk drugs. Bulk drugs are defined as "any substance including pharmaceutical, chemical, biological, or plant product or medicinal gas conforming to pharmacopoeial or other standards, which is used as such or as an ingredient in any formulations". They are also alternatively known as the active pharmaceutical ingredient (API). Price control in this setting meant that the price of API was regulated, and the price of formulations (defined as the final form of the drug consumed by patients), which contained these APIs was also regulated. The number of formulations under price regulation often exceeds the number of bulk drugs under regulation as formulations of different doses (but made from the same active ingredient) still fall under regulation.

The DPCO 1970 was also the first of many which based the pricing of regulated formulations on the costs of manufacturing the formulation. However, the lengthy, multi-step manufacturing process makes cost-verification difficult. Thus, a firm could get away with charging higher formulation prices if they subtly inflate their costs. The Drug Price Control Order of 1979 was more selective and decreased the number of bulk drugs covered under the DPCO 1970. Under the DPCO 1979, the government took into consideration rates of return on net worth and capital employed, and manufacturers could fix prices subject to certain profitability limits.[104] There have been three more drug price control orders since 1979, we describe them in some detail below.

Drugs price control order 1987

According to the DPCO 1987, the approach was to reduce the ambit of regulation by bringing down the number of drugs under price control. Thus, the number of drugs covered under the control orders were drastically reduced to the most essential and commonly used medicines. The government looked at which drugs were used in the National Health Program, and thus medicines were selected based on an *essentiality-based criterion.* Before 1987, 347 molecules were subject to price control. The DPCO 1987, reduced this number to 141.

Drugs price control order 1995

The DPCO 1995, introduced new *market-based criteria* to select drugs for price regulation. Several conditions had to be satisfied by the drug to fall under the regulatory ambit. First, the turnover of a drug was assessed; if the annual turnover exceeded Rs. 40 million, then the level of competition for the drug became the deciding criteria. If there were fewer than five producers of these bulk drugs and fewer than 10 formulators, with the market leader possessing at least a 40% share of the market, then the drug was put under regulation. For bulk drugs with a turnover of less than Rs. 40 million but at least Rs. 10 million, price control was introduced if the market leader selling the formulations resulting from the bulk drug had at least a 90% market share. Fewer bulk drugs were covered under this DPCO, with the number falling further down to 74.[105]

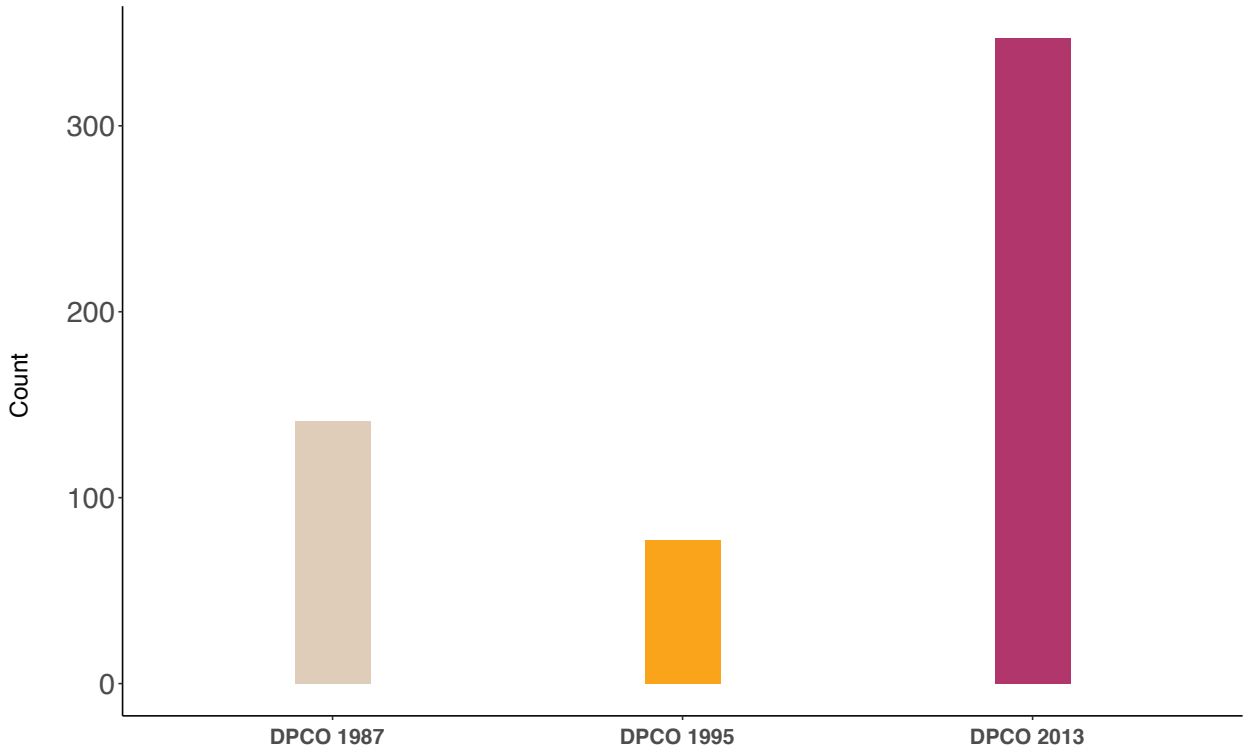
The DPCO 1995 also created the National Pharmaceutical Pricing Authority (NPPA) to enforce such price ceilings. The NPPA continues to operate today. Its main functions include the revision of drug prices, inclusion and exclusion of drugs from price control, and supervision of drug prices outside price control.

[102] Section 3, The Essential Commodities Act, 1955.
[103] Sudip Chaudhuri (2005), *The WTO and India's Pharmaceuticals Industry,* New Delhi: Oxford University Press India, 273.
[104] Chaudhuri, *The WTO*, 278.
[105] The original DPCO 1995 lists 76 drugs. However, Amikacin Sulphate and Mefenamic Acid were petitioned as not meeting the market criteria to be regulated in court.

Drugs price control order 2013

The latest and current DPCO switches back to the *essentiality-based* method of selecting which drugs fall under price control. However, contrary to the DPCO 1995, this order targeted the formulations—what the patient actually consumes—as opposed to the active ingredient.[106] The reasoning behind this change is that the active pharmaceutical ingredient may not reflect which formulations are essential for the public. This also makes the regulation more direct and in the interest of the consumer. Formulations deemed essential are compiled in the National List of Essential Medicines (NLEM) by government experts and based on those outlined by the World Health Organization. The NLEM may change from time-to-time, thus allowing the specific drugs under price regulation to change.[107] The number of bulk drugs under price control has risen to 347 under the NLEM 2011.[108]

Figure 26: Total number of bulk drugs covered under each drug price control order



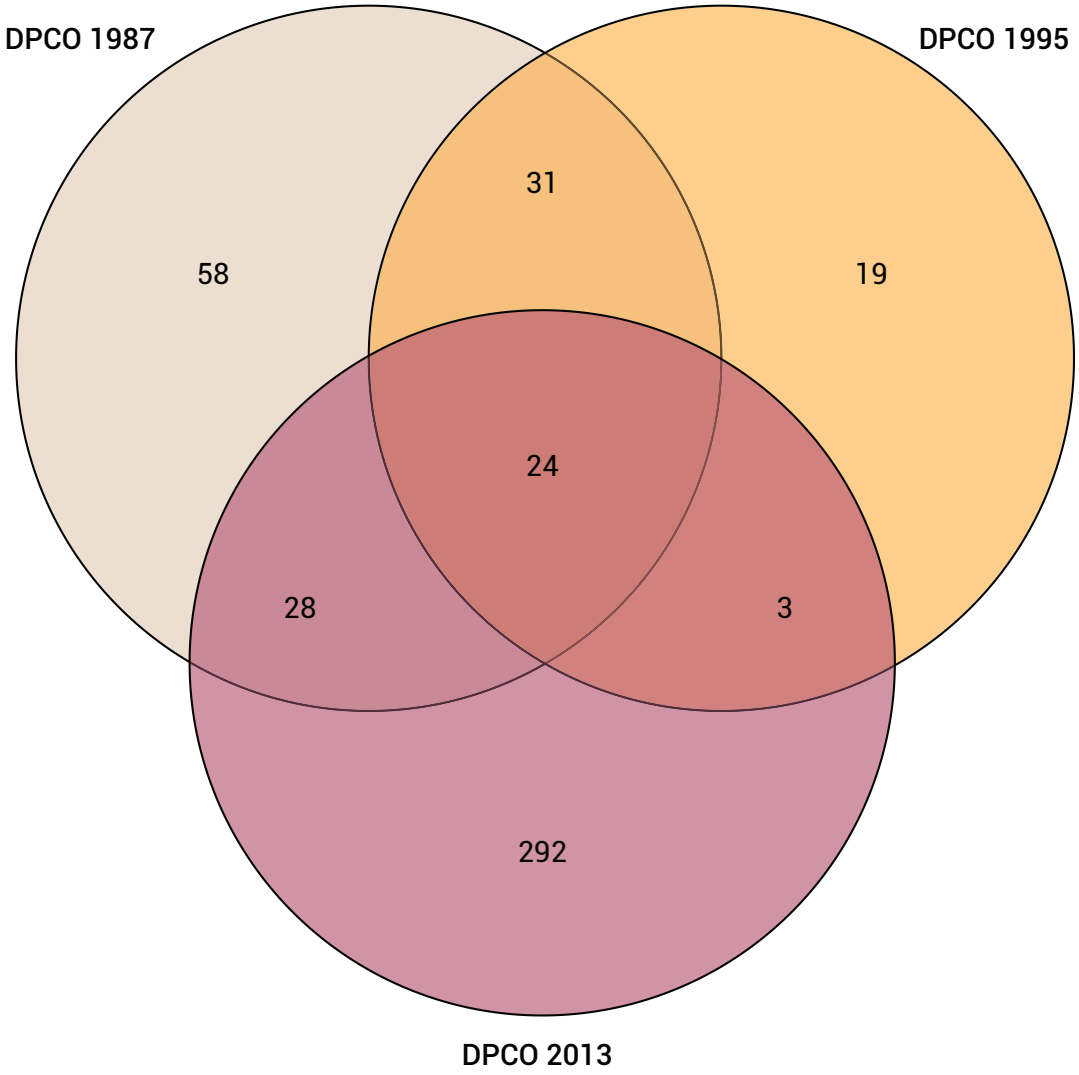
Source: DPCO 1987, DPCO 1995, DPCO 2013

The bar chart in Figure 26, shows how the total number of bulk drugs changed under the last three DPCOs. While it is clear that the total number of bulk drugs covered under each DPCO varies, we are also interested in the number of bulk drugs that have been covered by either all DPCOs, by two of them, or by just one of them. Thus, the following venn diagram (Figure 27) maps the number of overlapping bulk drugs that the three DPCOs have in common with each other.

Over the past four decades, 24 bulk drugs have always been under regulation. 31 bulk drugs were regulated under both the DPCO 1987 and DPCO 1995, but fell out of regulation in 2013. The DPCO 2013, introduced the largest number of new drugs that had not been regulated under the previous two DPCOs.

[106] Section 3.2, National Pharmaceuticals Pricing Policy, 2012.
[107] Section 4.1, National Pharmaceuticals Pricing Policy, 2012.
[108] The official National List of Essential Medicines, 2011 puts the number at 348. However, the NLEM 2011 lists the molecule "Gentian Violet" twice, first as "Gentian Violet" and second as "Methylrosanilinium Chloride (Gentian Violet)." We count this as the same molecule, so we have a final count of 347 bulk drugs for DPCO 2013.

Figure 27: Number of overlapping bulk drugs covered in DPCO's



Other forms of price regulation within DPCO 2013

While scheduled formulations are those that fall under regulation and subject to price control, non-scheduled formulations are still monitored by the government. The NPPA monitors the maximum retail prices (MRP) of all drugs and prevents manufacturers from increasing the MRP by more than 10% for non-scheduled formulations, from year-to-year.[109] Additionally, the government maintains its power to direct manufacturers of active pharmaceutical ingredients, bulk drugs, or formulations to increase such production and sell it accordingly.[110] Paragraph 19 grants the government power to fix the ceiling or the retail price of any drug for any length of time, as long as it is within the public's interest. This power was invoked by the government when it placed a 30% trade margin cap on manufacturers of 42 cancer medications in a February 27, 2019 order.[111] While trade margins are regulated for scheduled formulations under Paragraphs 7 and 8, not much is mentioned for non-scheduled formulations, which the government still monitors. The order cites high trade margins and the essentiality of 42 cancer drugs as a motivation for additional regulation. Thus, manufacturers of these drugs had to fix their retail prices, where the trade margin could not exceed 30%.

[109] Paragraph 20, Drug Price Control Order, 2013.
[110] Paragraph 3, Drug Price Control Order, 2013.
[111] Drugs Price Control Order, Notification, February 2019.

Medical devices

Medical devices follow the same regulatory framework that bulk drugs follow. Medical devices are also considered drugs under the Drugs and Cosmetics Act, 1940, and 19 of the 23 mentioned in the Drugs and Cosmetics Act, 1940, are subject to price regulation under the DPCO 2013.[112]

The Medical Devices Rules, 2017, came into effect in 2018 to better regulate the medical devices sold in the country, as their regulations had often been grouped under the same umbrella category of "drugs". The rules established several major provisions, dividing the devices into four different risk categories and expanding beyond the devices listed in the Drugs and Cosmetics Act, 1940. Unlike bulk drugs, India is still largely dependent on imports of medical devices. The industry faces a 75% import dependency.[113] This dependency will have huge implications for proposed amendments to the current Drug Price Control Order 2013, which currently favours domestic firms.

Another amendment could increase the availability of medical devices in India. Prior to the amendment of Rule 63 of Chapter VIII in the Medical Devices Rules of 2017,[114] imported or manufactured medical devices that did not have a predicate medical device had to submit an application after the successful completion of a clinical trial. The original Rule 63 waived the clinical trial requirement for devices approved by regulatory authorities in either the United Kingdom, United States, Australia, Canada, or Japan, as long as the device had been on the market for at least two years. The Drugs Technical Advisory Board approved an amendment to Rule 63 in June 2019 to include countries of the European Union in the clinical investigation requirement waiver.[115] While the move could allow EU medical devices to reach Indian markets faster, critics point to the failure of many foreign devices in the past as evidence that foreign regulators cannot be trusted.

Amendments to the DPCO 2013

The Department of Pharmaceuticals proposed several amendments to the DPCO 2013, including extending patent protection to manufacturers of new drugs regardless of the manufacturer's origin.[116] Previously, only new drugs developed by indigenous firms received product patents for five years. Now, any manufacturer, including foreign firms, can receive patent protection for five years for a new drug. Developers of new drugs, which include medical devices listed in the NLEM, could have more market power.

While one can only file patents for bulk drugs if they are new, medical device makers can tweak a device and claim it as innovation. Growing fears result from the already import-dependent medical devices industry, where multi-national corporations could use the amendment to obtain a price exemption for five years.[117] These amendments could push for foreign firms to more quickly introduce their products to the Indian market, which could have a positive impact.

Despite relatively cheaper drug prices compared to other countries, out-of-pocket drug costs remain high in India.[118] This suggests that the number of producers and drug price control orders alone does not alleviate affordability problems.

Ayushman Bharat (also known as Pradhan Mantri Jan Arogya Yojana, or PMJAY) is an ambitious national programme launched during the latter half of 2018 to

[112] "Monitoring of price movement of notified medical devices as 'Drugs' under the Drugs and Cosmetics Act, 1940 and the Drugs and Cosmetics Rules, 1945." Department of Pharmaceuticals, National Pharmaceutical Pricing Authority.
[113] Department of Pharmaceuticals, Annual Report.
[114] Rule 63, Chapter VIII, The Medical Devices Rules, 2017.
[115] Minutes of the 83rd Meeting of Drugs Technical Advisory Board. June 11, 2019 at Directorate General of Health Services, Nirman Bhawan, New Delhi, India.
[116] Department of Pharmaceuticals, ORDER S.O. 39(E).
[117] Sohini Das (2009), "DPCO Amendment May Benefit MNC Device Makers by Allowing Price Control," Business Standard, January 05, 2019, Accessed January 23, 2019, https://www.business-standard.com/article/economy-policy/dpco-amendment-may-benefit-mnc-device-makers-by-allowing-price-control-119010500782_1.html.
[118] Anamika Pandey, George B. Ploubidis, Lynda Clarke, and Lalit Dandona, "Trends in Catastrophic Health Expenditure in India: 1993 to 2014," *Bulletin of the World Health Organization* 96, no. 1 (January 2018): 1-76, doi:http://dx.doi.org/10.2471/BLT.17.191759.

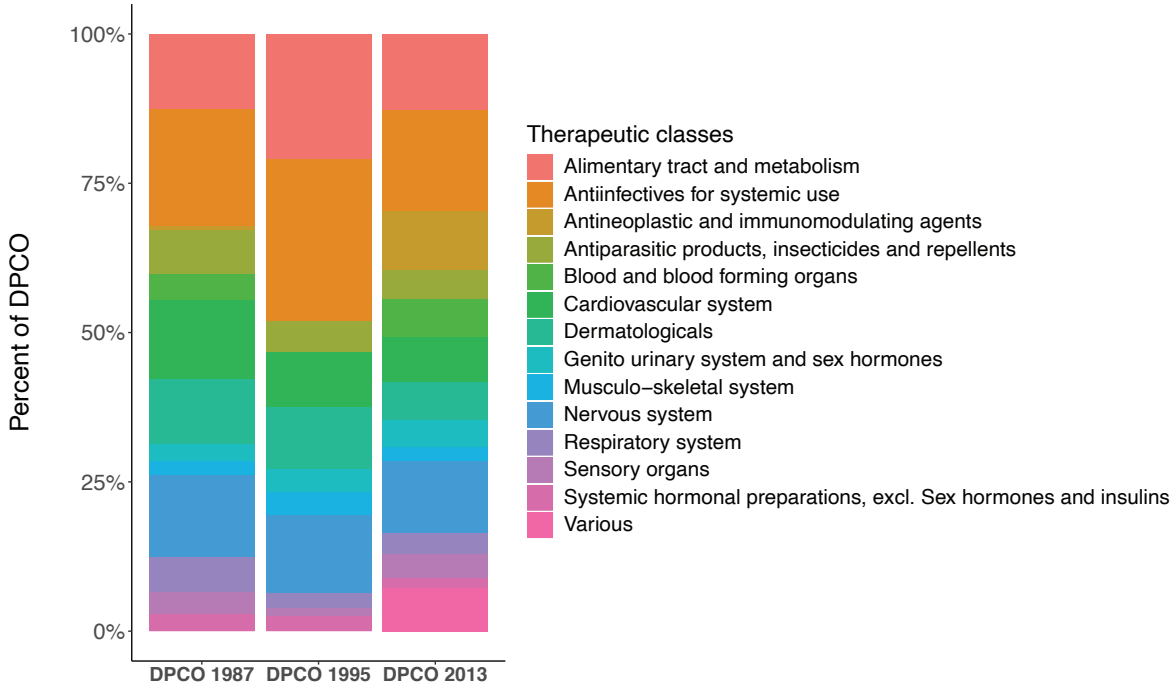
address the affordability of India's healthcare system as a whole.[119] The programme aims to cover hundreds of millions of beneficiaries, with 1,350 medical insurance packages that cover (among other things) surgery, medical treatments, and even the costs of medicines. This would reduce the out-of-pocket burden of medicines for eligible consumers. In the PMJAY beneficiary guidebook, the program covers expenses incurred for up to three days of medicines during pre-hospitalisation and up to 15 days for post-hospitalisation. Medicine, medical consumables, and medical implant services are also listed as covered, but no additional details are listed.[120] The government should ensure that high-quality drugs are part of these medical packages, and generic medicines are included (if available). This allows the government to save on costs without sacrificing quality.

3.3 Therapeutic classes of drugs under regulation

The bulk drugs listed in each of the DPCOs refer to their molecular names. Using these molecular names, we can map each bulk drug (molecule) with its therapeutic purpose[121] using the Anatomical Therapeutic Chemical classification (ATC) system.[122] The ATC classifies molecules into 14 different therapeutic classes. These 14 therapeutic classes encompass a variety of common diseases that are treated by drugs covered under the drug price control orders. For example, drugs that treat diseases such as diabetes and other illnesses related to the digestive system belong to the "Alimentary Tract and Metabolism" therapeutic class. "Antineoplastic and Immunomodulating Agents" refers to bulk drugs used to treat cancers and fight tumours. The ATC classification system also considers a bulk drug's therapeutic properties as opposed to solely looking at the organ or system upon which it acts. Thus, tuberculosis vaccines belong in "Anti-infectives for Systemic Use" as opposed to "Respiratory System," where active pharmaceutical ingredients that address chronic respiratory illnesses belong.

Figure 28 is a graphical representation of the composition of three DPCOs, split into proportion contributed by drugs belonging to different therapeutic classes.

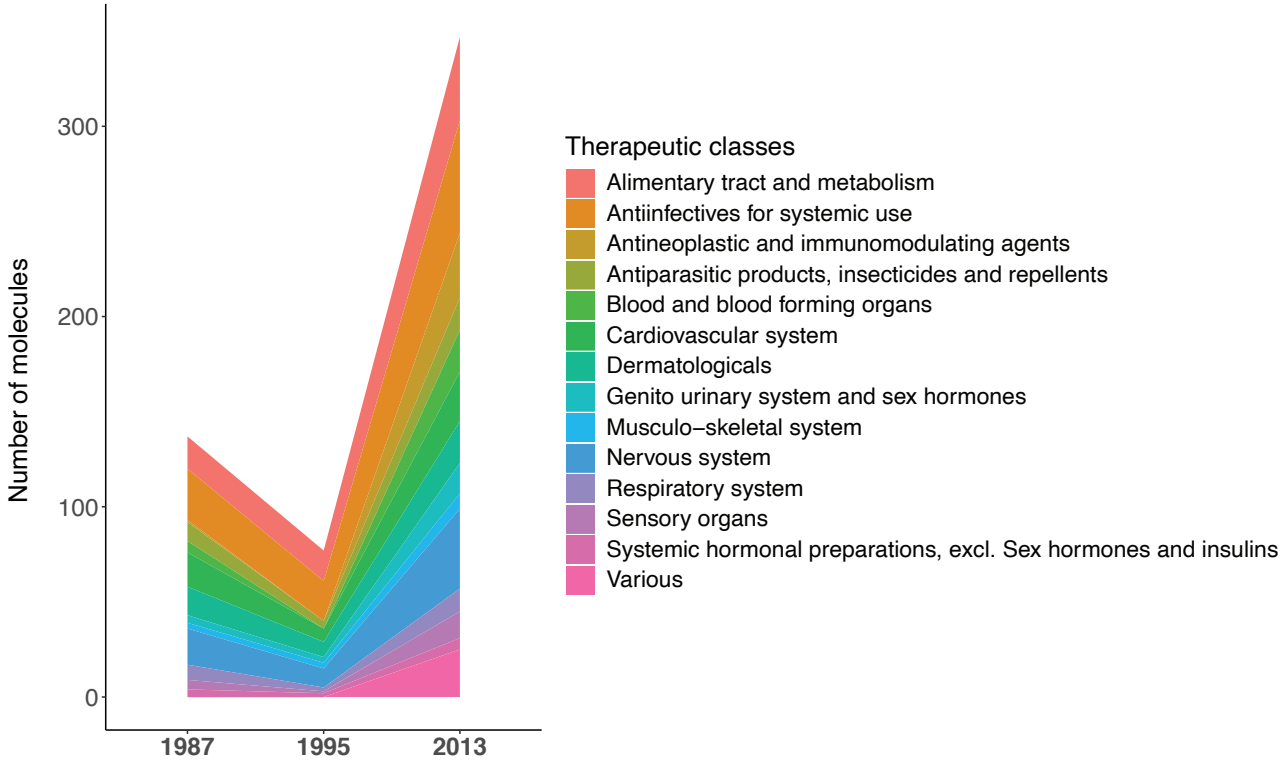
Figure 28: Percentage of therapeutic classes covered by each DPCO



[119] https://www.pmjay.gov.in/about-pmjay
[120] "Beneficiary Empowerment Guidebook" (2019), Ayushman Bharat Pradhan Mantri Jan Arogya Yojana.
[121] There are molecules that fall under multiple therapeutic classes. The DPCOs do classify the molecules based on their therapeutic purposes, so we choose the class that best corresponds with the DPCO's intent.
[122] https://www.genome.jp/kegg-bin/get_htext

These proportions show the compositional make of each DPCO. Drugs that fall under the "Anti-infectives for Systemic Use" therapeutic class make up the largest proportion of each DPCO. "Anti-infectives for System Use" peaked in the DPCO 1995, with the proportion of molecules under this category making up nearly a quarter of the entire drug price order. The proportion of molecules that fall under "Cardiovascular System" appears to decrease over time. While the proportion of certain therapeutic classes may decrease, the absolute number of molecules covered under each therapeutic class increased following the DPCO 2013. Figure 29 shows the raw number of molecules that are covered by each DPCO by therapeutic class.

Figure 29: Therapeutic classes covered by each DPCO by absolute number of molecules

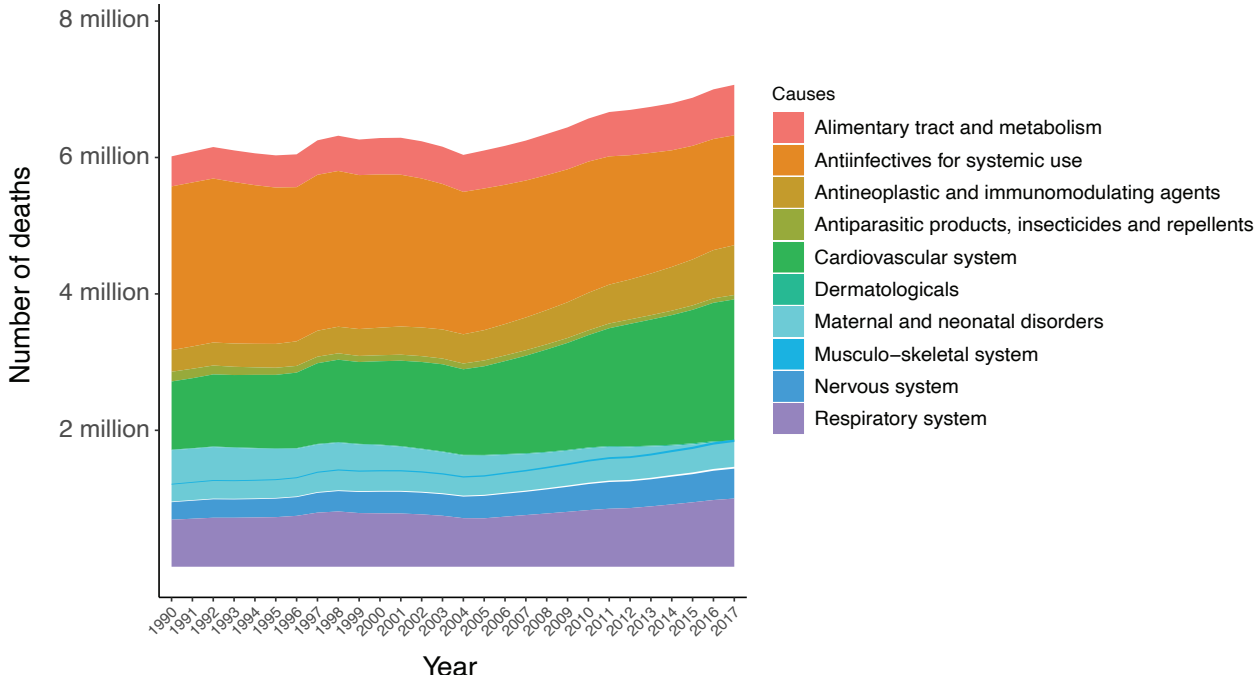


3.4 India's burden of diseases

We extend our analysis further by examining whether the changes in therapeutic class coverage follow India's burden of diseases. Because the DPCOs select drugs that are deemed essential to the population, understanding this relationship is paramount to examining an effective DPCO policy that controls prices on medicines that the population needs most. India's burden of diseases is calculated using the Global Disease Burden database, and we use level 2 causes of diseases by prevalence, incidence, and deaths number, dating back to 1990.[123] We find that many of the causes of diseases correspond with the therapeutic classes of the bulk drugs, where the therapeutic classes are the treatment for their disease-cause counterparts, such as anti-infectives for infectious diseases. Therefore, these causes have been mapped to the ATC categories to provide an easier comparison across disease burden and therapeutic class coverage under DPCOs. "Anti-infectives for Systemic Use," "Antineoplastic and Immunomodulating Agents," and "Antiparasitic Products, Insecticides, and Repellents" refer to their disease counterparts of infectious diseases, cancers, and parasitic-related diseases, respectively.

[123] http://ghdx.healthdata.org/gbd-results-tool

Figure 30: India's burden of disease, number of deaths

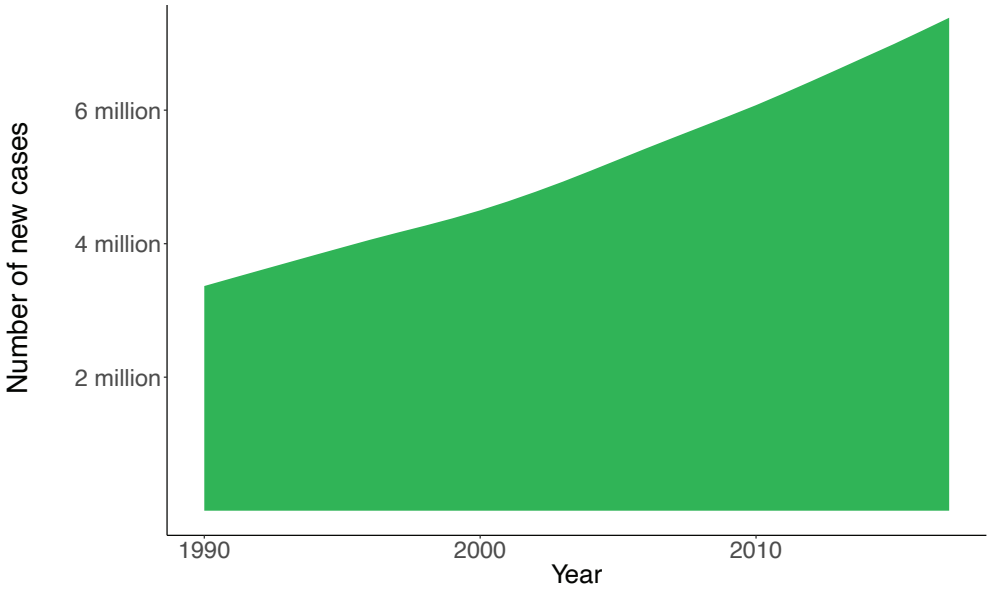


Source: Global Burden of Disease Database Institute for Health Metrics and Evaluation.

For the past two decades, India's disease burden has shifted towards non-communicable diseases, such as cardiovascular and respiratory illnesses, and towards lifestyle diseases such as diabetes. Figure 30 shows that the number of deaths attributed to diseases that are categorised under "Cardiovascular System" have risen, and now make up the biggest cause of death in 2017. Other diseases on the rise are those related to the alimentary tract and metabolism, such as diabetes, and those related to the respiratory system. Infectious diseases (therapeutic class counterpart is "Anti-infectives for Systemic Use") still cause a large number of deaths in India, but their share has decreased over the past two decades.

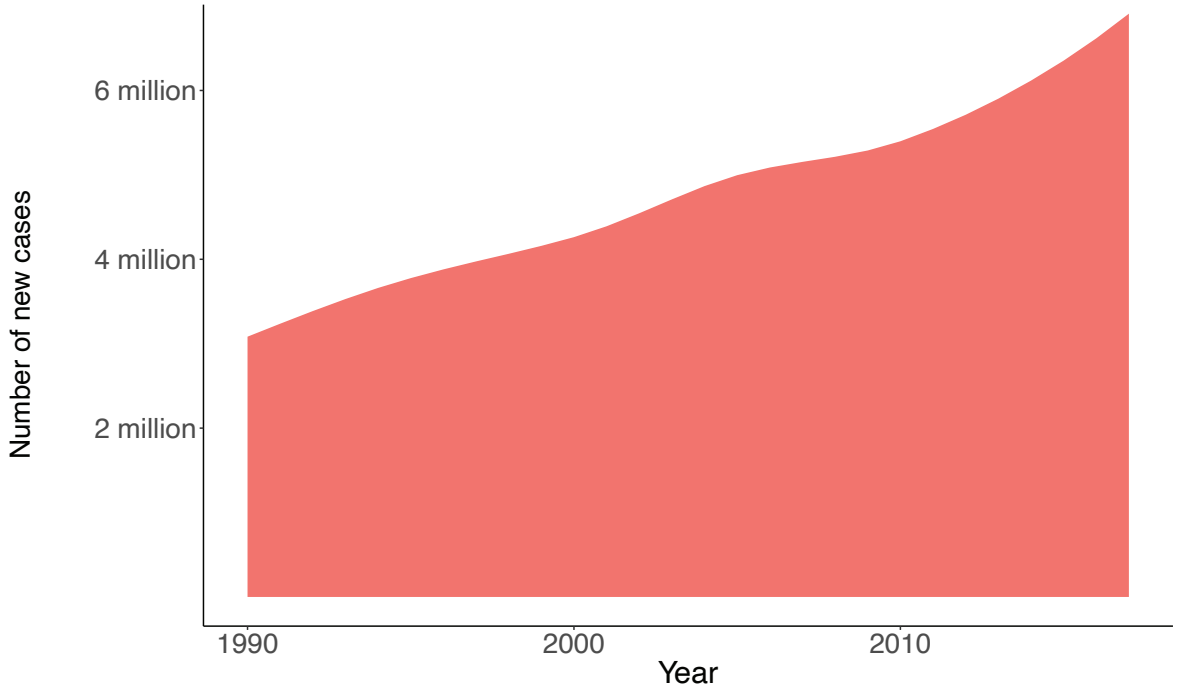
We also look at another outcome, that is the incidence of diseases or the number of new cases of that disease in a given year in Figure 31 to 33. We focus our attention on mostly non-communicable diseases (and also respiratory diseases) which contribute substantially to mortality.

Figure 31: Incidences of diseases related to cardiovascular system



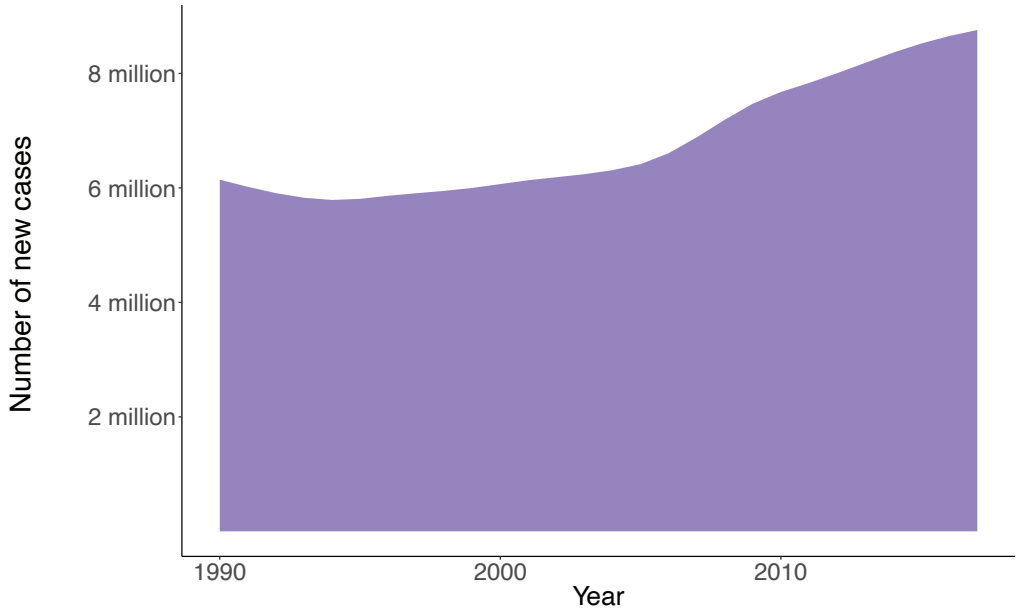
Source: Global Burden of Disease Database, Institute for Health Metrics and Evaluation.

Figure 32: Incidences of diseases related to diabetes and kidney diseases



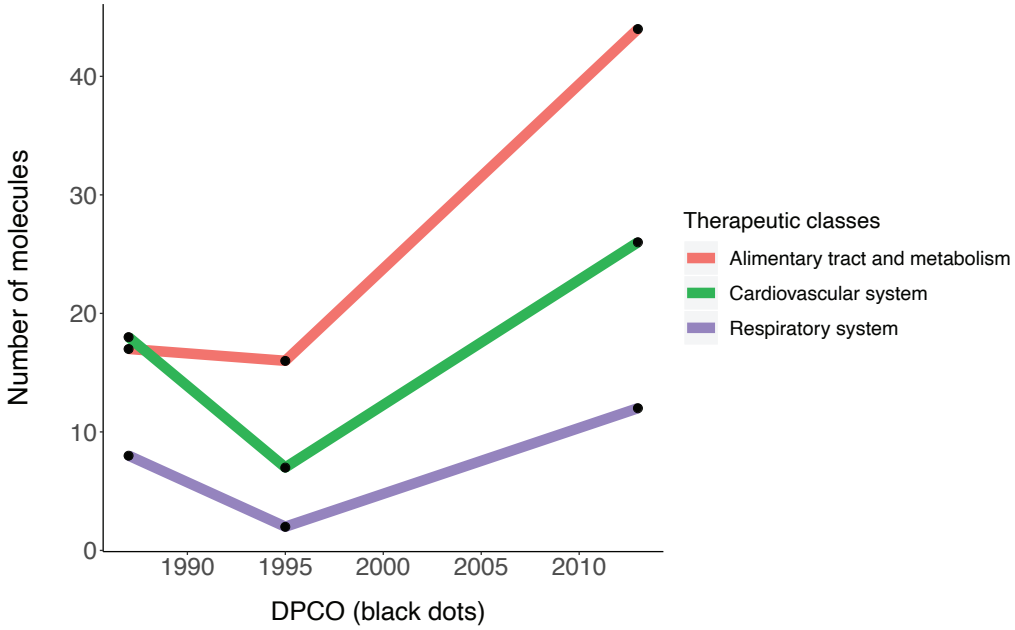
Source: Global Burden of Disease Database, Institute for Health Metrics and Evaluation.

Figure 33: Incidences of diseases related to respiratory system



Source: Global Burden of Disease Database, Institute for Health Metrics and Evaluation.

Figure 34: Count of selected bulk drugs under regulation



Source: Data from Drug Price Control Orders (1987, 1995, 2013).

As the number of new cases of these three diseases rises, the number of bulk drugs that belong to these diseases' therapeutic counterparts has also increased since 1987 (see Figure 34), in part due to a big spike in the number of bulk drugs covered by DPCO 2013. However, when looking at the entire composition of the DPCOs, the proportion of these therapeutic classes have remained the same, or even decreased in the case of "Alimentary Tract and Metabolism." This could suggest that the DPCOs are incorporating more drugs in general, but more of these drugs belong to other therapeutic classes that are not as much of a burden as those listed here. Ideally, the DPCOs should focus more on diseases that have a higher burden on society.

However, we acknowledge that there are several limitations to this descriptive analysis. First, the Global Disease Burden provides only estimates that may or may not be nationally representative of India's disease burdens. Second, there may only be a few drugs that lead to formulations that cure certain diseases. Even as the burden of cardiovascular diseases rises, the proportional representation of cardiovascular therapeutic class may not increase under drug price control order due to the limited total numbers of bulk drugs in that category. In an extreme hypothetical case, the proportion of bulk drugs under the "Cardiovascular System" therapeutic class can decrease in future DPCOs because the DPCO is already including all bulk drugs that exist in that therapeutic class. Our analysis can be enriched with data regarding retail sales of drugs in the market. We could then explore the proportion of a bulk drug of a certain therapeutic class (out of all available bulk drugs in the market) covered under the DPCOs.

In July 2018, the Ministry of Health & Family Welfare called together a Standing National Committee on Medicines (SNCM) to revise the National List of Essential Medicines of 2015. The members of the committee include experts from multiple medical fields, researchers, and regulators. The scope of the committee includes not only revising the NLEM, but also including medical devices, medical disposables, medical consumables, and other health- and hygiene-related products that they see fit.[124] The SNCM is also tasked with obtaining views from stakeholders, as well as considering anti-microbial resistance while recommending which drugs to include or delete from the list. The first stakeholder meeting took place in late July 2019, and the agenda focused on comments regarding oncology and cardiology drugs, penicillin preparations, and information about antimicrobial resistance. An updated NLEM has the potential to better address India's burden of diseases.

[124] "Constitution of Standing National Committee on Medicines (SNCM) for revision of National List of Essential medicines (NLEM)" (2018). Ministry of Health and Family Welfare.

3.5 Costs and benefits of price control

Price controls restrict a seller's ability to charge prices in the market. While the drug price controls have the potential to increase consumer welfare by establishing a price ceiling, they also come with tradeoffs. Too low of a price ceiling can disincentivise firms from joining, or continuing to operate, in the market.

In the pharmaceutical industry, drug manufacturers bear high costs of research and development with the hope of earning large profits after the drug is approved. Multiple research papers over the years have shown the costly and lengthy process of developing a new drug. DiMasi, Hansen, and Grabowski (2003) found that the average pre-approval cost estimates for new drugs were $802 million (in 2000 dollars).[125] Adams and Brantner (2006), reported that average to be higher at $868 million using the same base year, but costs ranged from as low as $500 million to over $2,000 million depending on the therapeutic class of the drug and the firm.[126] DiMasi, Grabowski, and Hansen followed with another study in 2016, which found the average pre-approval costs to be well over $1 billion (in base year 2000 dollars).[127] While these figures are from the U.S. pharmaceutical industry, their Indian counterparts could still be substantial. Capping how much these manufacturers can make from their medicines can stymie innovation. Achieving this balance between affordability and innovation is crucial for both a productive pharmaceutical market and a healthy public.

Thus, patents have been crucial in maintaining this incentive. They allow the inventor to retain exclusive manufacturing and distribution rights of a product for a set amount of time. Patents become even more crucial for the pharmaceutical industry due to the low costs of manufacturing a new bulk drug once it is discovered.[128] Without these exclusive production rights, other firms can cheaply imitate the new products such that the discoverer never regains the losses from researching the drug. But it is important to note that in India's case, abolishing its drug patent structure for over three decades actually enabled the growth of its domestic pharmaceutical industry into what it is today.

Historically, the Patents and Designs Act, 1911 allowed manufacturers of new drugs to effectively enjoy product patent rights for 16 years.[129] During this time in the Indian pharmaceutical industry, multinational corporations (MNCs) dominated the market, and mostly focused on developing new drugs, while local Indian companies were extremely innovative in establishing new manufacturing processes.[130] The MNCs were able to use the existing patent legal structure to their advantage, as they registered all the known and possible methods of manufacturing their drugs—effectively giving them product patent rights—due to the Patents and Designs Act, 1911's vague criteria.[131] However, Section 5 of The Patents Act, 1970 (later omitted in 2005) abolished drug patents, and only the claims for a single process of manufacturing a drug could be patented.[132] Given India's strength in innovative manufacturing techniques, the domestic pharmaceutical industry in India flourished in the late 1970s and onwards.[133] Drug patent protections came back into effect in January 2005 when India became a part of the World Trade Organization (WTO).

This historical context is essential to examine India's drug prices. In the early 1970s, when few drug producers operated within the country, the country's drug prices matched those in other countries, whereas India ranks among the lowest drug prices in the world today, in part due to a large number of producers.[134] A study found that after the DPCO 1995, drugs under price control maintained current price levels or even fell.[135] Those

[125] Joseph A. DiMasi, Ronald W. Hansen, and Henry G. Grabowski (2003). "The Price of Innovation: New Estimates of Drug Development Costs." *Journal of Health Economics* 22, no. 2: 151-85. doi:10.1016/s0167-6296(02)00126-1.
[126] Adams, Christopher P. (2006), and Van V. Brantner. "Estimating The Cost Of New Drug Development: Is It Really $802 Million?" *Health Affairs* 25, no. 2: 420-28. doi:10.1377/hlthaff.25.2.420.
[127] DiMasi, Joseph A., Henry G. Grabowski, and Ronald W. Hansen (2016). "Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs." *Journal of Health Economics* 47: 20-33. doi:10.1016/j.jhealeco.2016.01.012.
[128] Henry Grabowski, (2002), "Patents, Innovation, and Access to New Medicines," *Journal of International Economic Law*, Vol. 5, No. 4, December.
[129] Section 14, Patents and Designs Act, 1911.
[130] Chaudhuri, *The WTO*, 129.
[131] Ibid., 10.
[132] Section 5, The Patents Act, 1970.
[133] Chaudhuri, *The WTO*, 39.
[134] Report of the Task Force to Explore Options Other Than Price Control for Achieving the Objective of Making Available Life-Saving Drugs At Reasonable Prices," September 2005, 19.
[135] Sakthivel Selvaraj, (2007). "How Effective Is India's Drug Price Control Regime?", Boston, MA, USA: Harvard School of Public Health; 2007, Available at: https://www.hsph.harvard.edu/wp-content/uploads/sites/114/2012/10/RP256.pdf.

that were regulated under DPCO 1987 but deregulated in 1995 saw at times double-digit percent increases in their prices.[136] The evidence suggests that price controls do have their intended effects, but governments should proceed with caution.

Margaret Kyle's cross-country study looked at how price controls impacted the time drugs reached the market. One interpretation of the study's results is that firms operating under a price ceiling only innovate drugs that are slightly different from existing ones.[137] Firms also prefer markets without price controls, so these drugs reach price-controlled markets last.

Price ceilings reduce the potential profits that firms generate by placing a limit on the prices of drugs these firms can charge. This decrease in profits can hurt innovation incentives for firms. A study that modeled the hypothetical implementation of price controls on the U.S. pharmaceutical industry found that a cut in prices by 40%-50% led to a 30%-60% decrease in research and development projects.[138] Such projections can be extended to any other pharmaceutical industry, including India's. Globally, innovative firms invest approximately 15% of their sales turnover in research and development, but India's pharmaceutical firms hovered under 2% up until 2000.[139] Price controls have been implemented throughout this period with the absence of drug product patents. This percent grew and peaked at 5% in 2005, when India reinstated drug product patent regimes, and has stabilised under 5% ever since.

These firms can still be innovative while spending less on research and development. Generics dominate India's pharmaceutical industry, and process patents are the focus of many drug manufacturers.[140] Process patents, which protect a method of manufacturing a drug, are much cheaper to develop and obtain as opposed to developing a new drug. The patents filed and published in India up until 2015 suggest that the Indian pharmaceutical industry has largely focused on creating new processes of manufacturing and new formulations as opposed to new molecules.[141] Thus, the Indian pharmaceutical industry falls short in inventions that generate the most lucrative and transformative medicines. These medicines require incentives for firms to embark on costly research, and price ceilings are a disincentive.

The last time any drug price control order regulated these many bulk drugs was in 1979. In the period between 1980 to 1985, manufacturers shifted production away from drugs under price control, which created shortages of essential medications.[142] In response, the DPCO 1987 covered only 141 bulk drugs. Debates still continue on whether these price controls have hindered India's levels of innovation, especially of new drugs, and the opportunity cost of foreign investment being diverted away from the country.

But markets break down, and given the essentiality of many of the drugs, price controls are warranted for the pharmaceutical industry. Within this industry, the demand for many drugs is close to being inelastic. This means that the number of drugs consumed will remain the same (or change a little) regardless of the changes in prices. This inelasticity, especially for essential drugs that patients depend on for survival, means that price hikes would cause huge financial burdens—on top of the health burden—for households. Price controls are more important than ever for these essential medicines.

Rather, the debate should turn towards what the future of price controls should look like. The question of which drugs should be covered and which should be left out is one that needs serious thought, and the government should prioritise how to achieve this balance.

[136] Ibid.
[137] Kyle, Margaret K. "Pharmaceutical Price Controls and Entry Strategies." *Review of Economics and Statistics* 89, no. 1 (February 7, 2007): 88-99. doi:10.1162/rest.89.1.88.
[138] Thomas Abbott, and John Vernon (2005), "The Cost of US Pharmaceutical Price Reductions: A Financial Simulation Model of R&D Decisions," *National Bureau of Economic Research* Working Paper No. 11114, February 2005, doi:10.3386/w11114.
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[141] Ibid.
[142] "Regulatory Capture and Access to Health Care," *Oxfam-India*. https://www.oxfamindia.org/sites/default/files/INDIA%20CASE%20STUDY.pdf

3.6 Recommendations

There should be more strategic price controls on drugs which are used to treat new prevalent diseases. Price control is a double-edged sword which should be carefully used, keeping in mind the two objectives - the growth of industry (innovation and investment) and interest of consumers.

Doctor prescriptions should focus more on generic medications than branded ones: Branded medications are more expensive, regardless of whether the bulk drug is patented. An increase in generic prescriptions not only creates more demand and competition among the generic producers, but saves consumers needless extra spending. Quality standards for generic medicines should be maintained for the eventual benefit of consumers.

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