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Impact of National Drug Pricing Policy 2018 on Access to Medicines in Lahore Division, Pakistan: A Pre-Post Survey Study Using WHO/HAI Methodology

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Impact of National Drug Pricing Policy 2018 on Access to Medicines in Lahore Division, Pakistan: A Pre-Post Survey Study Using WHO/HAI Methodology

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Abstract

Objective: To evaluate the impact of new national drug pricing policy (NDPP) 2018 on access to medicines in terms of prices, availability and affordability.

Design: Two cross-sectional surveys were undertaken before and after the launch of NDPP 2018, using a modified WHO/HAI methodology.

Setting: Four districts of Lahore division, Pakistan.

Participants: 16 public sector hospitals and 16 private sector retail pharmacies.

Measures: The pre and post survey data on price and availability of Lowest Price Generics (LPGs) and Originator Brands (OBs) of 50 medicines were obtained by visiting the same public and private sector health facilities (n=32). 46 out of 50 surveyed medicines were from National Essential Medicines List. Inflation-adjusted median unit prices (MUPs) and median price ratios (MPRs) from 2019 were used for price comparison. Affordability was calculated in terms of number of days' wages required to get a standard treatment by the lowest paid unskilled government worker.

Results: The overall mean percent availabilities remained poor in both years i.e. far less than 80%. In public sector, the mean percent availability of OBs improved from 6.8% to 33.1% whereas, in case of LPGs it was reduced from 35.1% to 9%. In private sector, the mean percent availability of both OBs and LPGs demonstrated slight improvements in 2019 i.e. 55.0% to 58.3% and 20.3% to 32.3%. The adjusted MUPs and MPRs of OBs significantly increased by a median of 4.29% (Wilcoxon test $p=0.001$, $p=0.0001$). Whereas, the adjusted MUPs and MPRs of LPGs were increased by a median of 15.7% ($p=0.002$, $p=0.0002$). Overall the affordability of many medicines for common ailments reduced significantly in 2019.

Conclusions: The availability of medicines has been slightly improved, except in the case of LPGs which was reduced at public sector. Although the main aim of the NDPP 2018 was to make the drugs affordable, but its implementation has led to increased drug prices which has made standard treatment for some of the most prevalent ailments, unaffordable. This policy needs to be improved further to have strict price control especially for the essential medicines, to improve their access.

Strengths

- This is the first study of its kind from Pakistan, where pre-post surveys were conducted and analyzed to estimate the impact of a national drug pricing policy, using the WHO/HAI methodology.
- The data was collected from the same health facilities in both years. So, the comparison is reliable. This study provides an objective evidence to the policy makers for improving the current pricing policies.

Limitations

- The study is limited to only one division of Pakistan, although the medicine prices are fixed centrally and are supposed to be same across the country – affecting generalizability of the findings.
- Moreover, this study is conducted after about a year from the launch of new drug pricing policy 2018, so the results do not reflect the long term impact of the policy.

Introduction

Access to quality assured and affordable essential medicines is considered as a key component of an effective healthcare system. It has also been pledged under Sustainable Development Goal (SDG) 3 by United Nations (UN) that the equitable access to affordable essential medicines will be ensured as a basic human right [1, 2]. Pakistani government, like many other Low and Middle Income Countries (LMICs), has been grappling with the issue of high medicine prices and poor availability of medicines that compromises the accessibility of medicines [1, 3-6]. The medicines are provided free of cost at public sector health facilities, while patient pays out of pocket to get medicines from private sector, in Pakistan [5]. In fact, the poor availability of medicines at public sector compels the patients to buy medicines from private sector that escalates the burden on patient's pocket, while 24.3% (in 2015) of the population is living below the national poverty line [3, 4, 7, 8]. Besides, medicine prices have increased up to 100%, both legally or illegally, in the past few years [3]. The ministry of National Health Services Regulation and Coordination (NHSRC) of Pakistan has been taking different policy measures to curb these issues through Drug Regulatory Authority of Pakistan (DRAP). The first ever National Drug Pricing Policy (NDPP) was launched in 2015 for making the pricing mechanism transparent but it had minimal impact on medicine prices, suitable for both patients and manufacturers as per media reports and available literature evidences [3, 9]. So, a new drug pricing policy was launched in 2018[10]. The objectives of this policy were to improve the access to essential medicines, to devise rational prices, to ensure a transparent mechanism for pricing of medicines and to discourage illegal price increases.

Many modifications have been made to the pricing strategies in the NDPP 2018 compared to NDPP 2015, the most important one is the inclusion of all drugs (n=414) from National Essential Medicines List (NEML) under scheduled drugs category where drugs are kept under strict price control as compared to other drugs. Whereas in NDPP 2015, only 160 drugs from NEML were enlisted in this category [9, 10]. In NDPP 2018, the annual adjustment in prices has been linked with the Consumer Price Index (CPI), the Maximum Retail Prices (MRPs) of scheduled drugs (all drugs from NEML) could be increased up to 70% of the CPI, whereas the MRPs of all other drugs could be increased equivalent to CPI of the immediate preceding year. This step seems to improve the affordability of essential medicines (EMs) for patients in Pakistan. If several generics are already available in the market then in NDPP 2015, the MRP of new entrant was fixed by taking the average of other generics, while in NDPP 2018, MRP will be fixed equivalent to the highest MRP of the available generics [9, 10]. However, this would lead to even higher priced generics in the market that could compromise patient's affordability. Some media reports are claiming that the current increase (up to 200%) in medicines prices is the highest in the last 40 years, while others are claiming that government is taking action against this illegal rise in medicine prices [11, 12]. But there is no objective evidence to prove or disapprove these claims. The NDPP 2018, allows the MRPs of the New Chemical Entities (NCEs) to be fixed while using External Reference Pricing (ERP) mechanism by considering India, Bangladesh, Indonesia, Sri Lanka, Philippines, Lebanon and Malaysia as reference countries. However, the reason behind using the MRPs of these countries as reference is not clear, though some of them practice free market economy model and don't impose any price control measures over the MRPs in community pharmacies that may lead to high prices. The NDPP 2018 also takes into account the wholesale or procurement prices

from British National Formulary, Australian Pharmaceutical Benefit Scheme and New Zealand Pharmaceutical Management Agency while fixing the MRPs of NCEs, whereas these may not be the true prices because as a common practice discounts and rebates are given while making the payments. So, these ambiguities in the policy necessitate the evaluation of actual impact of these policies on the access to medicines in Pakistan.

In this context, we designed a study to measure the impact of new NDPP 2018 on access to essential medicines in terms of their prices, availability and affordability in Lahore division Punjab. We undertook a survey after the implementation of NDPP 2018 and compared it with a similar survey performed before the launch of this policy in 2017. Considering the objectives of the NDPP 2018, we hypothesized that it will improve the availability and affordability while decrease the prices of EMs.

Methodology

Study Design

Two cross-sectional studies were conducted in 2016-17 and 2019 using a variant of World Health Organization/Health Action International (WHO/HAI) methodology in four districts of Lahore division, Pakistan [13]. Since, the focus of this study was to measure the impact of NDPP 2018 in terms of changes in medicines prices, availability and affordability after its implementation, thus, the data on these parameters was collected to evaluate the accessibility of medicines in both years [10]. The first survey was conducted from November 2016 to March 2017, while the second survey was from March-May 2019, representing two fiscal years of Pakistan. For optimal and reliable comparison, the list of medicines, survey region and survey outlets selected for the survey 2019 were similar to those selected for 2017. The details of survey region, medicine selection, sampling of medicine outlets and data collection are given elsewhere and are briefly described in this paper [7].

Survey Areas

Lahore is the largest division of Pakistan in terms of population i.e. 16.28 Million (2017) and estimated to be 19.4 Million as of 2018[14]. It consists of four districts named as Lahore, Kasur, Sheikhpura and Nankana Sahib which are further subdivided into 17 Tehsils. All the four districts were selected for the surveys.

Sampling of Medicine Outlets

Medicine outlets or health facilities from both public and private sectors were sampled systematically using WHO/HAI manual as a guiding principle in both the surveys [13]. Total 32 medicine outlets were surveyed (16 from public sector and 16 from private sector). From public sector, hospitals from all three tiers of healthcare system i.e. primary, secondary and tertiary were selected. One main hospital in each district was selected as a survey anchor along with additional three more hospitals selected randomly and situated within three hours' drive from the main hospital. In this way, 4 hospitals were selected in each district making up a total of 16 hospitals from Lahore division. From private sector, one registered pharmacy was selected situated within 10 kilometers range of each public sector hospital. So, a total of 16 pharmacies were selected from

Lahore division, i.e. 4 retail pharmacies from each district. It is important to note that each survey unit, one hospital and one nearby pharmacy, was located in different Tehsils, so out of 17 Tehsils of Lahore division, 16 were surveyed in both years.

Selection of Medicines

50 medicines were selected for survey as per WHO/HAI methodology, which included all 14 medicines from WHO core global list of medicines and 36 supplementary medicines. The criterion of selecting medicines for supplementary list was local disease burden and inclusion of medicines in NEML [15].

Data Collection

The data were collected using a data collection form by the trained data collectors. The data collectors visited the health facilities and physically checked the medicines prices and availability for both OBs and LPGs of each medicine and entered in to data collection forms. The data for each year were entered separately in to the WHO/HAI workbook by using double data entry process, to avoid any mistake [13]. The patient prices or the prices charged to patients were entered in to the forms for private sector only because in public sector, the medicines are provided free of charge in Pakistan. Thus, the availability of medicines was documented only for public sector facility.

Data Analysis

Data were analyzed by using WHO/HAI preprogrammed Excel workbook[13], IBM Statistical Package for the Social Sciences (SPSS) version 22.0 and R version 3.5.1 (codenamed “Feather Spray”).

The availability was calculated as percentage of particular medicine available at each facility on the day of data collection. The mean percentage availabilities were also calculated and compared between different sectors (public and private), product types (OBs and LPGs) and among different groups (global medicines, supplementary medicines, medicines from NEML, medicines used to treat NCDs and IDs). Availability was documented as follows; Absent: 0% of facilities had surveyed enlisted medicines at the time of survey; Low: < 50% of facilities had the surveyed enlisted medicines; Fairly high: 50 -80% of facilities had surveyed enlisted medicines; High: > 80% of facilities, survey enlisted medicines were found in most of the facilities [16, 17].

Medicine prices were calculated as Median Unit Prices (MUPs) in Pakistani Rupees (PKR) and were also compared with International Reference Prices (IRPs) to calculate the Median Price Ratios (MPRs). The IRPs were obtained from Management Sciences for Health (MSH) drug price indicator guide 2015[18]. An MPR of greater than 1 for public sector and greater than 2 for private sector would lodge any medicine into high priced medicines category [7]. For comparing the prices between two years, the MUPs from 2019 were deflated by 3.33%, taking 2017 as base year. 70% of the CPI was used for calculating this deflation factor, because the medicine prices can be increased annually by 70% of the CPI as per NDPP 2018 [19]. Whereas MPR was calculated as follows:

Median Price Ratio(MPR) = Median local unit price/International reference unit price

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Affordability for treatment of different common diseases with selected medicines was calculated and compared in terms of Number of Days Wages (NDWs) required for a lowest paid government employee to get the standard treatment courses. Whereas, if a patient had to spend more than one day of his wage for treatment with a specific medicine in a month, that medicine was considered unaffordable [13]. For affordability comparison, NDWs in two years, the prices in 2019 were not deflated because the salary has also been increased in 2019. So, the salary of the lowest paid unskilled government worker was taken as 14000PKR per month (2016-17) and 15000PKR per month (2018-19) [20].

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Comparative analysis: Two patient prices were required to be included in the comparative analysis, one from 2017 and other from 2019. The difference in prices, availability and affordability were computed as percentage changes for each product. The mean availability and MUPs were also compared between different categories of medicines (NEML and non-NEML medicines; global and supplementary medicines; medicines for IDs and NCDs) across the years. We compared affordability in terms NDWs to get the standard treatment from the surveyed medicines. These were also compared among medicines for different disease groups (asthma, cardiovascular diseases, infectious diseases, brain disorders, diabetes, ulcer and arthritis; IDs and NCDs). To identify whether the difference between MUPs, MPRs and NDWs was significant across two years, we used Wilcoxon signed rank test. We took $p < 0.01$ as an indicator of significant difference in all the statistical testing.

28 29 **Patient and Public Involvement**

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Patients or the public were not involved in the design, or conduct, or reporting, or dissemination of this study.

33 34 **Results**

35 36 **Availability of medicines**

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The overall availability of surveyed medicines was improved in 2019 when compared with 2017, except for LPGs in public sector, where it demonstrated reduction.

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Availability in Public Sector: In public sector, the availability of both OBs and LPGs was poor in both years. None of the mean availabilities touched the benchmark of 80%. The mean percent availability of OBs improved from 6.8% to 33.1% whereas, in case of LPGs it reduced from 35.1% to 9%. The individual percent availabilities of each medicine (OB and LPG) are given in table S1. For better understanding of the data, we have used the data visualization tool in R and plotted a box plot of the data as shown in figure 1. The box plot showed distributional characteristics of the percent availability of medicines in two groups (OB and LPG) for the years 2017 and 2019. The mean percent availability is represented by the dot inside the box. In 2017, availabilities of 75% of the OBs in public sector were less than 11.2% as shown by the 3rd quartile or the upper bar of the 1st box plot. Whereas, in 2019, 75% of the OBs had availabilities higher than 6.3% which is almost equivalent to the mean percent availability (6.8%) in 2017. This indicates a substantial increase in the availability of OBs in public sector. In 2019, 75% of the LPGs had availability less than 12.5% (3rd quartile) whereas before the implementation of the

NDPP 2018, 75% of the LPGs had availabilities greater than 14.3% (1st quartile). This showed a remarkable decrease in the availability of LPGs in public sector in 2019.

Availability in private sector: In both years, the overall availability was better in private sector than the public sector. Mean percent availability of both OBs and LPGs were improved in 2019 i.e. 55.0% to 58.3% and 20.3% to 32.3%, respectively. Availability of LPGs was less than OBs in both years. For OBs, the mean percent availability improved slightly by 3.3% while data distribution remained almost the same across the years, as shown in the box plot (figure 1). For LPGs, a substantial increase in the availability was observed in terms of mean percent availability, maximum value and change in data distribution (figure 1). In 2017, the IQR (range between upper and lower bar of the box) for percentage availability of LPGs ranged from 6% to 31% whereas it got improved in 2019 and ranged from 6% to 50%.

Availability in different subgroups of medicines: When we compared availability of LPGs and OBs in different subgroups of medicines as shown in table 1, we found that mean percent availabilities of all global list medicines were higher than supplementary medicines in both years. Similarly, the availability of NEML medicines were higher than non-NEML medicines except for the non-NEML LPGs in public sector, which were higher than NEML LPGs (19.2% vs 8.1%). In 2017, in public sector, the availability of OBs for NCD medicines (6.7%) were lower than OBs for ID medicines (7.7%) whereas the availability of LPGs (35.9%) were better than LPGs of ID medicines (33%). Surprisingly, in 2019, the situation inversed completely for NCD medicines, increased and decreased availability of OBs (33.2%) and LPGs (33.1%), respectively, whereas, the availability decreased for LPGs (8.8%) and increased for OBs (9.5%) for ID medicines.

Table 1. Mean Percent Availabilities of Originator Brands (OBs) and Lowest Price Generics (LPGs) at both public and private sectors.

	Availability in 2017 (Mean, SD), %				Availability in 2019 (Mean, SD), %				Change in mean percent availability (%)			
	Public Sector		Private Sector		Public Sector		Private Sector		Public Sector		Private Sector	
	OBs	LPGs	OBs	LPGs	OBs	LPGs	OBs	LPGs	OBs	LPGs	OBs	LPGs
All medicines (n=50)	6.8 (10.4)	35.1 (23.6)	55 (31.1)	20.3 (14.4)	33.1 (27.8)	9 (14.9)	58.3 (32.3)	32.3 (26)	26.3	-26.1	3.3	12
Global Medicines (n=14)	11.2 (15.2)	50.1 (32.1)	64.3 (22.5)	25.9 (14.5)	48.4 (31.5)	14.3 (19.9)	66.5 (31.2)	43.8 (27.8)	37.2	-35.8	2.2	17.9
Supplementar y medicines (n=36)	5 (7.0)	29.2 (21.4)	51.4 (33)	18.1 (14)	27.2 (24.1)	7 (12.1)	55 (32.6)	27.8 (24.1)	22.2	-22.3	3.6	9.7
NEML medicines (n=46)	7.2 (10.7)	35.5 (26)	55.3 (31)	20.7 (14.6)	33.9 (28.1)	8.1 (15.1)	58.4 (32.9)	33.3 (26.3)	26.7	-27	3.1	12.6
Non-NEML medicines (n=4)	1.8 (3.0)	35.5 (34)	51.6 (36)	15.6 (11)	24.8 (25)	19.2 (7)	56.3 (28)	20.3 (21)	23	-16	4.7	4.7

NCD medicines (n=36)	6.4 (9.2)	35.9 (25.5)	55.7 (28.8)	20 (14.3)	33.2 (27)	8.8 (14)	62.3 (29.3)	31.3 (25)	26.8	-27.1	6.6	11.1
ID medicines (n=14)	7.7 (13.3)	33 (29)	53.1 (37.3)	21 (15)	33.1 (30.5)	9.5 (17.4)	47.8 (38.1)	34.8 (29.2)	25.4	-23.5	-5.3	13.8

Availability at different levels of healthcare: When we compared the availability at different levels of public healthcare sectors i.e. primary, secondary and tertiary, the availability of OBs improved in 2019, while it was decreased for LPGs. The pattern of overall medicines availability remained almost the same as of 2017 i.e. tertiary care>secondary care>primary care as shown in table S2.

Medicine Prices

An overall increase was noted in all adjusted MUPs and adjusted MPRs between 2017 and 2019 for both OBs and LPGs as shown in Table 2. In 2019, for all 42 available OBs, the adjusted MUPs and MPRs significantly increased by a median of 4.3% (Wilcoxon test $p=0.001$, $p=0.0001$). Whereas in case of all 37 available LPGs, the adjusted MUPs and MPRs were increased by a median of 15.7% ($p=0.002$, $p=0.0002$). The MPRs of OBs ranged from 0.58 to 60.62 in 2017 and 0.73 to 77.59 in 2019. 63% of the OBs had MPR of more than 2 in 2017. Whereas, in 2019 almost 75% of the OBs had MPR greater than 2. The MPRs of LPGs ranged from 0.42 to 19.95 in 2017 and 0.39 to 19.89 in 2019. For LPGs in 2017, the median value of MPR was less than 2 (i.e. 1.36) while in 2019 this median value became greater than 2 (i.e. 2.26). Which means many LPGs which were previously affordable got shifted to the high priced medicines category in 2019. The MUPs and MPRs for all OBs is given in table S3 and for all LPGs is given in table S4.

Table 2. Median price ratios (MPRs) and median unit prices (MUPs) of originator brands (OBs) and lowest price generics (LPGs) in private sector among different subgroups across the years 2017 and 2019.

	Originator Brands (OBs)				
	MPR-2017	MPR-2019	MUP 2017 (PKR)	Adjusted MUP 2019 (PKR)	Median percent change in MUPs/MPR
All medicines (n=42)	2.5	3.2	6.99	8.49	4.29%
Global Medicines (n=13)	2.8	3.2	7.66	8.22	3.35%
Supplementary medicines (n=29)	2.5	3.3	6.38	10.1	5.1%
NEML medicines (n=39)	2.4	3.3	6.38	8.51	5.1%
Non-NEML medicines (n=3)	3	3.2	7.66	8.22	1.93%
NCD medicines (n=36)	2.6	3.3	6.19	7.83	3.35%
CD medicines	2.3	2.9	24.3	31.2	7.36%

(n=10)					
Lowest Price Generics (LPGs)					
	MPR- 2017	MPR- 2019	MUP 2017 (PKR)	Adjusted MUP 2019 (PKR)	Median percent change in MPR/MUP
All medicines (n=37)	1.4	2.3	5.8	6.29	15.7%
Global Medicines (n=13)	1.6	2.7	5.8	6.56	19.2%
Supplementary medicines (n=24)	1.3	2.2	5.9	6.04	14.8%
NEML medicines (n=34)	1.4	2.2	5.4	6	15.8%
Non-NEML medicines (n=3)	2.5	2.7	6.5	6.7	3.97%
NCD medicines (n=26)	1.2	2.2	4.1	5.4	16.3%
CD medicines (n=11)	1.8	2.4	8.4	10.9	14.8%

The price data was also analyzed in different subgroups as shown in table 2. There was an increase in MUPs and MPRs for OBs of supplementary list of medicines compared to medicines from global list (5.5% vs 3.35%). However, it was inverse in case of LPGs, i.e. the prices of global medicines increased compared to supplementary medicines (19.2% vs 14.8%). Increment in prices of NEML medicines was more as compared to non-NEML medicines. Next, we compared medicines used for NCDs and IDs. Data suggested that the increase in the MUPs and MPRs of OBs for IDs was significant in comparison to NCDs (11.2% vs 7.36%). Whereas it was the opposite case for LPGs, where the increase was greater for NCD than ID medicines (16.3% vs 14.8%). It is also noteworthy that increase in prices for LPGs is more significant than OBs for all subgroups of medicines.

Affordability

Between 2017 and 2019, the median NDWs required for treatment with all OBs (n=36) increased from 1.05 to 2 and 0.5 to 0.7 for all LPGs (n=31), respectively. In 2019, the median percent increase in NDWs for LPGs (n=31) was much higher as compared to OBs (n=36) i.e. 12.5% (p=0.008) and 3% (p=0.081) respectively. So, an overall increase in NDWs for both OBs and LPGs was observed between 2017 and 2019. Similarly the Median Treatment Prices (MTPs) for OB and LPGs also increased significantly i.e. 464 PKR to 563 PKR (p<0.001) and 244 PKR to 350 PKR (p<0.001), respectively. The MTPs and NDWs for each medicine are given in tables S5 and S6. The medicines were categorized into seven disease groups to further analyze the changes in affordability between 2017 and 2019. In figure 2, a bar graph shows Median NDWs required for both OBs and LPGs in each disease group and the values above 1 are considered unaffordable. In 2017, the median NDWs of OBs to treat three types of diseases i.e. CVDs (1.2), diabetes (1.4) and ulcers (2.75) were more than 1. Whereas in 2019, medicines for one more

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3 disease category made its place into this list i.e. the medicines for IDs (1.18). Compared to 2017,
4 the median NDWs for all OBs increased in 2019 except for OBs acting on Central Nervous System
5 (CNS) and OBs to treat ulcers. The treatment for ulcer remained highly unaffordable in both years.
6 The median NDWs for LPGs increased in 2019 for the treatment of Arthritis, CNS disorders,
7 CVDs and IDs, while the modest decrease in median NDWs for LPGs was observed for some
8 diseases i.e. asthma, diabetes and ulcers as shown in figure 2.
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11 12 13 **Discussion**

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15 This study gives a conscionable insight in to the effects of NDPP 2018 associated changes on
16 medicine prices, availability and affordability in both public and private healthcare sectors of
17 Lahore division, Pakistan. The main objective of this refined policy was to improve the access to
18 essential medicines (EMs) and improvise rational drug pricing. Our study has shown that the
19 overall availability of medicines improved in 2019 in comparison to 2017 i.e. before the
20 implementation of this policy, except for the LPGs in public sector, demonstrating reduction.
21 Overall the medicine prices were increased significantly, making majority of the EMs used for the
22 common ailments unaffordable, with much higher price increases for LPGs in comparison to OBs.
23 The medicines used to treat ulcer, diabetes and CVDs remained most unaffordable in both years.
24 Thus, it can fairly be assumed that the current pricing policy, to some extent, ensures the
25 availability of medicines, nonetheless, significant policy refinements targeting essential medicines
26 are pivotal to make medicine prices affordable to patients. Although, this study provides an
27 objective evidence to the policy makers for improving the current pricing policies. Our study has
28 some limitations as well. The study includes medicines with specific strengths and dosage forms
29 to compare with IRPs. There might be other strengths/dosage forms of the surveyed medicines,
30 available in the health facilities, so the availability of the medicines may be under estimated.
31 Moreover, the affordability was calculated for single medicine for each disease, whereas patients
32 are usually taking more than one drug at a time – under-estimating the extent of affordability of a
33 specific treatment for a specific disease.
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40 Despite improvements in the availability of medicines between 2017 and 2019, the
41 availability of medicine remained below the optimal benchmark of 80% [13]. In public sector the
42 availability of OBs improved remarkably probably be due to decentralization procurement of
43 medicines in public sector. Before 2018, the medicines were procured centrally for all the public
44 sector hospitals except for teaching hospitals, within a province. But after 2018, the medicines
45 procurement was decentralized for public sector hospital to allow hospitals in each district a free
46 choice to select desired manufactures, thus, ending up in the selection of more OBs than LPGs,
47 possibly due to quality concerns about medicines. Another factor that improved medicines
48 availability after 2018 was authorization of hospitals to acquire medicines directly without any
49 delays. However, as practiced in the previous central supply system, the medicines were received
50 centrally from the manufacturers before reaching the concerned hospital with considerable effect
51 on timely availability of medicines. In both years, the mean percentage availabilities for all
52 medicines were found higher in the private sector compared to the public sector, corroborating
53 similar previous studies conducted in Bangladesh and Malawi in 2019 [21, 22]. The overall
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3 availability of medicines from NEML was slightly better than non-NEML medicines in both public
4 and private sectors. This might be attributed to the active role of DRAP in the revision and
5 subsequent dissemination of the revised NEML i.e. NEML 2018 [15]. Furthermore, the public
6 hospitals are encouraged to procure drugs from the latest NEML 2018 that has been standardized
7 in line with WHO essential medicines model list 2017 [23]. Besides, a mobile application was
8 launched in 2018 with user friendly interface to better disseminate the information on enlisted
9 medicines [24]. So, the NDPP 2018, doesn't seem to be solely responsible for the availability of
10 medicines.
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14 Although we found some improvements in the availability of medicines, there was a
15 substantial increase in medicine prices, making them inaccessible for most of the population.
16 According to one estimate approximately 46 million people are living below the national poverty
17 line in Pakistan (as per 2015) [8]. The increases in prices of both OBs and LPGs may fairly be
18 attributable to the NDPP 2018, that allows an annual increase in the prices of scheduled drugs up
19 to 70% of CPI compared to 50% of CPI as per NDPP 2015 [9, 10]. These changes in price
20 calculations seems to accentuate the substantial impact on overall prices of medicines, thus,
21 making them more expensive. The increase in LPGs prices were more significant as compared to
22 OBs suggesting that with already expensive OBs, the price increase in LPGs would impoverish
23 the overall access to medicines, imputable to the changes in formula for LPGs (new entrants) price
24 calculation. According to NDPP 2018, the MRP of new entrant first generic should be fixed at
25 20% less than that of OB compared with 30% less than MRP of OB as per NDPP 2015. Another
26 possible variable is the prior availability of generics in the market for price calculation, where,
27 according to NDPP2018, the MRP of a new entrant (LPGs) was fixed equal to the highest MRP
28 of the available generics in the market, while as per NDPP2015 practice, MRP was fixed by taking
29 the average of other generics in the market. Therefore, these changes in price calculating
30 mechanisms might have led to higher prices of many new LPGs in the market. Hence, contrary to
31 NDPP 2018's price steerage objectives, the increase in medicine prices was more distinct for
32 NEML medicines as compared to non-NEML medicines.
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38 Data from further analysis on affordability of standard treatment by selected OBs and LPGs
39 suggested that majority of the medicines have become more unaffordable in 2019. When the
40 affordability was compared for medicines of different disease groups, the three top most
41 unaffordable OBs were found for the treatment of ulcers, diabetes and CVDs. Additionally, the
42 treatment for ulcers remained awfully unaffordable with OBs and LPGs in both years.
43 Nevertheless, the treatment of CVDs and diabetes with LPGs remained affordable in 2017 but the
44 NDWs for CVDs surpassed affordability threshold in 2019. Among the disease categories, NCDs
45 harbor the top three unaffordable slots. It is noteworthy, that the burden of NCDs is increasing
46 worldwide and is responsible for higher mortality rates than all other diseases combined [25-27].
47 The CVDs, diabetes, cancer and chronic respiratory diseases are responsible for about 80% of
48 these deaths [28]. Pakistan is among top 10 countries where prevalence of diabetes is very high.
49 Besides, one third of Pakistanis, above 45 years of age have hypertension [29-31]. Thus, the
50 unaffordability of the essential medicines for NCDs, such as CVDs and diabetes, has worse bearing
51 on affordability associated therapeutic outcomes that ultimately leads to increased morbidity and
52 mortality due to un-controlled disease.
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Additionally, we also compared the median drug prices in 2019 with the prices published/allowed by DRAP in its latest Statutory Regulatory Orders (SROs). DRAP revised and published the maximum retail prices (MRPs) of about 1084 drugs on December 31, 2018 through SRO-1608, SRO-1609 and SRO-1610 [32]. Eighteen OBs from our study sample were part of these price revisions (table 3). Surprisingly, after comparing the MUPs of 18 selected OBs with prices allowed by the government, we found that most of the OBs, 14 out of 18, were sold at higher prices than the allowable prices – with median percent increase of 29.37%. These data suggested that these intentional malpractices by the drug sellers might be driven by poor price control regulation by price enforcement authorities. Therefore, the current drug pricing policy NDPP 2018, is not the sole reason of price hike, probably main stakeholders in drug supply chain are also contributing towards medicine inflated prices. Thus, it's reasonable to deduce that these factors may interfere with measuring the direct impact of current pricing policy.

Table 3. Maximum retail unit prices (MRPs) of Originator Brands (OBs) allowed by the government versus median unit prices (MUPs) found in private sector pharmacies.

Medicine Name	Strength (Dosage form)	Allowed Unit Price (PKR)	MUP 2019 (PKR)	Percentage difference
Aciclovir	200mg (tab)	52.6	75	42.5%
Amlodipine	5mg (tab)	8.5	13	52.9%
Amoxicillin	250mg (cap)	3.75	3.75	0%
Amoxicillin	500mg (cap)	5.58	8.75	56.8%
Atorvastatin	20mg (cap)	141.37	203.5	43.9%
Bisoprolol	5mg (tab)	15.35	16.72	8.9%
Carbamezipine	200mg (tab)	4	5	25%
Ceftriaxone	1g (inj)	783	783	0%
Ciprofloxacin	500mg (tab)	39.25	52.5	33.7%
Digoxin	0.25mg (tab)	1.75	2.68	53.1%
Fluconazole	200mg (cap)	425	585	37.6%
Insulin N	100IU (vial)	88.47	75.88	-14.2%
Insulin R	100IU (vial)	93.88	75.88	-19.1%
Methyldopa	250mg (tab)	7.71	8.1	5.05%
Omeprazole	20mg (cap)	42.9	52.29	21.8%
Propranolol	40mg (tab)	1.1	3.16	187.2%
Pyremethamine+Sulfadoxime	(25+500)mg (tab)	12.01	12.02	0.08%
Simvastatin	20mg (cap)	47.01	68	44.6%
Medians		27.3	34.505	29.3%

There could be many policy implications having an impact on drug pricing, availability and affordability. The procurement of medicines should be strictly based on the NEML. Clear cut mechanism for NEML based procurement should be devised and implemented specially in the

public sector hospitals. Besides this, the hospital pharmacy and therapeutics committees must actively evaluate the safety, efficacy and cost-effectiveness of drugs before purchasing. Pharmacoeconomic evaluations of drugs must be promoted by allocating research funds to experts. Not all drugs should be fully reimbursed in the hospitals, only essential medicines must be included in this list. So, the profits from other drugs can be used to purchase essential drugs when needed. Smooth functioning of the drug supply chain with proper quality control must be ensured. The current inflated prices would have a grave impact on the access to essential medicines, especially for the lower and middle income population in Pakistan. Thus, there is dire need to develop more clear, evidence based and stringent price control policy, especially for essential medicines. Exempting or reducing taxes and tariffs on EMs and promotion of local generic manufacture by providing subsidies on raw materials may improve both the availability and affordability of these medicines. While using the External Reference Pricing (ERP) mechanism, the reference countries should be chosen critically e.g. countries with similar pharmaceutical market and economic status. For costly medicines, regressive markups must be encouraged over progressive markups. The drug prices must be monitored on regular basis using a validated and well-designed scientific methodology and pricing policy must be revised based on such evidences. The essential medicines for most prevalent diseases such as diabetes and CVDs must be preferentially made affordable by devising some specific pricing strategies for these medicines. Besides, efforts must be made to enforce the pricing policy effectively by introducing reward and punishment system to induce a healthy competition among the drug manufacturers and sellers.

In Conclusion, the availability of medicines has been improved after the launch of a new drug pricing policy by Pakistani government but it is still poor, forcing the patients to buy medicines from private sector at their own expense. The prices of both LPGs and OBs of EMs have increased remarkably in 2019, when compared with 2017. The medicines to treat most prevalent non-communicable diseases (diabetes and CVDs) have become more expensive and unaffordable. The maximum retail prices of several originator brands have been illegally increased in the market, adding more burden on patients' pockets. The pricing policy needs to be improved further to bring a strict price control, especially on the EMs and on the medicines for most prevalent diseases.

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Contributions

AS, ZB and YF conceptualize the study. ZA, HS, AS and ZB designed methodology. ZS, HS, AS trained the data collectors and obtained the data. YF provided resources and supervised the project. ZS worked as survey area manager. MA, AH, NA, FK and MZ did data cleaning, validation and entry. AS, HS, CY, MJ analyzed the data. AS and HS wrote original draft. YF, ZB, ZS, CY and MJ, WJ reviewed and edited the manuscript.

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Competing Interests

None

Patient Consent for Publication

Not Required

Ethics Approval

Ethics approval was obtained from the Medical Ethics Committee of Xi’an Jiaotong University under study ID 2019-067.

Data availability statement

Data are available on reasonable request.

References

1. United Nations Development Group, United Nations. Statistical Division. Indicators for monitoring the millennium development goals: definitions, rationale, concepts and sources. United Nations Publications 2003:95.
2. World Health Organization. Medicine prices and access to medicines in the Eastern Mediterranean Region. 2007.
3. Lee KS, Shahidullah A, Zaidi ST, *et al*. The Crux of the Medicine Prices' Controversy in Pakistan. *Frontiers in pharmacology* 2017;8:504.
4. Kiani A, Qadeer A, Mirza Z, *et al*. Prices, availability and affordability of medicines in Pakistan. Geneva: Health Action International (HAI); 2006.
5. Zaidi S, Bigdeli M, Aleem N, *et al*. Access to essential medicines in Pakistan: policy and health systems research concerns. *PloS One* 2013;8:e63515.
6. Cameron A, Ewen M, Ross-Degnan D, *et al*. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. *The Lancet* 2009;373:240.

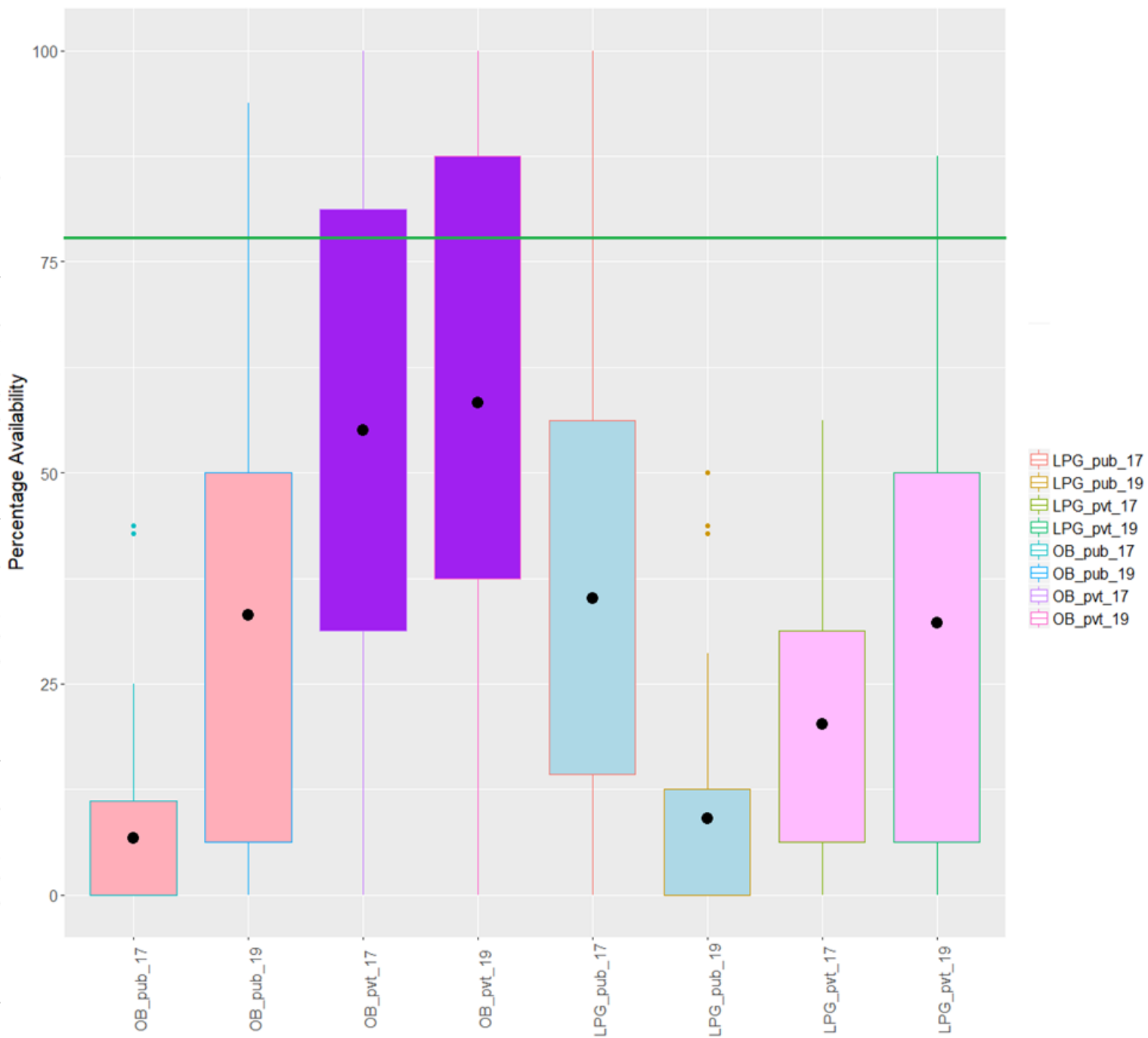
7. Saeed A, Saeed H, Saleem Z, *et al.* Evaluation of prices, availability and affordability of essential medicines in Lahore Division, Pakistan: A cross-sectional survey using WHO/HAI methodology. *PloS One* 2019;14:e0216122.
8. The World Bank. Poverty and Equity data portal. 2015. Available: <http://povertydata.worldbank.org/poverty/country/PAK>. [Accessed: 16 June 2019].
9. Costing and Pricing Division, Drug Regulatory Authority of Pakistan. Drug Pricing Policy 2015.
10. Costing and Pricing Division, Drug Regulatory Authority of Pakistan. Drug Pricing Policy 2018.
11. Durrani F. Increase in drug prices highest in last 40 years. *The News* 2019. Available: <https://www.thenews.com.pk/print/454864-increase-in-drug-prices-highest-in-last-40-years>. [Accessed: 3 September 2019].
12. Junaidi I. Minister orders crackdown on firms increasing medicine prices. *DAWN News* 2019. Available: <https://www.dawn.com/news/1473573>. [Accessed: 3 September 2019].
13. World Health Organization. Measuring medicine prices, availability, affordability and price components 2008.
14. Pakistan Bureau of Statistics. Population Census. 2017. Available: <http://www.pbs.gov.pk/content/population-census>. [Accessed: 18 August 2019].
15. Drug Regulatory Authority of Pakistan. National Essential Medicines List. 2018.
16. Yang H, Dib HH, Zhu M, *et al.* Prices, availability and affordability of essential medicines in rural areas of Hubei Province, China. *Health policy and planning* 2009;25:219.
17. Fang Y, Wagner AK, Yang S, *et al.* Access to affordable medicines after health reform: evidence from two cross-sectional surveys in Shaanxi Province, western China. *The Lancet Global Health* 2013;1:e227.
18. Management Sciences for Health. International Medical Products Price Guide 2015.
19. Pakistan Bureau of Statistics, Government of Pakistan. Price Statistics. Available: <http://www.pbs.gov.pk/content/officially-published-consumer-prices-data-imf-template>. [Accessed 18 August 2019].

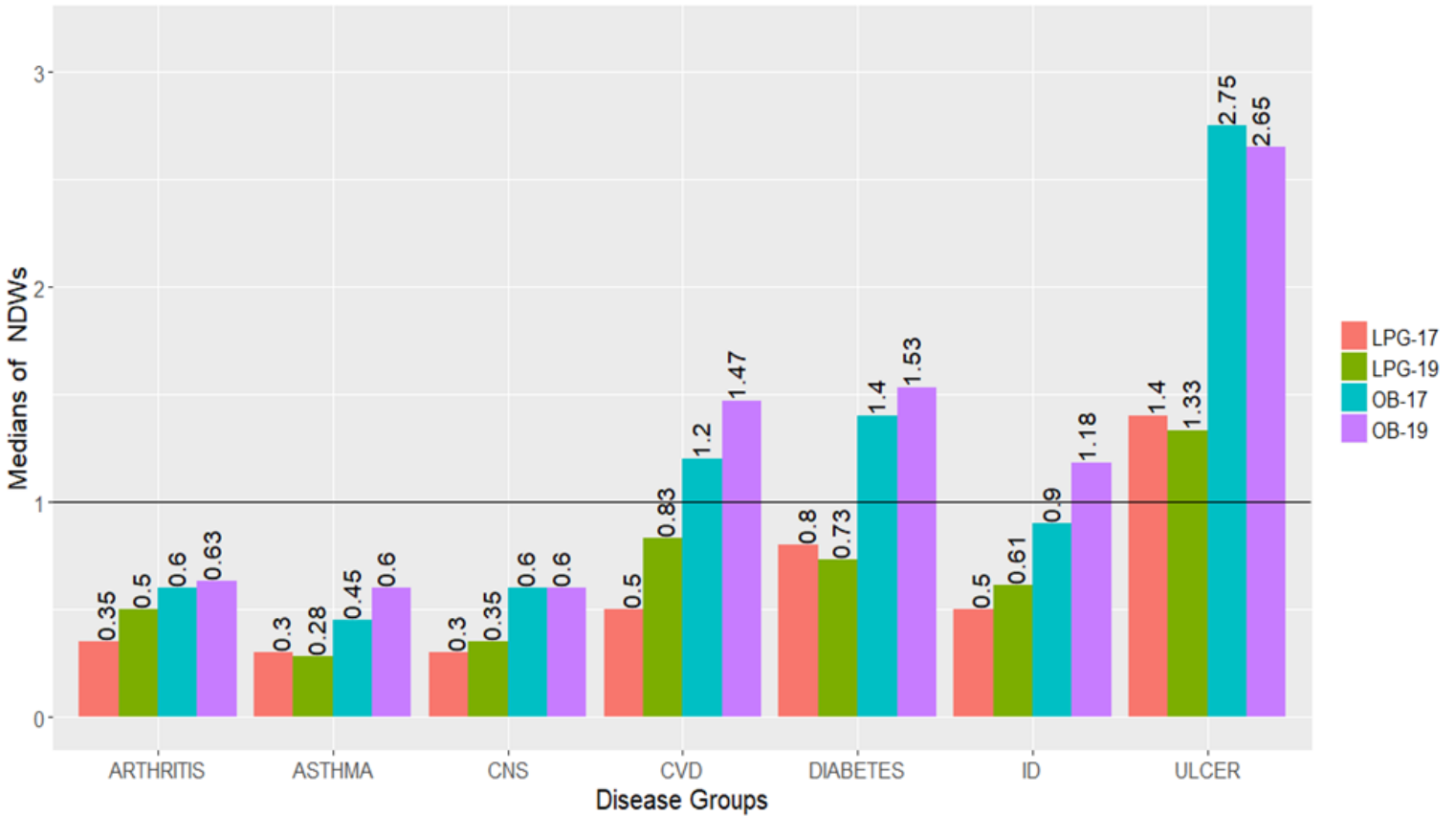
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 - 60
20. Wage Indicator Foundation. Minimum wages in Pakistan 2018. Available: <https://wageindicator.org/Wageindicatorfoundation>. [Accessed 15 April 2019].
21. Kasonde L, Tordrup D, Naheed A, *et al.* Evaluating medicine prices, availability and affordability in Bangladesh using World Health Organisation and Health Action International methodology. *BMC health services research* 2019;19:383.
22. Khuluza F, Haeefele-Abah C. The availability, prices and affordability of essential medicines in Malawi: A cross-sectional study. *PloS One* 2019;14:e0212125.
23. Jabri P. National essential medicine list -2018 to be implemented in all provinces: Kiani. *Business Recorder* 2018. Available: <https://www.brecorder.com/2018/10/06/444080/national-essential-medicine-list-2018-to-be-implemented-in-all-provinces-kiani/> . [Accessed: 3 September 2019].
24. Govt. launches WHO backed national essential medicine list. *Pakistan Today* 2018. Available: <https://www.pakistantoday.com.pk/2018/10/05/govt-launches-who-backed-national-essential-medicine-list/>. [Accessed: 3 September 2019].
25. Dans A, Ng N, Varghese C, *et al.* The rise of chronic non-communicable diseases in southeast Asia: time for action. *The Lancet* 2011;377:680.
26. Siegel KR, Patel SA, Ali MK. Non-communicable diseases in South Asia: contemporary perspectives. *British medical bulletin* 2014;111:31.
27. Habib SH, Saha S. Burden of non-communicable disease: global overview. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2010;4:41.
28. World Health Organization. Global action plan for the prevention and control of non-communicable diseases 2013-2020, 2013.
29. Ghaffar A, Reddy KS, Singhi M. Burden of non-communicable diseases in South Asia. *BMJ* 2004;328:807.
30. Jafar TH, Haaland BA, Rahman A, *et al.* Non-communicable diseases and injuries in Pakistan: strategic priorities. *The Lancet* 2013;381:2281.
31. Wasay M, Zaidi S, Jooma R. Non communicable diseases in Pakistan: burden, challenges and way forward for health care authorities. *Journal of Pakistan Medical Association* 2014; 64:1218.
32. Drug Regulatory Authority of Pakistan. SRO: Pricing division 2018. Available: <https://www.dra.gov.pk/Home/Pricing>. [Accessed: 17 July 2019].

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11 **Figure 1. Box plot of percent availability of lowest price generics (LPGs) and originator**
12 **brands (OBs) in both public (pub) and private (pvt) sectors in 2017 and 2019.** This box plot
13 shows the distributional characteristics of the percent availability of medicines in two groups (OB
14 and LPG) for the years 2017 and 2019. The mean percent availability is represented by the dot
15 inside the box.
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18 **Figure 2.** Bar graph of affordability of originator brands (OBs) and lowest price generics (LPGs)
19 for different diseases in both years i.e. 2017 and 2019.
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Supplementary Tables

Table S1. Percent availabilities and of originator brands (OBs) and lowest price generics (LPGs) of all medicines in public and private sector in 2017 and 2019 (%)

Names of meds	OB (Public) 2017	OB (Pvt.) 2017	LPG (Public)) 2017	LPG (Pvt.) 2017	OB (Public) 2019	OB (Pvt) 2019	LPG (Public) 2019	LPG (pvt.) 2019
Acetylsalicylic Acid	0.0	25.0	56.3	25.0	18.8	75.0	50.0	18.8
Aciclovir	0.0	50.0	25.0	37.5	6.3	18.8	0.0	50.0
Amiodarone	7.1	62.5	21.4	6.3	0.0	62.5	21.4	0.0
Amitriptyline	0.0	31.3	0.0	25.0	0.0	0.0	50.0	50.0
Amlodipine	6.3	75.0	62.5	31.3	37.5	93.8	12.5	56.3
Amoxicillin	43.8	93.8	18.8	25.0	93.8	68.8	0.0	37.5
Amoxicillin (250)	18.8	100.0	12.5	31.3	50.0	87.5	0.0	37.5
Atenolol	12.5	87.5	81.3	43.8	43.8	81.3	0.0	56.3
Atorvastatin	7.1	50.0	21.4	25.0	42.9	62.5	21.4	18.8
Azithromycin	0.0	25.0	25.0	31.3	31.3	25.0	25.0	75.0
Beclometasone inhaler	0.0	6.3	35.7	12.5	35.7	43.8	0.0	0.0
Bisoprolol	6.3	87.5	18.8	25.0	37.5	81.3	0.0	56.3
Captopril	0.0	81.3	85.7	25.0	50.0	93.8	28.6	50.0
Carbamazepine	12.5	87.5	56.3	25.0	25.0	31.3	0.0	56.3
Ceftriaxone injection	14.3	68.8	71.4	31.3	21.4	75.0	50.0	87.5
Ciprofloxacin	0.0	81.3	100.0	37.5	64.3	93.8	14.3	25.0
Clarithromycin	0.0	87.5	35.7	25.0	50.0	93.8	0.0	56.3
Co-trimoxazole suspension	6.3	31.3	62.5	6.3	6.3	6.3	43.8	6.3
Diazepam	6.3	62.5	12.5	0.0	43.8	68.8	0.0	0.0
Diclofenac	42.9	50.0	35.7	6.3	85.7	93.8	0.0	81.3
Digoxin	21.4	62.5	28.6	0.0	28.6	68.8	0.0	56.3
Enalapril	0.0	68.8	62.5	18.8	12.5	68.8	12.5	50.0
Fluconazole	0.0	37.5	18.8	25.0	43.8	43.8	0.0	50.0
Fluoxetine	0.0	43.8	12.5	43.8	6.3	62.5	6.3	62.5
Fluphenazine Decanoate	0.0	0.0	0.0	12.5	0.0	0.0	7.1	6.3
Furosemide	12.5	93.8	50.0	6.3	50.0	87.5	0.0	0.0
Glibenclamide	18.8	68.8	56.3	12.5	68.8	93.8	0.0	12.5
Gliclazide	0.0	75.0	0.0	18.8	7.1	75.0	0.0	31.3
Hydrochlorothiazide	0.0	0.0	0.0	12.5	18.8	0.0	0.0	0.0
Indinavir	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Insulin Isophane (NPH)	0.0	75.0	50.0	25.0	56.3	68.8	0.0	18.8
Insulin Neutral Soluble (Regular)	0.0	68.8	50.0	25.0	68.8	68.8	0.0	18.8
Losartan	7.1	43.8	14.3	43.8	0.0	43.8	42.9	43.8
Lovastatin	0.0	0.0	6.3	0.0	6.3	37.5	12.5	0.0

Metformin	25.0	81.3	56.3	31.3	68.8	93.8	0.0	50.0
Methyldopa	12.5	81.3	25.0	0.0	75.0	68.8	0.0	0.0
Metronidazole	25.0	93.8	56.3	37.5	75.0	87.5	0.0	56.3
Nevirapine	0.0	0.0	14.3	0.0	0.0	0.0	0.0	0.0
Nifedipine Retard	0.0	75.0	28.6	12.5	0.0	31.3	14.3	12.5
Omeprazole	6.3	56.3	75.0	37.5	62.5	62.5	6.3	50.0
Omeprazole (10)	0.0	12.5	43.8	18.8	18.8	0.0	12.5	31.3
Paracetamol suspension	6.3	68.8	87.5	25.0	81.3	87.5	0.0	81.3
Phenytoin	0.0	6.3	12.5	6.3	0.0	50.0	6.3	0.0
Propranolol	12.5	68.8	12.5	6.3	18.8	87.5	0.0	25.0
Pyrimethamine with sulfadoxine	0.0	75.0	21.4	6.3	21.4	68.8	0.0	6.3
Ranitidine	0.0	81.3	31.3	25.0	50.0	100.0	0.0	50.0
Salbutamol inhaler	0.0	81.3	56.3	31.3	62.5	68.8	0.0	12.5
Simvastatin	0.0	25.0	21.4	56.3	0.0	37.5	7.1	25.0
Spironolactone	6.3	62.5	25.0	0.0	12.5	93.8	6.3	43.8
Zidovudine	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Mean availabilities	6.8	55.0	35.1	20.3	33.1	58.3	9.0	32.3

Table (S2). Change in availability at different levels of healthcare (Public Sector).

	Primary level (n=2 outlets)		Secondary level (n=13 outlets)		Tertiary level (n=1 outlet)	
	All medicines (n=50)		All medicines (n=50)		All medicines (n=50)	
	OB	LPG	OB	LPG	OB	LPG
Mean Availability 2017 (SD),%	0.0 (0.0)	25.8 (44.5)	7.1 (11.2)	35.2 (27.5)	12.0 (32.8)	50.0 (50.5)
Mean Availability 2019 (SD) ,%	21.0 (31.0)	3.2 (18)	32.3 (29.1)	7.4 (13.4)	68.0 (47.1)	22.0 (41.8)
Change in mean percent availability,%	21.0	-22.6	25.2	-27.8	56.0	-28.0

Table S3. Change in median unit prices (MUPs) and median price ratios (MPRs) of the Originator Brands (OBs) at private sector.

Sr. no.	Medicines (OB)	MUPs 2017 (PKR)	MPR 2017	Adjusted MUP in 2019	MPR 2019	Percentage change in MUPs/MPRs
1	Acetylsalicylic Acid	1.16	0.8	1.12	0.7	-3.41%
2	Aciclovir	70	20	72.5	21	3.48%
3	Amiodarone	17.78	2.2	17.4	2.2	-2.15%
4	Amlodipine	11.93	7.3	12.6	7.7	5.1%
5	Amoxicillin	8.616	2.8	8.46	2.7	-1.83%
6	Amoxicillin (250)	3.56	2.1	3.63	2.2	1.83%
7	Atenolol	6.19	5.6	6.14	5.5	-0.81%
8	Atorvastatin	201.9	18	197	18	-2.6%
9	Azithromycin	40	1.7	118	5	66.2%
10	Beclometasone inhaler	1.25	1.2	1.84	1.8	32%
11	Bisoprolol	11.28	1.2	16.2	1.7	30.2%
12	Captopril	7.66	3	8.22	3.2	6.81%
13	Carbamazepine	4.91	2.6	4.84	2.5	-1.55%
14	Ceftriaxone injection	672	16	757	18	11.2%
15	Ciprofloxacin	50.4	13	50.8	13	0.72%
16	Clarithromycin	65.7	2.5	76.4	2.9	14%
17	Co-trimoxazole suspension	0.29	0.6	0.44	0.9	33.4%
18	Diazepam	2	2	1.93	1.9	-3.41%
19	Diclofenac	5.625	12	5.61	12	-0.29%
20	Digoxin	2.52	2.4	2.59	2.5	2.76%
21	Enalapril	5.85	5.4	6	5.6	2.43%
22	Fluconazole	442	61	566	78	21.9%
23	Fluoxetine	43.42	9.7	43	9.6	-0.9%
24	Furosemide	1.89	3	2.34	3.7	19.2%
25	Glibenclamide	1.69	2.9	2.09	3.5	19.1%
26	Gliclazide	7.6	1.5	16.4	3.3	53.8%
27	Insulin Isophane (NPH)	64.5	1.1	73.4	1.3	12.1%
28	Insulin Neutral Soluble (Regular)	64.5	1.1	73.4	1.2	12.1%
29	Losartan	51.67	4.3	50.3	4.2	-2.76%
30	Metformin	1.54	1	1.62	1	5.21%
31	Methyldopa	6.38	1.9	7.83	2.3	18.5%
32	Metronidazole	1.57	1.3	1.52	1.2	-3.41%
33	Nifedipine Retard	5.69	2.7	5.8	2.8	1.93%
34	Omeprazole	49.78	34	50.6	35	1.55%
35	Paracetamol suspension	0.85	1.6	2.2	4.1	61.4%
36	Phenytoin	5.2	4.8	23.2	22	77.6%
37	Propranolol	1.55	2.2	3.06	4.3	49.3%

38	Pyrimethamine with sulfadoxine	5.83	1.4	11.6	2.8	49.8%
39	Ranitidine	8.8	3.7	8.51	3.6	-3.41%
40	Salbutamol inhaler	1	1	1.03	1.1	3.35%
41	Simvastatin	67.13	12	65.8	12	-2.09%
42	Spirolactone	8.6	0.8	10.1	1	14.5%
	Medians	6.99	2.5	8.49	3.2	4.29%

Table S4. Change in median unit prices (MUPs) and median price ratios (MPRs) of the lowest price generics (LPGs) in private sector.

Sr. no.	Medicines	MUPs 2017 (PKR)	MPR 2017	Adjusted MUP in 2019	MPR 2019	Percentage change in MUPs/MPRs
1	Acetylsalicylic Acid	1.015	0.7	1.06	0.7	4.58
2	Aciclovir	12.4	3.6	13.5	3.9	8.41
3	Amitriptyline	1.19	1.4	1.24	1.4	3.86
4	Amlodipine	1.8	1.1	6.29	3.8	71.4
5	Amoxicillin	5.8	1.9	8.32	2.7	30.3
6	Amoxicillin (250)	3	1.8	3.48	2.1	13.8
7	Atenolol	2.05	1.8	2.47	2.2	16.9
8	Atorvastatin	37.5	3.4	35.8	3.2	-4.8
9	Azithromycin	40	1.7	19.3	0.8	-107
10	Bisoprolol	6.55	0.7	6.56	0.7	0.1
11	Captopril	6.5	2.5	6.77	2.7	3.97
12	Carbamazepine	3.3	1.7	4.35	2.3	24.2
13	Ceftriaxone injection	280	6.8	290	7	3.48
14	Ciprofloxacin	11	2.8	24.2	6.2	54.5
15	Clarithromycin	36	1.4	42.7	1.6	15.8
16	Co-trimoxazole suspension	0.21	0.4	2.32	4.7	91
17	Diclofenac	3.5	7.5	4.79	10	26.9
18	Enalapril	2.05	1.9	2.84	2.6	27.8
19	Fluconazole	145.5	20	145	20	-0.3
20	Fluoxetine	13.8	3.1	13.5	3	-1.9
21	Fluphenazine Decanoate	90.5	1	93.8	1.1	3.5
22	Glibenclamide	1.57	2.7	1.42	2.4	-10
23	Gliclazide	4.75	0.9	5.8	1.1	18.1

24	Insulin Isophane (NPH)	48	0.8	62.3	1.1	22.9
25	Insulin Neutral Soluble (Regular)	48	0.8	62.3	1	22.9
26	Losartan	11	0.9	13.1	1.1	15.7
27	Metformin	1.5	1	1.86	1.2	19.2
28	Metronidazole	1.5	1.2	1.93	1.6	22.4
29	Nifedipine Retard	2.65	1.3	5.14	2.4	48.4
30	Omeprazole	15.35	10	11.4	7.8	-35
31	Omeprazole (10)	12.14	0.9	5.13	0.4	-137
32	Paracetamol suspension	0.47	0.9	1.02	1.9	53.7
33	Propranolol	0.66	0.9	2.03	2.8	67.5
34	Pyrimethamine with sulfadoxine	5	1.2	4.84	1.2	-3.4
35	Ranitidine	6.93	2.9	7.78	3.3	11
36	Salbutamol inhaler	0.64	0.7	0.68	0.7	5.45
37	Simvastatin	8.5	1.6	16.6	3	48.7
	Medians	5.8	1.4	6.29	2.3	15.7

Table S5. Affordability of originator brands (OBs) for different diseases in 2017 and 2019, in private sector.

Disease	Medicine	Strength	Dosage form	No. of units needed per treatment	Durati on of treatment	MTP 2017 (PKR)	NDWs 2017	MTP 2019 (PKR)	NDWs 2019
ASTHMA	Salbutamol Inhaler	100mcg/dose	Inhaler	200	As needed	200	0.4	214	0.4
	Beclomethasone	50mcg/dose	inhaler	200	As needed	250	0.5	380	0.8
Cardiovascular Diseases	Bisoprolol	5mg	tab	60	30	676.8	1.5	1003	2
	Atenolol	50mg	tab	30	30	185.7	0.4	190.5	0.4
	Captopril	25mg	tab	60	30	459.6	1	510	1
	Amlodipine	5mg	tab	60	30	715.8	1.5	780	1.6
	Amiodarone	200mg	tab	60	30	1066.8	2.3	1080	2.2
	Losartan	50mg	tab	60	30	3100.2	6.6	3120	6.2
	methyldopa	250mg	tab	90	30	574.2	1.2	729	1.5
Nifedipine retard	20mg	tab	90	30	512.1	1.1	540	1.1	

	Spironolactone	100mg	tab	30	30	258	0.5	312	0.6
	Propranolol	40mg	tab	90	30	139.5	0.3	284.4	0.6
	Acetylsalicylic acid	75mg	tab	30	30	34.8	0.1	34.8	0.1
Anti hyperlipide mics	Simvastatin	20mg	Cap/tab	30	30	2013.9	4.3	2040	4.1
	Atorvastatin	20mg	Cap/tab	30	30	6057	13	6105	12
Infections-Adult respiratory tract infection	Ceftriaxone Injection	1g/vial	Inj.	1	1	672	1.4	783	1.6
	Ciprofloxacin	500mg	tab	14	7	705.6	1.5	735	1.5
	Azithromycin	500mg	tab	3	3	120	0.3	367	0.7
	clarithromycin	500mg	tab	28	14	1839.6	3.9	2212	4.4
	Amoxicillin	500mg	cap	42	14	361.87	0.8	367.5	0.7
	Amoxicillin	250mg	cap	84	14	299.04	0.6	315	0.6
Fungal Infection	Fluconazole	200mg	cap	1	1	442	0.9	585	1.2
Viral Infection	aciclovir	200mg	tab	25	5	1750	3.8	1875	3.8
Amoebiasis	metronidazole	400mg	tab	21	7	32.97	0.1	32.97	0.1
CNS Drugs-Anti epileptics	Carbamezipine	200mg	tab	60	30	294.6	0.6	300	0.6
	Phenytoin	100mg	tab	90	30	468	1	2160	4.3
Anxiety	diazepam	5mg	tab	90	30	180	0.4	180	0.4
Anti Diabetics	Metformin	500mg	tab	90	30	138.6	0.3	151.2	0.3
	Glibenclamide	5mg	tab	90	30	152	0.3	194.4	0.4
	Gliclazide	80mg	tab	60	30	456	1.5	1020	2
	Insulin Isophane (NPH)	100IU/ml	vial	10	30	645	1.4	758.8	1.5
	Insulin Neutral Soluble (Regular)	100IU/ml	vial	10	30	645	1.4	758.8	1.5
Ulcer Treatment	Omeprazole	20mg	cap	30	30	1493.4	3.2	1569	3.1
	ranitidine	150mg	tab	120	30	1056	2.3	1056	2.1
Pain/Inflam mation Arthritis	Paracetamol	24mg/ml	susp	45	3	38.25	0.1	102.6	0.2
	Diclofenac	50mg	tab	90	30	506.25	1.1	522	1

Where, MTP: Median treatment price, NDWs: Number of days' wages

Table S6. Affordability of lowest price generics (LPGs) for different diseases in 2017 and 2019, in private sector.

Disease/Condition	Medicine	Strength	Dosage form	No. of units needed per treatment	Duration of treatment	MTP 2017 (PKR)	NDWs 2017	MTP 2019 (PKR)	NDWs 2019
ASTHMA	Salbutamol Inhaler	100mcg/dose	Inhaler	200	As needed	128	0.3	140	0.3
Cardiovascular Diseases/ Anti Hypertensives	Bisoprolol	5mg	tab	60	30	393	0.8	406.8	0.8
	Atenolol	50mg	tab	30	30	61.5	0.1	76.5	0.2
	Captopril	25mg	tab	60	30	390	0.8	420	0.8
	Amlodipine	5mg	tab	60	30	108	0.2	390	0.8
	Losartan	50mg	tab	60	30	660	1.4	810	1.6
	Nifedipine retard	20mg	tab	90	30	238.5	0.5	478.4	1
	Propranolol	40mg	tab	90	30	59.4	0.1	189	0.4
	Acetylsalicylic acid	75mg	tab	30	30	30.45	0.1	33	0.1
Anti hyperlipidemics	Simvastatin	20mg	Cap/tablet	30	30	255	0.5	513.8	1
	Atorvastatin	20mg	Cap/tablet	30	30	1125	2.4	1110	2.2
Infections-Adult respiratory tract infection	Ceftriaxone Injection	1g/vial	Inj.	1	1	280	0.6	300	0.6
	Ciprofloxacin	500mg	tab	14	7	154	0.3	350	0.7
	Azithromycin	500mg	tab	3	3	120	0.3	60	0.1
	clarithromycin	500mg	tab	28	14	1008	2.2	1238	2.5
	Amoxicillin	500mg	cap	42	14	243.6	0.5	361.2	0.7
	Amoxicillin	250mg	cap	84	14	252	0.5	302.4	0.6
Fungal Infection	Fluconazole	200mg	cap	1	1	145.5	0.3	150	0.3
Viral Infection	aciclovir	200mg	tab	25	5	310	0.7	350	0.7
Amoebiasis	metronidazole	400mg	tab	21	7	31.5	0.1	42	0.1
CNS Drugs-Anti epileptics	Carbamezipine	200mg	tab	60	30	198	0.4	270	0.5
Depression	Amitriptyline	25mg	tab	60	30	71.4	0.2	76.8	0.2

Anti Diabetics	Metformin	500mg	tab	90	30	135	0.3	180	0.4
	Glibenclamide	5mg	tab	90	30	141	0	132.3	0.3
	Gliclazide	80mg	tab	60	30	285	0.8	360	0.7
	Insulin Isophane (NPH)	100IU/ml	vial	10	30	480	1	644	1.3
	Insulin Neutral Soluble (Regular)	100IU/ml	vial	10	30	480	1	644	1.3
Ulcer Treatment	Omeprazole	20mg	cap	30	30	460.5	1	353.7	0.7
	ranitidine	150mg	tab	120	30	831.6	1.8	966	1.9
Pain/Inflammation	Paracetamol	24mg/ml	susp	45	3	21.15	0	47.25	0.1
Arthritis	Diclofenac	50mg	tab	90	30	315	0.7	445.5	0.9

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Research Checklist

Dear editor,

We submit the manuscript entitled “**Impact of National Drug Pricing Policy 2018 on Access to Medicines in Lahore Division, Pakistan: A Pre-Post Survey Study Using WHO/HAI Methodology**”, for your consideration to be published in *BMJ Open*. And we confirm that we have prepared submission materials according to the guideline.

And our main document has covered everything required, which including the following:

Title page

Abstract

Introduction

Methods

Results

Discussion

Other Information

Funding

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Impact of National Drug Pricing Policy 2018 on Access to Medicines in Lahore Division, Pakistan: A Pre-Post Survey Study Using WHO/HAI Methodology

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1 Abstract

2 **Objective:** To evaluate the impact of new national drug pricing policy (NDPP) 2018 on access to
3 medicines in terms of prices, availability and affordability.

4 **Design:** Two cross-sectional surveys were undertaken before and after the launch of NDPP 2018,
5 using a modified WHO/HAI methodology.

6 **Setting:** Four districts of Lahore division, Pakistan.

7 **Participants:** 16 public sector hospitals and 16 private sector retail pharmacies.

8 **Measures:** The pre and post survey data on prices and availability of Lowest Price Generics
9 (LPGs) and Originator Brands (OBs) of 50 medicines were obtained by visiting the same public
10 and private sector health facilities (n=32). 46 out of 50 surveyed medicines were from National
11 Essential Medicines List (NEML). Inflation-adjusted median unit prices (MUPs) and median price
12 ratios (MPRs) from 2019 were used for price comparison. Affordability was calculated in terms
13 of number of days' wages required to get a standard treatment by the lowest paid unskilled
14 government worker.

15 **Results:** The overall mean percent availabilities remained poor in both years i.e. far less than 80%.
16 In public sector, the mean percent availability of OBs improved from 6.8% to 33.1% whereas, in
17 case of LPGs it was reduced from 35.1% to 9%. In private sector, the mean percent availability of
18 both OBs and LPGs demonstrated slight improvements in 2019 i.e. 55.0% to 58.3% and 20.3% to
19 32.3%. The adjusted MUPs and MPRs of OBs significantly increased by a median of 4.29%
20 (Wilcoxon test p=0.001, p=0.0001). Whereas, the adjusted MUPs and MPRs of LPGs were
21 increased by a median of 15.7% (p=0.002, p=0.0002). Overall the affordability of many medicines
22 for common ailments reduced significantly in 2019.

23 **Conclusions:** The availability of medicines slightly improved, except in the case of LPGs which
24 was reduced at public sector. Although the main aim of NDPP 2018 was to make the drugs
25 affordable, but its implementation led to increased drug prices thereby making standard treatment
26 for some of the most prevalent ailments, unaffordable. This policy needs to be improved further to
27 have strict price control especially for essential medicines, in order to improve their access.

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36 Strengths

- 37 • This is the first study of its kind from Pakistan, where pre-post surveys were conducted
38 and analyzed to estimate the impact of a national drug pricing policy, using the WHO/HAI
39 methodology.
- 40 • The data was collected from the same health facilities in both years. So, the comparison is
41 reliable. This study provides an objective evidence to the policy makers for improving the
42 current pricing policies.

43 Limitations

- 44 • The study is limited to only one division of Pakistan, although the medicine prices are fixed
45 centrally and are supposed to be same across the country – affecting generalizability of the
46 findings.
- 47 • Moreover, this study is conducted after about a year from the launch of new drug pricing
48 policy 2018, so the results do not reflect the long term impact of the policy.

64 Introduction

65 Access to affordable and quality assured essential medicines is considered as a key component of
66 an effective healthcare system. It has also been pledged under Sustainable Development Goal
67 (SDG) 3 by United Nations (UN) that the equitable access to affordable essential medicines will
68 be ensured as a basic human right [1, 2]. Pakistani government, like many other Low and Middle
69 Income Countries (LMICs), has been grappling with the issue of high medicine prices and poor
70 availability of medicines that compromises the accessibility of medicines [1, 3-6]. The medicines
71 are provided free of cost at public sector health facilities, while patient pays out of pocket to get
72 medicines from private sector, in Pakistan [5]. In fact, the poor availability of medicines at public
73 sector compels the patients to buy medicines from the private sector that escalates the burden on
74 patient's pocket, as 24.3% (in 2015) of the population is living below the national poverty line [3,
75 4, 7, 8]. Besides, medicine prices have increased up to 100%, both legally or illegally, in the past
76 few years [3]. The drug prices are fixed by the federal government and the National Health Services
77 Regulation and Coordination (NHSRC). The regional drug inspectors (DIs) are responsible for
78 monitoring of drug prices in the pharmacies of their area. The NHSRC has been taking different
79 policy measures to curb these issues through Drug Regulatory Authority of Pakistan (DRAP). The
80 first ever National Drug Pricing Policy (NDPP) was launched in 2015 for making the pricing
81 mechanism transparent but it had minimal impact on medicine prices, suitable for both patients
82 and manufacturers as per media reports and available literature evidences [3, 9]. So, a new drug
83 pricing policy was launched in 2018[10]. The objectives of this policy were to improve the access
84 to essential medicines, devise rational prices, ensure a transparent mechanism for medicine pricing
85 and to discourage illegal increase in drug prices.

86 Many modifications have been made to the pricing strategies in the NDPP 2018 compared to
87 NDPP 2015, the most important one is the inclusion of all drugs (n=414) from National Essential
88 Medicines List (NEML) under scheduled drugs category where drugs are kept under strict price
89 control as compared to other drugs. Whereas in NDPP 2015, only 160 drugs from NEML were
90 enlisted in this category [9, 10]. In NDPP 2018, the annual adjustment in prices has been linked
91 with the Consumer Price Index (CPI), the Maximum Retail Prices (MRPs) of scheduled drugs (all
92 drugs from NEML) could be increased up to 70% of the CPI, whereas the MRPs of all other drugs
93 could be increased equivalent to CPI of the immediate preceding year. This step seems to improve
94 the affordability of essential medicines (EMs) for patients in Pakistan. If several generics are
95 already available in the market then in NDPP 2015, the MRP of new entrant was fixed by taking
96 the average of other generics, while in NDPP 2018, MRP will be fixed equivalent to the highest
97 MRP of the available generics [9, 10]. However, this would lead to even higher priced generics in
98 the market that could compromise patient's affordability. Some media reports are claiming that
99 the current increase (up to 200%) in medicines prices is the highest in the last 40 years, while
100 others are claiming that government is taking action against this illegal rise in medicine prices [11,
101 12]. But there is no objective evidence to prove or disapprove these claims. The NDPP 2018,
102 allows the MRPs of the New Chemical Entities (NCEs) to be fixed by using the External Reference
103 Pricing (ERP) mechanism by considering India, Bangladesh, Indonesia, Sri Lanka, Philippines,
104 Lebanon and Malaysia as reference countries. However, the reason behind using the MRPs of
105 these countries as reference is not clear, though some of them practice free market economy model

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3 106 and don't impose any price control measures over the MRPs in community pharmacies that may
4 107 lead to high prices. The NDPP 2018 also takes into account the wholesale or procurement prices
5 108 from British National Formulary, Australian Pharmaceutical Benefit Scheme and New Zealand
6 109 Pharmaceutical Management Agency while fixing the MRPs of NCEs, however these may not be
7 110 the true prices because discounts and rebates are given as a common practice, while making the
8 111 payments. So, these ambiguities in the policy necessitate the evaluation of actual impact of these
9 112 policies on the access to medicines in Pakistan.

12 113 In this context, we designed a study to measure the impact of new NDPP 2018 on access to
13 114 essential medicines in terms of their prices, availability and affordability in Lahore division
14 115 Punjab. We undertook a survey after the implementation of NDPP 2018 and compared it with a
15 116 similar survey performed before the launch of this policy in 2017. Considering the objectives of
16 117 the NDPP 2018, we hypothesized that it will improve the availability and affordability, meanwhile
17 118 decrease the prices of EMs.

20 21 119 **Methodology**

22 23 120 **Study Design**

24 121 Two cross-sectional studies were conducted in 2016-17 and 2019 using a variant of World Health
25 122 Organization/Health Action International (WHO/HAI) methodology in four districts of Lahore
26 123 division, Pakistan [13]. Since, the focus of this study was to measure the impact of NDPP 2018 in
27 124 terms of changes in medicines prices, availability and affordability after its implementation, thus,
28 125 the data on these parameters was collected to evaluate the accessibility of medicines in both years
29 126 [10]. The first survey was conducted from November 2016 to March 2017, while the second survey
30 127 was from March-May 2019, representing two fiscal years of Pakistan. For optimal and reliable
31 128 comparison, the list of medicines, survey region and survey outlets selected for the survey 2019
32 129 were similar to those selected for 2017. The details of survey region, medicine selection, sampling
33 130 of medicine outlets and data collection are given elsewhere and are briefly described in this paper
34 131 [7].

35 36 132 **Survey Areas**

37 133 Lahore is the largest division of Pakistan in terms of population i.e. 16.28 Million (2017) and
38 134 estimated to be 19.4 Million as of 2018[14]. It consists of four districts named as Lahore, Kasur,
39 135 Sheikhpura and Nankana Sahib which are further subdivided into 17 Tehsils. All the four districts
40 136 were selected for the surveys.

41 42 137 **Sampling of Medicine Outlets**

43 138 Medicine outlets or health facilities from both public and private sectors were sampled
44 139 systematically using WHO/HAI manual as a guiding principle in both the surveys [13]. Total 32
45 140 medicine outlets were surveyed (16 from public sector and 16 from private sector). From public
46 141 sector, hospitals from all three tiers of healthcare system i.e. primary, secondary and tertiary were
47 142 selected. One main hospital in each district was selected as a survey anchor along with additional
48 143 three more hospitals selected randomly and situated within three hours' drive from the main

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3 144 hospital. In this way, 4 hospitals were selected in each district making up a total of 16 hospitals
4 145 from Lahore division. From private sector, one registered pharmacy was selected situated within
5 146 10 kilometers range of each public sector hospital. So, a total of 16 pharmacies were selected from
6 147 Lahore division, i-e. 4 retail pharmacies from each district. It is important to note that each survey
7 148 unit, one hospital and one nearby pharmacy, was located in different Tehsils, so out of 17 Tehsils
8 149 of Lahore division, 16 were surveyed in both years.

11 150 **Selection of Medicines**

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13 151 50 medicines were selected for survey as per WHO/HAI methodology, which included all 14
14 152 medicines from WHO core global list of medicines and 36 supplementary medicines. The criterion
15 153 of selecting medicines for supplementary list was local disease burden and inclusion of medicines
16 154 in NEML [15].

18 155 **Data Collection**

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21 156 The data were collected using a data collection form by the trained data collectors. The data
22 157 collectors visited the health facilities and physically checked the medicines prices and availability
23 158 for both OBs and LPGs of each medicine and entered it into data collection forms. The data for
24 159 each year were entered separately in to the WHO/HAI workbook by using double data entry
25 160 process, to avoid any mistake [13]. The patient prices or the prices charged to patients were entered
26 161 into the forms for private sector only, since the medicines are provided free of charge in public
27 162 sector, in Pakistan. Thus, the availability of medicines was documented only for public sector
28 163 facility.

30 164 **Data Analysis**

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33 165 Data were analyzed by using WHO/HAI preprogrammed Excel workbook [13], IBM Statistical
34 166 Package for the Social Sciences (SPSS) version 22.0 and R version 3.5.1 (codenamed “Feather
35 167 Spray”).

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38 168 *The availability* was calculated as percentage of particular medicine available at each facility
39 169 on the day of data collection. The mean percentage availabilities were also calculated and
40 170 compared between different sectors (public and private), product types (OBs and LPGs) and
41 171 among different groups (global medicines, supplementary medicines, medicines from NEML,
42 172 medicines used to treat NCDs and IDs). Availability was documented as follows; absent: 0% of
43 173 facilities had surveyed enlisted medicines at the time of survey; Low: < 50% of facilities had the
44 174 surveyed enlisted medicines; fairly high: 50 -80% of facilities had surveyed enlisted medicines;
45 175 High: > 80% of facilities, survey enlisted medicines were found in most of the facilities [16, 17].

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48 176 *Medicine prices* were calculated as Median Unit Prices (MUPs) in Pakistani Rupees (PKR)
49 177 and were also compared with International Reference Prices (IRPs) to calculate the Median Price
50 178 Ratios (MPRs). The IRPs were obtained from Management Sciences for Health (MSH) drug price
51 179 indicator guide 2015[18]. An MPR of greater than 1 for public sector and greater than 2 for private
52 180 sector would lodge any medicine into high priced medicines category [7]. For comparing the prices
53 181 between two years, the MUPs from 2019 were deflated by 3.33%, taking 2017 as base year. 70%
54 182 of the CPI was used for calculating this deflation factor, because the medicine prices can be

183 increased annually by 70% of the CPI as per NDPP 2018 [19]. Whereas MPR was calculated as
184 follows:

185 $Median\ Price\ Ratio(MPR) = Median\ local\ unit\ price/International\ reference\ unit\ price$

186 *Affordability* for treatment of different common diseases with selected medicines was
187 calculated and compared in terms of Number of Days Wages (NDWs) required for a lowest paid
188 government employee to get the standard treatment courses. Whereas, if a patient had to spend
189 more than one day of his wage for treatment with a specific medicine in a month, that medicine
190 was considered unaffordable [13]. For affordability comparison, NDWs in two years, the prices in
191 2019 were not deflated because the salary has also been increased in 2019. So, the salary of the
192 lowest paid unskilled government worker was taken as 14000PKR per month (2016-17) and
193 15000PKR per month (2018-19) [20].

194 *Comparative analysis:* Two patient prices were required to be included in the comparative
195 analysis, one from 2017 and other from 2019. The difference in prices, availability and
196 affordability were computed as percentage changes for each product. The mean availability and
197 MUPs were also compared between different categories of medicines (NEML and non-NEML
198 medicines; global and supplementary medicines; medicines for IDs and NCDs) across the years.
199 We compared affordability in terms NDWs to get the standard treatment from the surveyed
200 medicines. These were also compared among medicines for different disease groups (asthma,
201 cardiovascular diseases, infectious diseases, brain disorders, diabetes, ulcer and arthritis; IDs and
202 NCDs). To identify whether the difference between MUPs, MPRs and NDWs was significant
203 across two years, we used Wilcoxon signed rank test. We took $p < 0.01$ as an indicator of significant
204 difference in all the statistical testing.

205 **Patient and Public Involvement**

206 Patients or the public were not involved in the design, or conduct, or reporting, or
207 dissemination of this study.

208 **Results**

209 **Availability of medicines**

210 The overall availability of surveyed medicines was improved in 2019 when compared with 2017,
211 except for LPGs in public sector, where it demonstrated reduction.

212 *Availability in Public Sector:* In public sector, the availability of both OBs and LPGs was
213 poor in both years. None of the mean availabilities touched the benchmark of 80%. The mean
214 percent availability of OBs improved from 6.8% to 33.1% whereas, in case of LPGs it reduced
215 from 35.1% to 9%. The individual percent availabilities of each medicine (OB and LPG) are given
216 in table S1. For better understanding of the data, we have used the data visualization tool in R and
217 plotted a box plot of the data as shown in figure 1. The box plot showed distributional
218 characteristics of the percent availability of medicines in two groups (OB and LPG) for the years
219 2017 and 2019. The mean percent availability is represented by the dot inside the box. In 2017,
220 availabilities of 75% of the OBs in public sector were less than 11.2% as shown by the 3rd quartile

221 or the upper bar of the 1st box plot. Whereas, in 2019, 75% of the OBs had availabilities higher
 222 than 6.3% which is almost equivalent to the mean percent availability (6.8%) in 2017. This
 223 indicates a substantial increase in the availability of OBs in public sector. In 2019, 75% of the
 224 LPGs had availability less than 12.5% (3rd quartile) whereas before the implementation of the
 225 NDPP 2018, 75% of the LPGs had availabilities greater than 14.3% (1st quartile). This showed a
 226 remarkable decrease in the availability of LPGs in public sector in 2019.

227 *Availability in private sector:* In both years, the overall availability was better in private sector
 228 than the public sector. Mean percent availability of both OBs and LPGs were improved in 2019
 229 i.e. 55.0% to 58.3% and 20.3% to 32.3%, respectively. Availability of LPGs was less than OBs in
 230 both years. For OBs, the mean percent availability improved slightly by 3.3% while data
 231 distribution remained almost the same across the years, as shown in the box plot (figure 1). For
 232 LPGs, a substantial increase in the availability was observed in terms of mean percent availability,
 233 maximum value and change in data distribution (figure 1). In 2017, the IQR (range between upper
 234 and lower bar of the box) for percentage availability of LPGs ranged from 6% to 31% whereas it
 235 got improved in 2019 and ranged from 6% to 50%.

236 *Availability in different subgroups of medicines:* When we compared availability of LPGs
 237 and OBs in different subgroups of medicines as shown in table 1, we found that mean percent
 238 availabilities of all global list medicines were higher than supplementary medicines in both years.
 239 Similarly, the availability of NEML medicines were higher than non-NEML medicines except for
 240 the non-NEML LPGs in public sector, which were higher than NEML LPGs (19.2% vs 8.1%). In
 241 2017, in public sector, the availability of OBs for NCD medicines (6.7%) were lower than OBs for
 242 ID medicines (7.7%) whereas the availability of LPGs (35.9%) were better than LPGs of ID
 243 medicines (33%). Surprisingly, in 2019, the situation inversed completely for NCD medicines,
 244 increased and decreased availability of OBs (33.2%) and LPGs (33.1%), respectively, whereas,
 245 the availability decreased for LPGs (8.8%) and increased for OBs (9.5%) for ID medicines.

246 **Table 1.** Mean Percent Availabilities of Originator Brands (OBs) and Lowest Price Generics
 247 (LPGs) at both public and private sectors.

	Availability in 2017 (Mean, SD) ,%				Availability in 2019 (Mean, SD) ,%				Change in mean percent availability (%)			
	Public Sector		Private Sector		Public Sector		Private Sector		Public Sector		Private Sector	
	OBs	LPGs	OBs	LPGs	OBs	LPG	OBs	LPG	OB	LPGs	OB	LPG
All medicines (n=50)	6.8 (10.4)	35.1 (23.6)	55 (31.1)	20.3 (14.4)	33.1 (27.8)	9 (14.9)	58.3 (32.3)	32.3 (26)	26.3	-26.1	3.3	12
Global Medicines (n=14)	11.2 (15.2)	50.1 (32.1)	64.3 (22.5)	25.9 (14.5)	48.4 (31.5)	14.3 (19.9)	66.5 (31.2)	43.8 (27.8)	37.2	-35.8	2.2	17.9
Supplementar y medicines (n=36)	5 (7.0)	29.2 (21.4)	51.4 (33)	18.1 (14)	27.2 (24.1)	7 (12.1)	55 (32.6)	27.8 (24.1)	22.2	-22.3	3.6	9.7

NEML medicines (n=46)	7.2 (10.7)	35.5 (26)	55.3 (31)	20.7 (14.6)	33.9 (28.1)	8.1 (15.1)	58.4 (32.9)	33.3 (26.3)	26.7	-27	3.1	12.6
Non-NEML medicines (n=4)	1.8 (3.0)	35.5 (34)	51.6 (36)	15.6 (11)	24.8 (25)	19.2 (7)	56.3 (28)	20.3 (21)	23	-16	4.7	4.7
NCD medicines (n=36)	6.4 (9.2)	35.9 (25.5)	55.7 (28.8)	20 (14.3)	33.2 (27)	8.8 (14)	62.3 (29.3)	31.3 (25)	26.8	-27.1	6.6	11.1
ID medicines (n=14)	7.7 (13.3)	33 (29)	53.1 (37.3)	21 (15)	33.1 (30.5)	9.5 (17.4)	47.8 (38.1)	34.8 (29.2)	25.4	-23.5	-5.3	13.8

248 Where, SD refers to Standard deviation, NEML refers to National Essential Medicine List, NCD
249 refers to Non Communicable Diseases and ID refers to Infectious Diseases.

250 *Availability at different levels of healthcare:* When we compared the availability at different
251 levels of public healthcare sectors i.e. primary, secondary and tertiary, the availability of OBs
252 improved in 2019, while it was decreased for LPGs. The pattern of overall medicines availability
253 remained almost the same as of 2017 i.e. tertiary care>secondary care>primary care as shown in
254 table S2.

255 Medicine Prices

256 An overall increase was noted in all adjusted MUPs and adjusted MPRs between 2017 and
257 2019 for both OBs and LPGs as shown in Table 2. In 2019, for all 42 available OBs, the adjusted
258 MUPs and MPRs significantly increased by a median of 4.3% (Wilcoxon test p=0.001, p=0.0001).
259 Whereas in case of all 37 available LPGs, the adjusted MUPs and MPRs were increased by a
260 median of 15.7% (p=0.002, p=0.0002). The MPRs of OBs ranged from 0.58 to 60.62 in 2017 and
261 0.73 to 77.59 in 2019. 63% of the OBs had MPR of more than 2 in 2017. Whereas, in 2019 almost
262 75% of the OBs had MPR greater than 2. The MPRs of LPGs ranged from 0.42 to 19.95 in 2017
263 and 0.39 to 19.89 in 2019. For LPGs in 2017, the median value of MPR was less than 2 (i.e. 1.36)
264 while in 2019 this median value became greater than 2 (i.e. 2.26). Which means many LPGs which
265 were previously affordable got shifted to the high priced medicines category in 2019. The MUPs
266 and MPRs for all OBs is given in table S3 and for all LPGs is given in table S4.

267
268 **Table 2.** Median price ratios (MPRs) and median unit prices (MUPs) of originator brands (OBs) and
269 lowest price generics (LPGs) in private sector among different subgroups across the years 2017 and 2019.

	Originator Brands (OBs)				
	MPR- 2017	MPR- 2019	MUP 2017 (PKR)	Adjusted MUP 2019 (PKR)	Median percent change in MUPs/MPR
All medicines (n=42)	2.5	3.2	6.99	8.49	4.29%
Global Medicines (n=13)	2.8	3.2	7.66	8.22	3.35%
Supplementary medicines (n=29)	2.5	3.3	6.38	10.1	5.1%

NEML medicines (n=39)	2.4	3.3	6.38	8.51	5.1%
Non-NEML medicines (n=3)	3	3.2	7.66	8.22	1.93%
NCD medicines (n=36)	2.6	3.3	6.19	7.83	3.35%
CD medicines (n=10)	2.3	2.9	24.3	31.2	7.36%
Lowest Price Generics (LPGs)					
	MPR- 2017	MPR- 2019	MUP 2017 (PKR)	Adjusted MUP 2019 (PKR)	Median percent change in MPR/MUP
All medicines (n=37)	1.4	2.3	5.8	6.29	15.7%
Global Medicines (n=13)	1.6	2.7	5.8	6.56	19.2%
Supplementary medicines (n=24)	1.3	2.2	5.9	6.04	14.8%
NEML medicines (n=34)	1.4	2.2	5.4	6	15.8%
Non-NEML medicines (n=3)	2.5	2.7	6.5	6.7	3.97%
NCD medicines (n=26)	1.2	2.2	4.1	5.4	16.3%
CD medicines (n=11)	1.8	2.4	8.4	10.9	14.8%

270 Where PKR is Pakistani Rupee.

271 The price data was also analyzed in different subgroups as shown in table 2. There was an
 272 increase in MUPs and MPRs for OBs of supplementary list of medicines compared to medicines
 273 from global list (5.5% vs 3.35%). However, it was inverse in case of LPGs, i.e. the prices of global
 274 medicines increased compared to supplementary medicines (19.2% vs 14.8%). Increment in prices
 275 of NEML medicines was more as compared to non-NEML medicines. Next, we compared
 276 medicines used for NCDs and IDs. Data suggested that the increase in the MUPs and MPRs of
 277 OBs for IDs was significant in comparison to NCDs (11.2% vs 7.36%). Whereas it was the
 278 opposite case for LPGs, where the increase was greater for NCD than ID medicines (16.3% vs
 279 14.8%). It is also noteworthy that increase in prices for LPGs is more significant than OBs for all
 280 subgroups of medicines.

281 Affordability

282 Between 2017 and 2019, the median NDWs required for treatment with all OBs (n=36)
 283 increased from 1.05 to 2 and 0.5 to 0.7 for all LPGs (n=31), respectively. In 2019, the median
 284 percent increase in NDWs for LPGs (n=31) was much higher as compared to OBs (n=36) i.e.
 285 12.5% (p=0.008) and 3% (p=0.081) respectively. So, an overall increase in NDWs for both OBs
 286 and LPGs was observed between 2017 and 2019. Similarly the Median Treatment Prices (MTPs)
 287 for OB and LPGs also increased significantly i.e. 464 PKR to 563 PKR (p<0.001) and 244 PKR

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288 to 350 PKR ($p < 0.001$), respectively. The MTPs and NDWs for each medicine are given in
289 supplementary tables S5 and S6. The medicines were categorized into seven disease groups to
290 further analyze the changes in affordability between 2017 and 2019. In figure 2, a bar graph shows
291 Median NDWs required for both OBs and LPGs in each disease group and the values above 1 are
292 considered unaffordable. In 2017, the median NDWs of OBs to treat three types of diseases i.e.
293 CVDs (1.2), diabetes (1.4) and ulcers (2.75) were more than 1. Whereas in 2019, medicines for
294 one more disease category made its place into this list i.e. the medicines for IDs (1.18). Compared
295 to 2017, the median NDWs for all OBs increased in 2019 except for OBs acting on Central Nervous
296 System (CNS) and OBs to treat ulcers. The treatment for ulcer remained highly unaffordable in
297 both years. The median NDWs for LPGs increased in 2019 for the treatment of Arthritis, CNS
298 disorders, CVDs and IDs, while the modest decrease in median NDWs for LPGs was observed for
299 some diseases i.e. asthma, diabetes and ulcers as shown in figure 2.

300

301 Discussion

302 This study gives a conscionable insight in to the effects of NDPP 2018 associated changes on
303 medicine prices, availability and affordability in both public and private healthcare sectors of
304 Lahore division, Pakistan. The main objective of this refined policy was to improve the access to
305 essential medicines (EMs) and improvise rational drug pricing. Our study has shown that the
306 overall availability of medicines improved in 2019 in comparison to 2017 i.e. before the
307 implementation of this policy, except for the LPGs in public sector, demonstrating reduction.
308 Overall the medicine prices were increased significantly, making majority of the EMs used for the
309 common ailments unaffordable, with a much higher price increases for LPGs in comparison to
310 OBs. The medicines used to treat ulcers, diabetes and CVDs remained most unaffordable in both
311 years. Thus, it can fairly be assumed that the current pricing policy, to some extent, ensures the
312 availability of medicines, nonetheless, significant policy refinements targeting essential medicines
313 are pivotal in making medicine prices affordable to patients.

314 Despite improvements in the availability of medicines between 2017 and 2019, the
315 availability of medicine remained below the optimal benchmark of 80% [13]. In public sector the
316 availability of OBs improved remarkably probably be due to decentralization procurement of
317 medicines in public sector. Before 2018, the medicines were procured centrally for all the public
318 sector hospitals except for teaching hospitals, within a province. But after 2018, the medicines
319 procurement was decentralized for public sector hospital to allow hospitals in each district a free
320 choice to select desired manufactures, thus, ending up in the selection of more OBs than LPGs,
321 possibly due to quality concerns about medicines. Another factor that improved medicines
322 availability after 2018 was authorization of hospitals to acquire medicines directly without any
323 delays. However, as practiced in the previous central supply system, the medicines were received
324 centrally from the manufacturers before reaching the concerned hospital with considerable effect
325 on timely availability of medicines. In both years, the mean percentage availabilities for all
326 medicines were found higher in the private sector compared to the public sector, corroborating
327 similar previous studies conducted in Bangladesh and Malawi in 2019 [21, 22]. The overall
328 availability of medicines from NEML was slightly better than non-NEML medicines in both public

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3 329 and private sectors. This might be attributed to the active role of DRAP in the revision and
4 330 subsequent dissemination of the revised NEML i.e. NEML 2018 [15]. Furthermore, the public
5 331 hospitals are encouraged to procure drugs from the latest NEML 2018 that has been standardized
6 332 in line with WHO essential medicines model list 2017 [23]. Besides, a mobile application was
7 333 launched in 2018 with user friendly interface to better disseminate the information on enlisted
8 334 medicines [24]. So, the NDPP 2018, doesn't seem to be solely responsible for the availability of
9 335 medicines.

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12 336 Although we found some improvements in the availability of medicines, there was a
13 337 substantial increase in medicine prices, making them inaccessible for most of the population.
14 338 According to one estimate approximately 46 million people are living below the national poverty
15 339 line in Pakistan (as per 2015) [8]. The increases in prices of both OBs and LPGs may fairly be
16 340 attributable to the NDPP 2018, that allows an annual increase in the prices of scheduled drugs up
17 341 to 70% of CPI compared to 50% of CPI as per NDPP 2015 [9, 10]. These changes in price
18 342 calculations seems to accentuate the substantial impact on overall prices of medicines, thus,
19 343 making them more expensive. The increase in LPGs prices were more significant as compared to
20 344 OBs suggesting that with already expensive OBs, the price increase in LPGs would impoverish
21 345 the overall access to medicines, imputable to the changes in formula for LPGs (new entrants) price
22 346 calculation. According to NDPP 2018, the MRP of new entrant first generic should be fixed at
23 347 20% less than that of OB compared with 30% less than MRP of OB as per NDPP 2015. Another
24 348 possible variable is the prior availability of generics in the market for price calculation, where,
25 349 according to NDPP2018, the MRP of a new entrant (LPGs) was fixed equal to the highest MRP
26 350 of the available generics in the market, while as per NDPP2015 practice, MRP was fixed by taking
27 351 the average of other generics in the market. Therefore, these changes in price calculating
28 352 mechanisms might have led to higher prices of many new LPGs in the market. Hence, contrary to
29 353 NDPP 2018's price steerage objectives, the increase in medicine prices was more distinct for
30 354 NEML medicines as compared to non-NEML medicines.

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37 355 Data from further analysis on affordability of standard treatment by selected OBs and LPGs
38 356 suggested that majority of the medicines have become more unaffordable in 2019. When the
39 357 affordability was compared for medicines of different disease groups, the three foremost
40 358 unaffordable OBs were ones for treatment of ulcers, diabetes and CVDs. Additionally, the
41 359 treatment for ulcers remained exceptionally unaffordable with OBs and LPGs in both years.
42 360 Nevertheless, the treatment of CVDs and diabetes with LPGs remained affordable in 2017 but the
43 361 NDWs for CVDs surpassed affordability threshold in 2019. Among the disease categories, NCDs
44 362 harbor the top three unaffordable slots. It is noteworthy, that the burden of NCDs is increasing
45 363 worldwide and is responsible for higher mortality rates than all other diseases combined [25-27].
46 364 The CVDs, diabetes, cancer and chronic respiratory diseases are responsible for about 80% of
47 365 these deaths [28]. Pakistan is among top 10 countries where prevalence of diabetes is very high.
48 366 Besides, one third of Pakistanis, above 45 years of age have hypertension [29-31]. Thus, the
49 367 unaffordability of the essential medicines for NCDs, such as CVDs and diabetes, has worse bearing
50 368 on affordability associated therapeutic outcomes that ultimately leads to increased morbidity and
51 369 mortality due to un-controlled disease.

370 Additionally, we also compared the median drug prices in 2019 with the prices
 371 published/allowed by DRAP in its latest Statutory Regulatory Orders (SROs). DRAP revised and
 372 published the maximum retail prices (MRPs) of about 1084 drugs on December 31, 2018 through
 373 SRO-1608, SRO-1609 and SRO-1610 [32]. Eighteen OBs from our study sample were part of
 374 these price revisions (table 3). Surprisingly, after comparing the MUPs of 18 selected OBs with
 375 prices allowed by the government, we found that most of the OBs, 14 out of 18, were sold at higher
 376 prices than the allowable prices – with median percent increase of 29.37%. These data suggested
 377 that these intentional malpractices by the drug sellers might be driven by poor price control
 378 regulation by price enforcement authorities. Therefore, the current drug pricing policy NDPP 2018,
 379 is not the sole reason for the price hike. Most probably main stakeholders in the drug supply chain
 380 are also contributing towards medicine inflated prices. Thus, it's reasonable to deduce that these
 381 factors may interfere with measuring the direct impact of current pricing policy.

382 **Table 3.** Maximum retail unit prices (MRPs) of Originator Brands (OBs) allowed by the
 383 government versus median unit prices (MUPs) found in private sector pharmacies.

Medicine Name	Strength (Dosage form)	Allowed Unit Price (PKR)	MUP 2019 (PKR)	Percentage difference
Aciclovir	200mg (tab)	52.6	75	42.5%
Amlodipine	5mg (tab)	8.5	13	52.9%
Amoxicillin	250mg (cap)	3.75	3.75	0%
Amoxicillin	500mg (cap)	5.58	8.75	56.8%
Atorvastatin	20mg (cap)	141.37	203.5	43.9%
Bisoprolol	5mg (tab)	15.35	16.72	8.9%
Carbamezipine	200mg (tab)	4	5	25%
Ceftriaxone	1g (inj)	783	783	0%
Ciprofloxacin	500mg (tab)	39.25	52.5	33.7%
Digoxin	0.25mg (tab)	1.75	2.68	53.1%
Fluconazole	200mg (cap)	425	585	37.6%
Insulin N	100IU (vial)	88.47	75.88	-14.2%
Insulin R	100IU (vial)	93.88	75.88	-19.1%
Methyldopa	250mg (tab)	7.71	8.1	5.05%
Omeprazole	20mg (cap)	42.9	52.29	21.8%
Propranolol	40mg (tab)	1.1	3.16	187.2%
Pyremethamine+Sulfadoxim	(25+500)mg (tab)	12.01	12.02	0.08%
Simvastatin	20mg (cap)	47.01	68	44.6%
Medians		27.3	34.505	29.3%

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 385 Although the formation of a national scale pricing policy is laudable but it seems to be a
 386 collection of drug price calculation formulas only. It could also include the mechanism for price
 387 monitoring, an aspect which seems to be one of the major reasons behind failure to achieve the

goals of NDPP 2018. Inclusion of WHO/HAI based surveys on regular basis could also be an option, in this case. The WHO has developed a mobile application named “WHO Essential Medicines and Health Products Price and Availability Monitoring (WHO EMP MedMon)”, which can be used to collect and analyze price and availability data from health care outlets. This application is based on standard WHO/HAI methodology and it can be used both online and offline, make it both time saving and cost effective [33]. The drug inspectors or a third party can be given this responsibility to monitor and report the prices using WHO EMP MedMon on a regular basis, ensuring the compliance by drug manufacturers and sellers to NDPP. There could be many other policy implications having an impact on drug pricing, availability and affordability. The procurement of medicines should be strictly based on the NEML. Clear cut mechanism for NEML based procurement should be devised and implemented specially in the public sector hospitals. Besides this, the hospital pharmacy and therapeutics committees must actively evaluate the safety, efficacy and cost-effectiveness of drugs before purchasing. Pharmaco-economic evaluations of drugs must be promoted by allocating research funds to experts. Not all drugs should be fully reimbursed in the hospitals, only essential medicines must be included in this list. Hence, the profits from other drugs can be used to purchase essential drugs when needed. Smooth functioning of the drug supply chain with proper quality control must be ensured. The current inflated prices would have a grave impact on the access to essential medicines, especially for the lower and middle income population in Pakistan. Thus, there is dire need to develop clearer evidence based and stringent price control policy, especially for essential medicines. Exempting or reducing taxes and tariffs on EMs and promotion of local generic manufacture by providing subsidies on raw materials may improve both the availability and affordability of these medicines. While using the External Reference Pricing (ERP) mechanism, the reference countries should be chosen critically e.g. countries with similar pharmaceutical market and economic status. For costly medicines, regressive markups must be encouraged over progressive markups. The drug prices must be monitored on regular basis using a validated and well-designed scientific methodology and pricing policy must be revised based on such evidences. The essential medicines for most prevalent diseases such as diabetes and CVDs must be preferentially made affordable by devising some specific pricing strategies for these medicines. Besides, efforts must be made to enforce the pricing policy effectively by introducing reward and punishment system to induce a healthy competition among the drug manufacturers and sellers.

Although, this study provides an objective evidence to the policy makers for improving the current pricing policies. It has some limitations as well. The study includes medicines with specific strengths and dosage forms to compare with IRPs. There might be other strengths/dosage forms of the surveyed medicines, available in the health facilities, so the availability of the medicines may be under estimated. The affordability was calculated for single medicine for each disease, whereas patients are usually taking more than one drug at a time – under-estimating the extent of affordability of a specific treatment for a specific disease. Moreover, the post survey was conducted after about a year from the launch of new drug pricing policy 2018, so the results do not reflect the long term impact of the policy. Further surveys could be conducted in future to gauge the long term effects of the policy as it was done by Fang et al in two such surveys conducted after the health reform in China [17].

430 In Conclusion, the availability of medicines has been improved after the launch of a new drug
431 pricing policy by Pakistani government but it is still poor, forcing the patients to buy medicines
432 from private sector at their own expense. The prices of both LPGs and OBs of EMs have increased
433 remarkably in 2019, when compared with 2017. The medicines to treat most prevalent non-
434 communicable diseases (diabetes and CVDs) have become more expensive and unaffordable. The
435 maximum retail prices of several originator brands have been illegally increased in the market,
436 adding more burden on patients' pockets. The pricing policy needs to be improved further to bring
437 a strict price control, especially on the EMs and on the medicines for most prevalent diseases.

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442 institutions, data collectors and partners from research area who made this research possible.

443 **Contributions**

444 AS, ZB and YF conceptualize the study. ZS, HS, AS and ZB designed methodology. ZS, HS, AS
445 trained the data collectors and obtained the data. YF provided resources and supervised the project.
446 ZS worked as survey area manager. MA, AHG, NA, FK and MZ did data cleaning, validation and
447 entry. AS, HS, CY, MJ analyzed the data. AS and HS wrote original draft. YF, ZB, ZS, CY and
448 MJ, WJ reviewed and edited the manuscript.

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452 **Competing Interests**

453 None

454 **Patient Consent for Publication**

455 Not Required

456 **Ethics Approval**

457 Ethics approval was obtained from the Medical Ethics Committee of Xi'an Jiaotong University
458 under study ID 2019-067.

459 **Data availability statement**

460 Further data will be available upon reasonable request from the first author (<https://orcid.org/0000-0002-4144-9272>).

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References

1. United Nations Development Group, United Nations. Statistical Division. Indicators for monitoring the millennium development goals: definitions, rationale, concepts and sources. United Nations Publications 2003:95.
2. World Health Organization. Medicine prices and access to medicines in the Eastern Mediterranean Region. 2007.
3. Lee KS, Shahidullah A, Zaidi ST, *et al*. The Crux of the Medicine Prices' Controversy in Pakistan. *Frontiers in pharmacology* 2017;8:504.
4. Kiani A, Qadeer A, Mirza Z, *et al*. Prices, availability and affordability of medicines in Pakistan. Geneva: Health Action International (HAI); 2006.
5. Zaidi S, Bigdeli M, Aleem N, *et al*. Access to essential medicines in Pakistan: policy and health systems research concerns. *PloS One* 2013;8:e63515.
6. Cameron A, Ewen M, Ross-Degnan D, *et al*. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. *The Lancet* 2009;373:240.
7. Saeed A, Saeed H, Saleem Z, *et al*. Evaluation of prices, availability and affordability of essential medicines in Lahore Division, Pakistan: A cross-sectional survey using WHO/HAI methodology. *PloS One* 2019;14:e0216122.
8. The World Bank. Poverty and Equity data portal. 2015. Available: <http://povertydata.worldbank.org/poverty/country/PAK>. [Accessed: 16 June 2019].
9. Costing and Pricing Division, Drug Regulatory Authority of Pakistan. Drug Pricing Policy 2015.
10. Costing and Pricing Division, Drug Regulatory Authority of Pakistan. Drug Pricing Policy 2018.
11. Durrani F. Increase in drug prices highest in last 40 years. The News 2019. Available: <https://www.thenews.com.pk/print/454864-increase-in-drug-prices-highest-in-last-40-years>. [Accessed: 3 September 2019].

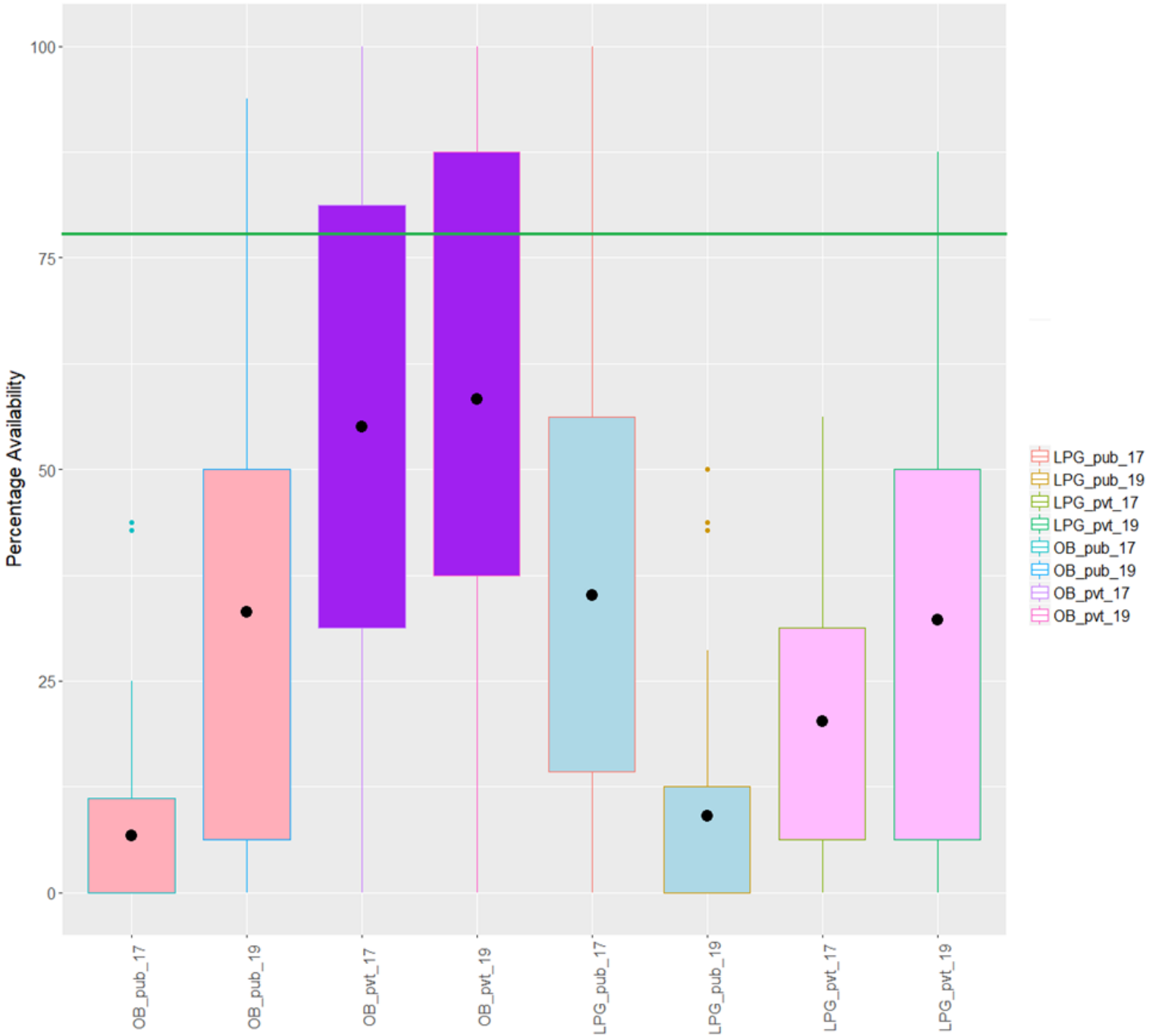
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2
3 491 12. Junaidi I. Minister orders crackdown on firms increasing medicine prices. DAWN
4 492 News 2019. Available: <https://www.dawn.com/news/1473573>. [Accessed: 3
5 493 September 2019].
6
7
8 494 13. World Health Organization. Measuring medicine prices, availability, affordability and
9 495 price components 2008.
10
11 496 14. Pakistan Bureau of Statistics. Population Census. 2017. Available:
12 497 <http://www.pbs.gov.pk/content/population-census>. [Accessed: 18 August 2019].
13
14 498 15. Drug Regulatory Authority of Pakistan. National Essential Medicines List. 2018.
15
16 499 16. Yang H, Dib HH, Zhu M, *et al*. Prices, availability and affordability of essential
17 500 medicines in rural areas of Hubei Province, China. *Health policy and planning*
18 501 2009;25:219.
19
20 502 17. Fang Y, Wagner AK, Yang S, *et al*. Access to affordable medicines after health reform:
21 503 evidence from two cross-sectional surveys in Shaanxi Province, western China. *The*
22 504 *Lancet Global Health* 2013;1:e227.
23
24 505 18. Management Sciences for Health. International Medical Products Price Guide 2015.
25
26 506 19. Pakistan Bureau of Statistics, Government of Pakistan. Price Statistics. Available:
27 507 [http://www.pbs.gov.pk/content/officially-published-consumer-prices-data-imf-](http://www.pbs.gov.pk/content/officially-published-consumer-prices-data-imf-template)
28 508 [template](http://www.pbs.gov.pk/content/officially-published-consumer-prices-data-imf-template). [Accessed 18 August 2019].
29
30 509 20. Wage Indicator Foundation. Minimum wages in Pakistan 2018. Available:
31 510 <https://wageindicator.org/Wageindicatorfoundation>. [Accessed 15 April 2019].
32
33 511 21. Kasonde L, Tordrup D, Naheed A, *et al*. Evaluating medicine prices, availability and
34 512 affordability in Bangladesh using World Health Organisation and Health Action
35 513 International methodology. *BMC health services research* 2019;19:383.
36
37 514 22. Khuluza F, Haeefele-Abah C. The availability, prices and affordability of essential
38 515 medicines in Malawi: A cross-sectional study. *PloS One* 2019;14:e0212125.
39
40 516 23. Jabri P. National essential medicine list -2018 to be implemented in all provinces:
41 517 Kiani. Business Recorder 2018. Available:
42 518 [https://www.brecorder.com/2018/10/06/444080/national-essential-medicine-list-](https://www.brecorder.com/2018/10/06/444080/national-essential-medicine-list-2018-to-be-implemented-in-all-provinces-kiani/)
43 519 [2018-to-be-implemented-in-all-provinces-kiani/](https://www.brecorder.com/2018/10/06/444080/national-essential-medicine-list-2018-to-be-implemented-in-all-provinces-kiani/) . [Accessed: 3 September 2019].
44
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47
48
49
50
51
52
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54
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56
57
58
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- 1
2
3 520 24. Govt. launches WHO backed national essential medicine list. Pakistan Today 2018.
4 Available: [https://www.pakistantoday.com.pk/2018/10/05/govt-launches-who-](https://www.pakistantoday.com.pk/2018/10/05/govt-launches-who-backed-national-essential-medicine-list/)
5 521 [backed-national-essential-medicine-list/](https://www.pakistantoday.com.pk/2018/10/05/govt-launches-who-backed-national-essential-medicine-list/). [Accessed: 3 September 2019].
6 522
7
8 523 25. Dans A, Ng N, Varghese C, *et al*. The rise of chronic non-communicable diseases in
9 southeast Asia: time for action. *The Lancet* 2011;377:680.
10 524
11 525 26. Siegel KR, Patel SA, Ali MK. Non-communicable diseases in South Asia:
12 contemporary perspectives. *British medical bulletin* 2014;111:31.
13 526
14 527 27. Habib SH, Saha S. Burden of non-communicable disease: global overview. *Diabetes*
15 *& Metabolic Syndrome: Clinical Research & Reviews* 2010;4:41.
16 528
17 529 28. World Health Organization. Global action plan for the prevention and control of non-
18 communicable diseases 2013-2020, 2013.
19 530
20 531 29. Ghaffar A, Reddy KS, Singhi M. Burden of non-communicable diseases in South Asia.
21 *BMJ* 2004;328:807.
22 532
23 533 30. Jafar TH, Haaland BA, Rahman A, *et al*. Non-communicable diseases and injuries in
24 Pakistan: strategic priorities. *The Lancet* 2013;381:2281.
25 534
26 535 31. Wasay M, Zaidi S, Jooma R. Non communicable diseases in Pakistan: burden,
27 challenges and way forward for health care authorities. *Journal of Pakistan Medical*
28 *Association* 2014; 64:1218.
29 536
30 537 32. Drug Regulatory Authority of Pakistan. SRO: Pricing division 2018. Available:
31 <https://www.dra.gov.pk/Home/Pricing>. [Accessed: 17 July 2019].
32 538
33 539 33. World Health Organization. MedMon - WHO Essential Medicines and Health Products
34 Price and Availability Monitoring Mobile Application. 2016. Available:
35 <https://www.who.int/medicines/areas/policy/monitoring/empmedmon/en/>
36 540
37 541 [Accessed: 30 March 2020].
38 542
39 543
40 544
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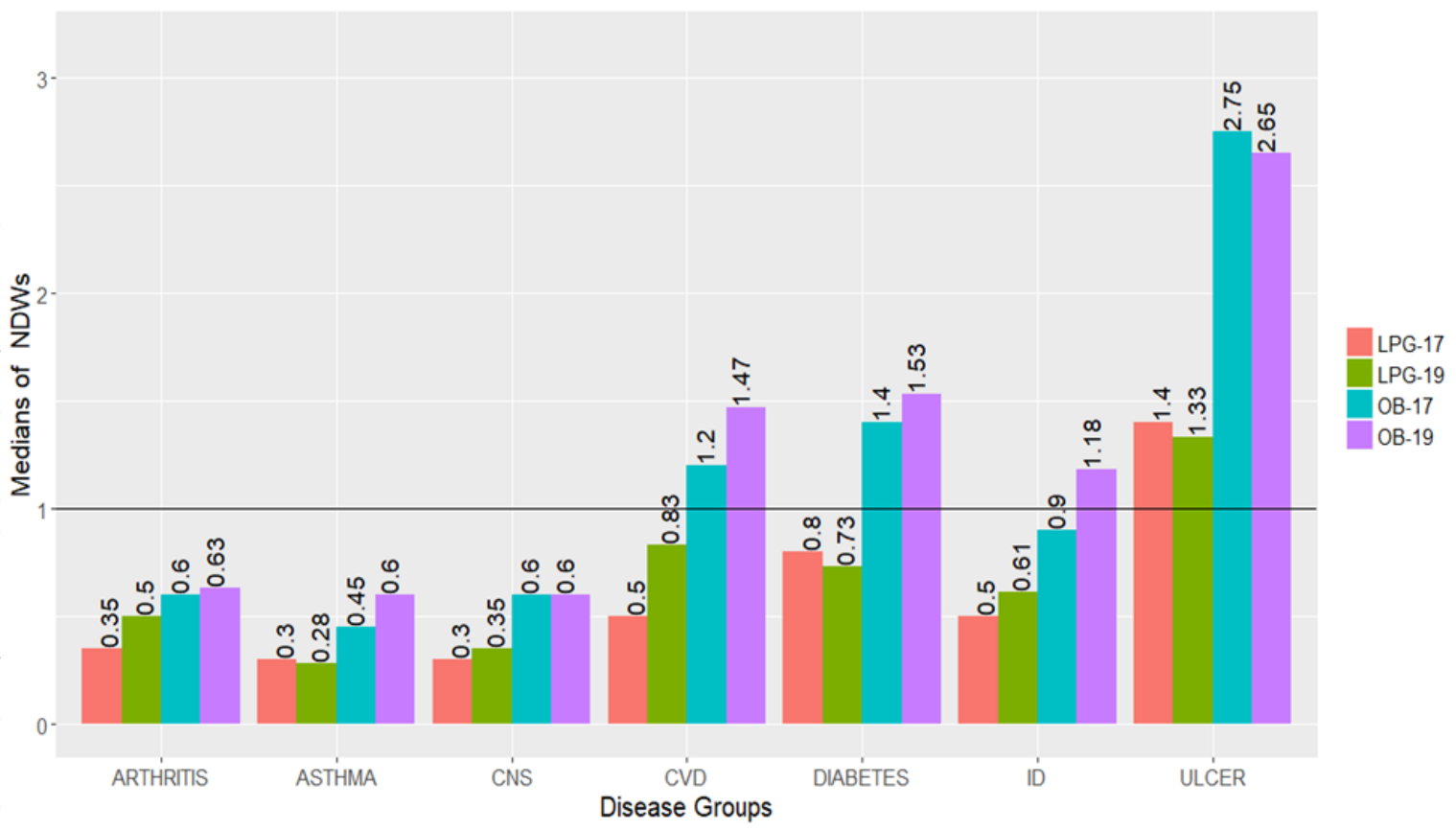
Figure 1. Box plot of percent availability of lowest price generics (LPGs) and originator brands (OBs) in both public (pub) and private (pvt) sectors in 2017 and 2019. This box plot shows the distributional characteristics of the percent availability of medicines in two groups (OB and LPG) for the years 2017 and 2019. The mean percent availability is represented by the dot inside the box.

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3 551 **Figure 2.** Bar graph of affordability of originator brands (OBs) and lowest price generics (LPGs)
4 552 for different diseases in both years i.e. 2017 and 2019.
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Supplementary Tables

Table S1. Percent availabilities and of originator brands (OBs) and lowest price generics (LPGs) of all medicines in public and private sector in 2017 and 2019 (%)

Names of meds	OB (Public) 2017	OB (Pvt.) 2017	LPG (Public) 2017	LPG (Pvt.) 2017	OB (Public) 2019	OB (Pvt) 2019	LPG (Public) 2019	LPG (pvt.) 2019
Acetylsalicylic Acid	0.0	25.0	56.3	25.0	18.8	75.0	50.0	18.8
Aciclovir	0.0	50.0	25.0	37.5	6.3	18.8	0.0	50.0
Amiodarone	7.1	62.5	21.4	6.3	0.0	62.5	21.4	0.0
Amitriptyline	0.0	31.3	0.0	25.0	0.0	0.0	50.0	50.0
Amlodipine	6.3	75.0	62.5	31.3	37.5	93.8	12.5	56.3
Amoxicillin	43.8	93.8	18.8	25.0	93.8	68.8	0.0	37.5
Amoxicillin (250)	18.8	100.0	12.5	31.3	50.0	87.5	0.0	37.5
Atenolol	12.5	87.5	81.3	43.8	43.8	81.3	0.0	56.3
Atorvastatin	7.1	50.0	21.4	25.0	42.9	62.5	21.4	18.8
Azithromycin	0.0	25.0	25.0	31.3	31.3	25.0	25.0	75.0
Beclometasone inhaler	0.0	6.3	35.7	12.5	35.7	43.8	0.0	0.0
Bisoprolol	6.3	87.5	18.8	25.0	37.5	81.3	0.0	56.3
Captopril	0.0	81.3	85.7	25.0	50.0	93.8	28.6	50.0
Carbamazepine	12.5	87.5	56.3	25.0	25.0	31.3	0.0	56.3
Ceftriaxone injection	14.3	68.8	71.4	31.3	21.4	75.0	50.0	87.5
Ciprofloxacin	0.0	81.3	100.0	37.5	64.3	93.8	14.3	25.0
Clarithromycin	0.0	87.5	35.7	25.0	50.0	93.8	0.0	56.3
Co-trimoxazole suspension	6.3	31.3	62.5	6.3	6.3	6.3	43.8	6.3
Diazepam	6.3	62.5	12.5	0.0	43.8	68.8	0.0	0.0
Diclofenac	42.9	50.0	35.7	6.3	85.7	93.8	0.0	81.3
Digoxin	21.4	62.5	28.6	0.0	28.6	68.8	0.0	56.3
Enalapril	0.0	68.8	62.5	18.8	12.5	68.8	12.5	50.0
Fluconazole	0.0	37.5	18.8	25.0	43.8	43.8	0.0	50.0
Fluoxetine	0.0	43.8	12.5	43.8	6.3	62.5	6.3	62.5
Fluphenazine Decanoate	0.0	0.0	0.0	12.5	0.0	0.0	7.1	6.3
Furosemide	12.5	93.8	50.0	6.3	50.0	87.5	0.0	0.0
Glibenclamide	18.8	68.8	56.3	12.5	68.8	93.8	0.0	12.5
Gliclazide	0.0	75.0	0.0	18.8	7.1	75.0	0.0	31.3
Hydrochlorothiazide	0.0	0.0	0.0	12.5	18.8	0.0	0.0	0.0
Indinavir	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Insulin Isophane (NPH)	0.0	75.0	50.0	25.0	56.3	68.8	0.0	18.8
Insulin Neutral Soluble (Regular)	0.0	68.8	50.0	25.0	68.8	68.8	0.0	18.8
Losartan	7.1	43.8	14.3	43.8	0.0	43.8	42.9	43.8
Lovastatin	0.0	0.0	6.3	0.0	6.3	37.5	12.5	0.0

Metformin	25.0	81.3	56.3	31.3	68.8	93.8	0.0	50.0
Methyldopa	12.5	81.3	25.0	0.0	75.0	68.8	0.0	0.0
Metronidazole	25.0	93.8	56.3	37.5	75.0	87.5	0.0	56.3
Nevirapine	0.0	0.0	14.3	0.0	0.0	0.0	0.0	0.0
Nifedipine Retard	0.0	75.0	28.6	12.5	0.0	31.3	14.3	12.5
Omeprazole	6.3	56.3	75.0	37.5	62.5	62.5	6.3	50.0
Omeprazole (10)	0.0	12.5	43.8	18.8	18.8	0.0	12.5	31.3
Paracetamol suspension	6.3	68.8	87.5	25.0	81.3	87.5	0.0	81.3
Phenytoin	0.0	6.3	12.5	6.3	0.0	50.0	6.3	0.0
Propranolol	12.5	68.8	12.5	6.3	18.8	87.5	0.0	25.0
Pyrimethamine with sulfadoxine	0.0	75.0	21.4	6.3	21.4	68.8	0.0	6.3
Ranitidine	0.0	81.3	31.3	25.0	50.0	100.0	0.0	50.0
Salbutamol inhaler	0.0	81.3	56.3	31.3	62.5	68.8	0.0	12.5
Simvastatin	0.0	25.0	21.4	56.3	0.0	37.5	7.1	25.0
Spironolactone	6.3	62.5	25.0	0.0	12.5	93.8	6.3	43.8
Zidovudine	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Mean availabilities	6.8	55.0	35.1	20.3	33.1	58.3	9.0	32.3

Table (S2). Change in availability at different levels of healthcare (Public Sector).

	Primary level (n=2 outlets)		Secondary level (n=13 outlets)		Tertiary level (n=1 outlet)	
	All medicines (n=50)		All medicines (n=50)		All medicines (n=50)	
	OB	LPG	OB	LPG	OB	LPG
Mean Availability 2017 (SD),%	0.0 (0.0)	25.8 (44.5)	7.1 (11.2)	35.2 (27.5)	12.0 (32.8)	50.0 (50.5)
Mean Availability 2019 (SD) ,%	21.0 (31.0)	3.2 (18)	32.3 (29.1)	7.4 (13.4)	68.0 (47.1)	22.0 (41.8)
Change in mean percent availability,%	21.0	-22.6	25.2	-27.8	56.0	-28.0

Table S3. Change in median unit prices (MUPs) and median price ratios (MPRs) of the Originator Brands (OBs) at private sector.

Sr. no.	Medicines (OB)	MUPs 2017 (PKR)	MPR 2017	Adjusted MUP in 2019	MPR 2019	Percentage change in MUPs/MPRs
1	Acetylsalicylic Acid	1.16	0.8	1.12	0.7	-3.41%
2	Aciclovir	70	20	72.5	21	3.48%
3	Amiodarone	17.78	2.2	17.4	2.2	-2.15%
4	Amlodipine	11.93	7.3	12.6	7.7	5.1%
5	Amoxicillin	8.616	2.8	8.46	2.7	-1.83%
6	Amoxicillin (250)	3.56	2.1	3.63	2.2	1.83%
7	Atenolol	6.19	5.6	6.14	5.5	-0.81%
8	Atorvastatin	201.9	18	197	18	-2.6%
9	Azithromycin	40	1.7	118	5	66.2%
10	Beclometasone inhaler	1.25	1.2	1.84	1.8	32%
11	Bisoprolol	11.28	1.2	16.2	1.7	30.2%
12	Captopril	7.66	3	8.22	3.2	6.81%
13	Carbamazepine	4.91	2.6	4.84	2.5	-1.55%
14	Ceftriaxone injection	672	16	757	18	11.2%
15	Ciprofloxacin	50.4	13	50.8	13	0.72%
16	Clarithromycin	65.7	2.5	76.4	2.9	14%
17	Co-trimoxazole suspension	0.29	0.6	0.44	0.9	33.4%
18	Diazepam	2	2	1.93	1.9	-3.41%
19	Diclofenac	5.625	12	5.61	12	-0.29%
20	Digoxin	2.52	2.4	2.59	2.5	2.76%
21	Enalapril	5.85	5.4	6	5.6	2.43%
22	Fluconazole	442	61	566	78	21.9%
23	Fluoxetine	43.42	9.7	43	9.6	-0.9%
24	Furosemide	1.89	3	2.34	3.7	19.2%
25	Glibenclamide	1.69	2.9	2.09	3.5	19.1%
26	Gliclazide	7.6	1.5	16.4	3.3	53.8%
27	Insulin Isophane (NPH)	64.5	1.1	73.4	1.3	12.1%
28	Insulin Neutral Soluble (Regular)	64.5	1.1	73.4	1.2	12.1%
29	Losartan	51.67	4.3	50.3	4.2	-2.76%
30	Metformin	1.54	1	1.62	1	5.21%
31	Methyldopa	6.38	1.9	7.83	2.3	18.5%
32	Metronidazole	1.57	1.3	1.52	1.2	-3.41%
33	Nifedipine Retard	5.69	2.7	5.8	2.8	1.93%
34	Omeprazole	49.78	34	50.6	35	1.55%
35	Paracetamol suspension	0.85	1.6	2.2	4.1	61.4%
36	Phenytoin	5.2	4.8	23.2	22	77.6%
37	Propranolol	1.55	2.2	3.06	4.3	49.3%

38	Pyrimethamine with sulfadoxine	5.83	1.4	11.6	2.8	49.8%
39	Ranitidine	8.8	3.7	8.51	3.6	-3.41%
40	Salbutamol inhaler	1	1	1.03	1.1	3.35%
41	Simvastatin	67.13	12	65.8	12	-2.09%
42	Spirolactone	8.6	0.8	10.1	1	14.5%
	Medians	6.99	2.5	8.49	3.2	4.29%

Table S4. Change in median unit prices (MUPs) and median price ratios (MPRs) of the lowest price generics (LPGs) in private sector.

Sr. no.	Medicines	MUPs 2017 (PKR)	MPR 2017	Adjusted MUP in 2019	MPR 2019	Percentage change in MUPs/MPRs
1	Acetylsalicylic Acid	1.015	0.7	1.06	0.7	4.58
2	Aciclovir	12.4	3.6	13.5	3.9	8.41
3	Amitriptyline	1.19	1.4	1.24	1.4	3.86
4	Amlodipine	1.8	1.1	6.29	3.8	71.4
5	Amoxicillin	5.8	1.9	8.32	2.7	30.3
6	Amoxicillin (250)	3	1.8	3.48	2.1	13.8
7	Atenolol	2.05	1.8	2.47	2.2	16.9
8	Atorvastatin	37.5	3.4	35.8	3.2	-4.8
9	Azithromycin	40	1.7	19.3	0.8	-107
10	Bisoprolol	6.55	0.7	6.56	0.7	0.1
11	Captopril	6.5	2.5	6.77	2.7	3.97
12	Carbamazepine	3.3	1.7	4.35	2.3	24.2
13	Ceftriaxone injection	280	6.8	290	7	3.48
14	Ciprofloxacin	11	2.8	24.2	6.2	54.5
15	Clarithromycin	36	1.4	42.7	1.6	15.8
16	Co-trimoxazole suspension	0.21	0.4	2.32	4.7	91
17	Diclofenac	3.5	7.5	4.79	10	26.9
18	Enalapril	2.05	1.9	2.84	2.6	27.8
19	Fluconazole	145.5	20	145	20	-0.3
20	Fluoxetine	13.8	3.1	13.5	3	-1.9
21	Fluphenazine Decanoate	90.5	1	93.8	1.1	3.5
22	Glibenclamide	1.57	2.7	1.42	2.4	-10
23	Gliclazide	4.75	0.9	5.8	1.1	18.1

24	Insulin Isophane (NPH)	48	0.8	62.3	1.1	22.9
25	Insulin Neutral Soluble (Regular)	48	0.8	62.3	1	22.9
26	Losartan	11	0.9	13.1	1.1	15.7
27	Metformin	1.5	1	1.86	1.2	19.2
28	Metronidazole	1.5	1.2	1.93	1.6	22.4
29	Nifedipine Retard	2.65	1.3	5.14	2.4	48.4
30	Omeprazole	15.35	10	11.4	7.8	-35
31	Omeprazole (10)	12.14	0.9	5.13	0.4	-137
32	Paracetamol suspension	0.47	0.9	1.02	1.9	53.7
33	Propranolol	0.66	0.9	2.03	2.8	67.5
34	Pyrimethamine with sulfadoxine	5	1.2	4.84	1.2	-3.4
35	Ranitidine	6.93	2.9	7.78	3.3	11
36	Salbutamol inhaler	0.64	0.7	0.68	0.7	5.45
37	Simvastatin	8.5	1.6	16.6	3	48.7
	Medians	5.8	1.4	6.29	2.3	15.7

Table S5. Affordability of originator brands (OBs) for different diseases in 2017 and 2019, in private sector.

Disease	Medicine	Strength	Dosage form	No. of units needed per treatment	Durati on of treatm ent	MTP 2017 (PKR)	NDWs 2017	MTP 2019 (PKR)	NDWs 2019
ASTHMA	Salbutamol Inhaler	100mcg/dose	Inhaler	200	As needed	200	0.4	214	0.4
	Beclomethasone	50mcg/dose	inhaler	200	As needed	250	0.5	380	0.8
Cardiovascular Diseases	Bisoprolol	5mg	tab	60	30	676.8	1.5	1003	2
	Atenolol	50mg	tab	30	30	185.7	0.4	190.5	0.4
	Captopril	25mg	tab	60	30	459.6	1	510	1
	Amlodipine	5mg	tab	60	30	715.8	1.5	780	1.6
	Amiodarone	200mg	tab	60	30	1066.8	2.3	1080	2.2
	Losartan	50mg	tab	60	30	3100.2	6.6	3120	6.2
	methyldopa	250mg	tab	90	30	574.2	1.2	729	1.5
Nifedipine retard	20mg	tab	90	30	512.1	1.1	540	1.1	

	Spironolactone	100mg	tab	30	30	258	0.5	312	0.6
	Propranolol	40mg	tab	90	30	139.5	0.3	284.4	0.6
	Acetylsalicylic acid	75mg	tab	30	30	34.8	0.1	34.8	0.1
Anti hyperlipide mics	Simvastatin	20mg	Cap/tab	30	30	2013.9	4.3	2040	4.1
	Atorvastatin	20mg	Cap/tab	30	30	6057	13	6105	12
Infections-Adult respiratory tract infection	Ceftriaxone Injection	1g/vial	Inj.	1	1	672	1.4	783	1.6
	Ciprofloxacin	500mg	tab	14	7	705.6	1.5	735	1.5
	Azithromycin	500mg	tab	3	3	120	0.3	367	0.7
	clarithromycin	500mg	tab	28	14	1839.6	3.9	2212	4.4
	Amoxicillin	500mg	cap	42	14	361.87	0.8	367.5	0.7
	Amoxicillin	250mg	cap	84	14	299.04	0.6	315	0.6
Fungal Infection	Fluconazole	200mg	cap	1	1	442	0.9	585	1.2
Viral Infection	aciclovir	200mg	tab	25	5	1750	3.8	1875	3.8
Amoebiasis	metronidazole	400mg	tab	21	7	32.97	0.1	32.97	0.1
CNS Drugs-Anti epileptics	Carbamezipine	200mg	tab	60	30	294.6	0.6	300	0.6
	Phenytoin	100mg	tab	90	30	468	1	2160	4.3
Anxiety	diazepam	5mg	tab	90	30	180	0.4	180	0.4
Anti Diabetics	Metformin	500mg	tab	90	30	138.6	0.3	151.2	0.3
	Glibenclamide	5mg	tab	90	30	152	0.3	194.4	0.4
	Gliclazide	80mg	tab	60	30	456	1.5	1020	2
	Insulin Isophane (NPH)	100IU/ml	vial	10	30	645	1.4	758.8	1.5
	Insulin Neutral Soluble (Regular)	100IU/ml	vial	10	30	645	1.4	758.8	1.5
Ulcer Treatment	Omeprazole	20mg	cap	30	30	1493.4	3.2	1569	3.1
	ranitidine	150mg	tab	120	30	1056	2.3	1056	2.1
Pain/Inflam mation Arthritis	Paracetamol	24mg/ml	susp	45	3	38.25	0.1	102.6	0.2
	Diclofenac	50mg	tab	90	30	506.25	1.1	522	1

Where, MTP: Median treatment price, NDWs: Number of days' wages

Table S6. Affordability of lowest price generics (LPGs) for different diseases in 2017 and 2019, in private sector.

Disease/Condition	Medicine	Strength	Dosage form	No. of units needed per treatment	Duration of treatment	MTP 2017 (PKR)	NDWs 2017	MTP 2019 (PKR)	NDWs 2019
ASTHMA	Salbutamol Inhaler	100mcg/dose	Inhaler	200	As needed	128	0.3	140	0.3
Cardiovascular Diseases/ Anti Hypertensives	Bisoprolol	5mg	tab	60	30	393	0.8	406.8	0.8
	Atenolol	50mg	tab	30	30	61.5	0.1	76.5	0.2
	Captopril	25mg	tab	60	30	390	0.8	420	0.8
	Amlodipine	5mg	tab	60	30	108	0.2	390	0.8
	Losartan	50mg	tab	60	30	660	1.4	810	1.6
	Nifedipine retard	20mg	tab	90	30	238.5	0.5	478.4	1
	Propranolol	40mg	tab	90	30	59.4	0.1	189	0.4
	Acetylsalicylic acid	75mg	tab	30	30	30.45	0.1	33	0.1
Anti hyperlipidemics	Simvastatin	20mg	Cap/tab	30	30	255	0.5	513.8	1
	Atorvastatin	20mg	Cap/tab	30	30	1125	2.4	1110	2.2
Infections-Adult respiratory tract infection	Ceftriaxone Injection	1g/vial	Inj.	1	1	280	0.6	300	0.6
	Ciprofloxacin	500mg	tab	14	7	154	0.3	350	0.7
	Azithromycin	500mg	tab	3	3	120	0.3	60	0.1
	clarithromycin	500mg	tab	28	14	1008	2.2	1238	2.5
	Amoxicillin	500mg	cap	42	14	243.6	0.5	361.2	0.7
	Amoxicillin	250mg	cap	84	14	252	0.5	302.4	0.6
Fungal Infection	Fluconazole	200mg	cap	1	1	145.5	0.3	150	0.3
Viral Infection	aciclovir	200mg	tab	25	5	310	0.7	350	0.7
Amoebiasis	metronidazole	400mg	tab	21	7	31.5	0.1	42	0.1
CNS Drugs-Anti epileptics	Carbamezipine	200mg	tab	60	30	198	0.4	270	0.5
Depression	Amitriptyline	25mg	tab	60	30	71.4	0.2	76.8	0.2

1	Anti Diabetics	Metformin	500mg	tab	90	30	135	0.3	180	0.4
2		Glibenclami	5mg	tab	90	30	141	0	132.3	0.3
3		de								
4		Gliclazide	80mg	tab	60	30	285	0.8	360	0.7
5		Insulin	100IU/ml	vial	10	30	480	1	644	1.3
6		Isophane								
7		(NPH)								
8		Insulin	100IU/ml	vial	10	30	480	1	644	1.3
9		Neutral								
10		Soluble								
11		(Regular)								
12	Ulcer Treatment	Omeprazole	20mg	cap	30	30	460.5	1	353.7	0.7
13		ranitidine	150mg	tab	120	30	831.6	1.8	966	1.9
14	Pain/Inflammati	Paracetamol	24mg/ml	susp	45	3	21.15	0	47.25	0.1
15	on									
16	Arthritis	Diclofenac	50mg	tab	90	30	315	0.7	445.5	0.9

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Research Checklist

Dear editor,

We submit the manuscript entitled “**Impact of National Drug Pricing Policy 2018 on Access to Medicines in Lahore Division, Pakistan: A Pre-Post Survey Study Using WHO/HAI Methodology**”, for your consideration to be published in *BMJ Open*. And we confirm that we have prepared submission materials according to the guideline.

And our main document has covered everything required, which including the following:

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		Supplementary material
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Impact of National Drug Pricing Policy 2018 on Access to Medicines in Lahore Division, Pakistan: A Pre-Post Survey Study Using WHO/HAI Methodology

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Impact of National Drug Pricing Policy 2018 on Access to Medicines in Lahore Division, Pakistan: A Pre-Post Survey Study Using WHO/HAI Methodology

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1 Abstract

2 **Objective:** To evaluate the impact of new national drug pricing policy (NDPP) 2018 on the access
3 to medicines in terms of prices, availability and affordability.

4 **Design:** Two cross-sectional surveys were undertaken before and after the launch of NDPP 2018,
5 using a modified WHO/HAI methodology.

6 **Setting:** Four districts of Lahore division, Pakistan.

7 **Participants:** 16 public sector hospitals and 16 private sector retail pharmacies.

8 **Measures:** The pre and post survey data on prices and availability of Lowest Price Generics
9 (LPGs) and Originator Brands (OBs) of 50 medicines were obtained by visiting the same public
10 and private sector health facilities (n=32). Out of 50, 46 surveyed medicines were from National
11 Essential Medicines List (NEML). Inflation-adjusted median unit prices (MUPs) and median price
12 ratios (MPRs) from 2019 were used for price comparison. Affordability was calculated in terms
13 of number of days' wages required to get a standard treatment by the lowest paid unskilled
14 government worker.

15 **Results:** The overall mean percent availabilities remained poor in both years i.e. far less than 80%.
16 In public sector, the mean percent availability of OBs improved from 6.8% to 33.1% whereas, in
17 case of LPGs it was reduced from 35.1% to 9%. In private sector, the mean percent availability of
18 both OBs and LPGs demonstrated slight improvements in 2019 i.e. 55.0% to 58.3% and 20.3% to
19 32.3%. The adjusted MUPs and MPRs of OBs significantly increased by a median of 4.29%
20 (Wilcoxon test $p=0.001$, $p=0.0001$). Whereas, the adjusted MUPs and MPRs of LPGs were
21 increased by a median of 15.7% ($p=0.002$, $p=0.0002$). Overall the affordability of many medicines
22 for common ailments reduced significantly in 2019.

23 **Conclusions:** The availability of medicines slightly improved, except in the case of LPGs which
24 was reduced at public sector. The implementation of NDPP 2018 led to increase in drug prices,
25 making the standard treatment for some of the most prevalent ailments unaffordable. So verily, the
26 drug pricing policy must be reviewed to ensure the access to essential medicines.

35 **Strengths and limitations of this study**

- 36 • This study is the first attempt to estimate the impact of a drug pricing policy, on the prices
37 of essential medicines in four districts of Lahore division, Pakistan using validated
38 WHO/HAI methodology.
- 39 • The data were collected from the same health facilities in both years to make the
40 comparison of results reliable.
- 41 • This study provides an objective evidence to the policy makers, in terms of impact of NDPP
42 2018 on access to medicines, for improving the current pricing policies.
- 43 • The study is limited to only one division of Pakistan, although the medicine prices are fixed
44 centrally and are supposed to be the same across the country – affecting generalizability of
45 the findings.
- 46 • The cross-sectional design of the study might not reflect the long term impact of NDPP
47 2018 - the average monthly, quarterly or yearly availability of medicines at individual
48 outlets.

64 Introduction

65 Access to affordable and quality assured essential medicines is considered as a key component of
66 an effective healthcare system. It has also been pledged under Sustainable Development Goal
67 (SDG) 3 by United Nations (UN) that the equitable access to affordable essential medicines will
68 be ensured as a basic human right [1, 2]. Pakistani government, like many other Low and Middle
69 Income Countries (LMICs), has been grappling with the issue of high medicine prices and poor
70 availability of medicines that compromises the accessibility of medicines [1, 3-6]. In Pakistan, the
71 medicines are provided free of cost at public sector health facilities, while patient pays out of
72 pocket to get medicines from private sector [5]. In fact, the poor availability of medicines at public
73 sector compels the patients to buy medicines from the private sector that escalates the burden on
74 patient's pocket, as 24.3% (in 2015) of the population is living below the national poverty line [3,
75 4, 7, 8]. Besides, medicine prices have increased up to 100%, both legally or illegally, in the past
76 few years [3]. The drug prices are fixed by the federal government and the National Health Services
77 Regulation and Coordination (NHSRC). The regional drug inspectors (DIs) are responsible for
78 monitoring of drug prices in the pharmacies of their area. The NHSRC has been taking different
79 policy measures to curb these issues through Drug Regulatory Authority of Pakistan (DRAP). The
80 first ever National Drug Pricing Policy (NDPP) was launched in 2015 for making the pricing
81 mechanism transparent but it had minimal impact on medicine prices, suitable for both patients
82 and manufacturers as per media reports and available literature evidences [3, 9]. So, a new drug
83 pricing policy was launched in 2018[10]. The objectives of this policy were to improve the access
84 to essential medicines, devise rational prices, ensure a transparent mechanism for medicine pricing
85 and to discourage illegal increase in drug prices.

86 Many modifications have been made to the pricing strategies in the NDPP 2018 compared to
87 NDPP 2015, importantly the inclusion of all drugs (n=414) from National Essential Medicines List
88 (NEML) under scheduled drugs category where the drugs are kept under strict price control as
89 compared to other drugs. Whereas in NDPP 2015, only 160 drugs from NEML were enlisted in
90 this category [9, 10]. In NDPP 2018, the annual adjustment in prices has been linked with the
91 Consumer Price Index (CPI), the Maximum Retail Prices (MRPs) of scheduled drugs (all drugs
92 from NEML) could be increased up to 70% of the CPI, whereas the MRPs of all other drugs could
93 be increased equivalent to CPI of the immediate preceding year. This step seems to improve the
94 affordability of essential medicines (EMs) for patients in Pakistan. If several generics are already
95 available in the market then in NDPP 2015, the MRP of new entrant was fixed by taking the
96 average of other generics, while in NDPP 2018, MRP will be fixed equivalent to the highest MRP
97 of the available generics [9, 10]. However, this would lead to even higher priced generics in the
98 market that could compromise patient's affordability. Some media reports are claiming that the
99 current increase (up to 200%) in medicines prices is the highest in the last 40 years, while others
100 are claiming that government is taking action against this illegal rise in medicine prices [11, 12].
101 But there is no objective evidence to prove or disapprove these claims. The NDPP 2018, allows
102 the MRPs of the New Chemical Entities (NCEs) to be fixed by using the External Reference
103 Pricing (ERP) mechanism by considering India, Bangladesh, Indonesia, Sri Lanka, Philippines,
104 Lebanon and Malaysia as reference countries. However, the reason behind using the MRPs of
105 these countries as reference is not clear, though some of them practice free market economy model

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3 106 and don't impose any price control measures over the MRPs in community pharmacies that may
4 107 lead to high prices. The NDPP 2018 also takes into account the wholesale or procurement prices
5 108 from British National Formulary, Australian Pharmaceutical Benefit Scheme and New Zealand
6 109 Pharmaceutical Management Agency while fixing the MRPs of NCEs, however these may not be
7 110 the true prices because discounts and rebates are given as a common practice, while making the
8 111 payments. So, these ambiguities in the policy necessitate the evaluation of actual impact of these
9 112 policies on the access to medicines in Pakistan.

12
13 113 In this context, we designed a study to measure the impact of new NDPP 2018 on access to
14 114 essential medicines in terms of their prices, availability and affordability in Lahore division
15 115 Punjab. We undertook a survey after the implementation of NDPP 2018 and compared it with a
16 116 similar survey performed before the launch of this policy in 2017. Considering the objectives of
17 117 the NDPP 2018, we hypothesized that it will improve the availability and affordability, meanwhile
18 118 decrease the prices of EMs.

20 21 119 **Methodology**

22 23 120 **Study Design**

24
25 121 Two cross-sectional studies were conducted in 2016-17 and 2019 using a variant of World Health
26 122 Organization/Health Action International (WHO/HAI) methodology in four districts of Lahore
27 123 division, Pakistan [13]. Since, the focus of this study was to measure the impact of NDPP 2018 in
28 124 terms of changes in medicines prices, availability and affordability after its implementation,
29 125 therefore, the data on these parameters was collected to evaluate the accessibility of medicines in
30 126 both years [10]. The first survey was conducted from November 2016 to March 2017, while the
31 127 second survey was from March-May 2019, representing two fiscal years of Pakistan. For optimal
32 128 and reliable comparison, the list of medicines, survey region and survey outlets selected for the
33 129 survey 2019 were similar to those selected for 2017. The details of survey region, medicine
34 130 selection, sampling of medicine outlets and data collection are given elsewhere and are briefly
35 131 described in this paper [7].

36 37 132 **Survey Areas**

38
39 133 Pakistan consists of four provinces which are sub-divided into several administrative units called
40 134 "divisions", each division is further sub-divided into districts, and districts into tehsils. Lahore is
41 135 the largest division of Pakistan in terms of population i.e. 16.28 Million (2017) and estimated to
42 136 be 19.4 Million as of 2018 [14]. It consists of four districts named as Lahore, Kasur, Sheikhpura
43 137 and Nankana Sahib and 17 Tehsils. All the four districts were selected for the surveys.

44 45 138 **Sampling of Medicine Outlets**

46
47 139 Medicine outlets or health facilities from both public and private sectors were sampled
48 140 systematically using WHO/HAI manual as a guiding principle in both the surveys [13]. Total 32
49 141 medicine outlets were surveyed (16 from public sector and 16 from private sector). From public
50 142 sector, hospitals from all three tiers of healthcare system i.e. primary, secondary and tertiary were
51 143 selected. One main hospital in each district was selected as a survey anchor along with additional

144 three more hospitals selected randomly and situated within three hours' drive from the main
145 hospital. In this way, 4 hospitals were selected in each district making up a total of 16 hospitals
146 from Lahore division. From private sector, one registered pharmacy was selected situated within
147 10 kilometers range of each public sector hospital. So, a total of 16 pharmacies were selected from
148 Lahore division, i-e. 4 retail pharmacies from each district. It is important to note that each survey
149 unit, one hospital and one nearby pharmacy, was located in different Tehsils, so out of 17 Tehsils
150 of Lahore division, 16 were surveyed in both years.

151 **Selection of Medicines**

152 50 medicines were selected for survey as per WHO/HAI methodology, which included all 14
153 medicines from WHO core global list of medicines and 36 supplementary medicines. The criterion
154 of selecting medicines for supplementary list was local disease burden and inclusion of medicines
155 in NEML [15].

156 **Data Collection**

157 The data were collected using a data collection form by the trained data collectors. The data
158 collectors visited the health facilities and physically checked the medicines prices and availability
159 for both OBs and LPGs of each medicine and entered it into data collection forms. The data for
160 each year were entered separately in to the WHO/HAI workbook by using double data entry
161 process, to avoid any mistake [13]. The patient prices or the prices charged to patients were entered
162 into the forms for private sector only, since the medicines are provided free of charge in public
163 sector, in Pakistan. Thus, the availability of medicines was documented only for public sector
164 facility.

165 **Data Analysis**

166 Data were analyzed by using WHO/HAI preprogrammed Excel workbook [13], IBM Statistical
167 Package for the Social Sciences (SPSS) version 22.0 and R version 3.5.1 (codenamed "Feather
168 Spray").

169 *The availability* was calculated as percentage of particular medicine available at each facility
170 on the day of data collection. The mean percentage availabilities were also calculated and
171 compared between different sectors (public and private), product types (OBs and LPGs) and
172 among different groups (global medicines, supplementary medicines, medicines from NEML,
173 medicines used to treat NCDs and IDs). Availability was documented as follows; absent: 0% of
174 facilities had surveyed enlisted medicines at the time of survey; Low: < 50% of facilities had the
175 surveyed enlisted medicines; fairly high: 50 -80% of facilities had the surveyed enlisted medicines;
176 High: > 80% of facilities, survey enlisted medicines were found in most of the facilities [16, 17].

177 *Medicine prices* were calculated as Median Unit Prices (MUPs) in Pakistani Rupees (PKR)
178 and were also compared with International Reference Prices (IRPs) to calculate the Median Price
179 Ratios (MPRs). The IRPs were obtained from Management Sciences for Health (MSH) drug price
180 indicator guide 2015[18]. An MPR of greater than 1 for public sector and greater than 2 for private
181 sector would lodge any medicine into high priced medicines category [7]. For comparing the prices
182 between two years, the MUPs from 2019 were deflated by 3.33%, taking 2017 as base year. 70%

183 of the CPI was used for calculating this deflation factor, because the medicine prices can be
184 increased annually by 70% of the CPI as per NDPP 2018 [19]. Whereas MPR was calculated as
185 follows:

186 *Median Price Ratio(MPR) = Median local unit price/International reference unit price*

187 *Affordability* for treatment of different common diseases with selected medicines was
188 calculated and compared in terms of Number of Days Wages (NDWs) required for a lowest paid
189 government employee to get the standard treatment courses. Whereas, if a patient had to spend
190 more than one day of his wage for treatment with a specific medicine in a month, that medicine
191 was considered unaffordable [13]. For affordability comparison, NDWs in two years, the prices in
192 2019 were not deflated because the salary has also been increased in 2019. So, the salary of the
193 lowest paid unskilled government worker was taken as 14000PKR per month (2016-17) and
194 15000PKR per month (2018-19) [20].

195 *Comparative analysis:* Two patient prices were required to be included in the comparative
196 analysis, one from 2017 and other from 2019. The difference in prices, availability and
197 affordability were computed as percentage changes for each product. The mean availability and
198 MUPs were also compared between different categories of medicines (NEML and non-NEML
199 medicines; global and supplementary medicines; medicines for IDs and NCDs) across the years.
200 We compared affordability in terms NDWs to get the standard treatment from the surveyed
201 medicines. These were also compared among medicines for different disease groups (asthma,
202 cardiovascular diseases, infectious diseases, brain disorders, diabetes, ulcer and arthritis; IDs and
203 NCDs). To identify whether the difference between MUPs, MPRs and NDWs was significant
204 across two years, we used Wilcoxon signed rank test. We took $p < 0.01$ as an indicator of significant
205 difference in all the statistical testing.

206 **Patient and Public Involvement**

207 Patients or the public were not involved in the design, or conduct, or reporting, or
208 dissemination of this study.

209 **Results**

210 **Availability of medicines**

211 The overall availability of surveyed medicines was improved in 2019 when compared with 2017,
212 except for LPGs in public sector, where it demonstrated reduction.

213 *Availability in Public Sector:* In public sector, the availability of both OBs and LPGs was
214 poor in both years. None of the mean availabilities touched the benchmark of 80%. The mean
215 percent availability of OBs improved from 6.8% to 33.1%, whereas, in case of LPGs it reduced
216 from 35.1% to 9%. The individual percent availabilities of each medicine (OB and LPG) are given
217 in table S1. For better understanding of the data, we have used the data visualization tool in R and
218 plotted a box plot of the data as shown in figure 1. The box plot showed distributional
219 characteristics of the percent availability of medicines in two groups (OB and LPG) for the years
220 2017 and 2019. The mean percent availability is represented by the dot inside the box. In 2017,

221 availabilities of 75% of the OBs in public sector were less than 11.2% as shown by the 3rd quartile
 222 or the upper bar of the 1st box plot. Whereas, in 2019, 75% of the OBs had availabilities higher
 223 than 6.3% which is almost equivalent to the mean percent availability (6.8%) in 2017. This
 224 indicates a substantial increase in the availability of OBs in public sector. In 2019, 75% of the
 225 LPGs had the availability of less than 12.5% (3rd quartile) whereas before the implementation of
 226 the NDPP 2018, 75% of the LPGs had availabilities of more than 14.3% (1st quartile). This showed
 227 a remarkable decrease in the availability of LPGs in public sector in 2019.

228 *Availability in private sector:* In both years, the overall availability was better in private sector
 229 than the public sector. Mean percent availability of both OBs and LPGs were improved in 2019
 230 i.e. 55.0% to 58.3% and 20.3% to 32.3%, respectively. Availability of LPGs was less than OBs in
 231 both years. For OBs, the mean percent availability improved slightly by 3.3% while data
 232 distribution remained almost the same across the years, as shown in the box plot (figure 1). For
 233 LPGs, a substantial increase in the availability was observed in terms of mean percent availability,
 234 maximum value and change in data distribution (figure 1). In 2017, the IQR (range between upper
 235 and lower bar of the box) for percentage availability of LPGs ranged from 6% to 31% whereas it
 236 got improved in 2019 and ranged from 6% to 50%.

237 *Availability in different subgroups of medicines:* When we compared availability of LPGs
 238 and OBs in different subgroups of medicines as shown in table 1, we found that mean percent
 239 availabilities of all global list medicines were higher than supplementary medicines in both years.
 240 Similarly, the availability of NEML medicines were higher than non-NEML medicines except for
 241 the non-NEML LPGs in public sector, which were higher than NEML LPGs (19.2% vs 8.1%). In
 242 2017, in public sector, the availability of OBs for NCD medicines (6.7%) were lower than OBs for
 243 ID medicines (7.7%), whereas the availability of LPGs (35.9%) were better than LPGs of ID
 244 medicines (33%). Surprisingly, in 2019, the situation inversed completely for NCD medicines,
 245 increased and decreased availability of OBs (33.2%) and LPGs (33.1%), respectively, whereas,
 246 the availability decreased for LPGs (8.8%) and increased for OBs (9.5%) for ID medicines.

247 **Table 1.** Mean Percent Availabilities of Originator Brands (OBs) and Lowest Price Generics
 248 (LPGs) at both public and private sectors.

	Availability in 2017 (Mean, SD) ,%				Availability in 2019 (Mean, SD) ,%				Change in mean percent availability (%)			
	Public Sector		Private Sector		Public Sector		Private Sector		Public Sector		Private Sector	
	OBs	LPGs	OBs	LPGs	OBs	LPGs	OBs	LPGs	OBs	LPGs	OBs	LPGs
All medicines (n=50)	6.8 (10.4)	35.1 (23.6)	55 (31.1)	20.3 (14.4)	33.1 (27.8)	9 (14.9)	58.3 (32.3)	32.3 (26)	26.3	-26.1	3.3	12
Global Medicines (n=14)	11.2 (15.2)	50.1 (32.1)	64.3 (22.5)	25.9 (14.5)	48.4 (31.5)	14.3 (19.9)	66.5 (31.2)	43.8 (27.8)	37.2	-35.8	2.2	17.9
Supplementar y medicines (n=36)	5 (7.0)	29.2 (21.4)	51.4 (33)	18.1 (14)	27.2 (24.1)	7 (12.1)	55 (32.6)	27.8 (24.1)	22.2	-22.3	3.6	9.7

NEML medicines (n=46)	7.2 (10.7)	35.5 (26)	55.3 (31)	20.7 (14.6)	33.9 (28.1)	8.1 (15.1)	58.4 (32.9)	33.3 (26.3)	26.7	-27	3.1	12.6
Non-NEML medicines (n=4)	1.8 (3.0)	35.5 (34)	51.6 (36)	15.6 (11)	24.8 (25)	19.2 (7)	56.3 (28)	20.3 (21)	23	-16	4.7	4.7
NCD medicines (n=36)	6.4 (9.2)	35.9 (25.5)	55.7 (28.8)	20 (14.3)	33.2 (27)	8.8 (14)	62.3 (29.3)	31.3 (25)	26.8	-27.1	6.6	11.1
ID medicines (n=14)	7.7 (13.3)	33 (29)	53.1 (37.3)	21 (15)	33.1 (30.5)	9.5 (17.4)	47.8 (38.1)	34.8 (29.2)	25.4	-23.5	-5.3	13.8

249 Where, SD refers to Standard deviation, NEML refers to National Essential Medicine List, NCD
250 refers to Non Communicable Diseases and ID refers to Infectious Diseases.

251 *Availability at different levels of healthcare:* When we compared the availability at different
252 levels of public healthcare sectors i.e. primary, secondary and tertiary, the availability of OBs
253 improved in 2019, while it was decreased for LPGs. The pattern of overall medicines availability
254 remained almost the same as of 2017 i.e. tertiary care>secondary care>primary care as shown in
255 table S2.

256 Medicine Prices

257 An overall increase was noted in all adjusted MUPs and adjusted MPRs between 2017 and
258 2019 for both OBs and LPGs as shown in Table 2. In 2019, for all 42 available OBs, the adjusted
259 MUPs and MPRs significantly increased by a median of 4.3% (Wilcoxon test p=0.001, p=0.0001).
260 Whereas in case of all 37 available LPGs, the adjusted MUPs and MPRs were increased by a
261 median of 15.7% (p=0.002, p=0.0002). In 2017, the MPRs of OBs ranged from 0.58 to 60.62 in
262 2017 and 0.73 to 77.59 in 2019. 63% of the OBs had MPR of more than 2. Whereas, in 2019
263 almost 75% of the OBs had MPR greater than 2. The MPRs of LPGs ranged from 0.42 to 19.95 in
264 2017 and 0.39 to 19.89 in 2019. In 2017, for LPGs, the median value of MPR was less than 2 (i.e.
265 1.36) while in 2019 this median value became greater than 2 (i.e. 2.26). This means that many
266 LPGs which were previously affordable got shifted to the high priced medicines category in 2019.
267 The MUPs and MPRs for all OBs is given in table S3 and for all LPGs is given in table S4.

268 **Table 2.** Median price ratios (MPRs) and median unit prices (MUPs) of originator brands (OBs) and
269 lowest price generics (LPGs) in private sector among different subgroups across the years 2017 and 2019.

	Originator Brands (OBs)				
	MPR- 2017	MPR- 2019	MUP 2017 (PKR)	Adjusted MUP 2019 (PKR)	Median percent change in MUPs/MPR
All medicines (n=42)	2.5	3.2	6.99	8.49	4.29%
Global Medicines (n=13)	2.8	3.2	7.66	8.22	3.35%
Supplementary medicines (n=29)	2.5	3.3	6.38	10.1	5.1%
NEML medicines	2.4	3.3	6.38	8.51	5.1%

(n=39) Non-NEML medicines	3	3.2	7.66	8.22	1.93%
(n=3) NCD medicines	2.6	3.3	6.19	7.83	3.35%
(n=36) CD medicines	2.3	2.9	24.3	31.2	7.36%
(n=10)					
Lowest Price Generics (LPGs)					
	MPR- 2017	MPR- 2019	MUP 2017 (PKR)	Adjusted MUP 2019 (PKR)	Median percent change in MPR/MUP
All medicines (n=37)	1.4	2.3	5.8	6.29	15.7%
Global Medicines (n=13)	1.6	2.7	5.8	6.56	19.2%
Supplementary medicines (n=24)	1.3	2.2	5.9	6.04	14.8%
NEML medicines (n=34)	1.4	2.2	5.4	6	15.8%
Non-NEML medicines (n=3)	2.5	2.7	6.5	6.7	3.97%
NCD medicines (n=26)	1.2	2.2	4.1	5.4	16.3%
CD medicines (n=11)	1.8	2.4	8.4	10.9	14.8%

270 Where PKR is Pakistani Rupee.

271 The price data was also analyzed in different subgroups as shown in table 2. There was an
 272 increase in MUPs and MPRs for OBs of supplementary list of medicines compared to medicines
 273 from global list (5.5% vs 3.35%). However, it was inverse in case of LPGs, i.e. the prices of global
 274 medicines increased compared to supplementary medicines (19.2% vs 14.8%). Increment in the
 275 prices of NEML medicines was more as compared to non-NEML medicines. Next, we compared
 276 the medicines used for NCDs and IDs. Data suggested that the increase in the MUPs and MPRs of
 277 OBs for IDs was significant in comparison to NCDs (11.2% vs 7.36%). Whereas it was completely
 278 opposite in the case of LPGs, where the increase was greater for NCD than ID medicines (16.3%
 279 vs 14.8%). It is also noteworthy that increase in prices for LPGs is more significant than OBs for
 280 all subgroups of medicines.

281 Affordability

282 Between 2017 and 2019, the median NDWs required for treatment with all OBs (n=36)
 283 increased from 1.05 to 2 and 0.5 to 0.7 for all LPGs (n=31), respectively. In 2019, the median
 284 percent increase in NDWs for LPGs (n=31) was much higher as compared to OBs (n=36) i.e.
 285 12.5% (p=0.008) and 3% (p=0.081) respectively. So, an overall increase in NDWs for both OBs
 286 and LPGs was observed between 2017 and 2019. Similarly the Median Treatment Prices (MTPs)
 287 for OB and LPGs also increased significantly i.e. 464 PKR to 563 PKR (p<0.001) and 244 PKR
 288 to 350 PKR (p<0.001), respectively. The MTPs and NDWs for each medicine are given in

10

289 supplementary tables S5 and S6. The medicines were categorized into seven disease groups to
290 further analyze changes in the affordability between 2017 and 2019. In figure 2, a bar graph shows
291 Median NDWs required for both OBs and LPGs in each disease group, where the values above 1
292 were considered unaffordable. In 2017, the median NDWs of OBs to treat three types of diseases
293 i.e. CVDs (1.2), diabetes (1.4) and ulcers (2.75) were more than 1. Whereas in 2019, medicines
294 for another disease category made its place into this list i.e. the medicines for IDs (1.18). Compared
295 to 2017, the median NDWs for all OBs increased in 2019 except for OBs acting on Central Nervous
296 System (CNS) and OBs to treat ulcers. The treatment for ulcer remained highly unaffordable in
297 both years. The median NDWs for LPGs increased in 2019 for the treatment of Arthritis, CNS
298 disorders, CVDs and IDs, while the modest decrease in median NDWs for LPGs was observed for
299 some diseases i.e. asthma, diabetes and ulcers as shown in figure 2.

300 Discussion

301 This study provides a valuable insight in to the effects of NDPP 2018 associated changes on
302 medicine prices, availability and affordability in both public and private healthcare sectors of
303 Lahore division, Pakistan. The main objective of this updated policy was to improve the access to
304 essential medicines (EMs) and improve rational drug pricing. Our study has shown that the
305 overall availability of medicines improved in 2019 in comparison to 2017 i.e. before the
306 implementation of this policy, except for the LPGs in public sector, demonstrating reduction.
307 Overall the medicine prices were increased significantly, making majority of the EMs used for the
308 common ailments unaffordable, with a much higher price increases for LPGs in comparison to
309 OBs. The medicines used to treat ulcers, diabetes and CVDs remained most unaffordable in both
310 years. Despite the modest improvements in the availability of surveyed medicines after NDPP
311 2018, the increased unaffordability of the surveyed medicines earnestly require significant
312 revisions and improvements in the current pricing policy to ensure the affordability of surveyed
313 medicines to the patients.

314 Despite improvements in the availability of medicines between 2017 and 2019, the
315 availability of medicine remained below the optimal benchmark of 80% [13]. In public sector the
316 availability of OBs improved remarkably probably be due to decentralization procurement of
317 medicines in public sector. Before 2018, the medicines were procured centrally for all the public
318 sector hospitals except for teaching hospitals, within a province. But after 2018, the medicines
319 procurement was decentralized for public sector hospital to allow hospitals in each district a free
320 choice to select desired manufactures, thus, ending up in the selection of more OBs than LPGs,
321 possibly due to quality concerns about medicines. Another factor that improved medicines
322 availability after 2018 was authorization of hospitals to acquire medicines directly without any
323 delays. However, as practiced in the previous central supply system, the medicines were received
324 centrally from the manufacturers before reaching the concerned hospital with considerable effect
325 on timely availability of medicines. In both years, the mean percentage availabilities for all
326 medicines were found higher in the private sector compared to the public sector, corroborating
327 similar previous studies conducted in Bangladesh and Malawi in 2019 [21, 22]. The overall
328 availability of medicines from NEML was slightly better than non-NEML medicines in both public
329 and private sectors. This might be attributed to the active role of DRAP in the revision and

330 subsequent dissemination of the revised NEML i.e. NEML 2018 [15]. Furthermore, the public
331 hospitals are encouraged to procure drugs from the latest NEML 2018 that has been standardized
332 in line with WHO essential medicines model list 2017 [23]. Besides, a mobile application was
333 launched in 2018 with user friendly interface to better disseminate the information on enlisted
334 medicines [24]. So, the NDPP 2018, doesn't seem to be solely responsible for the availability of
335 medicines.

336 Although we found some improvements in the availability of medicines, there was a
337 substantial increase in medicine prices, making them inaccessible for most of the population.
338 According to one estimate approximately 46 million people are living below the national poverty
339 line in Pakistan (as per 2015) [8]. The increases in prices of both OBs and LPGs may fairly be
340 attributable to the NDPP 2018, that allows an annual increase in the prices of scheduled drugs up
341 to 70% of CPI compared to 50% of CPI as per NDPP 2015 [9, 10]. These changes in price
342 calculations seems to accentuate the substantial impact on overall prices of medicines, thus,
343 making them more expensive. The increase in LPGs prices were more significant as compared to
344 OBs suggesting that with already expensive OBs, the price increase in LPGs would impoverish
345 the overall access to medicines, imputable to the changes in formula for LPGs (new entrants) price
346 calculation. According to NDPP 2018, the MRP of new entrant first generic should be fixed at
347 20% less than that of OB compared to NDPP2015, where it was 30% less than MRP of OB.
348 Another possible variable is the prior availability of generics in the market for price calculation,
349 where, according to NDPP2018, the MRP of a new entrant (LPGs) was fixed equal to the highest
350 MRP of the available generics in the market, while as per NDPP2015 practice, MRP was fixed by
351 taking the average of other generics in the market. Therefore, these changes in price calculating
352 mechanisms might have led to higher prices of many new LPGs in the market. Hence, contrary to
353 NDPP 2018's price steerage objectives, the increase in medicine prices was more distinct for
354 NEML medicines as compared to non-NEML medicines.

355 Data from further analysis on affordability of standard treatment by selected OBs and LPGs
356 suggested that majority of the medicines have become more unaffordable in 2019. When the
357 affordability was compared for medicines of different disease groups, the three foremost
358 unaffordable OBs were ones for treatment of ulcers, diabetes and CVDs. Additionally, the
359 treatment for ulcers remained exceptionally unaffordable with OBs and LPGs in both years.
360 Nevertheless, the treatment of CVDs and diabetes with LPGs remained affordable in 2017 but the
361 NDWs for CVDs surpassed affordability threshold in 2019. Among the disease categories, NCDs
362 harbor the top three unaffordable slots. It is noteworthy, that the burden of NCDs is increasing
363 worldwide and is responsible for higher mortality rates than all other diseases combined [25-27].
364 The CVDs, diabetes, cancer and chronic respiratory diseases are responsible for about 80% of
365 these deaths [28]. Pakistan is among top 10 countries where prevalence of diabetes is very high.
366 Besides, one third of Pakistanis, above 45 years of age have hypertension [29-31]. Thus, the
367 unaffordability of the essential medicines for NCDs, such as CVDs and diabetes, has worse bearing
368 on affordability associated therapeutic outcomes that ultimately leads to increased morbidity and
369 mortality due to un-controlled disease.

370 Additionally, we also compared the median drug prices in 2019 with the prices
 371 published/allowed by DRAP in its latest Statutory Regulatory Orders (SROs). On December 31,
 372 2018, the DRAP revised and published the maximum retail prices (MRPs) of about 1084 drugs
 373 through SRO-1608, SRO-1609 and SRO-1610 [32]. Eighteen OBs from our study sample were
 374 part of these price revisions (table 3). Surprisingly, after comparing the MUPs of 18 selected OBs
 375 with prices allowed by the government, we found that most of the OBs, 14 out of 18, were sold at
 376 higher prices than the allowable prices – with median percent increase of 29.37%. These data
 377 suggested that these intentional malpractices by the drug sellers might be driven by poor price
 378 control regulation by price enforcement authorities. Therefore, the current drug pricing policy
 379 NDPP 2018, is not the sole reason for the price hike. Most probably main stakeholders in the drug
 380 supply chain are also contributing towards medicine inflated prices. Thus, it's reasonable to deduce
 381 that these factors may interfere with measuring the direct impact of current pricing policy.

382 **Table 3.** Maximum retail unit prices (MRPs) of Originator Brands (OBs) allowed by the
 383 government versus median unit prices (MUPs) found in private sector pharmacies.

Medicine Name	Strength (Dosage form)	Allowed Unit Price (PKR)	MUP 2019 (PKR)	Percentage difference
Aciclovir	200mg (tab)	52.6	75	42.5%
Amlodipine	5mg (tab)	8.5	13	52.9%
Amoxicillin	250mg (cap)	3.75	3.75	0%
Amoxicillin	500mg (cap)	5.58	8.75	56.8%
Atorvastatin	20mg (cap)	141.37	203.5	43.9%
Bisoprolol	5mg (tab)	15.35	16.72	8.9%
Carbamezipine	200mg (tab)	4	5	25%
Ceftriaxone	1g (inj)	783	783	0%
Ciprofloxacin	500mg (tab)	39.25	52.5	33.7%
Digoxin	0.25mg (tab)	1.75	2.68	53.1%
Fluconazole	200mg (cap)	425	585	37.6%
Insulin N	100IU (vial)	88.47	75.88	-14.2%
Insulin R	100IU (vial)	93.88	75.88	-19.1%
Methyldopa	250mg (tab)	7.71	8.1	5.05%
Omeprazole	20mg (cap)	42.9	52.29	21.8%
Propranolol	40mg (tab)	1.1	3.16	187.2%
Pyremethamine+Sulfadoxim	(25+500)mg (tab)	12.01	12.02	0.08%
Simvastatin	20mg (cap)	47.01	68	44.6%
Medians		27.3	34.505	29.3%

384 Although the formation of a national scale pricing policy is laudable but it seems to be a
 385 collection of drug price calculation formulas only. It should also include the mechanism for price
 386 monitoring, an aspect which seems to be one of the major reasons behind failure to achieve the
 387 goals of NDPP 2018. Inclusion of WHO/HAI based surveys on regular basis could also be an
 388 option, in this case. The WHO has developed a mobile application named “WHO Essential

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3 389 Medicines and Health Products Price and Availability Monitoring (WHO EMP MedMon)”, which
4 390 can be used to collect and analyze price and availability data from health care outlets. This
5 391 application is based on standard WHO/HAI methodology and it can be used both online and
6 392 offline, making it both time saving and cost effective [33]. The drug inspectors or a third party can
7 393 be given this responsibility to monitor and report the prices using WHO EMP MedMon on a
8 394 regular basis, ensuring the compliance by drug manufacturers and sellers to NDPP. There could
9 395 be many other policy implications having an impact on drug pricing, availability and affordability.
10 396 The procurement of medicines should be strictly based on the NEML. Clear cut mechanism for
11 397 NEML based procurement should be devised and implemented specially in the public sector
12 398 hospitals. Besides, the hospital pharmacy and therapeutics committees must actively evaluate the
13 399 safety, efficacy and cost-effectiveness of drugs before purchasing. Pharmaco-economic
14 400 evaluations of drugs must be promoted by allocating research funds to experts. Not all drugs should
15 401 be fully reimbursed in the hospitals, only essential medicines must be included in this list. Hence,
16 402 the profits from other drugs can be used to purchase essential drugs when needed. Smooth
17 403 functioning of the drug supply chain with proper quality control must be ensured. The current
18 404 inflated prices would have a grave impact on the access to essential medicines, especially for the
19 405 low and middle income population of Pakistan. Thus, there is dire need to develop clearer evidence
20 406 based and stringent price control policy, especially for essential medicines. Exempting or reducing
21 407 taxes and tariffs on EMs and promotion of local generic manufacture by providing subsidies on
22 408 raw materials may improve both the availability and affordability of these medicines. While using
23 409 the External Reference Pricing (ERP) mechanism, the reference countries should be chosen
24 410 critically e.g. countries with similar pharmaceutical market and economic status. For costly
25 411 medicines, regressive markups must be encouraged over progressive markups. The drug prices
26 412 must be monitored on regular basis using a validated and well-designed scientific methodology
27 413 and pricing policy must be revised based on such evidences. The essential medicines for most
28 414 prevalent diseases such as diabetes and CVDs must be preferentially made affordable by devising
29 415 some specific pricing strategies for these medicines. Besides, efforts must be made to enforce the
30 416 pricing policy effectively by introducing reward and punishment system to induce a healthy
31 417 competition among the drug manufacturers and sellers.

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40 418 Although, this study provides an objective evidence to the policy makers for improving the current
41 419 pricing policies. It has some limitations as well. The study includes medicines with specific
42 420 strengths and dosage forms to compare with IRPs. There might be other strengths/dosage forms of
43 421 the surveyed medicines, available in the health facilities, so the availability of the medicines may
44 422 be underestimated. The affordability was calculated for single medicine for each disease, whereas
45 423 patients are usually taking more than one drug at a time – under-estimating the extent of
46 424 affordability of a specific treatment for a specific disease. Moreover, the post survey was
47 425 conducted after about a year from the launch of new drug pricing policy 2018, so the results do
48 426 not reflect the long term impact of the policy. Further surveys could be conducted in future to
49 427 gauge the long term effects of the policy as it was done by Fang et al in two such surveys conducted
50 428 after the health reform in China [17].

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54 429 In Conclusion, the availability of medicines has been improved after the launch of a new drug
55 430 pricing policy by Pakistani government but it still below the benchmark, thus, forcing the patients

431 to buy medicines from private sector at their own expense. The prices of both LPGs and OBs of
432 EMs have increased remarkably in 2019, when compared with 2017. The medicines to treat most
433 prevalent non-communicable diseases (diabetes and CVDs) have become more expensive and
434 unaffordable. The maximum retail prices of several OBs have been illegally increased in the
435 market, adding more burden on patients' pockets. Thus, the pricing policy should be improved
436 with strict price control measures, especially for the EMs, such as ensuring transparency on the
437 costs of drug development process and distribution, NEML based procurement, and reduction in
438 the taxes and tariffs on local production of EMs.

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444 **Contributions**

445 AS, ZB and YF conceptualize the study. ZS, HS, AS and ZB designed methodology. ZS, HS, AS
446 trained the data collectors and obtained the data. YF provided resources and supervised the project.
447 ZS worked as survey area manager. MA, AHG, NA, FK and MZ did data cleaning, validation and
448 entry. AS, HS, CY, MJ analyzed the data. AS and HS wrote original draft. YF, ZB, ZS, CY and
449 MJ, WJ reviewed and edited the manuscript.

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453 **Competing Interests**

454 None

455 **Patient Consent for Publication**

456 Not Required

457 **Ethics Approval**

458 Ethics approval was obtained from the Medical Ethics Committee of Xi'an Jiaotong University
459 under study ID 2019-067.

460 **Data availability statement**

461 Extra data can be accessed via the Dryad data repository at <http://datadryad.org/> with the
462 doi:10.5061/dryad.tjq2bvwq

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References

1. United Nations Development Group, United Nations. Statistical Division. Indicators for monitoring the millennium development goals: definitions, rationale, concepts and sources. United Nations Publications 2003:95.
2. World Health Organization. Medicine prices and access to medicines in the Eastern Mediterranean Region. 2007.
3. Lee KS, Shahidullah A, Zaidi ST, *et al*. The Crux of the Medicine Prices' Controversy in Pakistan. *Frontiers in pharmacology* 2017;8:504.
4. Kiani A, Qadeer A, Mirza Z, *et al*. Prices, availability and affordability of medicines in Pakistan. Geneva: Health Action International (HAI); 2006.
5. Zaidi S, Bigdeli M, Aleem N, *et al*. Access to essential medicines in Pakistan: policy and health systems research concerns. *PloS One* 2013;8:e63515.
6. Cameron A, Ewen M, Ross-Degnan D, *et al*. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. *The Lancet* 2009;373:240.
7. Saeed A, Saeed H, Saleem Z, *et al*. Evaluation of prices, availability and affordability of essential medicines in Lahore Division, Pakistan: A cross-sectional survey using WHO/HAI methodology. *PloS One* 2019;14:e0216122.
8. The World Bank. Poverty and Equity data portal. 2015. Available: <http://povertydata.worldbank.org/poverty/country/PAK>. [Accessed: 16 June 2019].
9. Costing and Pricing Division, Drug Regulatory Authority of Pakistan. Drug Pricing Policy 2015.
10. Costing and Pricing Division, Drug Regulatory Authority of Pakistan. Drug Pricing Policy 2018.
11. Durrani F. Increase in drug prices highest in last 40 years. The News 2019. Available: <https://www.thenews.com.pk/print/454864-increase-in-drug-prices-highest-in-last-40-years>. [Accessed: 3 September 2019].
12. Junaidi I. Minister orders crackdown on firms increasing medicine prices. DAWN News 2019. Available: <https://www.dawn.com/news/1473573>. [Accessed: 3 September 2019].

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2
3 494 13. World Health Organization. Measuring medicine prices, availability, affordability and
4 price components 2008.
5 495
6 496 14. Pakistan Bureau of Statistics. Population Census. 2017. Available:
7 <http://www.pbs.gov.pk/content/population-census>. [Accessed: 18 August 2019].
8 497
9 498 15. Drug Regulatory Authority of Pakistan. National Essential Medicines List. 2018.
10 499 16. Yang H, Dib HH, Zhu M, *et al*. Prices, availability and affordability of essential
11 medicines in rural areas of Hubei Province, China. *Health policy and planning*
12 500 2009;25:219.
13 501
14 502 17. Fang Y, Wagner AK, Yang S, *et al*. Access to affordable medicines after health reform:
15 evidence from two cross-sectional surveys in Shaanxi Province, western China. *The*
16 *Lancet Global Health* 2013;1:e227.
17 503
18 504 18. Management Sciences for Health. International Medical Products Price Guide 2015.
19 505 19. Pakistan Bureau of Statistics, Government of Pakistan. Price Statistics. Available:
20 [http://www.pbs.gov.pk/content/officially-published-consumer-prices-data-imf-](http://www.pbs.gov.pk/content/officially-published-consumer-prices-data-imf-template)
21 [template](http://www.pbs.gov.pk/content/officially-published-consumer-prices-data-imf-template). [Accessed 18 August 2019].
22 506
23 507 20. Wage Indicator Foundation. Minimum wages in Pakistan 2018. Available:
24 <https://wageindicator.org/Wageindicatorfoundation>. [Accessed 15 April 2019].
25 508
26 509 21. Kasonde L, Tordrup D, Naheed A, *et al*. Evaluating medicine prices, availability and
27 affordability in Bangladesh using World Health Organisation and Health Action
28 International methodology. *BMC health services research* 2019;19:383.
29 510
30 511 22. Khuluza F, Haefele-Abah C. The availability, prices and affordability of essential
31 medicines in Malawi: A cross-sectional study. *PloS One* 2019;14:e0212125.
32 512
33 513 23. Jabri P. National essential medicine list -2018 to be implemented in all provinces:
34 Kiani. Business Recorder 2018. Available:
35 [https://www.brecorder.com/2018/10/06/444080/national-essential-medicine-list-](https://www.brecorder.com/2018/10/06/444080/national-essential-medicine-list-2018-to-be-implemented-in-all-provinces-kiani/)
36 [2018-to-be-implemented-in-all-provinces-kiani/](https://www.brecorder.com/2018/10/06/444080/national-essential-medicine-list-2018-to-be-implemented-in-all-provinces-kiani/) . [Accessed: 3 September 2019].
37 514
38 515 24. Govt. launches WHO backed national essential medicine list. Pakistan Today 2018.
39 Available: [https://www.pakistantoday.com.pk/2018/10/05/govt-launches-who-](https://www.pakistantoday.com.pk/2018/10/05/govt-launches-who-backed-national-essential-medicine-list/)
40 [backed-national-essential-medicine-list/](https://www.pakistantoday.com.pk/2018/10/05/govt-launches-who-backed-national-essential-medicine-list/). [Accessed: 3 September 2019].
41 516
42 517 25. Dans A, Ng N, Varghese C, *et al*. The rise of chronic non-communicable diseases in
43 southeast Asia: time for action. *The Lancet* 2011;377:680.
44 518
45 519
46 520
47 521
48 522
49 523
50 524

- 1
2
3 525 26. Siegel KR, Patel SA, Ali MK. Non-communicable diseases in South Asia:
4 526 contemporary perspectives. *British medical bulletin* 2014;111:31.
5
6 527 27. Habib SH, Saha S. Burden of non-communicable disease: global overview. *Diabetes*
7 528 *& Metabolic Syndrome: Clinical Research & Reviews* 2010;4:41.
8
9 529 28. World Health Organization. Global action plan for the prevention and control of non-
10 530 communicable diseases 2013-2020, 2013.
11
12 531 29. Ghaffar A, Reddy KS, Singhi M. Burden of non-communicable diseases in South Asia.
13 532 *BMJ* 2004;328:807.
14
15 533 30. Jafar TH, Haaland BA, Rahman A, *et al*. Non-communicable diseases and injuries in
16 534 Pakistan: strategic priorities. *The Lancet* 2013;381:2281.
17
18 535 31. Wasay M, Zaidi S, Jooma R. Non communicable diseases in Pakistan: burden,
19 536 challenges and way forward for health care authorities. *Journal of Pakistan Medical*
20 537 *Association* 2014; 64:1218.
21
22 538 32. Drug Regulatory Authority of Pakistan. SRO: Pricing division 2018. Available:
23 539 <https://www.dra.gov.pk/Home/Pricing>. [Accessed: 17 July 2019].
24
25 540 33. World Health Organization. MedMon - WHO Essential Medicines and Health Products
26 541 Price and Availability Monitoring Mobile Application. 2016. Available:
27 542 <https://www.who.int/medicines/areas/policy/monitoring/empmedmon/en/>
28
29 543 [Accessed: 30 March 2020].
30
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40 546 **Figure 1. Box plot of percent availability of lowest price generics (LPGs) and originator**
41 547 **brands (OBs) in both public (pub) and private (pvt) sectors in 2017 and 2019.** This box plot
42 548 shows the distributional characteristics of the percent availability of medicines in two groups (OB
43 549 and LPG) for the years 2017 and 2019. The mean percent availability is represented by the dot
44 550 inside the box.

45 551 **Figure 2. Bar graph of affordability of originator brands (OBs) and lowest price generics (LPGs)**
46 552 **for different diseases in both years i.e. 2017 and 2019.**

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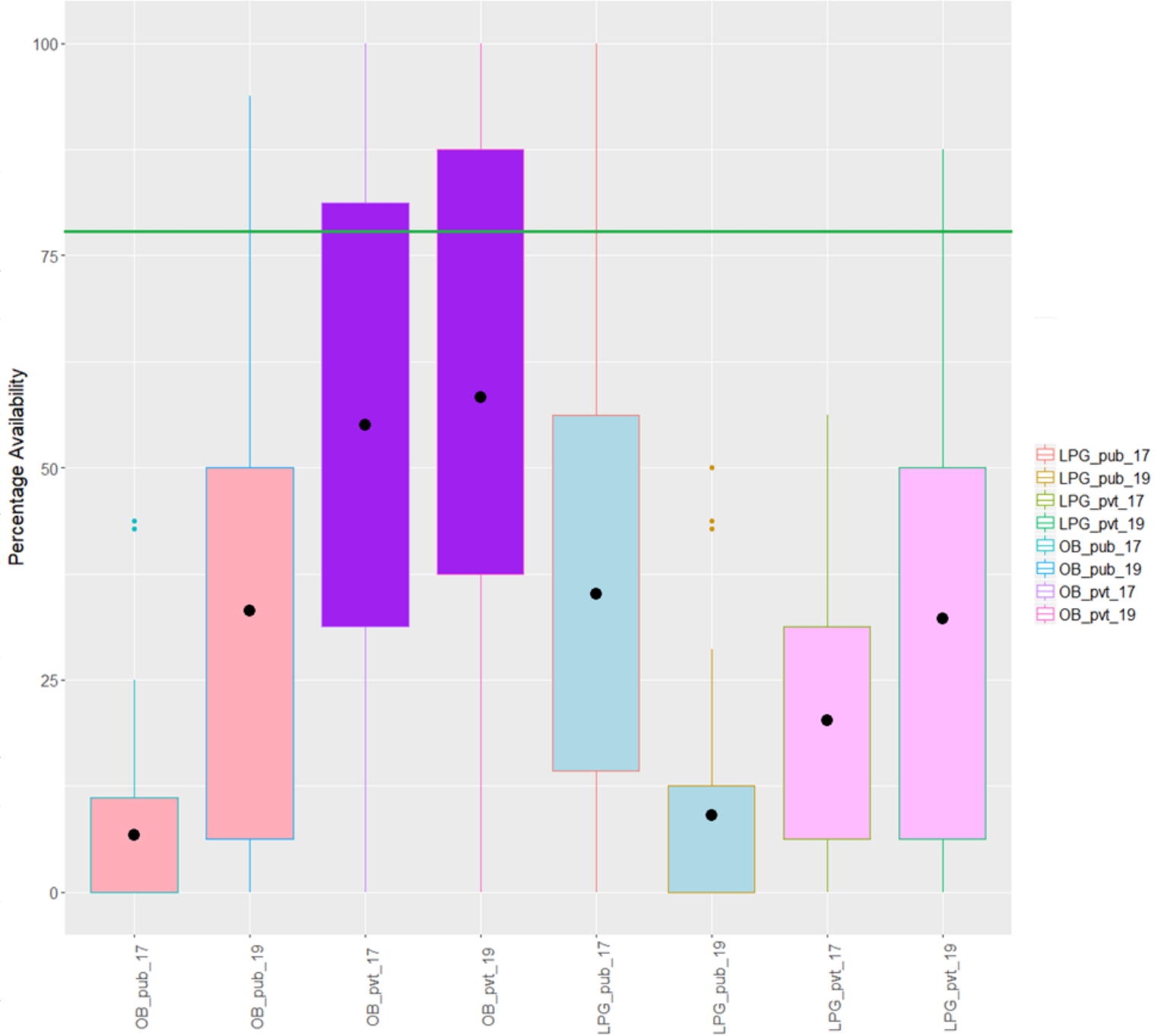
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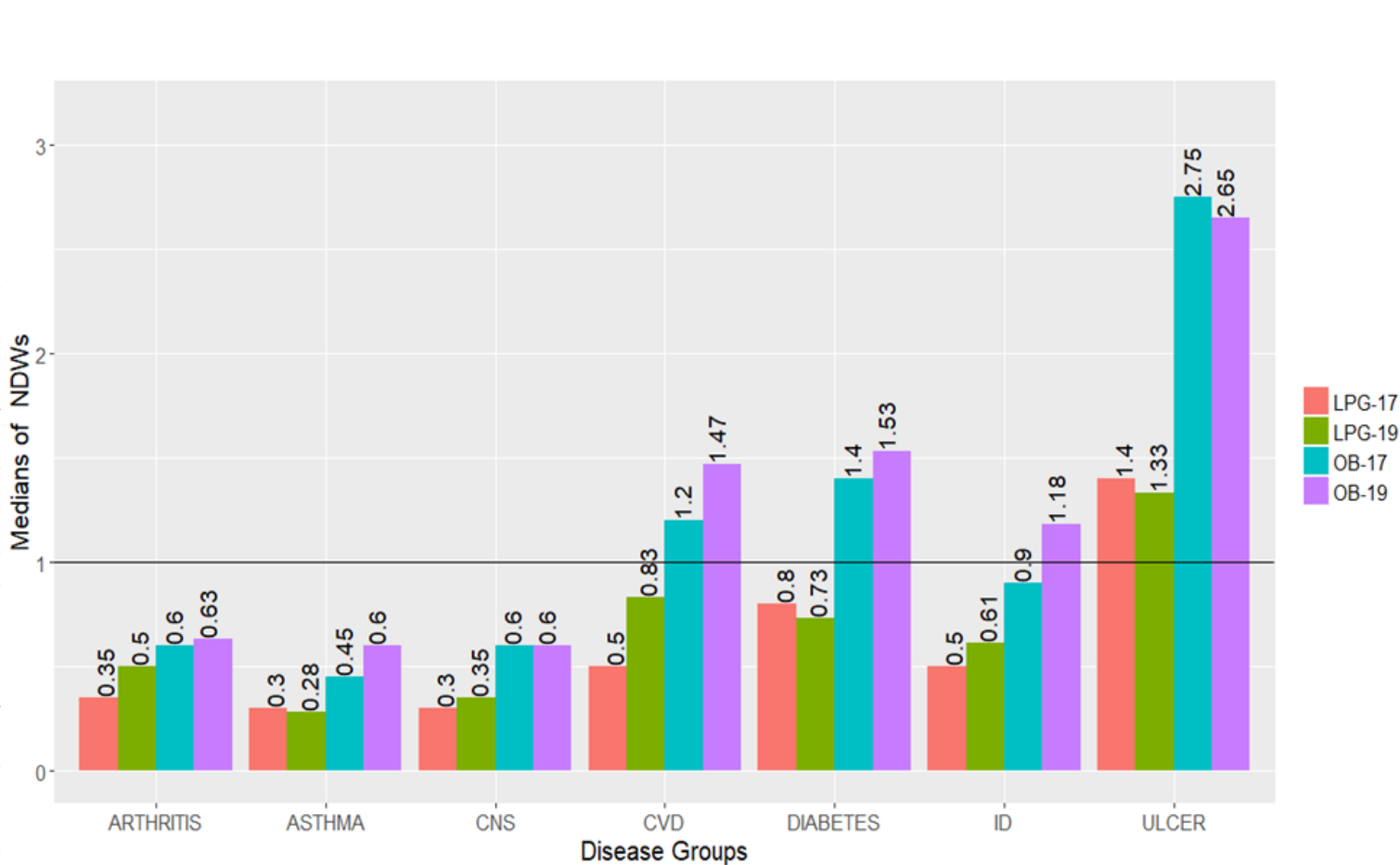
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Supplementary Tables

Table S1. Percent availabilities and of originator brands (OBs) and lowest price generics (LPGs) of all medicines in public and private sector in 2017 and 2019 (%)

Names of meds	OB (Public) 2017	OB (Pvt.) 2017	LPG (Public)) 2017	LPG (Pvt.) 2017	OB (Public) 2019	OB (Pvt) 2019	LPG (Public) 2019	LPG (pvt.) 2019
Acetylsalicylic Acid	0.0	25.0	56.3	25.0	18.8	75.0	50.0	18.8
Aciclovir	0.0	50.0	25.0	37.5	6.3	18.8	0.0	50.0
Amiodarone	7.1	62.5	21.4	6.3	0.0	62.5	21.4	0.0
Amitriptyline	0.0	31.3	0.0	25.0	0.0	0.0	50.0	50.0
Amlodipine	6.3	75.0	62.5	31.3	37.5	93.8	12.5	56.3
Amoxicillin	43.8	93.8	18.8	25.0	93.8	68.8	0.0	37.5
Amoxicillin (250)	18.8	100.0	12.5	31.3	50.0	87.5	0.0	37.5
Atenolol	12.5	87.5	81.3	43.8	43.8	81.3	0.0	56.3
Atorvastatin	7.1	50.0	21.4	25.0	42.9	62.5	21.4	18.8
Azithromycin	0.0	25.0	25.0	31.3	31.3	25.0	25.0	75.0
Beclometasone inhaler	0.0	6.3	35.7	12.5	35.7	43.8	0.0	0.0
Bisoprolol	6.3	87.5	18.8	25.0	37.5	81.3	0.0	56.3
Captopril	0.0	81.3	85.7	25.0	50.0	93.8	28.6	50.0
Carbamazepine	12.5	87.5	56.3	25.0	25.0	31.3	0.0	56.3
Ceftriaxone injection	14.3	68.8	71.4	31.3	21.4	75.0	50.0	87.5
Ciprofloxacin	0.0	81.3	100.0	37.5	64.3	93.8	14.3	25.0
Clarithromycin	0.0	87.5	35.7	25.0	50.0	93.8	0.0	56.3
Co-trimoxazole suspension	6.3	31.3	62.5	6.3	6.3	6.3	43.8	6.3
Diazepam	6.3	62.5	12.5	0.0	43.8	68.8	0.0	0.0
Diclofenac	42.9	50.0	35.7	6.3	85.7	93.8	0.0	81.3
Digoxin	21.4	62.5	28.6	0.0	28.6	68.8	0.0	56.3
Enalapril	0.0	68.8	62.5	18.8	12.5	68.8	12.5	50.0
Fluconazole	0.0	37.5	18.8	25.0	43.8	43.8	0.0	50.0
Fluoxetine	0.0	43.8	12.5	43.8	6.3	62.5	6.3	62.5
Fluphenazine Decanoate	0.0	0.0	0.0	12.5	0.0	0.0	7.1	6.3
Furosemide	12.5	93.8	50.0	6.3	50.0	87.5	0.0	0.0
Glibenclamide	18.8	68.8	56.3	12.5	68.8	93.8	0.0	12.5
Gliclazide	0.0	75.0	0.0	18.8	7.1	75.0	0.0	31.3
Hydrochlorothiazide	0.0	0.0	0.0	12.5	18.8	0.0	0.0	0.0
Indinavir	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Insulin Isophane (NPH)	0.0	75.0	50.0	25.0	56.3	68.8	0.0	18.8
Insulin Neutral Soluble (Regular)	0.0	68.8	50.0	25.0	68.8	68.8	0.0	18.8
Losartan	7.1	43.8	14.3	43.8	0.0	43.8	42.9	43.8
Lovastatin	0.0	0.0	6.3	0.0	6.3	37.5	12.5	0.0

Metformin	25.0	81.3	56.3	31.3	68.8	93.8	0.0	50.0
Methyldopa	12.5	81.3	25.0	0.0	75.0	68.8	0.0	0.0
Metronidazole	25.0	93.8	56.3	37.5	75.0	87.5	0.0	56.3
Nevirapine	0.0	0.0	14.3	0.0	0.0	0.0	0.0	0.0
Nifedipine Retard	0.0	75.0	28.6	12.5	0.0	31.3	14.3	12.5
Omeprazole	6.3	56.3	75.0	37.5	62.5	62.5	6.3	50.0
Omeprazole (10)	0.0	12.5	43.8	18.8	18.8	0.0	12.5	31.3
Paracetamol suspension	6.3	68.8	87.5	25.0	81.3	87.5	0.0	81.3
Phenytoin	0.0	6.3	12.5	6.3	0.0	50.0	6.3	0.0
Propranolol	12.5	68.8	12.5	6.3	18.8	87.5	0.0	25.0
Pyrimethamine with sulfadoxine	0.0	75.0	21.4	6.3	21.4	68.8	0.0	6.3
Ranitidine	0.0	81.3	31.3	25.0	50.0	100.0	0.0	50.0
Salbutamol inhaler	0.0	81.3	56.3	31.3	62.5	68.8	0.0	12.5
Simvastatin	0.0	25.0	21.4	56.3	0.0	37.5	7.1	25.0
Spironolactone	6.3	62.5	25.0	0.0	12.5	93.8	6.3	43.8
Zidovudine	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Mean availabilities	6.8	55.0	35.1	20.3	33.1	58.3	9.0	32.3

Table (S2). Change in availability at different levels of healthcare (Public Sector).

	Primary level (n=2 outlets)		Secondary level (n=13 outlets)		Tertiary level (n=1 outlet)	
	All medicines (n=50)		All medicines (n=50)		All medicines (n=50)	
	OB	LPG	OB	LPG	OB	LPG
Mean Availability 2017 (SD),%	0.0 (0.0)	25.8 (44.5)	7.1 (11.2)	35.2 (27.5)	12.0 (32.8)	50.0 (50.5)
Mean Availability 2019 (SD) ,%	21.0 (31.0)	3.2 (18)	32.3 (29.1)	7.4 (13.4)	68.0 (47.1)	22.0 (41.8)
Change in mean percent availability,%	21.0	-22.6	25.2	-27.8	56.0	-28.0

Table S3. Change in median unit prices (MUPs) and median price ratios (MPRs) of the Originator Brands (OBs) at private sector.

Sr. no.	Medicines (OB)	MUPs 2017 (PKR)	MPR 2017	Adjusted MUP in 2019	MPR 2019	Percentage change in MUPs/MPRs
1	Acetylsalicylic Acid	1.16	0.8	1.12	0.7	-3.41%
2	Aciclovir	70	20	72.5	21	3.48%
3	Amiodarone	17.78	2.2	17.4	2.2	-2.15%
4	Amlodipine	11.93	7.3	12.6	7.7	5.1%
5	Amoxicillin	8.616	2.8	8.46	2.7	-1.83%
6	Amoxicillin (250)	3.56	2.1	3.63	2.2	1.83%
7	Atenolol	6.19	5.6	6.14	5.5	-0.81%
8	Atorvastatin	201.9	18	197	18	-2.6%
9	Azithromycin	40	1.7	118	5	66.2%
10	Beclometasone inhaler	1.25	1.2	1.84	1.8	32%
11	Bisoprolol	11.28	1.2	16.2	1.7	30.2%
12	Captopril	7.66	3	8.22	3.2	6.81%
13	Carbamazepine	4.91	2.6	4.84	2.5	-1.55%
14	Ceftriaxone injection	672	16	757	18	11.2%
15	Ciprofloxacin	50.4	13	50.8	13	0.72%
16	Clarithromycin	65.7	2.5	76.4	2.9	14%
17	Co-trimoxazole suspension	0.29	0.6	0.44	0.9	33.4%
18	Diazepam	2	2	1.93	1.9	-3.41%
19	Diclofenac	5.625	12	5.61	12	-0.29%
20	Digoxin	2.52	2.4	2.59	2.5	2.76%
21	Enalapril	5.85	5.4	6	5.6	2.43%
22	Fluconazole	442	61	566	78	21.9%
23	Fluoxetine	43.42	9.7	43	9.6	-0.9%
24	Furosemide	1.89	3	2.34	3.7	19.2%
25	Glibenclamide	1.69	2.9	2.09	3.5	19.1%
26	Gliclazide	7.6	1.5	16.4	3.3	53.8%
27	Insulin Isophane (NPH)	64.5	1.1	73.4	1.3	12.1%
28	Insulin Neutral Soluble (Regular)	64.5	1.1	73.4	1.2	12.1%
29	Losartan	51.67	4.3	50.3	4.2	-2.76%
30	Metformin	1.54	1	1.62	1	5.21%
31	Methyldopa	6.38	1.9	7.83	2.3	18.5%
32	Metronidazole	1.57	1.3	1.52	1.2	-3.41%
33	Nifedipine Retard	5.69	2.7	5.8	2.8	1.93%
34	Omeprazole	49.78	34	50.6	35	1.55%
35	Paracetamol suspension	0.85	1.6	2.2	4.1	61.4%
36	Phenytoin	5.2	4.8	23.2	22	77.6%
37	Propranolol	1.55	2.2	3.06	4.3	49.3%

38	Pyrimethamine with sulfadoxine	5.83	1.4	11.6	2.8	49.8%
39	Ranitidine	8.8	3.7	8.51	3.6	-3.41%
40	Salbutamol inhaler	1	1	1.03	1.1	3.35%
41	Simvastatin	67.13	12	65.8	12	-2.09%
42	Spirolactone	8.6	0.8	10.1	1	14.5%
	Medians	6.99	2.5	8.49	3.2	4.29%

Table S4. Change in median unit prices (MUPs) and median price ratios (MPRs) of the lowest price generics (LPGs) in private sector.

Sr. no.	Medicines	MUPs 2017 (PKR)	MPR 2017	Adjusted MUP in 2019	MPR 2019	Percentage change in MUPs/MPRs
1	Acetylsalicylic Acid	1.015	0.7	1.06	0.7	4.58
2	Aciclovir	12.4	3.6	13.5	3.9	8.41
3	Amitriptyline	1.19	1.4	1.24	1.4	3.86
4	Amlodipine	1.8	1.1	6.29	3.8	71.4
5	Amoxicillin	5.8	1.9	8.32	2.7	30.3
6	Amoxicillin (250)	3	1.8	3.48	2.1	13.8
7	Atenolol	2.05	1.8	2.47	2.2	16.9
8	Atorvastatin	37.5	3.4	35.8	3.2	-4.8
9	Azithromycin	40	1.7	19.3	0.8	-107
10	Bisoprolol	6.55	0.7	6.56	0.7	0.1
11	Captopril	6.5	2.5	6.77	2.7	3.97
12	Carbamazepine	3.3	1.7	4.35	2.3	24.2
13	Ceftriaxone injection	280	6.8	290	7	3.48
14	Ciprofloxacin	11	2.8	24.2	6.2	54.5
15	Clarithromycin	36	1.4	42.7	1.6	15.8
16	Co-trimoxazole suspension	0.21	0.4	2.32	4.7	91
17	Diclofenac	3.5	7.5	4.79	10	26.9
18	Enalapril	2.05	1.9	2.84	2.6	27.8
19	Fluconazole	145.5	20	145	20	-0.3
20	Fluoxetine	13.8	3.1	13.5	3	-1.9
21	Fluphenazine Decanoate	90.5	1	93.8	1.1	3.5
22	Glibenclamide	1.57	2.7	1.42	2.4	-10
23	Gliclazide	4.75	0.9	5.8	1.1	18.1

24	Insulin Isophane (NPH)	48	0.8	62.3	1.1	22.9
25	Insulin Neutral Soluble (Regular)	48	0.8	62.3	1	22.9
26	Losartan	11	0.9	13.1	1.1	15.7
27	Metformin	1.5	1	1.86	1.2	19.2
28	Metronidazole	1.5	1.2	1.93	1.6	22.4
29	Nifedipine Retard	2.65	1.3	5.14	2.4	48.4
30	Omeprazole	15.35	10	11.4	7.8	-35
31	Omeprazole (10)	12.14	0.9	5.13	0.4	-137
32	Paracetamol suspension	0.47	0.9	1.02	1.9	53.7
33	Propranolol	0.66	0.9	2.03	2.8	67.5
34	Pyrimethamine with sulfadoxine	5	1.2	4.84	1.2	-3.4
35	Ranitidine	6.93	2.9	7.78	3.3	11
36	Salbutamol inhaler	0.64	0.7	0.68	0.7	5.45
37	Simvastatin	8.5	1.6	16.6	3	48.7
	Medians	5.8	1.4	6.29	2.3	15.7

Table S5. Affordability of originator brands (OBs) for different diseases in 2017 and 2019, in private sector.

Disease	Medicine	Strength	Dosage form	No. of units needed per treatment	Durati on of treatm ent	MTP 2017 (PKR)	NDWs 2017	MTP 2019 (PKR)	NDWs 2019
ASTHMA	Salbutamol Inhaler	100mcg/dose	Inhaler	200	As needed	200	0.4	214	0.4
	Beclomethasone	50mcg/dose	inhaler	200	As needed	250	0.5	380	0.8
Cardiovascular Diseases	Bisoprolol	5mg	tab	60	30	676.8	1.5	1003	2
	Atenolol	50mg	tab	30	30	185.7	0.4	190.5	0.4
	Captopril	25mg	tab	60	30	459.6	1	510	1
	Amlodipine	5mg	tab	60	30	715.8	1.5	780	1.6
	Amiodarone	200mg	tab	60	30	1066.8	2.3	1080	2.2
	Losartan	50mg	tab	60	30	3100.2	6.6	3120	6.2
	methyldopa	250mg	tab	90	30	574.2	1.2	729	1.5
Nifedipine retard	20mg	tab	90	30	512.1	1.1	540	1.1	

	Spironolactone	100mg	tab	30	30	258	0.5	312	0.6
	Propranolol	40mg	tab	90	30	139.5	0.3	284.4	0.6
	Acetylsalicylic acid	75mg	tab	30	30	34.8	0.1	34.8	0.1
Anti hyperlipidemics	Simvastatin	20mg	Cap/tab	30	30	2013.9	4.3	2040	4.1
	Atorvastatin	20mg	Cap/tab	30	30	6057	13	6105	12
Infections-Adult respiratory tract infection	Ceftriaxone Injection	1g/vial	Inj.	1	1	672	1.4	783	1.6
	Ciprofloxacin	500mg	tab	14	7	705.6	1.5	735	1.5
	Azithromycin	500mg	tab	3	3	120	0.3	367	0.7
	clarithromycin	500mg	tab	28	14	1839.6	3.9	2212	4.4
	Amoxicillin	500mg	cap	42	14	361.87	0.8	367.5	0.7
	Amoxicillin	250mg	cap	84	14	299.04	0.6	315	0.6
Fungal Infection	Fluconazole	200mg	cap	1	1	442	0.9	585	1.2
Viral Infection	aciclovir	200mg	tab	25	5	1750	3.8	1875	3.8
Amoebiasis	metronidazole	400mg	tab	21	7	32.97	0.1	32.97	0.1
CNS Drugs-Anti epileptics	Carbamezipine	200mg	tab	60	30	294.6	0.6	300	0.6
	Phenytoin	100mg	tab	90	30	468	1	2160	4.3
Anxiety	diazepam	5mg	tab	90	30	180	0.4	180	0.4
Anti Diabetics	Metformin	500mg	tab	90	30	138.6	0.3	151.2	0.3
	Glibenclamide	5mg	tab	90	30	152	0.3	194.4	0.4
	Gliclazide	80mg	tab	60	30	456	1.5	1020	2
	Insulin Isophane (NPH)	100IU/ml	vial	10	30	645	1.4	758.8	1.5
	Insulin Neutral Soluble (Regular)	100IU/ml	vial	10	30	645	1.4	758.8	1.5
Ulcer Treatment	Omeprazole	20mg	cap	30	30	1493.4	3.2	1569	3.1
	ranitidine	150mg	tab	120	30	1056	2.3	1056	2.1
Pain/Inflammation Arthritis	Paracetamol	24mg/ml	susp	45	3	38.25	0.1	102.6	0.2
	Diclofenac	50mg	tab	90	30	506.25	1.1	522	1

Where, MTP: Median treatment price, NDWs: Number of days' wages

Table S6. Affordability of lowest price generics (LPGs) for different diseases in 2017 and 2019, in private sector.

Disease/Condition	Medicine	Strength	Dosage form	No. of units needed per treatment	Duration of treatment	MTP 2017 (PKR)	NDWs 2017	MTP 2019 (PKR)	NDWs 2019
ASTHMA	Salbutamol Inhaler	100mcg/dose	Inhaler	200	As needed	128	0.3	140	0.3
Cardiovascular Diseases/ Anti Hypertensives	Bisoprolol	5mg	tab	60	30	393	0.8	406.8	0.8
	Atenolol	50mg	tab	30	30	61.5	0.1	76.5	0.2
	Captopril	25mg	tab	60	30	390	0.8	420	0.8
	Amlodipine	5mg	tab	60	30	108	0.2	390	0.8
	Losartan	50mg	tab	60	30	660	1.4	810	1.6
	Nifedipine retard	20mg	tab	90	30	238.5	0.5	478.4	1
	Propranolol	40mg	tab	90	30	59.4	0.1	189	0.4
	Acetylsalicylic acid	75mg	tab	30	30	30.45	0.1	33	0.1
Anti hyperlipidemics	Simvastatin	20mg	Cap/tablet	30	30	255	0.5	513.8	1
	Atorvastatin	20mg	Cap/tablet	30	30	1125	2.4	1110	2.2
Infections-Adult respiratory tract infection	Ceftriaxone Injection	1g/vial	Inj.	1	1	280	0.6	300	0.6
	Ciprofloxacin	500mg	tab	14	7	154	0.3	350	0.7
	Azithromycin	500mg	tab	3	3	120	0.3	60	0.1
	clarithromycin	500mg	tab	28	14	1008	2.2	1238	2.5
	Amoxicillin	500mg	cap	42	14	243.6	0.5	361.2	0.7
	Amoxicillin	250mg	cap	84	14	252	0.5	302.4	0.6
Fungal Infection	Fluconazole	200mg	cap	1	1	145.5	0.3	150	0.3
Viral Infection	aciclovir	200mg	tab	25	5	310	0.7	350	0.7
Amoebiasis	metronidazole	400mg	tab	21	7	31.5	0.1	42	0.1
CNS Drugs-Anti epileptics	Carbamezipine	200mg	tab	60	30	198	0.4	270	0.5
Depression	Amitriptyline	25mg	tab	60	30	71.4	0.2	76.8	0.2

Anti Diabetics	Metformin	500mg	tab	90	30	135	0.3	180	0.4
	Glibenclamide	5mg	tab	90	30	141	0	132.3	0.3
	Gliclazide	80mg	tab	60	30	285	0.8	360	0.7
	Insulin Isophane (NPH)	100IU/ml	vial	10	30	480	1	644	1.3
	Insulin Neutral Soluble (Regular)	100IU/ml	vial	10	30	480	1	644	1.3
Ulcer Treatment	Omeprazole	20mg	cap	30	30	460.5	1	353.7	0.7
	ranitidine	150mg	tab	120	30	831.6	1.8	966	1.9
Pain/Inflammation	Paracetamol	24mg/ml	susp	45	3	21.15	0	47.25	0.1
Arthritis	Diclofenac	50mg	tab	90	30	315	0.7	445.5	0.9

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STROBE—checklist

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1 2	Cross-sectional
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	
Objectives	3	State specific objectives, including any prespecified hypotheses	5	
Methods				
Study design	4	Present key elements of study design early in the paper	5	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5,6	
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	6	WHO/HAI methodology N.A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6,7	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6,7	
Bias	9	Describe any efforts to address potential sources of bias	5,6,7,	WHO/HAI validated methodology
Study size	10	Explain how the study size was arrived at	5,6,7	

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6,7	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7	
		(b) Describe any methods used to examine subgroups and interactions	N.A	
		(c) Explain how missing data were addressed	N.A	
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	N.A	
		(e) Describe any sensitivity analyses	N.A	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	N.A	
		(b) Give reasons for non-participation at each stage		
		(c) Consider use of a flow diagram		
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	N.A	
		(b) Indicate number of participants with missing data for each variable of interest	N.A	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	N.A	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	N.A	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	N.A	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	N.A	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7,9,10	Main results
		(b) Report category boundaries when continuous variables were categorized	N.A	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N.A	

Continued on next page

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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	1
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	1-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15