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Review Article

Overview of Drug Availability and Influencing Factors in Several Low, Lower and Upper- Middle Countries: A Systematic Review

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ABSTRACT

Drugs are vital to saving and improving public health. However, medicines are often not available at the facility because stocks run out or in particular, pharmaceuticals are not available due to a shortage of supplies. Implementation of pharmacy services should ensure safe, quality, usable and affordable availability drug. A systematic review was conducted to identify related studies. Electronic databases used to identify relevant studies are, ScienceDirect, Plos, PubMed and Google Scholar. This study is limited to English and publications from 2007 to 2017. The electronic database search earned 33 articles while only six studies met the criteria for review. There is the relatively low availability of drugs in some developing countries and the average availability of generic drugs is better than Innovator Brand drugs, especially in the public sector. Most of the factors that may affect drug availability are related to government policies to improve drug access and lower prices so that national drug policy review in each country is required. Overall, the method used to measure the availability of drugs using a reference method used by WHO Health Action International. The availability of drugs in low, lower and upper middle countries still need to be improved by increasing drug access and enhancing prices by using appropriate government policies. The WHO HAI method is effectively used to measure the availability of drugs by using the core drug and supplementary drug references by the established reference.

Key word: Drug Availability, Overview, Influencing Factors, Several Low, Lower and Upper-Middle Countries.

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INTRODUCTION

Patient's satisfaction with health services is directly related to the availability of medicines at the facility. Factors affecting the availability of medicines should be checked to improve the availability status of the drug. The purpose of drug selection is the availability of better supply, more rational drug use, more effective cost and high quality of care. The purpose of rational drug selection is to increase the availability of drugs; regular drug supplies can improve health outcomes, reduce polypharmacy, improve drug therapy and lower costs, procurement, storage and distribution can be more straightforward.[1] The selection of procurement time is part of procurement technical which is the primary determinant of drug availability and total health cost.[2] Proper inventory management has a significant impact on optimal hospital financial and operational management.[3]

The disadvantages of an irrational prescription have been estimated to reduce the availability of drugs by 50%.[4] The promotion of rational use of drugs as part of a health system that strengthens the approach to making quality drugs and pharmaceutical services more widely available and accessible in low-and-middle-income countries.[5] Rational use of drugs should be included with drug information. More than 50% of drug expenditure is wasted due to irrational prescription,[6] outlining factors from doctors who affect drug availability is that medical practitioners provide/prescribe unnecessary drugs or administer some medications to address the medical problem can be treated only one drug.

According to,[7] the factors of the patients affected by the availability of drugs are that the patient asks for drugs for other purposes or is incompatible with current medical conditions. Drugs should be used in an appropriate, safe and available manner. Irrational drug use includes overuse, underuse, due to lack of adequate system regulation, incomplete information and the strong influence of drug promotion on prescriber and patients. Logistic managers should be able to increase drug availability and reduce distribution costs. Community participant (contributing, consulting, managing) can improve the availability of drugs and supply health providers and can ensure low availability and price of drug.[6]

Drug prices are considered as one of the most significant barriers to access.[8] Drug purchases contribute significantly to the healthcare budget of developing countries and drug expenditure can reach 50%-90% of nonpersonal costs.[6] In 2002, Pharmaceutical Management Agency (PHARMAC) began negotiating a new price contract for 90% of hospital medicines for all New Zealand public hospitals (pricing management). This look at became carried out to examine the impact of 3 years of price management on pharmacy hospital expenditures and the impact of new contracts on the availability of medicines. Growth In-Patient Expenditure (IPE) slowed for all hospitals from 2003 to 2004. Some availability issues occurred with new contract items. Price management managed to save considerably and slow growth in IPE.[9] Studies in developed and growing countries show that discriminating prices by Multinational Corporations can reduce the issue of drug availability in developing countries compared to a uniform pricing strategy.[10]

To control availability and marketing, it is necessary to drug registration, national essential drug list, prescription and dispensing rules, labeling, generic labeling, manufacture and substitution, pharmacovigilance, information and advertising, education, fees, price controls and specialty products.[6] Quality Assurance drug-related policies will affect drug availability. Ineffective use of drugs, poor quality, harmful drugs can lead to therapeutic failure, disease exacerbations, resistance and sometimes death. It also undermines trust in health systems, healthcare professionals, pharmaceutical manufacturers and distributors in addition to a significant amount of money spent on poor quality medicines.[11] Also, using appropriate inventory management systems can also increase the availability of drugs, which using the ABC-VED matrix in the drug supply management system can save time and increase the availability of medicines by carefully monitoring the category I of 40% all drugs.[12]

Policies are undertaken by the government to improve the availability, affordability and rational use of drugs by which the supply of 60% to 90% of drugs are consumed in many developing countries. In the pharmaceutical sector, licenses must be held to reduce competition for price reductions and to ensure the availability of the necessary drugs. In developing countries, the availability of drugs is strongly emphasized by the National Medicine Policy. Implementation of National Health Insurance (NHI) using the National Formulary as a list of drugs chosen to ensure the availability of quality drugs.[13] Countries should update their medicines legislation and regulations regularly to address new pharmaceutical issues as they arise.[11] It is recommended to increase the availability of drugs in Northeastern District, Belo Horizonte; Brazil is doing research analyzing financing issues, expanding the adoption of the Essential Medicines List, avoiding interruptions inpatient care and stock monitoring.[14]

METHODS

Systematic searches are conducted in Science Direct, Plos and Google Scholar to identify all article descriptions, methods and matters affecting the availability of published drugs from 2007 to 2017. We aim to identify all articles related to the availability of drugs in their research to make a comparison of these studies together. The search method consists of search terms for systematic review, search terms for drug availability analysis methods and a drug availability search description filter. Boolean (AND, OR) words, field specifications (Title, Abstract, All fields), duplication checks, a comparison between articles and criteria are also used as a technique for making progress. The complete syntax used in this study is Availability of Drugs AND Key Drugs AND Factors Influencing* [Title / Abstract]). The following inclusion criteria were used in studies of the availability of drugs performed at hospitals, clinics and pharmacies in several low, lower and upper- middle countries. On the other hand, exclusion criteria were used: (1) the study was conducted by methods outside WHO HAI; (2) availability of drug-related to bioavailability in the body is excluded; (3) publications published in non-English journals were also excluded; (4) publications that prejudice incomplete discussions, for example, there is no quantitative data describing drug availability and no discussion of factors that influence drug availability; (5) articles are not listed completely (abstract only). Six results from this study were compared together, using health technology assessments as the same method. Search progress based on article selection is provided in Figure 1.

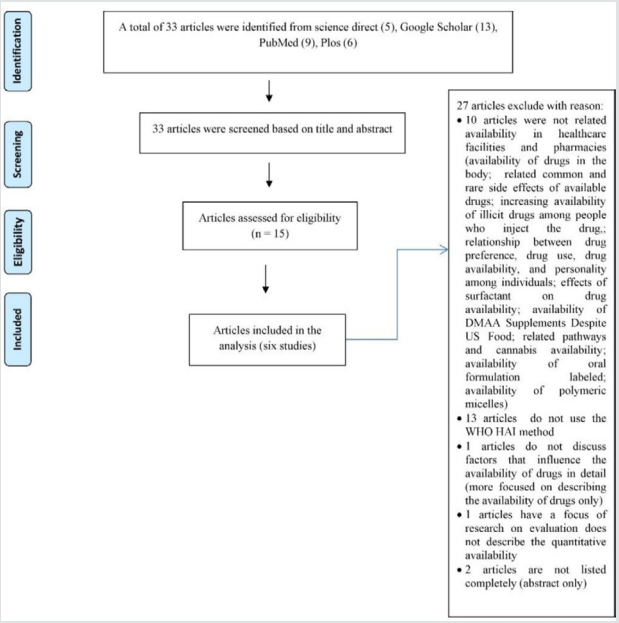

Figure 1: PRISMA diagram of retrieved studies.

RESULT

Search results

A diagram depicts steps of searching followed PRISMA diagram is introduced in Figure 1. As proven in the figure, electronic databases produced a complete of 33 articles (science direct (5), Google Scholar (13), PubMed (9), Plos (6). Title and abstracts of the 58 identified articles were independently assessed by the four authors, of which, 27 were excluded. Finally, six articles are included in the review.

Studies characteristics

Studies were conducted in some countries (Malawi, India, Malaysia, Cina, Thailand, Srilanka). Studies have been done using a standard survey instrument in each country developed by WHO and HAI.

Description of the availability of drugs

In the public sector, availability is very low and only 25% of generic drugs are available. In private pharmacies, the availability of all the drugs surveyed was 43% for Lowest Price Generic (LPG), 18% for Most Sold Generic (MSG) and 39% for Innovator Brand (IB). For the 41 drugs found in both sources, the combined analysis showed that in the public sector, the median availability was 40% for LPG, 0% for MSG and 5% for IB. In private-sector retail pharmacies, the median availability was 43.8% for generic drugs at the lowest price, 18.8% for the most-sold generic drugs and 40.6% for IB. In Dispensing Doctor Sector (DDS), median availability is 45% for LPG, 10% for MSG and 10% for IB.[15]

The average availability of medicines surveyed in all surveyed facilities under Government National Capital Territory (GNCT), Delhi and Municipal Corporation of Delhi (MCD) was 41.3% and 23.2%. The availability of drugs surveyed in three tertiary care hospitals under CG and one tertiary care hospital under GNCT, Delhi and MCD respectively was 60.0%, 40.0%, 42.0%, 60.0 % and 28.0%. Five drugs have 0% availability in New Delhi, i.e., inhalers, beclomethasone inhaler, budesonide+ formoterol inhaler, captopril, gliclazide and dispersible zinc tablets. The five drugs are not in the EML state government of Delhi. On the other hand, MCD has 15 drugs with 0% availability at the surveyed facility. Nine drugs are available in the range of 81-100% in facilities under the Delhi state government and these are amlodipine, amoxicillin 250 mg, atenolol, ibuprofen, norfloxacin, omeprazole, paracetamol suspension, ranitidine and salbutamol inhalers. In general, the availability of medicines is lower at MCD facilities compared to state government facilities in Delhi. The paracetamol suspension, the core drug, is available in almost all public outlets but 75% availability in MCD facilities. Overall availability of two antibacterial core drugs, amoxicillin suspension and cotrimoxazole suspension was poor in the public sector. Zinc sulfate dispersion tablets are not available at any facility.[16]

In 15 public facilities under study, the availability of antimalarial tablets of artemether/lumefantrine and sulfadoxine/pyrimethamine tablets was 93% and in the Malawi Christian Association (CHAM) 100% facility. Amoxicillin tablets/capsules are found to be available in 100% of hospitals, but only in 75% of CHAM facilities and 40% of public health centers. Amoxicillin combination clavulanic acid is not available in the

central hospital and also in seven of the eight CHAM facilities. Two licensed pharmacies included in our study had a good inventory, had ten or even twelve existing inquiry drugs. The four EML compliant drugs that should be available at all levels of the public health care system shows 100% availability in public hospitals but only 65% in public health centres. The availability of twelve drugs included in the study was found to be highest (92%) in private pharmacies.[17]

A fairly high availability (50-80%) of the medicines for Non-Communicable Diseases (NCD) was seen in the survey sample. The average availability of the survey area ranges from 50 - 80% at 8 and over 80% of one region. Only one survey area showed less than 50% (45%) availability outside the community healthcare facility. Two survey areas show less than 50% availability in pharmacies outside private hospitals. Rajya Osu Sala and private pharmacies show more than 50% availability in all survey areas. Although 45/50 of the drugs surveyed should be available in public hospital level 4, availability was only 64.6%. The single drug (alendronic acid) supplied only to the 4th level institution, indicating 30.8% availability. Twenty EM has availability in the range of 50% to 80%. The average availability of these 11 drugs is between 30% and 49%. There is 0% availability of sodium valproate syrup at a community healthcare facility. Very low availability (0 - 30%) was seen with aspirin 100 mg, 80 mg gliclazide, ipratropium bromide 40 µg, levodopa-carbidopa 100 + 25 mg, lithium carbonate 300 mg, ranitidine 150 mg and 25% timolol eye drop solution in sector. Seven originators have high enough availability (50 - 80%). The three brands of originators have availability between 50-30% while 20 indicate less than 30% .[18]

In China, the availability of 100% LPG is the central facility, for only 11.5% IB is available in the central facility and only four Amlodipine medicines, Captopril, Ciprofloxacin and Metformin have> 50% drug availability. The average LPG and IB availability is 32.6% and 36.8% in secondary and tertiary facilities. Also, only 24 IBs in secondary and tertiary facilities and 4 in retail pharmacies have> 50% availability. Although the average IB availability at secondary and tertiary facilities (36.8%) is low, this value is the highest of the surveyed sectors. Overall, the highest availability of LPG (100%) and the lowest IB (11.5%) was observed in primary health facilities, whereas the most widely available IBs (36.8%) and LPG were least available (32.6%) at the facility secondary and tertiary.[19]

In the public sector, the availability of median brands of innovators and generic drugs at the lowest prices are 10% and 75%, respectively. In the private sector, the availability of each type of drug is 28.6%. Low availability of drugs in beclometasone inhalers (15% brand innovators and 10% generic). Drugs used to treat HIV/ AIDS have poor availability in the public sector (except lamivudine) and are not found in private pharmacies surveyed.[20]

Factors influencing drug availability

The factors that influence the availability of drugs in Malaysia are the inaccessibility of drug prices, especially generic drugs. Thus price policy is required and should be incorporated into national drug policy. This policy aims to increase the availability of affordable generic drugs.[15] Low drugs in the public sector can be attributed to factors such as underbudgeting, the purchase of drugs not included in the essential drugs list, inability to accurately predict the needs and inefficient purchases in the supply chain.[16] Cooperation between government and non-government in providing access to essential medicines in Malawi dramatically affects the availability of medicines.[17] There are many generic and generic brands available for most of the pharmacies in government pharmacies of the private and semi-government thus increasing the availability and affordability of medicine.[18] In Jiangsu Province, the high availability of LPG at primary care facilities reflects the success of the government's drug policy, while low availability at secondary and tertiary levels and private pharmacies reflects the failure to implement policies at this level. National essential treatment policies should be fully developed and enforced at the secondary and tertiary levels and in private pharmacies of the Chinese health system to ensure fair access to essential health services. Government policies that support drug access sufficiently affect the availability of drugs.[19] Based on research results required review of policies, regulations and educational interventions that impact on drug prices and availability.[20]

Method of measuring drug availability

Studies in Malaysia follow the WHO HAI methodology. Among the total 48 medicines included in the survey, 28 were included in the main list of drugs recommended by WHO HAI for international comparison and 20 were added as complementary drugs. The main list of drugs is selected based on global disease burden. Additional lists are prepared by local disease burden, local needs as determined by community surveys, while other factors, such as the availability of medicines, are considered.[15]

A total of 50 drugs were surveyed in India based on the WHO/HAI Methodology which used 30 main drugs, 14 essential drugs for global diseases and 16 specifics for Southeast Asia. Outside of these core drugs, the list of drug supplements (20) is added. The supplementary list includes 17 commonly used antibiotics based on inclusion in the state of Delhi EML; two commonly used inhalers for asthma and zinc sulfate tablets recommended by WHO for acute diarrhea in children.[16]

The samples in the study in southern Malawi were six antimalarial drugs and 6 antibiotics collected in 31 health facilities in four districts including 15 public facilities, eight CHAM and eight private facilities. These data were analyzed using standard methodologies developed by the WHO HAI.[17]

The methodology is based on the second WHO HAI. The survey was drawn from 50 drugs taken from global, regional and additional lists. An additional list for this research is the NEML for Sri Lanka. The list of drugs surveyed included 9 drugs from the global core list, 10 drugs from the regional core list and the rest from Sri Lanka essential medicines list (SL-EML). Identified diseases include cardiovascular disease, diabetes, asthma and COPD, gastric ulcers, osteoporosis, thyroid disease, epilepsy, Parkinsonism, psychiatric disorders, osteoarthritis joint disorders and glaucoma.[18]

This research in China method adopted the modified WHO HAI methodology according to the research requirements undertaken in the provinces of China. Finally selected for this survey, including 23 main drugs and 27 complementary drugs. The first represents the drugs commonly used in the treatment of various chronic and acute conditions, while the latter is urgently needed. The study also used STROBE guidelines for observational studies.[19]

Field studies to measure the availability and price of selected medicines were conducted in Thailand during October and December 2006, using the standard methodology developed by WHO and HAI 2003. 43 drug data were collected in 20 public sector health facilities (20 hospitals) and 21 private pharmacies selected using a validated sampling frame.[20]

The following is a summary of the results as listed in Table 1.

DISCUSSION

There is the relatively low availability of medicines in some countries. Average availability of generic drugs is better than IB drugs, especially in the public sector. The availability of innovator brand drugs is low in the public sector, while the availability of drugs at low prices is great because most would instead buy generic drugs at lower prices than more expensive innovator brands. This is because the government's health budget is

Table 1: Summary of the results of articles

No	Authors	Years	Target population	World Bank income group (2010)	Overview	Methods	Factors influencing drug availability
1.	Zaheer Ud Din Babar, Mohamed Izham Mohamed Ibrahim, Harpal Singh, Nadeem Irfan Bukahri, Andrew Creese	2007	20 public sector facilities, 32 private sector retail pharmacies and 20 dispensing doctors in four geographical regions of West Malaysia	Upper-middle	In the public sector, the availability of drugs is very low and only 25% of generic drugs are available. In private pharmacies, the availability of all drugs surveyed was 43% for LPG, 18% for MSG, and 39% for IB. For 41 drugs found in both sources, the combined analysis showed that in the public sector, the average availability was 40% for LPG, 0% for MSG, and 5% for IB. In private-sector retail pharmacies, the median availability was 43.8% for generic drugs at the lowest price, 18.8% for the most-sold generic drugs and 40.6% for IB. In DDS, the median availability is 45% for LPG, 10% for MSG, and 10% for IB	WHO HAI	The factors that influence the availability of drugs in Malaysia are the inaccessibility of drug prices, especially generic drugs. Thus price policy is required and should be incorporated into national drug policy. This policy aims to increase the availability of affordable generic drugs.
2.	Anita Kotwani	2013	Public healthcare providers: the federal (central) government, state government and Municipal Corporation of Delhi (MCD)	Middle Income	The overall average availability of the drugs surveyed at facilities under the state government and MCD is 41.3% and 23.2. The overall availability of medicines in three tertiary care facilities was 49.3%. The availability of generic drugs is much higher in the private sector.	WHO HAI	Low drugs in the public sector can be attributed to factors such as under-budgeting, the purchase of drugs not included in the essential drugs list, inability to accurately predict the needs and inefficient purchases in the supply chain.
3.	Felix Khuluza1, Lutz Heide2	2017	15 public facilities (i.e. health centers, district hospitals and central hospitals), eight CHAM and eight private facilities in Malawi	Low Income	Availability of antimalarial artemether/lumefantrine and sulfadoxine/pyrimethamine have high public and CHAM facilities (93% and 100% respectively). However, the availability of antibiotics is much lower (eg 40% availability of amoxicillin tablets/capsules in public health centers).	WHO HAI	Cooperation between government and non-government in providing access to essential medicines in Malawi dramatically affects the availability of medicines
4	Panthihage Ruvini L Dabare, Chandanie A Wanigatunge, and BVS Hemantha Beneragama	2014	A country survey was conducted and facilities representing both public and private pharmacies were selected in Srilanka	Lower-middle	Semi-government drug pharmacies have the highest availability (> 80%) while pharmacies outside public health care facilities, private pharmacies, and pharmacies outside private hospitals show high availability (50-80%) of the drugs surveyed.	WHO HAI	There are many generic and generic brands available for most of the pharmacies in government pharmacies of the private and semi-government thus increasing the availability and affordability of medicine

5.	Xiaoyu Xi, Weixia Li, Jun Li, Xuan Zhu, Cong Fu, Xu Wei and Shuzhen Chu*	2015	public hospitals and private pharmacies in Jiangsu Province	Upper middle income	The average availability of innovators and drug brands with the LPG was 11.5% and 100% in primary health facilities, 36.8% and 32.6% in the secondary and tertiary sectors, and 18.7% and 42%, respectively.	WHO HAI	In Jiangsu Province, the high availability of LPG at primary care facilities reflects the success of the government's drug policy, while low availability at secondary and tertiary levels and private pharmacies reflect the failure to implement policies at this level. National essential treatment policies should be fully developed and enforced at the secondary and tertiary levels and in private pharmacies of the Chinese health system to ensure fair access to essential health services. Government policies that support drug access sufficiently affect the availability of drugs
6.	Cha-once Sooksriwong, Worasuda, Arthorn Riewpaiboon, Petcharat Pongcharoensuk, Montarat Thavorncharoensab, Usa Chaikledkaew, Siriwat Suwattanapreeda	2007	Health facilities and pharmacies in the capital city, Bangkok, and three randomly selected districts in each part of Thailand: Phitsanulok (North), Suratthani (South), and Nakornrachaseema (Northeast).	Upper middle income	In the public sector, the availability of median brands of innovators and generic drugs at the lowest price is 10% and 75%. In the private sector, the median availability of each type of product is 28.6%. The public sector obtaining the most product is generic.	WHO HAI	Based on research results required review of policies, regulations and educational interventions that impact on drug prices and availability.

given to limited public hospitals where public hospitals should allocate their budget efficiently by purchasing generic drugs at lower prices. The low availability of medicines on the National List of Essential Medicines and Drugs Formularies at government hospitals can have direct implications for access since patients must purchase these drugs from private pharmacies. While private pharmacies have fewer generic drugs, so patients have to spend a higher cost. Due to the unavailability of many drugs, the patient's impacts pay more significant. Better availability in the public sector will put pressure on the private sector to lower generic prices. The limited availability of medicines in government facilities is due to factors such as budgetary constraints, the purchase of drugs not included in the EML, the inability to accurately predict the need and inefficient purchases/distributions in the supply chain.[16,21] High availability of drugs in the private sector is found, although higher medicinal prices inhibit access. The availability of some drugs was found to be less than optimal; for many medications, but only one version of the product available is expensive or branded drugs (popular trade names). Therefore, the patient has no choice but to buy such expensive branded products while the Pharmacist will make the most commonly prescribed medication so this should be controlled. The lack of availability of essential drugs is a problem for the treatment of the dominant diseases affecting developing countries.[22] Providing universal access to essential drugs is a key challenge in low- and middle-income countries, although there is sufficient information from developed countries on access to essential medicines, data from Low Middle-Income Countries (LMICs) common drug in the public sector is only 35%.[21]

Based on the description of the most factors that can increase the availability of drugs is related to government policies to improve drug access and lower prices, so reviews of drug policy are needed. This is also consistent with studies conducted by WHO in 36 countries with medium and growing incomes where results from regulatory and legislative options such as the increased promotion of generic drugs and alternative funding mechanisms are needed to improve drug availability, reduce prices and improve affordability. Pricing policy is required and should be incorporated into national drug policy where this policy should aim to increase the availability of affordable generic drugs. To control availability and marketing it is necessary to register drugs, list essential national drugs, prescription and dispensing rules, labeling, generic labeling, manufacture and substitution, pharmacovigilance, information and advertisements, education, fees, price controls and specialty products.[18] Factors contributing to inadequate access to drugs include the economic aspects, laws, policies, lack of knowledge, social behavior, legislation, policies and the lack of highly interlinked knowledge.[23] Based on research conducted in Saudi Arabia obtained the result that the level of use of generic drugs is shallow. Majority Doctors and Pharmacists are convinced that the drug is branded better outcomes to patients and this attitude has the potential to make Government policy of generic drug usage ineffective.[24] So it takes regulation and legislation from the government to be able to overcome this; thus the use and availability of drugs, especially generic drugs can be increased.

The WHO HAI method is effectively used to measure the availability of drugs by using the core drug and supplementary drug references by the established reference. The list of global and regional core drugs is part of the WHO/HAI methodology standard. By drug standardization surveyed at global and regional can compare their findings with other countries and other international comparisons can do. Up to 50 medicines are included in the survey. The list of survey medicines is generally composed of 14 global core medicines; 16 regional core medicines; and

20 supplementary medicines. Supplementary drugs are selected at the country level by their respective national interests or for collecting data on specific therapeutic classes. The limitations of this systematic review are the focus of the literature review is not specific to one influencing factor but analyzes the factors that influence the availability of the drug. So that in the systematic review in the next stage can be advanced analysis with a focus on policies and regulations that most affect the availability of drugs.

CONCLUSION

There is the relatively low availability of medicines in some countries. The availability of drugs in developing countries still needs to be improved by increasing drug access and control prices by using appropriate government policies. The WHO HAI method is effectively used to measure the availability of drugs by using the core drug and supplementary drug references by the established reference.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

CHAM: Malawi Christian Association; **LMICs:** Low Middle-Income Countries; **COPD**: Chronic Obstructive Pulmonary Disease; **DDS**: Dispensing Doctor Sector; **EML**: Essential Medicines List; **GNCT**: Government National Capital Territory; **HAI**: Health Action International; **IB**: Innovator Brand; **IPE**: In-Patient Expenditure; **LPG**: Lowest Price Generic equivalent; **MSG**: Most Sold Generic equivalent; **MCD**: Municipal Corporation of Delhi; **NCD**: Non-Communicable Diseases; **PHARMAC**: Pharmaceutical Management Agency.

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