IFMSA Policy Document
Access to Medicines

Proposed by the IFMSA Team of Officials
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Policy Statement

Introduction

Access to medication is a fundamental pillar in the link between global health, human rights, and sustainable development. However, issues such as medication inequity and access barriers pose significant threats. Ensuring availability, affordability, and quality requires a focused, cross-disciplinary approach involving regulations, pricing, and supply chain management.

IFMSA Position

The International Federation of Medical Students' Association (IFMSA) strongly believes that every human has the right to access safe, efficient, affordable, and accessible medication. We believe the current market is profit-focused and must prioritise the positive health outcomes of accessible medicine. We support the inclusion of medicine accessibility in the development of Universal Health Coverage (UHC). The current research and development systems need re-allocation towards existing global health issues in new drug development and production of generic alternatives. Transparency in research, with public-oriented incentives, greatly propels innovation and the availability of affordable medicine. We support pharmacovigilance systems aiming to eliminate counterfeit medications and mitigate their impact. We believe that agreements promoting patent monopolies, especially Trade-Related Aspects of Intellectual Property Rights (TRIPS) and TRIPS-plus, are among the main barriers to equitable access to medicine.

Call to Action

Therefore, the IFMSA calls on:

Governments to:

- Allocate financial and human resources to strengthen the Universal Health Coverage and health insurance system, especially in low and medium Human Development Index countries.
- Ensure availability, quality, and accessibility of essential medications to the population in health institutions.
- Implement stronger registration laws and strategies, including monitoring and evaluation tools, to improve the functioning of local pharmacovigilance systems trafficking for counterfeit medicines.
- Allocate specific funding priorities and incentives for drug innovation and research in diseases impacting the community.
- Implement varied price control strategies whilst ensuring these mechanisms are done carefully without compromising the quality production of medicines.
- Implement policies promoting the production, approval, and prescription of biosimilar and generic drugs to increase competition among pharmaceutical companies and the availability of alternatives for price regulation. Assess and review existing legislation concerning the control of me-too drugs and ensure its enforcement and implementation.
- Oppose the addition of TRIPS-plus clauses to upcoming free trade agreements while supporting the TRIPS flexibilities.

World Health Organization (WHO) and Global Health Institutions to:

- Establish standard, globally applicable guidelines and instructions for countries worldwide on identifying, reporting, and sharing information on falsified medicine.
- Enforce global standards for transparency in clinical trials by pharmaceutical companies and research institutes.
- Promote and lead the implementation of the roadmap for access to medicines and vaccines 2019– 2023 and continue providing guidance and standards on health products' quality, safety, and efficacy.

- Create a unified, international, open-source database on medicine prices and patents.
- Implement the WHO guidelines on clinical trial reporting and registration to ensure data sharing between companies and organisations.
- Encourage collaborations and programs to raise funding and awareness about access and rational use of medicines.

Pharmaceutical companies to:

- Invest in research and development of efficient medicine that aligns with health needs globally.
- Adopt open innovation such as crowdsourcing for a cost-effective Research and Development(R&D)
- Disclose the expenditure of R&D to the public.
- Endorse Open Access Publications and open-source data for clinical trials and drug research.
- Establish Product Development Partnerships (PDP) between the private and governmental sectors to improve the provision of health products and thus enhance health equity.
- Commit to Collaborating with the WHO in times of health emergencies to ensure their products are accessible globally.

Healthcare Professionals and Facilities to:

- Organise educational initiatives about medicine accessibility for healthcare professionals focused on prescribing medication for physicians.
- Collaborate with the government to support providing and distributing affordable subsidised medicines of good quality and sufficient quantities.
- Educate patients on purchasing medicine through accredited online pharmacies and rational use of drugs.

IFMSA National Members Organizations (NMOs) and Healthcare Students:

- Organise campaigns for members, medical students, and critical stakeholders on access to medicines and how to engage in them.
- Organise campaigns and programs to raise public awareness about counterfeit medicines.

Position Paper

Background information

Access to healthcare is a global priority that involves a multisectoral approach towards major elements of the healthcare system. Access to medicine is defined as "the availability and financial and physical ability of an individual to obtain and receive medicines, and this is an essential element to attain the best possible health standards".(1) Ensuring that access to available, affordable, safe, and efficient medicine is crucial to achieving the Sustainable Development Goals (SDG) 3, particularly SDG 3.8 and 3. b.In 2019, 381 million people were pushed into poverty due to out-of-pocket payments for health, including medicine. (2)This heavily impacts patients, especially people suffering from chronic diseases. The WHO also estimates that 30% of people are deprived of access to essential medicine regularly. (3)
Therefore, the availability and affordability of medicine are crucial to reducing the health burden on the population and the government. This also affects the progress of many countries hoping to attain universal health coverage and Health for All. Furthermore, profit-driven approaches and a lack of innovative research lead to further challenges in reducing the burden of NCDs and infectious diseases. (4) It is also crucial that the products available are assessed for quality, effectiveness, and Impact on the community to avoid adverse health impacts and economic impacts. (5) Accessibility to medicine has also been highlighted amid the COVID-19 pandemic, including the current barriers and opportunities of global distribution in health crises regarding medicines and vaccinations. On December 5th, 2018, the WHO published the "WHO Roadmap on access to medicines and vaccines" for 2019-2023, providing a unified goal towards access to medicine for countries. (6)
Therefore, achieving accessible medicine requires a multidisciplinary approach to regulations, Pricing, supply chain management, and rational use of these products.

Discussion

1. Availability of Medicine

1.1 Overview of Essential Medicine

Essential medicines are necessary for healthcare; they provide and satisfy the population's healthcare needs and are efficient and safe. The World Health Organization 1977 defined essential medicines as "those that satisfy the priority health care needs of the population".(7) It is intended to be available in all functioning health systems in adequate amounts and appropriate dosage forms. (8) Essential medicines are also intended to be adaptable and flexible to different situations, providing distribution responsibility; they are selected considering disease prevalence, public health relevance, and evidence of efficacy, safety, and cost-effectiveness. The elements of essential medicine are procurement, supply, prescribing and dispensing of medicines, financing, rational use of medicine, and the careful selection of essential medicines. The latest list of essential medicines by the WHO is the 2023 Edition.

1.2 Causes of Shortage of Medicine

There are current problems in the healthcare system due to drug shortages. This problem has existed since the first drug scarcity in the early 1920s with insulin shortage, then started to become more widespread. Drug shortage is a problem that affects high, middle, and low-income countries, causing health and economic crises. Causes include business decisions, manufacturing problems, raw material unavailability, and regulatory issues. In low-middle-income countries, the causes of the shortage of medicine are different, including licensing of manufacturers and products, shortage of raw material for a local manufacturer, drug smuggling, and lodging tax government policies. One of the principal problems of drug shortages is its Impact on different stakeholders, especially patients. These impacts include delayed care, continuous referral, increased length of hospitalisation, and ultimately increased mortality rate. Countries have developed strategies to tackle the current problem, including improved reporting systems, policy changes, drug shortage platforms, and accelerated drug approval. (9)Generally, the shortage of medicine is a multidisciplinary problem involving health, economic, and social issues that need a multidisciplinary approach to satisfy the community's health needs.

1.3 Rational use of medicine

The Rational use of medicine is a complex topic to discuss as it involves specific criteria, including policies, structures, information, and education; it also requires evidence-based clinical guidelines for decision-making, a list of essential medicines, and continuing medical education. A national body to coordinate policies and adequate funding is needed to ensure the availability of medicines and health personnel. (10) The World Health Organization says that rational use of medicines requires patients to receive medications appropriate to their clinical needs, in doses meeting their requirements, and at the lowest cost. It is estimated that half of all medicines are prescribed, sold, or dispensed inappropriately and that half of all patients fail to take them correctly, making irrational use of drugs a major problem worldwide; some examples of this are inappropriate use of antimicrobials, inappropriate self-medication, non-adherence to dosing regimes, often of prescription-only medicines, etc. The goal is to promote the rational use of medicines through strategies for teamwork between health professionals and consumers. (11)

2. Affordability & pricing strategies

2.1 Barriers to Affordable Medicine

Data suggests that up to one-fifth of healthcare spending could be utilised more effectively by avoiding waste, which occurs (a) when healthcare products are overpriced, (b) when lower-cost but similarly efficient alternatives are not used, and (c) when bought items are not used at all. (4)

Prescription medicine prices that are relatively expensive can threaten healthcare budgets and reduce funds available for other sectors that require public investment. (12)There is a disparity between the funds to support essential medications and the medicine's overall cost. Medicine affordability has been defined as "the cost of medicines or treatment with medicine that the lowest paid government employee income would be required to pay to purchase from the private sector a one-month course of medicine at the standard dose. (13) Yearly, millions of people die, particularly in LMICs (Africa), due to the high expenses of medication as one of the significant hurdles in their treatment process. Malaria, T.B., and HIV-related ailments claimed the lives of roughly 1.6 million African people in 2015, which can be avoided or cured if affordable medications, vaccinations, and health services are made available on time.
Patent medicine markets have traditionally been seen as both renewable and self-evident. (14)Pharmaceutical corporations set medicine prices based on what society can pay without a systematic pricing structure since individuals are willing to bear a significant financial burden when treating life-threatening illnesses. (15)This is also known as the price that society will pay if a disease is not addressed or is treated with a substandard treatment. They have been the source of income for extremely successful pharmaceutical companies but can also be severely impacted by changes in medication life cycles. (14) The presence of monopolies is the primary cause of the high cost of prescription medications. As patents expire, generic competition should ultimately arise; monopolies should only last temporarily. However, this seldom occurs in cases of cancer and other chronic, life-threatening illnesses. A medication is already deemed outdated (planned obsolescence) and no longer the standard of care by the time its patent expires. A new and improved version will be created, with another monopoly protection and a new patent life. (12) Pharmaceutical corporations argue that maintaining innovation requires high medicine prices. However, the capacity to set high costs for each new medication may limit the rate of invention. Developing medications that are substantially safer or more effective than current medications is a less hazardous approach than developing entirely novel medications. (12) The industry's high level of deal-making activity, coupled with failure in the market, resulted in price hikes for even unlicensed medications. (14)

There are also visible global variations in medicine prices. Disparities appear in the costs health systems spend to purchase necessary cancer drugs. Price differences according to region suggest that these variables may affect the affordability of vital cancer medications. (16) Anti-cancer medicine costs exhibit significant regional variation in Southeast Asia, the Western Pacific, and the Eastern Mediterranean. Studies have indicated a correlation between anti-cancer drug prices and a country's economic situation. Therefore, a review of pricing

policies is required to increase the affordability and accessibility of cancer medications in the chosen nations. (15)
Another example is the significant pricing difference in critical cardiovascular medications. Patient's financial savings heavily depend on the selected brand for their cardiovascular disease. Therefore, patient-physician communication regarding socioeconomic factors is essential in drug prescription. (17) Instead of implementing laws for an abrupt price reduction, the government should advocate for value-based Pricing and establish treatment guidelines to address the problem of physicians prescribing costly drugs due to incentives. (12)

2.2 Improving Pricing

PDPs

Product development partnerships (PDPs) are "*public–private partnerships established to develop and provide access to new health products – especially vaccines, therapeutics, and diagnostics – for poverty-related and neglected diseases. PDPs are non-profit-making and typically funded by public and philanthropic organisations.*" (18)
Certain PDPs acknowledge that to decrease global health inequities, they must generate access to their goods and enhance research capacity in developing countries. For example, PDPs can help LMICs conduct their research to create low-cost products for neglected diseases and to improve their healthcare systems. (19)

Subsidies

Specific finance structures encourage price reductions for essential drugs, resulting in quick acceptance. For instance, The Global Fund's Affordable Medicines Facility for Malaria is designed to give significant subsidies to the private sector, as many individuals get medicines primarily through private markets. (20)

Increased Competition and Generic Medicine

As more generic drug companies enter the market, prices will continue to decline, making efforts to maintain successful competition among suppliers crucial to price control. Generic substitution is one of the best strategies utilised by health authorities in many countries to keep drug prices at an acceptable range while reducing healthcare costs. To put it quantitatively, an empirical study states that once ten generic drugs from competitors enter the market, the price of a branded drug is expected to decrease by around 25%.(21) Since 2019, the FDA has started to increase approval of biosimilar drugs after patent expiry, which has proven to increase competition in the pharmaceutical market and allow prices to fall from the brand-only monopoly price. (22) However, concerns about their safety and efficiency are raised compared to original branding drugs due to physicians' and patient's need for more confidence and knowledge about generic drugs. (23)

Risk Pooling

The WHO defines risk-pooling as the "*accumulation and management of revenues in such a way as to ensure that the risk of having to pay for health care is borne by all members of the pool and not by each contributor individually*" (24)
The WHO views high-risk pooled health funding models, such as health insurance and prepaid plans, as a viable way to promote health care and achieve universal health coverage. (24)
Pooled procurement has been directly advocated to solve several issues associated with restricted access to reasonably priced pharmaceuticals, including insufficient technical capability and incentives to produce or supply certain drugs or vaccines. Several objectives have been met by implementing pooled procurement mechanisms, such as price decreases brought about by demand grouping, increased efficiency and quality standards through sharing technical and human resources, and enhanced accessibility and sustainability through supplier benefits, consequently increasing supplier competition. (25)

2.3 Solutions

It is challenging to produce and distribute low-cost medications. (20) Because no single approach is sufficient, stakeholders must continue to engage in partnerships that promote knowledge and technology transfer to ensure essential medicines are manufactured and distributed in low-income and middle-income countries (LMICs) at affordable prices. (20) Regulation change is desperately needed to control costs and ensure everyone can access novel medications. (14)

Governments have attempted to affect medication pricing through market interventions and using healthcare quality-adjusted life year(QALY) measurements, but they frequently run into unwanted effects. The most viable short-term policy solutions include outcome-oriented Pricing, reference pricing, patent reform legislation, and encouraging doctors and pharmacists to recommend low-cost medications. (14)Policymakers in several high-income countries have extensively employed price regulation techniques, such as international or external reference pricing, to control the cost of prescription drugs. (14,15) The WHO defines external reference pricing as: "*The practice of using the price[s] of a medicine in one or several countries in order to derive a benchmark or reference price to set or negotiate the price of the product in a given country*".(26) Asia Pacific countries implement different pricing strategies and varied methods of implementation. For example, they implement different drug types and formulas that a strategy applies to, regardless of whether the strategy is a regulation or an instruction. Strategies are used partly to reduce costs but may also encourage price consistency, invention, and wider availability in the near and long term. (27)

3. Health Systems & Infrastructure

3.1 Universal Health Coverage and Health Insurance

The World Health Organization (WHO) emphasises the importance of Universal Health Coverage (UHC), ensuring that all individuals can access necessary health services without financial hardships. (28) Health insurance serves to achieve this goal, offering financial protection against healthcare costs. (29)While progress towards UHC was notable until 2015, there has been a limited increase of 3% in the UHC service coverage index in the past eight years. 2019, the index showed no improvement, leaving 4.5 billion people without coverage. Various challenges and obstacles hinder the effective implementation of UHC.(30) In the 2019 report from the World Bank Group, people in low-income countries spend over half a trillion dollars every year—more than $80 per person—using their own money for healthcare. (31)This indicates a significant financial strain on patients when purchasing medicines, especially for those dealing with chronic diseases. (32)

3.2 Barriers in the Healthcare System & Infrastructure

Overcoming the obstacles of Universal Health Coverage (UHC) involves addressing various barriers within the health system, impacting both the fundamental right to access health and the availability of medicines. (33)

Transportation is widely recognised as a barrier to getting medications and health services owing to road closures, poor infrastructure, and transportation limitations. (13) Developing countries need more infrastructure to improve access to medicines. Most diagnostics, for example, are not designed for use in non-optimal laboratory circumstances, such as those seen in developing countries, where there is a shortage of air conditioning, reliable electrical power, and freezers to keep samples and reagents. (20)

Furthermore, The inability of competent dispensary workers at the medical centre level and supply work has become a pivotal barrier to enhancing access to vital medications and primary healthcare service delivery. Significant deficiencies of highly educated health professionals found in African countries have been worsened in the current crisis by gaps in workforce distribution, compromising the implementation of efficient public health Interventions for people in need, particularly in distant rural regions. (13)

Infrastructure and supply challenges within health systems reveal a predominant concern with logistics and equipment, constituting 31% of reported issues. "The Human Development Index (HDI) is a measure of a country's achievement level of human knowledge, health and standard of living". Low and medium HDI countries

grapple with infrastructure, logistics, and equipment challenges at 35% and 41%, respectively. At the same time, high and very high HDI nations report issues associated with the cost of drugs and technologies, "24% and 27% respectively". Consequences of these challenges span medication shortages, expiration problems, and irregular stock control, affecting both low and very-high HDI countries. (34)
Leadership and governance challenges in healthcare encompass strategic policies and governance (31%), oversight and accountability (26%), and horizontal coordination (25%) across diverse HDI groups. Robust oversight and accountability mechanisms are indispensable, evidenced by struggles with drug quality in low HDI nations and collusion between healthcare providers and the pharmaceutical sector in high HDI nations. (34) These challenges encompass fragile public health leadership and inadequate health-related legislation and enforcement, contributing to issues observed in countries where government and non-governmental organisations' cooperation in providing access to essential medicines is lacking. (13)

3.3 Solutions

Reducing Out-of-Pocket Healthcare Expenses in Asia and Africa

Developed Asian and African nations, strategies encompass medical subsidies, universal health coverage, selective pharmacies, performance-based payments, contraception cost elimination, and telehealth for enhanced primary care. This approach addresses financial barriers to healthcare access, ensuring more inclusive and sustainable access to medicines. (35)

Government Support for Healthcare Initiatives

Governments play a central role in strengthening access to medicines by supporting public health insurance, subsidising expensive diseases, providing physician training, and formulating clinical guidelines. Innovative financing methods, including collection, pooling, and purchasing strategies, are strategically employed to ensure a sustainable and effective healthcare infrastructure. (34)

Global Healthcare Strategy

To overcome healthcare challenges, a unified approach is crucial. In low-development countries, tailor evidence-based practices locally and enhance knowledge accessibility. In high-development nations, systematically evaluate new technologies, build health technology, and assess capacity. An integrated, adaptable approach is essential for global access to medicine and healthcare. (34)

4. Regulations and Quality Assurance

Pharmaceutical regulation in developing countries needs more effective laws, quality manufacturing capability, suitable personnel resources, and adequate time for pharmaceutical registration. (13)

4.1 Counterfeit Medications

The WHO defines falsified medicine as' *products that deliberately/fraudulently misrepresent their identity, composition and source'*, also known as unregistered and unlicensed drugs that fail to meet the quality standard outlined by National Pharmacopoeia. (36) It also encompasses expired medications sold with modified labels and expiry dates, often motivated by financial gains. (37) Although low and middle-income countries represent one-tenth of the falsified medicine issue, it has become a widespread concern affecting all nations, with an estimated 10% of the medicine globally being counterfeit. (38)

4.1.1 Impact of falsified medicine

Counterfeit medicine varies from lacking active ingredients to having dangerously excessive ones, posting risks from no therapeutic benefits to fatalities. In developed countries, around 56.3% reported incidents involving health consequences. However, a comparable figure of 43.7% was documented in sub-Saharan Africa(LMIC). (39) Based on the WHO 2017 report, ineffective antimalarial drugs resulted in approximately 529 deaths per 1

million cases. (40,41) A 1% prevalence of counterfeit antibiotics correlates with 8688 cases; the cases rise to 72430 with a 10% prevalence. (41) Additional treatment due to falsified medicine leads to an estimated loss of 12 to 44 billion dollars. It was estimated that the global market of falsified medicine is worth US$200-432 billion. (42)

4.1.2 Barrier to Tackle Counterfeit Medicine

Counterfeit medicine is a global issue requiring universal Action and attention. Global capacity to detect falsified drugs is limited, with only 126 Member states and 400 regulatory personnel being equipped and trained, according to WHO's 2017 report. (43) According to the Pharmaceutical Security Institute, Asia remains the primary source of falsified drugs globally. (44) As cases are underrepresented, it challenges fair regulation and resource allocation.WHO databases heavily rely on the company's routine investigation report, which potentially overlooked drugs that were perceived to be less crucial and life-saving. This led to countries receiving the least resources and attention to detect falsifiability. Insufficient awareness, corruption, lack of reporting practices, and undetectable packaging further contribute to unreported cases. (45) Without comprehensive and standardised reporting rules, addressing and reporting falsified medicine relies mainly on individual company's decisions.

Public awareness and education about falsified medicine need to be increased. (46) One's ability to identify faulty medications is linked to geographical status, education level, employment status, and age. (46,47) This association is particularly notable and evident in LMICs, such as Middle Eastern countries, whose awareness rate is only 26.6%. (46) Hence, this highlights the need to address social determinants before effectively tackling this issue. Learning about the economic impacts, such as how it deters pharmaceutical companies from investing in research and development, is also necessary, especially in LMIC, whose markets are more vulnerable. (48) Counterfeit medicine will diminish revenue generated by the original brand company, leading to less investment in developing essential new drugs and less disease being combatted. (48)There is an urgent need for universal, consistent, and transparent legislation for counterfeit medication. (49)

Self-diagnosing and self-prescribing cultures have accelerated using Artificial Intelligent Self-diagnosing Digital platforms. Yet, doubts about their accuracy remain, and the regulation of this technology is still in the early stages. (50) Amplified by the COVID-19 pandemic, consumers tend to purchase drugs on social media and unregistered websites due to non-availability and high cost. (48) For example, there has been a surge of approximately 15% in global online purchases of drugs since March 2020. (51) According to the Alliance for Safe Online Pharmacies (ASOP), approximately 96% do not meet U.S. FDA law, and 89% of illegal websites do not require a prescription. (51,52) Evidence shows that engagement of healthcare providers in navigating patients' online medication purchases significantly reduces the number of counterfeit medication buying. (53)

4.1.3 Solutions

Shared Database

Creating open-access databases is essential to ensure every country has equal and fair access to evidence-based information. This is especially crucial in notifying countries about the ongoing unacceptable and unethical practices, aiding them in enhancing their medicine surveillance and regulatory system. For example, the OECD has researched fake pharmaceuticals based on the data collected and compiled by the World Customs Organization, the European Commission's Directorate, the United States Department of Homeland Security, and U.S. Immigration and Customs Enforcement. This enables the identification of trends of substandard medicine by examining past instances and detecting ongoing patterns of criminal activity, facilitating risk profiling, and encouraging international sharing of cases with detailed descriptions. (54) Additionally, when countries face similar challenges of counterfeit medicine exchange information, they can promptly react upon detecting hazardous and life-threatening medication.

Pharmacovigilance system

Identification and detection of counterfeit medicine are considered the primary defense against their establishment in the market. However, training an ample workforce and utilising lab tools pose a challenge. The

implementation of the Pharmacovigilance system was a remedy for these obstacles. WHO defines it as *"the science and activities relating to the detection, assessment, understanding, prevention of adverse effects or any other drugs related problem*". (55) This system consists of 3 core functions: case management (active surveillance), signal management, and benefit-risk management. Signal management encompasses accessing drug safety databases and handling reports of complaints about post-medication adverse effects, serving as a primary information source. (56) As simple as using social media and online platforms, it can function as a method of communication and reporting under the system. (57) However, beyond pharmaceutical companies in OECD countries, other nations have not shown commitment and dedication towards pharmacovigilance systems. (55) Barriers such as limited funding, lack of information dissemination tools, infrastructure, and passive reporting systems hinder the system's effectiveness. Hence, there is a need for a multistakeholder approach and regional collaboration that apply a comprehensive view to tackle policy and systematic gaps in each country. (58)

5. Research & Development (R&D)

5.1 Drug Innovation

5.1.1 Current Barriers towards Innovation

Challenges in drug trials

Drugs cost millions in R&D before being placed on a pharmacy shelf. The cost estimate of R&D on 106 randomly selected drugs from 10 multinational companies has shown an increase at an annual rate of 8.5% above general price inflation. Also, cancer clinical trials often inadequately represent patient populations with historically limited finance, dramatically advanced and minority patients. Likewise, individuals with higher socioeconomic status appear to participate more frequently in cancer clinical trials. These imbalances in enrollment significantly impact downstream outcomes, contributing to the need for more data regarding the real-world Impact of specific therapies on patients. (59) Due to financial barriers, research institutions and companies need more support to participate actively in drug development.

High risk and cost of clinical failure

Drug innovation involves creating formulations that are convenient to store, transport, and administer, safe and environmentally friendly for children. However, proving a concept to establish a drug in the market is lengthy and uncertain. For instance, the FDA has halted 20 clinical trials between 2020 and 2023 due to technology issues. (60) Meanwhile, the estimated success rate for both technical and regulatory trials only stands at approximately 4.2%. The investment for R&D and clinical trials is substantial- studies indicate that initial R&D approval will take 10-15 years, with an approximate cost of 1.2 to 1.8 billion dollars. (61,62)

Lack of effective new drugs

Me-too pharmaceutical products are defined as active compounds with the same therapeutic purpose, which might have different pharmacokinetic effects. About 60% of drugs are categorised as me-too drugs in the WHO essential drugs list. (7) The substantial investment into the development of me-too drugs is driven by its significant returns. As me-too drugs require minimal modification on their active ingredients and staff are trained from producing first candidate drugs, it offers cost-advantages in launching and marketing, benefiting pharmaceutical companies. While me-too drugs offer enhanced therapeutic effects and fewer side effects than first-class medicine, it leads to the trend where similar drugs are not competing based on lower prices but on their marginal difference in therapeutic effects. This is where companies over-stretch their budget advertising me-too drugs, resulting in reduced investment in the R&D of new essential drugs. (63)For instance, pharmaceutical firms have halted antibiotic innovation gradually due to financial barriers despite an estimated 10 million deaths annually projected by 2050 due to antimicrobial resistance. (64)

5.1.2 Solution

Pharmaceutical companies can enhance research efficiency by embracing open innovation through crowdsourcing, involving submitting and evaluating ideas and proposals from experts and the public. (60)
To address me-too drugs, the government has to review and improve the currently available legislation to control it. The U.S. Orphan Drug Act is a policy that safeguards original drugs/treatments from being replicated and gaining generic approval. It also provides tax credit, encouraging pharmaceutical researchers to focus and invest in rare disease drug development. (65). However, it only comprises seven years of protection. Despite their more considerable societal Impact, it excludes diseases involving pregnant women and the impoverished. (66)
Implementing a more plausible regulating strategy, such as mandating the release of an R&D expenditure breakdown, must be enforced. Authorities must instigate user confidence in generic drugs by implementing and executing detailed guidance covering post-approval safety monitoring and risk management plans. This advancement can improve drug surveillance and boost the patients' and physicians' trust and usage confidence. Moreover, manufacturers are encouraged to apply for interchangeability and product switching for biosimilar/generic drugs, aiming to demonstrate consistent clinical outcomes between patients. (67)

5.2 Emerging Technologies in Drug Innovation

DUBs

Our understanding of deubiquitylating enzyme (DUB) functions, mechanisms of Action, regulation, and disease linkages has dramatically advanced in the past decade. Simultaneously, there have been significant enhancements in DUB biochemical assays and screening technologies. These improvements have led to the creation of an increasing number of small-molecule DUB inhibitors. Researchers are currently exploring the selectivity of these inhibitors and refining them where possible. These inhibitors are the foundation for drug-like molecules suitable for clinical evaluation and versatile tools to investigate DUB cell biology, regulation, and biochemical mechanisms. Additionally, they are employed to test therapeutic hypotheses in disease models. While it is still premature to predict the full extent of the broad therapeutic potential of DUBs, the next few years are expected to bring further exciting developments in the realms of DUB biology and drug discovery. (68)

Artificial Intelligence (A.I.) and Machine Learning in Drug Innovation:

Administering an incorrect drug dose to a patient can result in undesirable and lethal side effects. Therefore, determining a safe drug dose for treatment purposes is crucial. Over the years, ascertaining the optimal dose of a drug that can achieve the desired efficacy with minimal toxic side effects has posed a challenge. (69)

With the rise of A.I., numerous researchers are actively using Machine learning (ML) and Data learning (DL) algorithms to determine appropriate drug dosages. For example, An AI-based platform, AI-PRS, was used to identify the optimal dosage and combinations of drugs for HIV treatment through antiretroviral therapy. Employing the PRS method, the dose of Tenofovir was reduced by 33% from the initial dose without causing virus relapse. Therefore, AI-PRS can also actively determine optimal drug dosages for various other diseases. (70)

This development has fostered enthusiasm within the scientific community and increased collaboration between pharmaceutical companies and A.I. enterprises. (71)According to research, the overall effectiveness of 21,143 drugs was approximately 5.2% in 2013, a decline from 11.2% in 2005. Consequently, the integration of A.I. is primarily linked to the imperative of minimising attrition and cutting costs. (72)Most pharmaceutical companies tend to withhold pharmacokinetic and pharmacodynamic measurements of drugs until they receive approval. Furthermore, there is a need for more available data related to drug discovery for training A.I. models. (73)Establishing a community responsible for overseeing and organising preclinical and clinical pharmacology data is essential to expedite the advancements of A.I. in this field. Recent strides in A.I. have significantly influenced clinical pharmacology, encompassing activities such as literature searching and processing, engagement with online predictive ML models, using ML methods to formulate policies promoting healthcare in various nations, and attaining predictive analyses for drug-related information. (74)

Following the implementation of A.I. technology, there has been a remarkable enhancement in the success rates of clinical trials. (75) A.I. models can contribute to cost reduction in clinical trials by improving success rates by analysing parameters such as toxicity, side effects, and other relevant factors. (76)

5.3 Transparency in Drug Trials and Data

Publication Bias and Access to Full Trial Data:

Publication bias occurs when published studies systematically differ from unpublished results. The tests available for publication bias lack statistical power, especially in situations of high heterogeneity or a low number of studies. Their validity relies on assumptions that often need to be met in practice. Currently, there is no single recommended test. Systematic reviewers should consistently utilise multiple publication bias detection methods and non-statistical approaches, like comparing published evidence from clinical trial registries, records from drug-approving agencies such as the Food and Drug Administration, and scientific conference proceedings. Searching trial registries is a crucial step that can unveil unpublished registered trials. Three commonly searched registries include ClinicalTrials.gov (http://www.clinicaltrials.gov), the International Standard Randomised Controlled Trial Number Register (http://isrctn.org), and the Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au). (77)

Clinical Trial Registration and Reporting

Registering studies before data collection establishes a comprehensive record of the research schedule, including hypotheses, methods, analyses, and outcomes. Researchers must be accountable for adhering to the prespecified methods and justifying any deviations. The World Health Organization promotes the registration of clinical trials through approved primary registries, and funders and publishers increasingly expect this practice. The International Committee of Medical Journal Editors mandates trial registration before publication, and the FDA Amendments Act 2007 in the USA made registration mandatory. This has led to widespread trial registration and facilitated mandatory reporting, ensuring that full findings are disseminated. Systematic reviews are also routinely registered before study commencement. While registration is a valuable tool to encourage result-sharing and discourage unjustified deviations, there are more comprehensive solutions. Undeclared "outcome switching" between registration and publication is common, but journals can ensure that reported outcomes align with prespecified registered outcomes. Despite some caveats, the importance of registration should be considered, as it allows for detecting deviations that would otherwise go unnoticed. (78)

6. Global Supply Chain and Distribution

6.1 Global Trade Agreements

The Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement is formed through the World Trade Organisation (WTO) to set standards for regulating and protecting intellectual property. TRIPS restricts companies' ability to use intellectual property to produce generic drugs. (79)

6.1.1 Issue related to TRIPS

Doha Declaration highlights issues regarding global access to medicine under the implementation of TRIPS, which includes

1. ensuring effective competition policies,
2. maintaining the safety and quality of medicine,
3. exempting taxes and tariffs transparently,
4. enforcing competitive procurement procedures

Additionally, the Doha Declaration also acknowledges the positive impacts of alternative funding mechanisms, donations, partnership programs, and licensing agreements by pharmaceutical companies to tackle the current accessibility problem. However, the challenges are influenced by stakeholders across multiple levels, emphasising the importance of coherence and cooperation among crucial holders.

WTO set standardised I.P. laws to minimise variability but may hinder innovation in under-resourced nations like Brazil. Particularly in pharmaceutical industries, due to deficient infrastructure, issues with compliance to new patent laws, dependency on imported drugs, and banned local production of patented medicines, the medication price will increase under TRIPS, posting more significant issues with inequality. (80)

In recent years, many developing countries have been pressured to implement restrictive conditions in their patent laws that the TRIPS Agreement requires – known as 'TRIPS-plus' provisions. Countries are not inherently bound by international law to adhere to these measures. However, several nations, including Brazil, China, and countries in Central America, have found themselves compelled to integrate these requirements into trade agreements with either the United States or the European Union. Such obligations can severely impede access to essential medications.(81)

Free Trade Agreements (FTAs), negotiated independently of the World Trade Organization (WTO), impose even stricter standards for intellectual property protection on pharmaceuticals than those stipulated by the TRIPS Agreement. These heightened requirements directly impact the accessibility of medicines. FTAs negotiated by the USA are more comprehensive and elaborated than those negotiated by the European Union (E.U.) and European Free Trade Association (EFTA) countries. (82)

6.1.2 Promoting TRIPS flexibility

TRIPS flexibilities aim to permit developing and least-developed countries to use TRIPS-compatible norms in a manner that enables them to pursue their public policies in specific fields like access to pharmaceutical products. (83)

Compulsory licensing

The 'paragraph 6 system' under the DOHA Declaration and article 1.1 in the TRIPS agreement allows for compulsory licensing for under-resourced countries, production, and importation of low-cost generic drugs without a patent holder's permission. (84) However, careful implementation and planning are crucial due to the safety concerns of generic medications. Some LMIC regions need the proper infrastructure of trade relations and potentially drop patent and generic drug prices due to extensive competition, which impacts the R&D of new drugs for diseases required. (85–87)

African countries show minimal patenting activity, emphasising the importance of building and enhancing health innovation systems. This allows the WHO Regional Office for Africa to collaborate closely with ARIPO and OAPI to create and promote a responsive Regional I.P. framework for addressing the region's public health challenges. Additionally, supporting countries in reviewing national I.P. laws is crucial, considering available flexibilities, such as LDC transition waivers, and less commonly used exceptions like research, regulatory review, and patent term extension. (88)

Parallel importation within TRIPS allows members to import patent drugs at reduced prices. Although some studies show that it has a limited impact on drug price reduction, it generally promotes the growth of generic firms, reduces governmental healthcare spending, and enhances public welfare. (86) Pharmaceutical companies often argue that immediate profit is crucial for long-term R&D investment. However, a study has contradicted this assertion, demonstrating that lower-priced drugs will result in more significant welfare benefits. The same study also shows that parallel trade approvals have boosted drug quality under price regulation, minimising profit loss. (89) For instance, parallel importation notably increased access to antiretroviral medications in Africa. (90)

Control of TRIPS-plus

Trips plus limits flexibilities of I.P. laws, benefiting patent-holding countries. Actions like extending patents beyond 20 years, restricting compulsory licensing, and extending data exclusivity and patent evergreening occur outside WTO purview and control. (86) For instance, prolonged data exclusivity increased drug prices in Canada. To counter TRIPS-plus effects, measures include limiting patent extension, imposing heavier punishments on companies for providing false information, encouraging faster generic company entry via automatic price

reduction, and implementing market-size-based compensation for delays in price reduction under the Pharmaceutical Benefits Scheme. These successful strategies by Australia can serve as a model for countries that seek similar benefits for their people. (90)

6.2 Distribution of Medicines and Vaccines in Global Health Emergencies

The COVID-19 Pandemic highlighted the current gaps in supply chains in global health emergencies. During Global health emergencies such as the COVID-19 pandemic, the disruption of the international system immediately affects the capability of low- and middle-income countries. To ensure equitable access, community-based strategies such as mobile clinics and fee exemptions for vulnerable and under-served segments of society need to be considered. Innovative and sustainable strategies informed by comparative risk assessment are increasingly required to ensure that local economic, social, demographic, and epidemiological risks and potentials are accounted for in the national COVID-19 responses and future health emergencies. (91)

7. Multisectoral Collaborations for Access to Medicine

7.1 Intergovernmental Collaborations

As reported in the 72nd World Health Assembly, extensive national policies and initiatives address the multidimensional problem of promoting accessibility to health products. These must also be in line with the applicable laws and regulations, address the entire product life cycle—from research and development to quality assurance and management of supply chains, and link public health needs with goals of socioeconomic growth. Additionally, and importantly, they must encourage collaboration with different industry sectors and stakeholders. (4)
The report also contained a deliverable of encouragement of technology transfer, health product manufacturing in low- and middle-income nations, and assistance for enhanced technological coordination and collaboration in the Action of supporting improved capacity for research and development and clinical trials in countries. (4)

7.2 Partnerships (PPPs and PDPs)

Public-private partnerships (PPPs)are long-term contracts between a private party and a government entity for providing a public asset or service in which the private party bears significant risk and management responsibility, and reimbursement is linked to performance. (92)
PDPs are also a crucial partnership strategy for accessible and affordable product development. They create novel health technologies and often engage in activities to provide equal access to these technologies, thereby improving the health of groups economically marginalised in countries with low or middle incomes. It is estimated that 60+ new health innovations developed by PDPs have benefited over 2.4 billion people. PDPs are likely to significantly contribute to global health, alleviate poverty, and increase global security, with several hundred new items in the queue.
Accordingly, WHO regularly releases target product profiles (TPPs) to assist PDPs in their product R&D for new health technologies. TPPs presently tackle more than 25 diseases. TPPs outline the envisioned characteristics of an anticipated product that targets specific diseases. TPPs identify the intended purpose, serve populations of focus, and other desired product qualities, such as effectiveness and security of use. These profiles can help design missing health items while emphasising public health concerns. (18)

7.3 Solutions

In conclusion, national and international regulations and laws must be formulated to guide new technologies and innovations, the delivery of medications, and, most importantly, within the scope of quality control. Moreover, partnerships between the public and private sectors are highly encouraged since they positively contribute to health equity and innovations and improve the economic status of the countries and individuals.

8. List of Abbreviations

AI: Artificial Intelligence
ARIPO: African Regional Intellectual Property Organization
ASOP: Alliance for Safe Online Pharmacies
DL: Data Learning
DUBs: Deubiquitylating enzyme
EFTA: European Free Trade Association
EU: European Union
FDA: Food and Drug Administration
FTAs: Free Trade Agreements
HDI: Human Development Index
IFMSA: International Federation of Medical Students
IP: Intellectual Property
LMICs: Low-Medium Income countries
LDC: Less Developed Countries
ML: Machine Learning
NCDs: Non Communicable Diseases
NMO: National Member Organization
OECD: Organization for Economic Cooperation and Development
OAPI: African Intellectual Property Organization
PDP: Product Development Partnerships
PDPs: Product Development Partnership
PPPs: Public-Private Partnerships
QALY: Quality-Adjusted life year
R&D: Research and Development
SDGs: Sustainable Development Goals
TPPs: Target Product Profile
TRIPS: Trade-Related Aspects of Intellectual Property Rights
UHC: Universal Health Coverage
WHO: World Health Organization
WTO: World Trade Organization

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