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Contents

Foreword

Neurological disorders are the leading cause of disability globally and access to essential medicines for neurological disorders remains a critical global health challenge. Disorders such as epilepsy, Parkinson disease, and other neurological disorders significantly impact the quality of life for millions of individuals and their families, making timely access to effective treatment paramount. However, disparities in access to necessary medications persist, particularly in low- and middle-income countries, where resources are limited, and healthcare systems are underdeveloped.

Concerted action is needed by all stakeholders to achieve the global targets of the *Intersectoral global action plan on epilepsy and other neurological disorders 2022-2031*, including having 80% of countries providing the essential medicines and basic technologies required to manage neurological disorders in primary care by 2031.

This report addresses the multifaceted barriers to accessing neurological medications and proposes strategic initiatives to overcome these obstacles. Key issues include the insufficient health financing and the high cost of drugs, inadequate healthcare infrastructure, lack of healthcare provider training, and insufficient public awareness about neurological disorders. Furthermore, the lack of an appropriate selection of essential medicines, combined with regulatory hurdles exacerbate the problem, leaving many patients without the medications they need.

Collaboration among governments, pharmaceutical companies, healthcare providers, and non-governmental organizations are crucial to improving access to these essential medicines. Innovative solutions such as differential pricing, generic drug production, and telemedicine can help bridge the gap between patients and the treatments they require.

By addressing these challenges head-on, we can make significant strides in reducing the burden of neurological disorders worldwide. This report serves as a call to action for all stakeholders to commit to tangible, sustainable improvements in the accessibility of medicines for neurological disorders. Together, we can enhance the lives of millions and move closer to a future where no one is denied the treatment they need due to geographic or economic barriers.

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Abbreviations

CRP	Collaborative Registration Procedure
DALYs	Disability-adjusted life years
DMTs	Disease-modifying therapies
EEG	Electroencephalogram
EML	WHO Model list of essential medicines
EMLc	WHO Model list of essential medicines for children
GBD	Global burden of disease
HAI	Health Action International
HICs	High-income countries
IEHK	Interagency Emergency Health Kit
IGAP	Intersectoral global action plan on epilepsy and other neurological disorders
ILAE	International League Against Epilepsy
LICs	Low-income countries
LMICs	Low- and middle-income countries
LPGW	Lowest paid government worker
MedMon	WHO Essential Medicines and Health Products Price and Availability Monitoring Mobile Application
MHK	WHO Mental Health Kit
MRI	Magnetic resonance imaging
NCD	Noncommunicable disease
NRA	National regulatory authority
mhGAP	Mental Health GAP Action Programme
PHC	Primary health care
UHC	Universal health coverage
UNODC	United Nations Office on Drugs and Crime
YLDs	Years lived with disability
YLLs	Years of life lost

Photo credit (next page): Pharmacist at Hargeisa General Group Hospital and laboratory, Somalia, 2019. © WHO / Fouzia Bano

Executive summary

Disorders and conditions of the nervous system (hereafter referred to as neurological disorders) are the leading cause of disability-adjusted life years (DALYs) and years of life lost (YLL) globally, emphasizing the enormous public health challenge posed by these conditions. The prevalence and impact of neurological disorders is also growing dramatically and, based on data from the Global Burden of Disease (GBD) 2021 study, resulted in an 85.6% increase in years lived with disability (YLDs) between 1990 and 2021.

Treatment gap and the lack of access to medicines for neurological disorders

Neurological disorders have a high treatment gap - i.e. the disparity between the number of individuals with a condition and those receiving appropriate treatment. Exceeding 75% in low-income countries (LICs), treatment gaps result from factors such as misconceptions about diseases and the resulting stigma, the capacity of the health-care workforce to diagnose and manage diseases, and the accessibility of essential medicines. Addressing challenges around neurological disorders and the associated treatment gap has been shown to yield positive returns for health systems and society. Investment case studies conducted in several countries have demonstrated, for example, a high cost-benefit ratio for epilepsy interventions.

Despite the existence of effective medicines that can prevent, treat and/or manage symptoms and that can substantially improve the quality of life of persons affected by neurological disorders, the sustained lack of access contributes significantly to the treatment gap. Consequently, many people with neurological disorders do not receive the treatment and care they need and deserve, thus increasing the risk of disability and premature mortality. Lack of access to medicines has a direct impact on quality of life and has multiple social and economic consequences. This impact is compounded by health inequities, whereby persons living in poverty and those in rural areas, as well as other vulnerable groups, are particularly affected. Despite being a global issue, low- and middle-income countries (LMICs) are affected the most, and the challenges associated with inaccessibility span across the health sector.

Global policy context

In May 2022, Decision WHA75 *(1)* – the Intersectoral global action plan on epilepsy and other neurological disorders 2022-2031 (IGAP) – was endorsed at the 75th World Health Assembly. IGAP aims to improve access to care and treatment for people living with neurological disorders, while preventing new cases and promoting brain health and development across the life course. This report is published within the context of IGAP's global target 2.2 which is a global target of 80% of countries providing essential medicines and technologies to manage neurological disorders in primary care by 2031.

The aims and scope of this report

This report seeks to provide a comprehensive understanding of the challenges and health system components that have an impact on access to medicines for neurological disorders, and to highlight, with data from across all WHO regions, the magnitude of the issues that need to be addressed. On the basis of these data, the report proposes an approach for improving the accessibility of medicines for neurological disorders that countries can adopt and implement. Components will have different impacts depending on the country and situation. Countries and regions will experience one – or many – of the challenges highlighted in this report. The target audiences of this report are policy-makers, public health professionals, health programme managers and planners, health-care insurance authorities, health-care providers, researchers, the pharmaceutical industry, and prescribers working in national health ministries, in subnational health offices, or at the district level, as well as health initiatives led by nongovernmental organizations.

Due to the wide scope of neurological disorders globally, this report uses tracer conditions to represent the broader disease area and to assess activities related to the provision of health services for those living with neurological disorders. The tracer conditions used in this report are epilepsy and Parkinson disease – two high-burden diseases that bear a disproportionately higher burden in LMICs, are unlikely to be addressed by other health programmes, and for which effective and essential medicines exist.

Methodology of this report

This report involved a landscape analysis and an expert consultation, drawing on existing access to medicine frameworks. The landscape analysis was undertaken following WHO's guide to performing a landscape analysis to map the extent, range and nature of research activity and policy on access to medicines for neurological disorders. The two-day consultation in September 2023 involved 38 experts and persons with lived experience representing all six WHO regions with the goal of developing an approach to improve access to medicines for neurological disorders.

Components affecting access to medicines for neurological disorders

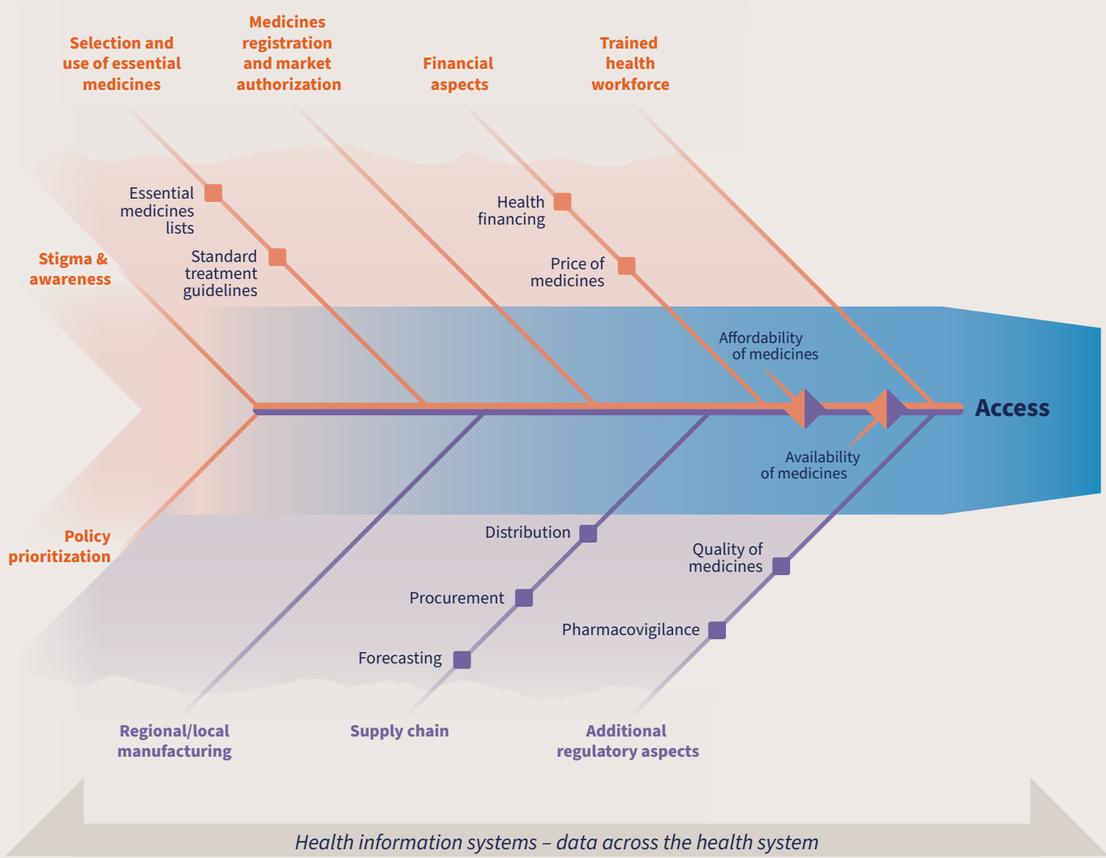
A multitude of challenges affect access to medicines. The components found to impact access to medicines for neurological disorders directly encompass stigma and awareness, policy prioritization, selection and use of essential medicines, registration and market authorization, financial aspects, availability of medicines and the availability of a trained health workforce. Broader health system elements that influence access to medicines include health information systems, supply chains, regional and local manufacturing, and additional regulatory elements such as the quality of medicines and pharmacovigilance (Figure ES1).

Stigma is a major barrier to accessing wider health services. Consequently, the high amount of stigma associated with neurological disorders has a direct impact on access to medicines for these conditions. Stigma can also result in discrimination, can reduce access to education and work for people with neurological disorders, can affect social and family relations and can result in abuse or violations of human rights. For example, children with epilepsy in WHO's African and Eastern Mediterranean regions are less likely to attend school, while adults with epilepsy face employment barriers in WHO's Region of the Americas and Western Pacific Region. Similarly, people with Parkinson disease experience challenges in securing paid work opportunities across the regions. Stigma and discrimination can therefore have negative health, social and financial outcomes acting as barriers to health-seeking, delaying diagnosis, and, consequently, timely access to appropriate and essential medicines.

Efforts to advocate for neurological disorders at the community and policy level are needed. Raising awareness at the community level will address misconceptions and create more inclusive communities, encouraging people to access health services and, therefore, access medicines. Likewise, at the policy level, creating policies and laws to support people living with neurological disorders and protect their human rights will increase their ability and confidence to access health services, which will ultimately lead to improved access to medicines and reduce treatment gaps for these conditions.

FIGURE ES1.

Fishbone diagram of barriers and health systems components affecting access to medicines for neurological disorders



Selection and use include the alignment of medicines in WHO's Model List of Essential Medicines (WHO EML) with national EMLs along with appropriate clinical guidance (standard treatment guidelines). Challenges with the selection of medicines and absence of standard treatment guidelines are barriers to access to medicines for neurological disorders across all WHO regions. For example, the inclusion of medicines for Parkinson disease in national EMLs of WHO's African Region is low, as is the inclusion of some medicines for epilepsy (e.g. lamotrigine and levetiracetam) and specific formulations of antiseizure medicines (e.g. for children). Additionally, many national EMLs have not been updated for several years. Medicines not included in a country's EML are unlikely to be prioritized for procurement or reimbursement, thus reducing their accessibility.

Strengthening the selection of essential medicines offers a key action for Member States to improve access. National EMLs and standard treatment guidelines should be updated periodically following evidence-based methods and based on WHO's EML and WHO's EML for children (EMLc) and on local epidemiological trends and evidence-based guidelines.

Registration and market authorization are important components of regulatory systems which play a key role in assuring the quality, safety and efficacy of medical products. However, the under-registration of essential medicines for neurological disorders by regulatory authorities is a major barrier to access in many parts of the world. Unregistered medicines do not possess licences for sale and distribution, thus impeding accessibility. The under-registration of essential medicines for epilepsy and Parkinson disease has been identified as an issue in the African, Eastern Mediterranean and Western Pacific regions.

Strengthening the capacity of regulatory systems and improving the registration of essential medicines are key opportunities for intervention. Improved registration will enable the procurement, sale and distribution of medicines and will facilitate public procurement, thereby improving access. A number of WHO processes are in place to support countries in streamlining regulatory processes and facilitating the availability of essential medicines. Examples include WHO's prequalification programme, WHO's Collaborative Registration Procedure (CRP) and WHO's programme for regulatory systems strengthening.

Financial aspects that influence access include the appropriate health financing, pricing and affordability of medicines. Poor health financing for neurological disorders and/or the lack of inclusion of essential medicines for neurological disorders in universal health coverage (UHC) packages, particularly in LICs, means that many people across the world must pay out-of-pocket for their medicines. Therefore, inadequate coverage in terms of public funded entitlements coupled with unaffordable prices of medicines present significant barriers to accessing medicines for neurological disorders and optimizing health and treatment outcomes. Medicines for epilepsy, Parkinson disease, and other neurological disorders have been determined as unaffordable across several countries in the African, Americas, South-East Asia, and Western Pacific regions, costing, in some cases, over 30 days' wages of the lowest paid government worker for a 30 day supply.

Improving the coverage under publicly funded schemes (or private schemes mandated by government) to include essential medicines for neurological disorders is needed to prevent catastrophic and impoverishing out-of-pocket spending and to achieve UHC. Medicines for neurological disorders also need to be made available at a fair price – one that is affordable and sustainable for health systems and patients.

Lack of availability of medicines for neurological disorders is a major barrier to access across world regions, with disparities within countries, between urban and rural areas, and across public and private sectors. The availability of essential medicines for epilepsy, Parkinson disease and other neurological disorders is particularly low in the regions of Africa and South-East Asia, and in LICs and LMICs, particularly at the primary care level.

Improved availability of essential medicines for neurological disorders will be a downstream benefit of action for other components – including action to improve awareness, prioritization, selection and use and to strengthen regulatory systems and supply chains.

A trained health workforce, including non-specialist health workforce, that is able to identify, diagnose and manage neurological disorders, as well as appropriately prescribe and dispense medication, is essential for improving access to medicines. The availability of the neurological workforce is a significant problem in LICs, and in countries in the African and South-East Asia regions, as well as in rural areas across all income groups and all regions. However, the situation in LICs is particularly dire, with no countries reporting a practising neurologist in rural areas.

Awareness-raising and educational efforts within health-care systems will help to identify and manage neurological disorders at the primary care level and should be coupled with specialized training to build the neurological workforce at the tertiary level – including the multidisciplinary workforce required for the holistic management of neurological disorders.

Additional components affecting access to medicines for neurological disorders

Additional components have a broader impact on health systems, and consequently affect access to medicines for neurological disorders. These include health information systems and the availability of data across the health system; regional and local manufacturing of medicines; supply chains; and pharmacovigilance and quality of medicines as additional regulatory related aspects.

The **lack of data** on neurological disorders presents challenges in the delivery of high-quality health services and in the accessibility of medicines. Limited data on burden, for example, relating to unreliability of health facility records or lack of data on long-term health, social and economic benefits of investing in neurological disorders, create challenges in understanding the need for prioritization, particularly in low-resource settings. Supply chains are also affected by the lack of data, including on availability, pricing, forecasting and distribution. Streamlining information across the health system can ensure that data are readily available to drive political prioritization and enable evidence-based decisions, considering specific needs across regions and populations for the appropriate allocation of resources.

Challenges along supply chains can impact the availability and affordability of medicines for neurological disorders. Key issues include the poor accountability and fragmentation of responsibilities, uncertainties in financing and underfunding, complexity of supply chains, mismanaged procurement and the aforementioned lack of data. Functioning supply chains are needed to ensure affordable essential medicines for neurological disorders move effectively and efficiently from the manufacturer to the patient.

Regional and local manufacturing has the potential to address several challenges in access to medicines for neurological disorders. By strengthening local manufacturing capacity and prioritizing essential medicines, countries can increase their availability and improve affordability as a result of the absence of importation taxes and facilitated distribution, among other reasons. Examples of regional initiatives in the African Region, such as the African Union's Pharmaceutical Manufacturing Plan for Africa, demonstrate the potential to enhance regional capacity to produce high-quality, affordable essential medicines. However, it is important to note that local and regional production has not always led to lower prices and better availability, and its incentivization should be accompanied by appropriate policies to protect local manufacturing, ensure sustained demand, and ultimately guarantee fair prices of medicines for neurological disorders.

Robust regulatory environments can facilitate the supply and maintenance of high-quality medicines in the market, alongside functioning pharmacovigilance to monitor the safe and appropriate use of medicines for neurological disorders. Substandard and falsified medicines are more likely to reach patients where there is limited access to safe, high-quality medicines, poor governance, and insufficient capacity for appropriate monitoring. The WHO estimates that a significant proportion of medicines circulating globally are substandard or falsified. For example, substandard antiseizure medicines, resulting from exposure to environmental variables, have been identified in countries across the African and South-East Asia regions. By strengthening pharmacovigilance and monitoring safety profiles, adverse events can be identified promptly, and risk minimization measures can be implemented. This approach increases patient compliance and prevents unnecessary restrictions on use or removal of a product from the market, facilitating continuous access to essential medicines.

Additional neurological disorders

In addition to the tracer conditions, data for headache disorders, multiple sclerosis and

> "The money you have is little, the drug cannot be found. We called pharmacies, they said there's none. We went around the capital, there was no chemist that sells it. In a day, I did nothing from morning to evening, I just looked for Parkinson's medication"
>
> **Carer of person with Parkinson disease, Kenya**

stroke are presented to demonstrate that challenges are shared among different disorders and that actions aimed at improving access to medicines for the selected tracer conditions are likely to have an impact on a larger group of neurological medicines. Common medications for acute treatment of headache disorders (e.g. aspirin, ibuprofen, paracetamol) are generally available, inexpensive and cost-effective across WHO regions. However, LMICs in particular are reported to have fewer pharmacological options for headache disorder management compared to high-income countries (HICs). With regard to multiple sclerosis, the availability and cost of disease-modifying therapies (DMTs) are barriers to access in many countries and particularly in LICs. The high costs of DMTs place a huge economic burden on health-care systems and persons in all countries, but particularly in LMICs. Of all neurological disorders, stroke is the leading cause of DALYs. However, the uneven availability of warfarin, a commonly used anticoagulant for stroke prevention, is a major barrier to access at the primary care level, particularly in the African and South-East Asia regions. Aspirin, used in secondary prevention of stroke, is consistently available across income groups yet is unaffordable for individuals living in LICs.

Special considerations influencing access to medicines for neurological disorders

The lack of access to medicines for neurological disorders can be exacerbated by unique and complex situations. This report refers to specific contexts that may affect access, namely: 1) emergency contexts; 2) specific gaps in attending to populations with neurological disorders (paediatrics); and 3) specific regulations and legislation that create barriers to access (controlled medicines).

Emergency contexts, such as the COVID-19 pandemic, human-caused disasters (including humanitarian emergencies) and armed conflicts, as well as natural disasters, can result in major disruptions to health-care systems and can limit or negate access to medicines. These disruptions also tend to affect vulnerable populations the most. Emergency situations raise the urgency of ensuring consistent equitable access through health systems that are resilient to emergencies, and the need to adopt policies and responses that ensure minimal disruption to access to medicines.

Pharmacists working to provide essential medicines at a health centre, Occupied Palestinian Territory, 2024.
© WHO / Christopher Black

Limited access to **paediatric medicines and formulations** is a challenge that affects the safe and effective treatment of children living with neurological disorders and is a significant contributor to child mortality. Due to differences in absorption, metabolism and clearance of the required dosing, medicines for children require adjustment to achieve the desired target exposure. However, child-appropriate formulations are often not available, and few countries have a specific essential medicines list for children. Access to appropriate medication should be facilitated across the life course, with particular care to include paediatric formulations when addressing access to medicines for neurological disorders.

Controlled medicines are essential for the provision of adequate medical care and for optimal health outcomes. However, the use of such medicines for non-medical purposes can lead to addiction and dependence, necessitating regulation of their use. Several antiseizure medicines (e.g. barbiturates and benzodiazepines) are classified as "controlled medicines" because of the risk of misuse, despite being essential (and in some instances lifesaving). The inaccessibility of controlled essential medicines such as these in low-resource contexts has been described as a human rights concern. Accessibility challenges result from national and international drug-control frameworks, negative perceptions about controlled medicines, fear of addiction and criminal sanctions, limited education on rational use and prescribing for health-care professionals, and lack of legal frameworks regarding use. Implementation of available tools, such as technical guidance from the United Nations Office on Drugs and Crime, could facilitate better access to controlled medicines.

How can barriers to access to medicines for neurological disorders be addressed?

To address the barriers and health system challenges that affect access to medicines for neurological disorders, this report presents an approach to improve access using epilepsy and Parkinson disease as tracer conditions, which can also be used to drive better access to other neurological medicines. Given the complexity and variety of challenges faced in different contexts, eight key action areas have been identified. If implemented, these will significantly improve access to medicines for neurological disorders. The actions include:

1. **Strengthen leadership** – Achieving strong leadership requires proactive steps to coordinate advocacy campaigns, facilitate collaboration in the field at different levels and develop tools such as investment cases for neurological disorders. These actions will empower global leaders, enhancing their capacity to prioritize neurological disorders effectively. Technical experts and policy-makers are encouraged to establish technical working groups to equip leaders with evidence-based arguments to make informed decisions and to advocate for increased investment to address the issue of access to medicines for neurological disorders.
2. **Promote appropriate selection and use of essential medicines** – Actively engage global and national experts in the revision of WHO's EML, EMLc and national EMLs in order to include all necessary essential medicines for neurological disorders, as well as in the development and revision of global and national clinical guidelines, including standard treatment guidelines, for neurological disorders in order to guide diagnosis and management.
3. **Strengthen regulatory environments** – Enhance regional collaboration by implementing convergence and reliance mechanisms between national regulatory agencies (NRAs), leading to improved registration and market authorization processes for essential medicines for neurological disorders and ensuring their quality, safety and efficacy. Strengthen regulatory authorities and pharmacovigilance services to facilitate the availability of high-quality generic formulations while simultaneously reducing the incidence of adverse effects and enhancing monitoring capabilities.
4. **Strengthen supply chain and procurement systems** – Deliver comprehensive training throughout the supply chain, covering areas such as forecasting, procurement, storage and distribution. Engage in pooled procurement initiatives to increase demand and bargaining power, thereby enhancing efficiency, availability, sustainability and adherence to quality standards across the supply chain.
5. **Improve financing for and affordability of neurological medicines** – Advocate for the integration of medicines for epilepsy and Parkinson disease into national benefit packages, alongside the implementation of fair pricing policies in order to ensure equitable, sustainable and safe access to these medicines. Tailored measures, aligned with each country's context, should be pursued – such as regulating mark-ups, employing referencing pricing, fostering trust in high-quality generic formulations and promoting pricing transparency. Successful strategies also entail limiting co-payments and reducing or exempting taxes/charges on essential medicines, particularly for the most economically vulnerable households.
6. **Build health system workforce capacity** – Develop and implement clinical guidance to support training of the health workforce, enabling health workers to identify, diagnose and manage neurological disorders. This should be done alongside and in combination

with the implementation of WHO's mhGAP modules to build the capacity of primary health-care workers across health systems. Other cadres should also receive training which includes strengthening the capacity of the supply chain workforce, regulators and persons working at point-of-care facilities.

7. **Strengthen data and health information systems** – Establish comprehensive data collection, monitoring and reporting systems to gather robust information on the burden of neurological disorders, the status of health facilities and the supply of medicines. This data will serve to inform supply chain management decisions and catalyse political commitment and prioritization efforts. Additionally, conduct country-level surveys to assess the availability and affordability of medicines, providing insights into evolving access concerns and facilitating the monitoring of interventions.

8. **Encourage coordination, partnership and convening** – Encourage and facilitate regular communication, information exchange and collaboration between stakeholders, in consultation with people with lived experience, in order to increase global prioritization of neurological disorders and to operationalize the above activities. Improving access to medicines for neurological disorders will require effective harmonization of national policies and coordination between stakeholders. A key action is to ensure the alignment between medicine selection procedures, insurance and/or UHC benefit packages, together with treatment and service delivery guidelines and procurement services.

Photo credit (next page): Portrait of a man sitting outside of the Reference Health Center of Ménaka, Mali, 2022. © WHO / Fatoumata Diabaté

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Introduction

1. Introduction

In 2022, all Member States of the World Health Organization (WHO) adopted WHO's *Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031* (herein referred to as IGAP), which represents an unprecedented opportunity to address the impact of neurological disorders through a comprehensive response (Box 1) *(1)*. Improving access to treatment and care and improving the quality of life of people with neurological disorders, their carers and families, requires concerted actions by all stakeholder groups towards addressing the five strategic objectives in the action plan (Figure 1).

BOX 1

Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031 (IGAP)

IGAP aims to improve access to care and treatment for people living with neurological disorders globally, while preventing new cases and promoting brain health and development across the life course. It seeks to support the recovery, well-being and participation of people living with neurological conditions, while reducing associated mortality, morbidity and disability, promoting human rights, and addressing stigma and discrimination through interdisciplinary and intersectoral approaches.

The vision of IGAP is a world in which:

- brain health is valued, promoted and protected across the life course.
- neurological disorders are prevented, diagnosed and treated, and premature mortality and morbidity are avoided.
- people affected by neurological disorders and their carers attain the highest possible level of health, with equal rights, opportunities, respect and autonomy.

FIGURE 1.
Five strategic objectives of IGAP *(1)*

The six guiding principles of IGAP which frame this report at a macro level are:

- people-centred primary health care (PHC) and universal health care;
- integrated approach to care across the life course;
- evidence-informed policy and practice;
- intersectoral action;
- empowerment and involvement of persons with neurological disorders and their carers;
- gender, equity and human rights.

Despite the considerable progress made in developing safe, effective and cost-effective interventions (including medication), the treatment gap for neurological disorders in many countries remains high. A major driver of the treatment gap for neurological disorders is the lack of access to neurological medicines – a challenge that is particularly profound in low- and middle-income countries (LMICs). One of the action areas of IGAP pertains to appropriate access to medicines, diagnostics and other health products, with a global target of 80% of countries providing essential medicines and basic technologies required to manage neurological disorders in primary care by 2031.

1.1 Epidemiology of neurological disorders

According to the GBD 2021 study, neurological disorders contribute significantly to the global burden of disease as the leading cause of disability adjusted life years (DALYs) and leading cause of years of life lost (resulting in over 11 million deaths per year) *(2)*. Most of the burden of neurological disorders, with respect to DALYs, results from non-communicable conditions. Among the top fifteen leading contributors of neurological DALYs in 2021 were stroke, migraine, dementia, epilepsy and Parkinson disease *(2)* (Figure 2).

Data from the GBD study 2021 showed that 3.1 billion people worldwide were living with headache disorders (including migraine and tension-type) *(2)*. In the same year, there were approximately 94 million cases of stroke, and the condition caused 145 million years of life lost (YLL) and over 7 million deaths *(2)*. Likewise, around 50 million people worldwide are estimated to have epilepsy (idiopathic and secondary epilepsy), a condition that results in about 140,000 deaths per year, of which more than 80% are reported from LMICs *(2, 3)*. In addition, the impact of neurological disorders, such as dementia, multiple sclerosis and Parkinson disease has grown dramatically in the past few decades *(2, 4)*.

Addressing the burden of neurological disorders requires well-prepared and supported health systems to provide adequate treatment, care and support. However, the high burden associated with neurological disorders is compounded by profound health inequities – approximately 70% of people with neurological disorders live in LMICs, where health systems are not adequately prepared for the impact of these conditions *(1)*.

FIGURE 2.
Top 15 causes of neurological DALYs *(2)*

Global rank	Disease
1	Stroke
2	Migraine
3	Alzheimer disease and other dementias
4	Meningitis
5	Epilepsy
6	Spinal cord injury
7	Traumatic brain injury
8	Brain and other central nervous system cancer
9	Tension-type headache
10	Encephalitis
11	Parkinson disease
12	Other neurological disorders
13	Tetanus
14	Multiple sclerosis
15	Motor neuron diseases

Source: GBD 2021 study (2)

1.2 The treatment gap for neurological disorders

A treatment gap refers to the difference between the number of people with a condition and the number of people with the condition being appropriately treated. Despite the existence of effective and affordable medicines globally, access to these essential medicines varies worldwide. The treatment gap for neurological disorders results from several factors, such as misconceptions about diseases and the resulting stigma, the capacity of the health-care workforce to diagnose and manage conditions and, as presented throughout this report, the accessibility of effective and affordable medicines.

Data on the treatment gap for epilepsy, for instance, highlight the magnitude of the problem *(5–7)*. Worldwide, around 50 million people live with epilepsy, yet access to first-line medicines that represent a cost-effective use of resources for health is limited *(1)*. Many people do not receive the necessary treatment to control their seizures, and the gap varies markedly, exceeding 75% in most LICs and 50% in most middle-income countries *(1)*, with larger gaps reported

in rural areas *(8)*. Although some data are relatively dated, the epilepsy treatment gap was reportedly as high as 95% in Myanmar in 2018 *(9)*, 90% in Azerbaijan in 2023 *(10)*, 90% among children in Lao People's Democratic Republic (Lao PDR) in 2011 *(11)*, and 85% in Ghana in 2018 where epilepsy was identified as one of the five most burdensome medical problems *(12)*. The treatment gap for epilepsy is observed not only in LMICs; data from WHO's European Region from 2010 estimated an epilepsy treatment gap of up to 40% in Europe *(10)*, similar to 2019 estimates from the United States of America (USA) of 36.7% *(13)*.

For other neurological disorders such as Parkinson disease, global data on the treatment gap are lacking, with country-level studies highlighting estimates. For example, a prevalence study of Parkinson disease in a rural area of the United Republic of Tanzania found that 78% of the people identified with Parkinson disease were previously undiagnosed *(14)*, and therefore not accessing treatment. While these data give an insight into the potential treatment gap for Parkinson disease globally, further data are needed to truly understand how many people with Parkinson disease are not accessing the medication they need and are not being appropriately treated.

Addressing challenges around neurological disorders and the associated treatment gap has been shown to yield positive returns for health systems and society. Investment case studies for mental health and neurological disorders conducted in several countries across sub-Saharan Africa, as well as in Central, South, and Southeast Asia, have demonstrated a significant benefit-cost ratio for investing in epilepsy. These studies found that the median return on investment for epilepsy interventions was US$8.2 and could reach up to US$24.3 for every US$1 invested, with overall higher rates observed when considering both productivity and social effects (Table 1) *(15)*.

As one of the main drivers of the treatment gap for neurological disorders, the lack of access to essential medicines underscores the urgent need for comprehensive and targeted interventions across the health system to address this challenge.

TABLE 1.
Benefit-cost ratio of epilepsy interventions

	Bangladesh	Kenya	Nepal	Philippines	Uganda	Uzbekistan	Zimbabwe
Benefit-cost ratio (productivity effects alone)	5.8	5.5	6.6	6.7	1.3	9.7	5.1
Benefit-cost ratio (productivity + social effects)	14.5	11.1	16.2	16.6	3.2	24.3	12.6

1.3 Access to medicines frameworks

Existing access to medicines frameworks can help to demonstrate and address the complex and dynamic relationships between medicines and health systems and offer pathways to address barriers impeding access to medicines. This report draws on three frameworks (Figure 3):

1. *WHO Medicines Strategy 2000–2003,* a framework for action to secure access to essential medicines for priority health problems *(16)*;
2. WHO's *Equitable access to essential medicines: a framework for collective action,* developed in line with the Millennium Development Goals to guide and coordinate collective action on access to essential medicines *(17)*;
3. Bigdeli and colleagues' framework on access to medicines from a health systems perspective *(18)*.

Considering access to medicines from a health system perspective – within the broader context of accelerating the achievement of universal health coverage (UHC) – also requires consideration of WHO's health system building blocks:

- Leadership and governance
- Service delivery
- Health system financing
- Health workforce
- Medical products, vaccines and technologies
- Health information systems

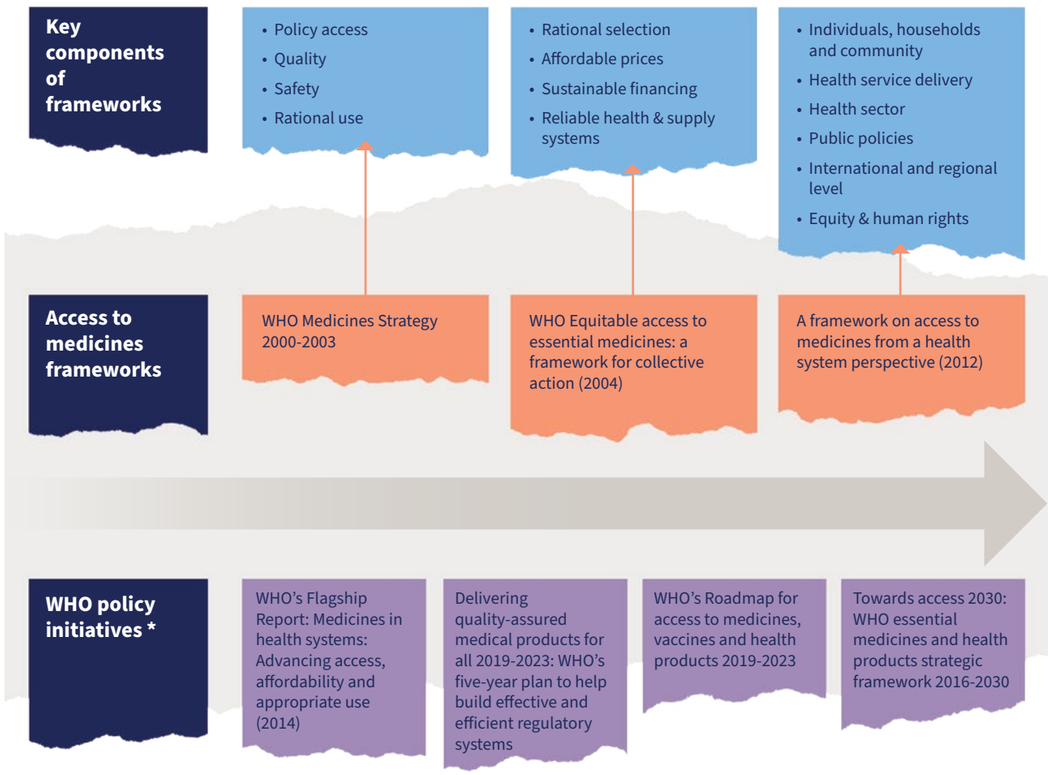
Patients line up to get free medicine from the drug store in district headquarters hospital in Kasur, Pakistan, 2018. © WHO / Asad Zaidi

This report also draws on WHO's *Flagship Report: Medicines in health systems* *(19)* and is situated within previous and ongoing work by WHO departments to achieve access to UHC. These include (Figure 3):

- *Delivering quality-assured medical products for all 2019–2023* – WHO's five-year plan to help build effective and efficient regulatory systems *(20)*.
- WHO's *Roadmap for access to medicines, vaccines and other health products 2019–2023 (21)*.
- *Towards Access 2030* – WHO Medicines and Health Products Programme Strategic Framework 2016–2030 *(22)*.

FIGURE 3.

Key components of access to medicines frameworks and examples of relevant WHO policy initiatives relating to access to medicines



**Examples of relevant WHO initiatives relating to access to medicines*

1.4 Scope of this report

This report addresses access to medicines for chronic, noncommunicable neurological disorders, with a focus on epilepsy and Parkinson disease. Chronic neurological disorders can be effectively managed, prevented or controlled with appropriate pharmacological treatments, and rehabilitation. Poor access to medicines for these neurological disorders is a significant contributor to the high treatment gap across the world.

Tracer conditions addressed in this report

This report uses two tracer conditions to represent the wider disease area and to assess activities involved in the provision of health services for a specified population – i.e. persons living with neurological disorders globally. Epilepsy presents a significant burden across the life course, although can be effectively managed with appropriate medication – up to 70% of people with epilepsy could achieve seizure freedom with appropriate antiseizure medicines following accurate diagnosis *(1)*. The global prevalence of Parkinson disease is rapidly growing – effective symptomatic medicines that can significantly reduce the impact of the disease exist but are often not accessible. The tracer conditions selected – epilepsy and Parkinson disease – have the following characteristics:

- high disease burden globally;
- diseases that bear a disproportionately higher burden in LMICs;
- diseases for which effective medications exist and have been identified as "essential medicines" by WHO;
- diseases that are unlikely to be addressed by other health programmes;
- diseases that collectively represent a life course perspective with distinct needs across different age groups.

In addition to the tracer conditions, other neurological disorders are also covered in this report (Section 4). Data for headache disorders, multiple sclerosis and stroke are presented to demonstrate that challenges are shared among different disorders and that actions aimed at improving access to medicines for the selected tracer conditions are likely to impact a larger group of neurological medicines.

What this report does not cover

This report acknowledges the burden of dementia; however, due to the limited evidence on the benefits of medicines in effectively managing symptoms or slowing the progression of underlying diseases, dementia is not included in the report. Similarly, cerebral palsy and attention deficit hyperactivity disorder, which are among the five leading causes of childhood disability, are not included in the report because medicines for these conditions are currently not included in the WHO EML (see Box 3 in Section 3.2 on ongoing efforts to update the list). WHO recommends non-pharmacological interventions for Alzheimer disease, other dementias, cerebral palsy and attention deficit hyperactivity disorder. Data on acute neurological conditions, caused by injuries or belonging to communicable disease categories, are also not covered in this report. However, strategies to improve access presented in this report may also be applicable to these groups.

1.5 Aims of this report

An estimated two billion people around the world do not have access to essential medicines, effectively precluding them from the benefits of advances in modern science and medicine *(23)*. Supporting the essential medicines component of IGAP's global target 2.2, WHO is working with diverse stakeholders to identify and address key barriers impeding continuous access to high-quality medicines for people living with neurological disorders. This comprehensive approach requires interventions at all levels tackling global issues, while supporting actions that focus on the specific needs of regions and countries. In carrying out this work, WHO will support systematic change across health systems to improve access to medicines for neurological disorders and potentially build wider health system capacity to improve access to all medicines. The first step in generating these interventions and actions is to understand the global landscape of neurological disorders and the factors that influence access to medicines.

This report has three aims:

1. To map the extent, range and nature of information available regarding access to medicines for neurological disorders at global, regional and country levels, and to identify the major barriers to access.
2. To identify opportunities and best practice examples that lead to improved access to medicines for neurological disorders.
3. To provide an approach that countries can adopt and implement to improve access to medicines for neurological disorders.

Target audience of this report

The report is intended for use by policy-makers, public health professionals, health programme managers and planners, healthcare insurance authorities, health-care providers, researchers, the pharmaceutical industry, and prescribers working in national health ministries, in subnational health offices, or at the district level, as well as health initiatives led by nongovernmental organizations to address challenges relating to access to medicines for people living with neurological disorders.

Photo credit (next page): Health worker and WHO staff inspecting medical supplies in a health centre, South Sudan, 2023. © WHO / Peter Louis Gume

2

Methodology

2. Methodology

This report utilized standard WHO methodology for a landscape analysis *(24)* and an expert consultation in order to address the aims described above. Existing access to medicines frameworks (Section 1.3) were used to guide the identification and definition of components that impact access to medicines for neurological disorders.

2.1 Landscape analysis

The aim of the landscape analysis was to map the extent, range, and nature of research activity and policy on access to medicines for neurological disorders, and to summarize the findings. This was undertaken in five stages in accordance with WHO's guide to performing a landscape analysis.

Stage 1: Developing the research question

Literature was sought on neurological disorders broadly and on the specific conditions relating to the scope of this report. This initial broad scope lent itself to the development of sub-questions.

Research question: What is known from the existing literature about access to medicines for people living with neurological disorders globally?

Sub-questions:

1. What are the causes of lack of access to medicines?
2. How do these causes vary between neurological disorders?
3. What are the specific barriers and challenges faced by LMICs?
4. Are there special considerations or scenarios that have an impact on access to neurological medicines?
5. What strategies can be used to address these barriers, and how effective are they?
6. What can be learned from other disease programmes?

Stage 2: Developing the method

Relevant sources were identified, including published research studies and grey literature (e.g. WHO MedMon survey reports) from electronic databases (Scopus, EBSCO, ProQuest databases, Scopus, Web of Science), snowballing (searching reference lists), and manual searching in key journals and in WHO's publications library. The

Health care worker in front of medicine shelves, French Polynesia, 2021. © WHO / Grégoire Le Bacon

broader term of "neurological disorders" was used initially, followed by focused searches on the specific conditions included in this report and specific WHO regions. Targeted searches were used to address sub-questions to better understand emerging issues of relevance (e.g. emergency contexts, including the COVID-19 pandemic).

Example search terms included: availab* OR accessib* OR "access to medicines" AND epilepsy OR antiseizure OR anti-seizure OR anti-epileptic OR antiepileptic OR anticonvuls* AND Africa OR "sub-Sahara* Africa".

Stage 3: Collecting the data

Sources were screened and reviewed for inclusion. Minimal inclusion criteria were applied initially to the searches, and criteria were devised post hoc on the basis of increasing familiarity with the literature. The inclusion criteria included relevance of the study/report to the research question (including specifically relating to one or more of the tracer conditions or additional neurological conditions). Papers or reports solely on other disorders were excluded.

Stage 4: Analysing and visualizing the results

Data from the resources identified were extracted and analysed. Information recorded included: type of resource; year of publication; study or report location; disease and medicines being reported; aims of the study/report; methodology; outcome measures; important results.

Stage 5: Disseminating the findings

The analysed data are summarized in this report which seeks to present a narrative overview of all material reviewed. The themes draw on existing access to medicines frameworks and consider a health system perspective.

2.2 Expert consultation

In September 2023, WHO organized a consultation with 38 global experts working on access to medicines, neurological disorders, and other disease areas that share similar challenges regarding access to medicines, such as noncommunicable diseases (NCDs) and mental health. The consultation involved a two-day workshop with experts representing all six WHO regions. Declarations of interests were received from all experts. WHO processes were used to assess declared interests and to manage any potential conflicts of interest. Experts that have reviewed and provided comments to the draft of this report have declared the following interests: research associated with their academic positions, non-financial collaborations with non-governmental organizations and honoraria to attend scientific conferences. After review and due diligence by the WHO Secretariat, it was concluded that these interests did not interfere with the development of this report.

The main objectives of the workshop were the following:

1. Present the results of the global landscape analysis.
2. Discuss challenges associated with the health system components that have an impact on access to medicines for neurological disorders.
3. Explore how to leverage learnings from other disease areas such as NCDs and mental health.
4. Identify a set of actions to improve access to medicines for neurological disorders.

The actions identified during the consultation are summarized as an "approach" at the end of this report. Experts were also invited to review a draft of the landscape analysis and to provide additional comments and evidence.

Photo credit (next page): Medical supplies being delivered to Kamal Adwan hospital, Occupied Palestinian Territory, 2024. © WHO

3

Components affecting access to medicines for neurological disorders

3. Components affecting access to medicines for neurological disorders

The structure of the landscape analysis considered existing access to medicines frameworks (Section 1.3). Through the landscape analysis and during the expert consultation, specific components were found to have a direct impact on access to medicines for neurological disorders, while others, although also directly influencing access to such medicines, represented broader aspects of health systems.

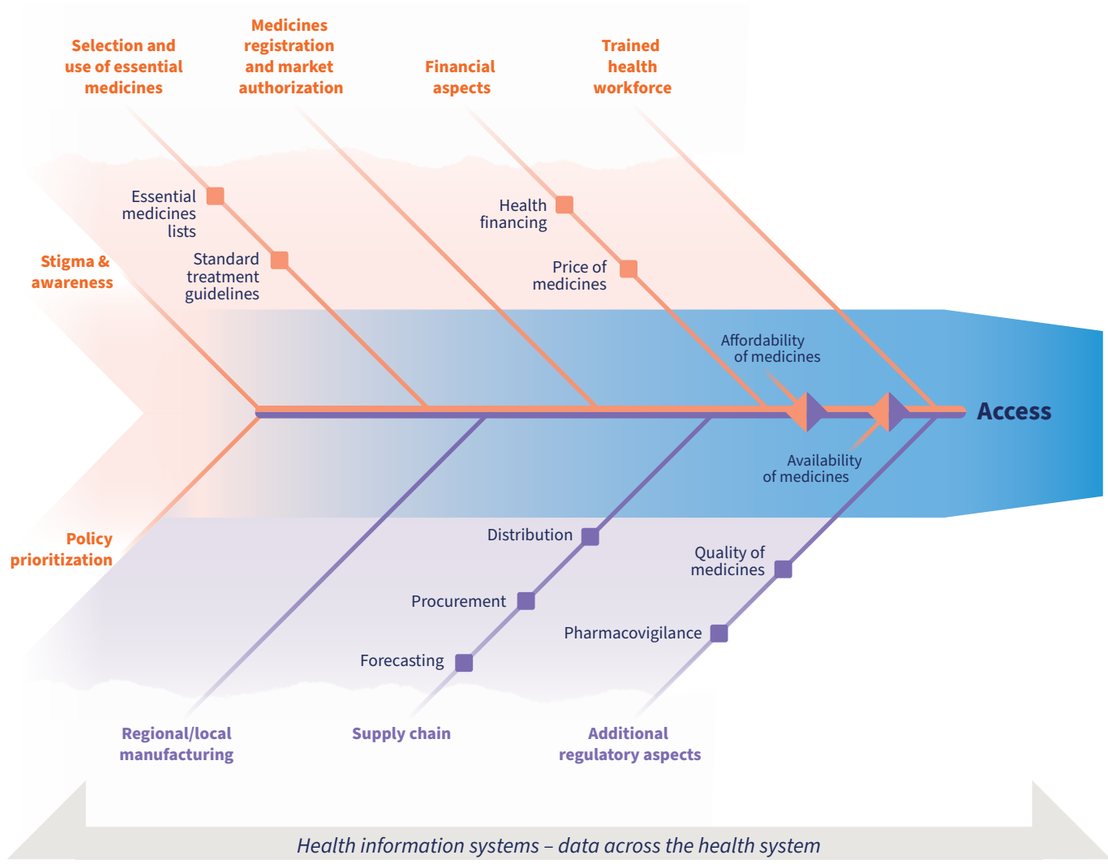
Components that have an impact on access to medicines for neurological disorders are illustrated as a "fishbone diagram" (Figure 4). The key components identified as having a direct impact on access to medicines are:

1. Stigma and awareness, and policy prioritization
2. Selection and use of essential medicines
3. Medicines registration and market authorization
4. Financial aspects
5. Availability and affordability of medicines
6. Trained health workforce.

The broader health systems aspects include health information systems as a cross-cutting component, regional and local manufacturing, supply chains (including forecasting, procurement and distribution) and additional regulatory aspects, including quality of medicines and pharmacovigilance.

FIGURE 4.

Fishbone diagram of barriers and health systems components affecting access to medicines for neurological disorders



The challenges and components illustrated in the fishbone diagram highlight the complexity and myriad potential barriers to be addressed. Many of these challenges are shared between countries, while others may be more pronounced in some countries than in others. Likewise, components may affect disorders differently, even within the same country.

The report also highlights three scenarios which have been found to exacerbate challenges relating to access to medicines for neurological disorders. These "special considerations" are:

1. Access to medicines in emergency contexts
2. Access to paediatric medicines and formulations
3. Regulation around controlled medicines.

This report attempts to comprehensively capture data regarding access to medicines for neurological disorders; however, data from specific regions, countries or disorders may not have been included. It is also important to note that, although a large number of studies were found (representing a comprehensive overview of the situation), substantial data are still lacking and concerted research efforts are warranted to fill gaps across the components that have been identified.

3.1 Stigma and awareness

Stigma and awareness: summary

Stigma is a major barrier to access to medicines and wider health services. Both self-stigma and stigma by other people towards an individual (enacted) are common among people with neurological disorders and are widely reported across all WHO regions. Enacted stigma can result in discrimination, including at a systemic and policy level (institutional stigma), and has been shown to affect access to education and work for people with epilepsy and Parkinson disease. For example, children with epilepsy in WHO's African and Eastern Mediterranean regions are less likely to attend school, while people with epilepsy face employment barriers in WHO's Region of the Americas and Western Pacific Region. People with Parkinson disease face exclusion from communities and from paid employment across all regions. Stigma also affects social and family relations and results in violations of human rights. Stigma and discrimination can therefore have negative health, social and financial outcomes, acting as barriers to health-seeking and delaying access to health services, diagnoses and medicines.

Addressing these challenges is key to improving access to medicines and reducing treatment gaps for neurological disorders. At the community level, education and awareness initiatives can improve understanding, address misconceptions and help create more inclusive communities. At a policy level, improving access to medicines requires innovative strategies to strengthen national leadership in order to support policies and laws for people living with neurological disorders, while removing existing discriminatory legislation and protecting human rights (Box 2).

The association between stigma and neurological disorders is a widely-recognized global health issue *(25–27)*. Lack of awareness and multilevel stigma are major barriers that impede the prioritization of neurological disorders and have a direct impact on access to care and support, while contributing to treatment gaps. IGAP proposes that addressing the needs of people with neurological conditions begins with increasing understanding and awareness and addressing stigma and discrimination *(1)*.

Stigma relating to neurological disorders is common and experienced at different levels.

Self-stigma is associated with shame or embarrassment, enacted stigma (interpersonal and/or institutional) is discrimination by others towards an individual, while families and caregivers experience affiliate or associative stigma. The drivers and facilitators of stigma relating to neurological disorders include poor awareness, lack of health policy and legislation on neurological disorders, and a limited health workforce able to diagnose neurological disorders. In many regions and countries, stigma is also observed through beliefs of contagion, blame and associations with supernatural beliefs or witchcraft *(28, 29)* which can be perpetuated by misdiagnoses. Stigma can

> "It is beliefs. Because many people think bewitched, which is the commonest thing. So, they try all those things (traditional healing) before getting to you. And then they see it's not improving and then eventually they are convinced that this is not subsiding."
>
> **Epilepsy healthcare professional, Uganda**

have devastating consequences which can result in human rights violations *(30)*.

Stigma has consequences across multiple domains of daily living *(31)* that ultimately have an impact on access to medicines. Persons with epilepsy and Parkinson disease have been shown across all WHO regions to experience exclusion from school *(32, 33)* and paid work opportunities *(34, 35)*, as well as from their families and societies *(28, 36, 37)*, thus reducing social and financial capacity and ultimately limiting the ability to access and afford medicines. In the United Republic of Tanzania, for example, 50% of children with epilepsy at one demographic surveillance site did not access school regularly *(38)*, affecting their future financial outcomes.

Stigma and discrimination result in negative health and social outcomes and, combined with low awareness of neurological disorders among health workers, can create barriers to accessing timely and appropriate health-care services *(39)* and accurate diagnoses *(40)*, delaying access to medicines. Difficulty in accessing medicines results in adverse health consequences, further intensifying stigma and ultimately forming a vicious closed loop. Stigma and discrimination, poor awareness and low health literacy as well as limited access to, and mistrust of, health services can also drive people with neurological disorders to seek herbal, traditional or religious/faith healing *(29, 41)*, which can be ineffective, could result in worsening symptoms and delayed commencement of appropriate medication.

BOX 2.

The need for advocacy, awareness and prioritization of neurological disorders

Although poor awareness influences multiple issues relating to access to medicines for neurological disorders, stigma is also facilitated by structural constraints. These include lack of policy concerning neurological disorders, limited health-care capacity, poor accessibility of services, lack of financial protection from health-care costs, absence of social protection schemes, and limited rights for people living with disabilities. These constraints can influence the ability of people living with neurological disorders to access the medicines they need and, therefore, can negatively influence health and well-being.

The presence of bidirectional, complex relationships between barriers highlights the need to address multiple issues in tandem in order to achieve optimal outcomes. For instance, lack of awareness is a barrier to accessing health services and results in misdiagnoses. However, without access to appropriate medication, symptoms are poorly controlled, thus perpetuating stigma. Consequently, awareness needs to be addressed at all levels of society (e.g. among communities, health-care workers and policy-makers).

At a policy level, improving awareness can drive disease prioritization of health conditions. Lack of data on the long-term health, social and economic benefits of investment in neurological disorders leads to difficulties in advocating for the prioritization of these disorders in health budgets and policies. Economic evaluations, such as cost-effectiveness or benefit-cost analyses, are needed to set priorities (Section 3.7.1) to ensure evidence-informed resource allocation within health systems and the greatest health impact. For example, Kenya Mental Health Investment Case 2021 identified that the highest return on investment over 10 years for the six conditions included was for epilepsy, at 5.5 Kenyan shillings for every 1 Kenyan shilling invested *(42)*. Concerted brain health advocacy *(43)* represents the first step in raising awareness and better public understanding of neurological disorders in order to drive prioritization.

Nurse provides essential medicines to child at Manushi Dispensary in Moshi, United Republic of Tanzania, 2023. © WHO / Mwesuwa Ramsey

3.2 Selection and use of essential medicines

Selection and use of essential medicines: summary

WHO's EML, updated every two years, indicates the medicines that should be available within countries' health systems, in adequate amounts and appropriate dosage forms, with assured quality and adequate information, and at a price the individual and community can afford. The WHO EML is a guide for developing national EMLs. However, challenges with the selection of medicines on national EMLs alongside the absence of appropriate clinical guidance (standard treatment guidelines) are barriers to access to medicines for neurological disorders across all WHO regions. For example, the inclusion of medicines for Parkinson disease in national EMLs of countries in the African region is limited, as is the inclusion of some medicines for epilepsy (e.g. lamotrigine and levetiracetam) and specific formulations (e.g. for children) (Box 5). Additionally, many national EMLs have not been updated for several years. Medicines which are not included on a country's national EML are unlikely to be prioritized for procurement or reimbursement, thus limiting their accessibility.

Strengthening the selection of essential medicines is crucial for Member States to improve access to medicines for neurological disorders. National EMLs and standard treatment guidelines should be updated periodically following evidence-based methods and should be based on the WHO's EML, evidence-based guidelines and local epidemiological trends. National EMLs and standard treatment guidelines should also consider the inclusion of neurological medicines for children (based on WHO's EMLc), which are vital to improve access to medicines and ensure coverage across the life course.

WHO's EML and EMLc include those medicines which are intended to be available within the context of functioning health systems, in adequate amounts and appropriate dosage forms, with assured quality and adequate information and at a price the individual and community can afford *(44)*. WHO is committed to supporting Member States in sharing and developing processes for the selection of medicines for national EMLs, consistent with the evidence-based methods used for updating the WHO EML *(45)*.

There are important real-world implications when a medicine is included on the WHO EML, as these medicines are more likely to be included in a country's national EML (Box 3). National EMLs can: raise disease awareness and political will; guide procurement, regulation policies and legislative interventions; guide reimbursement by national insurers; and facilitate access to affordable medicines by prioritizing the most important medicines that countries should make available, which also depends on local epidemiological trends. Essential medicines have

been shown to be more available than other medicines around the world *(46)*, suggesting that national EMLs have influenced the provision and improved the availability of medicines, and facilitated progress towards UHC, particularly in LMICs *(47, 48)*. The selection of medicines on national EMLs should be followed by monitoring of the prescribing and use of medicines *(45)*. This can be facilitated by the alignment of national EMLs with standard treatment guidelines – which are evidence-based clinical guidelines developed to assist health-care professionals, prescribers, health facility managers and policy-makers in appropriate health-care decisions.

BOX 3.

The public health importance of updating the WHO EML

The importance of the inclusion of medicines on the WHO EML is exemplified in the case of multiple sclerosis and the drive of the Multiple Sclerosis International Federation to add disease-modifying treatments to the 2023 WHO EML as an initial and important step to increase their availability worldwide, and particularly in LMICs *(49–51)*. Regular updating and expanding of the number and scope of medicines on the EML, EMLc and national EMLs are key priorities in addressing gaps, responding to lack of coverage of diseases and medicines, and responding to emerging epidemiological trends, emergencies and updated evidence on therapeutic benefits (Box 4) *(52)*. For example, levetiracetam – an antiseizure medicine for which there is robust evidence of its effectiveness for all seizure types, limited drug interactions and its safety for use during pregnancy – was added to the WHO EML in 2023.

The alignment – or lack thereof – of national EMLs with the WHO EML and EMLc is both a key factor that influences access to neurological medicines and an opportunity for intervention. A comparison of the 2017 WHO EML with 137 national EMLs across 406 medicines (all disease categories) identified gaps in the selection of medicines at the national level compared to the WHO EML *(53)* resulting from differences in prioritization or challenges with national EML development processes. Even in countries where national EMLs do align with the WHO EML, barriers to access still exist due to the absence of regulatory or legislative frameworks to support compliance to national EMLs or as a result of medicines not being supplied by pharmaceutical manufacturers unless profitability is addressed *(54)*. Greater clarity on the relationship between national EMLs and wider regulatory, financing, procurement and delivery of pharmaceuticals is needed (see Section 3.3). Without a commitment to using essential medicines as the basis for preferred procurement, reimbursement and clinical care, the efficiency goals of the selection of priority medicines are unlikely to be realized. This applies not only to LMICs but also to HICs; large differences are seen between the national EMLs of HICs compared to the WHO EML *(55)*, while many HICs do not have national EMLs (although positive reimbursement lists often act as national EMLs in HICs). HICs could also benefit by implementing the essential medicines concept according to their context and evaluating implementation systematically as part of their national medicines policy *(56)*.

BOX 4.

Ongoing WHO efforts to update the WHO EML and EMLc for neurological disorders and developmental conditions

WHO's Brain Health unit, in collaboration with partners, is working on a review of the WHO EML and EMLc to identify potential gaps and to coordinate action towards a comprehensive update and appropriate representation of neurological disorders and developmental conditions in the EML and EMLc. The aims of the activities are:

1. to identify medicines for neurological disorders and developmental conditions that have established evidence-based efficacy and cost-effectiveness but are not represented or included in the EML and EMLc;
2. to identify missing formulations and strengths of medicines that are already included in the EML and EMLc;
3. to identify medicines included in the EML and EMLc for the management of other conditions but which are also relevant for neurological disorders;
4. to coordinate evidence-based applications for the inclusion of medicines for neurological disorders and developmental conditions in the EML and EMLc.

Pharmacist and WHO staff working at a pharmacy in Jordan, 2020. © WHO

BOX 5.

Case study on the inclusion of medicines for epilepsy and Parkinson disease in national EMLs in the WHO African Region

Using countries in the WHO African Region as an example, this analysis sought to understand the alignment of 47 African Region national EMLs to the WHO EML and EMLc using antiseizure medicines and medicines for Parkinson disease as tracer conditions for neurological disorders. The medicines are effective in managing the diseases, although their availability and affordability varies around the world. The goal of the case study was to identify gaps or misalignments and to leverage these findings to guide the selection of medicines in countries, with the goal of increasing prioritization and access. The analysis used the 23rd WHO EML and 9th WHO EMLc (updated September 2023). Latest publicly-available versions of African Region national EMLs were sourced through the Internet, websites of ministries of health, WHO's Essential Medicines and Health Products Information Portal, or by contacting local, relevant stakeholders directly.

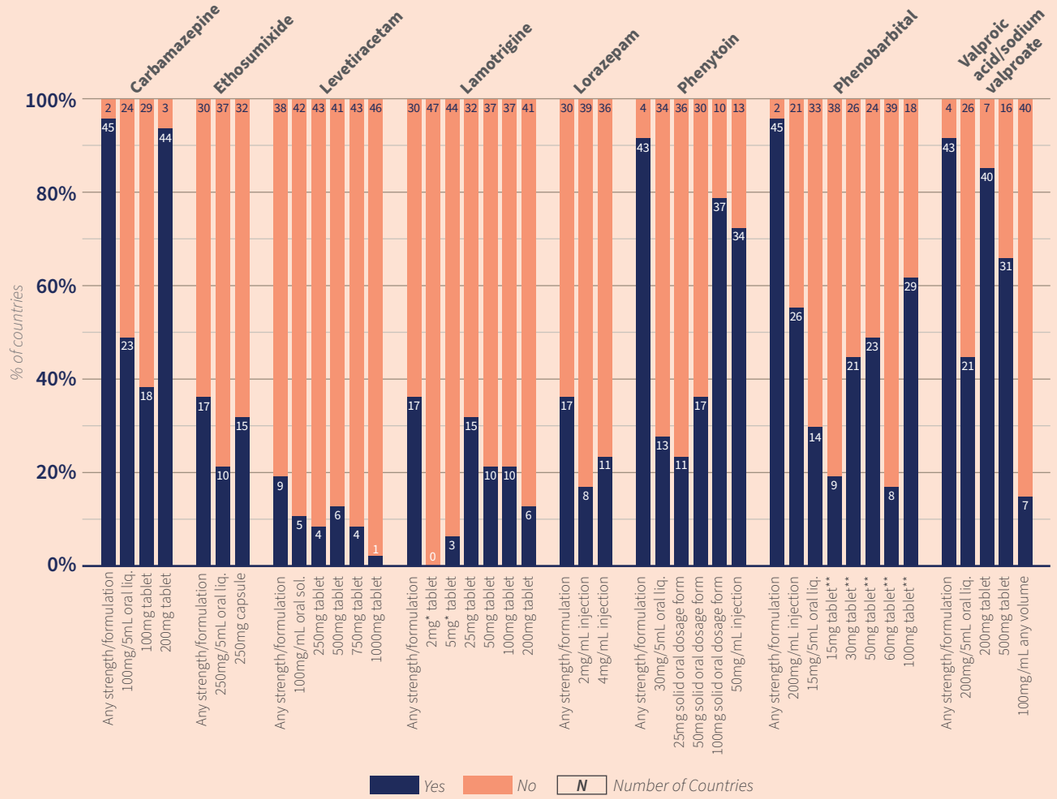
The national EMLs of 23 of the African countries (49%) were most recently updated between 2015 and 2019, while national EMLs from 14 countries (30%) were last updated after 2020. Eight countries (17%) have not updated their national EML since 2014 or earlier, with some lists last updated (or created) in 2006. The national EMLs of two countries did not have a specific date attributed to them. National EMLs should reflect the epidemiological transition that has occurred in recent years in order to ensure the availability of appropriate essential medicines. Older national EMLs may not be up to date and aligned with emerging epidemiological trends or newer medicines.

Antiseizure medicines

The alignment of national EMLs to the WHO EML for antiseizure medicines varied considerably (Figure 5). Although good alignment (above 91%) was seen for most first generation antiseizure medicines considering any formulation and strength (e.g. carbamazepine, phenobarbital, phenytoin, valproic acid), certain formulations and preparations were absent on many national EMLs. Valproic acid in liquid form was included in less than 50% of national EMLs. Low-dose lamotrigine (2mg and 5mg) was included in 0 and 3 countries respectively – these formulations and preparations are commonly prescribed for children. Other antiseizure medicines, such as any dose of ethosuximide, lamotrigine and lorazepam were all included in 36% of national EMLs. Levetiracetam was included in less than 20% of national EMLs, although this medication was only added to the WHO EML in 2023 and a low rate of inclusion was expected. Solutions for infusion of levetiracetam were not included in any of the national EMLs (not shown in Figure 5). Other antiseizure medicines such as diazepam (rectal gel and solution), magnesium sulphate (injection), and midazolam (oromucosal solution and injection) were often included in national EMLs without complete information, thus not allowing for a fair and appropriate analysis. These medicines were therefore not included.

FIGURE 5.

Inclusion of antiseizure medicines in national EMLs in the African Region



** chewable, dispersible tablets*

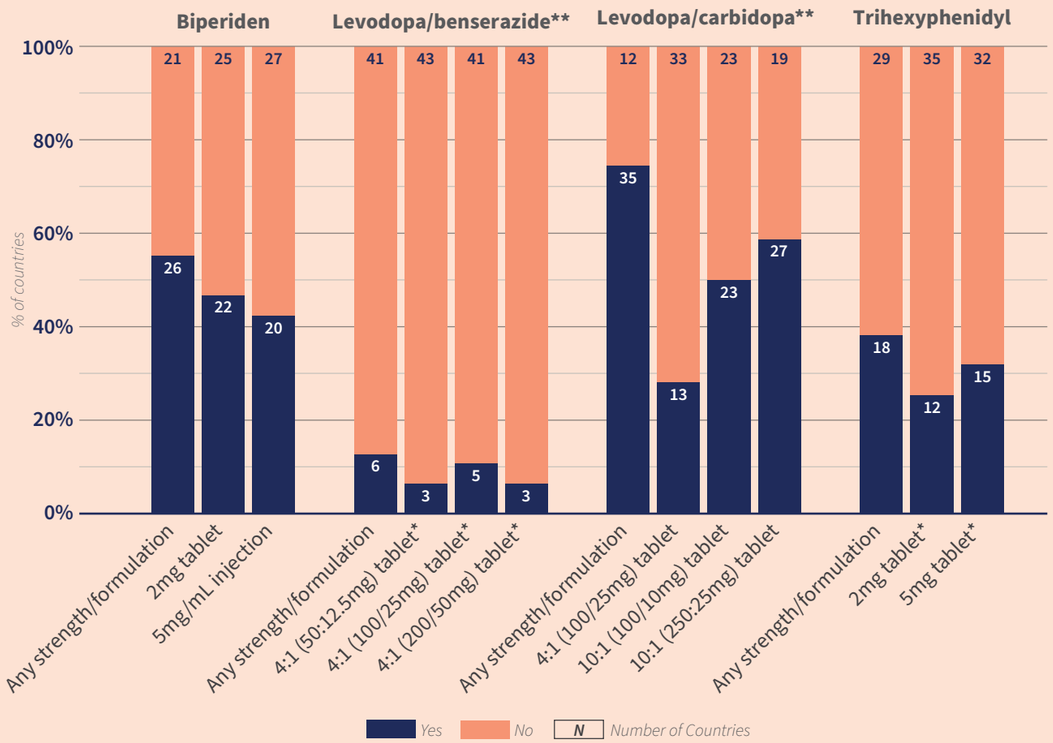
*** representative strengths for the range listed (15mg to 100mg)*

Medicines for Parkinson disease

Levodopa/carbidopa (any formulation or strength) was included in 74% of national EMLs (Figure 6). Levodopa/carbidopa 100/25 (4:1 ratio) was the least common preparation included on national EMLs (27% of countries) for Parkinson disease, despite being the most recommended formulation – especially at earlier disease stages due to the higher ratio of levodopa to carbidopa and better tolerability. Levodopa/carbidopa 100/10 and 250/25 (both 10:1 ratios) were included on 50% and 57% of national EMLs, respectively. Biperiden (an anticholinergic) was included in 55% of national EMLs; trihexyphenidyl (also an anticholinergic) in 38%; and levodopa/benserazide (therapeutic alternative to levodopa/carbidopa) in only 13%.

FIGURE 6.

Inclusion of medicines for Parkinson disease in national EMLs in the African Region



** Medicines under square box listing. Representative strengths available in national EMLs.*
*** Absolute number of countries does not add up to the total of 47 countries as information about strength or formulation was missing in one national EML.*

Conclusion

The inclusion of essential medicines for Parkinson disease, and specific medicines and formulations for epilepsy, on national EMLs in the WHO African Region remains relatively low, highlighting a key opportunity for intervention at the country level. Updating national EMLs offers a first step towards improving access to essential medicines. However, this needs to be part of a comprehensive approach involving action across multiple components.

3.3 Registration and market authorization

Registration and market authorization: summary

Many countries do not have sufficient capacity to provide effective regulatory oversight that includes the registration, or market authorization, of medicines and medical products. Medicines that are not registered by national regulatory authorities (NRAs) do not possess a licence for sales and distribution in the country. The under-registration of essential medicines for neurological disorders has been identified as a concern in the African, Eastern Mediterranean and Western Pacific regions for medicines for epilepsy and Parkinson disease. For instance, document analyses from Kenya and Pakistan found that no essential medicines for Parkinson disease were registered in those countries.

The under-registration of essential medicines is a major barrier to access and presents an opportunity for intervention. It is key to foster the registration of essential medicines listed on national EMLs and their authorizations for use, as well as to allow procurement, sale and distribution. The in-country registration of neurological medicines can facilitate public procurement, thereby improving access. Capacity-building of country regulatory systems is also needed to ensure that appropriate essential medicines undergo registration. For instance, a number of WHO processes (e.g. WHO's programmes on prequalification and regulatory systems strengthening) are in place to support countries in order to streamline their regulatory processes and facilitate the availability of medicines.

Regulatory systems play a key role in assuring the quality, safety and efficacy of medical products. Effective regulatory systems are an essential component of health systems and contribute to desired public health outcomes and innovation. Registration – or market authorization – are key regulatory processes that enable access to medicines. NRAs are entrusted by governments with ensuring that medical products on the market are legally authorized, safe and perform appropriately when used according to directions *(57)*. Medicines that are not registered by NRAs cannot be procured by normal procedures and do not possess the licence for sale and distribution in countries.

Many countries worldwide do not have the capacity to provide effective regulatory oversight (previously reported in Africa *(58, 59)*), a situation that represents a threat to global public health and that can delay access to essential medical products *(57)*. For example, a 2018 document analysis of medicine registration in Uganda found that only 51% of medicines listed as essential (unique dosage forms/strengths) included a product registered with the NRA *(60)*. Therefore, it is of critical importance to help regulatory authorities to fulfil their mandate in an effective, efficient and transparent manner (Box 6).

Evidence of the under-registration of neurological medicines emerges from the African, Eastern Mediterranean and Western Pacific regions. A 2018 document analysis drawing on national EMLs and drug registers of Kenya, United Republic of Tanzania and Uganda showed that the most severe under-registration across all therapeutic classes was for medicines for Parkinson disease *(61)*. In a similar analysis from Pakistan in 2018, 100% of essential medicines for Parkinson disease and 42% of antiseizure medicines were not registered *(62)*. Of the 10 antiseizure medicines available in pharmacies surveyed in Lao PDR in 2020, only three medicines/doses were registered (phenobarbital 60mg, phenobarbital 100mg and phenytoin 50mg) *(63)*. This suggests that unregistered medicines enter country markets through either illegal methods or alternative routes (e.g. parallel importation or special import licences). However, parallel importation can create challenges with pricing and regulation, while public procurement – which can enable access through public outlets at lower costs – is not possible for these medicines. Further, ensuring high standards of medicines that enter the country through illegal methods is not possible and creates other challenges regarding safety and efficacy. More data are needed to better understand the relationships between registration and the availability of essential medicines globally.

> "Even if patients come to us with money to buy their medication, we have challenges importing the medicines. In the past 6 months, I have ordered medicines for 10 Parkinson disease patients, but they get stuck because they are not registered in the country. These patients have been untreated for 6 months"
>
> **Pharmacist, Kenya**

BOX 6.

WHO's role in strengthening country-level regulatory systems

The process of registration can take considerable time, particularly in countries with limited regulatory capacity. WHO has responded to this situation by creating: 1) a collaborative procedure to facilitate the assessment and acceleration of national registration of WHO-prequalified finished pharmaceutical products (FPPs) *(64)*; and 2) a collaborative procedure to accelerate the registration of FPPs that have already received approval from a stringent regulatory authority *(65)*.

The prequalification programme enables NRAs to make use of work already carried out by WHO and to strengthen their own regulatory oversight processes in line with international best practices. Repeating NRA assessments and inspections consumes scarce regulatory resources and extends the time before making medicines available to patients. As well as aiming to ensure that much-needed medicines reach patients more quickly, both procedures incorporate strong elements of capacity-building and regulatory harmonization. The successful application of both procedures is highly dependent on the ability and willingness of pharmaceutical companies (the applicants), manufacturers, regulatory authorities and WHO to work together to meet public health goals. This is, in turn, of great interest to manufacturers since the application of the procedure enables faster registration and market authorization in countries.

Within the prequalification programme, WHO launched the Collaborative Registration Procedure (CRP) for finished pharmaceutical products. As of 2024, the procedure involved more than 65 participating countries in various regions. The CRP for WHO prequalified products aims to accelerate registration through improved information sharing between WHO prequalification and NRAs. The CRP builds on the collaboration between WHO, NRAs and manufacturers by leveraging the work of WHO prequalification in order to reduce duplication and facilitate in-country registration of quality-assured products, thus making these products more widely available.

Further, WHO provides support through the Regulatory Systems Strengthening (RSS) programme and the Global Benchmarking Tool (GBT) *(66)* which is used to evaluate national regulatory systems of medical products objectively and to identify strengths and areas for improvement. In 2021, WHO published the Good Regulatory Practices and Good Reliance Practices documents *(67)* to support countries in improving the oversight and regulation of medicines and health products and to promote greater collaboration between regulators both regionally and internationally to leverage resources more efficiently and to ensure that quality health products reach people faster.

3.4 Financial aspects

Financial aspects: summary

Low levels of public financing for neurological disorders, means that many people across the world must either pay for their medicines out-of-pocket, often resulting in significant financial hardship, or they must go without medicines. Price and affordability of medicines is one of the most significant barriers to accessing medicines for neurological disorders. Several studies have investigated the price and affordability of medicines for neurological disorders, with the overwhelming conclusion that medicines are unaffordable across countries in the African, Americas, South-East Asia and Western Pacific regions, despite most being off-patent, with generic formulations available and low international market prices. For example, purchasing one month's supply of antiseizure medicines, or medicines for Parkinson disease, could cost, in some cases, over 30 days' wages of the lowest-paid government worker.

Improved access to publicly funded benefit packages (which include essential medicines for neurological disorders) is necessary to prevent catastrophic and impoverishing out-of-pocket spending on health care and to achieve UHC. Moreover, medicines for neurological disorders need to be made available at a fair price – i.e. one that is affordable and sustainable for both health systems and patients. WHO proposes several measures to reduce the costs of medicines both to governments and households – including the use of pooled procurement, regulation of mark-ups, use of referencing pricing, fostering trust in high-quality generic formulations, and promoting pricing transparency. Measures to ensure fair and sustainable pricing of medicines will require regulatory and health system capacity-building (Box 7).

3.4.1 Health financing

At the health system level, adequate public funding for neurological disorders in many parts of the world is limited. Of the countries surveyed in the 2017 second edition of the WHO's Neurology atlas, 12% reported a separate budget line for neurological disorders – defined as a source of funds available and allocated for action directed to the treatment and care of neurological disorders (Figure 7) *(69)*.

BOX 7.

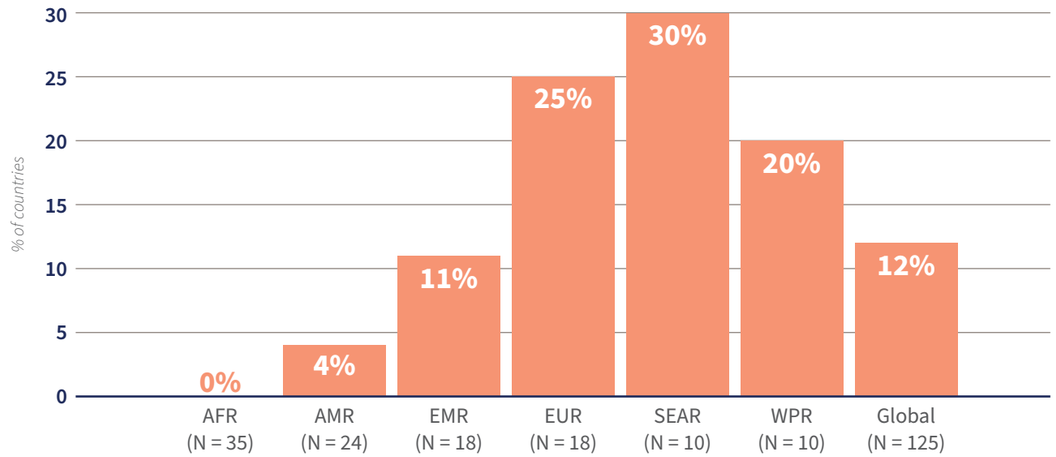
The role of health financing in achieving universal health coverage

Health financing is a core function of health systems that can enable progress towards UHC by improving effective service coverage and financial protection. UHC means that all people have access to the full range of quality health services they need, when and where they need them, without financial hardship. It covers the full continuum of essential health services across the life course, from health promotion to prevention, treatment, rehabilitation and palliative care. Financial hardship due to out-of-pocket health spending occurs when direct payments for health threatens people living standard by pushing them into poverty or further into poverty (are impoverishing) and compromises access to essential goods such as food, shelter, clothing and education (are catastrophic).

Removing financial barriers to accessing services, and protecting people from the financial consequences of using health services, both addresses unmet needs and reduces the risk that people will face financial hardship due to out-of-pocket health spending, often trying to cope by using up life savings, selling assets or borrowing money/going into debt. Consequently, it is crucial to advance UHC in order to ensure financial protection from the cost of medicines, diagnostics and other health products *(68)*, particularly in the lowest-income countries and households. Poor health financing presents a significant barrier to optimizing health and treatment outcomes because of the unaffordable costs of medicines.

FIGURE 7.

Countries with a separate budget line for neurological disorders, by WHO region *(69)*



Note: AFR = African Region; AMR = Region of the Americas; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asia Region; WPR = Western Pacific Region.

The reported availability of monetary support (e.g. disability benefit payments or income support) for people with neurological disorders in LICs is 24%, compared to 86% in HICs.

At the population level, low levels of public funding in health leads to catastrophic out-of-pocket spending. Neurological disorders are unlikely to be an exception. Indeed, out-of-pocket payments represent the primary method of financing neurological care in 84.2% of LICs (compared to 25.6% worldwide) *(70)*.

3.4.2 Price and affordability of medicines

Affordability is determined by the price of the medication and an individual's financial capacity or ability to pay for the medication (Box 8). Different barriers affect the affordability of neurological medicines in distinct ways. While standing patents can drive the prices of some medicines to levels that are unaffordable for most people (e.g. certain medicines for multiple sclerosis), the unaffordability of essential medicines for epilepsy and Parkinson disease is compounded by the lack of coverage of these conditions within public funded benefits or entitlements, issues across the supply chain that lead to higher prices, as well as by high tariffs, taxes, mark-ups and substantial out-of-pocket expenditure. Coverage for treatment of neurological disorders variers across countries. Regardless of whether countries adopt social health insurance schemes or have tax-financed health systems, access to care for neurological disorders is largely funded through out-of-pocket payments. This is particularly the case in LMICs *(71, 72)*. High out-of-pocket costs can impose financial hardship on people with neurological disorders (and their families) and may result in lower medication adherence. For example, studies from rural parts of the Democratic Republic of Congo and Nigeria, from 2019 and 2011 respectively, have shown that the cost of care for a family member living with epilepsy can be as high as half of the household income, with around 20% of the cost due to out-of-pocket purchases of antiseizure medicines *(73, 74)*.

The availability of lower-cost generic medicines offers the opportunity to create a culture where high-quality generics are trusted, prescribed and utilized (see section 3.7.4 on "*Quality of generic medicines*"), which could drive the market to lower prices, thereby making medicines more affordable.

Ultimately, the affordability of medicines is directly impacted by several health system components demonstrated in the fishbone diagram, such as appropriate selection of medicines, registration and market authorization, health financing, supply chains and other elements (Figure 4). Therefore, increased efficiency across these different components have the potential to improve the affordability of medicines to both health systems and the population, driving better access.

Epilepsy

The cost and affordability of antiseizure medicines was evaluated across 46 countries (across all income groups) through a study published in 2012, with the conclusion that the affordability of antiseizure medicines is poor *(76)*. The study identified that the highest prices for carbamazepine and phenytoin, for instance, were found in countries with the lowest income. Public sector patient prices for generic carbamazepine and phenytoin were about 5 and 18 times higher than international reference prices, respectively, whereas private sector patient prices were 11 and 25 times higher, respectively (as of 2011). One month's supply of originator carbamazepine could cost up to 16 days' wages for the LPGW. In 2022, the International League Against Epilepsy (ILAE) Task Force on Access to Treatment carried out a survey which determined that cost was the most prevalent barrier to access, reported by 80% of LMICs and 63% of upper-middle-income countries. Whether cost was identified as a barrier was also notably related to the country's income level, as significantly fewer HICs (35.9%, $p<0.05$) reported cost as a barrier *(72)*.

BOX 8.

Methodology used to determine the affordability of medicines

The World Health Organization/Health Action International (WHO/HAI) methodology is a tool for measuring medicine prices, availability, affordability and price components *(75)*. This methodology has been adopted by studies to understand the affordability of neurological medicines across different WHO regions. Unaffordability is defined as paying more than 1 day's wages of the lowest-paid government worker (LPGW) for a standard 30-day supply of medication. It is worth noting that using the LPGW wage as a measure of affordability may be an over-estimation of income in view of the large size of the informal labour workforce in many countries. Further, such measures reflect only the wages required to pay for medicines and do not take account of expenditure on additional care, food, shelter and other basic needs.

Data from the WHO African Region show similar findings related to cost and affordability, with a study from eastern Ethiopia in 2021 reporting that one month's supply of carbamazepine 200mg tablets (based on a defined daily dose of 1000mg) cost 30-days' wages *(77)*. In Malawi, the affordability of antiseizure medicines in 2017 was deemed to be "very poor" *(78)* – phenobarbital was the only affordable antiseizure medicine identified in the study and was also the most available. It is worth noting that the cost of epilepsy treatment not only includes medication cost but also cost associated with medical consultations and investigations, such as EEG[1], MRI[2] and travel to health-care appointments. By contrast, in the WHO European Region, a 2019 WHO survey from Ukraine found that carbamazepine was affordable (determined by the availability at a low cost in 84.6% of facilities surveyed) *(80)*.

The unaffordability of antiseizure medicines has also been reported in the WHO Western Pacific Region. In Cambodia, carbamazepine and sodium valproate were the most costly antiseizure medicines (up to 10.8 and 10.1 days' wages of the LPGW for a monthly treatment respectively), with similar costs seen across urban and rural areas *(81)*. In Lao PDR, all antiseizure medicines were sold at higher prices than the international reference prices – e.g. phenobarbital 100mg cost over 20 times the international reference price *(63)*. Sodium valproate was the most expensive medicine surveyed. A cross-sectional survey of health-care professionals across a number of LMICs in the South-East Asia and Western Pacific regions in 2023 determined that a number of antiseizure medicines, including lamotrigine and levetiracetam, were unaffordable in most Asian LMICs – requiring between 4.7 and 13 days' wages for a 30-day supply *(82)*. Also from the South-East Asia Region, a study in India found

1 EEG = Electroencephalogram.

2 MRI = Magnetic resonance imaging.

Medicines for epilepsy, Parkinson disease, and other neurological disorders have been determined as unaffordable across several countries in the African, Americas, South-East Asia, and Western Pacific regions, costing, in some cases, over 30 days' wages of the lowest paid government worker for a 30 day supply.

that one month's supply of medication would cost over 30 days' wages of the LPGW (except for carbamazepine, which would cost six days' wages) *(83)*.

Parkinson disease

Available evidence on medicines for Parkinson disease point towards their unaffordability, particularly in LMICs. A needs assessment on Parkinson disease care from 2020 (including representation from the African, Eastern Mediterranean and South-East Asia regions) reported high costs of medication based on cost of living and income ratios and lack of health insurance coverage *(84)*. However, data on affordability from studies using robust methodology is lacking globally.

A survey of health-care professionals from the African Region concluded that medicines for Parkinson disease are largely unaffordable in most African countries *(85)*. Studies from Ghana *(86)*, Kenya *(87)* and Nigeria *(88)* using WHO/HAI methodology have also determined that medicines for Parkinson disease, including levodopa/carbidopa, are unaffordable. Table 2 outlines the cost of one months' supply of levodopa/carbidopa from each country and days' wages from the LPGW required.

TABLE 2.
Cost and affordability of levodopa/carbidopa from Ghana, Kenya and Nigeria

Country	Year of survey	Cost of 30-day supply of levodopa/carbidopa tablets (range in US$ at time of survey)	No. of days' wages from the LPGW for a 30-day supply	Affordability
Ghana *(86)*	2017	35–71	Data not available	No
Kenya *(87)*	2014	28–82	Data not available	No
Nigeria *(88)*	2017	27–45	23	No

Note: range includes all formulations of levodopa/carbidopa; Kenya affordability deemed by pharmacist opinion (87); Nigeria and Ghana affordability calculated using WHO/HAI methodology.

3.5 Availability of medicines

Availability of medicines: summary

The lack of available medicines for neurological disorders is a major barrier to access. Poor availability is seen across world regions and within countries, with disparities between urban and rural areas, as well as across public and private sectors. The availability of essential medicines for neurological disorders is found to be a main challenge at PHC level and is particularly low in the African and South-East Asia regions, as well as across LMICs.

Improved availability is a downstream benefit of action across other components, including awareness and prioritization, selection, regulatory systems and the supply chain. A well-managed supply chain would enable consistent and efficient supplies of quality medicines to be available to those who need them while minimizing the occurrence and duration of stock-outs.

Poor availability of medicines for neurological disorders is a major barrier to access in many parts of the world (Box 9). The second edition of WHO's Neurology atlas determined that the availability of essential medications for neurological disorders is low in PHC settings across WHO regions, and particularly in the African and South-East Asia regions and in LMICs *(69)*. Low availability in the public sector, where medicines should be cheaper and/or covered by UHC, can drive individuals to the private sector where medicine prices are often much higher.

Epilepsy

Many essential antiseizure medications are not available in many parts of the world, particularly in the public sector *(30)*. The WHO Neurology atlas found that just 55% of countries globally report the availability of one or more antiseizure medicines (carbamazepine, phenobarbital, phenytoin, valproic acid) at all times in the PHC setting *(69)*. At the hospital level, 70% of countries report the availability of at least one antiseizure medication (see Figure 8 for availability across income groups).

A survey conducted by the ILAE Task Force on Access to Treatment in 2022 (including responses from 101 countries) noted that, although first-generation antiseizure medicines are, in general, widely available globally, the availability of other more recent antiseizure medications is limited in LMICs *(72)*. In the same survey, only 30% of LICs reported the availability of at least one non-first-generation antiseizure medicine (compared to more than 90% for HICs), while 60% of respondents from low- and lower-middle income countries cited limited access to lamotrigine. Disparities in availability in LICs are also seen across both public and private sectors. Data from the HAI global database on psychotropic medicines from 2023 show that the availability of carbamazepine in LIC public-sector facilities was 10%, compared to 55% in LIC private-sector facilities *(90)*. Furthermore, stock-outs have been reported as a barrier to access *(91)* – in Uganda, medication stock-outs were shown to be the most consistent barrier to accessing epilepsy care *(39)*.

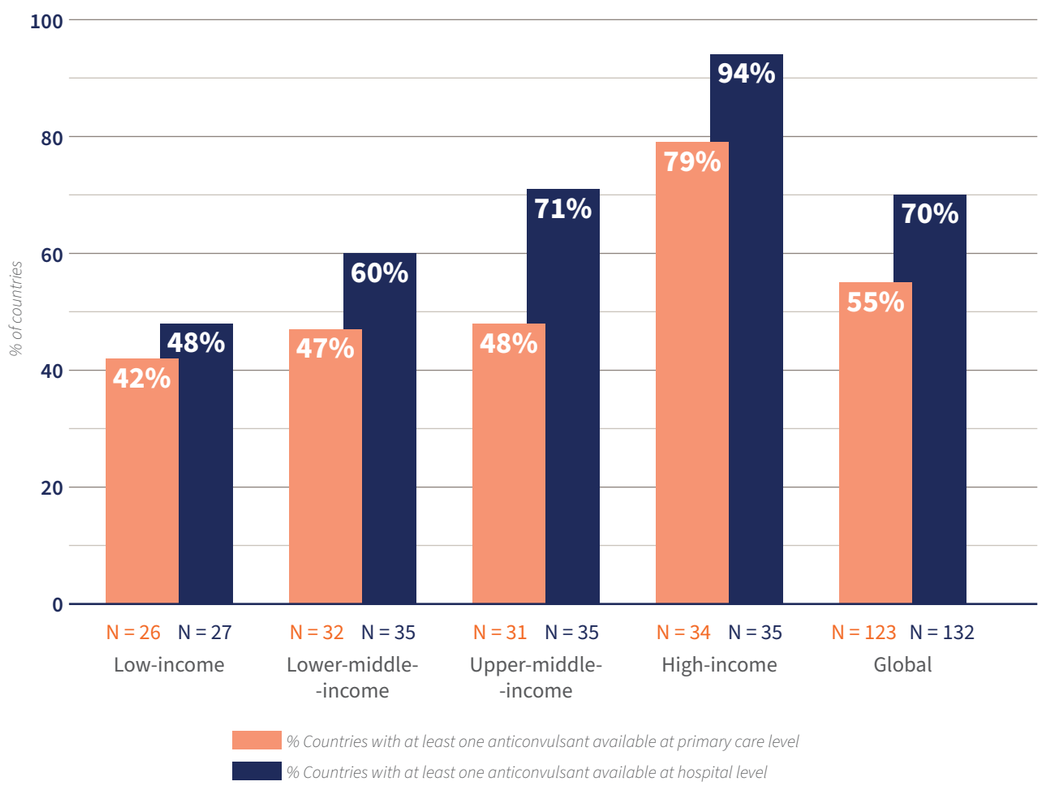
BOX 9.

Methodology used to determine the availability of medicines

Availability is expressed as the percentage of facilities in which a medicine is available at the time of the survey. The following levels have been used to determine availability: <30% very low; 30–49% low; 50–80% fairly high; 80% high *(89)*. Low availability should not be overemphasized because countries may have other strengths or dosage forms of a particular medicine available.

FIGURE 8.

Countries with at least one antiseizure medication (carbamazepine, phenobarbital, phenytoin, valproic acid) always available at primary care and hospital level, by World Bank income group *(69)*



In the European Region, a WHO survey conducted in Tajikistan found that the availability of carbamazepine was critically low in all areas surveyed, with a median total stock-out duration lasting 366 days *(92)*. The report adds that, although carbamazepine is listed in Tajikistan's national EML, it is not regularly available in pharmacies. A similar survey in Uzbekistan found a higher availability of carbamazepine, although sodium valproate was among the least available of all medicines surveyed, despite being included in the national EML and the national list of socially important medicines. Stock-outs for sodium valproate were reported by almost half of the facilities, lasting up to one month in public facilities. For carbamazepine, stock-outs were not as common (17% of facilities) and were resolved in less than seven days *(93)*. A slightly different picture emerges from the 2019 WHO survey conducted in Ukraine, where antiseizure medicines (including carbamazepine, sodium valproate, trihexyphenidyl) were widely available. While carbamazepine was deemed to be "available", magnesium sulphate was not (Table 3).

In the South-East Asia Region, the availability of essential antiseizure medication has been determined as low in Cambodia and Lao PDR *(63, 81)* (Table 2); in both countries, phenobarbital 100mg was the most available medication. A survey from north-west India showed the availability of antiseizure medicines to be poor and fragmented, with availability in just 10% of public facilities compared to 88% of private facilities *(83)*.

TABLE 3.

Availability of antiseizure medicines (determined using WHO/HAI methodology) across selected countries and WHO regions

WHO region	Country	Year of publication	Medication	Availability
South-East Asia Region	Cambodia *(81)*	2021	Carbamazepine, phenobarbital, phenytoin and sodium valproate	36%
	Lao PDR *(63)*	2020	Carbamazepine, phenobarbital, phenytoin and sodium valproate	15%
	India *(83)*	2020	Selection of 11 antiseizure medicines	22%
European Region	Tajikistan *(92)*	2023	Carbamazepine	7%
	Uzbekistan *(93)*	2023	Carbamazepine	60.7%
			Sodium valproate	19%
	Ukraine *(80)*	2021	Carbamazepine, magnesium sulphate, trihexyphenidyl and sodium valproate	93.8%

Parkinson disease

The low availability of medicines for Parkinson disease is a particular challenge in LMICs *(69, 71, 94, 95)*, while disparities in rural/urban availability are prevalent globally *(96)*. Yet data regarding availability are lacking from many regions and countries. The WHO Neurology atlas determined that 0% of LICs always had medicines for Parkinson disease available at PHC level and only 21% had them at hospital level *(69)*. Only 37 of 110 countries had levodopa/carbidopa consistently available in PHC settings.

In the South-East Asia Region, studies have reported on the disparities in availability and accessibility of dopaminergic medications across and within countries *(97)*. For example, levodopa/carbidopa is not universally available in Cambodia and Lao PDR *(98)*. In contrast, in Thailand, levodopa/carbidopa has been reported to be available across all 77 of the country's provinces *(99)*. A review of the challenges of Parkinson disease care in south-east Asia showed that levodopa/carbidopa in a 4:1 ratio was not available in three of the eight countries surveyed *(100)*.

A survey of neurologists regarding the availability of medicines for Parkinson disease across Africa identified that levodopa/carbidopa 100/25 (4:1 ratio) was "always available" in just nine of the 28 countries included in the survey *(85)*. Surveys from Ghana *(86)*, Kenya *(87)* and Nigeria *(88)* (Table 4) highlight low availability as a key barrier to accessing appropriate Parkinson disease medicines, in addition to affordability, awareness of Parkinson disease, and limited health-care provision. In Nigeria, anticholinergics were available in 77% of private and 34% of public pharmacies. In Ghana, stock-outs and shortages were experienced by half the pharmacies surveyed. Across all sites, levodopa/carbidopa 100/25 (4:1 ratio) – a frequently recommended formulation for Parkinson disease – was the least available. Formulations which contain a lower proportion of dopa-decarboxylase inhibitor (carbidopa) (i.e. 10:1 ratio) were more available yet can result in higher incidence of side-effects.

TABLE 4.
Availability of levodopa/carbidopa in three countries in the African Region

Country	Year of publication	No. of pharmacies surveyed	Availability of levodopa/carbidopa			
			Overall	Public	Private	4:1 ratio
Ghana *(86)*	2019	121	11%	5%	14.6%	5.8%
Kenya *(87)*	2016	48	50%	6.7%	73.7%	6.2%
Nigeria *(88)*	2019	123	48%	19.7%	75.8%	2.4%

> "As I write this I am in a clinic where we are struggling to find solutions for patients who have received a neurological diagnosis"
>
> **Neurologist, Tanzania**

3.6 Trained health workforce

Trained health workforce: summary

The overall shortage in the global neurological workforce able to diagnose and manage neurological disorders, as well as in the wider interdisciplinary workforce, are key barriers to access to medicines. The availability of an appropriately trained workforce that can identify, diagnose and manage neurological disorders, as well as prescribe and dispense medicines, is crucial to ensuring safe, appropriate and effective treatment. If individuals are not diagnosed, they cannot access medicines. The availability of the neurological workforce is a particular problem in LICs, and in countries in the African and South-East Asia regions. The availability of child neurologists is particularly low, with many countries in the world having no child neurologists. Disparities also exist within countries, with very few neurologists practising in rural areas across all income groups and all WHO regions. However, the situation in LICs is particularly dire, with no countries reporting a permanent practising neurologist in rural areas.

Awareness-raising and educational efforts are needed within health-care systems to identify neurological disorders at the PHC level (e.g. utilizing mhGAP to train non-specialists), particularly in LICs. This should be coupled with specialized training to build the neurological workforce at the secondary and tertiary levels, including the multidisciplinary workforce required for the holistic management of neurological disorders (e.g. pharmacists and supply chain).

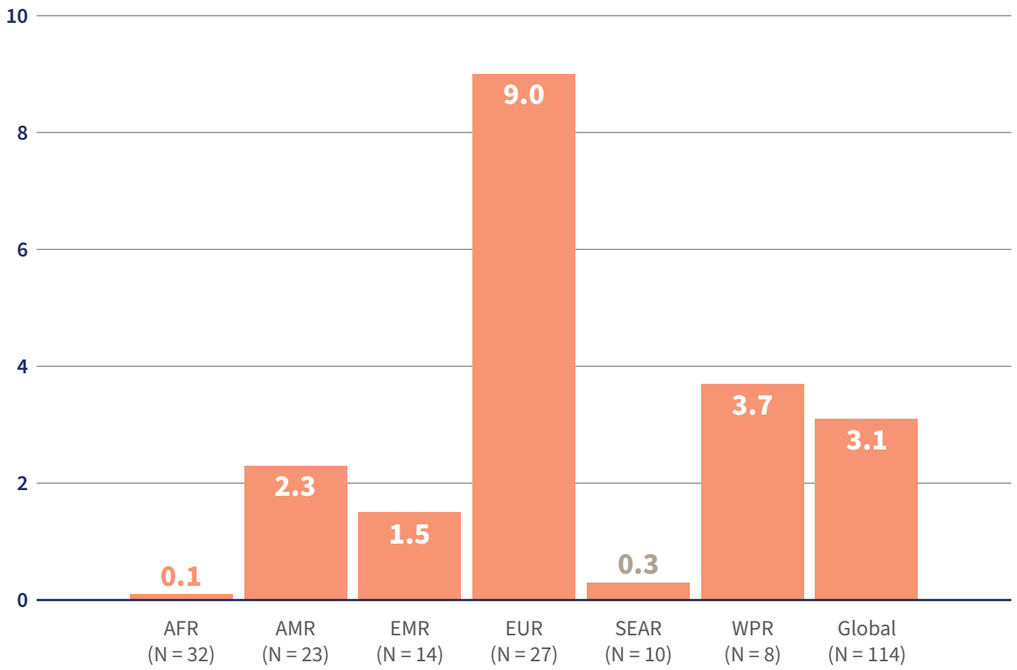
The capacity of the workforce to diagnose and manage the treatment of chronic, life-long neurological disorders is a key aspect of access to medicines. Once a diagnosis is made – which is challenging in itself because of the limited capacity of, and diagnostic instruments available to, the neurological workforce *(40)* – obtaining a prescription from a trained health-care professional is the next step in accessing appropriate and potentially life-saving medication. However, when workforces are limited, this too becomes challenging. The lack of a trained health-care workforce across all levels of care able to diagnose and manage neurological disorders is significantly associated with treatment gaps, resulting in untreated or unmanaged disease. Particularly at the PHC level, the ability of the non-specialist workforce to diagnose and treat neurological disorders is limited. This is what the WHO mhGAP aims to address. It is also important to note that, even in countries with some capacity, health professionals can be left with limited options due to the unaffordability and unavailability of medicines. This shows that comprehensive action across different sectors is needed to improve access.

The size of the neurological workforce varies across WHO regions (Figure 9). Numbers also vary by country income categories. Most LICs and lower-middle income countries have low

numbers of neurologists and a small overall neurological workforce *(69, 85, 98, 101)*. The global median of the total neurological workforce (defined as the total number of neurologists, neurosurgeons and child neurologists) is 3.1 per 100 000 population *(69)*. In LICs, the median is 0.1 per 100 000 population compared to 7.1 per 100 000 in HICs.

FIGURE 9.

Median neurological workforce per 100 000 population, by WHO region *(69)*



Note: AFR = African Region; AMR = Region of the Americas; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asia Region; WPR = Western Pacific Region.

The number of adult neurologists is lowest in the African Region, with a median of 0.04 per 100 000 population – in Malawi, for instance, there is one neurologist for a population of over 19 million *(85)* – and also in the South-East Asia Region, with a median of 0.1 neurologists per 100 000 population. The European Region has 6.6 adult neurologists per 100 000 population – the highest number of all WHO regions.

Although there is a deficiency of adult neurologists in LICs *(69)*, the situation regarding the availability of child neurologists is significantly worse (Figure 10) *(69)*. A survey by the International Child Neurology Association *(102)* identified that 73% of LICs lack access to child neurologists, with the majority of these countries in the African and South-East Asia regions. There are 52 countries in the world that have no child neurologists.

FIGURE 10.

Median number of neurological workforce per 100 000 population by World Bank income group *(69)*

World Bank income group	Adult neurologists		Neurosurgeons		Child neurologists	
	Number of responding countries	Median	Number of responding countries	Median	Number of responding countries	Median
Low-income	23	**0.03**	23	**0.02**	18	**0.002**
Lower-middle-income	29	**0.13**	28	**0.11**	27	**0.02**
Upper-middle-income	32	**1.09**	28	**0.6**	25	**0.1**
High-income	30	**4.75**	29	**1.24**	23	**0.39**
Global	114	**0.43**	108	**0.34**	93	**0.05**

Disparities also exist within countries. The WHO Neurology atlas shows no LICs reporting any neurologists practising in rural areas, compared with 45% in HICs *(69)*. A systematic review of the determinants of the epilepsy treatment gap in resource-limited settings found that persons from rural locations were 1.63 times more likely to have untreated epilepsy *(103)*.

In many countries, the lack of neurological workforce means that most neurological care is provided by non-specialist health-care providers. However, specialty care is essential to maintain a continuum of care, and specialists are also needed to provide education, training, supervision and support to non-specialists working at the PHC level. Many health-care professionals at the PHC level lack the expertise to diagnose and manage neurological conditions; consequently, awareness about neurological disorders is often limited *(40)*. Appropriately trained non-physician health-care workers could potentially diagnose and manage epilepsy and Parkinson disease in rural clinics *(96, 104)*, as has been demonstrated for epilepsy in China *(105)*, particularly if aided by culturally contextualized and appropriate technologies. This would require education and training of the PHC workforce, as has been demonstrated by WHO's Programme on reducing the epilepsy treatment gap which was launched in 2012 in Ghana, Mozambique, Myanmar and Viet Nam *(106)*, and by the implementation in several countries of the mhGAP *(104)* which was launched in 2008.

The achievement of improved health outcomes depends greatly on the combination of an adequate neurological workforce, other health-care providers – including psychologists, psychiatrists, radiologists, physical therapists, occupational therapists and speech therapists – and competent health workers serving at the PHC level, who are trained in identifying and managing neurological disorders *(1)*. Furthermore, the training and education of an interdisciplinary workforce – including social care workers, rehabilitation specialists trained in neurological conditions, technicians, pharmacists, community health workers, family members, carers and traditional, religious and herbal healers, where appropriate – is required to support the delivery of person-centred care to people with neurological disorders, to reduce their mortality and morbidity and to improve their quality of life.

3.7 Additional components affecting access to medicines for neurological disorders

The components that affect access to medicines for neurological disorders are manifold. This report has highlighted the components which appear to have the most significant impact relating to chronic, noncommunicable neurological disorders. However, there are also multiple components which have a broader impact on wider health systems and on access to all medicines. Consequently, medicines for neurological disorders are also affected.

3.7.1 Health information systems

Health information systems: summary

The lack of available data on neurological disorders presents challenges for prioritization and the need for intervention, as well as supply chain processes. Strong health information systems play a major role in delivering high-quality health services. Therefore, the availability of data collected systematically across the health system is a crucial and cross-cutting component of access to medicines for neurological disorders. Particularly in low-resource settings, challenges arise in understanding the neurological disease burden and the need for prioritization due to unreliable health facility records, non-inclusion of neurological disorders in health management information systems, lack of regular data collection on stock, pricing and distribution of neurological medicines, shortage of cross-sectional community studies, lack of data on the long-term health, social and economic benefits of investment, and lack of inclusion in surveillance systems and registries.

Data on disease epidemiology, burden and return on investment are needed to advocate for prioritization and to generate political commitment, as well as to inform demand and forecasting within the supply chain, which in turn will improve availability and access.

Health information systems are an essential component of a health system, providing reliable information on the determinants of health, population health, health status and performance (e.g. human resources, health infrastructure and financing), while guiding activities across other health system building blocks *(107)*. Health information systems are defined as an integrated effort to collect, process, synthesize, report and use health information and knowledge to influence policymaking, programme action and research. They are critical systems which help to harmonize information and modernize health processes by integrating health functions and departments to deliver high-quality health-care services *(108, 109)*. Therefore, the availability of systematically collected data and a smooth flow of information throughout the health system are crucial and cross-cutting features that contribute to access to medicines for neurological disorders.

Data are needed to inform prioritization (e.g. burden of disease), supply chain processes (including demand and forecasting), return on investment (need for intervention) and to inform health information systems in general. Data reporting systems help to monitor trends in disease burden, identify high-priority health-care issues and develop plans for improvements in health services. In the WHO Neurology atlas, however, the lack of a data-reporting system for neurological disorders was identified in low- and lower-middle-income countries *(69)*. Within health information systems, data may be provided on new cases, although this is often difficult in low-resource settings, and routine data collection often lacks information on follow-up cases. This makes it difficult, for instance, to provide accurate estimates of service coverage.

Further challenges regarding the availability of data on neurological disorders in many parts of the world relate to unreliable health facility records, non-inclusion of neurological disorders as separate items in health information systems, and the lack of cross-sectional community studies *(110)*. Lack of inclusion of neurological disorders in disease surveillance systems, registries and censuses also create challenges in understanding the epidemiology of these conditions. This scenario is worsened by the lack of primary care physicians with specialized neurological training (see Section 3.6) and the existence of stigma (see Section 3.1) that makes epidemiological investigations of these neurological disorders extremely difficult.

Standard recording and reporting are also needed to improve supply forecasting and management *(18)*. Streamlining information across the health system can ensure that data are readily available to make the right decisions, considering specific needs across regions and populations for the appropriate allocation of resources (see section 3.7.2 on “Supply chain”). The regular collection and reporting of data and information on price, availability, quality, utilization, registration and procurement can be used to improve the access to and use of medicines *(111)*.

3.7.2 Supply chain

Supply chain: summary

Challenges along the supply chain can have an impact on the availability and affordability of medicines for neurological disorders, impeding continuous access. The main challenges are the lack of accountability and fragmentation of responsibilities, uncertainties in financing, complex supply chains, mismanaged procurement processes and inaccurate or inexistent forecasting, underfunded operating costs, and a lack of adequate planning and poor data on real needs.

Addressing the issue of access to medicines for neurological disorders and ensuring that essential medicines move efficiently and effectively from the manufacturer or distributor to the point of access, and therefore to the patient, would require improvements to the supply chain. Countries are encouraged to utilize WHO’s – and/or other internationally recognized – tools to build stronger medicines supply management systems to improve the availability and accessibility of essential medicines.

A supply chain refers to the ecosystem of organizations, people, technology, activities, information, and resources that ensure the cost-effective delivery of a product from manufacturer to the patient *(112)*. WHO's Medicines Management Cycle *(113)* shows how a supply chain involves selection, quantification and forecasting, procurement, storage and distribution. A well-managed supply and distribution chain is, therefore, critical to timely access to medicines as it ensures efficiency and continuity, maintains product quality and affordability, and prevents stock-outs. Resilient supply chains depend on effective supply sourcing and appropriate demand (i.e. market forces).

Despite increased investments in the procurement of essential medicines globally, availability at health facilities in many LMICs remains low *(114)*. The lack of a functioning and efficient in-country supply chain is a limiting factor in enabling access to essential medicines *(114–116)*. For example, an ILAE report identified challenges with local purchasing and distribution of antiseizure medicines, with 75% of African countries surveyed reporting such issues occurring more than twice a year *(72)*.

In many LMICs, governments (i.e. ministries of health) use publicly-managed "central medical stores" to procure, store and distribute medicines to regional warehouses and health facilities *(112)*. How much of a medical product is sent to a health facility is commonly determined by either a "push" or a "pull" system which depends on the health system's capacity to conduct stock planning and forecasting and the availability of information systems. Forecast data and demand consolidation are the cornerstones to procurement. However, problems such as internal fragmentation, inefficient or incipient logistics management information systems, poor forecasting data, challenges in stock management can weaken the entire medicines procurement system.

Challenges relating to supply chains include the lack of an accountability structure and fragmentation of responsibility, uncertainties in financing due to long procurement cycles, complex supply chain structures, long replenishment intervals and inaccurate forecasting, minimal funds for operating costs, and a lack of supply chain planning data and data on rates of product consumption *(112)*. Further challenges in the supply chain relate to creating an integrated logistics management and information system where there has been no bar-coding to track products, inefficient domestic transport, poor infrastructure and storage conditions, and poor inventory and waste management systems.

Supply chains should be responsive to the needs of patients in a cost-effective manner. Addressing the issue of access to medicines for neurological disorders would therefore require supply chain reform. However, this cannot be pursued in isolation and requires broader health system actions, including fundamental changes to the structure of health-care financing and regulation, strong leadership in the health sector and a strong supply chain workforce, again exemplifying the need for multisectoral action to improve access to medicines.

Medical supplies being delivered to Al-Awda hospital, Occupied Palestinian Territory, 2024. © WHO

3.7.3 Regional and local manufacturing

Regional and local manufacturing: summary

The reliance on imported medicines for neurological disorders in many parts of the world can create access challenges. However, many of the problems with importing medicines result from challenges with financing, registration and supply chain. Addressing these components can facilitate the process of importing medicines. Regional and local manufacturing has the potential to address these challenges by strengthening the ability and local capacity to produce pharmaceuticals, while prioritizing essential medicines. Examples of regional initiatives in the African Region – e.g. the African Union's Pharmaceutical Manufacturing Plan for Africa – demonstrate the potential to strengthen regional capacity to produce high-quality, affordable essential medicines. However, challenges with pharmaceutical infrastructure, the high costs of raw materials and active pharmaceutical ingredients (APIs), and poor technical capacity are among the challenges associated with local and regional manufacturing.

The reliance on imported medicines for neurological disorders in many parts of the world can create access challenges. For example, although Africa accounts for 24% of the global burden of disease, the continent produces just 3% of the world's pharmaceutical drugs *(115)* despite housing over 649 drug manufacturing plants across 29 countries *(117)*. The regional manufacturing of medicines for neurological disorders has the potential to improve access.

Manufacturing is characterized by three stages: 1) the manufacture of active pharmaceutical ingredients (APIs); 2) the manufacture of complete dosage forms from raw materials and excipients; and 3) the packaging and labelling of finished products *(118)*. Low manufacturing capacity can result from the high cost of importing raw materials and APIs, the market dominance of imported products, failure of products to meet internationally accepted quality standards, lack of technical capacity to enable diversification of portfolios and product lines, and lack of enabling policies and policy coherence *(118)*. In the United Republic of Tanzania, for example, local phenobarbital production ceased because imported products dominated public procurement.[3] In Ghana, the local association of pharmaceutical manufacturers reported that the low demand for phenobarbital made it financially and operationally unattractive and production was ceased.[4] Further challenges relating to infrastructure exist, including interruptions to electricity supplies and access to ports for export and import of goods, as well as challenges relating to regulators, regulatory frameworks and access to finance for enterprise *(117)*.

3 Based on reports from a WHO consultation workshop in the United Republic of Tanzania.

4 Based on reports from a WHO consultation workshop in Ghana.

While local manufacturing may not be feasible due to the issues outlined, regional manufacturing has been shown to have benefits. For instance, several programmes have been initiated in Africa to enhance local pharmaceutical production and increase access to essential medicines *(118)*. These include the African Union's Pharmaceutical Manufacturing Plan for Africa which aims to strengthen Africa's ability to produce high-quality, affordable pharmaceuticals across all essential medicines, while the African Medicines Agency and the African Continental Free Trade Area offer of opportunities to promote a single market for the continent. Another example is the second East African Community Regional Pharmaceutical Manufacturing Plan of Action 2017–2027 which was developed to serve as a blueprint for the pharmaceutical sector. It is important that essential medicines are prioritized by such initiatives *(119)*. However, local and regional production has not always led to lower prices and better availability, and its incentivization should be accompanied by appropriate policies to protect local manufacture, sustained demand and a guarantee of sustainable low prices *(120)*.

3.7.4 Quality of medicines and pharmacovigilance

Quality of medicines and pharmacovigilance: summary

The compromised quality of medicines in circulation, including substandard and falsified medicines, and inadequate capacity to monitor the safety of medicines, can result in challenges in accessing quality-assured and safe medicines for neurological disorders. Substandard and falsified medicines are more likely to reach patients where there is constrained access to quality and safe medicines, with poor governance and weak technical capacity. Furthermore, issues of storage and environmental factors can also contribute to the ineffectiveness of medicines and the risk of harm. WHO estimates that about 10% of medicines circulating globally are substandard or falsified. For example, substandard antiseizure medicines resulting from exposure to environmental variables have been identified in countries across the African and South-East Asia regions.

It is crucial to build capacity in pharmacovigilance in order to ensure the safe and effective use of medicines, and to monitor the safety of medicines indicated for neurological disorders – particularly in regions with diverse population profiles and high comorbidity rates with potential for polypharmacy. By monitoring safety profiles, adverse events can be identified promptly and risk minimization measures can be put in place to ensure that medicines are used optimally, thus increasing patient compliance and preventing unnecessary restrictions on use or removal of a product from the market.

Substandard and falsified medicines

The complex web that characterizes the global production and distribution of pharmaceutical products, including a long and convoluted supply chain, places all countries at risk of substandard and falsified products *(23)*. Substandard (or out-of-specification) medicines are authorized medical products that fail to meet either their quality standards or specifications, or both *(121)*. Falsified medical products deliberately and/or fraudulently misrepresent their identity, composition or source. Substandard and falsified medical products are most likely to reach patients in situations where there is constrained access to quality and safe medicines, poor governance and weak technical capacity, and are considered a public health threat *(122, 123)*.

Exposure to environmental variables is a common cause of substandard medicines, as well as suboptimal active ingredient content. A study from 2018 investigating the quality of antiseizure medicines in Gabon, Kenya and Madagascar identified that 32.3% of medicines were of poor quality as a result of inadequate storage and exposure to environmental factors *(124)*. The highest proportions of substandard medicines were seen in carbamazepine and phenytoin batches and were more common in public facilities. Other studies have identified proportions of poor-quality medicines ranging from 13.7% in Mauritania (regarding phenobarbital) in 2005 *(125)*, to 15% in Lao PDR in 2020 (phenobarbital 100mg) *(63)*, to 23.9% in Cambodia in 2021 (across several antiseizure medicines) *(81)* and to 65% in Viet Nam in 2008 (for several antiseizure medicines) *(126)*.

WHO provides guidance for storing pharmaceutical products in tropical areas, where environmental factors (e.g. temperature and humidity) *(127)* can lead to ineffective, substandard and potentially harmful medicines if they are stored inappropriately *(124)*. An analysis from 2018 of an opportunistic sample of paracetamol tablets from 13 countries identified that 12% of the samples examined were substandard *(128)*, in line with the WHO estimate of 10% of medicines worldwide being either substandard or falsified (with higher rates in LMICs). Estimates from the African Region indicate that up to 18.7% of medicines are substandard or falsified *(129)*. In Iraq, a 2021 study identified that 10% of medicines for the nervous system were substandard and/or falsified *(130)*.

Falsified (often referred to as counterfeit) medicines are designed to mimic real medicines but do not comply with intellectual property rights, and manufacturers are generally unknown. Falsified medicines can be difficult to detect; however, they will often fail to treat properly the disease or condition for which they were intended and can lead to serious health consequences, including death. Concerns about counterfeit or falsified antiseizure medicines have previously been reported in Guinea-Bissau and Nigeria *(131)*. In this instance, phenobarbital concentrations were either undetectable or extremely low, while tablets were brittle and varied in weight. Falsified antiseizure medicines are detrimental because a loss of seizure control can be life-threatening, withdrawal symptoms can be severe, and ineffective medicines can contribute to a lack of confidence in health-care systems and treatment adherence, further worsening the treatment gap *(131)*. In addition, the COVID-19 pandemic exacerbated the increase in circulation of falsified medicines, with some groups taking advantage of high market demands for medicines (including painkillers) *(132)*.

Quality of generic medicines

Generic and biosimilar medications must demonstrate bioequivalence to brand products using well-documented standards. The use of high-quality generics and biosimilars is crucial to improving affordability and decreasing the treatment gap for neurological disorders. However, despite the availability of several high-quality and effective formulations in the market, certain research findings suggest that

this does not uniformly hold true. A systematic review found that a high proportion of doctors, pharmacists and lay people have negative perceptions of generics *(133)*. A survey by the ILAE Task Force on Generic Substitution (predominantly involving respondents from the European, South-East Asia and Western Pacific regions) identified reports of adverse outcomes such as increased occurrence of seizures with use of generic substitutions (including carbamazepine, lamotrigine and valproic acid), as well as mistrust concerning regulatory control and quality *(134)*. In Germany, concerns related to the content of active substances and composition and amount of impurities in generic levodopa/benserazide were found in tested pharmacy samples, raising concerns for patient safety *(135)*.

Pharmacovigilance

To ensure continued accessibility of neurological medicines for those who need them, it is essential to prioritize their safe usage. Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem *(136)*. All medicines undergo rigorous testing for safety and efficacy through clinical trials. However, certain side-effects and adverse and/or rare events may emerge only once these products have been used by a larger heterogenous population, including people with other concurrent diseases, or with unknown conditions and over a long period of time *(136)*.

A number of antiseizure medicines have been associated with adverse events, drug interactions, complex pharmacokinetics, including teratogenicity (phenytoin and valproic acid) (Box 10) or serious cutaneous reactions (carbamazepine and lamotrigine) *(137)*. For Parkinson disease, dopamine agonists also cause adverse events associated with syncope, obsessive-compulsive behaviours, somnolence and psychosis *(138)*.

To ensure the safe and effective use of medicines, the establishment of robust systems for reporting undesired side-effects, known as "adverse events", is crucial. Pharmacovigilance should involve proactive risk monitoring as opposed to spontaneous reporting. However, this requires strong regulatory systems. Pharmacovigilance reporting should also be coupled with minimization measures to ensure that medicines are used optimally and that adverse events are managed appropriately, preventing harm and unnecessary restrictions on the use of medicines. The WHO Programme for International Drug Monitoring and associated tools (Box 11) supports countries in storing, monitoring and sharing essential information associated with adverse effects.

BOX 10.

Safety of the use of valproic acid (sodium valproate) for women and girls of childbearing potential

Valproic acid (sodium valproate) is a first-generation antiseizure medicine that is widely used for the treatment of epilepsy. However, evidence of teratogenic effects on the fetus of childbearing potential have grown in recent years. In updated mhGAP guidelines, WHO issued the following recommendation associated with its use.

Valproic acid (sodium valproate) should not be prescribed to women and girls of childbearing potential because of the high risk of birth defects and developmental disorders in children exposed to valproic acid (sodium valproate) in the womb. In women and girls of childbearing potential, lamotrigine or levetiracetam should be offered as first-line monotherapy for both generalized onset seizures and focal onset seizures.

The guideline also addresses the issue of women and girls of childbearing potential currently being prescribed the medication. Advice should be provided on the use of effective contraception, without interruption, for the duration of treatment. Women should be informed to consult physicians when planning pregnancy and particularly in case of pregnancy. Every effort should be made to switch to appropriate alternative treatment prior to conception. If switching is not possible, women should receive further counselling regarding the risks of valproic acid (sodium valproate) for the unborn child to support informed decision-making.

Increasing awareness of safety concerns associated with valproic acid (sodium valproate) among health-care workers and the wider population will support the effective implementation of the safety recommendations described above. Likewise, a robust pharmacovigilance system can support the prevention and monitoring of adverse effects, which is crucial to ensure the safety of, and assistance to, the population and to ensure the availability of essential medicines in the market for those who need them.

BOX 11.

WHO’s action on international drug monitoring

The WHO Programme for International Drug Monitoring consists of 179 Member States or territories, 156 of which share reports of adverse events associated with medicinal products (i.e. medicines and vaccines) with VigiBase – the WHO global database of Individual Case Safety Reports. Data in VigiBase are stored in a structured and comprehensive way in accordance with international standards. Pooled data from all contributing countries enables the rapid detection of potential safety signals at global or regional levels. The WHO Collaborating Centre for International Drug Monitoring (the Uppsala Monitoring Centre) has developed user-friendly tools to support data collection, management, analysis and interpretation. It is important that safety monitoring activities should be documented and monitored for all medicines for neurological disorders.

Photo credit (next page): Elderly women outside a local health centre in Hoa Binh City, Viet Nam, 2018. © WHO / Sebastian Liste

4

Additional neurological disorders

4. Additional neurological disorders

4.1 Headache disorders

According to GBD 2021, more than three billion people worldwide live with headache disorders (including migraine and tension-type) *(2)*. The availability of medicines for headache disorders differs across countries and regions; however, common medications for acute treatment (e.g. aspirin, ibuprofen, paracetamol) are generally available, inexpensive and cost-effective across regions *(77, 78, 80, 92, 93)*. The WHO Neurology atlas identified consistent global availability of at least one medication for headache disorders at PHC level (92% of countries) and hospital level (94% of countries) *(69)*, yet the treatment gap for headache disorders remains.

LMICs in particular are reported to have fewer pharmacological options for headache disorder management compared to HICs *(139)*. Triptans and medicines for prophylaxis (amitriptyline), for instance, are less available than common analgesics. A better representation of medicines for headache disorders and migraine is needed across WHO EML, national EMLs and standard treatment guidelines, given that response to treatment varies substantially among individuals. For example, while more options for acute treatment and prevention exist and should be considered, no medicines for cluster headache, an extremely debilitating condition, are currently included in the WHO EML. Further, many people with headache disorders globally are not evaluated in medical systems and, therefore, are not likely to benefit from appropriate pharmacological treatment *(139)*.

4.2 Multiple sclerosis

According to GBD 2021, almost two million people across the world live with multiple sclerosis *(2)*. However, the availability and cost of multiple sclerosis medication – disease-modifying therapies (DMTs) – are barriers to access in many countries *(101, 140)*. For instance, licensed DMTs were available in 30% of LICs, in 70% of lower-middle income countries, 97% of upper-middle income countries and 100% of HICs according to the 2021 Multiple sclerosis atlas *(140)*. In the Region of the Americas, studies from Latin America reported that more than 65% of persons with multiple sclerosis (as high as 90% in Dominican Republic) had challenges accessing medication, despite the medicines being approved by local regulatory agencies

> "I was left in a situation of being newly diagnosed, scared and with the prospect that I didn't have health coverage."
>
> **Person with multiple sclerosis, Argentina**

Man and woman leaving the Taytawasi Senior Center in Villa Maria del Triunfo after receiving medical care, Peru, 2018. © WHO / Sebastian Liste

(141, 142). Challenges with availability have also been reported in the Eastern Mediterranean *(143)* and South-East Asia *(144)* regions.

In terms of affordability, barriers in HICs relate to the costs to the government, health-care system or insurance provider, with out-of-pocket spending common even if medicines are subsidized by health insurance schemes *(145, 146)*. The costs of DMTs have risen dramatically over the past two decades *(147)*. In LMICs, barriers relate to the cost to individuals as out-of-pocket payments are not a viable option due to high prices. Additionally, many individuals cannot afford health insurance and, even when they can, there is often a lack of coverage for specific medicines by health insurance providers, which hampers access for most of the population in need *(141, 144, 148)*. Multiple sclerosis places a huge economic burden on health-care systems and societies in these countries *(149)*. Further data on the availability and affordability of DMTs are required in order to build a detailed picture of the global situation.

4.3 Stroke

Stroke is the leading cause of DALYs of all neurological disorders reported by the GBD 2021 study *(2)*. Hypertension is a major risk factor for stroke, which can be mitigated by the use of antihypertensives. Warfarin is a commonly-used anticoagulant that is included on the EML for stroke prevention in the context of atrial fibrillation. However, the WHO Neurology atlas identified that warfarin is always available in just 32% (36/114) of countries at the PHC level *(69)*. In the African and South-East Asia regions warfarin is always available in just 10% and 11% of countries, respectively. Stark differences are seen across income groups, with only one LIC having the medicine always available, compared to 73% of HICs. Warfarin has also been reported to be unaffordable – in Uganda, warfarin cost 3.2 days' wages of the LPGW for one month's supply in 2017 *(150)*.

Acetylsalicylic acid is an anti-platelet agent used in secondary prevention of stroke. Data from the Prospective Urban Rural Epidemiology (PURE) study, which explored the availability and affordability of cardiovascular medicines across 18 countries and involved data from 94 919 households across those countries *(151)*, found that acetylsalicylic acid was consistently available across income groups, with slight disparities between urban and rural communities. In Cameroon, a study found the availability of acetylsalicylic acid ranging from 47.6% in rural facilities to 82.4% in urban facilities *(152)*. Analysis of PURE data also highlights challenges with affordability – 60% of households in the LICs that were included would find the medicines needed to prevent cardiovascular disease unaffordable.

Photo credit (next page): Children receiving their medicines at Eles Primary School in Nguna Island, Vanuatu, 2016. © WHO / Yoshi Shimizu

5

Special considerations

5. Special considerations

The lack of access to medicines can be exacerbated by unique and complex situations. There are specific contexts that may have an impact on access (emergency contexts), to specific gaps within populations with neurological disorders (paediatrics) and to specific regulations and legislation that create barriers to access (controlled medicines).

5.1 Access to medicines in emergency contexts

Emergency situations – including pandemics, conflicts, forced displacements and natural disasters – can result in major disruptions to health-care systems, resulting in challenges with the overall accessibility, including the availability and affordability of medicines (Box 12). These disruptions tend mainly to affect vulnerable populations.

BOX 12.

The impact of COVID-19 on essential health services: WHO's pulse survey

The COVID-19 pandemic disrupted health-care services globally, with access to care and support for people with neurological conditions significantly affected *(153–156)*, particularly in resource-poor countries. The WHO pulse survey tracked the continuity of essential health services during the COVID-19 pandemic (2020–2023) *(157–160)*. The four rounds of the survey highlight the persistent disruption to essential health services seen across countries, including community services, PHC, specialist outpatient services and supply chains. The surveys report the "unavailability/stock-out of essential medicines" as a marker of service disruption and a common challenge faced by countries.

The COVID-19 pandemic compounded the challenges that people with neurological disorders in many regions face in accessing medicines – particularly the lack of insurance coverage *(155)*. A survey from 2020 exploring the impact of COVID-19 on access to medicines for Parkinson disease identified challenges across sub-Saharan Africa (80% of respondents), Central America (77% of respondents), and South America (64% of respondents) *(161)*. Similar disruptions were experienced in India for people with epilepsy, who reported difficulties in accessing antiseizure medications due to lockdown restrictions, lack of transport, out-of-date prescriptions, unavailability of medicines in pharmacies, and the closure of pharmacies *(162)*. Furthermore, 50% of individuals identified challenges with paying for medicines due to the widespread loss of jobs during lockdowns. Medicine prices for epilepsy were shown to increase in Azerbaijan and Georgia over the course of the COVID-19 pandemic from 2019 to 2021 *(163)*. In a survey involving 360 neurologists from 52 countries assessing the impact of COVID-19 on multiple sclerosis management, 45% of respondents indicated that the treatment of multiple sclerosis relapses had changed during the pandemic *(164)*. A study based in the United Kingdom of Great Britain and Northern Ireland identified reductions of 13% in the prescription of DMTs for multiple sclerosis in 2020 *(165)*. The COVID-19 pandemic resulted in unprecedented challenges in access to essential medicines, increasing the urgency of ensuring consistent equitable access through health systems that are resilient to emergencies *(166)*.

War, conflict, humanitarian crises and international sanctions can limit or negate access to medicines *(167, 168)*. However, the epidemiology of neurological disorders in humanitarian crises, and the treatment needs of persons in such situations, are not well understood *(169–171)*. Challenges in accessing essential medicines have also been reported in countries and territories affected by armed conflicts *(172–174)*, and among refugee and migrant populations across the world *(175)*. Epilepsy is the most common neurological disorder among forcibly displaced people in refugee camps globally *(176)* – in 2011 alone, epilepsy accounted for 91% of all neurological diseases in the webHIS[5] of the United Nations High Commissioner for Refugees *(177)*. However, a study exploring the availability of medicines in the context of conflict in Yemen, for example, found that antiseizure medicines were available in just 7% (2/30) of health-care facilities *(174)*. Access to DMTs for multiple sclerosis is also problematic in countries with ongoing conflicts, with delays to drug approvals, high costs and limited reimbursement presenting as challenges *(178)*. A study involving Syrian and Palestinian refugees with multiple sclerosis in Lebanon identified limited access to therapies posing challenges to disease management *(178)*. These groups should not be excluded from efforts to improve access to timely, necessary and affordable medicines for neurological disorders.

Natural disasters, including earthquakes, tsunamis and hurricanes, can also have a significant impact on health-care systems. A survey from Japan after the Great East Japan Earthquake of 2011 found that people with epilepsy experienced shortages of medicines, while some were forced to stop taking their medication as a result *(179)*. In 2021, a series of winter storms in Canada, northern Mexico and the USA resulted in power outages and severe disruptions to supply chains. A survey investigating the impact of these storms on children with epilepsy in Texas identified difficulties in obtaining medication refills, with some children running out of medicine. Evacuations from natural disasters can also result in loss of medicines and medical records or prescriptions, showing the need

5 HIS = Health Information System.

for field clinics or emergency hospitals where appropriate medicines can be sourced post-disaster *(180)*. Climate change is regarded as one of the main causes of increases in the frequency and severity of adverse weather events and environmental disasters, with lower-income and minority communities disproportionately impacted by such events *(181)*. It is therefore vital that health-care systems have the resilience to deal with climate disasters in the future by adopting climate policies and emergency responses that ensure minimal disruption to access to medicines. To support countries facing challenging situations, the WHO and other organizations have collaboratively developed emergency health kits. These kits address priority health needs, including access to essential medicines (Box 13).

BOX 13.

Interagency Emergency Health Kit and WHO Mental Health Kit

Interagency Emergency Health Kit (IEHK)

The IEHK is designed principally to meet the priority health needs of a population affected by emergencies and who have limited access to routine health-care services. The kit is designed primarily for "life-saving" purposes, not for health conditions requiring continued care. Given its use in emergency situations, the IEHK fills immediate medical gaps; it does not aim to replace existing medical supply chain mechanisms. The kit contains essential drugs, supplies and equipment, including medicines for neurological disorders, to be used for a limited period of time and targeting a defined number of people.

WHO Mental Health Kit (MHK)

WHO has developed the MHK which contains essential medicines and is designed to treat selected mental health and neurological conditions. The MHK, which can be ordered by countries, targets outpatient care in PHC settings and at hospital level following WHO's *mhGAP Humanitarian Intervention Guide (2015)*, the *mhGAP Intervention Guide 2.0 (2016)* and WHO's guidelines as described in the mhGAP Evidence Resource Centre. The MHK includes medicines such as biperiden, carbamazepine, phenytoin and valproic acid (sodium valproate) for neurological disorders. The MHK is intended to treat 10 000 people for three months and addresses supply chain disruptions while requiring adequate health system capacity to dispense its contents.

5.2 Access to paediatric medicines and formulations

Child-appropriate medicines are essential for the safe and effective treatment of children. In 2007, WHO published the first EMLc to provide guidance on the selection and use of medicines for children aged 0–12 years, particularly in LMICs, and to support the Sustainable Development Goals (SDGs) targets for the health of women and children. However, few countries have specific EMLs for children, while many national EMLs include only adult doses, creating access challenges for children. Limited availability of affordable essential medicines for children contributes to child mortality. Recent data suggest that more than 50 countries worldwide will fail to meet the targets of SDG 3.2 to end preventable deaths of children by 2030 *(182)*. Improving access to essential medicines is a priority for addressing this devastating situation *(183)*. Among chronic neurological disorders, this impact is felt most with epilepsy, which affects up to 1% of children. Data from the GBD 2021 study show that epilepsy ranks sixth in terms of DALYs across all neurological conditions for children under 5 years, and third for those aged 5–19 years *(2)*.

Due to differences in absorption, metabolism and clearance of the required dosing, medicines for children need adjustment to achieve the desired target exposure *(184)*. These medicines and preparations should also be easy to administer, safe for children and accepted by children. Therefore, child-appropriate formulations (e.g. dispersible, chewable) are often required in order to deliver optimal treatment but are rarely widely available. There is also a large gap in data needed to monitor access to these medicines for children adequately. Research efforts have traditionally focused on

> "Without pediatric friendly formulations to treat children with epilepsy, appropriate titration is difficult and the only options for dosing can have high risk of side effects, including in some instances being dangerously sedating."
>
> **Neurologist, United States of America**

measuring access to medicines for the general population without specific consideration of paediatric formulations. Deficiencies in the available data need to be addressed to implement appropriate interventions for improving access for this vulnerable population *(184)*. An adapted SDG indicator methodology has been developed to measure access to medicines for children, with suggestions for a child-specific indicator to be considered in the Global Indicator Framework for tracking SDG progress *(183)*. Box 14 describes a novel effort to increase access to paediatric medicines.

Challenges relating to the availability of paediatric strengths and formulations of antiseizure medicines emerge in studies, for instance from Lao PDR, where <1% of facilities surveyed were stocking appropriate medicines *(63)*. In this case, parents manipulated adult dosage forms and split tablets, with the risk that halving the tablet may not systematically result in equal shares of active ingredient, thus potentially resulting in altered absorption with suboptimal drug exposure. An analysis from Pakistan noted a shortage of registered paediatric antiseizure formulations which created challenges with regard to availability *(62)*. In India, paediatric formulations for epilepsy medications (phenytoin syrups) were shown to be available in just two of 29 public-sector outlets (6.9%) and four of eight (50%) private outlets *(83)*. It is vital that access to appropriate medication is facilitated across the life course, with particular care to include paediatric formulations when addressing access to medicines for neurological disorders.

BOX 14.

Enabling greater access to paediatric medicines through the GAP-f network

The Global Accelerator for Paediatric Formulations Network (GAP-f) is a coordinated response to the global lack of access to appropriate paediatric medicines that was conceived following the resolution at the Sixty-ninth World Health Assembly on promoting innovation and access to quality, safe, efficacious and affordable medicines for children. The vision of GAP-f is that all children have equitable access to the medicines they need. Recent work led by GAP-f and partners consulted experts and front-line health-care providers to explore gaps in medicine formulations for children *(185)*. A lack of paediatric forms of phenobarbital and valproic acid were reported, despite being available in many countries as adult formulations. Additional challenges with phenobarbital and valproic acid for use in children included lack of in-country marketing, shortages, lack of inclusion in the drug formulary, and physicians' difficulties when using the medicines. Concerns about valproic acid also related to the wide range of doses across age–weight bands, lack of safety data, requirements for therapeutic drug monitoring, and frequent dosing errors. In view of these challenges, antiseizure medicines are being considered for future paediatric drug optimization (PADO) processes *(186)* which WHO undertakes to gain greater clarity on the most needed priority formulations in each therapeutic area.

5.3 Regulation of controlled medicines

Controlled medicines are medicines for which distribution and use are regulated under international drug conventions or national drug-control law *(187)*. These medicines, if used in accordance with medical guidelines, are essential for the provision of adequate medical care. Rational use of internationally controlled essential medicines – i.e. medicines listed in the schedules of international drug control treaties and contained in the WHO EML – is essential for optimal health outcomes based on scientific evidence *(188)*. However, the use of such medicines for non-medical purposes can lead to addiction and dependence, thus necessitating regulation of the use of such substances to promote and protect public health *(189)*. Despite this, the inaccessibility of controlled essential medicines in low-resource contexts has been described as a human rights concern *(190, 191)*.

Several antiseizure medicines are classified as controlled medicines, including barbiturates (phenobarbital) and benzodiazepines (e.g. lorazepam, midazolam, diazepam) due to their risk of misuse *(192)*. The use of such medicines and their applications are recognized in international drug conventions which outline that States are obliged to make adequate provision to ensure the availability of controlled medicines for medical and scientific purposes *(187)*. There are significant concerns regarding the consumption and accessibility of these substances, while levels of consumption of psychotropic substances for the treatment of neurological disorders vary widely between countries and regions *(191)*. Insufficient or inadequate access to psychotropic substances seems to be particularly pronounced in LMICs. WHO considers that a balanced public health approach requires access to controlled medicines for scientifically sound clinical use to be maximized and that diversion to non-medical use should be minimized *(188)*. Supply chain management is particularly important to ensure appropriate forecasting and procurement of adequate supplies of these medicines.

Regulations on controlled medicines should enhance the safety of their use while improving accessibility for persons who need these life-saving medicines. Regulations should not preclude access. However, the status of controlled medicines contributes to challenges in accessibility owing to international drug-control frameworks that relate to international and domestic trade and distribution control measures *(190)*. Additional challenges relating to controlled medicines include challenges with perceptions and fear of addiction, limited education on rational use for health-care professionals, fear of criminal sanctions and lack of legal frameworks for use *(187, 190, 193)*. The restriction of sales of psychotropics to pharmacies with special licences has created further access challenges in Tajikistan *(92)*. In Zambia, complex administration and documentation procedures required of pharmacists in order to fulfil regulatory requirements on handling phenobarbital have been shown to impede access *(194)*. Implementation of the WHO *mhGAP Intervention Guide* could provide appropriate training on prescribing and could reduce the risk that controlled substances are handled inappropriately. Box 15 summarizes the approach by the United Nations Office on Drugs and Crime (UNODC) to improve access to controlled medicines.

BOX 15.

The role of the United Nations Office on Drugs and Crime in improving access to controlled medicines

UNODC provides technical guidance on increasing access to, and availability of, controlled medicines, and proposes three core areas that need to be addressed, as well as five cross-cutting themes *(188)*. The core areas are systems strengthening and integration, education and awareness, and supply chain management. The cross-cutting themes are: economic structure, consistent messaging, patient-centred care, prevention of diversion and non-medical use, and availability of data and research. A coordinated, multisectoral response is required to ensure a consistent momentum that results in a positive impact on patients with medical needs receiving the medication and treatment interventions that are appropriate for their care.

Photo credit (next page): Mother and child receiving medical care from a clinical officer at Manushi Dispensary in Moshi, United Republic of Tanzania, 2023. © WHO / Mwesuwa Ramsey

6

Country spotlight on improving access to medicines for epilepsy and Parkinson disease

6. Country spotlight on improving access to medicines for epilepsy and Parkinson disease

WHO works closely with Member States to support the implementation of IGAP. Two examples of these activities in Ghana and the United Republic of Tanzania are described below. Both aimed to support the countries in improving access to medicines for neurological disorders.

6.1 Improving the selection and use of medicines for epilepsy and Parkinson disease in Ghana

WHO and the Ministry of Health of Ghana convened a workshop in September 2022 with local stakeholders, including government representatives, health service providers, representatives from civil society and people with lived experience. The aims of the workshop were twofold, namely:

1. to discuss issues related to access to essential medicines in Ghana, focusing on medicines for people with neurological disorders, particularly epilepsy and Parkinson disease; and
2. to investigate the status of access to medicines for neurological disorders in Ghana, including potential challenges, design actions with realistic timelines, identification of the stakeholders responsible for taking actions, and how to monitor these actions.

Several barriers to access to medicines for epilepsy and Parkinson disease were identified. These included:

- stigma associated with epilepsy and Parkinson disease;
- several medicines for epilepsy and Parkinson disease were not listed in Ghana's national EML and standard treatment guidelines;
- lack of coverage of medicines for Parkinson disease in national insurance schemes, thus leading to high out-of-pocket spending;
- lack of data across the supply chain and the health system;
- frequent stock-outs of medicines for epilepsy and Parkinson disease; and
- lack of continuous and sizeable demand to enable local production of medicines for epilepsy and Parkinson disease.

National researchers also highlighted new and unpublished data on the availability and pricing of medicines for epilepsy and Parkinson disease in the country. For example, in 180 pharmacies surveyed in urban (n = 157) and rural (n = 27) areas of Ghana, the availability of carbamazepine (100% in urban and 20% in rural areas), levetiracetam (50% in urban and 0% in rural areas), phenobarbital (55% in urban and 34% in rural areas) and sodium valproate (97% in urban and 0% in rural areas) varied drastically, with much lower availability seen in rural areas.

In another survey, levodopa/carbidopa was available in only 5% of public and 13% of private facilities (hospitals and pharmacies), with prices ranging from US$ 29 to US$ 64 for a 30-day supply.

With a comprehensive understanding of the local challenges, several actions were proposed to address the above barriers. Since the consultation, WHO and local partners have been working together and several advances have already been made. For example, two strengths of levodopa/carbidopa have been included in the ongoing update of Ghana's national EML, and clinical guidance for its use, as well as for antiseizure medicines have been added to the country's standard treatment guidelines. Additionally, over 20 medicines for neurological disorders have been included in an ongoing MedMon survey to assess the availability, affordability and stock-outs of medicines. This will support efforts to improve the availability of data and ongoing monitoring of interventions. Finally, WHO is working with local partners to organize awareness campaigns to improve society's knowledge about epilepsy and Parkinson disease and reduce stigma attached to these conditions

6.2 Towards improvement of access to medicines for neurological disorders in the United Republic of Tanzania

WHO and the Ministry of Health of the United Republic of Tanzania are working together to address the issue of access to medicines to neurological disorders, using epilepsy and Parkinson disease as tracer conditions.

In May 2023, a two-day workshop was organized in Dar es Salaam on the implementation of IGAP and access to neurological medicines in the country. Participants included representatives from various government sectors, people with lived experience, health-care providers and civil society representatives.

The three objectives of the workshop were:

1. to bring together national stakeholders to improve awareness of IGAP and to identify avenues for its successful implementation in the country;
2. to promote epilepsy advocacy, drawing on opportunities provided by the Epilepsy Pathway Innovation in Africa (EPInA) project; and
3. to discuss issues related to access to essential medicines for neurological disorders in the country, focusing on medicines for epilepsy and Parkinson disease.

Several challenges were identified, namely:

- lack of public awareness, leading to stigma, discrimination and delayed diagnosis;
- knowledge gaps in the diagnosis and management of epilepsy and Parkinson disease among health-care providers, including lack of coordination of services;
- lack of sustained access to medicines, including frequent stock-outs;
- unaffordability of medicines with disparities in price across regions and public facilities;
- problems with the quality of medicines;
- financial hardship resulting from spending on treatment and care;
- complex supply chain systems (including procurement and distribution) with a lack of knowledge, experience and quality data to inform procurement, forecasting and budgeting;
- challenges with the registration of medicines, including high costs of registration and lack of information on the registration process;
- lack of insurance coverage and challenges with exemption policies that were not followed by health facilities; and
- lack of coverage of neurological disorders in the national NCD programme and policy.

Workshop participants proposed a range of actions to address the above barriers, to tackle challenges in registering essential medicines for neurological disorders, to resolve problems with supply chains, and to addressing awareness and stigma.

Portrait of a woman sitting in the Lodwar County Referral Hospital, Kenya, 2018. © WHO / NOOR / Sebastien Liste

In September 2023, WHO and Ministry of Health, convened a follow-up meeting in Moshi to continue the activities for IGAP implementation and to update participants on progress since the meeting in Dar es Salaam. Encouragingly, actions include: a proposal for the formation of a national committee on epilepsy and other neurological disorders; government procurement of medicines for neurological disorders, including for epilepsy and Parkinson disease; and ongoing activities to organize a survey to investigate the availability and affordability of neurological medicines.

As a consequence of the strong commitment from the United Republic of Tanzania's Ministry of Health, several neurological medicines are undergoing special procurement – including carbamazepine (tablets and syrup), lamotrigine, levetiracetam, levodopa/carbidopa, phenobarbital (tablets and injection), sodium valproate and trihexyphenidyl.

In a significant step towards improving access to medicines for neurological disorders, the National Health Insurance Fund package of 2024 (which was last updated in 2016) now includes several medicines for neurological disorders, including baclofen, donepezil, levetiracetam, levodopa/carbidopa, selegiline and additional preparations of lamotrigine and carbamazepine.

Photo credit (next page): Health workers part of the Eltomale Site Mobile Heath and Nutrition Team, Ethiopia, 2022. © WHO / Martha Tadesse

7

An approach to improve access to medicines for neurological disorders

7. An approach to improve access to medicines for neurological disorders

This landscape analysis identified several barriers and health system components that influence access to medicines for neurological disorders. Some of these barriers were found to affect access directly (e.g. lack of registration or marketing authorization of medicines), while other health system components have an impact on access to all medicines (e.g. issues associated with supply chains) and, consequently, medicines for neurological disorders are also affected. Both specific and broad health system actions are needed to address access to medicines, with input from a range of stakeholders.

Given the complexity of the components identified and the different challenges faced by countries, WHO, together with global experts, defined eight key action areas (Figure 11) that constitute a proposed approach to improve access to medicines for neurological disorders.

The approach uses epilepsy and Parkinson disease as tracer conditions, but it can also be used to drive better access to other neurological medicines. The following sections discuss these actions in greater detail.

FIGURE 11.
Approach to improve access to medicines for neurological medicines

Epilepsy and Parkinson disease as tracer conditions

7.1 Strengthen leadership

Strengthening leadership is key to improving access to medicines for neurological disorders. Actions should be multilevel and multisectoral. Strengthening leadership requires the convening of leaders across policy areas, health sectors, academia, the philanthropy sector, and people with lived experience of neurological disorders to advocate for improved diagnosis, treatment and care for these disorders. Strong leadership should be accompanied by good governance and the dedication of financial and human resources, and should generate political commitment and buy-in to take action towards the goals of IGAP.

Structured engagements and the formation of technical working groups that bring together experts and policy-makers will increase capacity and understanding and equip decision-makers with the knowledge to drive forward the neurological agenda and take the lead on actions. Working groups should involve coordination of interventions to facilitate continued access to medicines during humanitarian emergencies.

Strengthened advocacy and awareness campaigns can tackle stigma and empower global leaders to raise political will and drive the prioritization of neurological disorders. Advocacy should involve health literacy campaigns and the establishment of support groups for people with neurological disorders and their families. This, coupled with the promotion of education at all levels of the health system and with training of programme staff (see Section 7.1.6), will help address structural stigma.

Furthermore, investment cases for neurological disorders – both global and region/country-specific – should be developed to present an evidence-based argument for investing in the prevention and management of neurological disorders. This includes identifying the investment needed, estimating the global public benefits and the expected return on investment. The development of such investment cases will fill a significant gap in advocacy and provide an essential tool to foster the prioritization of neurological disorders, therefore facilitating access to medicines.

7.2 Promote appropriate selection and use of medicines

External stakeholders are encouraged to engage with the evidence-based application process for revising the WHO EML and EMLc, which are updated every two years on the basis of recommendations made by an independent WHO Expert Committee. Applications must present, inter alia, information on the public health relevance, evidence of efficacy and safety, comparative cost and cost-effectiveness of medicines being proposed for inclusion. For example, for the 2023 update an application was submitted by external stakeholders in collaboration with WHO's Brain Health unit that resulted in the inclusion of levetiracetam in the WHO EML and EMLc.

Further, updates to the WHO EML and EMLc should be accompanied by regular efforts in countries to translate changes into national EMLs. The lack of inclusion in national EMLs of essential medicines for epilepsy and Parkinson disease as listed on WHO's EML has been identified as an important barrier to access to these medicines. Countries are strongly encouraged to review and update their national EMLs periodically. However, where capacity is limited, countries should prioritize the inclusion of selected essential medicines on national EMLs and should work to establish adequate financing, training and procurement cycles to ensure that this core set of medicines is always available. Further, such efforts should always strive to meet the needs of special populations (e.g. inclusion of antiseizure medicines that are safe for use by women and girls of childbearing potential, as well as appropriate formulations for children).

Countries' standard treatment guidelines are based on global guideline recommendations, although they are not always available or updated. Therefore, concerted efforts should be made to develop new, and to update existing, clinical guidelines for neurological disorders on the basis of robust and emerging evidence, while ensuring appropriate implementation. Standard treatment guidelines are key to outlining clinical guidance on recommended treatment options and should be developed and updated in conjunction with national EMLs. Updating a country's standard treatment guidelines based on global guidance, with adaptation to the local context, will promote the appropriate prescribing and use of medicines, as well as facilitate training and standardization for procurement.

Actions to promote appropriate selection and use of medicines are important for LMICs and HICs. Updating of national EMLs and standard treatment guidelines is critical to achieving UHC as countries often use them as guides for priority-setting exercises associated with health benefit packages. Appropriate representation of essential medicines for neurological disorders in both national EMLs and standard treatment guidelines will support their addition and coverage in social benefit systems (see also Section 7.1.5).

7.3 Strengthen regulatory environments

Action is needed to develop robust and efficient regulatory systems. These are key to facilitating information-sharing, clarifying processes and procedures, promoting safety and driving better access to medicines. Countries are encouraged to facilitate appropriate registration/market authorization of essential medicines through NRAs to improve affordability, to ensure the quality and safety of medicines being purchased, and to reduce medication shortages and stock-outs. Registration is also key to overcoming barriers to international collaboration and collaborative procurement activities such as pooled procurement.

The lack of registration of neurological medicines evidenced in this report (see 3.3 Registration and market authorization) can be addressed by actions from different sectors. WHO's prequalification process can support countries in decreasing the burden on NRAs by relying on WHO's thorough evaluation to ensure that medicines are safe, appropriate and meet stringent quality standards. However, this needs to be met by an active interest from the pharmaceutical industry. Pharmaceutical manufacturers are therefore encouraged to actively submit an Expression of Interest for Product Evaluation (EoI) for prequalification when invited by WHO, as well as to apply for approval by NRAs. NRAs are also encouraged to prioritize and streamline processes to facilitate registration of essential medicines. For instance, establishing a maximum time to respond to applications associated with essential medicines will not only ensure the systematic prioritization of medicines considered as essential but is also likely to attract increased interest from manufacturers due to a streamlined and efficient process.

The large treatment gap highlighted in this report is clear evidence of a demand that needs to be addressed urgently. NRAs are encouraged to engage with a range of WHO activities and resources such as the CRP (see Box 6, Section 3.3) as well as to engage in reliance mechanisms. Such activities will help to build capacity, reduce duplication of efforts and foster collaboration to strengthen national regulatory systems.

Enhancing the impact of the CRP requires proactive steps from medicine manufacturers. Those routinely supplying medicines in LMICs should leverage the CRP either by registering their products with stringent regulatory agencies or by requesting WHO prequalification of their products. This approach will enable collaborative registration with NRAs through the CRP. Similarly, manufacturers frequently supplying neurological medicines in HICs often have their products registered with stringent agencies but may not extend their supply to LMICs. Encouragingly, these manufacturers can utilize the CRP to seek registration in LMICs and direct efforts towards improving supply in these areas. In addition to the CRP efforts, various regional initiatives are addressing registration challenges and are facilitating better access to medicines. Region-led initiatives, such as those spearheaded by the Africa CDC, African Medicines Agency, the East African Community, the ZaZiBoNa collaborative medicines registration procedure, and the Association of Southeast Asian Nations (ASEAN) joint assessment play pivotal roles in streamlining registration processes. Nevertheless, it is imperative that manufacturers take the lead by actively engaging with these initiatives to maximize their impact.

It is also important to strengthen regulatory authorities and pharmacovigilance services in order to ensure that formulations available in the market are of high quality and to restore trust in high-quality generic medicines. This will ensure that individuals are appropriately and effectively treated, the occurrence of adverse events is decreased and monitored, and that the availability of lower-cost options is increased, thereby making medicines more affordable (Section 3.4.2).

Additionally, to facilitate access during emergency situations, competent authorities should create special procedures to facilitate import and export of medicines, including controlled medicines, providing clear guidance to stakeholders on requirements and procedures, while following guidance established by the International Narcotics Control Board *(195)* where relevant.

Strengthening the regulatory environment will also require capacity-building of the workforce to carry out these actions (see Section 7.1.6).

Medical supplies being delivered to Ménaka, Mali, 2022. © WHO / Fatoumata Diabaté

7.4 Strengthen supply chain and procurement systems

Efficient supply chains require coordination at different levels of the health system and include activities such as forecasting the demand for neurological medicines and planning the procurement and distribution of medicines to facilities. This is only possible when the supply chain workforce is appropriately trained (see Section 7.1.6) and health systems data are available (see Section 7.1.7) to inform public health decisions.

It is essential to develop comprehensive standard operating procedures to institutionalize the efficient management of the supply chain, including aspects of transportation, storage, "first expire, first out method", inventory and waste management. Moreover, developing forecasting tools for neurological disorders will facilitate the estimation of future needs for medicines and will serve as an essential tool to ensure lower prices, sustainable availability of medicines, programme planning and scale-up.

Developing fair and sustainable pricing policies, as well as engaging in collaborative procurement systems such as pooled procurement, are also recommended to improve affordability, availability, efficiency of procurement, sustainability of supply and quality standards. WHO has provided guidance on pricing policies, for example, as outlined in *WHO guideline on country pharmaceutical pricing policies, second edition (196)* published in 2020, which includes conditional recommendations for pooled procurement *(197, 198)*. Pooled procurement refers to the formal arrangement whereby financial and nonfinancial resources are combined across various purchasing authorities to create a common mechanism for sourcing and purchasing medicines on behalf of individual purchasing entities *(196)*. Pooled procurement can result in price reductions by scaling up demand and increasing bargaining power, improving the efficiency of procurement methods, and improving availability, sustainability and quality standards *(197)*. It is essential that medicines for neurological disorders are routinely included in such efforts.

Action should also be taken to utilize tools developed by WHO to assess medicines supply management systems in countries. The Medicines Management Cycle *(113)* includes the main steps of effective management of medicines supply: selection, quantification and forecasting, procurement, storage, and distribution. A reliable health supply system will integrate supply management into health system development; develop an efficient mix of public–private partnerships; maintain medicine quality in distribution channels; and increase access to essential medicines. Another example of an important tool is the Supply Chain Maturity Model *(199)* developed by the United Nations Children's Fund (UNICEF) with support from WHO and other agencies. The tool can be used to measure the performance of key supply chain functions and to support countries to identify gaps in the supply chain, establish evidence-driven and government-owned strengthening plans, inform funding allocations and technical assistance schemes, and review the impact of the interventions deployed in a holistic and efficient manner.

Supply chains are also heavily affected by humanitarian emergencies. To improve emergency preparedness, it is crucial that essential medicines are maintained in buffer stocks, alongside revisions of estimates to ensure sufficient supply and to avoid stock-outs.

7.5 Improve financing for and affordability of neurological medicines

This report highlights multiple components that contribute to the poor financing for and lack of affordability of medicines for neurological disorders. Addressing these barriers will require concerted actions from a range of stakeholders. Direct engagement with government stakeholders is needed to support the inclusion of medicines for epilepsy and Parkinson disease in publicly funded benefit packages that promote equitable, sustainable and safe access to these medicines. Pricing policies implemented by countries should be fair, sustainable and transparent and set out in a way that is affordable for both health systems and patients, without creating unrealistic provisions that will hamper incentives for industry and without driving safe and high-quality medicines out of the market. Countries can refer to *WHO guideline on country pharmaceutical pricing policies, second edition (196)*, published in 2020, which was developed for use by policy-makers and decision-makers responsible for introducing and revising price management policies to improve access to medicines. The guidelines recommend overarching principles for formulating and implementing pricing policies, as well as specific recommendations that countries can use and adapt, alongside implementation considerations *(196)*.

A range of other measures to prevent high treatment costs and increase affordability for the public health system, as well as for individuals, should also be considered – e.g. the regulation of mark-ups in the pharmaceutical supply chain and the use of reference pricing; pooled procurement to increase purchasing power and efficiency; and promotion of, and building trust in, quality-assured generic medicines. Building trust would also require transparency from manufacturers on pricing, as stated in resolution WHA72.8 of the Seventy-second World Health Assembly on *Improving the transparency of markets for medicines, vaccines, and other health products (200)*.

Action should be taken to create limits on co-payments and/or to create or extend exemptions or reductions on taxes/charges for essential medicines which can significantly decrease the financial burden on individuals and families, especially for the poorest households and those affected by chronic neurological disorders. Successful strategies demonstrated in various countries also include mandating private insurances to cover essential medicines, as well as exemptions and caps based on family income and fixed co-payments, whereby the payment of low and consistent fees for medicines have the potential to limit financial family hardship.

Strengthening of the regulatory environment, including appropriate registration of medicines, will facilitate the procurement of medicines by government stores, which in turn has the potential to reduce the purchase price for both governments and households. Furthermore, efforts to implement streamlined and efficient processes across NRAs can enhance manufacturers' interest in entering these markets. This increased participation will result in a greater

supply of high-quality generic medicines and lower prices, driven by heightened competition (Box 16).

Incentivizing local and regional manufacturing is a beneficial strategy for driving better availability of medicines and significantly reducing costs. However, appropriate and sustained demand needs to be in place, as do policies that can protect local manufacturers – such as preferential treatment in government procurement, reduced tariffs and adequate mark-ups. Moreover, efforts should be made to ensure regular procurement of essential medicines in order to maintain the continuous production and availability of well-priced medicines in the market, which will facilitate better access.

BOX 16.

How to ensure fair and sustainable pricing of medicines

Action is needed to ensure that essential medicines for neurological disorders are available at a fair price – i.e. a price that strikes a balance between the public health needs for innovation and affordability while recognizing that sustainable production of quality health products comes at a cost *(201)*. Issues related to the fair pricing of medicines are framed by two extremes: prices so high they are unaffordable, and prices so low they drive high-quality manufacturers out of the market, leading to shortages *(23)*. Fair pricing models should ensure that essential medicines are available in sustainable quantities at prices that are affordable for patients, third-party payers and health system budgets.

International initiatives, including pooled procurement and licensing agreements, have been used to facilitate sustainable and affordable access to treatment for many noncommunicable and infectious diseases in LMICs *(202)*. Unfortunately, medicines for neurological conditions are rarely included in such initiatives. Tiered pricing agreements, whereby eligibility is defined according to global income classifications, are also used to enable affordable prices in LMICs; however, pricing agreements often omit middle-income countries and are often not sensitive to a country's burden of disease or levels of income inequality.

WHO released guidance on country pharmaceutical pricing policies in 2020 *(196)* including recommendations to facilitate affordable access to medicines. For instance, WHO strongly recommends the promotion and use of quality-assured generic and biosimilar medicines, with a view towards enabling early market entry of generics and biosimilars with supportive incentives and clinical education to facilitate uptake. Other conditional recommendations include: the use of internal and external reference pricing with regular price monitoring and revision; regulation of mark-ups in the pharmaceutical supply chain; tendering and price negotiation; exemptions or reductions of tax for essential medicines; promotion of price transparency; and use of health technology assessments to notify pricing and reimbursement decisions. Although many regions have mature pricing systems, lack of supporting frameworks and capacity in some regions can prevent the implementation of such pricing measures *(115, 196)*. Countries may need to choose, adapt and implement a combination of these interventions according to the context of their respective health systems.

7.6 Build health system workforce capacity

Building capacity across the entire health-care system is crucial to guarantee the appropriate prescription, accessibility and safe use of medicines by those who need them. Reducing the treatment gap and improving health outcomes requires that people living with neurological disorders have access to care at the PHC level and depends greatly on the availability of an appropriate neurological workforce (e.g. adult neurologists, child neurologists, neurosurgeons), as well as other health-care providers who are trained to identify and manage neurological disorders. Given the scarcity of the neurological workforce globally – and particularly in LMICs – sustained efforts should be made to empower the non-specialist workforce to diagnose and manage neurological disorders appropriately. This means developing tools for training, with clinical guidance for Parkinson disease and promoting its implementation in training activities alongside WHO's mhGAP module for epilepsy (Box 17).

In addition to PHC workers, there is a great need to scale up the specialized neurological workforce, particularly in public practice. Strengthening of the curricula and improving career prospects should be combined with adequate compensation and incentives to work in underserved areas. Comprehensive action in this area has the potential to decrease the "brain drain" that is often seen with this workforce and bring about positive outcomes in the long term. Other health-care professionals are also key to ensuring the safe and correct use of medicines for neurological disorders and appropriate training should be provided – for instance, community pharmacists are essential for providing the population with guidance on safety, adverse and side-effects and continuous management of disorders. They are also vital in decreasing misconceptions about generic medicines.

There is also a need to build the capacity of the supply chain workforce, the regulators and those working at point-of-care facilities, including pharmacists, technicians and other cadres. For example, well-trained supply chain managers can support the implementation and scale-up of forecasting capabilities (see Section 7.1.4). Regulators can ensure adherence to global standards from stringent regulatory agencies and can promote engagement through collaborative registration efforts (see 7.1.3). Countries are encouraged to enhance their pharmacovigilance capacity by engaging in specific training offered by WHO and its Programme for International Drug Monitoring *(203)*.

BOX 17.

The role of mhGAP in training the neurological workforce

Countries are encouraged to implement mhGAP in order to strengthen workforce capacity in non-specialist settings to deal with the growing burden of mental, neurological and substance use conditions and to narrow the treatment gap. Provision of training to non-specialists in PHC settings, particularly where the specialized neurological workforce is scarce, could significantly improve access to appropriate care, ultimately improving access to treatment (i.e. with a trained health workforce able to diagnose and to prescribe appropriately). The mhGAP guideline, or associated mhGAP derivative products (e.g. *mhGAP Intervention Guide*), include models of care for epilepsy, dementia and child and adolescent mental and behavioural disorders and have been used in more than 100 countries and have been translated into over 20 languages. Since 2018, 162 studies have reported use of mhGAP guidelines, providing evidence of positive effects on training, patient care, research and practice.

The third edition of the mhGAP guidelines, published in 2023, provides updated recommendations for psychotropic medicines based on current evidence. In the epilepsy module, the antiseizure medicines lamotrigine, levetiracetam and lacosamide, have been included for the first time. Intravenous levetiracetam and intravenous fosphenytoin have also been added for the treatment of established status epilepticus. The guidelines complement the inclusion of levetiracetam and intravenous levetiracetam on the WHO EML and EMLc which were updated in 2023.

7.7 Strengthen data and health information systems

The lack of data on neurological disorders and on medicines for neurological disorders across the health system needs to be addressed so that strategic decisions can be based on evidence. Action is needed: 1) to collect robust data on the burden of neurological disease through data-reporting systems and research (e.g. prevalence studies); 2) to disaggregate data from health facilities on diagnosis, treatment and numbers of persons with neurological disorders who are accessing care; 3) to collect data on the supply chain, including price, availability, quality, utilization and registration in order to inform procurement, distribution, forecasting and budgeting; and 4) to determine the return of investment in order to prioritize neurological disorders. Country-level surveys on the availability and affordability of medicines (e.g. using the WHO/HAI methodology, WHO MedMon tool etc.) should be conducted to support a holistic understanding of the status of access in countries, change in accessibility over time, and facilitate the monitoring of interventions aimed at improving access. The availability of robust data on neurological disorders is also a tool to generate political commitment and drive prioritization.

7.8 Encourage coordination, partnership and convening

The actions outlined here are not possible without coordination and partnership, with different stakeholders taking the lead on specific actions. Regular communication, information exchange and collaboration between stakeholders (including WHO experts and leaders, NGOs and patient communities, health ministries, regulators, health-care workers, researchers and the private sector) are essential for increasing the global prioritization of neurological disorders and operationalizing the activities described above to improve access to medicines for neurological disorders (Box 18). The creation of national committees for neurological disorders, such as the one proposed in the United Republic of Tanzania (see Case study 2), is a good example of country-level partnerships. Further, action should be taken to coordinate national plans, laws and education policies.

All activities should be carried out in consultation with persons with lived experience who are directly affected by, or experience first-hand, the many barriers to access. It is essential that these persons remain central to, and are directly involved in, all aspects of the activities. This engagement can be modelled on the *WHO framework for meaningful engagement of people living with noncommunicable diseases, and mental health and neurological conditions (204)*. Similarly, patient advocacy groups need to be equipped with the tools to engage with other stakeholders in order to be able to participate fully in partnerships.

BOX 18.

Aligning selection, registration and health financing

Improving access to medicines requires harmonization of national policies and coordination among national stakeholders. Many countries rely on their national EMLs to determine which medicines are procured, prescribed and included in UHC packages, publicly funded insurance schemes and reimbursement lists. This harmonization will also support appropriate budgeting and financing, ensuring that with a consistent, well-planned and coordinated selection of medicines, budgets can be allocated efficiently, minimizing unexpected expenditures and mismatches across the health system and providing clear insights into the overall costs involved. Countries' service delivery guidelines and procedures must also be aligned to ensure that such medicines are offered at the appropriate level of care (e.g. PHC level and/or specialized setting) and that staff have the appropriate training to prescribe them.

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