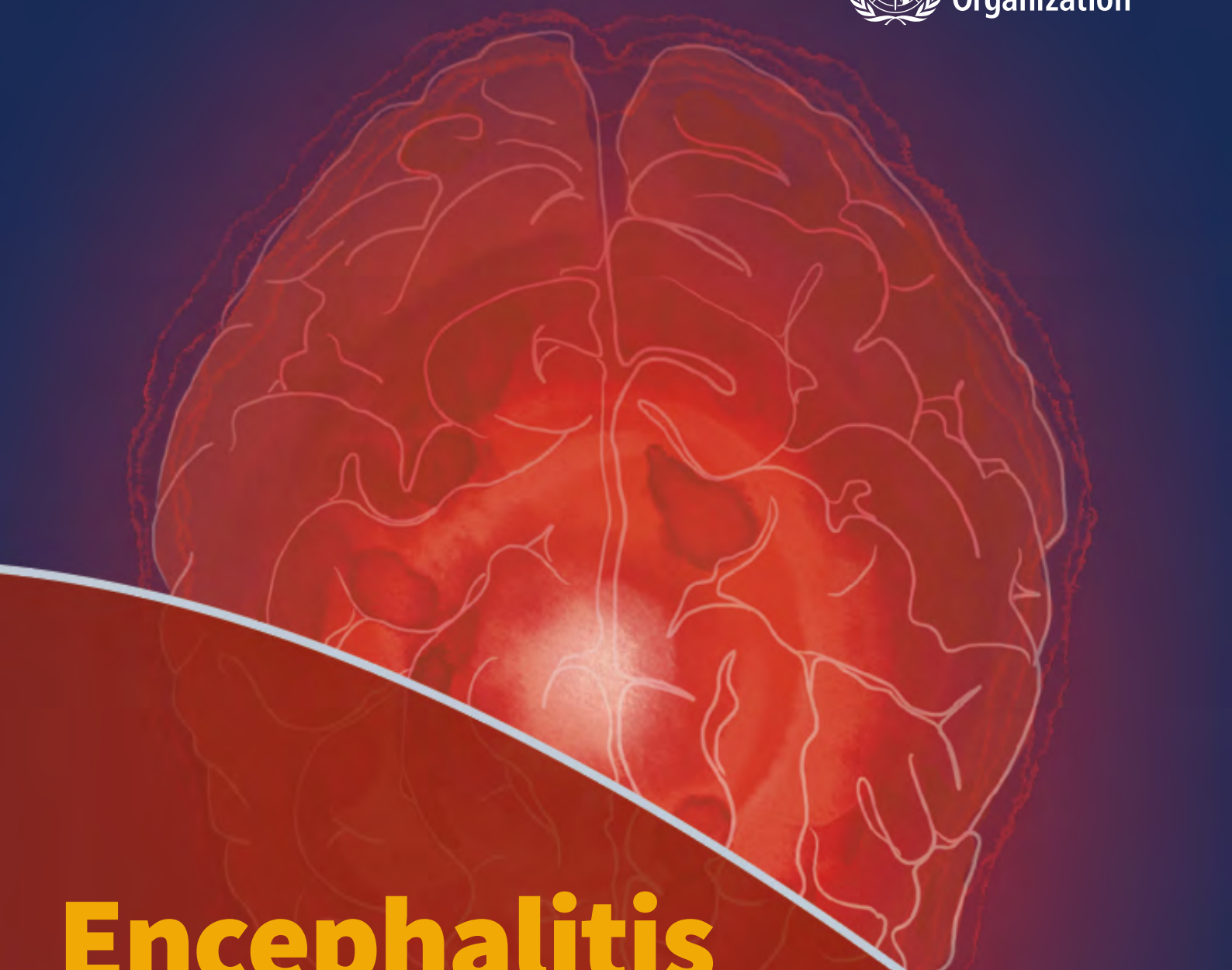
World Health Organization



Encephalitis

Global threats, trends and public health implications

Technical brief

World Health Organization

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A technical brief

Encephalitis: global threats, trends and public health implications. A technical brief

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Contents

Abbreviations and acronyms

CNS	central nervous system
CSF	cerebrospinal fluid
DALY	disability-adjusted life year
EEG	electroencephalography
EML	essential medicines list
HIC	high-income countries
HIV	human immunodeficiency virus
HSV	herpes simplex virus
IGAP	Intersectoral global action plan on epilepsy and other neurological disorders
IV	intravenous
JE	Japanese encephalitis
JEV	Japanese encephalitis virus
LIC	low-income countries
LMIC	low- and middle-income countries
MRI	magnetic resonance imaging
NGO	nongovernmental organization
RCT	randomized controlled trial
PHC	primary health care
TBE	tick-borne encephalitis
UHC	universal health coverage
VZV	varicella-zoster virus
WHO	World Health Organization

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Vision and conceptualization

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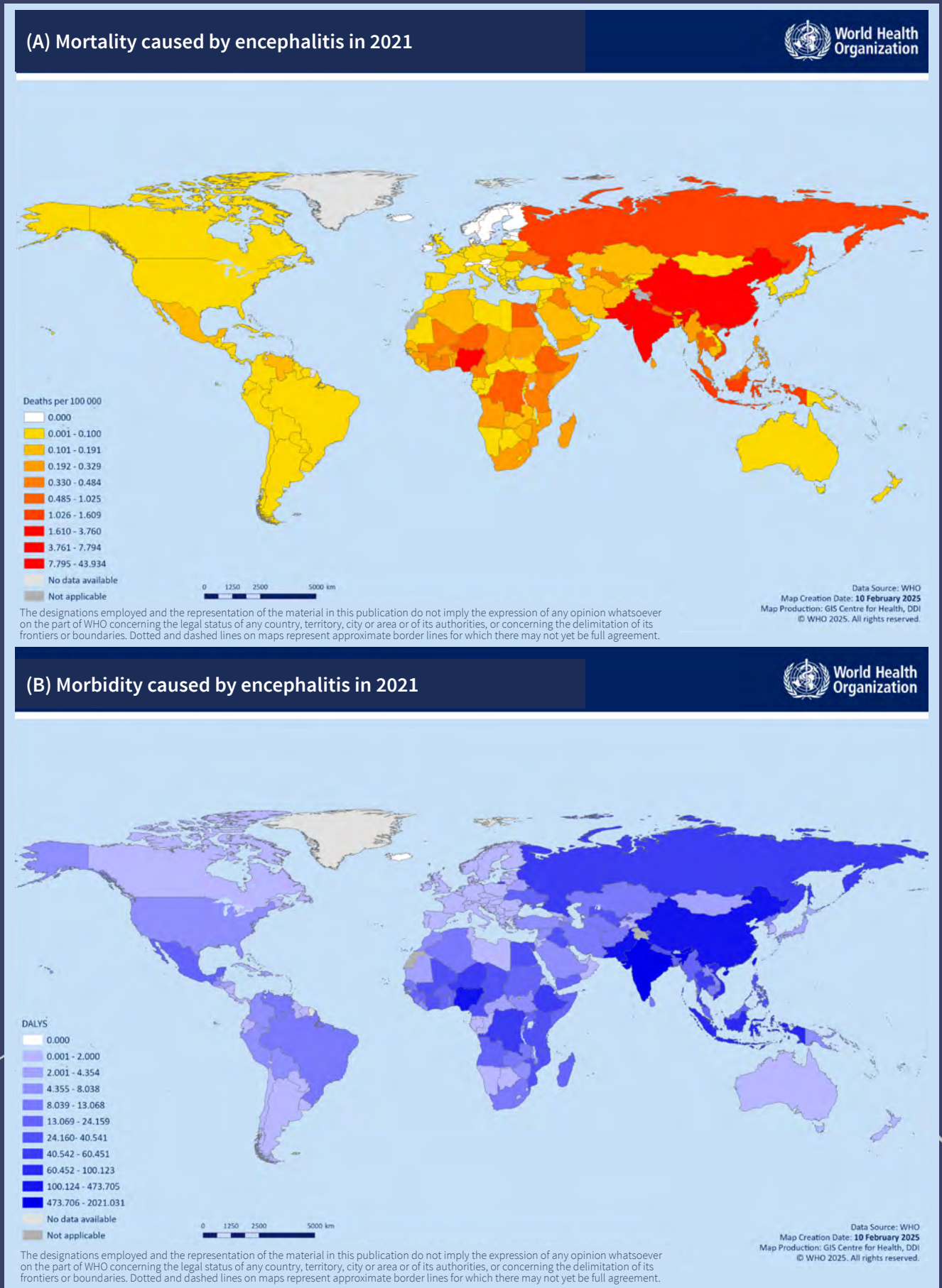
Introduction

Encephalitis is an inflammation of the brain; a serious, life-threatening neurological condition affecting people across all age groups, that has high mortality and often leads to significant long-term sequelae. Globally in 2021, encephalitis was the fourth leading cause of neurological health loss (i.e. disability-adjusted life years [DALYs]) in children aged under 5 years and the 13th overall across all age groups *(1, 2)*. In 2021, over 80 000 people died from encephalitis and up to 50% of people with encephalitis suffered long-term after-effects of the condition, losing independence, income and quality of life *(3-5)* (Map 1). Its burden was estimated at 5 million DALYs in 2021 annually *(1)*. Hospitalizations due to encephalitis in 2010 in the United States of America (USA) cost an estimated US$ 2 billion *(6)*. Data from a large Swedish registry in 2019 revealed that the total cost of illness and death for tick-borne encephalitis (TBE) alone was over €23 million *(7)*. Economic information is limited in low- and middle-income countries (LMIC), but encephalitis is likely to incur a substantial financial drain on families, as seen in studies on Japanese encephalitis (JE) in Bangladesh, China and Nepal *(8, 9)*.

Globally in 2021, encephalitis was the fourth leading cause of neurological health loss in children aged under 5 years and the 13th overall across all age groups.

Encephalitis has many causes, including infectious and autoimmune processes; however, the etiological agent often remains unidentified. Infectious encephalitis is an increasing public health concern globally, and mosquito-transmitted arboviruses (i.e. arthropod-borne viruses) addressed in the World Health Organization's (WHO's) upcoming preparedness and resilience for emerging threats (PRET) module will include those that cause encephalitis *(10)*. A few types of infectious encephalitis can be prevented by vaccination or treated with antimicrobials; however, in most cases, no specific treatment is available, making encephalitis an urgent public health imperative and underscoring the importance of prevention.

Over 100 different pathogens can cause infectious encephalitis, including vector-transmitted and vaccine-preventable pathogens *(11)*. Among pathogens with global geographical spread, herpes simplex virus (HSV) is the most common cause of encephalitis, whereas in Asia, JE virus (JEV) is associated with a substantial number of cases *(12)*. Autoimmune encephalitis, an immune-mediated inflammatory brain disorder, is increasingly recognized as a cause of encephalitis. Regardless of cause, all encephalitis types require rapid assessment, diagnosis and treatment to prevent mortality and morbidity. Although laboratory and imaging investigations provide information on etiology and can guide treatment decisions, care that is hospital based with specialists, and involves multidisciplinary support improves outcomes, even in the absence of etiology-specific treatments.



Map 1. Mortality (A) and morbidity (B) caused by encephalitis by country in 2021
DALY: disability-adjusted life year.

The consequences of encephalitis can be devastating, requiring long-term comprehensive support in the community, including access to rehabilitation, and financial and social assistance. Hence, integrated care for encephalitis requires a continuum of services through universal health coverage (UHC) *(13)*, and substantial political and financial commitment to health system strengthening. Additionally, at the population level, the detection, prevention and management of infectious encephalitis and its emerging causes requires surveillance systems, diagnostic capabilities and targeted public health measures.

Encephalitis disproportionately affects people living in LMIC, where health services and resources are most limited. Unless targeted actions are taken, encephalitis will continue to drive avoidable morbidity and mortality, fuelled by high population density in underresourced communities, globalization, vaccine hesitancy, intensive farming practices, climate change, and emerging and re-emerging infections *(14, 15)*.

Encephalitis disproportionately affects people living in LMIC, where health services and resources are most limited.

Several WHO initiatives support the organization's work on brain infections. The *Defeating meningitis by 2030* global roadmap was approved by the Seventy-third session of the World Health Assembly in November 2020 (Resolution WHA73.9) *(16)*. The roadmap sets a comprehensive vision for 2030 – "Towards a world free of meningitis" – with three visionary goals: elimination of bacterial meningitis epidemics, reduction of cases of vaccine-preventable bacterial meningitis by 50% and deaths by 70%, and reduction of disability and improvement of quality of life after meningitis due to any cause. Subsequently, in May 2022, Member States unanimously adopted the Intersectoral Global Action Plan on epilepsy and other neurological disorders 2022–2031 (IGAP) *(17)*. IGAP aims to improve access to diagnostics, treatment and care; improve the quality of life for people with neurological disorders, and their carers and families; and promote brain health across the life course. In alignment with IGAP, the *Defeating meningitis by 2023* roadmap and UHC, this technical brief aims to focus attention on the increasing global threat of encephalitis, and to highlight current geographical trends and gaps in diagnosis, treatment and care, with their associated public health implications.

The target audience for this brief includes policy-makers, public health professionals, health programme managers and planners, health care providers and researchers involved in service design and improving care for people with encephalitis.

Twenty-four countries in the WHO South-East Asia and Western Pacific Regions have Japanese encephalitis virus transmission risk, which includes more than 3 billion people.

The virus is transmitted to humans through bites from infected mosquitoes of the Culex species. In the tropics and subtropics, transmission can occur year-round but often intensifies during the rainy season and pre-harvest period in rice-cultivating regions.

A farmer planting rice in Indonesia. Traditionally, workers in paddy fields are at high risk of mosquito borne illnesses such as Japanese Encephalitis.

Methods

This technical brief is based on evidence from a WHO-commissioned scoping review, WHO's meeting titled "Why encephalitis matters?" *(18)*, and contributions from and reviews by technical experts from all six WHO regions, organizations *(11)*, and other WHO departments and initiatives. Conflicts of interest from all individual contributors were declared, assessed and managed in line with WHO procedures.

An extensive list of pathogens and autoantibodies can cause both encephalitis and overlapping conditions such as meningoencephalitis and meningitis. Hence, this brief encompasses a syndromic approach, rather than a pathogen-specific one. Much of the guidance contained herein is also applicable to diseases such as malaria, HIV, tuberculosis, neurocysticercosis, coronavirus disease (COVID-19) and other infectious diseases that can involve the central nervous system (CNS) but are not specifically associated with encephalitis *(19-23)*. Specific pathogen advice for the diseases listed above is beyond the scope of this brief; for the most part, WHO guidance on these diseases is provided elsewhere.

The brief follows the structure of the strategic objectives of IGAP, covering diagnosis, treatment and care of encephalitis (i.e. care pathways; diagnosis; treatment; care, including social protection and welfare; rehabilitation; and an interdisciplinary workforce). It then addresses surveillance and prevention (i.e. vaccines and vector control), followed by research, and advocacy and awareness.

This brief encompasses a syndromic approach, rather than a pathogen-specific one.

Fig. 1. A strong health system that embraces a people-centred and coordinated care approach

Diagnosis, treatment and care of encephalitis

Improving the lives of people with encephalitis, avoiding complications, and preventing premature death and disability requires a strong health system that embraces a people-centred and coordinated care approach, and is directed towards ensuring effective, timely and responsive diagnosis, treatment and care. Strong, comprehensive care pathways, access to treatment and care and an appropriately trained health workforce are all crucial components of a well-functioning and trained health system (Fig. 1).

The overall effectiveness of health systems rests in large part on the ability of first-contact workers to make accurate diagnoses, use evidence-based treatment plans and make appropriate referrals.

Care pathways

The delivery of integrated primary and acute care services is at the heart of country efforts to progress towards UHC through a primary health care (PHC) approach *(24)*. Effective primary and acute care ensures that people's health needs are met across the life course, that people can get care when and where needed, and that individuals and communities are actively engaged in their own health care. The overall effectiveness of health systems rests in large part on the ability of first-contact workers to make accurate diagnoses, use evidence-based treatment plans and make appropriate referrals. This is particularly important for addressing brain infections such as encephalitis, where prevention, early recognition, initial management and referral are critical to improving outcomes.

Packages of services are a key mechanism for achieving UHC *(25)*, but their impact is ultimately determined by how well they are implemented. Services for encephalitis as well as foundational services for first-contact primary and emergency care are rarely explicitly included in national packages *(26)*. These omissions can hamper a country's ability to adequately address the comprehensive health needs of its population and make progress towards UHC.

Owing to the complex needs and high levels of morbidity of people with encephalitis, a range of coordinated health and social care follow-up is essential, including interventions such as rehabilitation, psychosocial and spiritual support, and interventions to enhance quality of life. Rehabilitation should be integrated early within the care pathway from community care to comprehensive multidisciplinary post-acute care (Fig. 2).

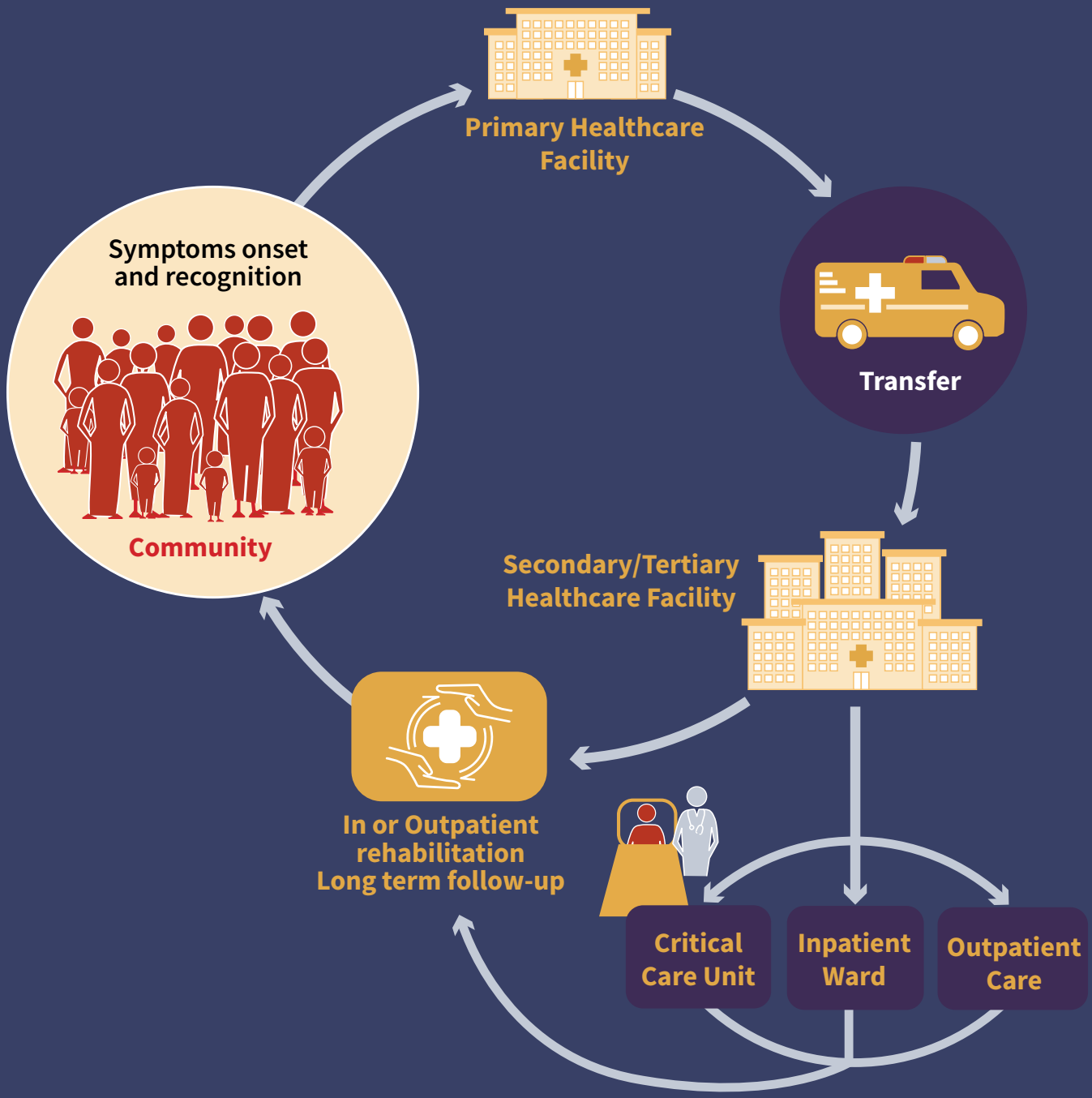
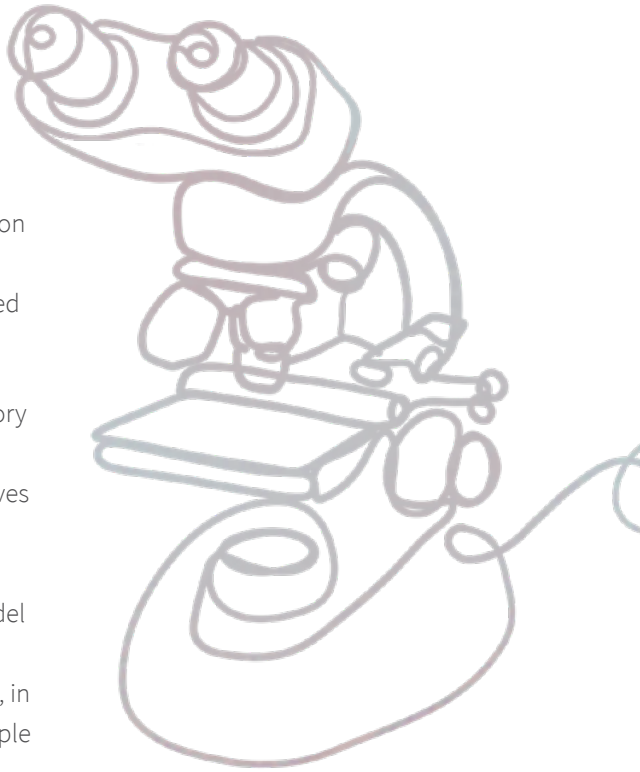


Fig. 2. Continuum of care for encephalitis and other brain infections

Key actions for care pathways

- Develop evidence-based care pathways of coordinated health and social services for people with encephalitis within UHC *(25)*. Such pathways should include integration at multiple levels of the health and social care system, the use of interdisciplinary care teams, service directories and medical health records, and referral mechanisms.
- Generate evidence and develop regionally adapted tools in local languages to support programmes that provide access to integrated care for people with encephalitis.



Diagnosis

Globally, challenges with encephalitis diagnosis result in delayed recognition and treatment, increasing the risk of death and severe complications. In low-resource settings, encephalitis outcomes are further impaired by limited health care access, facilities, workforce, diagnostics and treatments *(11)*.

The diagnosis of encephalitis requires early clinical recognition, confirmatory lumbar puncture, and additional tests such as brain imaging and electroencephalography (EEG). However, most of the world's population lives in areas with no immediate access to comprehensive or rapid encephalitis diagnostics. Testing of cerebrospinal fluid (CSF) obtained via lumbar puncture is especially important for the definitive diagnosis. The WHO model list of essential in vitro diagnostics includes basic CSF microscopy and measurement of cell counts, glucose and protein *(27)* (Box 1). Nevertheless, in many countries, lumbar punctures are performed on only some of the people with suspected brain infections *(16)*. This may be due to a lack of trained workforce or procedural kits, and misconceptions about lumbar puncture indications and safety. Additionally, pathogen-specific tests (e.g. virological polymerase chain reaction [PCR] testing of CSF) and autoantibody assays are often required for confirmation but are not available in many LMIC settings. Antibody testing for autoimmune encephalitis is primarily limited to high-income countries (HIC), and samples from countries with limited capacity are frequently assayed abroad causing delays. The lack of other diagnostic technologies (e.g. EEG and magnetic resonance imaging [MRI]) in many LMIC creates a barrier to confirming a diagnosis of encephalitis and related complications *(28)*. To establish laboratory networks, core development areas for LMIC are funding, workforce, equipment, training, infrastructure, utilities, management and regulation.

When it comes to the detection and prevention of emerging infectious diseases that can cause encephalitis, there are clear diagnostic gaps. The

BOX 1. WHO lists of essential diagnostics and medical devices

The WHO model list of essential in vitro diagnostics (2023) helps countries to establish priorities for inclusion of diagnostics in national essential diagnostics lists. Basic CSF profiling (cell counts, biochemistry and culture for bacteria, fungi and parasites) is included in the WHO model list but specific tests for the diagnosis of viral or autoimmune encephalitis are limited. Regional specificity for infectious encephalitis testing is needed because different pathogens are prevalent in different areas. Basic CSF profiling is essential, but insufficient, for pathogen detection; hence, countries should establish regional lists for priority encephalitis panels and work towards establishing better access. Diagnostic panels can include singleplex assays (i.e. testing for one pathogen at a time) or multiplex assays (i.e. testing for multiple pathogens simultaneously). Affordable, reliable and region-specific multiplex panels can simplify procurement and distribution, and improve access. However, they may need to be supplemented by additional assays, depending on sensitivity and the local epidemiology. Multiplex panels should combine testing for encephalitis with that of other CNS infections such as meningitis. *(27, 29-31)*

Early recognition is essential to providing lifesaving and outcome-changing treatment; however, many clinicians do not initially suspect encephalitis, often owing to a lack of knowledge or guidelines.

etiological agents responsible for such diseases are often novel or less common, requiring specialized diagnostics and interventions that may not be fully covered under the current UHC framework. These gaps highlight the need for enhanced surveillance, advanced diagnostic capabilities and targeted public health measures that go beyond the standard services covered by UHC. Addressing these gaps is crucial to ensure that health systems are fully equipped to detect, prevent and manage encephalitis caused by emerging infectious diseases. Diagnostic strategies in children in Asia have been explored starting with treatable causes (HSV-1, varicella-zoster virus [VZV], *Mycobacterium tuberculosis* and common bacteria such as *Orientia tsutsugamushi)* and, if endemic, malaria. If no causative agent is identified, secondary screening can be conducted for JEV, dengue virus, enterovirus A-71 (EV-A71), respiratory viruses (including influenza virus) and autoimmune encephalitis autoantibodies. This screening can be followed by testing for unknown or emerging pathogens *(32)*.

Early clinical recognition and knowledge of encephalitis among health professionals is also limited across a range of settings including traditional healers and primary care workers. Early recognition is essential to providing lifesaving and outcome-changing treatment; however, many clinicians do not initially suspect encephalitis, often owing to a lack of knowledge or guidelines, especially for autoimmune encephalitis.

Clinical knowledge of the differential diagnosis of encephalitis from other brain infections is also challenging in both surveillance and clinical settings.

WHO previously provided a clinical case definition of acute encephalitis syndrome as part of a surveillance strategy for JE, which was expanded to include other infectious agents as the etiological landscape evolved *(33-35)*. Other standardized clinical case definitions have also subsequently been proposed that attempt to balance sensitivity and specificity *(36, 37)*. Guidelines for encephalitis are available only in selected countries, generally those with high-income settings *(38-42)*. Consistent training across the health workforce is needed (especially where specialist services are lacking), and for community practitioners and healers.

Key actions for diagnosis

- Target early clinical recognition of encephalitis through public and health professional education.
- Aligned with the *Defeating meningitis by 2030* roadmap, aim to increase the acceptance and accessibility of lumbar punctures by educating the public, training the workforce, and ensuring the availability of affordable and sterile CSF testing kits.
- Use standardized clinical guidelines and the WHO list of essential diagnostics to aid the selection of encephalitis diagnostics for national lists and implementation plans, taking into account regional pathogen distribution.
- Leverage existing guidelines and laboratory quality standards and frameworks *(43-45)* to train leaders to implement improvements in laboratory testing, and to strengthen regulatory, production, procurement and distribution pathways for essential diagnostics.
- Leverage the momentum of IGAP and other initiatives to build capacity for MRI and EEG health products *(30, 46)*.
- Collaborate with industry and other stakeholders to facilitate the development of novel diagnostic assays to improve detection while ensuring scalability, affordability and specificity across regions.

Treatment

Owing to the complexity of the disease and frequent complications, people with encephalitis often require care in critical care or intensive care units, preferably with facilities and staff trained in neurological disorders. However, few countries report the presence of specialized neurology units *(47)*; also, in countries where such facilities exist, people with encephalitis may need to travel hundreds of kilometres to access appropriate care.

Medication costs, inadequate supply and distribution chains, and issues with quality and regulation all limit access to the essential encephalitis treatment

A baby with a doctor during a medical examination in Tajikistan.
© WHO / NOOR / Sebastian Liste

for many of the world's population *(48)*. Hospital treatment encompasses general supportive measures (e.g. hydration, analgesia, anti-pyrexial agents and nutritional support) as well as encephalitis-specific treatment (e.g. intravenous [IV] aciclovir, when available) and treatment of acute complications (e.g. seizures and electrolyte imbalance). In some cases, such as rabies, palliative care is also important *(49)*.

For autoimmune encephalitis, IV steroids are considered standard treatment; however, a combination of steroids with more costly therapies (e.g. plasma exchange or IV immunoglobulin) may also be warranted *(50)*. Recognition of autoimmune encephalitis by the physician can lead to curative interventions such as the removal of any underlying tumours (e.g. ovarian or testes teratoma).

The biannually updated WHO model list of essential medicines (EML) *(51)* includes IV aciclovir, oral valaciclovir, antimicrobials and immunosuppressive treatments, as well as supportive medicines such as anticonvulsants and analgesics. However, there are gaps between the WHO EML, national lists of essential medicines and actual on-the-ground availability. In 2017, of 123 responding countries, only 68 (55%) reported the availability of one or more anticonvulsants (carbamazepine, phenobarbital, phenytoin or valproic acid) at all times in the PHC setting *(47)*. Often, IV aciclovir is unavailable or unaffordable for many people living in LMIC. As with many other neurological disorders, out-of-pocket costs – such as medical bills, medications and lost earnings – due to encephalitis can be devastating to individuals and families *(48)*.

As with many other neurological disorders, out-of-pocket costs – such as medical bills, medications and lost earnings due to encephalitis can be devastating to individuals and families.

Untreated autoimmune encephalitis leads to death, coma or permanent brain injury. Although oral and IV steroids are generally available, access to more potent and advanced immunotherapies is limited, especially outside HIC. Many people with autoimmune encephalitis also require prolonged treatment and recurrent treatment cycles with other immunosuppressants because of disease relapse.

Key actions for treatment

- Prioritize relevant medicines (e.g. antiseizure medications, immunosuppressants, antivirals and vaccines included in WHO's EML) for inclusion into national essential medications lists and standardized treatment protocols.
- Include both autoimmune and infectious encephalitis and their treatments in publicly funded UHC packages, which, combined with the implementation of fair pricing policies, can increase affordability and consequently widen access.
- Use and expand existing surveillance systems for forecasting demand and supply chains to streamline procurement and distribution, to decrease the occurrence of stock-outs.
- Pair better availability and affordability of medicines with appropriate training and education of the health workforce to recognize and treat encephalitis in a timely manner.

Care

Following encephalitis, many people are unable to return to their premorbid functioning and require lifelong assistance in personal care and activities of daily living.

Common sequelae of encephalitis include developmental delay, cognitive deficits, behavioural difficulties, mood disturbance, hearing and vision loss, motor impairment and seizures. Some of these sequelae may be subtle or delayed. Their detection requires dedicated assessment, including functional, cognitive and sensory tests, not only during acute hospital admission but also in later recovery stages (e.g. during a return to schooling or employment). For young children, the consequences of encephalitis may only become evident later in childhood or adolescence. The sequelae arising from encephalitis are the same as those that occur after any brain infection such as meningitis and brain abscesses. Thus, a final common clinical pathway can address and treat people suffering not only from the consequences of encephalitis, but also from the consequences of any brain infection.

The 2023 WHO *Mental Health Gap Action Programme* (mhGAP) provides comprehensive recommendations on the management of seizures and the use of antiseizure medications *(52, 53)*.

CARER SUPPORT

Following encephalitis, many people are unable to return to their premorbid functioning and require lifelong assistance in personal care and activities of daily living. As with other chronic neurological conditions, challenges for carers include stress, role strain, financial burden, social isolation and bereavement in the event of loss. Roles and challenges may vary, including when caring for children, adolescents or older adults, which highlights the need for individualized support. Support networks are essential in mitigating the challenges of post-encephalitis adjustment and recovery. Palliative care and grief counselling services are also important for those who have lost family members or friends due to encephalitis.

Key actions for individual and carer support

- Provide accessible and evidence-based information on available resources in the community; for example, training programmes, respite care, neurological health services and other resources that are tailored to the needs of carers of people with brain infections and their sequelae *(28, 54)*.
- Develop or strengthen mechanisms to protect carers; for example, through the implementation of social and financial benefits (e.g. pension, leave or flexible workhours) and policies and legislation aimed at reducing stigma and discrimination, and supporting carers beyond their caregiving role *(55)*.

SOCIAL PROTECTION AND WELFARE

Given the impact of encephalitis on employment opportunities and prospects of independent living, a comprehensive encephalitis approach must include access to social protection and welfare. This involves disability allowances, nondiscriminatory disability practices, re-employment schemes and access to funding for the necessary rehabilitation and care. In 2017, 72 (58%) of 124 countries reported that financial support is available for people with neurological disorders, ranging from 86% among HIC to 24% among low-income countries (LIC) *(47)*. In total, 38% of the world's countries reported providing residential care to people with neurological diseases (83% in HIC and 8% in LIC). Substantial financial investment and political commitment are needed to make such support accessible and affordable.

Given the impact of encephalitis on employment opportunities and prospects of independent living, a comprehensive encephalitis approach must include access to social protection and welfare.

Along with inequities in health outcomes, people with sequelae due to brain infections often experience gaps in formal social support mechanisms. These people are often reliant on support from family members (frequently female) to access health services and engage in community activities. The WHO *Global report on health equity for persons with disabilities* calls on Member States to take action to advance health equity for people with disabilities, including disabilities that result from brain infections such as encephalitis *(56)*.

Key actions for social protection and welfare

- Develop financial and social protection mechanisms, including national health insurance plans and social security benefits, to address the direct and indirect costs related to accessing health care (e.g. transportation costs), and support affordable and accessible care for people with encephalitis, and their carers and families *(55)*.
- Conduct research on the socioeconomic impact of sequelae on children and adults and their families or carers, and on the effectiveness of aftercare and support interventions in reducing impact *(16)*.
- Map out existing services and support systems available by country for children and people with disabilities, including those with encephalitis sequelae and families or carers of people affected by encephalitis. Work with organizations for people with disabilities and other networks for encephalitis to identify barriers to access, availability and use and undertake a gap analysis to improve service provision.

Rehabilitation

People with encephalitis are often underserved, particularly at the point of discharge from acute hospital care, owing to underdeveloped multidisciplinary rehabilitation services, limited integration of those services into acute and post-acute care, and lack of rehabilitation services in the community.

The functional impairments and limitations experienced by people with encephalitis and other brain infections reflect those of the global unmet need for rehabilitation. Globally, in 2021, 2.6 billion people experienced conditions that could benefit from rehabilitation *(57)*; however, in some LMIC, less than 50% of such people receive rehabilitation *(58, 59)*, and even fewer have life-changing access to assistive devices *(60)*. As of 2017, only 16% of 105 countries reported the presence of specialized neurorehabilitation units, and only 17% reported the availability of neurorehabilitation in general rehabilitation settings *(47)*. People with encephalitis are often underserved, particularly at the point of discharge from acute hospital care, owing to underdeveloped multidisciplinary rehabilitation services, limited integration of those services into acute and post-acute care, and lack of rehabilitation services in the community.

Key actions for rehabilitation

- Integrate rehabilitation into national and subnational planning priorities, financing and evaluation programmes and workforce development strategies, and along the continuum of care from acute to post-acute care (Fig. 2). Most importantly, rehabilitation should be accessible at the PHC level with appropriately trained PHC workers, because many people do not have access to specialist facilities.
- Train all health professionals to appropriately refer people to rehabilitation services and involve caregivers in home-based rehabilitation, drawing on WHO resources to strengthen national rehabilitation programmes, competency-based approaches and general neurorehabilitation priorities *(61-63)*.
- Leverage existing support resources from professional and third-sector organizations to complement encephalitis care and recovery.

Interdisciplinary workforce

Diagnosis and management of encephalitis are complex, requiring multidisciplinary collaboration from neurologists, infectious disease specialists and clinical teams that comprise of, for example, specialist nurses, intensivists, psychologists, physiotherapists, occupational therapists, dietitians, and speech and language therapists. Yet, where the encephalitis burden is greatest, access to such an integrated, multidisciplinary workforce is lowest. Globally,

there are too few adult neurologists, with large inequalities between low- and high-income settings and between rural and urban areas. Further, the incidence of encephalitis is greater among children than adults, and many children with encephalitis will experience chronic neurological sequelae, exacerbated by the shortage of paediatric neurologists *(3, 47)*. There is also a global shortage of allied health professionals working in neurology and a global shortage of nurses in general, estimated at nearly 6 million in 2018 *(47, 64)*.

The lack of specialized professionals at the subnational level hampers the ability to accurately diagnose and manage neurological conditions such as encephalitis, particularly in people with complex symptoms requiring complex therapies. It also limits the effectiveness of public health interventions, because in many regions the expertise needed to guide and implement these measures is not readily available. Addressing this disparity is essential to improving overall health care capacity and response at all levels.

Globally, there are too few neurologists, with large inequalities between low- and high-income settings and between rural and urban areas.

Key actions for the interdisciplinary workforce

- Increase the number of specialist and nonspecialist people in the workforce by implementing national and regional neurology training programmes.
- Redistribute and incentivize health professionals to practise locally by improving wages, working conditions and professional development opportunities.
- Provide encephalitis-focused training to nonspecialist health workers including local healers and community health workers.
- Support the development of regional, etiology-driven standardized treatment guidelines to develop guidance and ensure their implementation. Given similarities in presentation, investigation and initial management, encephalitis can also be incorporated into existing workstreams, magnifying opportunities for funding and benefiting from priorities set in other WHO initiatives.

These actions should span across professions, including nurses, therapists, doctors, community workers and others. As a priority, training should aim to increase recognition of encephalitis, increase the frequency of lumbar punctures using non-physician supportive health workers (e.g. nurses), implement early treatment, promote preventive measures, and recognize and support the management of long-term sequelae.

To provide such training, global partnerships, knowledge exchange programmes, and expertise and resources from national and regional professional societies and independent organizations should be harnessed. International professional organizations can also provide technical support to implement formal training programmes resulting in certifications. Local knowledge exchange (e.g. via centre–centre training) should be encouraged.

A nurse gives a child a routine vaccination at a mobile health clinic in Ntiliya village, Kenya.
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Surveillance and prevention

When implemented effectively, prevention strategies such as surveillance, vaccination and vector control are highly successful public health measures to combat infectious encephalitis. Surveillance of encephalitis is crucial for understanding the epidemiology, burden and distribution of disease; for guiding preventive measures and immunization campaigns; and for determining the efficacy of interventions, vaccine campaigns and vector control programmes. Vaccination programmes remain one of the most powerful public health interventions to combat encephalitis and the types of campaigns described by WHO should be followed *(65)*. Demonstrating where vaccination or other interventions have been particularly successful for encephalitis and resulted in reduced disease burden can be highly effective. Vector control should be considered as one strategic tool in a larger toolbox because work on vector control must consider climate change, urbanization, land uses, water storage in urban and rural environments, and other environmental factors that affect vectors. Vector control should not come at the cost of vaccination *(18)*.

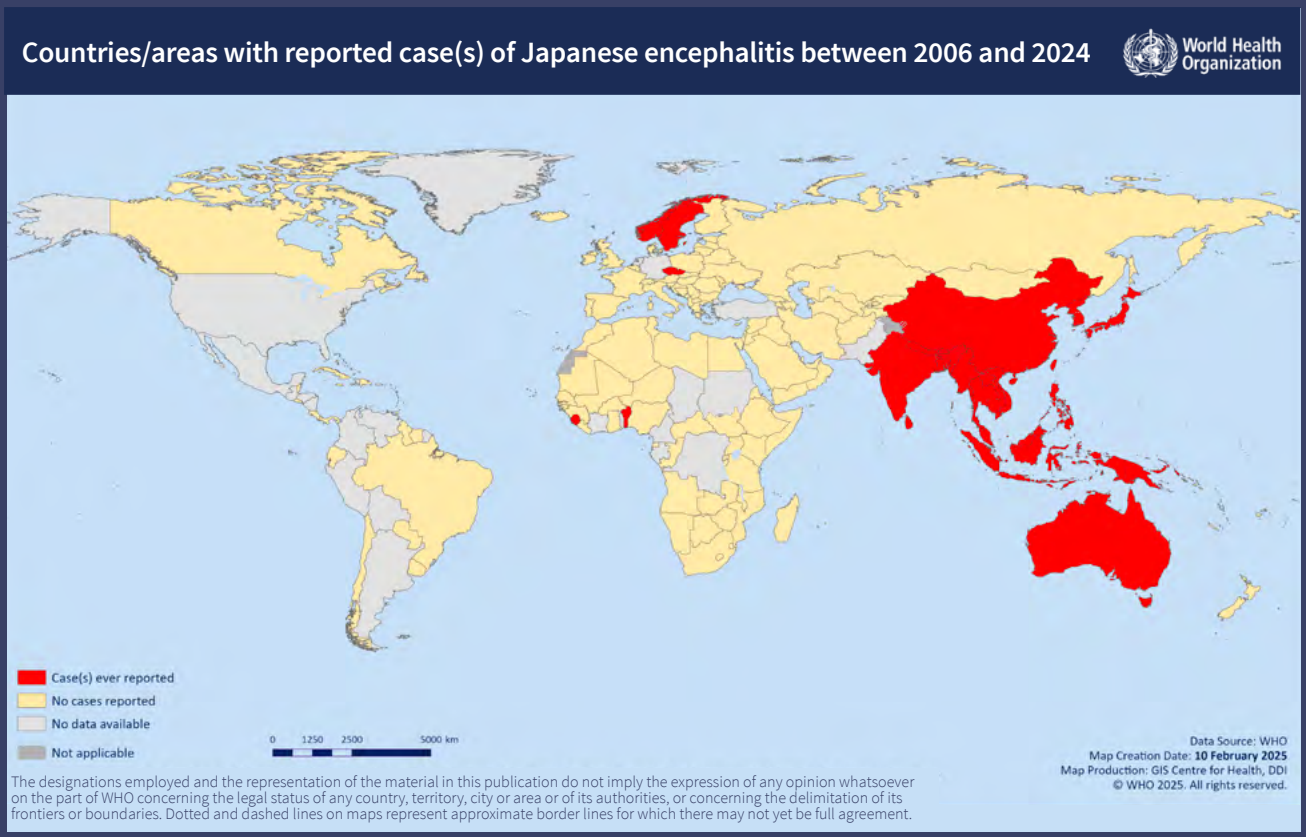
By strengthening disease surveillance capacity, countries can better recognize prevention priorities, plan ahead, sensitize communities, optimize workable evidence-based interventions and monitor disease trends.

Surveillance

By strengthening disease surveillance capacity, countries can better recognize prevention priorities, plan ahead, sensitize communities, optimize workable evidence-based interventions and monitor disease trends. WHO recommends surveillance of diseases with high impact, epidemic potential and active control programmes, where collected information could result in new public health measures *(66)*. Encephalitis surveillance is relevant to many of these goals (Box 2). Even so, encephalitis surveillance systems have not been universally developed, and the quality of existing systems varies. In addition, countries vary in their approaches to encephalitis surveillance, and fragmentation severely limits the estimation of the burden of encephalitis, the contribution of specific pathogens, information sharing, and the ability to detect outbreaks and emergent infections.

BOX 2.Objectives of surveillance systems for encephalitis

1) Monitoring of encephalitis incidence to estimate disease burden.
2) Monitoring of encephalitis etiologies (including autoimmune) to inform priorities for public health measures and standardized treatment guidelines.
3) Detection of new and emergent pathogens, including new strains and pathogens with expanding geographical distribution.
4) Detection and assessment of encephalitis outbreaks with potential for escalation to public health emergencies.
5) Incorporation of encephalitis sequelae into existing surveillance systems.
6) Evaluation of existing and proposed control programmes, including:
    - impact of vaccination programmes;
    - optimization of vaccination schedules;
    - reach of vaccination programmes and need for supplementary vaccination;
    - consideration of new vaccine introduction;
    - evaluation of encephalitis-specific vector control programmes; for example, interruption of the mosquito–human–mosquito transmission cycle through personal preventive measures including the use of mosquito or chigger repellents, long-sleeved clothes, coils and vaporizers; and
    - support and promotion of integrated reporting systems for human and animal rabies surveillance with integrated, quality data. *(33, 35, 66, 70)*



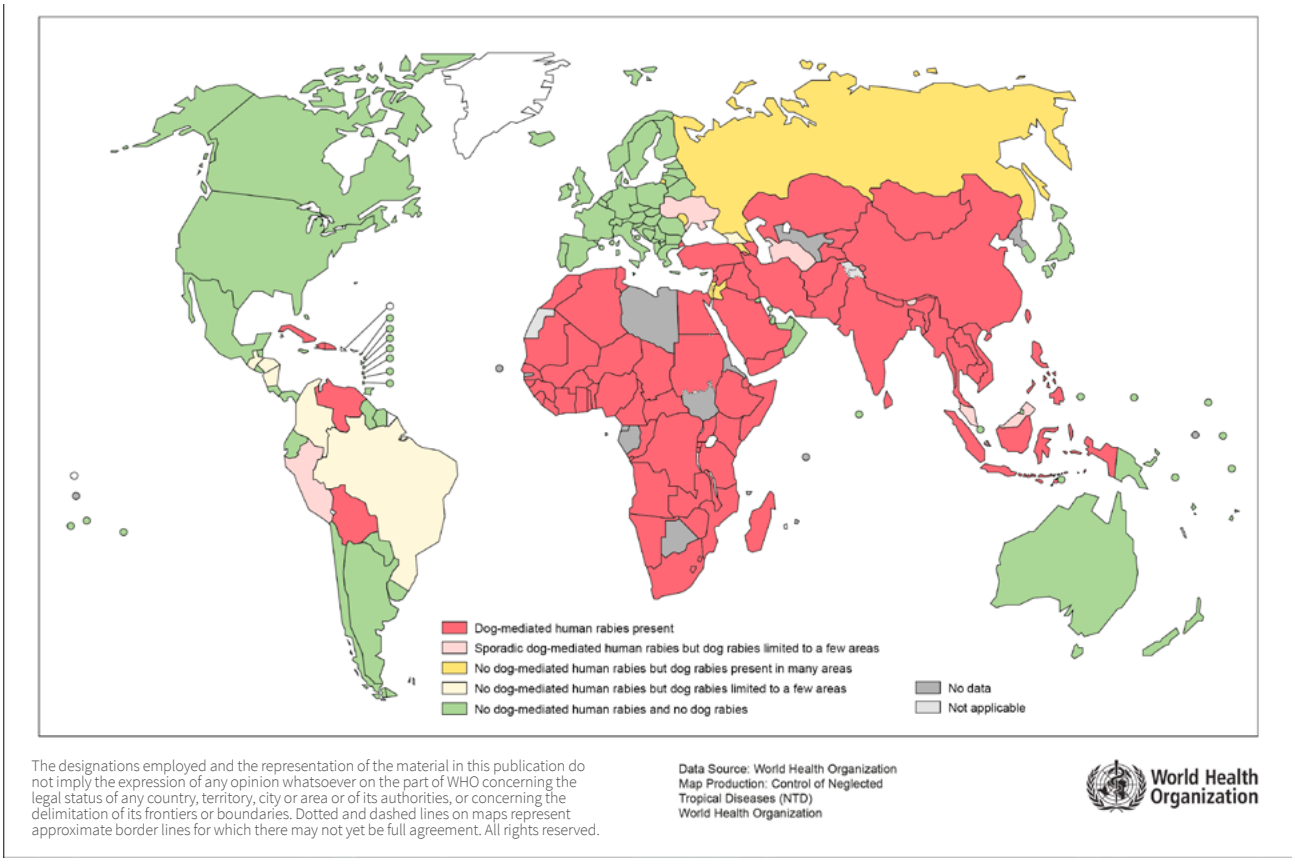
Map 2. Countries with reported case(s) of JE between 2006 and 2024

Some pathogen-specific systems already exist and could be scaled up to include more pathogens. Examples of robust existing surveillance systems include JE in the WHO regions of South-East Asia and the Western Pacific (Map 2), rabies (Map 3), West Nile and poliomyelitis (an under-recognized cause of encephalitis) *(12, 67-69)*. In addition to commitment, coordination and resources, effective encephalitis surveillance requires:

- awareness and recognition of the condition;
- access to health care, lumbar punctures and pathogen-diagnostic assays;
- local systems for sample collection, storage, transport and testing, delivered by trained staff across laboratory networks, with quality control and assurance; and
- data and communication systems to aggregate, analyse and act on information from the local networks *(66)*.

WHO's recommended surveillance standards serve as a guide for harmonizing and developing communicable disease surveillance activities, including specific standards for some pathogens relevant to encephalitis (e.g. JEV, mumps, measles and VZV) *(33, 70-73)*.

An increasing awareness of the importance of early recognition of sequelae of brain infections has led to initial efforts to incorporate sequelae surveillance into existing surveillance networks as part of the *Defeating meningitis by 2030* initiative *(16)*. The primary objective is to use existing country surveillance systems to measure the prevalence and types of sequelae at discharge or within 4 weeks of discharge among people with meningitis, meningoencephalitis or encephalitis in a given area. The resulting data can be used to inform public health policies for early detection and care of people with sequelae from brain infections.



Map 3. Presence of dog-mediated human rabies by country in 2022

Key actions for surveillance

- For countries with no encephalitis surveillance systems, elect to start with syndromic case-based notifications or sentinel surveillance for the highest priority pathogens. These should include pathogens for which control measures (e.g. vaccination) are in place or being considered, and pathogens with expanding spread or at risk of causing epidemics. National public health agencies, supported by external experts, should establish a list of priority pathogens and develop specific guidelines on which cases should be sampled and which data should be notified. The cases should reflect the broader encephalitis population, to improve the accuracy and relevance of surveillance data.
- Incorporate encephalitis surveillance into existing surveillance systems. Given shared syndromic presentation and diagnostic approaches, integrated meningoencephalitis surveillance is likely to reduce costs and aid implementation while collecting data on brain infections for which joint public health measures exist. From the laboratory standpoint, encephalitis surveillance may also be combined with surveillance of other vaccine-preventable diseases *(70)*.
- Adapt, integrate and implement WHO-recommended surveillance standards for local disease epidemiology, resources and information networks *(66)*. Given similarities in encephalitis etiologies, further technical support should also be exchanged between the countries via regional collaboration.
- Link national and regional surveillance networks (e.g. JEV, rabies) for coordinated information sharing, particularly to ensure global surveillance for emerging and remerging infections. Such global coordination should be supported by international organizations and partners.
- Leverage national encephalitis surveillance systems to additionally collect data on encephalitis sequelae. Surveillance of sequelae due to encephalitis can build on sequelae surveillance for meningitis and should be adapted according to the existing surveillance system (e.g. case-based or syndromic surveillance).

Vaccination

There are vaccines for several important causes of infectious encephalitis – JEV (Box 3), rabies (Box 5), dengue virus, TBE virus, VZV, measles and mumps – and for other infections that may cause encephalitis *(74-76)*. Many of these vaccines (e.g. for JEV, measles and mumps) should be a part of routine childhood vaccination schedules, whereas others (e.g. TBE virus and rabies vaccines) are recommended in at-risk populations *(77-79)*. Further vaccines, such as for the chikungunya virus, have recently been approved.

Global vaccination coverage decreased during the COVID-19 pandemic, with 14.5 million children not receiving a single vaccine in 2023 *(77)*. An estimated 2 million (17%) children missed their routine first dose of measles vaccine, and only 74% of children worldwide received two doses of that vaccine *(77)*. Consequently, owing to incomplete and pandemic-interrupted coverage, rising rates of diseases such as acute measles have been reported worldwide. This may result in not only concurrent encephalitis but also fatal subacute sclerosing panencephalitis (SSPE) – a devastating and uniformly fatal disease that can occur years after measles infection *(80)*. In countries with good access to vaccination, vaccine hesitancy can contribute to disease resurgence *(81)*.

Vaccination programmes remain one of the most powerful public health interventions to combat encephalitis.

BOX 3. Japanese encephalitis, surveillance and vaccination

JEV is a flavivirus transmitted by infected *Culex* mosquitoes; it is responsible for up to 100 000 cases of viral encephalitis and 25 000 deaths each year. Twenty-four countries in the WHO South-East Asia and Western Pacific regions have endemic JEV transmission, and more than 3 billion people are at risk of infection. Climate change poses a risk of extending the transmission window and geographical spread to previously unaffected regions.

Most JEV infections are mild (manifesting with fever and headache) or without apparent symptoms, but about 1 in 250 infections results in severe illness. The case fatality rate among those with encephalitis can be as high as 30% and, of those who survive, 20–30% suffer permanent cognitive, behavioural or neurological sequelae such as paralysis, recurrent seizures or the inability to speak. JE primarily affects children, because most adults in endemic countries have developed natural immunity after childhood infection. However, with climate change, JEV transmission is likely to affect new areas, where the adult population may have lower levels of immunity. This further emphasizes the importance of enhancing surveillance systems to better respond to this risk. There is no antiviral treatment for those with JE. Treatment is supportive to relieve symptoms and help the individual overcome the infection. However, vaccination against JEV is highly safe and effective. There is little evidence to support a reduction in JE burden from interventions other than the vaccination of humans. WHO recommends that JE vaccination be integrated into national immunization schedules in all areas where JE disease is recognized as a public health issue. *(12, 70, 82)*

Endemic causes of vaccine-preventable encephalitis should be addressed by targeted programmes for high-risk individuals living in or visiting endemic areas (e.g. TBE vaccination). Travel advice, including recommended vaccines, for people travelling to areas of high risk, can be provided by general practitioners and other relevant health workers *(83, 84)*.

If rabies disease, for example, develops it is invariably fatal, but pre-exposure vaccination is highly effective *(78)*. Similarly, post-exposure prophylaxis for rabies (consisting of wound washing, and administration of a timely vaccination series and rabies immunoglobulins) effectively prevents disease when given promptly *(78)*. However, factors that limit coverage of rabies pre- and post-exposure prophylaxis and other vaccines include a lack of central funding, inadequate supply chains, challenges of geographical distribution and poor health care seeking behaviours. To help mitigate this, further integration of programmes with the animal health sector in line with the WHO One Health approach is essential *(85)*.

Key actions for vaccination

- At the regional level, develop collaborations to exchange technical expertise, advocate for improved supply and distribution chains, and aggregate data for the expansion of vaccination programmes. Successful regional and national initiatives that have supported JEV immunization expansion can provide frameworks for other countries and other vaccinations.
- As recommended by WHO, incorporate measles, mumps and JEV vaccinations into national childhood immunization programmes and complement these by catch-up vaccinations of adults, and targeted programmes for endemic areas and high-risk groups.
- Develop, endorse and fund training of health professionals to manage programmes locally, as well as public education and information campaigns to promote vaccination uptake and sustain coverage.

Vector-borne and zoonotic disease control

Risk of vector-borne diseases are rapidly expanding owing to unplanned urbanization, increased movement of people and goods, climate change, and biological challenges (e.g. resistance to insecticides and evolving strains of pathogens) *(86)* (Box 4). This renders large populations at increasing risk of vector-borne diseases such as arboviruses (e.g. JE, TBE, dengue, Zika, chikungunya, West Nile and equine encephalitis) (Map 4). Given the absence of pathogen-specific treatments for arboviral encephalitides, preventive measures and vector control are paramount. The One Health concept recognizes that the health of humans, animals and the environment are linked, and it aims to address problems holistically by working across sectors to achieve the greatest impact *(85)*.

BOX 4. Scrub typhus

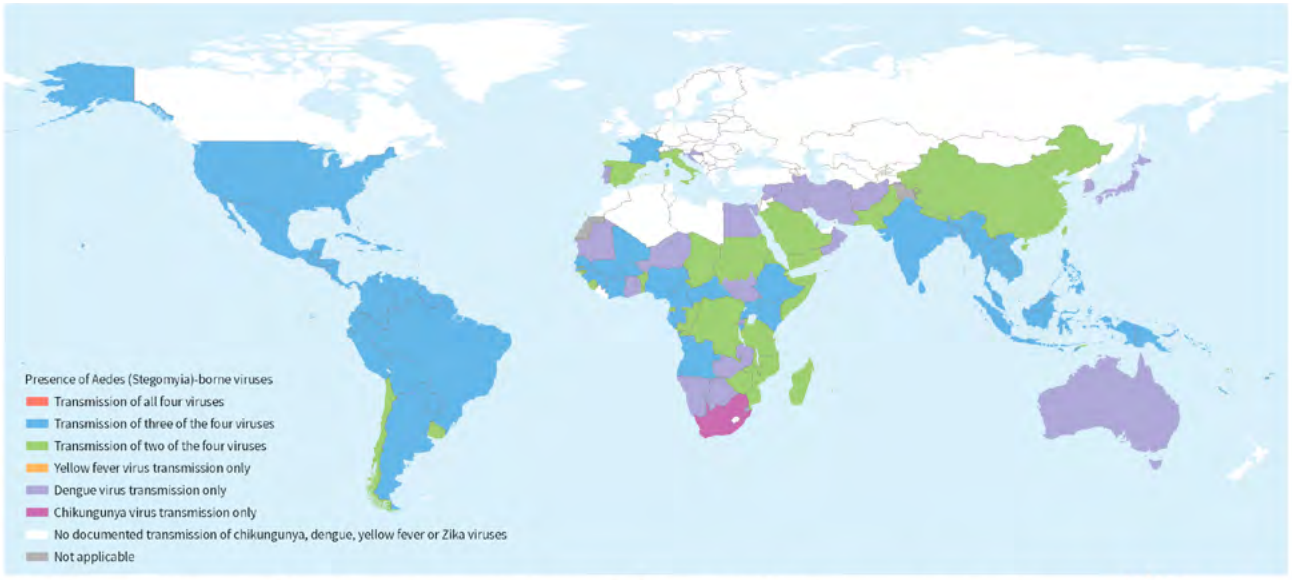
Scrub typhus ("bush disease" or "tsutsugamushi disease") is an acute febrile illness caused by an arthropod-borne Gram-negative bacillus, *Orientia tsutsugamushi.* It is endemic in regions of the Asia–Pacific and Northern Australia; these regions are termed the "tsutsugamushi triangle". However, recent expansion beyond known endemic areas signals an emerging global public health problem and emphasizes the importance of enhanced surveillance.

Scrub typhus is a major zoonotic disease spread by trombiculid mites infected with *O. tsutsugamushi.* An eschar at the site of mite or chigger feeding is a feature. If left untreated, the case fatality rate is high due to multiorgan failure with pulmonary, hepatic, renal, cardiac and neurological complications (meningitis, meningoencephalitis and encephalitis), which are seen in up to a fifth of hospitalized individuals.

An effective vaccine is yet to be developed. Hence, effective measures in the treatment, control and prevention of this disease must be implemented.

In synergy with a One Health approach and country strategies *(85, 87-89)*, improved surveillance and management of scrub typhus could include:

- prevention and control measures including provision of protective clothing to people working and living in areas of heavy scrub vegetation to prevent mite bites, insecticide repellents, vegetation clearance and rodent control to prevent mite transmission to humans;
- rapid case identification by health workers and prompt treatment, including pre-positioning diagnostic kits ahead of peak seasons;
- public awareness campaigns and sensitization of the community and health workers ahead of the peak seasons, especially during the pre-monsoon period; and
- audit of all cases by chief medical officers and district surveillance officers.



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Map 4. Countries and territories with current or previous transmission of chikungunya, dengue, yellow fever or Zika viruses (as of 16 October 2024)

In 2022, WHO launched the *Global Arbovirus Initiative* – a focused framework with objectives and priority activities to tackle emerging and re-emerging arboviruses with epidemic and pandemic potential *(90)*. The initiative includes risk monitoring, pandemic and epidemic prevention, coalition building and strengthening of vector control. There are many barriers to effective vector control, including systemic, structural, informational, environmental, human movement, political and financial challenges *(86)*. The influence of social and environmental factors on vector-borne pathogen transmission underscores the critical importance of addressing wider determinants of health, such as poverty, and a holistic approach to zoonotic diseases, in line with the One Health framework *(85)*.

The One Health approach has been effectively modelled in the case of rabies prevention. More than 90% of human rabies infections are due to bites from rabid dogs. Vaccination of dogs can remove or reduce the risk of rabies transmission to humans. In many countries, dogs are culled as part of a strategy to eliminate rabies, but this only reduces rabies transmission temporarily. Vaccinating dogs, including puppies, is the most cost-effective strategy for preventing rabies transmission in humans because it stops the transmission at its source and has been shown to be cost-effective in most settings *(67)* (Box 5).

BOX 5. Rabies and rabies control initiatives

Rabies is a vaccine-preventable, zoonotic, viral disease that is almost 100% fatal. Globally, rabies is present on all continents except Antarctica, but over 95% of human deaths occur in Africa and Asia. Almost 40% of the estimated 59 000 rabies annual deaths occur in children aged under 15 years.

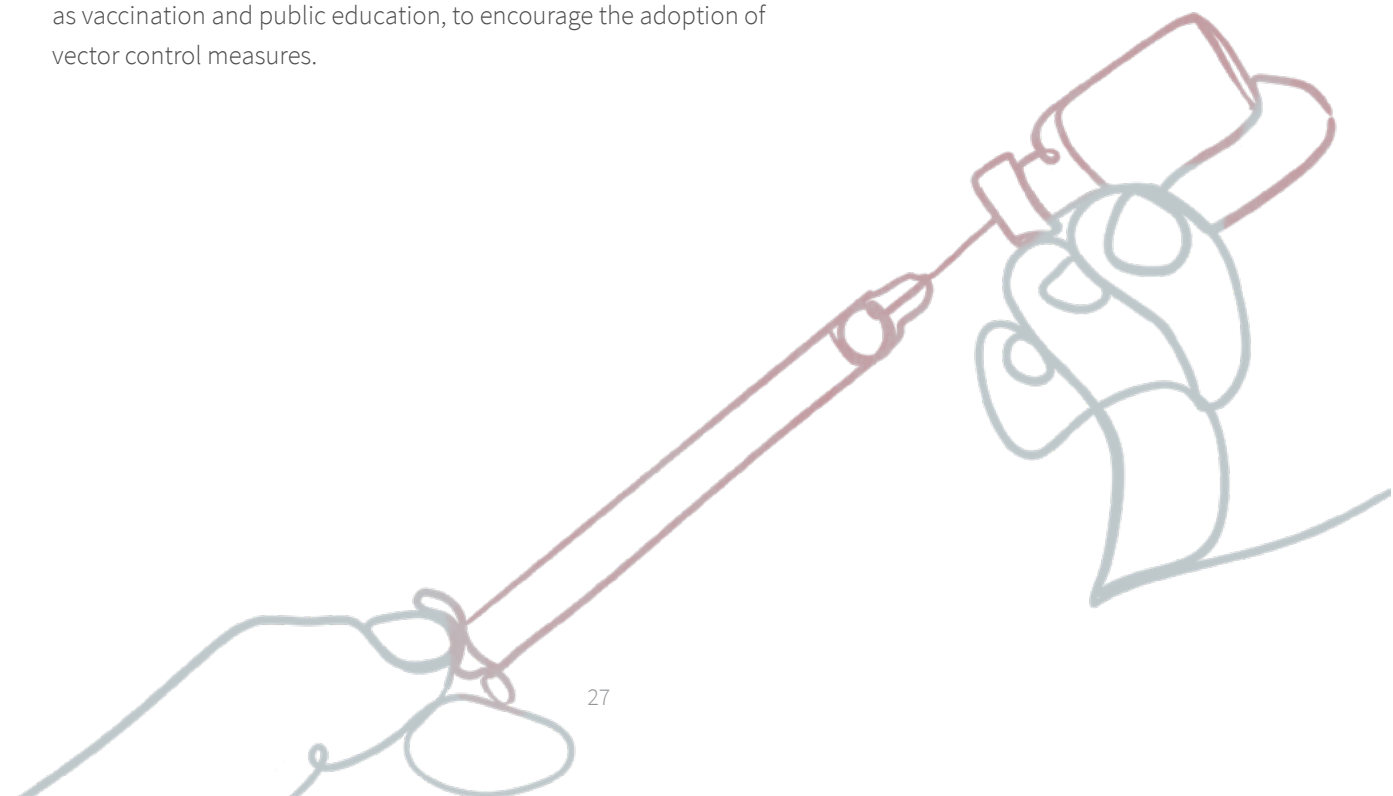
People are usually infected with rabies following a deep bite or scratch from an animal with the disease; in 99% of the cases, this animal is a dog. In regions where dog-mediated transmission is interrupted, rabies can be contracted from bats, cats, foxes, raccoons and other wild mammal species.

Pre-exposure vaccination and post-exposure prophylaxis are highly effective in preventing rabies. Even so, these are often not readily available or accessible to those in need; also, if they are available, they can trigger catastrophic health expenditures. Vaccinating dogs, including puppies, is the most cost-effective strategy for preventing rabies transmission in humans because it stops the transmission at its source. *(67, 78, 91)*

Key actions for vector-borne and zoonotic disease control

Multiple WHO initiatives provide guidance relevant to strengthening vector-borne and zoonotic disease control *(67, 86, 90)*. These include:

- promoting environmental modifications via interdisciplinary engagement with municipal planners or village local bodies and environmental management departments;
- improving guidance for the evaluation and implementation of vector control programmes; and
- integrating such programmes with other preventive actions, such as vaccination and public education, to encourage the adoption of vector control measures.



Young boy proudly showing the rabies vaccination certificate of his dog.
© Anna Czupryna

Research and innovation

Multiple areas of both infectious and autoimmune encephalitis remain under-researched, particularly in LMIC. Encephalitis research needs to include further information on the burden of encephalitis, including health economics data, particularly in LMIC; a better understanding of the severity of the disease (including disability and mortality); and information on strengthening routine health information systems. Further areas for research focus include the identification of biomarkers, a better understanding of the molecular mechanisms of disruption of the blood–brain barrier, an understanding of neurotropism, and the potential of immunomodulatory agents and antiviral medicines to reduce the sequelae from encephalitis.

For autoimmune encephalitis, in particular, data from LMIC are limited and antibody testing in Africa, Asia and South America is lacking; this affects both surveillance and clinical care. Given that autoimmune encephalitis is not yet fully understood, the way forward could be standard case definitions, standard approaches to surveillance and standard diagnostics, with subsequent pooling of data. Biobanks for infectious causes could be useful in parts of the world where diagnostics are less available, as a surveillance mechanism to revisit unappreciated outbreaks that may have occurred in the past and could inform empirical treatment regimens; such outbreaks may be useful in the future when newer technologies can be employed. Training on the practicalities of biobanking needs to focus on how to process samples, fund biobanks, ensure the functionality of freezers and ensure that samples are not degraded over time *(18)*.

Incentives are needed for the development of technology and products such as quality-assured multiplex assays or biomarkers for use in settings with the fewest resources and the greatest disease burden. Studies on the clinical applications of novel diagnostics, including host biomarkers, are needed to differentiate among different CNS disorders including autoimmune etiologies. In this context, research priorities should include biomarkers with short turnaround times and minimal implementation barriers in resource-limited settings.

For encephalitis sequelae, randomized controlled trials (RCTs) are required to investigate the efficacy and safety of discontinuation of antiseizure medication in individuals with acute symptomatic seizures or epilepsy due to

Priorities should include the development of affordable, accurate diagnostic tools; optimization of existing vaccines; creation of new treatments; and enhanced understanding of the long-term sequelae of encephalitis.

encephalitis *(92)*. The lack of observational studies on sequalae rehabilitation following encephalitis and of RCTs comparing different rehabilitation options indicates a neglected area of research within encephalitis management and care that should be prioritized.

These advances must be coupled with implementation research, and policy and programme evaluations to assess the effectiveness of on-the-ground strategies for encephalitis prevention, education and care. International partnerships between academic bodies, research funders and nonprofit organizations should help to secure funding and prioritize research with the greatest potential for impact.

Key actions for research and innovation

Prioritize research into infectious and autoimmune encephalitis, including sequelae that addresses the following top research gaps:

- data on the burden of encephalitis in terms of mortality, morbidity (including disability) and financial impact, particularly in LMIC;
- surveillance data on disease etiology and changes in seasonal and demographic patterns, especially outside HIC, to facilitate more accurate estimates of encephalitis burden and cost;
- optimization of current vaccines and the development of new vaccines;
- development of accurate and affordable diagnostic panels;
- development of new pathogen-specific and autoimmune treatments, and improved applications of existing treatments;
- increased understanding of brain infection sequelae and recovery trajectories; and
- increased research on autoimmune encephalitis – its mechanisms, new subtypes, affordable testing panels, long-term trajectories, and the therapeutic effectiveness of available and novel immunomodulatory agents; critically, such research must be coupled with expanding awareness and clinical recognition, to prevent misdiagnosis and implement appropriate treatment and care.

Policy prioritization and governance

As the threat of encephalitis continues to grow, effective and timely strategies need to be adopted as soon as possible, to respond to ongoing encephalitis epidemics and prepare for new ones. Political commitment is required to develop strategies, programmes and services that are effective for people with encephalitis and their families and carers.

Currently, some countries are formulating national plans for meningitis that are tailored to a local context, designed as multiyear plans that are regularly monitored, evaluated and updated. Other countries have indicated that their preferred option is to have a well-defined set of activities pertaining to brain infections and their sequelae that can be integrated into existing strategic and operational national plans (e.g. national communicable disease manual, national health strategic plans, and other plans, programmes or documents). These national plans, as well as regional plans on meningitis that have been or are being developed, give an ideal entry point to incorporate meningoencephalitis and encephalitis into regional and national plans *(93)*.

As outlined in IGAP's first strategic objective, political commitment, funding, legislation and advocacy are crucial to helping people with encephalitis, their families, caregivers and society. The IGAP implementation toolkit *(55)* and other WHO guidance recommend various strategic approaches that can be used concurrently.

Key actions for policy prioritization and governance

- Maintain political commitment and allocate funding by working with a range of stakeholders, including people with lived experience, their families and carers, industry, academia, nongovernmental organizations (NGOs), health care providers, and community members such as traditional healers.

- Harness resources such as those provided by WHO for neurological disorders *(17, 55)*, brain infections *(16, 93)* and rehabilitation *(61)* through UHC to create national action plans for neurological diseases. Such plans can include encephalitis directly; however, because they cover neurological disorders as a whole, they are also likely to improve the landscape for encephalitis.

- Introduce legislation to reduce stigma and discrimination, and to improve social participation for people with neurological conditions including the long-term sequelae of encephalitis *(28)*.

World Encephalitis Day, celebrated each year on February 22d, is a global awareness campaign dedicated to raising awareness about encephalitis.

Celebration of World Encephalitis Day 2020 in South Africa
© Encephalitis International

Public awareness and education

Raising awareness of brain infections as an urgent public health priority among funders and policy-makers can mobilize resources to address the current increasing trends of encephalitis seen today. Awareness can be raised, for example, by using the voices of national and international champions, civil society organizations, advocacy groups and health care providers, including the disability sector. Increasing public awareness of encephalitis is an important tool to improve health care seeking behaviour, vaccination uptake, adoption of preventive measures and compliance with investigations such as lumbar punctures and treatments.

There are insufficient encephalitis engagement and education campaigns, particularly those adapted to local languages and cultural contexts. Challenges to education also include limited knowledge of encephalitis

> *The first hospital I went to I was misdiagnosed. I was given psychotropic drugs, medication for schizophrenia and bipolar disorder and my situation got even worse. I was very erratic, out of control. Hallucinating. What they did was they handcuffed me to the bed. I could have died in that hospital.*
>
> *Luckily, my family was able to move me to another hospital. I was really lucky to have been able to go there. The whole thing started with olfactory hallucinations, visual hallucinations. Sleeplessness. Paranoia. These are all things that can be attributed to many things. But now that people know more and more about encephalitis, I'm really happy. I gave my entire medical file to several gynaecologists and they [subsequently] diagnosed a number of people with ovarian teratoma encephalitis.*
>
> *So when you talk about awareness and all that, it's really, really critical for this information to be available across all borders and in various languages.*
>
> *– A person with anti-NMDA receptor encephalitis*

Campaigns and appropriate use of social media can help to reduce the stigma and discrimination.

among health professionals, who may not be able to offer education to the public; possible mistrust of community health workers; social media misinformation; and poor previous experiences with the health systems.

Campaigns and appropriate use of social media can help to reduce the stigma and discrimination associated with some neurological sequelae such as epilepsy. They may also promote information and increase awareness of the impact of the condition on those affected.

Increasing the general public's understanding of encephalitis and its preventive measures can complement vaccination and vector control strategies. Education on preventive measures should be evidence based, easily comprehensible and culturally appropriate in local languages; also, it should build on partnerships with those delivering care to the communities including community health workers, NGOs and traditional healers *(17, 28)*. Education should also include information on support sources and sequelae management for people with encephalitis. Resources already developed by international organizations can be used, and encephalitis can be included in brain health education campaigns. Social media can be used as an education platform to increase reach and counteract misinformation.

Key actions for public awareness and education

- Support advocacy initiatives for encephalitis such as World Encephalitis Day, to target both national and international decision-makers and thus bring alignment and collaboration across countries, regions and independent international partners.
- Promote the inclusion of people with lived experience who also have training in health diplomacy, to further spread the message *(94)*.

Conclusion

Encephalitis represents a significant yet under-recognized global health challenge, marked by substantial mortality, disability burden and economic impacts. The disease is likely to further expand its reach owing to large population densities in resource-limited settings, proximity to animals through human encroachment, intensive farming practices, vaccine hesitancy, climate change, urbanization and global trade. Emerging and re-emerging viral outbreaks of encephalitis are increasing, and identification and recognition of autoantibodies are contributing to the expanding number of autoimmune encephalitis cases. The diverse etiology of encephalitis, ranging from over 100 infectious pathogens to autoimmune causes, underscores the complexity of diagnosis and management. Critical gaps persist in timely recognition, diagnostic capabilities, and access to treatment and care; these gaps are then exacerbated by global inequities in health care. The true global burden of encephalitis is currently unknown, particularly in LMIC; however, the heavy costs associated with neurological sequelae and the impact on families are undisputed and increasingly being recognized.

The true global burden of encephalitis is currently unknown, particularly in LMIC; however, the heavy costs associated with neurological sequelae and the impact on families are undisputed and increasingly being recognized.

Central to reducing the burden of encephalitis are vaccination strategies and the establishment of robust surveillance systems to monitor disease incidence, track emerging pathogens and guide evidence-based interventions. Vaccination programmes remain among the most effective public health measures; however, the challenges posed by vaccine hesitancy, inadequate supply chains and the complex interplay of climate change, intensive farming practices and urbanization on vector-borne diseases remain formidable. Vaccination campaigns and vector control strategies, supported by the One Health approach, offer a sustainable path forward to quantify and reduce the encephalitis burden, monitor etiological patterns, detect emergent and spreading pathogens, and prepare for future epidemics.

Strengthening health systems is equally critical. Delivery of comprehensive encephalitis care requires strengthening of all dimensions of health systems, including the explicit addition of integrated services for encephalitis in national UHC frameworks to foster accessibility and affordability and the provision of acute diagnostics, treatment, rehabilitation, long-term care, and social, financial and carer support services. These efforts must be partnered with people with lived experience who can advocate for a better response to neurological disorders.

Progress in these areas should be underpinned by quality medical and public health research, and the generation of new advances. Research and

innovation will continue to advance our understanding of encephalitis and improve outcomes. Priorities should include the development of affordable, accurate diagnostic tools; optimization of existing vaccines; creation of new treatments; and enhanced understanding of the long-term sequelae of encephalitis. The expansion of research in LMIC, where data are the most limited, is particularly important to inform localized, adapted interventions. Collaborative efforts between academia, industry and international organizations will be vital in driving this progress.

Public awareness and education also play a pivotal role in improving health care seeking behaviour, reducing stigma, and ensuring adherence to preventive measures such as vaccination and vector control. Targeted campaigns tailored to cultural contexts and local languages can empower communities and health care providers alike, fostering a shared understanding of the disease and its impacts.

Prioritizing encephalitis within global and national health agendas, mobilizing resources for targeted interventions, and fostering collaboration among stakeholders can significantly reduce the potential global threat and disease burden. Together, these efforts promise to improve health outcomes, enhance the quality of life for those affected, and build resilient health systems capable of responding to this growing public health challenge.

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