Encephalitis International
The brain inflammation non-profit

Encephalitis:

an in-depth review and gap analysis of key variables affecting global disease burden

Dr Julia Granerod · Alina Ellerington · Dr Nicholas Davies · Professor Benedict Michael · Professor Tom Solomon · Dr Ava Easton

Encephalitis

an in-depth review and gap analysis of key variables affecting global disease burden

Dr Julia Granerod, Alina Ellerington, Dr Nicholas Davies, Prof Benedict Michael, Professor Tom Solomon CBE, Dr Ava Easton MBE

Contents

List of Tables

List of Figures

Abbreviations

ABI	Acquired brain injury
ABLV	Australian bat lyssavirus
ADEM	Acute disseminated encephalomyelitis
AES	Acute encephalitis syndrome
ALS	Amyotrophic lateral sclerosis
AMPAR	α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor
AMR	Region of the Americas
AR	African region
CASPR2	Contactin-associated protein-2
CFR	Case fatality rate
CHW	Community health worker
CMV	Cytomegalovirus
CNS	Central nervous system
CSF	Cerebrospinal fluid
D2R	Dopamine-2 receptor
DALYs	Disability-adjusted life years
DNA	Deoxyribonucleic acid
DPPX	Dipeptidyl-peptidase-like protein-6
EAN	European Academy of Neurology
EBV	Epstein Barr virus
EBVL	European bat lyssavirus
ECDC	European Centre for Disease Prevention and Control
EEEV	Eastern equine encephalitis virus
EFNS	European Federation of Neurological Societies
EFTA	European Free Trade Association
ELISA	Enzyme-linked immunosorbent assay
EMR	Eastern Mediterranean Region
EU	European Union
EUR	European Region
EV	Enterovirus
GABAaR	γ-aminobutyric acid-A receptor
GABAbR	γ-aminobutyric acid-B receptor
GAVI	Global Alliance for Vaccines and Immunisation
GBD	Global Burden of Disease
GlyR	Glycine receptor
GOS	Glasgow Outcome Scale
GP	General practitioner
HHV-6	Human herpesvirus-6
HIC	High-income country
HSE	Herpes simplex encephalitis
HSV	Herpes simplex virus
ICD	International Classification of Disease
ICU	Intensive care unit
ID	Intradermal
IGAP	Intersectoral global action plan
IHME	Institute for Health Metrics and Evaluation
IM	Intramuscular
IQR	Interquartile range
IV	Intravenous
JE	Japanese encephalitis
JEV	Japanese encephalitis virus
LCMV	Lymphocytic choriomeningitis virus

LGI-1	Leucine-rich, glioma-inactivated 1
LIC	Low-income country
LMIC	Low- and middle-income country
mGluR5	Metabotropic glutamate receptor 5
MMSE	Mini mental state examination
MND	Motor neuron disease
MOG	Myelin oligodendrocyte glycoprotein
MRI	Magnetic resonance imaging
MS	Multiple sclerosis
MVEV	Murray Valley encephalitis virus
NMDAR	N-methyl-D-aspartate receptor
PCR	Polymerase chain reaction
PDR	People's Democratic Republic
PEP	Post-exposure prophylaxis
PICU	Paediatric intensive care unit
RDT	Rapid diagnostic test
RIG	Rabies immunoglobulin
RNA	Ribonucleic acid
RR	Rate ratio
RT-PCR	Reverse transcriptase- polymerase chain reaction
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SEAR	South-East Asian Region
SLEV	St. Louis encephalitis virus
SSPE	Subacute sclerosing panencephalitis
TB	Tuberculosis
TBE	Tick-borne encephalitis
TBEV	Tick-borne encephalitis virus
UMIC	Upper-middle-income country
UN	United Nations
US	United States
VEEV	Venezuelan equine encephalitis virus
VENICE	Vaccine European New Integration Collaboration Effort
VZV	Varicella zoster virus
WEEV	Western equine encephalitis virus
WFN	World Federation of Neurology
WHO	World Health Organization
WNV	West Nile virus
WPR	Western Pacific Region

1 Executive Summary

Encephalitis is a thief. In the same way that we have watched other neurological conditions rob people of their lives and loved ones, encephalitis has quietly been at work for hundreds—if not thousands—of years. It robs families of those they love, and even where life is spared, it often steals the very essence of a person: their memories, personality, and the abilities many of us take for granted—concentration, judgement, inhibition, and independence. For many, the consequences extend further, including epilepsy and profound, life-limiting fatigue that can make a return to work or education impossible. And for too many, survival is not the outcome.

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.

For decades, encephalitis has been overlooked—frequently mischaracterised as rare and relegated to the margins of neurological and global health priorities. Yet evidence, including that presented in this report and reinforced by the World Health Organization's technical brief on encephalitis, demonstrates that encephalitis is neither rare nor insignificant. In many countries, its incidence exceeds that of motor neuron disease/ALS, bacterial meningitis, and multiple sclerosis. The WHO further highlights encephalitis as a public health concern, and a complex and growing global health challenge, shaped by emerging and re-emerging infections, climate change, population movement, and persistent inequities in health systems, particularly in low- and middle-income countries.

Crucially, the WHO technical brief underscores long-standing and systemic gaps that this report also identifies: inconsistent surveillance, under-recognition and misdiagnosis, limited access to timely diagnostics (including cerebrospinal fluid testing), and inequitable access to treatment and rehabilitation. It also draws attention to the substantial, yet often hidden, long-term burden on individuals, families, and societies—burdens that extend far beyond the acute phase of illness and are insufficiently captured in current data systems.

At the same time, there is cause for optimism. Scientific advances, improved understanding of infectious and autoimmune causes, and the availability of effective vaccines for several encephalitis-causing pathogens mean that prevention, earlier diagnosis, and better outcomes are within reach. The WHO calls for a coordinated, multi-sectoral response—one that integrates surveillance, diagnostics, clinical care, vaccination, and long-term support—echoing the priorities and recommendations set out in this report.

Encephalitis International is over 30 years old and has developed unparalleled expertise in the condition and its lifelong impact on patients, families, and those bereaved. Strengthened governance, infrastructure, and a dedicated global approach have enabled us to annually update this comprehensive global baseline situational analysis. This report represents a collaborative effort involving our Chief Executive and leadership team, Global Scientific Advisory Panel, and Board of Trustees, alongside other global partners and stakeholders.

This report not only defines the scale and scope of the problem—from epidemiology and economic burden to prevention, diagnosis, treatment, and survivorship—but also sets out practical, evidence-informed solutions. Importantly, it aligns with and operationalises the priorities articulated by the WHO technical brief, positioning encephalitis firmly within the global health agenda.

Encephalitis International is uniquely placed to convene and lead a global, collaborative response. Building on the momentum generated by both this report and the WHO's calls to action, we will bring together international health organisations, governments, clinicians, researchers, and patient communities to drive meaningful change. This will include strengthening surveillance systems, improving access to diagnostics and vaccines, advancing research, and ensuring that the voices and needs of those affected are central to all efforts.

Now is the moment to act. The convergence of new global evidence, growing recognition, and clear strategic direction presents a rare opportunity to transform outcomes for people affected by encephalitis worldwide. This report is not just an analysis—it is a catalyst. It marks the beginning of a coordinated global commitment to reduce the incidence of encephalitis, minimise its devastating impacts, and build a future where fewer lives are lost, fewer futures are diminished, and more people are able to survive—and truly live—beyond encephalitis.

2 Overview

2.1 Purpose

This report, first published in 2021, was intended to inform the creation of a robust and ambitious strategic plan for Encephalitis International's global development and to provide a sound basis to inform its key priorities and collaborations with other global leaders in the fields of infectious and autoimmune disease. It has already contributed to the development of a seminal World Health Organization (WHO) Technical Brief on encephalitis (1). It is updated on an annual basis. Encephalitis International (formerly The Encephalitis Society; www.encephalitis.info) is an award-winning UK-based charity/non-profit with a global focus and has been in operation since 1994. It operates in three primary areas: providing support and information to patients and families affected by the condition; raising global awareness of the condition (its primary vehicle for this being World Encephalitis Day); and funding, promoting, and collaborating on research with academic, scientific, and medical partners around the world.

2.2 Scope

Encephalitis is inflammation and swelling of the brain, most often caused by an infection or by the body's immune defences. Encephalitis is a growing global threat due to a variety of factors such as climate change, vaccine hesitancy, co-circulation of viruses, continued unexplained cases, increasing identification of autoimmune causes, recurrence and spread of epidemics, as well as the high mortality and morbidity associated with the condition, and its economic impact for those affected and the wider community. This report provides an in-depth analysis of 12 variables where change could make an impact on the global encephalitis burden. The variables were selected by Encephalitis International and its expert scientific and medical advisors. These variables are:

1) Cause;
2) Incidence;
3) Morbidity and mortality;
4) Economic impact;
5) Prevention including vaccine programs, vector control, and epidemic control;
6) Diagnosis and treatment;
7) In-country neurologists and access to neurology training;
8) Surveillance;
9) New and emerging infections;

10) Advocacy;
11) Support and after-care for survivors and families; and
12) Availability of and access to information.

2.3 Methodology

For the scientific chapters (Chapters three to nine) a literature search was carried out via Pubmed for academic papers reporting on each above-mentioned variable. A comprehensive search strategy was devised for each variable separately based on search terms, keywords, and phrases (see details of specific searches in Appendix 16.1). Bibliographies of acquired articles were searched for further relevant papers. In addition, a free-text internet search for grey literature using the Google search engine was conducted. It is worth noting that as data acquisition relied largely on published data and internet searches, relevant data unavailable via these means may not be included in this report.

A traditional rather than systematic review was carried out for each pre-identified variable as a systematic review generally addresses a specific question whereas the remit of this work was very broad, hypotheses were not stated, and summary measures were not reported. In addition, systematic reviews require pre-defined article inclusion and exclusion criteria, search of multiple databases and websites including unpublished data, assessment of article quality, and two reviewers judge which articles should be included/excluded (at least for a proportion of articles retrieved). This was not considered feasible given the broad range and reach of the topics addressed in this report.

Chapters 10, 11, and 12 were composed from the observations, understanding, and lived experience of patients supported by Encephalitis International, published literature, and data from the Brain Infections Global study (2).

3 Epidemiology of encephalitis

3.1 Causes

Encephalitis or inflammation of the brain is a syndrome of multiple pathogeneses and aetiologies. Encephalitis can result from direct infection of the central nervous system (CNS) or it can be immune-mediated. More than 100 different organisms have been recognised as causative agents, some of which have a worldwide distribution and others which are geographically restricted (3).

3.1.1 Causes with worldwide distribution

Herpes simplex encephalitis (HSE) occurs worldwide; approximately 50% to 90% of adult populations in all parts of the world are seropositive for herpes simplex virus (HSV) infections and encephalitis occurs in a minority of those infected (4). HSV is the most common reported infectious cause of encephalitis in industrialized countries (5). Boucher et al. reviewed the literature for articles on infectious causes of encephalitis published between 2000 and 2015 (6). Twenty-five studies were retrieved, including prospective and retrospective studies from tropical and temperate countries. In 65% of studies, including those from North America, Europe, Australia/New Zealand, and one from Asia, HSV was the most common identified aetiological agent (Figure 1). There were limited studies from Africa and South and Central America included in the review by Boucher et al.; however, studies published subsequently identified HSV as a common cause of encephalitis in Peru and Colombia (7,8). Studies from Africa are lacking and diagnostic capacity limited (see Section 6.1.3.2); however, recent studies from Senegal and Egypt identified HSV as an important cause of encephalitis (9,10).

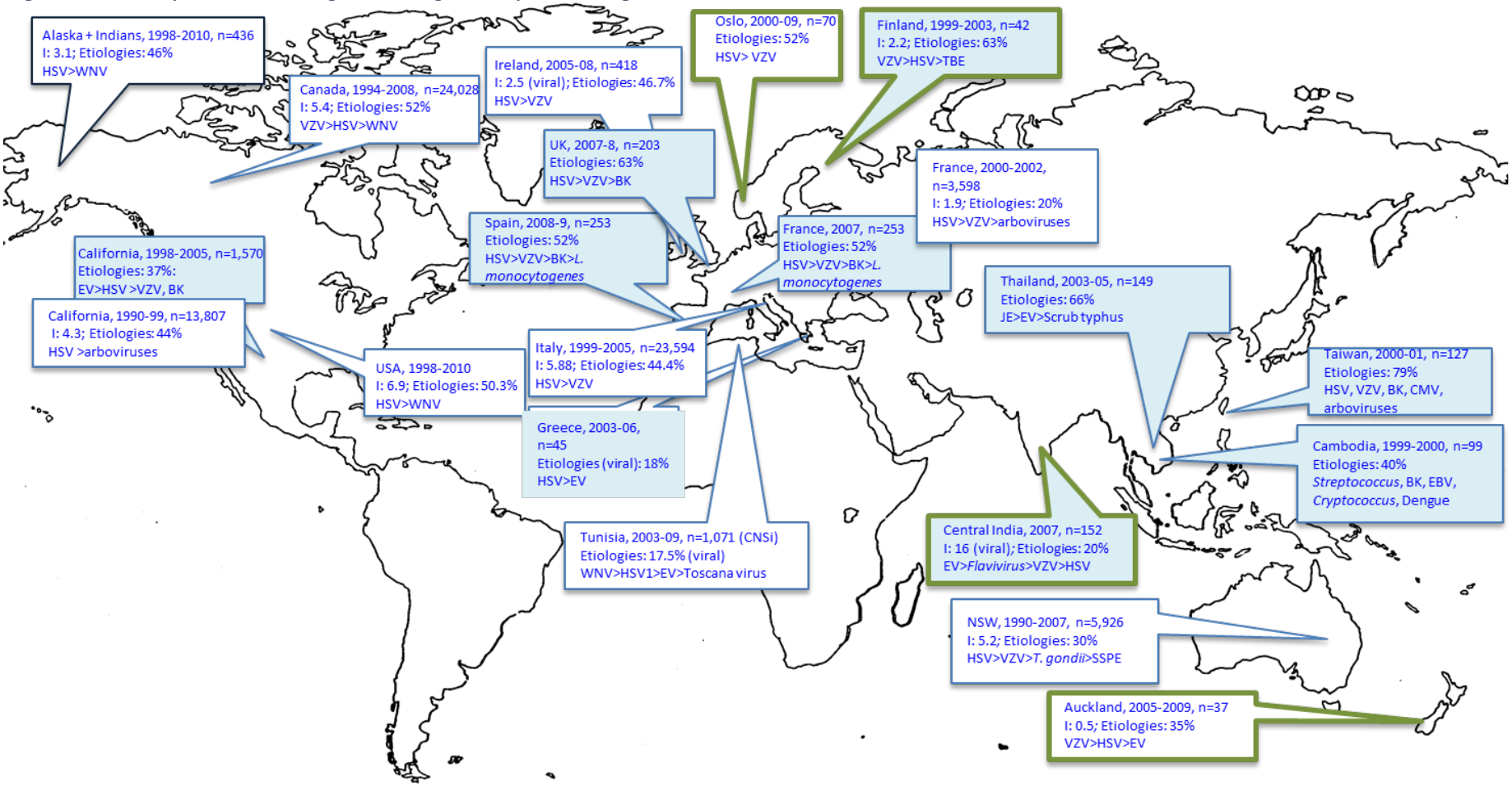
Varicella zoster virus (VZV) and enteroviruses (EV) were also reported by Boucher et al. as frequent causes of encephalitis in North America, Europe, Asia, and Australia/New Zealand (Figure 1). VZV is the second most common cause of encephalitis in industrialized countries, after HSV (11–14). EV71, which causes severe encephalitis in 3% of neurological presentations, has been responsible for epidemics in Southeast Asia and the Pacific since 1997 and there have been reports of a few epidemics outside Asia, notably in Australia/Oceania, United States of America (USA), Europe, Japan, and Brazil (6). Other causes of infectious encephalitis with a worldwide distribution include other herpesviruses (Epstein Barr virus [EBV], cytomegalovirus [CMV], human herpesvirus-6 [HHV-6]), mumps, measles, rubella, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), JC virus, human immunodeficiency virus (HIV), and lymphocytic choriomeningitis virus (LCMV; Table 1) (15).

Although viruses are responsible for most encephalitis cases due to infection, bacteria, parasites, and fungi can also cause encephalitis. As with viruses, these other causes of encephalitis can be distributed worldwide or restricted geographically. *Mycobacterium tuberculosis* and *Mycoplasma pneumoniae* are two important bacterial causes of encephalitis with a worldwide distribution. A prospective French study identified *M.tuberculosis* and *Listeria monocytogenes* as the most frequently identified bacterial causes of encephalitis in 2007 (14). *M.tuberculosis* was also identified as an important cause in a UK study (16). *M.pneumoniae*

is frequently associated with encephalitis, and infection with *M.pneumoniae* is established in 5-10% of paediatric encephalitis patients (17–19). However, *M.pneumoniae* is rarely found in the cerebrospinal fluid (CSF) suggesting an immunoinflammatory pathogenic mechanism rather than direct CNS infection (6).

About half of all encephalitides with known cause are thought to be immune-mediated (20). Autoimmune encephalitis may be predominantly demyelinating brain disease (e.g., acute disseminated encephalomyelitis [ADEM]), in the context of systemic autoimmune disorders (e.g., systemic lupus erythematosus), in the setting of a steroid-responsive condition associated with elevated antithyroid antibodies (e.g., Hashimoto's encephalopathy), or in association with antineuronal antibodies (21). ADEM predominantly affects children and can often be temporally linked to upper respiratory tract symptoms or an acute febrile illness in the days/weeks prior to neurological symptom onset. Granerod et al. identified viruses such as enteroviruses, EBV, HHV-6, and parainfluenza, and bacteria including *M.pneumoniae*, *Bartonella henselae*, and streptococci as the main microbes associated with ADEM worldwide (11). Different pathogenic mechanisms have been suggested for ADEM, and a subset of individuals have evidence of antibody-associated autoimmunity against myelin oligodendrocyte glycoprotein (MOG) (22). More recently, cortical encephalitis has been reported in patients with anti-MOG autoantibodies (23,24). Over the last two decades, technological improvements have enabled the discovery of autoimmune encephalitides associated with antibodies against neuronal surface targets (25) (Table 2; Figure 2). Anti N-methyl-D-aspartate receptor (NMDAR) encephalitis, first identified in 2007, is the most common of these in younger age groups, while leucine-rich, glioma-inactivated 1 (LGI-1)-antibody encephalitis appears most common in those >50 years of age (26). This will however likely change in the future with the discovery of further antibody epitopes and increasing testing specificity. Other causes include for example contactin-associated protein-2 (CASPR2)-antibody encephalitis, γ-aminobutyric acid-B receptor (GABAbR), and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) antibodies (27). Immune-mediated causes of encephalitis have a worldwide distribution as their pathogenesis is not dependent on external factors, including vectors and climate. However, one study showed higher incidence (and possibly more severe phenotype) of anti-NMDAR encephalitis in Maori and Pacific Island children compared to children without this ancestry, which may suggest a genetic predisposition in some populations perhaps affecting distribution (28). It is highly likely that further autoimmune causes account for some of the 30-40% of cases that lack an aetiological diagnosis (21).

Figure 1 – Encephalitis aetiologies from global epidemiological studies



Adapted from Boucher et al. (6) *Blue background: prospective studies; white background: retrospective studies. Green-boxed text: studies including adults; black-boxed text: studies including children and adults.*
BK = BK virus; CMV = Cytomegalovirus; EBV = Epstein Barr virus; EV = Enterovirus; HSV = Herpes simplex virus; I = Incidence per 100,000 population; JE = Japanese encephalitis; SSPE = Subacute sclerosing panencephalitis; TBE = Tick-borne encephalitis; VZV = Varicella zoster virus; WNV = West Nile virus

Table 1 – Global distribution of viral causes of encephalitis

Virus	Distribution	Transmission
Herpes viridae		
HSV	Worldwide	Human to human
VZV	Worldwide	Human to human
EBV	Worldwide	Human to human
CMV	Worldwide	Human to human
HHV-6	Worldwide	Human to human
Cercopithecine herpes virus 1	Old world except for Madagascar	Monkey bite or scratch or spitting
Arboviruses		
WNV	North and South America, Middle East, Africa, Europe, Australia/Oceania, and Southern Asia (Kunjin)	Vector (various mosquito species [mainly Culex spp.])
JEV	Asia and South East Asia, Australia/Oceania	Vector (*Culex spp*.)
SLEV	North and South America	Vector (*Culex spp.*)
TBEV	Central and Eastern Europe, Russia	Vector (*Ixodes spp*.)
EEEV	Eastern half of North and South America, from Canada to Argentina	Vector (various mosquito species)
WEEV	Western half of North and South America from Canada to Argentina	Vector (*Culex tarsalis*)
VEEV	North and South America	Vector (*Aedes, Psorophora spp.*)
LaCV	North America	Vector (*Aedes spp.*)
TOSV	Mediterranean Basin	Vector (*Phlebotomus perniciosus* and *P.perfiliewi)*
CTFV	North America	Vector (*Dermacentor spp*.)
Others		
Rabies virus	Worldwide except for Western Europe, Japan, other islands	Carnivorous mammals, or bat bite, or scratch, or licking on wounded skin or mucosae, graft transmission possible although rare
Mumps virus	Worldwide	Human to human
Measles virus	Worldwide	Human to human
Rubella virus	Worldwide	Human to human
Henipah viruses	Nipah: Malaysia, Bangladesh, India Hendra: Australia/Oceania	Probably airborne, or contact with animal feces, from fruit bats. Pigs may be possible intermediate hosts.
JC virus	Worldwide	Human to human
HIV	Worldwide	Human to human
Enteroviruses	Worldwide	Human to human
LCMV	Worldwide	Airborne from rodent feces
Influenza	Worldwide	Human to human, airborne

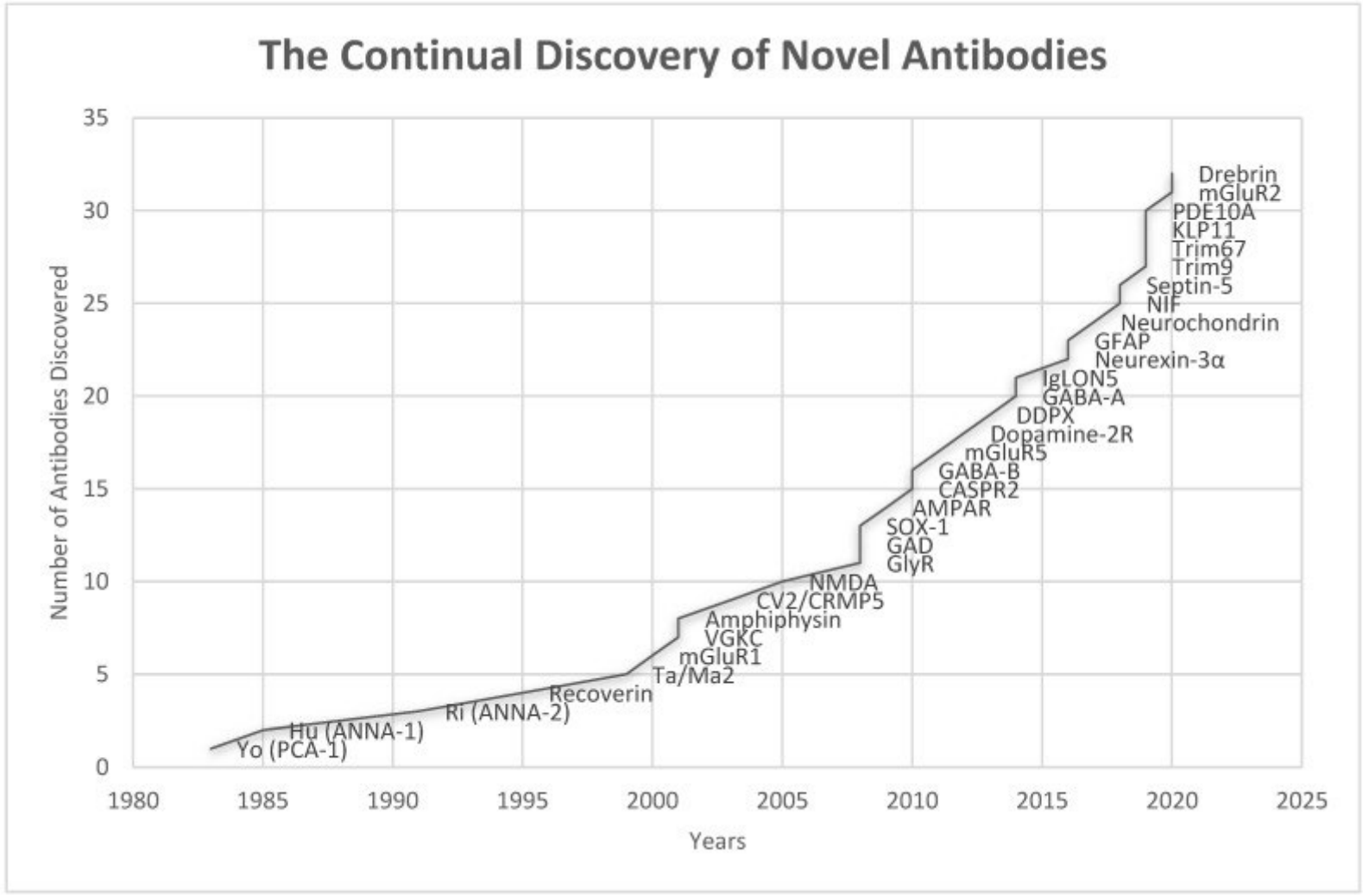
Adapted from Stahl et al. **(15)**; *CMV = Cytomegalovirus; CTFV = Colorado tick fever virus; EBV = Epstein Barr virus; EEEV = Eastern equine encephalitis virus; HHV-6 = Human herpesvirus-6; HIV = Human immunodeficiency virus; HSV = Herpes simplex virus; JEV = Japanese encephalitis virus; LaCV = La Crosse virus; LCMV = Lymphocytic choriomeningitis virus; SLEV = Saint Louis encephalitis virus; TBEV = Tick-borne encephalitis virus; TOSV = Toscana virus; VEEV = Venezuelan equine encephalitis virus; VZV = Varicella zoster virus; WEEV = Western equine encephalitis virus; WNV = West Nile virus*

Table 2 - Autoimmune causes of encephalitis associated with antibodies against neuronal surface targets

Neuronal surface antibody target	Distribution	First reported (reference)
MOG	Worldwide	2007 (22)
NMDAR	Worldwide	2007 (29)
GlyR	Worldwide	2008 (30)
AMPAR	Worldwide	2009 (31)
GABAbR	Worldwide	2010 (32)
LGI1	Worldwide	2010 (33)
CASPR2	Worldwide	2010 (33)
mGluR5	Worldwide	2011 (34)
D2R	Worldwide	2012 (35)
DPPX	Worldwide	2013 (36)
GABAaR	Worldwide	2014 (37)
Neurexin-3α	Worldwide	2016 (38)

Adapted from Zuliani et al. (39)
AMPAR = α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; CASPR2 = Contactin-associated protein-2; DPPX = Dipeptidyl-peptidase-like protein-6; D2R = Dopamine-2 receptor; GABAaR = γ-aminobutyric acid-A receptor; GABAbR = γ-aminobutyric acid-B receptor; GlyR = Glycine receptor; LGI1 = Leucine-rich, glioma-inactivated protein-1; mGluR5 = Metabotropic glutamate receptor 5; MOG = Myelin oligodendrocyte glycoprotein; NMDAR = N-methyl-D-aspartate receptor

Figure 2 – Timeline of the discoveries of antibodies associated with autoimmune encephalitis



From Patel et al. (40)

3.1.2 Causes which are geographically restricted

Infectious agents transmitted by vectors or animals, or that have an animal host, cause encephalitis in geographically restricted areas (Table 3). This is a result of the ecological range of the vector or the reservoir, or because of geographically or culturally specific behaviour that puts individuals at risk (3). Arboviruses are the most important of these. Most arboviral infections are asymptomatic and only a small proportion result in neurological disease. Approximately 100,000 global Japanese encephalitis virus (JEV) cases are thought to occur annually (41). Japanese encephalitis (JE) is a vector-borne zoonotic disease primarily transmitted by *Culex* mosquitoes. JEV transmission often occurs in rural agricultural areas associated with rice production and flooding irrigation as this is where mosquito vectors breed. The virus exists in a cycle between mosquitos, pigs, and/or water birds; humans are dead-end hosts. JE occurs throughout most of Asia and parts of the Western Pacific (Figure 1), and JEV has recently been detected in humans, animals, and mosquitoes in mainland Australia (6,42). Tick-borne encephalitis virus (TBEV) was more frequently reported in Eastern and Northern Europe as well as in Russia in the studies included in the review by Boucher et al. (Figure 1) (6). Tick-borne encephalitis (TBE) is caused by three subtypes of TBEV including European, Siberian, and Far-Eastern, and is endemic in central, eastern, and northern Europe; the Urals region, Siberia, and far-eastern Russia; and in forested regions of China and Japan (43). Boucher et al. reported that other arboviruses, mainly Flaviviruses and Alphaviruses, were more frequent in North American studies (Table 3) (6). These include predominantly West Nile virus (WNV), Saint Louis encephalitis virus (SLEV), and La Crosse virus. WNV, first detected in the Western hemisphere in 1999, has rapidly spread across North and South America and resulted in a massive outbreak across southern and central Europe in 2018 (44). Between 1999 and 2008 almost 30,000 cases of WNV were reported in the US; 41% of these were neuroinvasive (45). Rarer arboviral causes include Powassan virus, Eastern equine encephalitis virus (EEEV), and Western equine encephalitis virus (WEEV) amongst others (Table 3). Human rabies is a Lyssavirus and results in an acute progressive encephalitis that is almost always fatal after the onset of clinical symptoms (46). An estimated 59,000 human deaths occur each year due to rabies, mainly in Asia and Africa (47). The primary reservoir of the virus and main source of human infections are dogs. Although classical canine rabies is no longer observed in Western Europe, a few cases of rabies caused by European bat lyssaviruses has been reported (48). Apart from some viral causes of encephalitis, certain other infectious causes are also geographically restricted (Table 3). *Orientia tsutsugamushi*, the bacteria which causes scrub typhus and has been linked to encephalitis, is transmitted by mites and predominantly occurs in the Asia Pacific region (see Section 9.2.4 for more information) (49,50). *Trypanosoma brucei* is a parasite transmitted by tsetse flies and causes

sleeping sickness and encephalitis in Africa (Table 3). Parasites and fungi are rare causes of encephalitis in Europe (51).

Table 3 – Causes of encephalitis that are geographically restricted

Region	Causes	
Africa	Chikungunya virus Dengue virus Yellow fever virus HTLV WNV Rabies virus *Trypanosoma brucei* *Schistosoma*	
Asia	JEV TBEV Chandipura virus Nipah virus EV71 Chikungunya virus	Rabies virus *Orientia tsutsugamushi* *Angiostrongylus* sp.
Australia/Oceania	MVEV Kunjin virus Hendra virus ABLV JEV	Rabies virus
Europe	TBEV WNV Toscana virus Rabies virus *Anaplasma phagocytophilum* *Borrelia burgdorferi*	EBLV
Mediterranean region	Toscana virus WNV Dengue virus Rabies virus	
North America	WNV La Crosse virus SLEV EEEV WEEV California encephalitis virus Colorado tick fever virus Powassan virus Chikungunya virus Rabies virus EV71	*Rickettsia rickettsii* *Anaplasma phagocytophilum* *Borrelia burgdorferi* *Coccidioides* *Naegleria fowleri* *Acanthamoeba* spp. *Balamuthia mandrillaris* *Baylisascaris procyonis*
South and Central America	VEEV WNV EEEV SLEV Chikungunya virus Dengue virus Ilheus virus	Yellow fever virus Rabies virus HTLV *Bartonella bacilliformis* *Rickettsia* *Taenia solium*

Adapted from Boucher et al. **(6)**
ABLV = Australian bat lyssavirus; EBVL = European bat lyssavirus; EEEV = Eastern equine encephalitis virus; EV71 = Enterovirus 71; HTLV = Human T-cell lymphotropic virus; JEV = Japanese encephalitis virus; MVEV = Murray Valley encephalitis virus; SLEV = St. Louis encephalitis virus; TBEV = Tick-borne encephalitis virus; VEEV = Venezuelan equine encephalitis virus; WEEV = Western equine encephalitis virus; WNV = West Nile virus

3.1.3 New and emerging infections

Boucher et al. reported that the proportion of encephalitis patients in which a cause was identified ranged from 27.5% to 79% (6). Amongst the cases of unknown cause, new and as yet undiscovered agents may be responsible. Encephalitis is a marker syndrome for new and emerging infections and numerous pathogens have been detected in these cases, for example variegated squirrel bornavirus 1, Zika virus, SARS-CoV-2, and monkeypox (52–54). See Chapter 9 for more information on emerging infectious encephalitides.

3.2 Incidence

It is important to understand the incidence of encephalitis as the burden of encephalitis to health services is disproportionately high (see Section 4.2.1). Incidence must be examined in the global context as climate change, increased international travel, and emerging infections raise the possibility of wider geographical spread of microbes. We aimed to understand global encephalitis incidence to compare how rates vary among different subgroups/exposures and enable limited resources to be focused appropriately in settings where they are most needed.

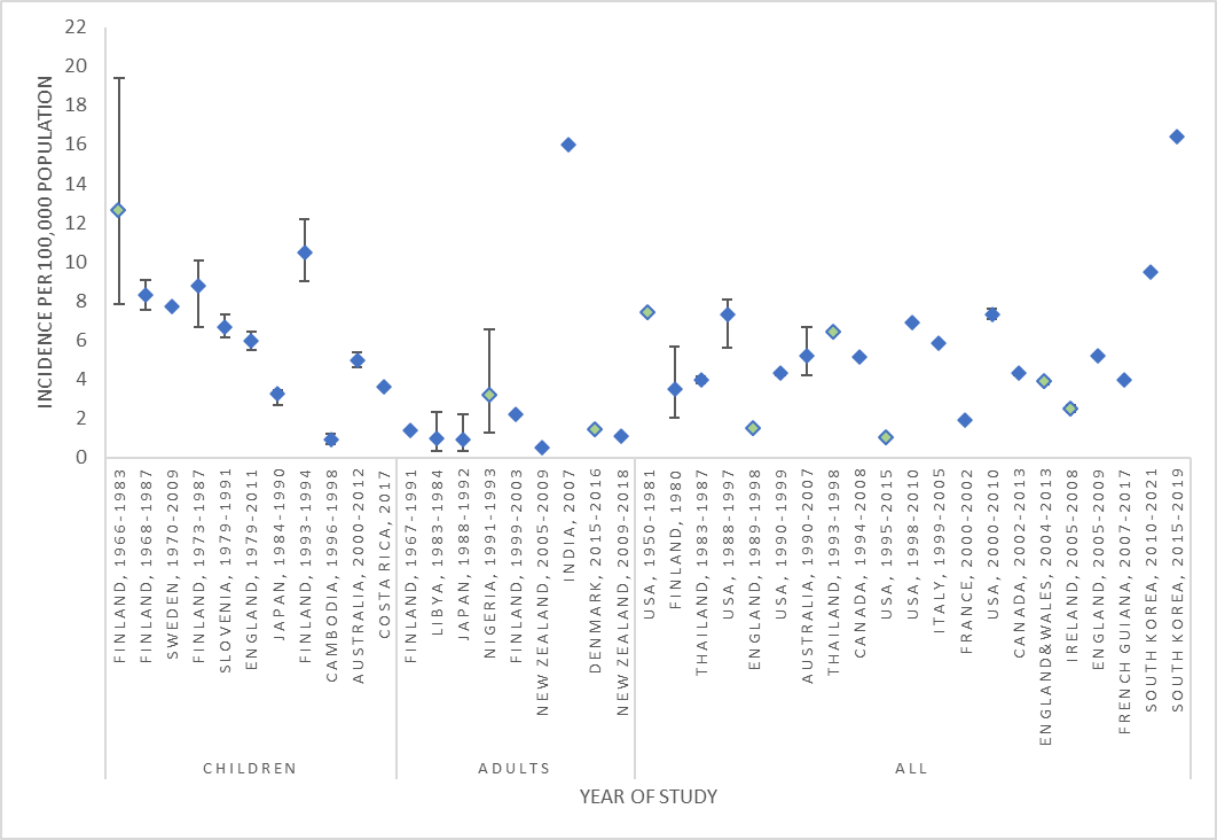
3.2.1 Global incidence of all-cause encephalitis in non-outbreak situations

Based on data from the Global Burden of Disease (GBD) 2019 study, the overall number of incident encephalitis cases was 1,444,720 globally in 2019 (55). This represents a 12.5% increase from 1,284,160 in 1990. There are however limitations with the GBD data as discussed below (see Section 3.2.2).

Incidence reported in studies of all-cause encephalitis in non-outbreak situations worldwide ranged from 0.5 to 16 cases/100,000/year (Figure 3; see Table A1 for further detail) (11–13,20,56–93). This related to studies of unspecified and infectious/viral encephalitis, while studies restricted to a specific cause of encephalitis from the outset (e.g., JEV, HSV) were not considered to keep the focus on the incidence of encephalitis in its broadest sense. In addition, outbreaks were excluded as the incidence in these situations is transient, increasing rapidly before falling again, and is thus not reflective of the true underlying incidence. The lowest incidence of 0.5/100,000 was reported in a study from Auckland, New Zealand where patients were identified via a database search of all patients with a request for CSF viral polymerase chain reaction (PCR) testing; medical notes were then retrieved to assess whether the patient fulfilled the criteria for encephalitis (13). The highest incidence (16/100,000) was a prospective study from India that reported on acute encephalitis syndrome (AES) and a retrospective

review of claims data in South Korea (72,91). Encephalitis incidence in children appeared generally higher than that in adults (Figure 3).

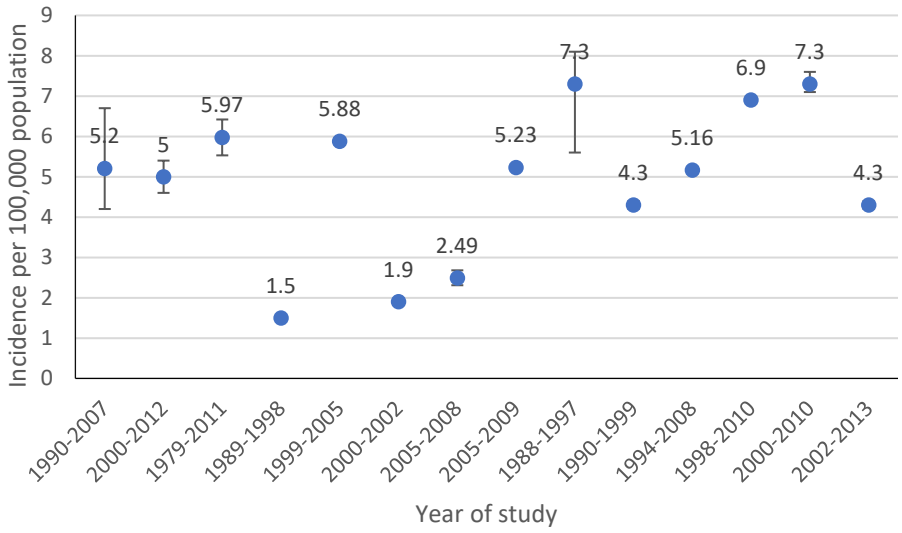
Figure 3 - Incidence per 100,000 population per year of unspecified and infectious/viral encephalitis, by age



Green represents infectious/viral encephalitis and blue represents unspecified encephalitis.
The error bars represent the 95% confidence interval around the incidence estimates.

When studies were restricted to those that used a similar hospitalisation data source and coding system (to facilitate better comparison across studies), incidence ranged from 1.5-7.3/100,000/year (Figure 4) (56–59,65,74–79,81,84,88). It should be noted that lower incidence studies were restricted to viral encephalitis (rather than all-cause unspecified encephalitis) (57,84).

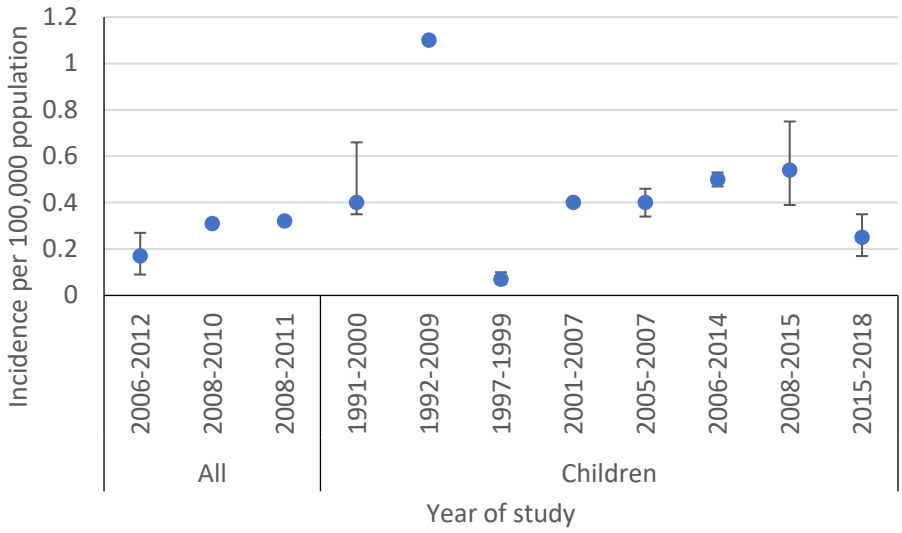
Figure 4 - Encephalitis incidence per 100,000 per year in studies using hospitalisation data



Vertical bars represent 95% confidence intervals where available

The incidence of ADEM ranged from 0.07-1.1/100,000/year, with most studies of ADEM restricted to children (Figure 5) (94–105).

Figure 5 - Incidence per 100,000 population per year of ADEM, by age



Vertical bars represent 95% confidence intervals where available

The estimated cumulative incidence of autoimmune encephalitis is 0.5-1.0 per 100,000 persons per year in adults and between 1.0-1.3 per 100,000 persons per year in children (106). The incidence of anti-NMDAR encephalitis ranged from 0.03-0.23 per 100,000 in all age groups and 0.07-0.22 per 100,000 in children (106). The incidence of anti-LGI1 encephalitis ranged from 0.06-0.14 per 100,000 adults (106).

3.2.2 Discussion

A wide range of incidence estimates were reported from the numerous studies included in this review. The lowest incidence of 0.07/100,000/year was reported in a German study of children with ADEM while the highest incidence of 16/100,000 was reported in both an Indian study of AES and a retrospective review of South Korean claims data (72,91,94). Incidence may vary due to biological factors, such as the geographic distribution of causative agents and vaccination histories of study populations. It may also vary due to methodological factors such as case definitions used and differences in diagnostic testing and ascertainment strategies. Encephalitis is a complex diagnosis, and symptoms often overlap with those of other neurological diseases that lack an infectious or inflammatory aetiology. Studies that use more stringent case definitions may report lower incidences than those where diagnosis is based on less specific clinical criteria. The study by Joshi et al., which reported the highest incidence, likely included some non-encephalitis cases (e.g., toxic encephalopathy, bacterial meningitis) as the case definition for AES is quite broad (72). The strategy used to ascertain cases may also impact on incidence; active case finding may result in a higher incidence estimate than a study using a passive reporting system. The study by Child et al. may have missed cases where no CSF PCR was requested as that was their main method of ascertainment (13). Thus, the studies included in this report are not directly comparable. When studies were restricted to those that used hospitalisation data only, they became more comparable. All studies that used hospitalisation data were from Europe, North America, and Australia. Studies that used hospitalisation data had a similar data source and data coding; however, some used encephalitis in the primary diagnostic coding field only and some in all diagnostic fields. Also, the diagnosis of encephalitis in hospitalisation data has not yet undergone validation so there is likely to be some misclassification if mimicker syndromes are coded using encephalitis codes. There was a lack of studies from Africa, Asia, and South America, which likely reflects the lack of resources and lack of surveillance infrastructure (i.e., national hospital data) in these parts of the world. However, incidence is likely to be higher in these countries. For example, a systematic review of the global incidence of JE reports a JE incidence of up to 3.7/100,000 in Cambodia, Indonesia, Lao People's Democratic Republic (PDR), parts of Malaysia, Myanmar, Philippines, and Timor-Lest (107). Given there are over 100 causes, the incidence of all-cause encephalitis in these parts of Asia is likely to be even higher.

Recent studies have shown that encephalitis may be more common than previously thought. The incidence of encephalitis in England, previously estimated at 1.5/100,000/year, is likely 5.23 but could be as high as 8.66/100,000/year (57,58). Importantly, in many countries

encephalitis has a higher incidence than motor neurone disease (MND)/amyotrophic lateral sclerosis (ALS), bacterial meningitis, and multiple sclerosis (MS) - conditions which have much higher clinical and public profiles (108–110).

There is a distinct lack of published data on the epidemiology of autoimmune encephalitis. Reviews that considered the incidence of autoimmune encephalitis included predominantly studies from USA and Europe, and a study each from New Zealand, Hong Kong, and Malaysia (106,111). No study from Africa or South America were included. The scarcity of data could be limited to a lack of clinical awareness and difficulties in autoimmune encephalitis diagnosis and testing.

Although the GBD study reported approximately 1.5 million incident cases of encephalitis in 2019, the study has some important limitations (55). The incidence estimate was derived using mathematical models which were based on data sources of varying quality. Also, data sources from some areas were extremely scarce, thus the GBD estimate may deviate from the actual data particularly in these areas. The GBD estimated a 12.5% increase in encephalitis incidence over the last 30 years which may relate to increased recognition of novel causes and improved surveillance. Previously, it was estimated that 500,000 cases of encephalitis occur globally each year (112) but this is thought to be an underestimate. Annually, 100,000, 60,000, and 15,000 cases of JE, rabies, and TBE, respectively, are thought to occur (113–115). Given 1:1,000 cases of childhood measles are complicated by encephalitis and that 9,232,288 estimated cases of measles occurred in 2022, approximately 9,000 cases of measles encephalitis likely occurred (116). Thus, just these four causes alone (of >100 possible causes) amount to 184,000 encephalitis cases per year, over a third of the total 500,000. The true incidence likely falls between 1 to 1.5 million cases per year.

In conclusion, the data from this review demonstrate the difficulty in comparing incidences across studies as biological and geographical factors differ between populations and case definitions and other methodological differences exist. Incidence in parts of the world (West) is higher than previously thought. However, there is a lack of incidence studies in parts of the world where incidence is likely to be even higher (South America, Africa). We also highlight the importance of immune-mediated causes which have been increasingly recognized over the last decade.

3.2.3 Gap analysis

Table 4 – Gap analysis for encephalitis incidence

Where we are	Where we want to be

The incidence of encephalitis likely falls between 1 to 1.5 million cases per year.	Need for more accurate assessment of incidence as global cases of encephalitis are underestimated
There is a lack of incidence studies from Africa, South America, and parts of Asia. Studies from Asia tend to be restricted to JE.	Need further studies to enable better assessment of encephalitis incidence in Africa, Asia, and South America
Studies vary in incidence partly due to biological factors of study populations (e.g., geographical area and vaccination history) but also due to methodological differences between studies.	Need standardisation of case definitions, diagnostic testing, and methods of case ascertainment to enable better comparison of incidence between studies and regions
Routine surveillance systems are either sub-standard or lacking in many countries.	Need to develop/improve routine surveillance systems to facilitate assessment of accurate incidence estimates

GBD = Global Burden of Disease; JE = Japanese encephalitis; TBE = Tick-borne encephalitis; WHO = World Health Organization

4 Burden of disease

4.1 Morbidity and mortality

It is important to assess the morbidity and mortality of encephalitis worldwide to understand the burden of encephalitis on global populations. In addition, it is important to assess specific long-term needs of survivors, so that strategies for long term care, support, and rehabilitation can be designed accordingly. We aimed to understand global encephalitis morbidity and mortality to compare how rates vary among different subgroups/exposures and enable limited resources to be focused appropriately.

4.1.1 Mortality for all-cause encephalitis

4.1.1.1 Mortality rate

Mortality rate measures the number of deaths due to encephalitis in a population scaled to the size of that population per unit of time. In 2021, the WHO estimated 80,286 deaths in all ages from encephalitis which equates to a crude mortality rate of 1.01/100,000 population (Table 5) (117). This is similar to the Institute for Health Metrics and Evaluation (IHME) estimate of 91,948 deaths for 2021 which equates to a rate of 1.17/100,000 (118).

Table 5 - Estimates of all-age encephalitis mortality by WHO region, 2021

	Number deaths	% of total deaths	Crude death rate (/100,000)
Global	**80,286**	**0.12**	**1.01**
African Region	12,281	0.14	1.04
Region of the Americas	902	0.01	0.09
South-East Asia Region	48,156	0.26	2.33
European Region	2,841	0.02	0.30

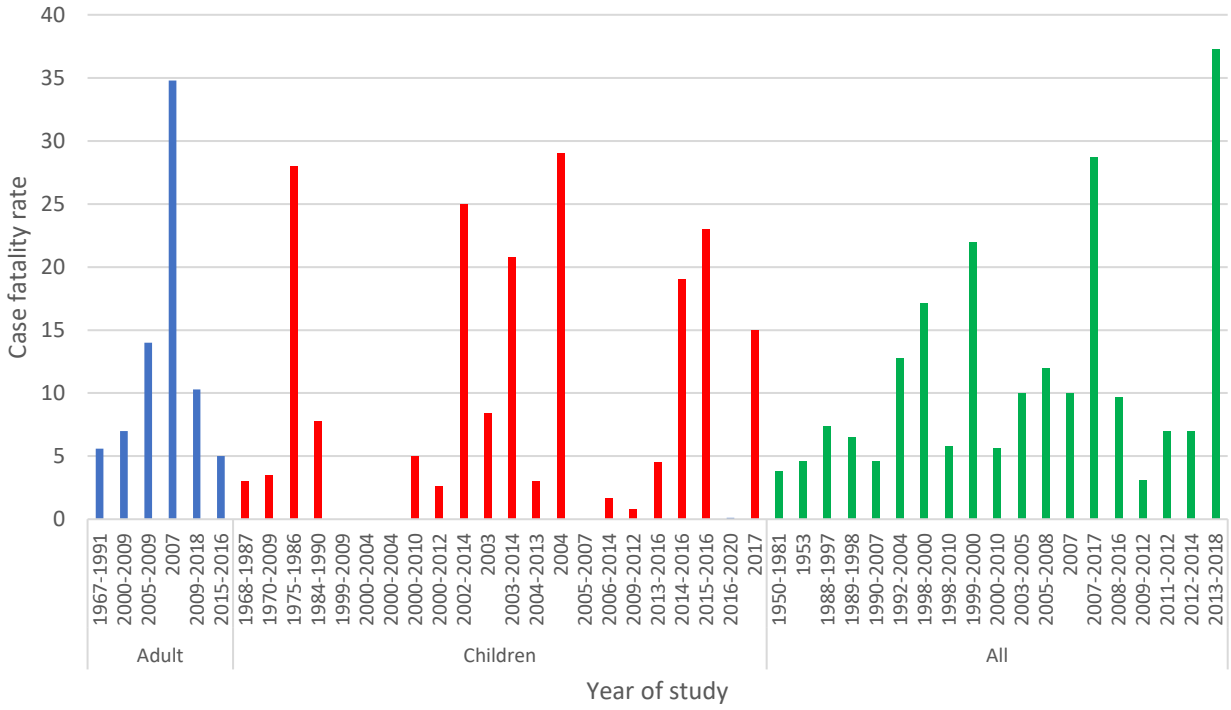
Eastern Mediterranean Region	10,358	0.21	1.33
Western Pacific Region	5,654	0.36	0.29

From WHO Global Health Estimates **(117)**

4.1.1.2 Case fatality rate

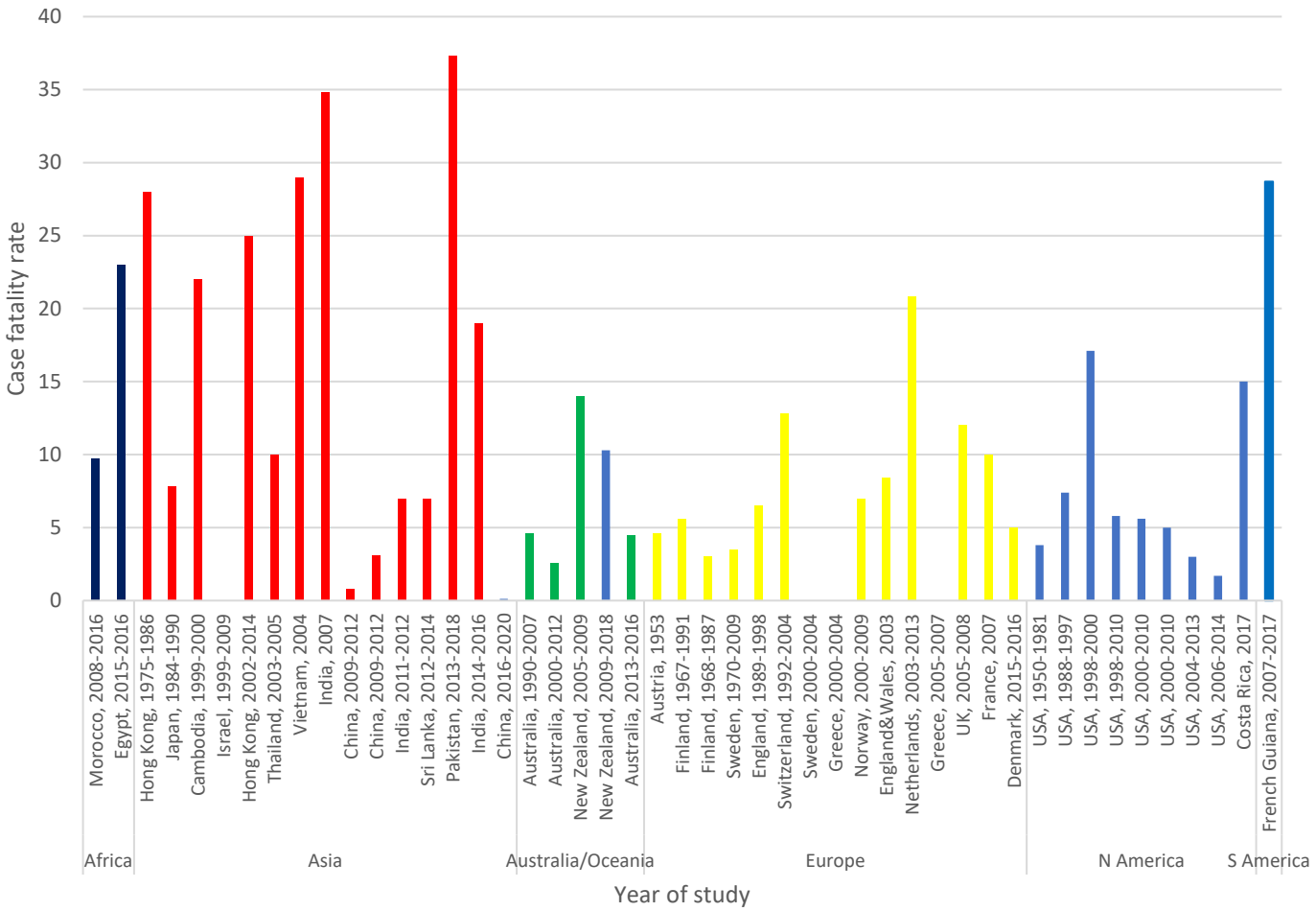
Case fatality rate (CFR) represents the proportion of deaths from encephalitis compared to the total number of people diagnosed for a certain time period. Studies of encephalitis in the literature report CFRs ranging from 0 to 37% (Figure 6) (12–14,16,56,57,60,61,72,74,78–83,89,89,92,103,119–142,142–147). Four identified studies reported zero deaths; these were all studies of children, three conducted in Europe and one in Israel (120,121,130,144). The highest identified CFR (37.3%) was reported from a retrospective study in Pakistan that included patients with severe encephalitis admitted to the intensive care unit (145). This was followed by CFRs of 34.8%, 29%, 28%, and >25% reported in four identified Asian studies (India, Vietnam, and two from Hong Kong) (72,129,131,133). See Table A2 in Appendix for further details of studies.

Figure 6 - Case fatality rates for encephalitis studies by age and year of study



CFRs from included African, Asian, and South American studies appeared higher than those from other continents (Figure 7).

Figure 7 – Case fatality rates for encephalitis studies by age and continent



4.1.1.3 Discussion

These results confirm that encephalitis is associated with high mortality on a global scale. The WHO/IHME estimate of 80-90,000 deaths worldwide (1.0-1.2/100,000 population) from encephalitis in 2021 is likely an underestimate (117). Rabies alone is estimated to cause 60,000-70,000 deaths and JE 25,000 deaths worldwide each year yielding a total of 85,000 deaths from these two causes of encephalitis alone (50,148,149). Given there are >100 different causes of encephalitis, the total number of deaths is likely to be higher than the estimate of 80-90,000 deaths. In addition, a recent study reported >24,000 human deaths from rabies annually in Sub-Saharan Africa alone, far higher than the approximately 12,000 deaths due to encephalitis reported by WHO for the whole of Africa in 2021 (150). Data for the IHME estimate were based on ICD codes; these included codes for arboviruses, sequelae of viral encephalitis, and general non-pathogen-specific rubric specifying encephalitis diagnoses, but omitted codes for rabies, HSE, and other specific known causes. Thus, deaths due to encephalitis are higher than current global estimates.

The CFRs reported varied between studies, and CFRs from African, Asian, and South American studies were higher than those reported from Australian/New Zealand, European, and North American studies. There are some possible explanations for this. Firstly, the main factor that influences outcome appears to be the aetiological agent involved, likely a reflection of an interplay between the pathogenesis of the organism, treatment available, and host factors (3). Different organisms are present in these regions that may cause more severe disease. Second, the regions with the highest CFRs have the fewest number of neurologists per 100,000 population (see Section 7.2.1) and lowest coverage of two doses of measles-containing vaccine (see Section 5.1.3.2), both which would contribute to better protection against and treatment of encephalitis. It is important to note however, that comparison is difficult due to between-study heterogeneity, which emphasizes the need for standardised surveillance systems across the board for incidence and mortality. Some studies may have been missed as this was not a systematic review; however, this is thought to be limited as the search used was very comprehensive. Data from Africa and South America were scarce. Two African studies conducted in Libya and Nigeria reported CFRs of 20% and 50%, respectively, in the abstract; however, the full text could not be obtained (68,71). These latter studies only included a very small sample size (five and seven patients).

4.1.1.4 Gap analysis

Table 6 - Gap analysis for encephalitis mortality

Where we are	Where we want to be

WHO/IHME estimated 80-90,000 deaths worldwide from encephalitis in 2021. However, 60,000 and 25,000 deaths from rabies and JE, respectively, occur each year in Asia and Africa which equates to 85,000 deaths per year from these two causes alone. Thus, it is certain that the global number of deaths from encephalitis per year is higher than the estimated 80-90,000.	Need for more accurate assessment and better recording of mortality as global deaths from encephalitis are underestimated
Comparison is difficult due to between-study heterogeneity.	Need for standardised surveillance systems to enable more accurate assessment and comparison of mortality/case fatality
Case fatality rates are higher in Africa, Asia, and South America compared to Europe, Australia/New Zealand, and North America.	Need to facilitate prevention, treatment, and management (e.g., increase number of neurologists and coverage of two doses of measles-containing vaccine) of encephalitis in these regions
Data from Africa and South America are scarce.	Need for more research to assess mortality in Africa and South America

IHME = Institute for Health Metrics and Evaluation; JE = Japanese encephalitis; WHO = World Health Organization

4.1.2 Morbidity for all-cause encephalitis

4.1.2.1 Sequelae in children

A systematic review and meta-analysis, which comprised articles published up until April 2016, quantified the long-term (i.e., follow-up period ≥12 months) outcomes of all-cause infective encephalitis in 1,018 children (151). Sixteen studies were included for quantitative meta-analysis, the majority (n=13/16, 81%) from high-income countries (HICs). Almost half (n=312, 42%) of survivors had incomplete recovery/neurodevelopmental sequelae (Table 7). The most common long-term sequelae included developmental delay (35%), abnormal behaviour (18%), intellectual deficit (IQ<85; 17.5%), and motor impairment (17%). Higher rates of sequelae were reported in studies from HICs compared to low- and middle-income countries (LMICs; 47% [36-58%] versus 26% [9-47%]). Children with HSV encephalitis had a higher proportion of long-term sequelae compared to those with other infections (64% [95%CI 34-89%] versus 38% [28.0-50.0%]). A recent systematic review from 2023 similarly reported neurological sequelae in over half (51%) of children following encephalitis associated with HSV (152).

Table 7- Meta-analysis of long-term outcomes of infective encephalitis in childhood

Long-term sequelae	Number of patients followed up	Number of patients who developed sequelae	Percentage with sequelae (95% CI)
Death	584	18	**2.7** (1.7-4.5)
Severe sequelae*	520	33	**6.7** (4.5-8.8)
Incomplete recovery**	890	312	**42.0** (31.6-53.1)
Motor impairment	705	86	**17.0** (10.0-26.0)

Seizure	566	52	**10.0** (6.0-14.0)
Developmental delay	227	50	**35.0** (10.0-65.0)
Abnormal behaviour	329	61	**18.0** (8.0-31.0)
Intellectual deficit (IQ<85)	285	41	**17.5** (4.3-37.1)
Intellectual deficit (IQ<70)	302	33	**12.5** (4.6-23.4)

**Persisting sequelae which impair everyday functions; **Residual neurocognitive symptoms*
Adapted from Khandaker et al. **(151)**
CI = Confidence interval

The presence of varying degrees of neurological sequelae in children following encephalitis has been confirmed in studies published since the aforementioned systematic review (i.e., post-April 2016; Table 8) (82,137–139,147,153).

Table 8 – Sequelae reported in post-April 2016 studies of childhood encephalitis

Study (sample size)	Date	Country	Type of encephalitis	Sequelae reported
Wickstrom et al. (n=408)	1970-2009	Sweden	All cause	26% mild and 18.25% moderate-severe sequelae
Elenga et al. (n=30)	2007-2018	French Guiana	All cause	17% severe neurological sequelae (epilepsy, quadriplegia, visual and cognitive impairments)
Ai et al. (n=255)	2009-2012	China	Viral encephalitis	7.5% neurological sequelae (coma, aphasia, secondary epilepsy, cognitive impairment, blindness, ataxia, dysphasia, hearing impairment, hemiplegia)
Britton et al. (n=287)	2013-2016	Australia	All cause	27% moderate to severe neurological sequelae
Meligy et al. (n=96)	2015-2016	Egypt	Viral encephalitis	74% of survivors mild to severe/vegetative neurological sequelae
Chen et al. (n=76)	2013-2017	Taiwan	Anti-NMDAR encephalitis	73% full recovery, 18% behavioural and school/working deficits, 9% multidomain deficits (self-care ability, behavioural-cognitive impairment, seizures)
Kim et al. (n=66)	2012-2024	Korea	Probable antibody-negative autoimmune encephalitis	95% good clinical outcome (mRS), 44.2% persistent seizures, 32.8% cognitive problems, 27.9% behavioural problems

From references (82,137–139,147,153,154)
mRS = modified Rankin Scale

4.1.2.2 Sequelae in adults

Studies report similar outcomes in adults as children following encephalitis (Table 9). Between 26% and 62% of adults suffer significant sequelae, including epilepsy, memory problems, inappropriate behaviour and poor social skills, fatigue/sleep disturbance, personality changes, cognitive problems, problems with pain and other sensations, and problems with daily living skills (155). A UK study of mainly adults (~80%) which assessed sequelae in encephalitis survivors relative to rates within the general population showed an increased risk of all

investigated outcomes, including epilepsy (adjusted rate ratio [RR] 31.9; 95%CI 25.38-40.08), bipolar disorder (6.34, 3.34-12.04), psychotic disorders (3.48, 2.18-5.57), depressive disorders, anxiety disorders, cognitive problems, dementia, headache, and alcohol abuse (156). The high rate of psychiatric disorders following encephalitis was confirmed by a large international survey conducted in 445 patients in 31 countries (157).

Table 9 - Sequelae reported in studies of adult/all-age encephalitis

Study	Age	Sample size	Date	Continent	Sequelae reported
Rantalaiho et al.	Adult	322	1967-1991	Europe	26% sequelae
Hansen et al.	All	340	2000-2017	USA	50.6% confirmed adverse clinical outcome (GOS 1-4)
Granerod et al.	All	198	2005-2008	Europe	44% of all or 50% of survivors severe or moderate disability (GOS 2-4)
Joshi et al.	Adult	152	2007	Asia	34% of survivors significant cognitive disability (MMSE<25)
Mailles et al.	All	253	2007	Europe	62% of survivors had neurological signs and 10% behavioural disorders
Roux et al.	All	108	2007-2017	South America	46.6% poor outcome*
Toudou-Daouda et al.*	All	31	2008-2016	Africa	9.7% temporal lobe epilepsy, 16.1% anterograde amnesia, and 19.4% severe cognitive impairment
Zhao et al.	All	1027	2009-2012	Asia	20.7% mild, 10% moderate, and 1.8% severe neurological sequelae
Rathore et al.	All	80	2011-2012	Asia	18% poor outcome**
Bodilsen et al.	Adult	89	2015-2016	Europe	62% unfavourable outcome (GOS 1-4)
Mailles et al.	Adult	494	2016-2019	Europe	0.5% persistent vegetative state, 11.4% severe disability, 27% moderate disability, 61.1% good recovery

**Study relates to limbic encephalitis*
***Includes death or severe disability*
From references (12,14,16,72,80,83,126,134,140,158,159)
GOS = Glasgow Outcome Scale; MMSE = Mini mental state examination

4.1.2.3 Carer burden

Sequelae following encephalitis do not only affect the survivor but can have a huge impact on their families and communities. Caregiving, particularly in neurological diseases, is costly and time-consuming and has been shown to increase the risk for depression and worse physical health (160). A study of 36 parents reported greater parental distress when their child experienced higher levels of behavioural symptoms following encephalitis (161). A recent study which assessed caregiver burden in 76 individuals caring for a person with anti-NMDAR encephalitis reported a mean Zarit Burden Interview (i.e., standardised 22-item questionnaire to assess burden) score of 44 (range 17-70), reflecting moderate to severe burden (162).

Caregivers of individuals with anti-NMDAR encephalitis in this study experienced higher levels of burden than those reported for dementia, stroke, and Alzheimer's (163–165).

4.1.2.4 Discussion

Data show that both children and adults suffer significant sequelae following encephalitis. A systematic review of encephalitis outcomes in children reported neurodevelopmental sequelae including developmental delay, abnormal behaviour, intellectual deficit, and motor impairment in almost half of survivors (151). In this study higher rates of sequelae were reported from HICs compared to LMICs, likely due to sequelae not being adequately assessed and recorded in the latter. A systematic review from 2010 of the global and regional risk of disabling sequelae from bacterial meningitis found that survivors in low income countries (LICs) were worst affected; the risk of major sequelae was twice as high in Africa and South-East Asia as in Europe (166). As for children, between a quarter and two thirds of adults suffer significant sequelae following encephalitis. Between-study heterogeneity exists in terms of study setting, aetiology, sample size, duration of follow-up, and variations in the reporting of the type of sequelae (i.e., one specific type or category of sequelae versus all sequelae, some include deaths as poor outcome, some reported all cases including deaths as denominator while others only survivors). A systematic review which assessed the range of outcome measures used in the long-term follow-up of patients with encephalitis, concluded that most of the 37 measures used assessed a single category of sequelae using 5–8-point scales and were not validated for use in encephalitis (167). Reported outcomes are often based on generic clinical outcome assessments that rarely capture the patient perspective. A further systematic review failed to identify a validated measuring tool for detecting neurocognitive, functional, and health status in encephalitis (168). Thus, standardisation is required in the way sequelae are measured and reported to facilitate comparison between regions, causes, and to better assess the extent of sequelae post-encephalitis. In addition, the development and/or validation of disease-specific patient-reported outcome measures for encephalitis patients is critical to improve patient management (168).

4.1.2.5 Gap analysis

Table 10 - Gap analysis for encephalitis morbidity

Where we are	Where we want to be
Data are available from HICs on the acute outcomes of HSE and from LMICs on the acute outcomes of JE.	Need data from LMICs on acute outcomes of encephalitis from other infectious causes
Data are available from HICs on the long-term outcomes of HSE.	Need data from LMICs on long-term outcomes of encephalitis

	Need data on long-term neurocognitive outcomes of infective encephalitis Need data on clinical predictors of long-term outcomes of infective encephalitis in children Need age stratification of follow-up studies on long-term outcomes of infective encephalitis
Evidence of significant caregiver burden associated with encephalitis	Need to consider possible interventions including psychoeducational interventions focused on coping and problem solving and educational sessions, which have shown to be successful in other neurological diseases **(169,170)**
Lack of standardized methods of outcome data collection and uniform definitions, and lack of validation of outcome measures for study population complicates comparison of studies/causes or full assessment of extent of sequelae following encephalitis **(171)**.	Need an encephalitis-specific outcome measure to aid standardization

Adapted from Khandaker et al. **(151)**
HICs = High-income countries; HSE = Herpes simplex encephalitis; JE = Japanese encephalitis; LMICs = Low- and middle-income countries

4.1.3 Morbidity and mortality by cause

Mortality and morbidity by the main causes of encephalitis are displayed in Table 11. Rabies encephalitis is invariably fatal, while HSV and JE are often associated with a CFR of around 20%. A recent systematic review and modelling analysis however, reported JE CFR estimates were <20% after 2000 (172). Post-encephalitis sequelae tend to affect cognitive (e.g., memory disorders) and psychiatric (e.g., mood impairments) domains with *Herpesviridae* and neurological (e.g., limb paralysis) and psychiatric (e.g., psychosis-like syndrome) domains in flavivirus encephalitis (173). Criminality has recently been reported as a serious and novel post-autoimmune encephalitic association (174).

Table 11 - Mortality and morbidity by main causes of encephalitis

Cause	Case fatality	Sequelae	Reference
Infectious			
HSV	20%	30-70%	Kvam et al.; Rocha et al.
JE	14-30%	30-60%	Simon et al.; Kumar et al.; Chow et al.; Cheng et al.
TBE			Taba et al.
European subtype	1%	26-46%	
Far Eastern subtype	6.4-33%*	N/A	
Siberian subtype	1.8-3%*	N/A	
Rabies	100%	N/A	Dacheux et al.
Immune-mediated			
ADEM	1-3%	20%	Bhatt et al.
NMDARE	5-7%	25% significant morbidity or mortality	Venkatesan et al.; Chi et al.; Kvam et al.

LGI1 encephalitis	6-19%	3%-21% functionally dependent; 32-90%** cognitive impairment	Kvam et al.
All-cause AE	N/A	18%	Abboud et al.

*Based on limited data
**Also includes Caspr2 patients
From references (103,152,172,173,175–184)
ADEM = Acute disseminated encephalomyelitis; AE = Autoimmune encephalitis; HSV = Herpes simplex virus; JE = Japanese encephalitis; LGI1 = Leucine rich glioma inactivated 1; N/A = Not available; NMDARE = N-methyl-D-aspartate receptor encephalitis; TBE = Tick-borne encephalitis

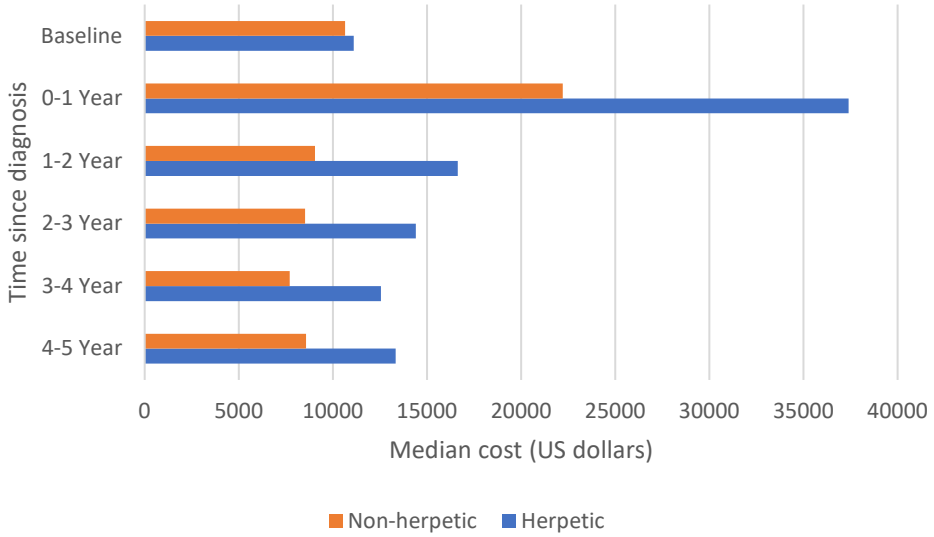
4.2 Economic burden and DALYs

4.2.1 Cost

Due to its high morbidity and mortality, encephalitis is associated with significant costs to individuals and society. An annual cost of >£23 million (US$35 million) has been estimated in England based on an incidence of 5.23 cases/100,000/year, a mean hospital length of stay of 34 days, and a bed-day cost of £261 (58). This, however, does not include the cost of intensive care, expensive investigations, in-patient rehabilitation, or long-term care and loss of productivity among many working-age survivors. Thus, the cost of encephalitis is likely substantially higher. In a USA study, the mean charges for hospitalization for a child with encephalitis was $64,604 and for those requiring critical care was $260,012. In this study, 40% of the 7,298 children admitted with encephalitis between 2004 and 2013 were admitted to paediatric intensive care, incurring a total cost of >$750 million (135). Encephalitis-associated hospitalisations in the USA were estimated to cost $2 billion in 2010 (78). Data obtained from the Paediatric Intensive Care Audit national Network database estimated a paediatric intensive care unit (PICU) encephalitis bed cost of £414,230/year (IQR: £198,111–£882,495) for this cohort of 1,031 children with severe encephalitis admitted to the PICU in England and Wales between 2003 and 2013 (141). This is however an underestimate of the PICU cost burden of encephalitis as treatment costs and costs for procedures such as invasive ventilation were not accounted for. A study by Kiyani et al. examined the longitudinal health economic impact of viral encephalitis over a five-year period following diagnosis using a national claims database (185). Healthcare resource utilisation was investigated in 1,635 patients between 2008 and 2015, 598 with herpetic and 1,037 with non-herpetic encephalitis. The median baseline total cost for the one-year period prior to diagnosis was $10,654 for the non-herpetic viral encephalitis group and $11,097 for the herpetic encephalitis group. The cost increased by 165% to $37,403 during the first year of diagnosis for the herpetic group and by 90% to $22,207 for the non-herpetic viral encephalitis group (Figure 8). Costs decreased after two years but remained elevated in the herpetic versus non-herpetic group. The longer length of hospital stay and more admissions associated with the disease have been suggested as possible reasons for the higher costs seen with HSE (185). An analysis of Swedish registry

data reported the cost of illness and death from TBE alone in Sweden in 2019 was €23.5 million (186).

Figure 8 – Annual total median costs of viral encephalitis in the USA at baseline and up to five years post-diagnosis



Adapted from Kiyani et al. (185)

Median hospital charges per autoimmune encephalitis patient (>$70,000) were nearly four times higher compared with HSE in a USA study (187). The hospital charges were significantly higher for autoimmune encephalitis patients admitted to the ICU than for those not admitted to the ICU ($173,000 versus $50,000; p<0.001). This was mainly driven by a longer length of hospital stay resulting from delayed diagnosis, prolonged treatment course, and lack of treatment response. The mean direct cost per patient with antibody-positive autoimmune encephalitis in West China was $14,219, and the authors noted a heavy financial burden of autoimmune encephalitis for Chinese patients (188).

Studies from LICs and lower-middle-income countries show great cost burden of encephalitis. In Nepal, for children with severe/moderate impairment due to AES the median out-of-pocket cost to families was US $1,151, 10 times their median monthly income (189). For children with mild/no impairment the median cost was $524, almost five times their income. Similarly, the mean cost of illness per child with encephalitis in Vietnam was estimated at US $2,820.43 and approximately half of direct medical costs attributed to hospitalisation resulted in out-of-pocket payments from the patients' family (190). For JE specifically, the mean total cost per acute JE episode was $3,371 and $2,005 in Vietnam and Lao PDR, respectively, with further costs due to sequelae, and 20-30% of households had sustained debts years after acute JE (191). Similarly, in Bangladesh the average societal cost of an acute JE episode was US $929, initial

sequelae US $75, and long-term sequelae US $47, with most families experiencing sustained debt for JE expenses (192).

4.2.2 DALYs

Disability-adjusted life years (DALYs) are used to measure the burden of disability associated with a disease and represent the total number of years lost to illness, disability, or premature death within a given population. In short, DALYs are the sum of the number of years of life lost and the years lived with disability for a specific disease. One lost DALY represents one lost year of healthy life (through death or illness/disability), and total DALYs (burden of disease) measure the gap between the current health of a population and an ideal situation where everyone lives into old age in full health. DALYs combine information on incidence/prevalence, mortality, and sequelae into a composite measure.

Smit et al. evaluated the burden of TBE in Slovenia using DALYs (193). Total DALYs amounted to 3,450 or 167.8 per 100,000 population (or 3.1 per case from the individual perspective) in 2011, with a greater burden resulting from the consequences of TBE. LaBeaud et al. used updated information on incidence, mortality, average age at death, and (in survivors) the duration and impact of disability outcomes to evaluate the disease burden of arboviral causes of encephalitis, including JE and chikungunya virus (194). Global DALYs estimates for JE ranged from 107,435 to 1,859,170 in 2005 (Table 12), with early mortality and long-term, related chronic conditions providing the largest DALY component. The total burden of JE in Zhejiang Province, China was 14.25 DALYS per million population; a separate Chinese study reported 9.2 as the median DALY lost to JE per subject (195,196).

Table 12 – Calculated global 2005 DALY estimates and inputs for specific arboviral causes of encephalitis

	Inputs				DALYs	
	Estimated clinical cases per year	Median age (years) for symptomatic disease	Case fatality rate	Survivor's risk for multiyear or permanent disability	Non-discounted	Discounted
JEV	35-50,000	10	10-30%	30-50%	265,778-1,859,170	107,435-755,670
CHIKV	33-93,000	40	0.1-28%	5-50%	2,124-1,411,904	1,481-780,234

Adapted from LaBeaud (194)
CHIKV = Chikungunya virus; DALYs = Disability-adjusted life-years; JEV = Japanese encephalitis virus

The GBD study estimated 4.8 million DALYs related to encephalitis globally in 2019 (55). This was down from 8.48 million in 1990; however, age-standardised DALY rates increased in some parts of the world, including New Zealand, UK, Australia, Greece, Switzerland, USA,

and Canada. This was attributed to more immunocompromised people in HICs (i.e., following tissue/organ transplantation), HSE being the most common cause and associated with poor prognosis, and a longer life expectancy in these parts of the world (55). Encephalitis was the fifth largest contributor to total neurological DALYS in India, just behind stroke, headache disorder, epilepsy, and CP (197). As previously noted, the encephalitis incidence estimated from the GBD Study is likely an overestimate; however, comparisons to other diseases should remain similar proportionally.

In addition to assessing disease burden, DALYs are often used to monitor health technologies. A cost-effectiveness study of routine immunisation to control JE in Shanghai showed that a program using inactivated or live attenuated JE vaccine would save 6,456 or 6,556 DALYs per 100,000 persons, respectively (198). A similar study conducted in Bali, Indonesia reported that a potential routine JE immunisation program would save 1,223 DALYs at a cost of US $31 per DALY saved, yielding it highly cost effective (199).

4.2.3 Gap analysis

Table 13 – Gap analysis for cost of encephalitis and associated DALYs

Where we are	Where we want to be
Studies report significant direct costs (e.g., hospitalisation) associated with encephalitis but data on indirect costs are lacking (e.g., lost productivity).	Need more data on direct and indirect costs from LMICs and on indirect costs from all countries
Encephalitis is associated with high DALYs, but these vary depending on input estimates.	Need more accurate input estimates including incidence/prevalence, mortality, and sequelae to more accurate assess DALYs
DALYs are mostly associated with encephalitis sequelae.	Need to reduce DALYs associated with encephalitis sequelae by implementing better tertiary prevention strategies
DALYs are often used to monitor health technologies and assess benefit of vaccination program against specific causes of encephalitis.	Need to use DALYs measure to assess further introduction of JE/TBE vaccine in endemic places where vaccine not already implemented or where disease may spread in future

DALYs = Disability-adjusted life years; JE = Japanese encephalitis; LMICs = Low- and middle-income countries; TBE = Tick-borne encephalitis

5 Prevention

5.1 Vaccines

Vaccines have had an enormous impact on global health, especially in LMICs. Smallpox became the first (and only) human infectious disease to be eradicated by vaccination in 1979

(200). There are currently vaccine programs in place for the elimination of other infectious diseases including polio and measles. Ozawa et al. used health impact models to estimate that vaccinations given between 2001 and 2020 in 73 LMICs will avert over 20 million deaths and save US $350 billion in cost of illness (201). Vaccines are available for well-established causes of encephalitis, including JEV, TBEV, measles, rabies, and VZV, and for emerging or re-emerging causes of encephalitis, including SARS-CoV-2, dengue virus, and chikungunya virus. We aimed to assess the global distribution of vaccine programs for vaccine-preventable causes of encephalitis to determine where the gaps are.

5.1.1 Japanese encephalitis vaccination programs

5.1.1.1 Recommended practice

Four classes of vaccines are available against JEV including inactivated mouse brain-derived vaccines, inactivated Vero cell-derived vaccines, live attenuated vaccines, and live recombinant (chimeric) vaccines (202). The WHO recommends that JE vaccination is included in the national immunisation schedule of all countries where JE is recognised as a public health priority (203). Since 2006, the WHO has urged inactivated mouse brain-derived vaccines be replaced with the newer generation vaccines for safety reasons (202).

5.1.1.2 Implementation status

Heffelfinger et al. reported on JE immunisation programs in Asia and the Western Pacific in 2016 (204). Data were obtained from published literature and websites, the 2015 WHO/ United Nations (UN) Children's Fund Joint Reporting Form on Immunization, notes and reports from JE meetings held during 2014–2016, and a survey of JE surveillance and immunisation practices administered to health officials in countries with JE virus transmission risk. Twelve of 24 countries (50%) with JEV transmission risk had a JE immunisation program in 2016, a slight increase from 46% in 2012 (204,205). Improvements were not only seen in implementation of a JE immunisation program but also in the breadth of existing programs (i.e., whether they were national or only covered some areas). The JE vaccine program covered all areas in 42% of countries in 2016 compared to 25% in 2012 (204,205). Since 2016, three further countries have implemented JE vaccination programs, including Myanmar (national), Indonesia (Bali), and the Philippines (Regions I, II, III, and the Cordillera Administrative Region; Table 14) (204,206). As of 2020, 15 of 24 (62%) countries with JEV transmission risk have a JE immunisation program, 10 of which are national programs (207).

Live attenuated vaccine is used in 11 countries (Cambodia, China, India, Indonesia [Bali], Lao PDR, Myanmar, Nepal, Philippines, South Korea, Sri Lanka, Thailand), live recombinant in

four (Australia, Malaysia, Thailand, and China's Taiwan province), and inactivated Vero cell culture-derived in three (Japan, Republic of Korea, and China's Taiwan province) (207). Mouse-brain derived vaccine is only used in Vietnam.

Table 14 - Presence of JE immunisation program in countries with JEV transmission risk

Country	JE immunisation program	Comment
Australia*	All risk areas	Vaccination recommended for people who live in (or are travelling to) a risk region of Australia and who may be bitten by mosquitoes. Risk regions are determined by states and territories and may change depending on areas in which JE virus is detected.
Bangladesh	None	
Bhutan	None	
Brunei	None	
Cambodia	National	
Myanmar	National	
China	National	Excluding the provinces of Qinghai, Tibet, and Xinjiang, which do not have endemic transmission
Taiwan**	All areas	
India	Subnational	In 216 districts with endemic JE
Indonesia	Subnational	In Bali
Japan	National	
Lao PDR	National	
Malaysia	Subnational	In Sarawak state; in peninsular Malaysia and Sabah, vaccination is provided to children aged <15 years in vicinity of outbreak
Nepal	National	
North Korea	None	JE vaccination campaign conducted in 2016
Pakistan	None	
Papua New Guinea	None	
Philippines	Subnational	Regions I, II, III, and the Cordillera Administrative Region CAR
Russia*	None	
Singapore	None	Decided not to introduce JE vaccine because only rare, sporadic human cases are reported in the country
Republic of Korea	National	
Sri Lanka	National	
Thailand	National	
Timor-Leste	None	
Vietnam	National	

**JE virus transmission risk in well-defined, limited areas; **A survey was not administered to health officials from Taiwan. Data for Taiwan were obtained from published literature and the Taiwan CDC website*

Adapted from Heffelfinger et al. and Letson et al. (204,208)

JE = Japanese encephalitis; JEV = Japanese encephalitis virus; PDR = People's Democratic Republic

5.1.1.3 Barriers to implementation and discussion

Recent improvements have been seen in the presence and breadth of JE vaccine programs. At present, 62% of countries with JEV transmission risk have JE immunization programs

compared to 50% in 2016 and 46% in 2012. Some countries with risk have decided against a program as only rare, sporadic human cases occur (e.g., Singapore) (204). However, non-functional health facilities and lack of vaccine availability are the reason for lack of a vaccine program in other countries (e.g., Papua New Guinea) (209). It is also evident that since 2012, mouse brain-derived vaccine is used in fewer countries as recommended by WHO with more countries using newer, less reactogenic vaccines with simpler dosing schedules (202,204). Lack of disease surveillance, inadequate financial resources, competing vaccine priorities, and need for technical assistance have been cited as the four main barriers for JE vaccine introduction by decision makers in JE-endemic countries (210). The introduction of the JE vaccine has resulted in a 72% reduction in JE in Nepal, reduced the risk of acquiring JE by 61% in Sarawak, Malaysia, reduced the proportion of encephalitis caused by JEV from 40% to 15% in Thailand, and reduced morbidity in China by 97% (211–214). This emphasizes the success of a vaccine program if it is properly implemented.

5.1.1.4 Gap analysis

Table 15 - Gap analysis for JE vaccination

Where we are	Where we want to be
Approximately 62% of countries with JEV transmission risk have JE immunization programs. Implementation of JE vaccination programs have improved over the years but is still patchy in some in endemic areas.	Need to improve access to health facilities, vaccine availability, financial resources, and education to enable access to JE vaccines in countries with JEV transmission risk Need good burden data as vaccine introduction in resource-limited settings often require prioritization of multiple public health interventions for diseases that affect populations
Vietnam continues to use mouse brain-derived vaccines despite the WHO recommendation that inactivated mouse brain-derived vaccines be replaced with the newer generation vaccines for safety reasons.	Need to replace mouse brain-derived vaccines with safer options
General vaccine hesitancy is on the rise including in countries affected by JE **(207)**.	Need to maintain confidence in vaccine programs and high JE vaccine coverage.

JE = Japanese encephalitis; JEV = Japanese encephalitis virus

5.1.2 Tick-borne encephalitis vaccination programs

5.1.2.1 Recommended practice

Worldwide there are six different TBE vaccines, two from Western Europe, three from Russia, and one from China (215). The WHO recommends vaccination should be offered to the whole population in areas where TBE is highly endemic (≥5 cases/100,000/year) and to targeted individuals at risk in regions with a moderate or low TBE incidence (<5 cases/100,000/year)

(216). Similarly, the Central European Vaccination Awareness Group recommends universal TBE vaccination for persons aged over one year for all countries at high risk of TBE (217).

5.1.2.2 Implementation status

Different immunisation strategies exist in European countries depending on the local epidemiological situation and regional/national risk assessment. Between 2020-2023, national government public health websites for countries of the UN Europe area were reviewed for information regarding country-specific vaccine recommendations (218). Where this could not be located, local Pfizer Medical Teams were consulted and authoritative websites and data sources that contained accurate information obtained. Data from 30 European countries showed a national recommendation in seven countries, a sub-national recommendation for vaccination of everyone within specific risk areas in nine countries, a sub-national recommendation for vaccination of individuals engaged in high-risk activities within certain areas in three countries, a recommendation for vaccination of at-risk occupational groups in 12 countries, and an explicit recommendation for travellers in 26 countries (Table 16). The four countries that did not explicitly recommend vaccination in travelers had a national TBE vaccination recommendation.

Although the focus has mainly been on Europe, countries outside Europe experience TBE too, namely China and Japan. The TBE immunisation policy in China recommends vaccination for people working or living in high-risk regions, especially forest workers or those who enter the forest areas for occupational reasons, including military personnel (219). Similarly, in Japan TBE vaccine is recommended for residents in at-risk regions and travellers to endemic areas (220).

Despite many European countries having some form of TBE vaccine policy in place, vaccination rates remain suboptimal. A population survey conducted in 2015 concluded that 25% across 10 European countries (i.e., Czech Republic, Estonia, Finland, Germany, Hungary, Latvia, Lithuania, Slovakia, Slovenia, and Sweden) had at least one injection (221). The lowest vaccination rates were seen in Finland and Slovakia (~10%) and the highest in Austria (85%). A belief that vaccination is unnecessary and that there is no risk of contracting TBE are the main reasons for not receiving vaccination.

Table 16 – TBE vaccine recommendations by country

Country	TBE vaccination program	Further details of vaccination recommendations
Austria	National	National; Travel
Belarus	Other	Occupational; Travel
Belgium	Other	Occupational; Travel
Croatia	Regional (activity)	Regional (for high-risk activities); Occupational; Travel
Czech Republic	National	National; Occupational
Denmark	Regional (activity)	Regional (for high-risk activities); Travel
Estonia	National	National; Occupational
Finland	Regional (all)	Regional (for all within region); Travel
France	Other	Travel
Germany	Regional (all)	Regional (for all within region); Travel
Greece	Other	Travel
Hungary	National	National; Occupational; Travel
Iceland	Other	Travel
Ireland	Other	Travel
Italy	Regional (all)	Regional (for all within region); Occupational; Travel
Latvia	National	National
Lithuania	National	National; Travel
Luxembourg	Other	Travel
Netherlands	Other	Travel
Norway	Regional (activity)	Regional (for high-risk activities); Travel
Poland	Regional (all)	Regional (for all within region); Occupational; Travel
Portugal	Other	Travel
Romania	Regional (all)	Regional (for all within region); Travel
Russia	Regional (all)	Regional (for all within region); Occupational; Travel
Slovakia	Regional (all)	Regional (for all within region); Occupational; Travel
Slovenia	National	National; Occupational
Spain	Other	Travel
Sweden	Regional (all)	Regional (for all within region); Travel
Switzerland	Regional (all)	Regional (for all within region); Occupational; Travel
United Kingdom	Other	Occupational; Travel

TBE = Tick-borne encephalitis

Adapted from Halsby et al. (218)

5.1.2.3 Barriers to implementation and discussion

TBE vaccines are highly effective and considered the most successful way to prevent TBE. A large proportion of European countries have some form of TBE vaccine policy in place, which is largely dependent on the local epidemiological situation and risk assessment. However, it has been suggested that prevention of TBE is suboptimal in some European countries where an increasing number of cases are occurring (222). This is likely due to underuse of vaccine in most countries with TBE, even in highly endemic areas. Some Asian countries like China and Japan, also experience TBE. Historically, TBE in China was considered an occupational disease. However, since the 1990s, 70%–95% of TBE patients were non-forest-working farmers, housewives, domestic workers, students or anyone with any occupation who entered the endemic forest areas (223). Thus, adjustments to the immunisation policy may need consideration with more TBE cases observed in people with occupations other than forest workers (219). Despite policies being in place, it is thought that vaccine uptake is limited. Only 158,000 and 255,000 doses of second-generation purified primary hamster kidney cell-derived inactivated vaccine were released on 28 November 2007 and 3 February 2008, respectively; however, the population of the endemic provinces (including the non-endemic areas) was 65.7 million (219). Japan reported its first case of TBE in 1993; since then only four further cases have been reported (between 2016 and 2018), all on the northern island of Hokkaido (224). A recent retrospective study of patients hospitalised with encephalitis and meningitis of unknown cause identified two previously undiagnosed TBE cases, demonstrating that TBEV infections and TBE cases may go undiagnosed in Japan (225). A TBE vaccine was only officially approved in Japan in March 2024 (220). Climate change may alter the current distribution of TBE, and low endemic countries may see an increase in TBE burden. Milder weather may prolong the exposure period to ticks and tick activity in endemic areas (43). Also, TBE endemic areas may be extended, and the distribution of vectors may increase.

5.1.2.4 Gap analysis

Table 17 - Gap analysis for TBE vaccination

Where we are	Where we want to be
Many European countries have some form of TBE vaccine policy in place; however, TBE vaccines are underused in most, even in highly endemic areas	Need to focus efforts on raising awareness (also outside endemic areas), improving surveillance and diagnostics, ensuring better vaccine uptake, and strengthening international collaborations to look beyond natural foci and national borders
There is a TBE immunization policy in place in China for people working or living in high-risk regions, especially forest workers or those who enter the forest areas for occupational reasons.	Need to consider adjustments to the immunization policy with more TBE cases observed in non-forest-working farmers, housewives, domestic workers, students, or anyone with any occupation who entered the endemic forest areas

TBE = Tick-borne encephalitis; TBEV = Tick-borne encephalitis virus

5.1.3 Measles vaccination programs

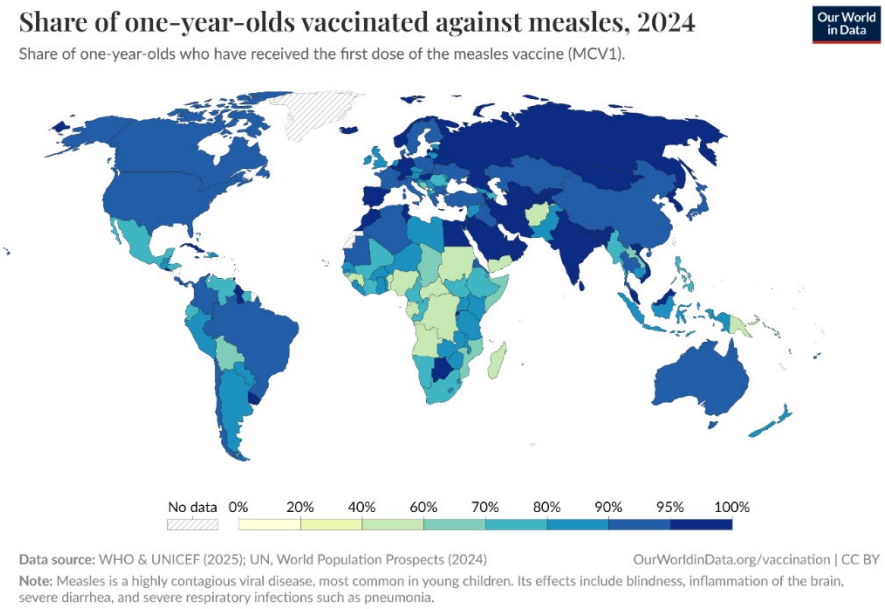
5.1.3.1 Recommended practice

Despite the availability of a safe and effective vaccine, measles still infects hundreds of thousands of people globally. Approximately 136,000 deaths due to measles occurred in 2022, mostly in children under the age of five years (226). It is estimated that 1-3 in 1,000 children who contract measles will develop encephalitis; 10–15% of those children will die and a further 25% will be left with permanent neurological damage (227). The WHO recommends 95% vaccination coverage with two doses of measles-containing vaccine in each country to protect the population from measles (228).

5.1.3.2 Implementation status

The WHO estimated that in 1980 only 16% of one-year olds received the first dose of a measles-containing vaccine (MCV1); this increased to 85% in 2016 and as a result deaths due to measles decreased by 84% between 2000 and 2016. Coverage of MCV1 by country in 2024 is displayed in Figure 9. The lowest coverage was seen in Montenegro (23%),Yemen (41%), and Central African Republic (41%) (229). A study on the trends of measles vaccine coverage in 204 countries from 1990 to 2019 reported only 74 (36%) reached the recommended MCV1 coverage rate of 95% (230). The global proportion of children who received a first dose of measles vaccine in 2024 was 84% (231).

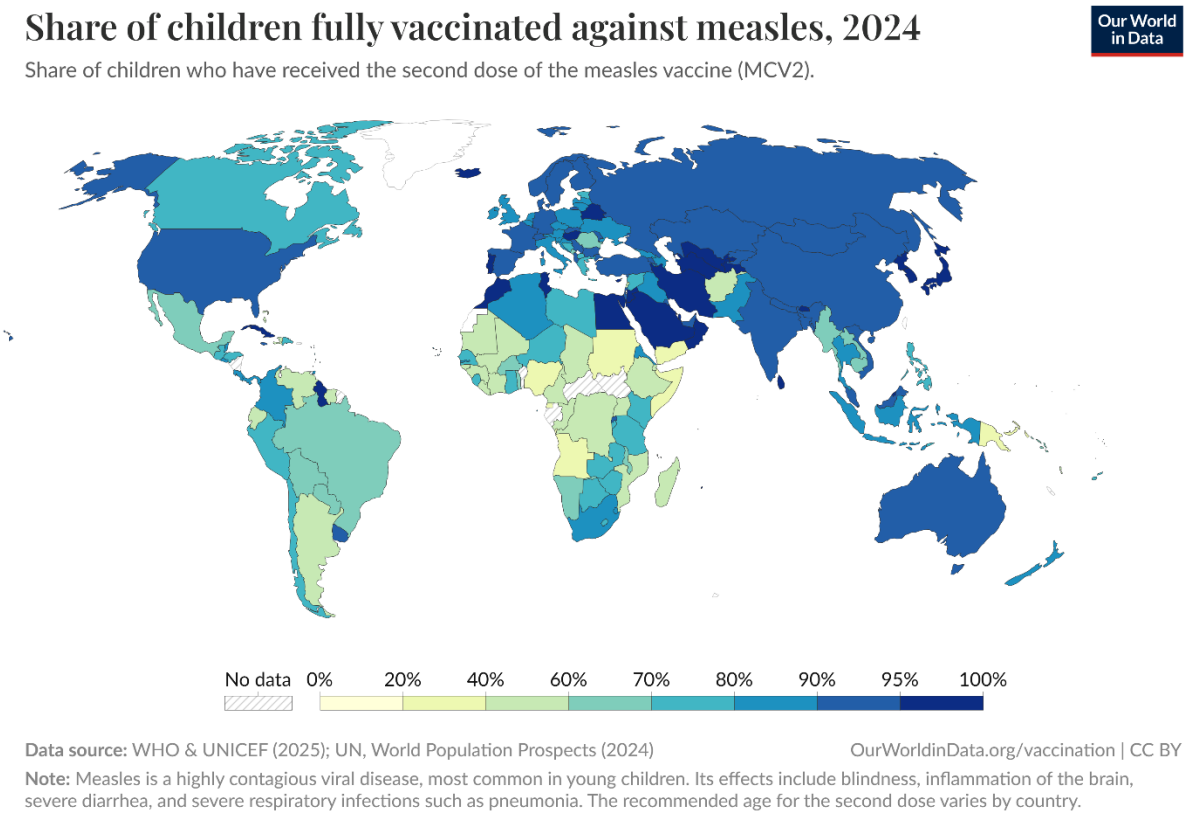
Figure 9 - Global coverage of first dose of measles-containing vaccine in one-year olds, 2024



From Our World in Data (229)

A higher level of protection is achieved with two doses of a measles-containing vaccine (MCV2). By the end of 2024, 76% of children globally received the second dose of measles-containing vaccine according to nationally recommend schedules (231). Coverage of MCV2 by country is displayed in Figure 10. In 2024, coverage was lowest in Papua New Guinea (26%), Equatorial Guinea (31%), and Angola (31%) (229). Furthermore, many countries in sub-Saharan Africa have yet to introduce MCV2 as part of routine immunisation (232). Only 36 (18%) countries reported a rate of MCV2 over 95% in a study on the trends of measles vaccine coverage in 204 countries from 1990 to 2019 (230).

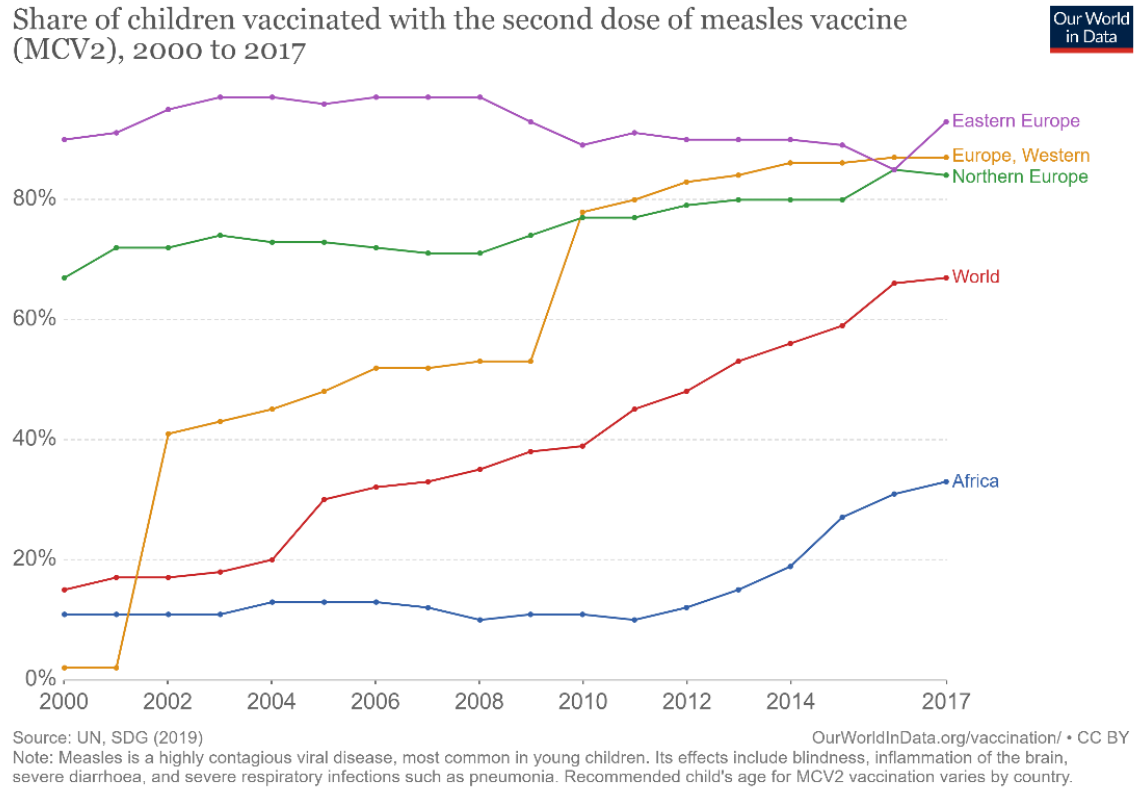
Figure 10 – Global coverage for second dose of measles-containing vaccine, 2024



From Our World in Data (229)

A substantially higher proportion of European children have been vaccinated with two doses of a measles-containing vaccine than African children (Figure 11).

Figure 11 – Proportion of children given second dose measles vaccine in Europe and Africa

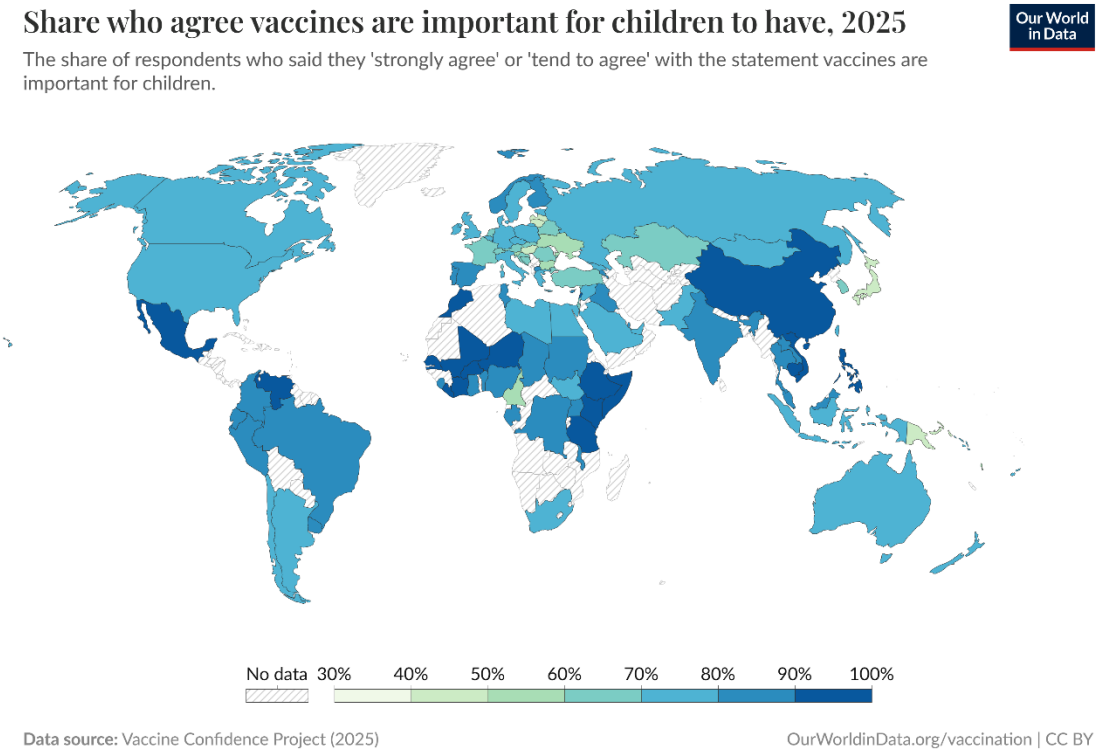


5.1.3.3 Barriers to implementation and discussion

5.1.3.3.1 Barriers to implementation

A survey by The Wellcome Trust in 2018, which included >140,000 people from 140 countries, found that >90% of the world's population believe childhood immunisation is important (233). Despite support for vaccination being generally high, some differences were observed between northern and southern countries. Data from the Vaccine Confidence Project, set up in 2010 to better understand growing vaccine scepticism around the world, reports highest vaccine support in Morocco (99%), Ethiopia (98%), and Tanzania (98%) and lowest vaccine support in Hungary (43%), Latvia (45%), and Papua New Guinea (46%) (Figure 12) (229,234).

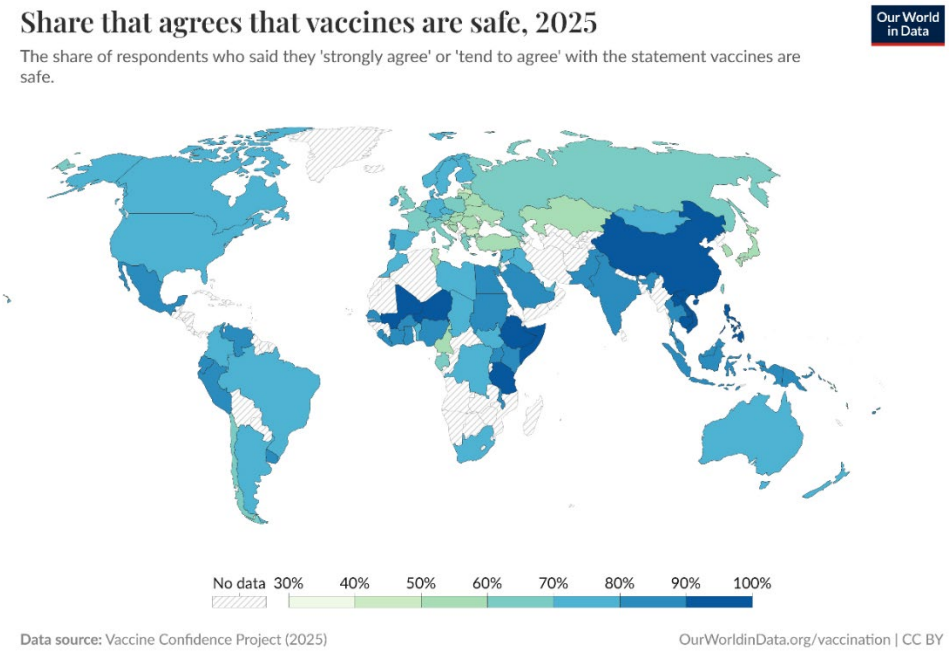
Figure 12 – Proportion of respondents by country who believe childhood immunisation is important, 2025



From Our World in Data (229)

Similarly, the proportion of individuals who agree vaccines are safe was lowest in Eastern European countries, including Latvia (42%), Bulgaria (47%), Slovenia (50%), and Hungary (50%) (Figure 13) (229). Countries with high confidence of vaccine safety included Cambodia (97%), China (95%), and Niger (95%) (229).

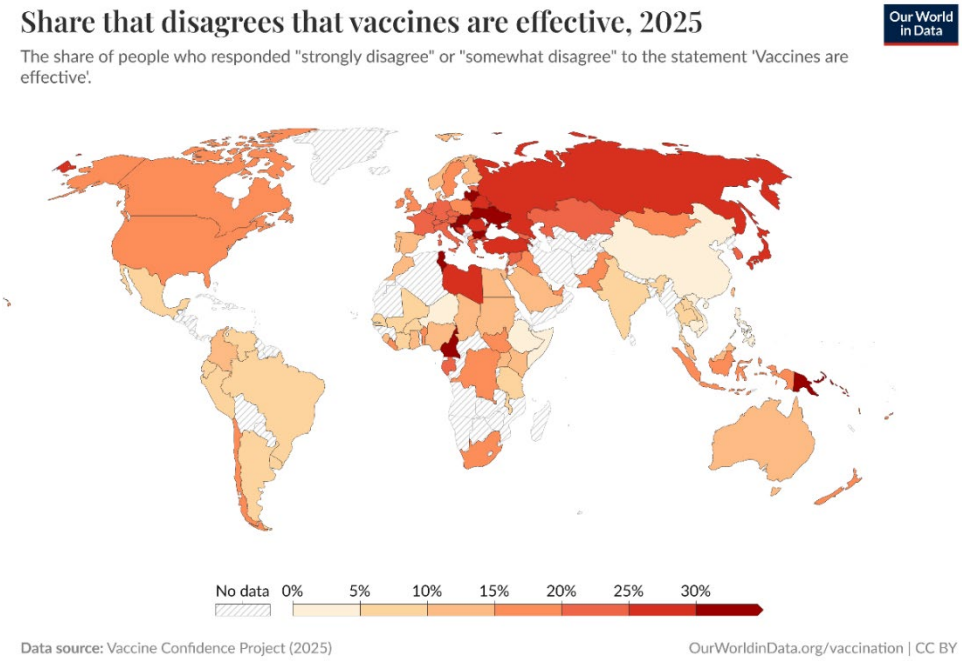
Figure 13 – Proportion of respondents by country who agree that vaccines are safe, 2025



From Our World in Data (229)

Skepticism of vaccine effectiveness was highest in Papua New Guinea (46%), Latvia (43%), and Bulgaria (41%) and lowest in China (2%) and Niger (3%) (Figure 14) (229).

Figure 14 - Proportion of respondents by country who disagree that vaccines are effective, 2025



From Our World in Data (229)

5.1.3.3.2 Discussion

Despite the availability of vaccine, cases of measles are increasing at an alarming rate. This is important as approximately 90% of people who are not already immune will become infected following exposure to the measles virus (233). In LMICs, it is estimated that 1 or 2 in every 1,000 children with measles will die from the disease or its complications (233). Global vaccine coverage has not reached sufficient levels to prevent outbreaks. The WHO recommends 95% vaccine coverage of two doses of measles-containing vaccine to protect the population against measles. Many countries in sub-Saharan Africa have yet to introduce a second dose, and in many other countries coverage remains low. In 2022, an estimated 136,000 deaths due to measles occurred globally, mainly in unvaccinated or under vaccinated children under five years of age (235). Measles remains an imminent threat in every region of the world due to declines in vaccine coverage, weakened measles surveillance, continued interruptions and delays in immunisation activities due to COVID-19, and persistent large outbreaks. Efforts must focus on improving routine immunisation and health systems and overcoming vaccine hesitancy.

5.1.3.4 Gap analysis

Table 18 - Gap analysis for measles vaccination

Where we are	Where we want to be
The average global coverage of second dose of measles-containing vaccine was estimated at 76% in 2024. Many countries in sub-Saharan Africa have yet to introduce a second dose, and in other countries coverage remains low (e.g., Papua New Guinea, Equatorial Guinea, Angola).	Need to increase the number of countries, especially in Africa, offering a second dose of measles-containing vaccine as part of routine immunization Need to increase the coverage of measles-containing vaccine to 95% in each country Need to focus efforts on improving routine immunisation and health systems and overcoming vaccine hesitancy

5.1.4 Rabies vaccination programs

5.1.4.1 Recommended practice

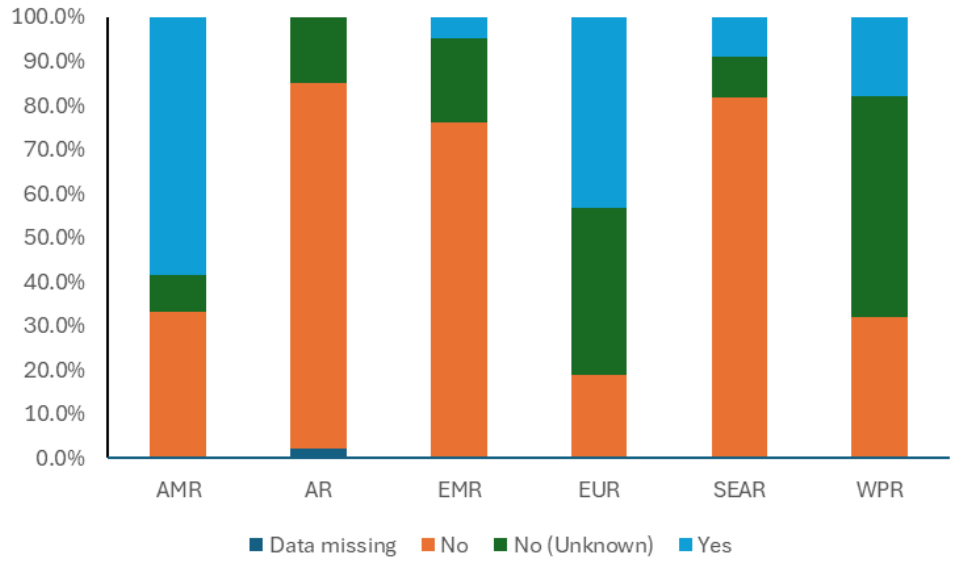
Rabies CNS involvement manifests as classic or furious encephalitic rabies in 80% of cases as opposed to paralytic rabies (236). To date, no effective therapy for rabies CNS involvement has been developed and most cases result in death. Vaccination against rabies can be used to protect against exposure to rabies (i.e., pre-exposure vaccination) or to prevent the development of clinical symptoms once exposure has occurred (i.e., post-exposure prophylaxis [PEP]). Rabies transmitted by dogs is most common in LMICs, whereas rabies transmitted by bats account for the few cases seen in industrialized countries. Pre-exposure vaccination with cell-culture- or embryonated-egg-based vaccine is recommended for individuals living in or travelling to countries or areas at risk and people at high risk of exposure

to rabies, including laboratory staff working with rabies virus, veterinarians, animal handlers, and wildlife officers. The WHO recommends intradermal (ID) administration of rabies vaccine for pre-exposure prophylaxis (237). Prompt PEP may be required in countries or areas at risk of rabies following an animal bite or other contact with an animal suspected to be rabid. PEP includes wound washing, vaccination with rabies vaccine, and administration of rabies immunoglobulin (RIG) where indicated (47). Four organisations including the WHO, World Organisation for Animal Health, Food and Agriculture Organization of the UN, and Global Alliance for Rabies Control, have joined forces, as the United Against Rabies collaboration, and set a global target to end human deaths from dog-mediated rabies by 2030 (238).

5.1.4.2 Implementation status

Data collated by CDC through international organisations (e.g., WHO, Pan American Health Organization), government reports, scientific publications, outbreak report alerts, and information provided by national and international rabies experts, show that out of 196 WHO region countries, 51 (26%) have implemented a robust national rabies control programme (239). A robust control program was evidenced by control measures (e.g., dog rabies vaccination coverage), significant reduction in cases, and/or transmission limited to focal areas as documented in the past five years. If data were not available, the country was not considered to have a robust control program. There is no robust national rabies control program in 97.9% of African Region (AR; 46/47), 95.2% of Eastern Mediterranean Region (EMR; 20/21), 90.9% of South-East Asian Region (SEAR; 10/11), 82.1% of Western Pacific Region (WPR; 23/28), 56.6% of European Region (EUR; 30/53), and 41.7% of Region of the Americas (AMR; 15/36) countries (Figure 15).

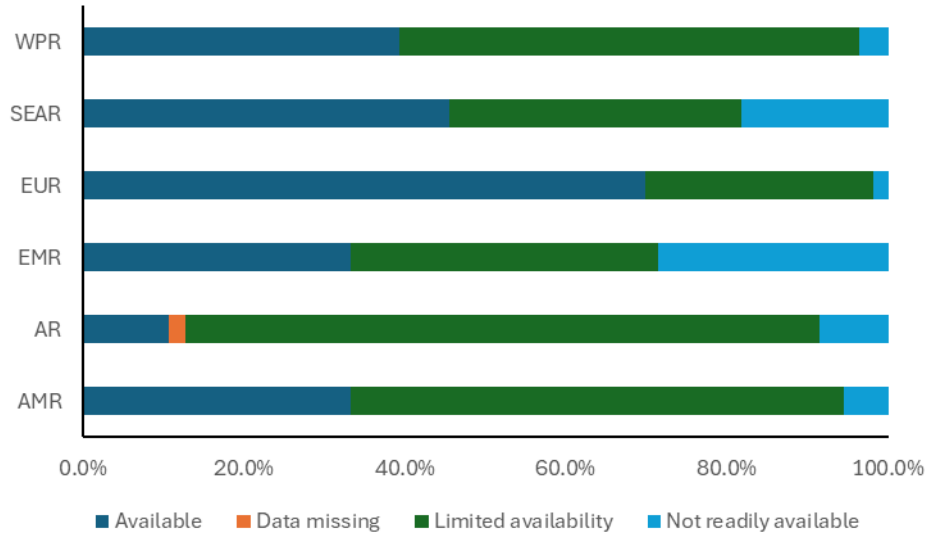
Figure 15 – Countries with robust rabies national control program implemented



Data from CDC (239)
AMR = Region of the Americas; AR = African Region; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asian Region; WPR = Western Pacific Region

Vaccine and RIG availability also vary globally. High-quality rabies vaccine for human use is available (throughout most of the country for PEP within 48 hours of patient presenting for care) in 77 countries, with limited availability (available only in major urban medical facilities for PEP within 48 hours of patient presenting for care) in 102 countries and not available (not readily available within 48 hours of patient presenting for care in most of the country) in 16 countries (239). Vaccine is available in 69.8% (37/53) of countries in EUR compared to 10.6% (5/47) in AR (Figure 16). National rabies vaccination policies for adults exist in some European countries. Rabies vaccine is recommended for specific risk groups in the Czech Republic and UK, and is mandatory for specific risk groups in Bosnia Herzegovina, Serbia, Montenegro, and North Macedonia. In the USA, individuals at high risk of exposure, such as vets, animal handlers, and laboratory workers, should be offered rabies vaccination (240).

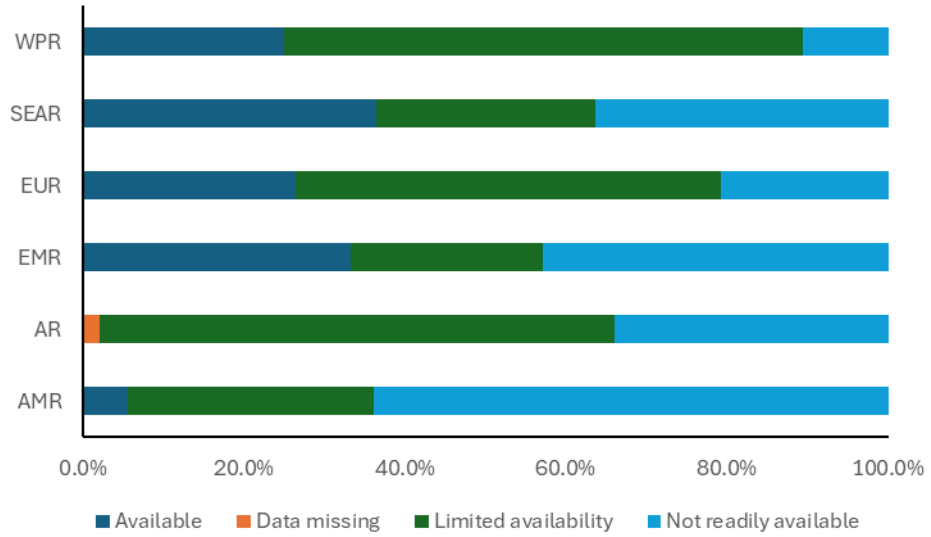
Figure 16 - Global availability of rabies vaccine



Data from CDC (239)
AMR = Region of the Americas; AR = African Region; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asian Region; WPR = Western Pacific Region

RIG is available in 34 countries, has limited availability in 95 countries, and is not readily available in 66 countries (239). RIG is available (throughout most of the country for PEP within 48 hours of patient presenting for care) in no AR countries (Figure 17).

Figure 17 - Global availability of rabies immunoglobulin



Data from CDC (239)
AMR = Region of the Americas; AR = African Region; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asian Region; WPR = Western Pacific Region

A survey of 35 key personnel at the national, county, sub-county, and health facility levels in five counties of Kenya showed considerable variability in the availability of rabies vaccine and immunoglobulin within Kenya, administration of PEP via the intramuscular (IM) route rather than intradermally (i.e., one ID dose is 0.1 mL of vaccine while one IM dose is an entire vial of vaccine irrespective of vial size), and a high cost of rabies PEP and immunoglobulin to patients with bites (47). A further study which assessed patient characteristics associated with initiation and completion of rabies PEP in Vietnam between 2014 and 2016 showed that only 70% and 41% of patients with animal exposures completed two and five doses, respectively, of their IM vaccine course (241). Sreenivasan et al. reported the results of a standardized assessment of rabies PEP procurement, forecasting, distribution, monitoring, and reporting in 23 LMICs in Asia and Africa (46). Data on administration route, cost, and accessibility of rabies vaccine and immunoglobulin in the public sector by country are displayed in Table 19. Almost 60% of countries (13/22) have a national program or guidelines (however not defined as "robust" as per aforementioned CDC data) for rabies control and prevention; these included seven countries in Asia and six in Africa. Rabies vaccine was available in all countries; however, accessibility and cost varied widely. Vaccine was widely accessible (i.e., defined based on availability and cost; see Table 19) in 36% (8/22), accessible in 32% (7/22), and limited in 32% of countries (7/32). Rabies vaccine was only widely accessible in one African country and limited in five. Almost 90% of countries with wide access to vaccine had a national rabies control program or guidelines. Rabies vaccine was reported to be consistently provided for free in the public sector in 43% (10/23) of countries. RIG was less accessible than vaccine; 65% (15/23) of countries had limited access of which 11 were in Africa. RIG was only widely accessible in two countries. Approximately half of countries (12/23) used the IM route exclusively for rabies vaccination; 10 of these were in Africa. A further five Asian countries reported using both IM and ID administration.

Table 19 - Administration route, cost, and accessibility of rabies vaccine and rabies immunoglobulin in the public and non-private sectors of Asian and African countries, 2017–2018

Country	National program/ guidelines	Route of administration	Vaccine accessibility*	Vaccine cost to patient	RIG accessibility	RIG cost
Cameroon		Intramuscular	Accessible	$13-17/dose	Limited	-
Chad		Intramuscular	Limited	$13/dose	Limited	-
Côte d'Ivoire		Intramuscular	Accessible	$13/dose	Limited	-
Ethiopia	Yes	Subcutaneous Intramuscular	Limited	$2-4/course $13/dose	Limited	-
Ghana		Intramuscular	Limited	Free	Limited	-
Kenya	Yes	Intramuscular	Accessible	$12-15/dose	Limited	$70/vial
Madagascar	Yes	Intradermal	Accessible	Free	Limited	Free
Mali		Intramuscular	Limited	$20/dose	Limited	-

Malawi (Blantyre district only)		Intramuscular	Information not available	Free	Limited	-
Nigeria	Yes	Intramuscular	Limited	Free	Limited	-
South Africa	Yes	Intramuscular	Widely accessible	Free	Widely accessible	Free
Tanzania	Yes	Intramuscular	Accessible	$13	Limited	-
Bangladesh	Yes	Intradermal	Widely accessible	Free	Accessible	Free - $15/vial
Bhutan	Yes	Intradermal	Widely accessible	Free	Accessible	Free
India	Yes	Intradermal Intramuscular	Accessible	Free	Limited	Free
Nepal		Intradermal Intramuscular	Accessible	Free	Limited	-
Sri Lanka	Yes	Intradermal	Widely accessible	Free	Accessible	Free
Pakistan		Intradermal Intramuscular	Limited	Free	Limited	Free
Cambodia		Intradermal Intramuscular	Limited	Free - $15/dose	Limited	$37/ patient
China	Yes	Intramuscular	Widely accessible	$50/course	Widely accessible	$25-50/ vial
Mongolia		Intramuscular	Widely accessible	Free	Limited	Free
Philippines	Yes	Intradermal	Widely accessible	Free	Accessible	$28-32/vial
Vietnam	Yes	Intradermal Intramuscular	Accessible	$7-13/dose	Accessible	$15-27/vial

**Widely accessible = vaccine or RIG available for free or at a subsidized cost at the central level, provincial, state or regional level, and at least one health facility in every district, county or zone; Accessible = vaccine or RIG available at the central level and provincial, state, or regional level but not in every district, county or zone, or available in every district but at a cost to patients (greater than US$ 5/dose); Limited accessibility = vaccine or RIG only available at the central level (regardless of cost) or being sporadically available at lower levels because of budget constraints or stock outs*
Adapted from Sreenivasan et al. (46)

Dog-mediated rabies in Latin American countries has decreased significantly over the last three decades but only 37% of countries surveyed in 2013/4 reported sufficient funds to sustain their rabies control program, which includes the use of PEP (242). A situational analysis of rabies in the Caribbean (conducted via survey and literature review) showed that pre-exposure rabies vaccination for at-risk groups (e.g., vets and laboratory personnel) was routinely conducted and vaccine was available for PEP in all endemic countries in 2014//5 (243). RIG for PEP however was only available in five of 10 endemic Caribbean countries; it was not available in Belize, Dominican Republic, Guyana, Suriname, and Trinidad despite these countries being endemic for rabies. It was also available in three non-endemic Caribbean countries, including Bonaire, Bermuda, and Guadeloupe.

5.1.4.3 Barriers to implementation and discussion

Rabies vaccine is effective yet an estimated 59,000 human deaths still occur each year due to rabies (47). In addition, there has been an alarming rise in rabies in the post-COVID era in

high-burden countries, for example India and parts of Africa and South America, due to vaccine hesitancy, disruptions in supply chains, and the reduction of mass dog vaccination campaigns (244). The availability and cost of rabies vaccine and PEP varies between and within countries and is often limited in the places that need it the most. In Africa in particular, vaccine is widely limited, RIG is less accessible than vaccine, and rabies vaccination is most often given via the IM route. The WHO recommends pre-exposure rabies vaccine be administered intradermally as 60-80% less vaccine volume is used via this route, which lowers the vaccination cost, extends supplies, and prevents shortages (245). Monoclonal antibodies for PEP might be preferable to RIG in terms of supply, cost, and efficacy (246). Almost 90% of Asian and African countries which reported wide access to rabies vaccine had a national rabies control program or guidelines. This highlights the importance of developing and ensuring such programs or guidelines are in place within endemic countries. PEP is almost 100% effective in preventing rabies when given appropriately and in a timely manner (46). However, it is evident that prompt provision of PEP remains a challenge in rabies endemic areas due to lack of steady supply of PEP for bite patients that seek care, delays in receiving PEP due to long distances bite patients have to travel to access health care, lack of affordability of PEP, or poor health care seeking by bite patients due to a lack of knowledge about the risk of rabies and its prevention (47). Efforts need to focus on shifting these barriers to reach the target of global elimination of human deaths due to dog-mediated rabies by 2030 (47,238). It should be noted that mass vaccination of dogs is a key component of national rabies elimination programmes and has been successful in eliminating dog-transmitted rabies in Europe, North and Latin America, and Japan (247).

5.1.4.4 Gap analysis

Table 20 - Gap analysis for rabies vaccines

Where we are	Where we want to be
Rabies vaccine is effective, yet an estimated 59,000 human deaths still occur each year due to rabies, mainly in Asia and Africa. In Africa in particular, vaccine is widely limited, and RIG is less accessible than vaccine.	Need to increase provision of readily available vaccine across all countries where rabies is endemic, as well as educate people about dog bite prevention. Canine vaccination programs should also be implemented in endemic areas.
A national rabies control program or guidelines are available in almost 90% of Asian and African countries which reported wide access to rabies vaccine.	Need to ensure development and implementation of such programs or guidelines in all rabies-endemic countries, which will increase government buy-in and funding
PEP is almost 100% effective in preventing rabies when given appropriately and in a timely manner, but prompt provision of PEP remains a challenge in rabies endemic areas.	Need to increase supply of PEP for bite patients that seek care, minimize delays in receiving PEP due to long distances bite patients have to travel to access health care, make PEP more affordable, and educate people about the risk of rabies and its prevention and the importance of seeking health care if bitten

In Africa in particular, rabies vaccination is predominantly given via the IM route.	Need to shift pre-exposure rabies vaccine administration from IM to ID in line with the WHO guidelines as 60-80% less vaccine volume is used via the ID route, thus lowering vaccination cost, extending supplies, and preventing shortages

ID = Intradermal; IM = Intramuscular; PEP = Post-exposure prophylaxis; RIG = Rabies immunoglobulin; WHO = World Health Organization

5.1.5 Varicella zoster virus vaccination programs

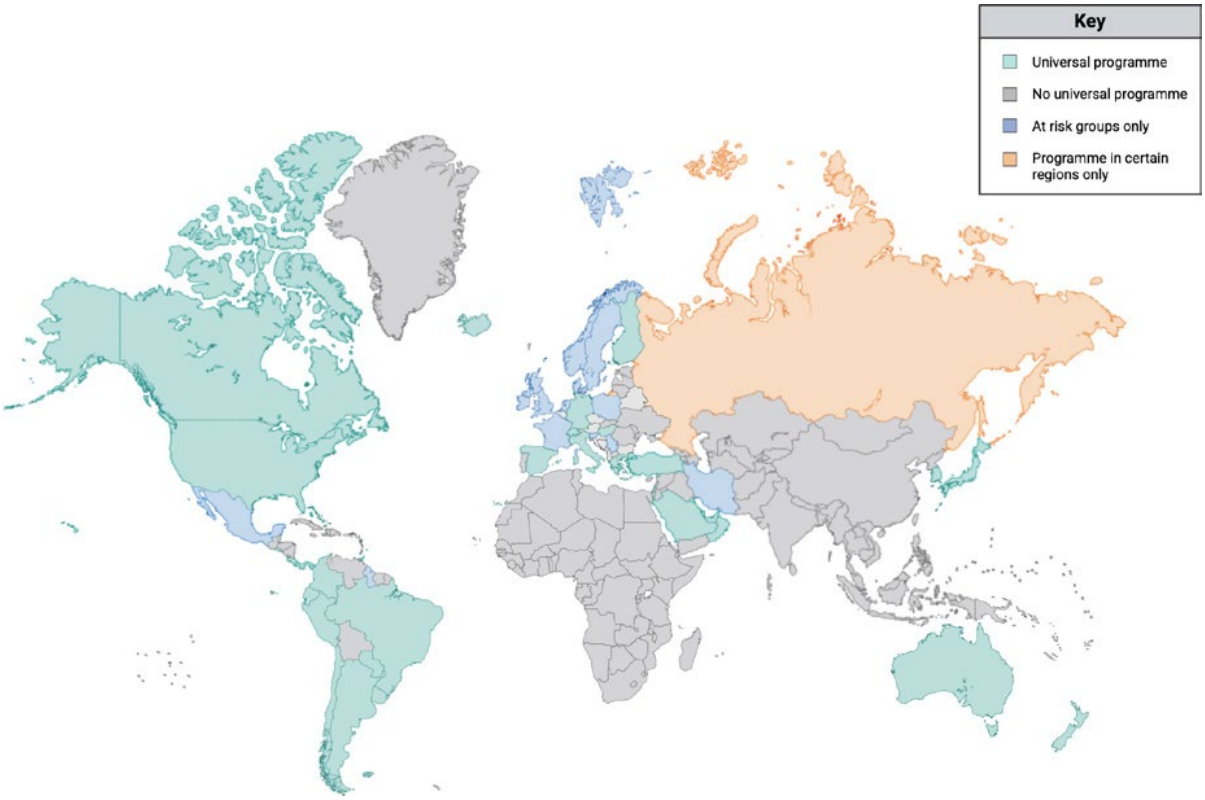
5.1.5.1 Recommended practice

VZV affects ~140 million individuals annually despite the availability of a safe, well-tolerated, and effective vaccine (248). Approximately 4.2 million severe complications requiring hospitalisation and ~4,200 deaths from VZV infections occur per year (249). The greatest disease burden has been reported in children, which represent 90% of cases, 70% of hospitalisations, and 50% of deaths (248). It is estimated that 2-4 per 1,000,000 individuals who contract VZV will develop encephalitis (250); 9–20% of those individuals will die and a further 33% will be left with neurological complications (251). The WHO recommends the varicella vaccine be considered for routine immunisation in countries where varicella constitutes a significant public health burden, and where resources and uptake are sufficient to achieve at least 80% vaccine coverage (249).

5.1.5.2 Implementation status

The vaccine effectiveness of the varicella vaccine is estimated at 55-87% for one dose and 84-98% for two doses *(252)*. However, despite the established efficacy, the varicella vaccine it is not universally part of routine immunisations. As of 2024, it has been recommended in 45 countries (Figure 18) *(253)*. A further 14 countries offer varicella vaccination for at-risk groups or in some areas of the country. Many countries around the world, particularly in Africa and Asia, have yet to recommend the varicella vaccine as part of routine immunisation.

Figure 18 – Global coverage of varicella vaccination programs, 2024



From Wooding et al. (253)

5.1.5.3 Barriers to implementation and discussion

There are several known barriers specific to the implementation of universal varicella vaccination. VZV is frequently perceived to have a low risk of complications with only immunocompromised children or those with underlying medical conditions being at risk (254). This is supported by a survey on parental attitudes to varicella vaccination in preschool and school children which was conducted in Hong Kong in 2015 and included >3,000 parents (255). The survey found that VZV infection being considered a “minor infection” was a key reason that parents did not vaccinate their children. Another key barrier is the potential impact that vaccination programmes could have on the epidemiology of VZV infections (254). In populations where varicella vaccinations have reduced natural infections from VZV, natural boosting of immunised individuals would also likely be reduced (254). This may lead to a shift in infections from young children to older age groups, who are at high risk from complications, resulting in increased morbidity and mortality, despite an overall decline in the number of VZV cases (256). Having reduced natural immunity may also led to an increase in the risk of viral reactivation in individuals with latent VZV through natural infection (257). Lastly, cost modelling based on hospital admission savings and societal costs (e.g., missed employment) show

significant projected/actual savings from varicella vaccine in high-resource settings; however, the benefit remains unclear in resource-limited settings (253).

Thus, despite the availability of a vaccine for VZV, many countries around the world have chosen not to recommended or include it in within their routine vaccinations. This is important as an effective vaccination program has been shown to reduce hospitalisations and complications at least three-fold with the greatest reduction in children under four years of age (258,259). VZV is the second leading cause of viral encephalitis, accounting for 5% of total cases within the UK and other HICs, and is highly preventable with the varicella vaccine (16). However, currently global vaccine coverage must significantly increase to reach levels to prevent outbreaks. The WHO recommends 80% coverage of two doses of varicella containing vaccine to protect the population against VZV. Many countries in Africa, Asia and Eastern Europe have yet to introduce or recommend vaccination.

5.1.5.4 Gap analysis

Table 21 - Gap analysis for varicella vaccination

Where we are	Where we want to be
As of 2024, 45 countries around the world recommend varicella vaccination. Many countries in Africa, Asia and Eastern Europe have yet to introduce or recommend the vaccine.	Need to increase the number of countries, which offer or recommend the varicella vaccine to be taken Need to increase the coverage of varicella vaccine to 80% in each country Need to focus efforts on improving routine immunisation and health systems and overcoming vaccine hesitancy

5.1.6 Vaccines in travelers

Travelers are advised to have a medical consultation prior to departure to acquire knowledge on disease risk in the country/ies they plan to visit and necessary steps to prevent illness, including vaccination. Specific vaccinations that may be recommended to prevent travel-associated encephalitis include for example JE, TBE, and rabies vaccine. The WHO recommends TBE vaccination in travelers to endemic areas, particularly if their visits include outdoor activities (260). JE vaccination is recommended for travelers spending extensive time in JE endemic areas (261). However, despite the availability of vaccine, cases of travel-associated encephalitis still occur. In 2014/15, three cases of JE were diagnosed in British travelers; all suffered severe, life-threatening illness and have been left with life-changing neurological sequelae (262). Similarly, 38 cases of TBE were documented in 2012 in Central/ Western Europe among international travelers (263). Reasons individuals contract travel-associated encephalitis include failure to vaccinate due to poor travel advice and cost of

vaccination. A survey of travelers from Canada, Germany, Sweden, and UK to TBE-endemic regions reported only 69% had heard of TBE, 32% had heard of TBE vaccine, and most sought information online rather than through family doctors or travel clinics (260). A survey of 85 travelers identified cost and 'lack of perceived necessity' as barriers to patient acceptance of pharmacist-provided recommendations for international travel and showed JE and rabies were the vaccines with the lowest acceptance (264). Efforts to increase awareness of travel risk and available vaccines and reduce costs associated with receiving advice and vaccination are needed to reduce the occurrence of travel-related encephalitis.

5.1.6.1 Gap analysis

Table 22 - Gap analysis for vaccines in travellers

Where we are	Where we want to be
Despite the availability of vaccine, cases of travel-associated encephalitis still occur.	Need efforts to increase awareness of travel risk and available vaccines Need efforts to reduce costs associated with receiving advice and vaccination

5.1.7 Other vaccines

Further vaccines have recently been approved or are in development that may prevent encephalitis from other causes in the future. Valneva's single-shot chikungunya vaccine (VLA1553/IXCHIQ®) is approved in some regions (EU, Canada, others) but now carries restrictions or warnings in older adults (≥60-65 years) due to safety concerns (265). For similar reasons, its US license was suspended in 2025 and development there is currently on hold (266). The virus-like particle chikungunya vaccine (VIMKUNYA) manufactured by Bavarian Nordic, was licensed in the US and Europe in February 2025 (267).

Dengue vaccine development has seen significant progress with the licensing of two live-attenuated vaccines. Dengvaxia® (CYD-TDV) is registered by the European Medicines Agency, US Food and Drug Administration, and in some Asian and Latin American countries; however, deployment is complex due to varying efficacy against dengue virus serotypes and the requirement to pre-screen for prior exposure to avoid the potential of severe dengue in those not previously infected (268–270). The newly authorized Qdenga® (TAK-003) vaccine is suitable for individuals aged ≥4 years regardless of baseline serostatus; however, there are concerns regarding its safety and efficacy against certain serotypes (268). The worst global dengue outbreak on record in 2024 emphasizes the need for further vaccines (271). Further candidates in clinical (i.e., phase-III Butantan-DV vaccine) and preclinical trials have shown promise; however, challenges remain with regards to the

various dengue serotypes and the potential for antibody-mediated disease enhancement (268).

A live attenuated vaccine against Venezuelan equine encephalitis virus (VEEV) was developed in 1961 and has been used exclusively for laboratory and military personnel at risk of contracting VEEV and to immunize horses. This vaccine however is associated with adverse events, serological nonresponse, and lacks full coverage of VEEV (272). There are currently no vaccines against EEEV, VEEV, or WEEV licensed for human use; however, several vaccines are currently under development to protect against these encephalitic alphaviruses.

The rapid development and implementation of vaccines against SARS-CoV-2 in response to the COVID-19 pandemic have shown how much can be achieved with financial commitment, determination, and engagement of the global scientific community. Novel vaccine platforms (e.g., mRNA), adoptive case-driven trial designs, and a rolling review process by regulators have facilitated this process (273). Lessons should be learned and applied to the development of future vaccines, including those against other causes of encephalitis.

5.2 Vector control

Vaccines are the most effective intervention for the aforementioned causes of encephalitis. However, other measures exist that could help reduce disease burden. Use of protective clothing and repellents to avoid mosquito and tick bites and avoiding the consumption of unpasteurized milk or dairy products in TBE risk areas (as infected dairy animals can shed TBEV in their milk) may reduce the burden of TBE (274). Mosquito nets have only proved effective in one study of JE; several other studies have shown no effect (202). Mass dog vaccination has resulted in elimination of canine rabies in Malaysia, Japan, Taiwan, Singapore, and across Western Europe (275). There is however little evidence that interventions apart from vaccination of humans, for example vaccination of pigs, environmental management for vector control, and chemical control of vectors, reduces JE disease burden (202). It is important to intensify efforts to prevent and control vector-borne diseases as climate change is likely to increasingly impact vector-borne disease transmission and spread (276).

5.3 Epidemic control

Encephalitis can either occur sporadically or in outbreaks. Encephalitis itself might be epidemic (e.g., arboviruses) or may occur as a feature of disease epidemics for which

encephalitis is a rare complication (e.g., COVID-19) (3). The control of encephalitis outbreaks, or epidemic control, is dependent on the underlying aetiology and availability of a vaccine. For example, a vaccination campaign may be considered if a JE outbreak occurs in an area where JE vaccination has not yet been introduced (277). Factors such as outbreak size, response timeliness, population affected, and program capacity should be taken into account, and the use of live vaccines are recommended for rapid production of protective antibodies (277). Following the outbreak vaccination campaign, introduction of JE vaccine into the routine immunisation schedule is recommended. In Nipah virus outbreaks, where a licensed vaccine is not available, successful epidemic control measures have included isolation of pig farms known to harbour Nipah virus, evacuation of farmers/pig handlers, and the culling of pigs to limit further transmission (278).

For disease outbreaks where encephalitis is a complication (e.g., influenza, COVID-19, measles), different epidemic control strategies can be adopted. Public health interventions such as self-isolation and social distancing have been implemented to reduce the spread of the coronavirus epidemic and thus the subsequent occurrence of resulting encephalitis cases (279). Similar non-pharmaceutical interventions have been used to control influenza outbreaks, as well as vaccination or prophylaxis with antiviral drugs (279,280).

6 Diagnosis and treatment

6.1 Diagnostics

6.1.1 Overview of diagnostic tests

Numerous diagnostic tests are available for the aetiological diagnosis of encephalitis **(281)**. CSF culture can be used for the diagnosis of bacterial encephalitis, while CSF microscopy is helpful for detection of acid-fast bacilli in tuberculous (TB) encephalitis. Serological techniques provide diagnostic support for some causes of encephalitis (e.g., arboviruses); however, when an organism is detected outside the CNS it can be difficult fully to attribute causality. The gold standard for the aetiological diagnosis of most viral encephalitides is CSF PCR. The CSF can also be examined for the presence of microbe-specific intrathecal antibodies present in excess of that predicted by passive transfer from the periphery indicating a local infectious or inflammatory process in the CNS. CSF biochemistry, microbiological tests performed on samples from outside the CNS, and neuroimaging results can provide important supporting diagnostic information in the absence of a lumbar puncture (LP). The diagnosis of ADEM relies primarily on magnetic resonance imaging (MRI). Serological tests are used to identify the precipitant infection of ADEM and to test for autoantibody encephalitis. Metagenomics

includes sequencing the total deoxyribonucleic acid (DNA)/ribonucleic acid (RNA) from a sample to enable the identification of genetic material from any (known or unknown) microorganism present in the specimen that might be causing encephalitis. This method might have a role to play in undiagnosed encephalitis but has yet to be implemented on a routine basis (282).

6.1.2 Recommended practice

The 4th WHO Model List of Essential Diagnostics was published in 2023 (updated from 1st edition in 2018) to help countries prioritize important diagnostic tests for their populations (283). The intention is for countries to use this list to decide which diagnostic tests to select and where to use them, depending on their epidemiology, resources, and infrastructure. The list does not recommend diagnostics specific to encephalitis but rather types of tests that can be used for the diagnosis of many communicable and non-communicable diseases, including encephalitis. The WHO List of Essential Diagnostics recommends microscopy and culture of CSF specimens for bacteriology, mycology, and parasitology. More specifically, the tests that pertain to neurology include CSF cryptococcal antigen (for cryptococcal meningitis), CSF nucleic acid amplification test (CNS TB), CSF bacterial culture, CSF Venereal Disease Research Laboratory test (neurosyphilis), CSF cell cytology, and CSF profile (i.e., red and white blood cells, glucose, protein) (283,284). Despite numerous diagnostic tests being available for the diagnosis of encephalitis, we focus on global access to the following four: 1) CSF examination, including microscopy/culture, 2) CSF HSV PCR, 3) MRI, and 4) autoantibody testing for the aetiological diagnosis of encephalitis.

6.1.3 Implementation status

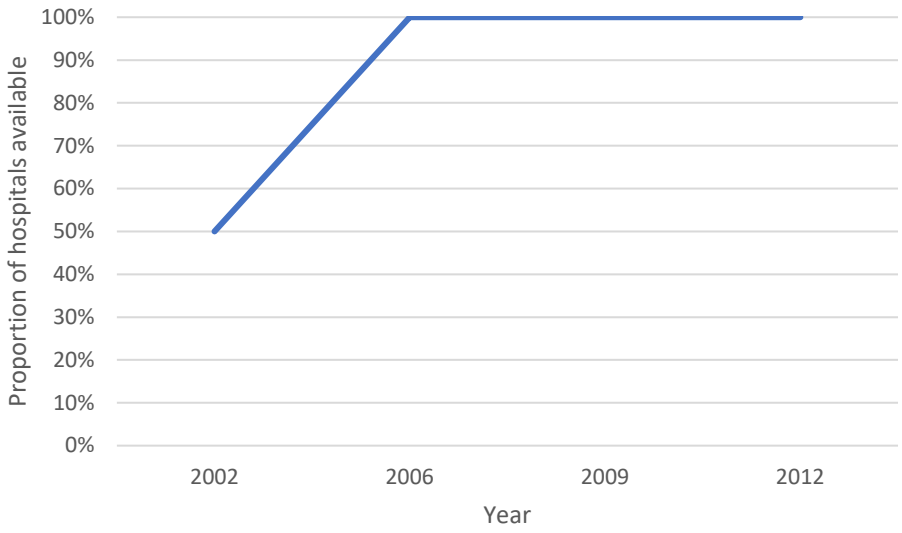
6.1.3.1 CSF examination

The vast majority of laboratories in HICs (i.e., Europe, North America, Australia/New Zealand) are able to conduct CSF investigations, including microscopy and culture. However, these basic diagnostic techniques are often superseded by more sophisticated laboratory diagnostic methods including PCR in these regions. A large survey was conducted of physician respondents engaged in neurology practice worldwide in 2014 to assess the availability of neurodiagnostic tests (285). Thirty-seven countries (n=119, 31% response rate) responded including eight (22%) LICs (Bangladesh, Burkina Faso, Ethiopia, Haiti, Myanmar, Somalia, Uganda, Zimbabwe), seven (19%) lower-middle-income countries (Bhutan, Ghana, India, Lao PDR, Nigeria, Pakistan, Zambia), 13 (35%) upper-middle-income countries (UMICs; Albania,

Botswana, Brazil, Cuba, Iran, Jamaica, Jordan, Macedonia, Mexico, Namibia, Panama, Peru, South Africa), and nine (24%) HICs (Canada, Czech Republic, Iceland, Israel, Japan, Kuwait, the Netherlands, US[1]). CSF studies were reported available in most (n=36, 97%) survey countries, except one LIC which was not specified. All 36 countries could test for white cells, protein, and glucose; 6% (n=2, Bangladesh, Ethiopia) could not obtain staining for bacteria; 17% (n=6, Burkina Faso, Bangladesh, Ethiopia, Jordan, Peru, Albania) were unable to send tests for *M.tuberculosis*; 33% (n=12) were unable to obtain an opening pressure; 36% (n=13) were unable to obtain HSV PCR; and 53% (n=19) were unable to obtain oligoclonal bands for intrathecal antibody testing. Bacterial culture was named by Haiti as the number one diagnostic test they would like that was not currently available.

Numerous studies have assessed the adoption of recommended practices and basic technologies for global health in Kenya, particularly in the context of children. A national survey of 14 hospitals covering 13 Kenyan districts reported 92.9% (n=13) of hospitals were able to do CSF microscopy in 2002 (286). A study which evaluated resources for providing effective paediatric/neonatal care in Kenyan district hospitals over an 11-year period (2002–2012) found that in 2002 only half (7/14) of hospitals could offer microscopy, Gram stain, and culture of CSF. This increased to 100% in 2006 (8/8), 2009 (17/17), and 2012 (22/22; Figure 19) (287).

Figure 19 – Proportion of hospitals in Kenya where microscopy, Gram stain, and culture for CSF available by year, 2002-2012



Data from English et al. (287)

[1] One country was missing from the paper, hence only eight countries were identified here.

Apart from the Kenyan studies, a survey was conducted of the availability and types of laboratory tests offered in clinical laboratories (public and non-public) in Kampala, Uganda (288). Data were obtained from 95% (907/954) of public and private laboratories in 2011. The study recorded the Availability Index (i.e., weighted the percentage of laboratories that offered a test by the laboratory-wide test volumes of those laboratories) of various tests, and CSF analysis was categorised as a minimal availability test (≤15%).

6.1.3.2 HSV PCR

Although no systematic review or survey specifically assessing the global availability of HSV PCR could be identified, studies of encephalitis in Europe, Australia/New Zealand, and the USA have shown widespread use of CSF HSV PCR as a first-line diagnostic test in cases of suspected encephalitis (14,16,139,143). This has also been reiterated in guidelines for the management of encephalitis produced by countries covering these regions (289–291).

Fewer data are available from Asia, Africa, and Latin America. In Asia, CSF HSV PCR is generally available in Middle Eastern countries, some Southeast Asian countries including Singapore and Hong Kong, and at many larger sites in India (292–294). Availability is however more sporadic in other Asian countries and is often not available routinely in government hospitals but can be available via private laboratories for those who can afford it. Studies of encephalitis from Sri Lanka, Vietnam, Taiwan, and Thailand have shown the availability of CSF HSV PCR; however, these research studies are often done in larger tertiary referral centres (123,133,295,296). Some CSF investigations were conducted locally (biochemistry, Gram stain, direct acid-fast bacilli smear examination) in a study of adults with presumed CNS infection who presented to a tertiary referral hospital in Manado, North Sulawesi, Indonesia between 2015 and 2017 but CSF HSV PCR was conducted retrospectively on samples sent to a larger institute in Jakarta (297). A study conducted in rural Nepal between 2014 and 2016 sent collected CSF samples to a collaborating laboratory in Sweden for HSV PCR testing (298). Similarly, samples from adults with CNS infection admitted to a tertiary referral hospital in Kathmandu, Nepal between 2009 and 2011 were investigated locally for CSF biochemistry, Gram stain, and culture but sent to the Oxford University Clinical Research Unit in Vietnam for molecular analysis (299).

In Africa, anecdotal evidence suggests CSF HSV PCR is not routinely available at most hospitals in Zambia, Mozambique, Nigeria, and Malawi (B Singh 2024, personal communication). A study of children with fever and altered consciousness (including encephalitis) conducted in Sudan in 2011 did not search for herpes immunoglobulin or conduct

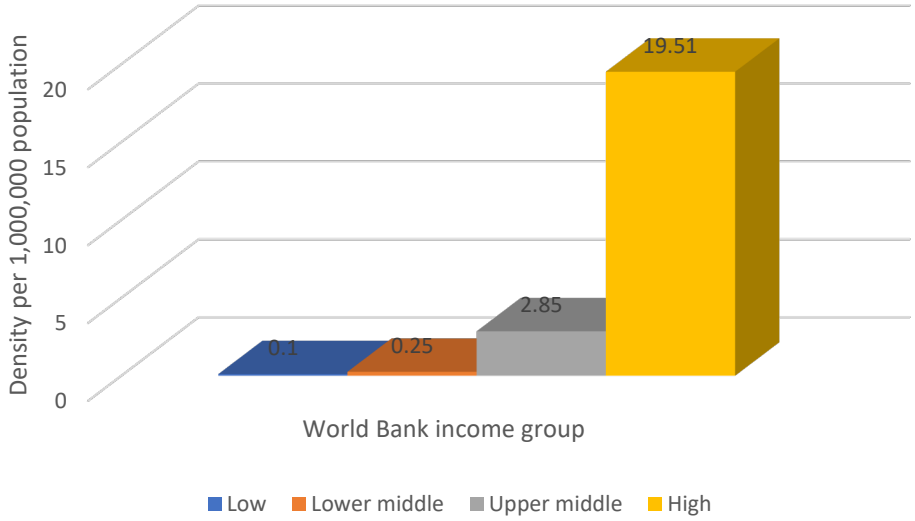
CSF PCR for viruses (300). Similarly, basic laboratory examinations and CSF analysis were carried out locally in a paediatric prospective study to assess the causes of acute neurologic diseases, including encephalitis, in the Democratic Republic of the Congo between 2015 and 2016; however, molecular analysis for the diagnosis of viral CNS infection was not available (301). When respondents in the aforementioned McLane et al. study were asked to list the top three diagnostic tests they would like that were not already available in their practice, PCR for CNS pathogens including HSV was mentioned by Ghana, Zambia, Ethiopia, Botswana, and Bangladesh (285). This study also reported 36% (13/36) of participating countries were unable to obtain HSV PCR; however, the exact countries are not specified in the paper.

Information from Latin America on the availability of laboratory testing in encephalitis is also lacking. Anecdotal evidence suggests CSF PCR is generally available in Brazil, but there is some within-country variation (D Brown 2020, personal communication). Bastos et al. reported that the tertiary public health hospital for infectious diseases in Manaus receives 90% of all CSF samples from patients in the Amazonas state and is the only hospital which performs viral molecular diagnosis (302). In Peru, a prospective study was conducted at 12 hospitals located in different settings (city, Amazon, Andes, and coast) between 2009 and 2012 (7). CSF glucose, protein, and cell count with differential were determined at local laboratories; however, CSF HSV PCR was not available in most Peruvian hospitals and samples were referred to the US Naval Medical Research Unit-6 in Lima for further testing. Following this study, improved diagnostic assays for CSF were identified as a major need through interviews with 48 neurologists across Peru (303). No participating laboratory was able to perform all the following assays: basic CSF chemistries (cell count, glucose, and protein), culture, PCR, immunoglobulin assays, and additional advanced diagnostic testing. Routine CSF biochemistry and culture were performed by most laboratories; however, some relied on private local laboratories for these assays. At present, a reference centre for CSF diagnostics is being developed at the only reference centre for neurological diseases in Peru, with the ultimate aim for CSF PCR testing capacity at regional hospitals.

6.1.3.3 MRI

A baseline country survey on medical devices was carried out in 145 WHO Member States in 2010 with the following response rate: 81.2% (26/32) in low, 75.8% (25/33) in lower middle, 78.9% (30/38) in upper middle, and 70.7% (29/41) in high income groups (304). Results demonstrated a higher density of MRI scanners per million population in high income countries (Figure 20).

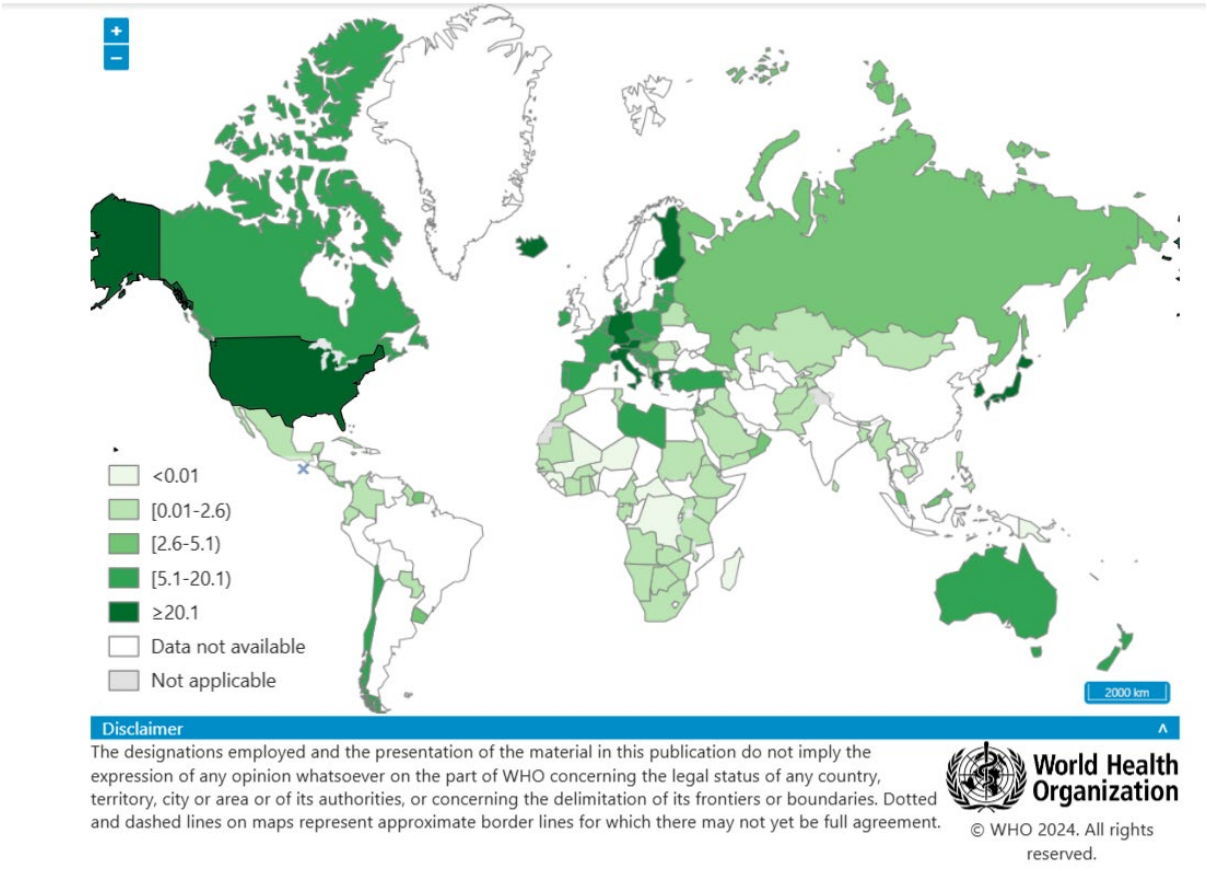
Figure 20 – Density of MRI scanners by income group, 2011



From reference (304)*; MRI = Magnetic resonance imaging*

Data from WHO showed that at present (2024) the lowest density of MRI scanners are in Africa, Asia, and South America (Figure 21) .

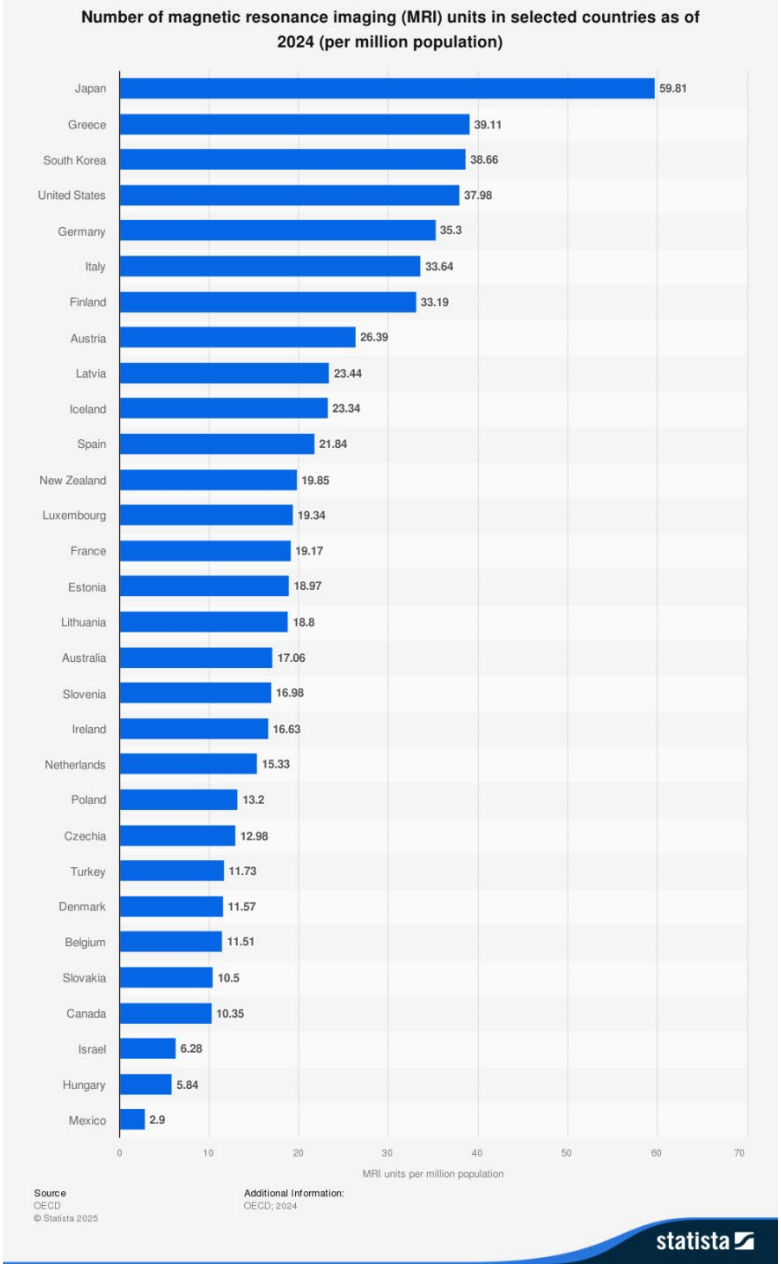
Figure 21 – Total MRI density per million population in 2024



From reference (305)

The presence of MRI scanners was assessed in Organisation for Economic Co-operation and Development (OECD) countries in 2024. The majority of OCED members are HICs with a high Human Development Index (measure of economic development and welfare). The availability of MRI scanners ranged from 2.9 per million population in Mexico to 59.81 per million in Japan (Figure 22) (306). Comparatively, the average MRI scanner density in Africa in 2023 was reported as 0.8 scanners per million population (307).

Figure 22 – MRI units per million population in selected countries as of 2024



From reference (306)

Ogbole et al. carried out a one-year survey between 2015 and 2016 (using both interview and online search) to assess the availability of MRI in the West African region (308). In 2016 there were 84 MRI units in West Africa; more than two-thirds of these were in Nigeria. All Nigerian MRI scanners were situated in urban areas, most were within the private (63%) rather than public health sector, and most (77.6%) were low-field strength (rather than high-field strength) systems. Despite Nigeria having the largest actual number of MRI scanners, Ghana had the highest number of MRI units per million population in West Africa (0.48 units/million compared to 0.30 units/million in Nigeria). This compares to 5.16/million MRI scanners in Libya, the North African country with the highest number of MRI units per million population, and 0.87 units/million in Namibia in the Southern African region (308). When respondents in the aforementioned McLane et al. study were asked to list the top diagnostic test they would like that was not already available in their practice, MRI was mentioned by Pakistan, Cuba, Namibia, and Israel (285).

6.1.3.4 Autoantibody test

The discovery of novel autoimmune encephalitides associated with antibodies against neuronal surface targets has exploded over the last decade. Autoantibody testing is widely and routinely available in most of Europe, the USA, and Australia (S Irani 2020, personal communication). However, variation in testing methods provide different levels of sensitivity and specificity (309–312). Data from Africa and Asia are scarce but autoantibody testing is likely limited in these parts of the world (313). A Moroccan study of limbic encephalitis noted limited access to systemic immunological tests, antineuronal antibodies, and HSV PCR; however, a cohort of Tunisian paediatric autoimmune encephalitis patients received autoantibody testing locally (134,314). The availability of autoantibody testing has been noted in larger tertiary referral centres in India, Sri Lanka, Thailand, and Vietnam (315–318). A recent review from the Philippines reported in-country availability of some autoimmune encephalitis antibody tests (i.e., NMDA, Hu, Ma, Ri) at a cost of USD 100-200 each and with a turnaround time of 3-4 weeks; however, CSF samples are often sent abroad for testing (319). A narrative review of autoimmune encephalitis in Latin America reported that CSF and blood samples for suspected cases of autoimmune encephalitis are usually sent to Europe or the USA for analysis (320). A tertiary hospital in Brazil reported that expensive tests such as the evaluation of serum autoantibodies must be approved by financial staff prior to being performed, which can lead to diagnostic delays, and then sent to an external laboratory for testing (321).

6.1.4 Barriers to implementation and discussion

The global inequity in the availability of laboratory tests for the aetiological diagnosis of encephalitis is stark. Basic CSF microscopy and culture are the most widely available of the four test types evaluated; however, these tests are predominantly for non-viral causes of encephalitis (which also cause meningitis) and most cases of encephalitis are viral or autoimmune. CSF analysis also relies on performance of an LP which is not always carried out due to lack of training, experience, sterile LP kits, and limited laboratory capacity **(322)**. A recent retrospective study in Kenya reported an LP ordered in a median of 66% (range 38%–95%) of children with meningitis and LP findings documented in laboratory or clinical records in a median of 58% (range 15%–79%) **(323)**. This suggests that an LP is not ordered in some children with meningitis, or they may be ordered and never carried out. As meningitis is more widely known and occurs in epidemics across sub-Saharan Africa LPs for encephalitis might be even lower.

The availability of CSF HSV PCR is variable; however, these data show that it is lacking in places that need it. For example, samples from studies in Peru and Indonesia were referred for CSF HSV PCR as testing was not available locally, but HSV was identified as a common cause of encephalitis in both these countries (7,297). This confirms the importance of diagnosing HSE as treatment is available and the outcome is better if treatment is instigated early in the illness. Despite slowly increasing, access to nucleic acid tests remains largely insufficient in LICs and remains limited to predominantly HIV and tuberculosis (324). Lack of availability of testing can be due to numerous factors. Some hospitals in some resource-limited countries lack even basic microbiology laboratories (325). Other laboratories have all the relevant instruments and reagents to carry out specific diagnostic tests but lack skilled staff. Further laboratories are able to amplify DNA but unable to report the results in a timely manner, and many laboratories neglect accreditation and quality assurance (325). Other factors apart from laboratory characteristics and capabilities may play a role. For example, clinician preference was recorded as the main reason further diagnostic testing was not performed in children with acute neurological illness or injury in the Democratic Republic of the Congo suggesting that there are significant gaps in knowledge of appropriate and necessary diagnostic strategies which can be improved through education (301). It is worth noting that even in areas where CSF HSV PCR is readily available it might be used sub-optimally, for example a study in the USA reported CSF HSV PCR was only repeated in 14.2 % of patients with an initial negative result (326).

The global inequity in MRI availability is stark, with a much higher number of MRI units per million population in high-income compared to lower income countries. Even within OCED, which includes predominantly HICs, the availability varies from 2.9 per million population in Mexico to 59.81 in Japan. The number of available MRI units in Africa is very small for the population. This is largely due to cost, poor infrastructure, shortage of healthcare workers, lack of capacity in the existing workforce, and substandard facilities (308). The price of an MRI scanner ranges from $150,000 to several million not including installation and maintenance costs, with the cost of single scan of up to $4,000 (327). The MRI units that are available are often located in urban areas and often accessible within the private, rather than public, healthcare sector. However, the latter serve only a minority of the population (328). It has been suggested that greater cooperation between the private and public healthcare sectors is required for future improvement of MRI use across the African region (308). Most developed countries use high magnetic field MRI machines while low magnetic field MRI machines are more widely available in West Africa. Although the basic imaging functions of these machines still play an important role in the management of neurological conditions in West Africa, the high cost is restricting access to more advanced imaging capability that comes with high magnetic field MRI (308). It is worth noting that even the presence of an MRI scanner does not ensure appropriate and timely scans are conducted in patients with suspected encephalitis, as other factors such as skilled technical staff to carry out the scan and knowledgeable medical staff to order the scan are required.

Antibody testing is widely available in Europe, North America, and Australia. Standardised, commercial diagnostic kits are available for the most common subtypes of autoantibody encephalitis; however, expensive kits or reagents, training, ongoing quality measures, pre-analytic pipelines, and sophisticated laboratory equipment are required for analysis and interpretation, severely limiting their availability in LMIC (329). However, studies confirm that these types of encephalitis do occur in these parts of the world (e.g., Africa, South America, Asia) but are likely under-recognized (313,330–332). In areas where antibody tests are available, doctors need to recognize and be aware of autoantibody encephalitis to ensure specimens are sent for diagnosis. Bedside assessment and clinical judgement remain critical in the diagnosis of immune-mediated encephalitis as treatment is available, effective, and often empiric based on presenting features. A worldwide survey of over 1,000 neurologists from 94 countries on their approach to autoimmune encephalitis found that those treating >5 cases per year were more likely to send antibodies in both serum and CSF, pursue empiric immunotherapy, and continue immunotherapy despite no response and negative antibodies at two weeks (333). In areas where antibody tests are unavailable, treatment initiation relies solely on bedside assessment and clinical judgement. Coincidentally, this usually requires

specialized neurological input, but antibody tests are mostly lacking in areas where there is also a lack of neurologists (see Section 7.2.1). Lack of necessary treatment may also be an issue in lower income countries. A high index of clinical suspicion combined with better access to autoantibody testing and availability of required therapy is needed.

We can only draw conclusions based on the data retrieved. However, this report is also intended to highlight inadequacies in information systems. A systematic survey is required to assess the availability of these diagnostic test types globally. For a summary of barriers to implementation of these different diagnostic methods see Table 23.

Table 23- Summary of barriers to implementation of various diagnostic tests for encephalitis

Diagnostic test	Barriers to implementation
CSF analysis	-Laboratories in LMICs are often sparsely distributed -Access may be limited by economic or geographical factors -Clinical laboratories are often under resourced -Amenities such as electrical supply and water may be unreliable -Shortage of skilled technical personnel, especially in rural areas - Due to their high cost or lack of robustness, some specific diagnostic tests may not be available to the majority population -Some manufacturers may be reluctant to supply countries if return on their investment is likely to be low or where it may be difficult to establish effective mechanisms for product distribution or technical support -Weak regulation has also contributed to the sub-optimal provision of diagnostic services and in some countries, tests of unknown or dubious quality are sold without hindrance
CSF HSV PCR	-Lack of basic microbiology labs in hospitals in some resource-limited countries -Lack of skilled staff to carry out tests -Lack of laboratory accreditation and appropriate quality assurance and quality control -Lack of timely reporting in labs able to amplify DNA -Clinician preference -Gaps in knowledge of appropriate and necessary diagnostic strategies
MRI	-High cost -Poor infrastructure -Shortage of healthcare workers -Lack of capacity in the existing workforce -Substandard facilities -MRI units that are available are often located in urban areas and often accessible within the private, rather than public, healthcare sector
Autoantibody testing	-Lack of awareness -Lack of neurologists -Lack of availability of antibody tests

CSF = Cerebrospinal fluid; DNA = Deoxyribonucleic acid; HSV = Herpes simplex virus; LMICs = Low- and middle-income countries; MRI = Magnetic resonance imaging; PCR = Polymerase chain reaction; Adapted from McNerney et al. (334)

6.1.5 Gap analysis

Table 24 - Gap analysis for diagnostic tests in encephalitis

	Where we are	Where we want to be
CSF examination	Some type of CSF examination is available in most countries but exactly what this consists of varies greatly.	-Need investment and participation from regional and local governments to sustain new diagnostic and treatment capacity -Need to increase lab capacity by training lab technicians, installing basic equipment, and implementing more advanced diagnostics -Need recognition at national and international level of importance of clinical laboratory services in health system -Need education, supervision and technical improvements and quality assurance networks to revitalize lab services as sub-standard services waste resources and result in clinical mismanagement and inaccurate health information -Need collaboration between laboratory professionals and clinicians to ensure effectiveness of lab services in guiding patient management -Need to ensure budget for laboratory equipment also covers servicing, repair, spare parts, and training in maintenance -Need to incorporate routine CSF testing in WHO essential diagnostics list
CSF HSV PCR	Widely available in Europe, North America, and Australia/New Zealand; variable availability in Asia often in larger tertiary referral centres; limited availability in Africa and South America, mainly only for research purposes.	-Need to emphasize importance of laboratory testing -Need to balance the allocation of financial resources -Need to strengthen the existing health care infrastructure -Need to routinely monitor test quality -Need to establish system for laboratory accreditation -Need to implement laboratory training programs -Need to encourage partnerships between public and private organizations -Need to develop affordable, rapid diagnostic tests -Need systematic survey to collect information on availability of CSF HSV PCR testing globally -Need to incorporate CSF PCR in the WHO essential diagnostics list
MRI	Low number of MRI units in African countries, often located in urban areas and in the private sector.	-Need better cooperation between public and private healthcare sectors for future improvement in MRI use across African region
Antibody testing	Widely available in Europe, North America, and Australia but likely limited in Asia, Africa, and South America despite the occurrence of cases in these areas.	-Need systematic survey to collect information on availability of autoantibody testing globally -Need to expand access to autoantibody testing globally

Adapted from (334,335)*; CSF = Cerebrospinal fluid; HSV = Herpes simplex virus; MRI = Magnetic resonance imaging; PCR = Polymerase chain reaction; WHO = World Health Organization*

6.2 Treatment

6.2.1 Recommended practice

The WHO List of Essential Medicines was first published in 1977 and most recently updated in 2025 for both adults (24th version) and children (10th version) (336). This list aids prioritization of key health products that should be widely available, accessible, and affordable throughout health systems, particularly in LMICs. JE and TBE vaccine are included in the WHO Essential Medicines list and their availability in terms of preventing encephalitis is discussed in Sections 5.1.1.2 and 5.1.2.2. Treatment for encephalitis is largely supportive but specific treatment is available for herpesvirus encephalitis, and non-viral and immune-mediated causes (5). Aciclovir is the first-line treatment for HSE. The WHO List of Essential Medicines includes aciclovir, antimicrobials, and immunosuppressive treatments as well as supportive medicines such as anticonvulsants and analgesics, and IV acyclovir is specified as a medicine for viral CNS infections (336). We focus on the availability of aciclovir for the treatment of encephalitis worldwide.

6.2.2 Implementation status

It has been shown that in the absence of aciclovir treatment the case fatality from HSE is up to 70%; aciclovir treatment has reduced this to below 20% but survivors still have significant sequelae (337). Early administration is key to improved outcomes. As HSV is the most common cause of encephalitis in Western countries, IV aciclovir is commenced upon suspicion of a case, often even prior to laboratory results being available. Aciclovir is widely available in HICs across Europe, North America, and Australia/New Zealand but often administered sub-optimally and not in accordance with recommended guidelines. A study of encephalitis patients in a tertiary referral centre in the UK showed that only 53% of patients had received aciclovir despite the recommendation to start empirical treatment with aciclovir upon clinical suspicion of encephalitis (338). Furthermore, a pragmatic cluster randomised controlled trial of a tailored intervention to improve the initial management of suspected encephalitis showed that less than a third of patients at participating UK hospitals were prescribed aciclovir within the recommended six hours of admission (339). Outside of the UK, one third of adults (n=241) admitted with encephalitis in the Houston area were not started on IV aciclovir upon suspicion of encephalitis (326).

Data suggests aciclovir availability across Asia is variable. Studies from India, Pakistan, Japan, Sri Lanka, and Vietnam report treatment of encephalitis with aciclovir (123,340–342). However, these studies are often conducted in larger tertiary referral centres, so aciclovir is perhaps less available in smaller rural hospitals and within-country variation likely exists. A

cross-sectional survey conducted in India showed aciclovir is not listed in the Haryana state Essential Medicines List and thus availability was poor in the public sector (343). A South American study that recruited patients from 12 hospitals between 2009 and 2012 reported treatment with IV aciclovir was not available in most Peruvian hospitals (7). However, a systematic review of herpes zoster in Latin America registered treatment with IV aciclovir in Argentina and Brazil (344).

Anecdotal evidence suggests that aciclovir is available only in African cities, and in Lusaka, Zambia the IV formulation is only available in private pharmacies rather than government-funded hospitals and is very costly at $40/dose or $120/day (D Saylor 2020, personal communication). IV aciclovir was not available in a study in Senegal, and patients with HSE were instead given oral aciclovir or valaciclovir with high mortality rates (345). A study that considered the availability of oral aciclovir for the treatment of genital ulcer disease in eight Sub-Saharan African countries in 2007 reported challenges that curtailed procurement and access to aciclovir in private and public health facilities (346). Aciclovir was largely procured centrally for the public sector in each country by the Ministry of Health or central medical store (CMS) facility however stock-outs at the CMS were reported in Kenya and Zambia. Zimbabwe reported inadequate financial resources to purchase aciclovir in the public sector. Due to lack of data on IV aciclovir in Africa, the availability of other drugs, which might indicate how likely a country is to have aciclovir, was considered. The Neurology Atlas 2017 assessed the availability of anticonvulsants, often used as supportive therapy in encephalitis and on the WHO Essential Medicines list, in countries worldwide (347). Only 55% (n=68/123) and 70% (n=65/132) of countries reported the availability of at least one anticonvulsant at all times in the primary care or hospital setting, respectively. The proportion with at least one anticonvulsant available in the primary care setting was lower in Africa, Southeast Asia, and the Western Pacific (≤50%) and also in LIC (42% compared to 79% in HIC).

6.2.3 Barriers to implementation and discussion

Aciclovir is widely available in Europe, North America, and Australia/New Zealand; however, use is often suboptimal and not always in line with available guidance for maximum patient benefit. Delays in starting aciclovir therapy might relate to failure to consider HSE promptly or awaiting HSV PCR laboratory results unnecessarily. When aciclovir is instigated promptly, treatment length might be too short (348).

Despite aciclovir being on the WHO Essential Medicines list, there are gaps between the WHO list and national lists of essential medicines and on-the-ground availability. Access to aciclovir

appears variable in Asia, with availability most likely in larger tertiary referral centres and with within-country variation. The price of aciclovir in Pakistan is 18 times higher than the international reference price resulting in significant out-of-pocket payments impacting affordability (349). Aciclovir availability was lacking in a Peruvian study; however, the high prevalence of HSE identified in this study (n=45/313, 14.4%) highlights the need for increased availability of IV aciclovir for the treatment of HSE in Peru and likely other South American countries. A subsequent study designed to set up a research network for encephalitis among twelve hospitals in five Peruvian cities indicated the lack of availability of IV aciclovir in Peru (303). IV aciclovir was purchased in bulk through a US hospital pharmacy; however, a national shortage led to a search for other suppliers. Shipping and manufacturing delays were amongst the challenges that occurred in the aciclovir supply chain, and the authors are currently exploring possibilities for acquiring and maintaining aciclovir supplies in Peru (303).

Data from Africa are sparse but aciclovir availability is likely lacking. A study from Senegal reported the availability of oral rather than the recommended IV aciclovir for HSE (345); however, oral aciclovir does not result in adequate CSF concentration to achieve antiviral efficacy (350). The availability of supportive therapy with anticonvulsants was only 70% globally in the hospital setting and <50% in the primary care setting in Africa, Southeast Asia, and the Western Pacific (347). The availability of these drug types in the primary care setting is important as patients in these regions often consult primary care physicians for neurological care in the absence of neurologists (see Section 7.2.1). LICs generally experience poor availability of essential medicines in health facilities, substandard-quality treatments, frequent stock-outs, and suboptimal prescription and use of medicines, poor transportation systems, lack of drug storage facilities, and weak manufacturing capacity (351). Furthermore, poor procurement practices often afflict the inefficient and bureaucratic public sector supply system in Africa leading to unavailable or costly drugs.

6.2.4 Gap analysis

Table 25 – Gap analysis for aciclovir use

Where we are	Where we need to be
IV aciclovir is widely available in most countries in Europe, Australia/New Zealand, and USA although use can be sub-optimal.	Need to promote adherence to available guidance and education on importance of early instigation of aciclovir in suspected encephalitis Need to educate on how to recognize suspected encephalitis
Variable aciclovir availability across Asia, limited availability in South America, and lack of data on availability in Africa but likely lacking.	Need efforts to improve availability of essential medicines in health facilities, prescribing practices, dispensing practices, quality of medicines, and access to drug information resources

	Need systematic survey needed to assess global availability of aciclovir Need to reduce aciclovir cost to facilitate availability in low-resource settings including Africa Need to incorporate routine IV acyclovir for encephalitis in national essential medicines lists

USA = United States of America

7 In-country neurologists and access to neurology training

7.1 Recommended practice

Neurological disorders account for a large proportion of the global burden of disease, and the number of people living with neurological disorders is growing worldwide (352). We reported in Section 3.2 that encephalitis incidence is higher than previously thought and in many countries surpasses that of MND/ALS, bacterial meningitis, and MS (108–110). Neurology healthcare professionals are important to care for and manage the growing number of people with neurological disorders. The WHO recommends at least one neurologist per 100,000 population (353). We assessed the global presence of neurologists and neurology training.

7.2 Implementation status

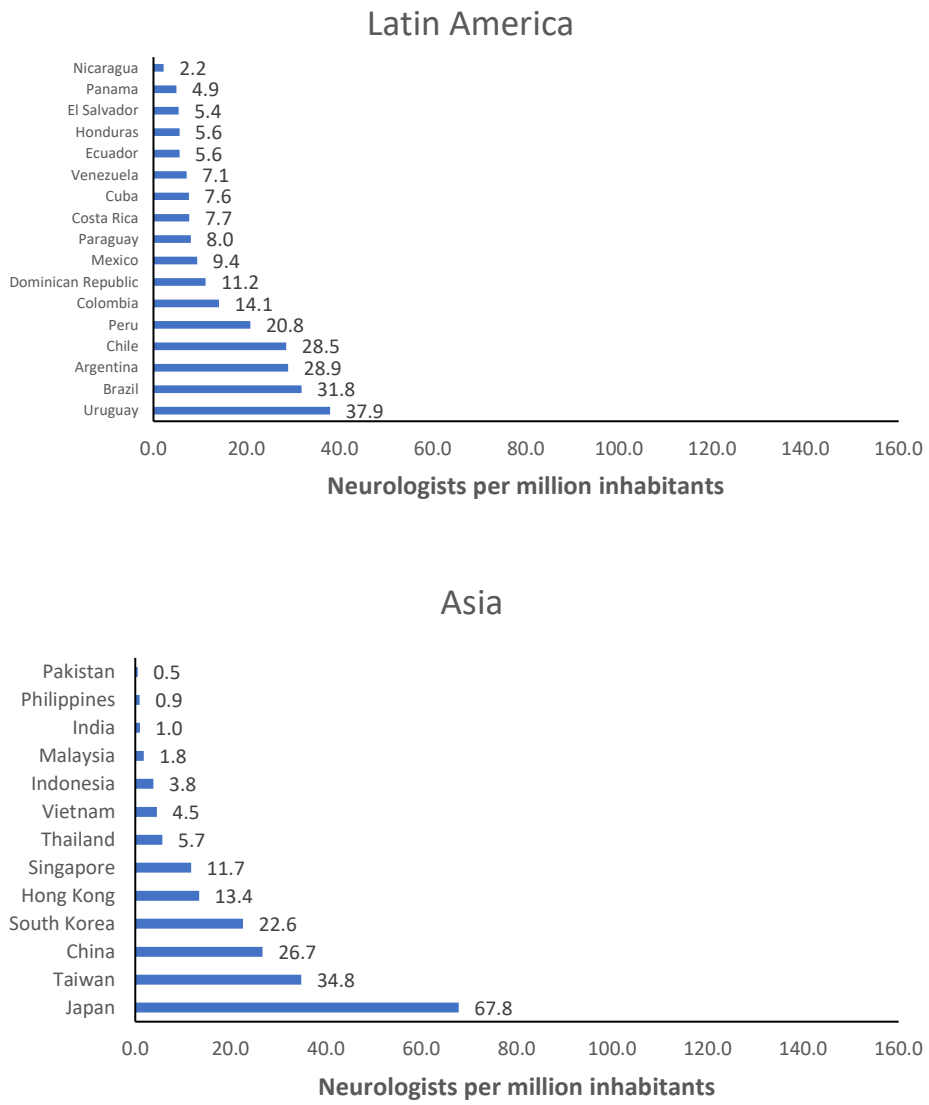
7.2.1 Presence of neurologists

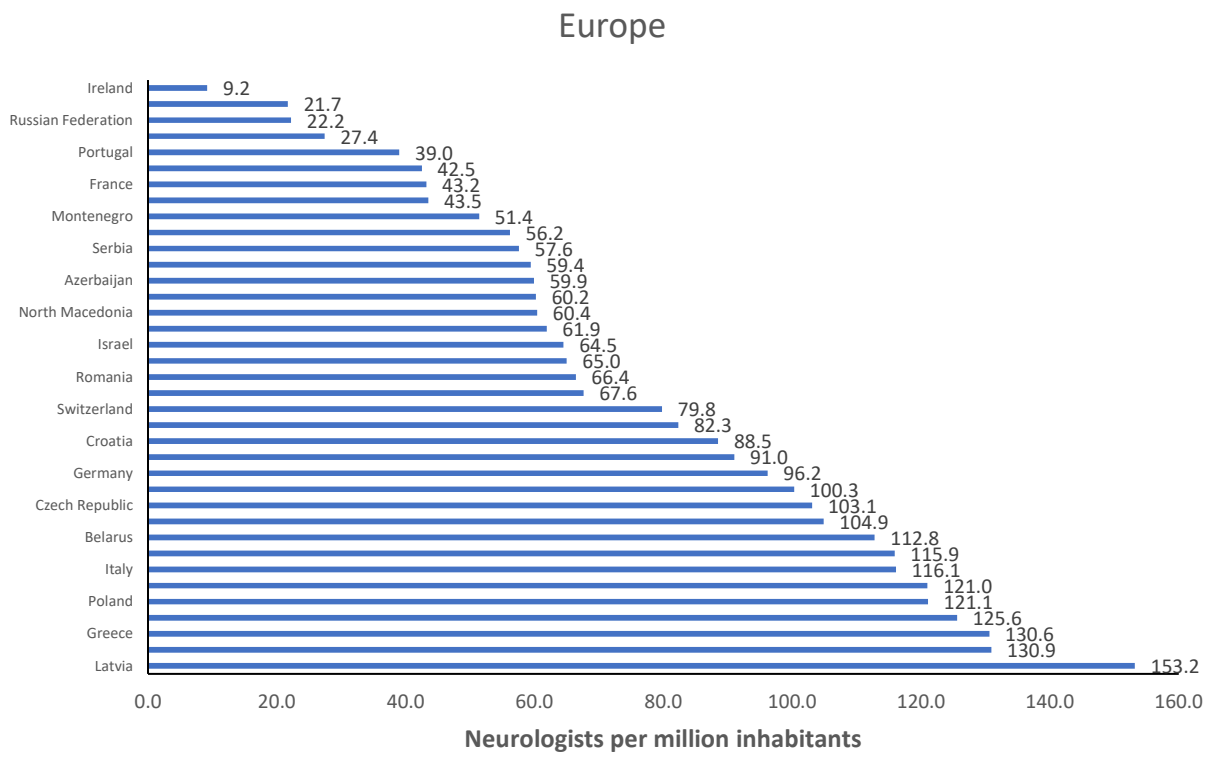
The Neurology Atlas 2017, a collaboration between WHO and the World Federation of Neurology (WFN) to assess available resources within countries to cope with neurological diseases, administered a questionnaire to 132 countries and two territories covering 94% of the world population (347). Data were collected from 36 countries (77%) in AR, 25 (71%) in AMR, 18 (86%) in EMR, 33 (62%) countries in EUR, 10 (91%) countries in SEAR, and 12 (44%) in WPR. The global median of the total neurological workforce (including adult neurologists, paediatric neurologists, and neurosurgeons) was estimated at 3.1 per 100,000 population among the 114 countries who responded (347). The largest number was reported in EUR (9/100,000) whereas the lowest number was reported in AR (0.1/100,000) and SEAR (0.3/100,000). When participating countries were grouped into World Bank income groups, LICs and HICs reported a median of 0.1 and 7.1 neurological workforce per 100,000 population, respectively. Almost all countries (111/114, 97%) reported neurologists practicing in the capital city; however, only 23% reported neurologists in rural regions. Of 105 countries

that responded, only 20% reported the availability of specialist neurology units, 16% specialized neurorehabilitation services, and 17% general rehabilitation units offering neurological rehabilitation (347). Primary care physicians may offer neurological care in 91% of responding countries (n=96/106), ranging from 78% in EMR to 100% in SEAR.

Bassetti et al. reported the number of neurologists per million population by individual country (Figure 23) (354). This ranged from 9.2 (Ireland) to 153.2 (Latvia) in Europe, 2.2 (Nicaragua) to 37.9 (Uruguay) in Latin America, and 0.5 (Pakistan) to 67.8 (Japan) in Asia.

Figure 23 - Number of neurologists per million people in Latin America, Asia, and Europe

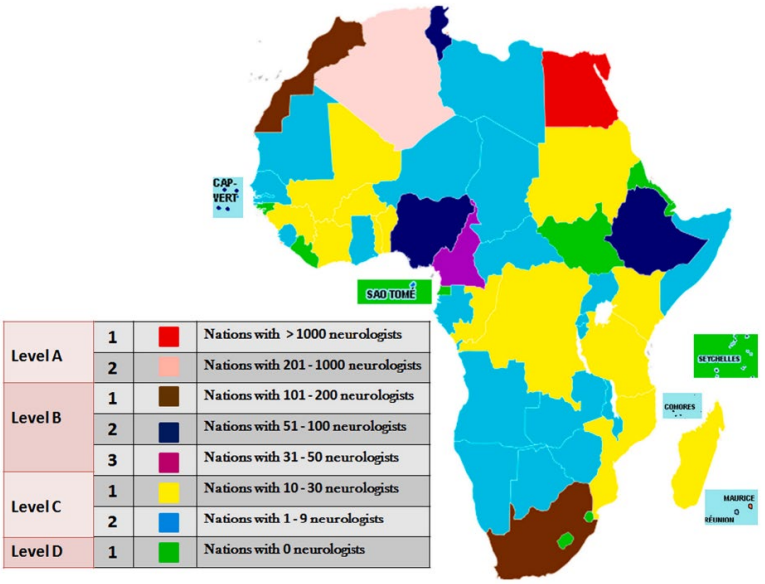




Adapted from Bassetti et al. (354)

In a survey of 50 African countries conducted in 2020, almost three-quarters (n=36/50; 72%) reported one to 30 neurologists per country and 10 (20%) reported having no neurologist (Figure 24) (353).

Figure 24 - Number of neurologists by African country



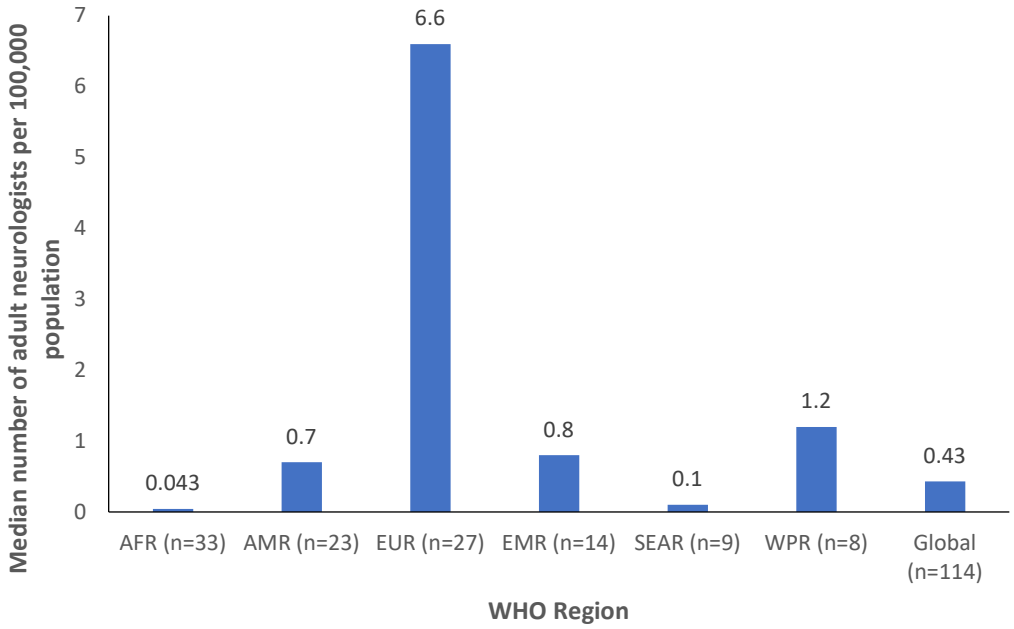
From Kissani et al. (353)

Neurologist numbers have increased in some regions (e.g., Latin America); however, growth of the neurological workforce remains slow in Africa and other regions (354). Even in regions with overall high numbers of neurologists (e.g., Europe, North America), distribution is unequal with some areas reporting an insufficient neurological workforce (354).

7.2.1.1 Adult neurology

The global median number of adult neurologists is 0.43 per 100,000 population. AFR and SEAR have the lowest number (medians 0.04 and 0.1/100,000, respectively) whereas the highest number is seen in EUR (median 6.6/100,000; Figure 25).

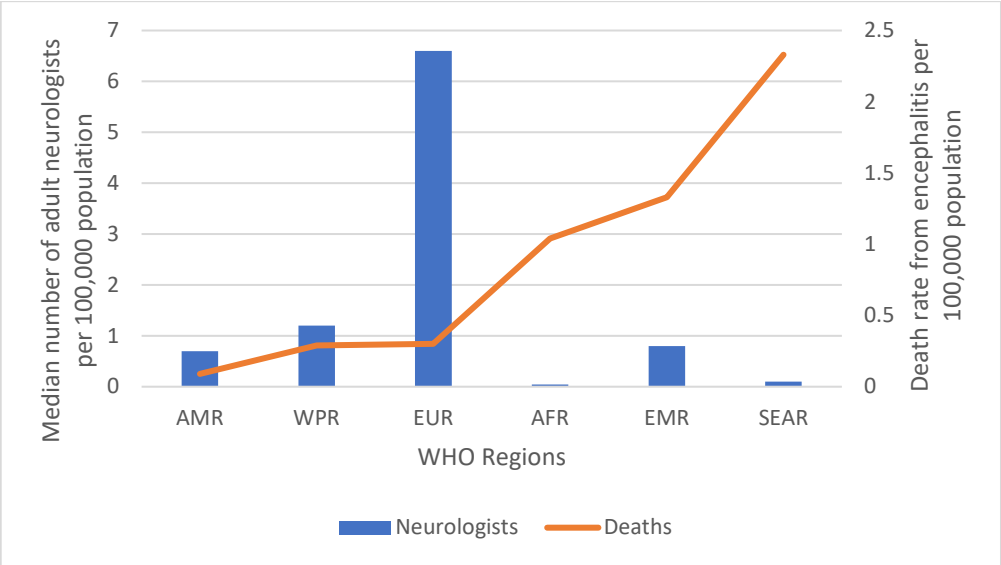
Figure 25 - Median number of adult neurologists per 100,000 population by WHO region



From Neurology Atlas 2017 (347)
AR = African Region; AMR = Region of the Americas; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asia Region; WPR = Western Pacific Region

The crude death rate from encephalitis, as estimated by the WHO in 2021, by the median number of adult neurologists per 100,000 population for each WHO region is displayed in Figure 26 (117,347). The highest death rate from encephalitis was reported in SEAR, also one of the regions with the lowest number of adult neurologists. A visible trend of lower encephalitis mortality rates in regions with a higher number of neurologists is evident.

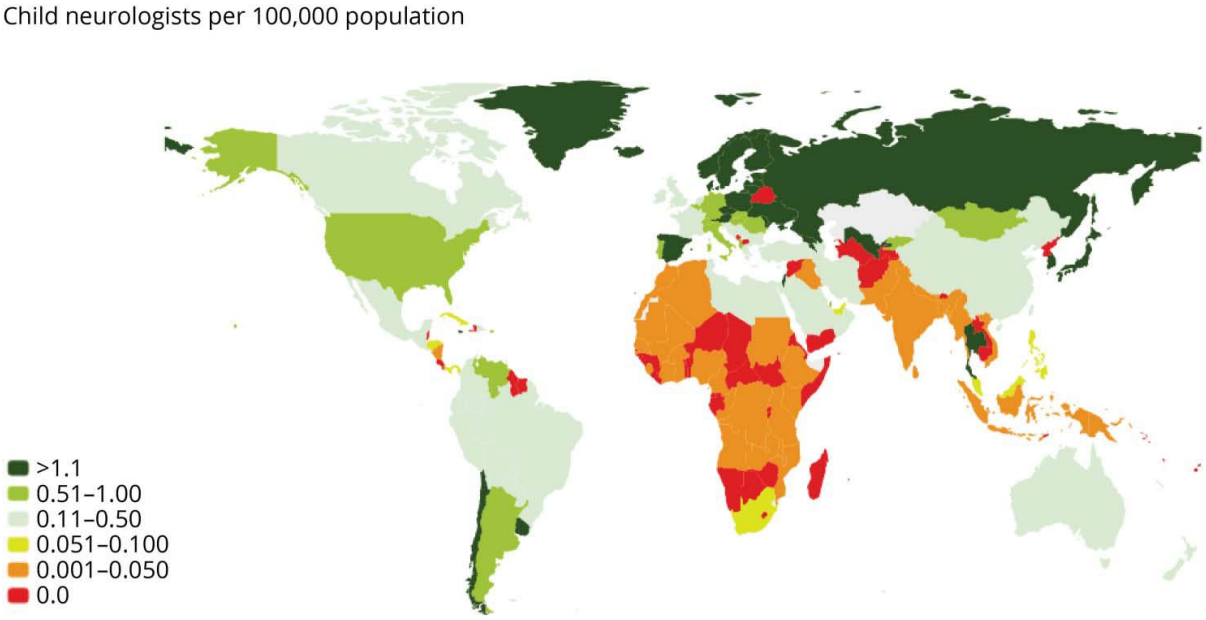
Figure 26 - Global mortality for encephalitis and number of adult neurologists by WHO region



7.2.1.2 Paediatric neurology

The global median number of paediatric neurologists is substantially lower than that reported for adult neurologists (Figure 27). A recent survey carried out in 177 countries on access to paediatric neurology services reported almost three-quarters of LICs (73%), predominantly in Africa and Southeast Asia, lack access to child neurologists (355). There is a median of 0.01 child neurologists per 100,000 population in Africa compared to 0.59 per 100,000 in HICs (355).

Figure 27- Ratios of child neurologists per 100,000 of country populations worldwide

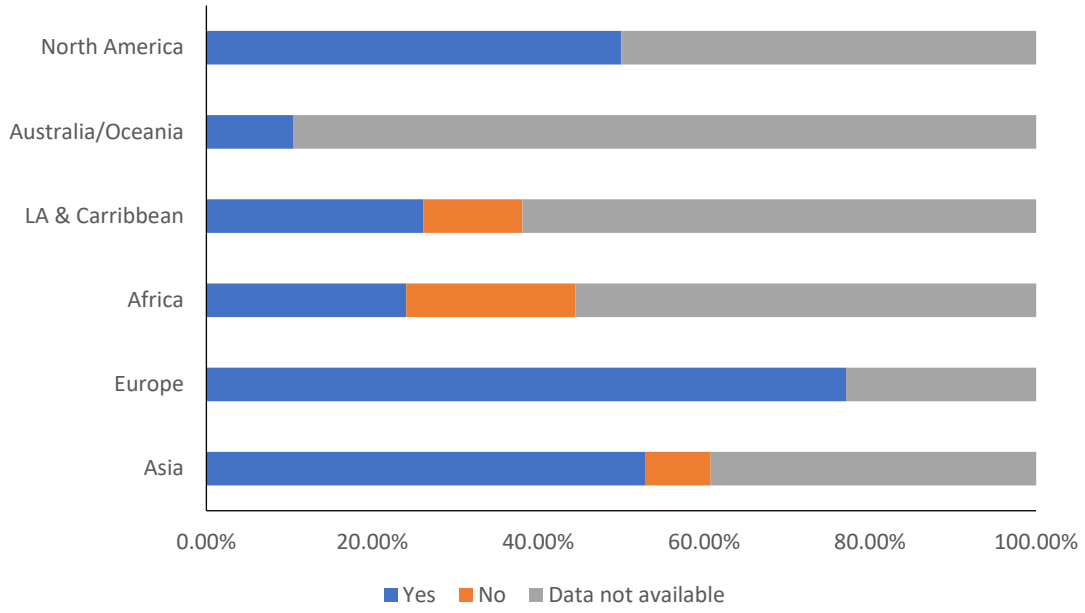


From Wilmshurst 2023 (355)

7.2.2 Neurology training

A 2018 review by Hillis et al. investigated the presence of neurology trainees, a marker of the presence of a neurology training program within a country (356). Of countries with data available, 58% (7/12), 24% (6/25), 10% (3/29), and 9% (4/46) of LICs, lower-middle-income countries, UMICs, and HICs, respectively, reported no trainees (356). Within each continent, the majority of countries reported they had a trainee with the exception of Africa, Latin America and the Caribbean, and Asia where 20% (11/54), 12% (5/42), and 8% (4/51) of countries, respectively, reported the presence of no trainee (Figure 28). Data on trainees was not available from 89% (17/19), 62% (26/42), and 56% (30/54) of countries in Australia/Oceania, Latin America and the Caribbean, and Africa, respectively (Figure 28).

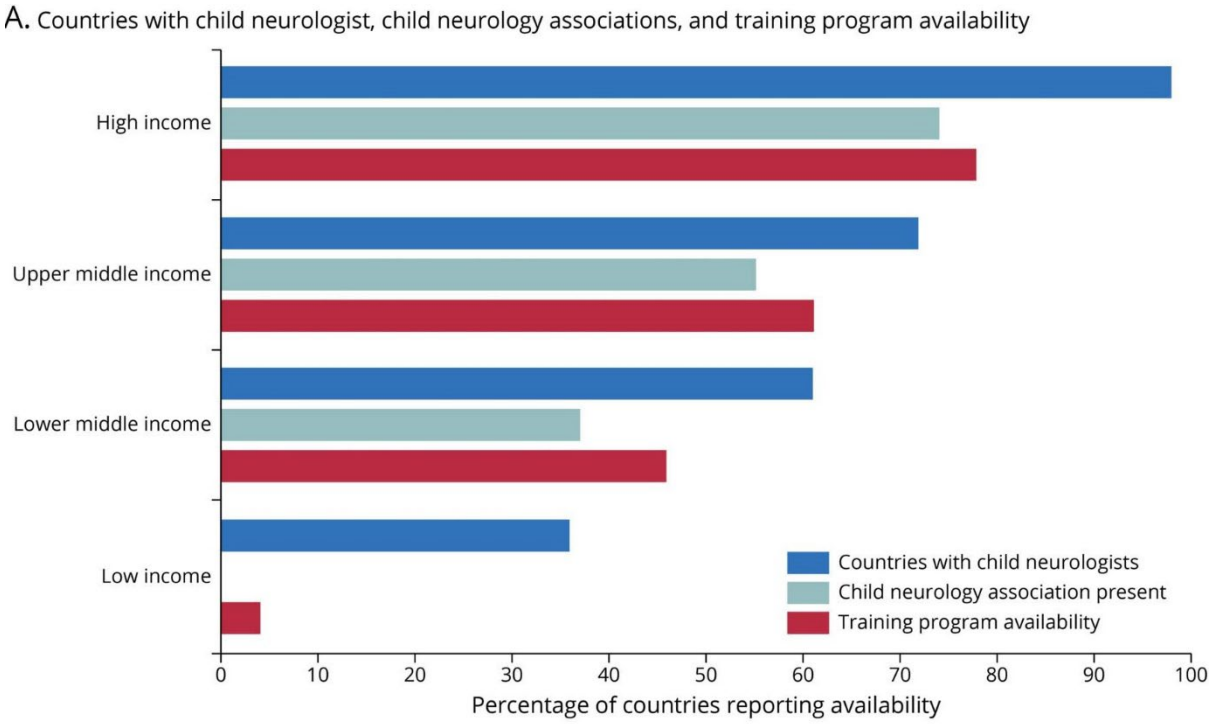
Figure 28 - Proportion of countries with neurology trainees by continent



Data obtained from Hillis et al. (356)

It has recently been reported that neurology training programs are available in nine of the 11 Association of Southeast Asian Nations (ASEAN) countries except Timor Leste and Cambodia (357). Of 177 countries recently surveyed about paediatric neurology training, the greatest deficits in access to training was evident in LICs (Figure 29).

Figure 29 - Worldwide access to paediatric neurology training programs



From reference (355)

7.3 Barriers to implementation and discussion

These data demonstrate that the available resources for neurological disorders globally are insufficient. Despite most countries in Asia and Africa reporting the presence of neurologists, the actual number of neurologists is very low. The number of paediatric neurologists in particular is strikingly low across all regions, which is significant as the incidence of encephalitis is higher in children that adults (58,88). A lack of neurology in rural areas and lack of neurorehabilitation services were also evident (358). In the absence of neurologists, many countries consult primary care physicians for neurological care; however, their level of training and expertise is unknown. Data from India and Peru suggest some patients with encephalitis are managed by internists, infectious disease specialists, or a combination of healthcare providers (303,333). The presence of a neurologist at an epilepsy clinic in rural Tanzania compared to a clinic mainly attended by nurses resulted in a reduced disease burden, emphasising the importance of specialist care (359). Neurology trainees, a marker of neurology training programs, were scarcer than neurologists. One reason for the lack of neurology training programs is the lack of neurologists to develop and support them (356). No trainees were reported in some African, Latin American and Caribbean, and Asian countries; however, data on this were lacking from the majority of countries. Recent initiatives have seen 1) the first postgraduate neurology training program started in Zambia in October 2018 developed by a Johns Hopkins faculty neurologist and 2) online training modules for LMICs

launched by Encephalitis International in partnership with BMJ (360,361). A recent cross-sectional survey of medical students and post-graduate trainees in internal medicine and paediatrics across Africa showed fear and discomfort with the subject of neurology (362). This highlights the need for strategies, including enhancing neurological educational, diagnostic, and treatment capacity, to mitigate so-called neurophobia.

The Neurology Atlas 2017 and review by Hillis et al. were two comprehensive data sources identified which provided detailed information on the global presence of neurologists and neurology trainees (347,356). The Neurology Atlas 2017 gathered data from key experts in the area of neurology identified by the WFN in 132 countries and two territories, representing 94% of the world population. Most of the surveys included in the review by Hillis et al. were also conducted through the WFN (356). As a confederation of national neurological societies, the WFN is well positioned to collect data from their member countries. However, surveys conducted by the WFN and EFNS/EAN omit countries without neurological societies and might be biased toward countries with more established neurology infrastructure (347). Also, countries that received surveys but did not respond were perhaps those with worse infrastructure. Thus, it is likely the global estimates presented here are an overestimate. A further limitation of Neurology Atlas 2017 is the fact that one key person in each country was the source of information. However, this individual was not only the WFN liaison officer, but could also consult other neurologists within the country and had access to both official and unofficial sources of information (347). Despite the limitations, the Neurology Atlas 2017 is considered a comprehensive compilation of neurological resources (347).

7.4 Gap analysis

Table 26 – Gap analysis for presence of neurologists and/or neurology training

Where we are	Where we want to be
Available resources for neurological disorders globally are insufficient given the increasing number of patients with neurological disorders.	Need to increase neurological services and training in order to care for these patients
In some Asian, African, and Latin American countries, the actual number of neurologists is very low.	Need to increase number of neurologists, especially in LMICs and rural areas
Neurology trainees, a marker of neurology training programs, were scarcer than neurologists. No trainees were reported in some African, Latin American and Caribbean, and Asian countries; however, data on this were lacking from the majority of countries.	Neurology training programs need to be developed across many areas, particularly Africa Need neurologists to develop and support training programs Need to strengthen data on the availability of these resources by country

There is an evident lack of neurorehabilitation services.	Need to consider increased access to neurorehabilitation services

LMICs = Low- and middle-income countries

8 Surveillance

8.1 Recommended practice

Surveillance, or the systematic collection, analysis, and interpretation of health-related data, is important for understanding the epidemiology and global burden of encephalitis and implementing the appropriate disease prevention and control measures. Surveillance also enables detection of and rapid response to encephalitis outbreaks, monitoring epidemiological trends over time, guiding public health policy, and monitoring the impact of any prevention and control measure (322). The latter is particularly important, and the WHO suggests that monitoring vaccine impact in settings where JE vaccine has been introduced is a research priority. The WHO recommends enhanced or minimal JE surveillance depending on the availability of resources within a country. National, case-based surveillance for JE and AES with laboratory confirmation comprises enhanced surveillance. The alternative minimal recommended surveillance includes sentinel surveillance with laboratory confirmation of JE in all JE-endemic countries (202). The WHO position paper suggests AES surveillance is important in the absence of JE confirmatory testing for monitoring vaccine programs and to understand all causes of encephalitis. The WHO Recommended Surveillance Standards (Second Edition) also includes measles and rabies, other causes of encephalitis with a vaccine available. In some HICs encephalitis is notifiable by law with a requirement to notify every case.

8.2 Implementation status

8.2.1 All-cause syndromic surveillance

Case ascertainment for encephalitis in higher income countries predominantly relies on routine laboratory reports, notifications, hospitalisation data, and mortality data (3). Surveillance of encephalitis using either of these systems alone; however, is incomplete. National hospitalisation data are available in Europe, North America, and Australia as is evident in Section 3.2.1. Cases of complex syndromes such as encephalitis might be over- or under-ascertained using hospital-only data. Cases of meningoencephalitis may for example be coded as meningitis rather than encephalitis, and patients with anti-NMDAR encephalitis who present with psychiatric symptoms might be classified as such. Hospitalisation data can also include non-encephalitis cases misdiagnosed as encephalitis due to overlapping

symptoms (58). Statutory notifications are grossly underreported with only eight, five, and five cases of acute encephalitis notified for England and Wales in 2021, 2022, and 2023, respectively (363).

The European Network for Diagnostics of 'Imported' Viral Diseases carried out a survey of existing surveillance systems for encephalitis in Europe in 2004 (364). The survey found that bacterial causes of meningitis/encephalitis were thoroughly investigated in all 27 EU Member States; however, notification of viral cases varied between countries because of non-standardised or not enforced reporting policies. The distribution of relevant viral causes of encephalitis reported in the surveillance systems varied greatly and depended on the diagnostic tests carried out and/or notification regulations. Only six countries (Austria, Czech Republic, Hungary, Poland, Slovakia, and Slovenia) could provide pathogen-specific data on common causes of encephalitis (e.g., HSV) and endemic causes (e.g., TBEV). Furthermore, other countries could only report pathogen-specific data for major arboviral causes of encephalitis including TBEV (Baltic States, Germany, Finland) and WNV (Romania). Just over half (n=15, 56%) of the 27 European countries provided information on unexplained neurological illnesses of possible infectious aetiology.

8.2.2 JE surveillance

Surveys were administered to health officials from 24 countries with endemic JE to obtain information on JE surveillance programs in 2016 (204). This was supplemented with data from relevant meetings, reports, and websites. Twenty-two of 24 (92%) countries carried out some form of JE surveillance; 14 (58%) national, 2 (8%) subnational in all JE risk areas, and 11 (46%) sentinel surveillance (Table 27). The latter also included five that also carried out national or subnational surveillance. Twenty-two countries (92%) used JE case definitions; however, the exact definition used varied between countries (from the WHO AES definition to country-specific case definitions). All countries that carried out JE surveillance reported use of JE-specific diagnostic testing in serum and/or CSF to confirm some/most suspected cases.

Table 27 - JE surveillance in countries with JEV transmission risk, 2016

Country	Surveillance program	Age groups included	Laboratory confirmation
Australia	All risk areas	All	Yes
Bangladesh	Sentinel (4 sites)	All	Yes
Bhutan	Sentinel (5 sites)	<15 years	Yes
Brunei	National	All	Yes
Burma	National	All	Yes
Cambodia	Sentinel (6 sites)	<15 years	Yes
China	National and sentinel (27 sites)	All	Yes
Taiwan	All areas	All	Yes

India	All risk areas and sentinel (223 sites)	All	Yes
Indonesia	Sentinel (34 sites)	All	Yes
Japan	National	All	Yes
Lao PDR	National and sentinel (3 sites)	All	Yes
Malaysia	National	All	Yes
Nepal	National	All	Yes
North Korea	National	<15 years	Yes
Pakistan	None	-	-
Papua New Guinea	Sentinel (1 site)	<15 years	Yes
Philippines	Sentinel (9 sites)	All	Yes
Russia	None	-	-
Singapore	National	All	Yes
South Korea	National	All	Yes
Sri Lanka	National	All	Yes
Thailand	National and sentinel (40 sites)	All	Yes
Timor Leste	National	All	Yes
Vietnam	National and sentinel (8 sites)	All	Yes

Adapted from Heffelfinger et al. (204)
PDR = People's Democratic Republic

It is worth noting that these JE systems are not always stand-alone surveillance systems. Cambodia successfully integrated JE surveillance into an established, working system for bacterial meningitis surveillance (365). Similarly, successful surveillance was established for acute meningitis-encephalitis syndrome in China and Bangladesh in 2006 and 2007, respectively, and for AES in India in 2007 using the polio-measles surveillance infrastructure and laboratory networks (366).

8.2.3 TBE surveillance

Surveillance for TBE in Europe is heterogenous. A review on TBE surveillance reported that TBE or a related condition (i.e., viral encephalitis or meningitis) was statutorily notifiable in 84% (37 of 44) of countries in the UN Europe Region in 2023 (367). Of the countries that report TBE data to ECDC, 24 countries reported having a comprehensive surveillance system in 2022 (Table 28). Reporting was compulsory in 24 countries, voluntary in three (Belgium, Denmark, and the Netherlands), and was not specified for one country (Croatia). Belgium and Bulgaria reported aggregated data, while all other countries reported case-based data (368). Twenty-two countries used the EU case definition, two countries (Germany and Italy) reported using a case definition other than the EU case definition, and four countries (Croatia, Denmark, France, and Malta) did not specify which case definition was used (368).

Table 28 – TBE surveillance systems overview for 2022 by European country

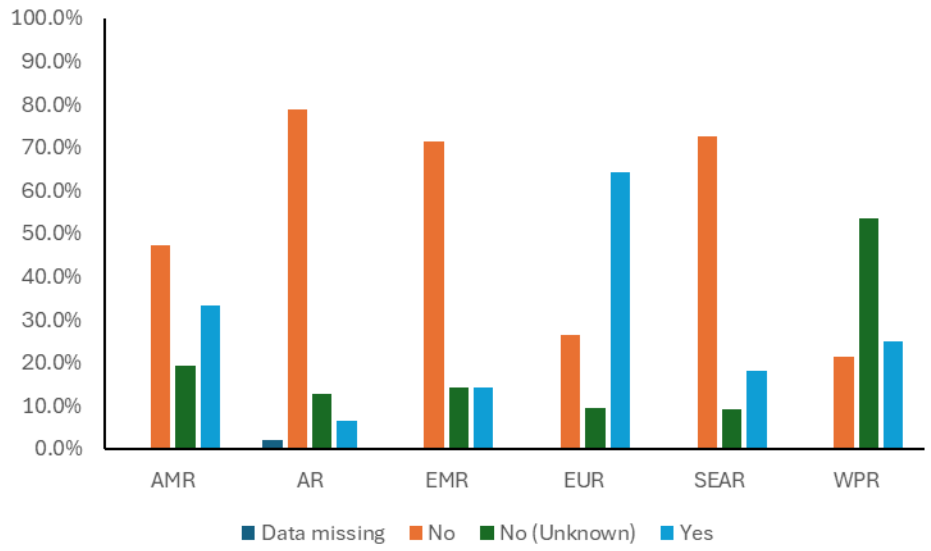
Country	Type of surveillance 1	Type of surveillance 2	Type of reporting	Type of data recorded	Data reported by				Case definition used
					Labs	***Physicians***	***Hospitals***	***Others***	
Austria	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	Yes	EU-2012
Belgium	Voluntary	Comprehensive	Active	Aggregated	Yes	No	No	No	EU-2018
Bulgaria	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	Yes	EU-2018
Croatia	.	.	.	Case-based	.	.	.	.	Not specified/unknown
Czechia	Compulsory	Comprehensive	Active	Case-based	Yes	Yes	Yes	No	EU-2012
Denmark	Voluntary	Comprehensive	Passive	Case-based	Yes	No	No	No	Not specified/unknown
Estonia	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	No	EU-2018
Finland	Compulsory	Comprehensive	Passive	Case-based	Yes	No	No	No	EU-2012
France	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	Yes	Not specified/unknown
Germany	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	Yes	Other
Greece	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	.	EU-2018
Hungary	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	No	EU-2012
Iceland	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	.	.	EU-2018
Ireland	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	No	EU-2012
Italy	Compulsory	.	Passive	Case-based	No	Yes	Yes	.	Other
Liechtenstein	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	.	EU-2012
Lithuania	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	No	No	EU-2018
Luxembourg	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	No	No	EU-2018
Malta	Compulsory	Comprehensive	Passive	Case-based	.	.	.	.	Not specified/unknown
Netherlands	Voluntary	.	Passive	Case-based	Yes	No	No	No	EU-2012
Norway	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	No	EU-2012
Poland	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	No	EU-2012
Portugal	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	.	No	EU-2018
Romania	Compulsory	Other	Passive	Case-based	No	No	Yes	No	EU-2018
Slovakia	Compulsory	Comprehensive	Active	Case-based	Yes	Yes	Yes	No	EU-2018
Slovenia	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	No	EU-2008
Spain	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	Yes	No	EU-2018
Sweden	Compulsory	Comprehensive	Passive	Case-based	Yes	Yes	No	No	EU-2018

From ECDC (368)
EU = European Union

8.2.4 Rabies surveillance

Data collated by CDC show that out of 196 WHO region countries, 61 (31.1%) have robust national rabies surveillance (239). Rabies surveillance was considered robust if formal surveillance reports (including methodologies and results) are available in the form of publications, government reports, or other submissions satisfying international reporting requirements. If data were not available, the country was not considered to have robust surveillance. Only 6.4% (3/47) of countries in AR have robust rabies surveillance compared to 64.2% (34/53) of countries in EUR (Figure 30).

Figure 30 - Countries with robust national rabies surveillance



Data from CDC (239)
AMR = Region of the Americas; AR = African Region; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asian Region; WPR = Western Pacific Region

A 2020 scoping review that assessed the current situation and gaps on rabies morbidity and mortality, integrated rabies surveillance programmes, and existing prevention and control strategies in Africa reported coordinated surveillance for rabies in seven of 18 African countries (39%), including Cameroon, Ivory Coast, Malawi, Senegal, Tanzania. South Africa, and Zimbabwe (247).

8.3 Barriers to implementation and discussion

It is evident from the literature that encephalitis surveillance exists and has improved over the years but there is still a way to go. HICs, in Europe, USA, and Australia/New Zealand, have

surveillance systems including national hospitalisation data, notification systems, and laboratory reports; however, under-reporting is common in many countries. In the UK, 97% of hospitalised cases were not formally reported in the routine notification system (57). Hospitalisation data will include most cases of encephalitis but cases with a milder presentation may be missed (3). In addition, hospitalisation data are limited by unknown accuracy of coding, lack of specific diagnostic criteria, and lack of timeliness (3). Many European countries have implemented surveillance systems for the systematic collection of TBE information, enabling the extent of TBE endemic regions and general surveillance trends to be described (368). However, some important differences (case definition, laboratory diagnosis, clinical syndromes reported) exist in these surveillances systems that might complicate interpretation and international comparisons (369). Standardisation of TBE surveillance would enhance the understanding of TBE disease burden in Europe (367).

In LMICs where resources are more scarce surveillance strategies are often targeted at vaccine-preventable causes. JE surveillance programs have expanded in recent years; over 90% of countries with JE transmission risk conducted JE surveillance in 2016 compared to three quarters in 2012. It is likely these surveillance programs relate only to people living in-country and not travellers who might be affected. This represents substantial progress, but challenges remain including incomplete case reporting, case misclassification, lack of monitoring data for immunisation programs, and suboptimal monitoring of vaccine coverage following introduction (204). Surveillance of vaccine-preventable causes of encephalitis is particularly important to assess burden, inform vaccination strategies, monitor vaccine safety, and monitor the impact and effectiveness of vaccines (204). The WHO also suggests AES surveillance is important to understand other causes of encephalitis and also to demonstrate the impact of the vaccination program in the absence of JE confirmatory testing (204). AES surveillance could be incorporated into other well-established surveillance systems, such as those for poliomyelitis, acute flaccid paralysis, or meningitis surveillance. This has been done in some countries and gives technical and logistical benefits of existing infrastructure and investments.

The WHO target is to eliminate human deaths from dog-mediated rabies by 2030. The means are there to achieve this but relies on many factors including strong surveillance systems. In countries where rabies was a notifiable disease, there was high variability in rabies surveillance systems. In high-risk areas such as AR, only 6% of countries reported a robust national surveillance system for rabies (239).Lack of specific anti-rabies legislation, lack of rabies policy, poor awareness, lack of funds in the health system, lack of accountability for doctors, and priority given to other diseases have been cited as barriers to human rabies

becoming a notifiable disease. Significant underreporting (e.g., in rural areas away from major hospitals), inadequate follow-up of unconfirmed cases to determine outcome or diagnostics to confirm cases, inadequate financial investment in surveillance systems, lack of enforcement or implementation of the legislation and guidance, human rabies deaths occurring at home and away from health centres, poor recognition of rabies by some health workers, rabies being neglected by politicians due to competing priorities, lack of coordination between veterinary and medical authorities, inadequate training of medical staff in surveillance and case definitions, and lack of understanding on when and how to seek treatment by bite victims were cited as reasons for rabies surveillance being ineffective (275). An evaluation of rabies surveillance in southern Vietnam recommended simplification of the report forms, training staff, and improvements in the timeliness of reporting and data usage for better implementation of rabies surveillance (370). India declared human rabies notifiable in 2021 to ensure accurate incidence data to help inform effective prevention and control measures (371). It is worth noting that for vector-borne and zoonotic diseases, surveillance should be a multi-pronged approach and also include environmental, entomological, and veterinary surveillance.

8.4 Gap analysis

Table 29 – Gap analysis for presence of encephalitis surveillance

What we know	Where we want to be
Surveillance systems for all-cause encephalitis exist in HICs including notification systems, hospitalisation data, and laboratory reports; however, cases are still under-reported.	Need to strengthen these surveillance systems by validation of codes in hospitalisation data, encouraging notification of cases, strengthening laboratory diagnosis, and standardisation of case definitions Need implementation of surveillance systems for all-cause encephalitis in lower income countries
Surveillance systems exist in LMICs, but these are more focussed on vaccine-preventable causes of encephalitis such as JE. JE surveillance has improved in countries at risk of JE transmission, but challenges still remain.	Need to implement JE surveillance systems in all areas where JE is a public health priority. This could involve integration with other infrastructure, i.e., polio-measles surveillance. Need to ensure complete case reporting, correct classification of cases, presence of immunisation program monitoring data, and adequate monitoring of JE vaccination coverage following vaccine introduction
Most European countries conduct TBE surveillance but differences in case definitions and laboratory diagnosis make international comparisons difficult.	Need to improve surveillance throughout Europe to obtain homogenous, comparable data Need to encourage uniform use of diagnostic methods for detection of TBE pathogens Need to recommend use of standard EU case definition for TBE
Rabies surveillance is particularly lacking in Asia and Africa.	Need to implement and strengthen rabies surveillance across all risk areas to meet WHO target of rabies elimination by 2030

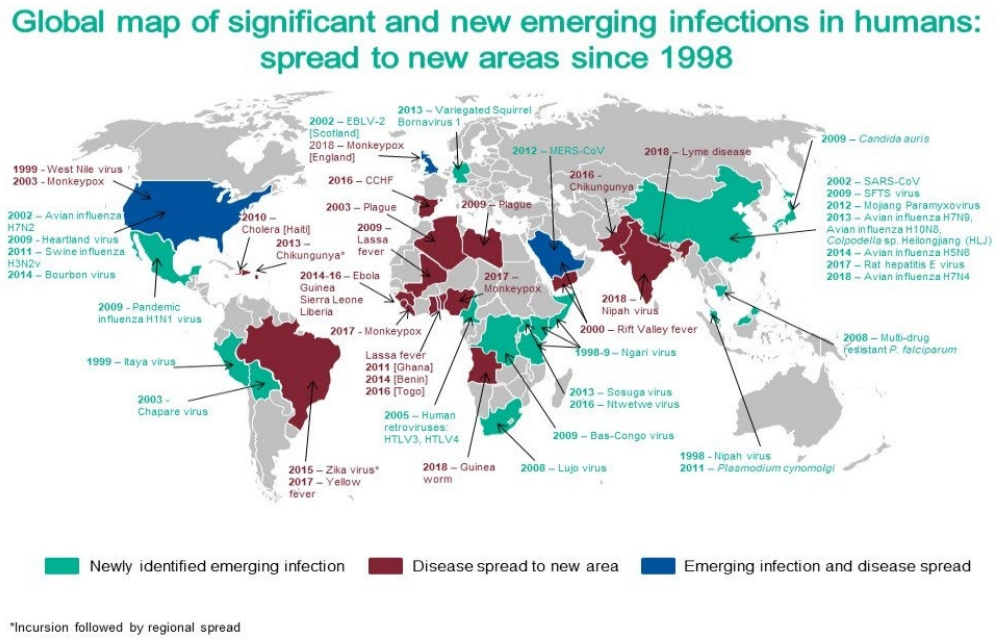
EU = European Union; HICs = High-income countries; JE = Japanese encephalitis; LMICs = Low- and middle-income countries; TBE = Tick-borne encephalitis

9 New and emerging infections

9.1 Introduction

Novel Infectious diseases have been emerging for thousands of years and will continue to do so in the future as a result of climate change, rapid urbanization, changing land-use patterns, and increasing interaction between humans, animals, and their environment (One Health) (372,373) (Figure 31). Approximately 60-80% of emerging infections are thought to be derived from an animal source (372). Many emerging infections can present as encephalitis, and there is potential to detect many more amongst the current pool of unknown causes. Recent years have seen the emergence and spread of arboviruses, such as Powassan, chikungunya, TBEV, and more recently JEV in Australia, and the unique role of bats in the transmission of novel viruses to humans, some of which can cause encephalitis (e.g., Nipah virus and likely SARS-CoV-2) (374). WHO monitors the spread of diseases globally and maintains a list of diseases with epidemic or pandemic potential (375). We aimed to assess the global situation in terms of emerging/re-emerging pathogens included in the WHO list that can cause encephalitis, including chikungunya, Nipah virus infection, and novel coronavirus (COVID-19). Importantly, we also considered scrub typhus, an emerging cause of encephalitis in South Asia for which effective treatment is available.

Figure 31 - Global map of significant and new emerging infections in humans: spread to new areas from 1998 to February 2019



From PHE **(372)**

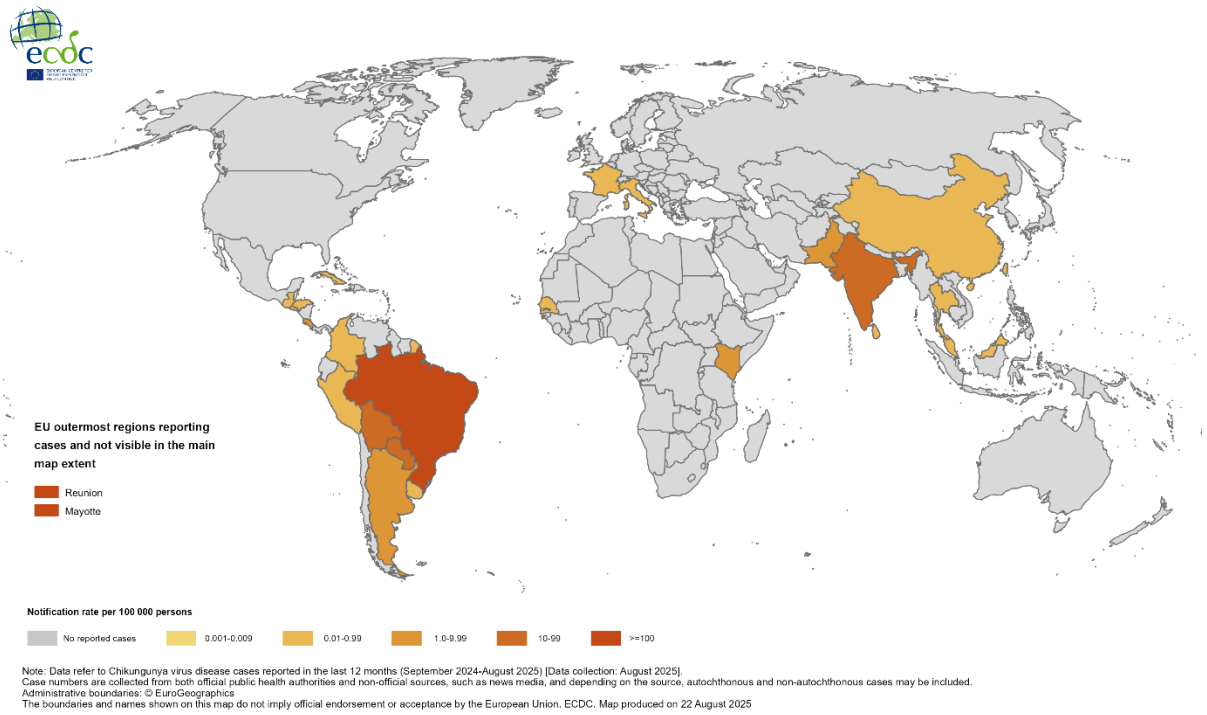
9.2 Selected examples

9.2.1 Chikungunya virus

Chikungunya, a mosquito-borne viral disease, was first recognised in 1952 during an outbreak in southern Tanzania; however, clinical descriptions suggest that chikungunya outbreaks may date as far back as the 1600s (376). Historically, chikungunya was considered a mild febrile self-limiting disease, possibly complicated by chronic disabling arthritis of the joints, restricted to Africa and Asia (377).

Chikungunya has been neglected compared to other arboviral diseases until its re-emergence in Kenya in 2004 (almost 500,000 cases), Reunion Island in 2005 (>266,000 cases), and India in 2006 (1.4 million cases) (378). Since 2004, chikungunya virus has caused large epidemics, spreading to the Pacific Islands in 2011, and the Americas in 2013 (379,380). Chikungunya virus has now been identified in 114 countries in Asia, Africa, Americas, Europe, and Oceania (376). This rapid global expansion has been the result of adaptation of the virus to other vector species (i.e., *Aedes Albopictus* in addition to *Ae. Aegypti*), expansion of mosquito vectors to more temperate climates, and increased air travel exporting chikungunya virus to other countries and possibly provoking autochthonous transmission by local *Aedes* populations (376,380) (Figure 32). The 2005/2006 outbreak on Réunion Island, which resulted in a cumulative incidence rate of 34%, demonstrated the explosive capacity and potential swift dissemination of chikungunya virus (381). In this outbreak, the incidence of chikungunya-associated encephalitis contributed to a two-fold increase of the regional overall incidence of all encephalitis (14.6 versus 6.0 cases per 100,000 persons per year at baseline) (382). Since the beginning of 2025 and as of August, there have been approximately 317,000 chikungunya cases and 135 chikungunya-associated deaths reported in 16 countries/territories in Americas, Africa, Asia, and Europe (383).

Figure 32 - Chikungunya virus disease case notification rate per 100,000 population, September 2024 to August 2025



From ECDC website (383)

The case fatality rate of chikungunya is 0.07% (range 0.012% to 1.8%); however, it results in chronic or permanent disability in 42.5% (7% to 89.7%) of cases (378). Neurological involvement ranging from 0.1% to 16.3% has been reported in case series during epidemics, with encephalitis and myelitis the most important neurological presentations of chikungunya infection (375,379). Neurological presentations of chikungunya are severe and often result in a poor neurocognitive outcome. The case fatality among patients with a neurological presentation in the 2005/2006 Réunion Island outbreak was 10%.

Treatment is symptomatic as no efficacious medical countermeasures exist despite >75% of the world population living in areas at risk of chikungunya virus transmission (376). Thus, prevention is of utmost importance and currently involves preventing mosquito bites and transmission from viraemic patients, and vector control through targeted limited spraying and destruction of breeding sites. The rapid detection of outbreaks is key to ensure prompt initiation of control measures. Current diagnostic strategies predominantly rely on reverse transcriptase (RT)-PCR and antibody detection by enzyme-linked immunosorbent assay (ELISA); however, these diagnostic technologies require complex instrumentation, sophisticated laboratories, and trained personnel rendering them not accessible or affordable to patients at the lower healthcare system levels where most chikungunya outbreaks occur

(385). Rapid Diagnostic Tests (RDTs) are available and have the potential to overcome some of these challenges; however, the landscape of chikungunya RDTs is fragmented and coordinated efforts are needed to ensure that patients in chikungunya-endemic areas have access to appropriate RDTs (385).

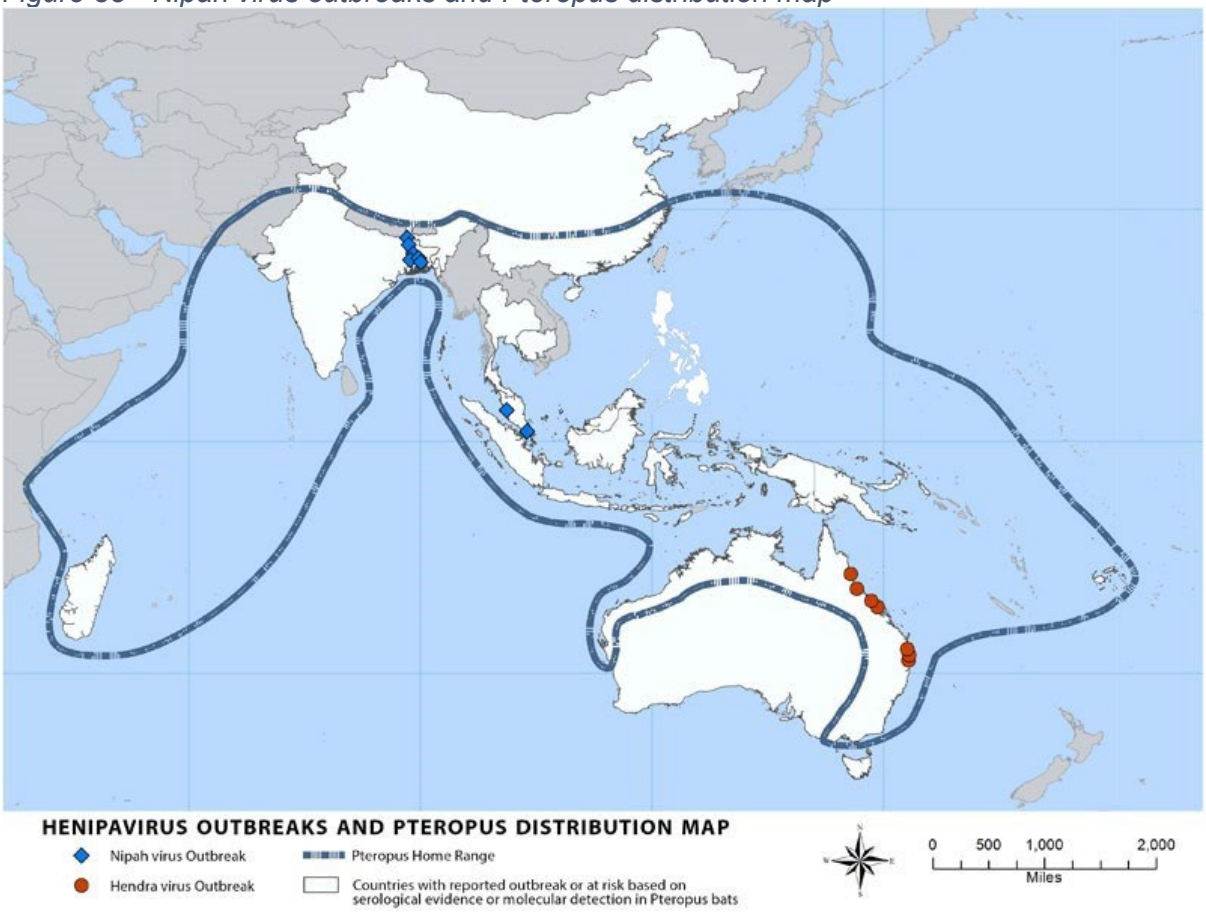
As previously mentioned, Valneva's VLA1553 vaccine has been granted approval in numerous countries (e.g., Canada, EU, UK, Brazil) and Bavarian Nordic's VIMKUNYA vaccine was recently licensed in US and Europe (265). Future research should focus on diagnostics, drug and further vaccine development, vector control programs, and surveillance activities to enable mitigation of any explosive increase in chikungunya cases.

9.2.2 Nipah virus

Nipah virus was first identified in Malaysia and Singapore in 1999 following an outbreak of respiratory and neurological disease in pigs and encephalitis in humans (386). Since then, further sporadic and unpredictable outbreaks have occurred in Bangladesh, India, and the Philippines (387). Symptoms in humans range from mild to severe and initially include fever, headache, and respiratory symptoms; encephalitis and potentially death may follow. Nipah virus infection is associated with a high case fatality rate (40-75%) (386).

Nipah is a zoonotic disease, and the animal host reservoir is the fruit bat (genus *Pteropus*) (387). Infected fruit bats can spread the disease to humans or other animals, including pigs. Humans can become infected through close contact with an infected animal or its body fluids. Fruit bats have a flying range that can cover vast areas, hence there is concern that outbreaks can affect further areas in the future (388) (Figure 33). Human-to-human transmission has been documented, accounting for 75% and 51% of cases in the India and Bangladesh outbreaks, respectively, raising further fears of Nipah's pandemic potential (388).

Figure 33 - Nipah virus outbreaks and Pteropus distribution map



From Dhaked et al. (389)

Despite the threat posed by Nipah virus, medical countermeasures do not exist. Intensive supportive therapy, where available, is the current standard of care for severe respiratory and neurological complications (390). Current prevention strategies focus on raising disease awareness in affected areas and behaviour modifications to prevent spill-over from bats (388). Rapid detection of Nipah outbreaks is required for prompt initiation of appropriate control measures. Various assays have been developed for laboratory confirmation of Nipah virus infections, with ELISA and RT-PCR the preferred methods (388). Currently available tests could be improved by validation of methods and standardization across laboratories. Further investment in strategies that can facilitate access to suitable diagnostics in all areas where Nipah virus outbreaks are likely to occur is important (388).

There is a diverse pipeline of medical countermeasures in development, including small molecules and antivirals, monoclonal antibodies, and vaccines, that have the potential to control future Nipah outbreaks (390). It is important to continue and progress these efforts given the high case fatality associated with the disease coupled with the potential for further spread. Investment in a combined portfolio of several medical countermeasures, including

surveillance systems, and active data exchange between developers of human and animal medical countermeasures should be encouraged (390).

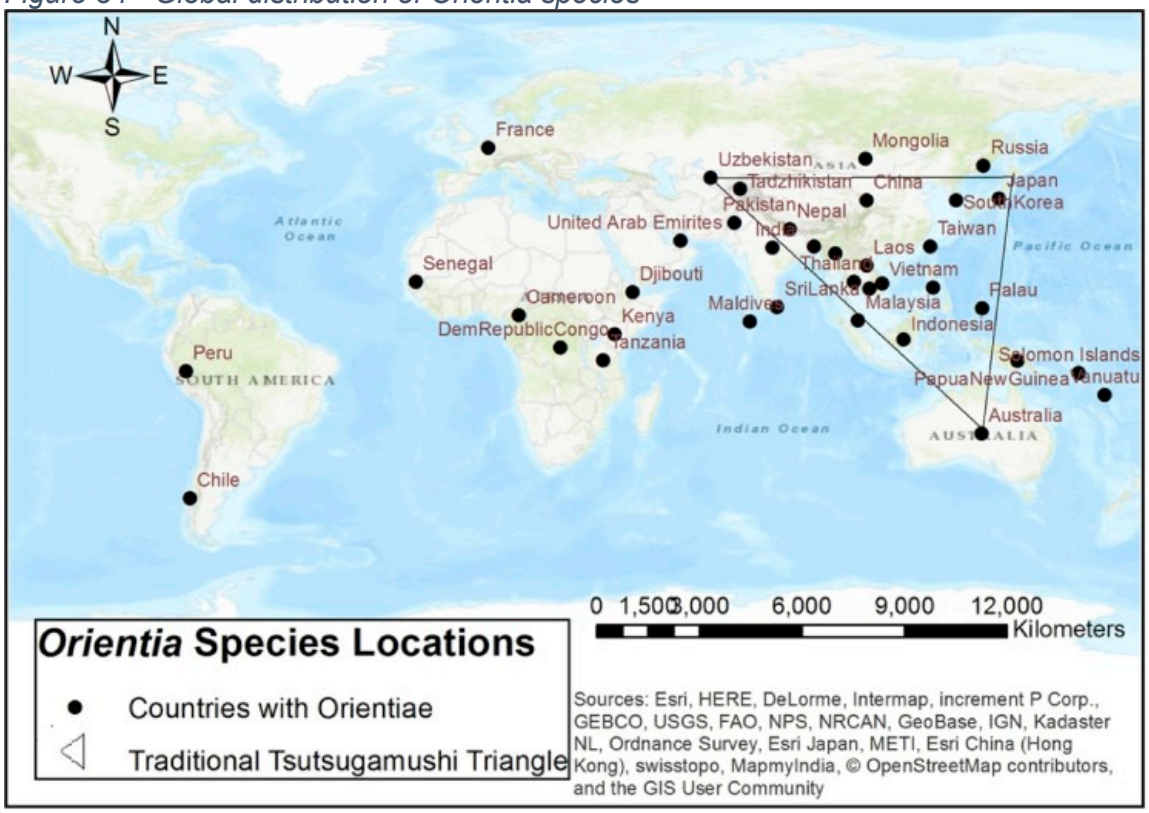
9.2.3 COVID-19

Since the first cases of SARS-CoV-2 were reported in Wuhan, China in 2019, the world has seen a global COVID-19 pandemic with >778 million cases, approximately 7.1 million deaths, and an unprecedented burden on economic and healthcare systems (391). Although COVID-19 predominantly affects the respiratory system, neurological disorders, such as stroke, Guillain-Barre syndrome, myelitis, and encephalitis, have been increasingly reported (392). A systematic review and meta-analysis reported the pooled incidence of encephalitis in COVID-19 patients was 0.215% (392). However, as most patients in this study had severe COVID-19 illness prior to developing encephalitis, the incidence of encephalitis due to COVID-19 infection in the general population is likely lower (as most infections are mild). The incidence of encephalitis increases significantly in COVID-19 patients who require ITU care (6.7%) (392). In addition, mortality in patients who suffer encephalitis as a complication of COVID-19 is four times higher than the general population of COVID-19 patients (13.4% versus 3.4%) (392). Encephalitis syndromes seen with COVID-19 are heterogeneous, including acute and post-infectious presentations, likely representing varied underlying neuropathogenesis (393). Response to treatment depends on the specific CNS manifestation. Various treatments have been used for COVID-19-associated encephalitis; one survey reported IV methylprednisolone/oral prednisone (36.11%), IV immunoglobulin (27.77%), and aciclovir (16.66%) as common treatment options (394). Several studies have confirmed the efficacy of IV immunoglobulin in severe cases of COVID-19 (395,396).
In December 2020, approximately one year after the initial case was reported, the UK became the first country to approve a COVID-19 vaccine (i.e., Pfizer-BioNTech) that has been tested in a large clinical trial (397). Further vaccines have since been developed and granted emergency use listing by WHO (398). The extraordinary success of the COVID-19 vaccines shows what can be achieved in the event of a true global emergency and sufficient resources. The COVID-19 pandemic has changed the future of vaccine science, as new vaccine manufacturing methods (e.g., messenger RNA) have been validated and it has been demonstrated that the development process can be accelerated substantially without compromising safety (399). Lessons from the coronavirus pandemic should be applied to preparedness efforts against Nipah virus and other pathogens of pandemic potential (390).

9.2.4 Scrub typhus

Scrub typhus, a disease caused by the rickettsia/bacteria *Orientia tsutsugamushi*, is spread to humans through bites of infected chiggers or larval mites. Although first described as early as the third century A.D., scrub typhus shot into prominence during the second world war when millions were affected in the China-Burma-India corridor of military action (49). Since then, scrub typhus has reemerged with a different geographical distribution and varied clinical presentation (400). Scrub typhus is endemic in the Asia–Pacific region (i.e., 'tsutsugamushi triangle') but has recently spread to Chile, Peru, and West Africa (Figure 34) (49).

Figure 34 - Global distribution of Orientia species



From Tilak et al. **(49)**

The most common symptoms of scrub typhus include fever, headache, body aches, and sometimes rash. The first sign of the disease prior to symptom development is the formation of a black crust or eschar close to the site of the vector bite (401). Eschars are present in 7-97% of patients with scrub typhus (49). Nervous system involvement occurs in up to one fifth of patients and can include encephalitis, meningitis, and less frequently opsoclonus, myoclonus, parkinsonism, and Guillain-Barre syndrome (402). Scrub typhus has emerged as an important cause of encephalitis in children in India. A prospective cohort study conducted at a tertiary care public hospital reported scrub typhus in 18.8% (n=66/352) of children with AES (403). Other studies in India have reported ranges from 12.5% in Notheast India to 63%

in Gorakphur (404,405). Seasonal outbreaks of AES have been occurring over numerous years in eastern Uttar Pradesh during the monsoon and post-monsoon months, affecting mainly children from rural areas and resulting in high case fatality (15-25%) (406). Scrub typhus has increasingly been identified as an important, and even main aetiology of these outbreaks. Moderate to severe disability is frequent amongst survivors of AES caused by scrub typhus (406). Of 146 survivors of AES caused by scrub typhus, 38.4% (n=56) had mild disability and 13% (n=19) had moderate to severe disability.

The gold standard for diagnosing rickettsial infections is immunofluorescence. However, the required fluorescence microscope is not easily available, the test is expensive and time-consuming, technical expertise is required, and cell culture facilities are ideally needed for sustaining rickettsial antigens (407). Serum IgM ELISA is the most widely used test for diagnosis; however, CSF IgM ELISA may be preferable but this requires further evaluation in larger studies (407,408). It is important however not to await laboratory confirmation when there is clinical and epidemiological suspicion as scrub typhus can successfully be treated with doxycycline, tetracycline, and azithromycin, and most of the neurological manifestations of scrub typhus, including encephalitis, respond to these antibiotics (401,402). Thus, it is important to consider scrub typhus high on the list of differential diagnoses among patients in endemic areas presenting with acute febrile illness, especially in the setting of multi-organ dysfunction and presence of an eschar (402).

There are ongoing efforts to develop a prophylactic vaccine against scrub typhus despite the availability of antibiotics (401). Poor cross-reactive immunity and the short life span of protective immunity results in frequent reinfection, and antibiotic resistance is a concern with the profuse use of antibiotics.

9.3 Discussion

Changes in climate, land use, proximity to animals, and human behaviours have and will continue to result in the emergence/re-emergence of numerous pathogens that cause encephalitis. Scrub typhus has re-emerged as a main cause of encephalitis in children in India, and Chikungunya virus has spread westwards since 2004 resulting in large epidemics with neurological involvement in a significant proportion of cases. Nipah virus outbreaks are restricted to Asia thus far, but there is real concern given the vast flying range of the bat vector, potential of human-to-human transmission, and high case fatality. The emergence of SARS-CoV-2, which can result in encephalitis, has shown the devastating impact a global pandemic can have on individuals, economic, and health systems. This emphasizes the importance of

pandemic preparedness and efforts to reduce the risk of emergence/re-emergence of dangerous pathogens.

A reduction in activities which contribute to environmental change, such as deforestation, intensive agricultural practices, biodiversity loss, and interactions with animals and live animal markets, would lower the risk of emerging zoonoses and spillover events (409). If a novel zoonoses or mutation does emerge, rapid and early identification is key to limit spread (393). As has been demonstrated by the coronavirus pandemic however, containment alone may prove difficult. A worldwide collaborative response, including international collaborative efforts of identification, classification, and knowledge sharing, is required to tackle a global disease that has spread (393). Expansion of global surveillance will reduce the risk of large-scale outbreaks of encephalitis in the future (374). The One Health approach is gaining global recognition as an effective way to fight health issues at the human-animal-environment interface (410,411). This approach applies global collaboration at the local level to achieve better public health outcomes, from addressing the impact of climate and environmental change through to the implementation of surveillance and early warning systems to detect emerging pathogens with the potential to cause future pandemics (409).

9.4 Gap analysis

Table 30 - Gap analysis for new and emerging infections

Where we are	Where we want to be
Novel Infectious diseases have been emerging for thousands of years and will continue to do so in the future. Some of these cause encephalitis and are included in the WHO list of diseases with epidemic or pandemic potential.	Need increased investment in outbreak response to help mitigate the threat from future emerging infections Need efforts to develop universal vaccines (e.g., against all strains of influenza viruses, flaviviruses, or coronaviruses) Need rapid and early identification of novel zoonoses or mutations to limit spread Need to improve and expand global surveillance Need One Health approach to fight health issues at the human-animal-environment interface Need a better understanding of disease ecology and investigations into infectious agents in wildlife to potentially prevent outbreaks in livestock and people
Chikungunya virus has spread westwards since 2004 resulting in large epidemics with neurological involvement in a significant proportion of cases.	Need to understand more about the epidemiology of chikungunya, especially granular data on disease incidence and age-specific infection rates Need to standardise procedures used to characterise this disease Need to better understand chikungunya disease dynamics with appropriate granularity and better insights into the duration of long-term

	population immunity to assist in the planning and success of vaccine development efforts pre and post licensure Need to improve surveillance and rapid outbreak detection Need coordinated efforts to ensure patients in chikungunya-endemic areas have access to appropriate rapid diagnostic tests Need to continue efforts to develop medical countermeasures Need to prepare mechanisms for the acceptance, procurement, and uptake of licensed chikungunya vaccines
Nipah virus outbreaks are restricted to Asia thus far, but there is real concern given the vast flying range of the bat vector, potential of human-to-human transmission, and high case fatality.	Need to establish or reinforce surveillance systems to ensure rapid detection of Nipah outbreaks and prompt initiation of appropriate control measures Need to increase efforts on behaviour change communication interventions to increase awareness of disease risks Need to validate and standardise laboratory diagnostic methods for Nipah Need to invest in strategies to facilitate access to suitable diagnostics in all areas where Nipah outbreaks are likely to occur Need to continue and increase efforts to develop medical countermeasures
The world has experienced a global COVID-19 pandemic with an unprecedented burden on individuals, economic, and healthcare systems.	Need to apply lessons from the coronavirus pandemic to preparedness efforts against other pathogens of pandemic potential
Scrub typhus is increasingly recognised as an important cause of encephalitis in children in India.	Need to consider scrub typhus high on the list of differential diagnoses among patients in endemic areas presenting with acute febrile illness as effective treatment is available

10 Advocacy

10.1 Introduction

The WHO defines advocacy for health as “a combination of individual and social actions designed to gain political commitment, policy support, social acceptance, and systems for a particular health goal or program” (412). At an individual level, advocacy should concentrate on empowering the individual to engage in planning and monitoring health services. At an organisation level, advocacy should concentrate on problem identification, acquisition of evidence for problem solving, and communication of knowledge to the public, decision-makers, opinion leaders/influencers, and key government stakeholders. Communities and organisations could together successfully advocate for accessible and high-quality healthcare, an imperative especially in LMICs.

Advocacy goals for encephalitis include better protection against preventable types of encephalitis, better diagnosis and treatment, and better support and after-care for survivors of encephalitis and their families. Particular attention should be dedicated to initiatives targeting vaccine-preventable encephalitis in LMICs where vaccine hesitancy and limitations of health systems contribute to gaps in vaccine coverage (413). Encephalitis professionals and those with personal experience are the strongest advocates for change, and it is essential that all involved in the management of encephalitis (health professionals, individuals affected, families, and patient organisations) contribute towards this advocacy. In addition, the commitment of decision-makers and the community is necessary. A joint effort is required to improve the lives of those affected by encephalitis. The specific advocacy goals for prevention, diagnosis and treatment, and aftercare and support in encephalitis are displayed in Table 31.

The ‘Encephalitis as a public health priority’ virtual meeting took place from June 28 to 29, 2022. This event was organised by the WHO and received support from Encephalitis International. The primary objective of the meeting was to discuss mechanisms and identify strategies to strengthen countries’ capacity to respond to the public health challenge posed by encephalitis and reduce the burden faced by individuals, families, communities, and societies. Two pivotal themes concerning advocacy emerged prominently during the meeting. The first theme emphasised the urgency of advocacy and awareness. This encompassed the imperative to combat stigma and discrimination surrounding encephalitis, while underscoring the invaluable role played by individuals affected by encephalitis, their families, and civil society organisations in this endeavour. By giving voice to their experiences and insights, they contribute significantly to shaping public perception and support. The second theme revolved around prevention and encompassed multifaceted advocacy strategies. This entailed advocating for encephalitis vaccines and promoting their integration into national health programmes. It also extended to the critical task of educating the general public about vaccines through primary healthcare providers and community leaders. This comprehensive approach aims not only to raise awareness, but also ensure proactive measures are taken to prevent the onset of encephalitis, thereby mitigating its impact on individuals and communities.

The WHO’s Intersectoral global action plan (IGAP) for epilepsy and other neurological disorders, spanning the years 2022 to 2031, similarly places a strong emphasis on advocacy (414). It highlights the critical role of effective advocacy in shaping political commitment and mobilising resources, particularly in LMICs (415). The broader objective is to secure backing for policies that prioritise the comprehensive management of neurological disorders. The

plan explicitly highlights the essential nature of advocacy across several key dimensions. These include elevating the quality of neurological care, combatting and diminishing the associated stigma and prejudice, preventing rights violations in the context of neurological care, and promoting a broader culture of human rights in the healthcare sphere (415).

Table 31 - Advocacy goals for encephalitis

Advocacy area	Goals
Prevention	-Encephalitis prioritised as a health issue in endemic areas and as a travel-related condition -More accurate data available on global burden of encephalitis, particularly in LMICs like Senegal (9) -Policies accessible and funding available to support introduction and optimisation of vaccine schedules and educational campaigns -Increased vaccine awareness and promotion of uptake, particularly in LMICs -Integration of vaccine awareness (including accurate and tailored information) into national programmes -Increased accuracy of information on risk, burden, and preventative measures for infectious encephalitis -Deliver vaccine education through primary care and community leaders -National and local policies to control vectors involved in transmitting specific causes of encephalitis (e.g., dogs in rabies, mosquitos in JE)
Diagnosis and treatment	-Development of diagnosis and treatment guidelines for encephalitis -Improved supply of free/affordable immunotherapies -Routine provision of evidence-based information on safety netting by health professionals -Provision of training for health professionals on all types of encephalitis -Inclusion of encephalitis and immunotherapies used for the treatment of autoimmune encephalitis on the insurance approved list -Implementation of health and social care assessments at discharge for detection of after-effects and for implementation of rehabilitation programmes
After-care and support	-Ensuring that healthcare and social services for after-care and support are accessible to affected individuals and families in a timely manner -Availability of educational programmes for the self-management of symptoms - Signposting of suitable after-care support by health services -Presence of a suitable legal framework that supports the rights of those with ongoing after-effects, impairments, and disabilities -Building meaningful partnerships between community health workers, communities, and policymakers to confront and address underlying structures of inequity

JE = Japanese encephalitis; LMICs = Low- and middle-income countries

10.2 Recommended practice

Advocacy is a powerful way to engage a diverse range of people with the encephalitis cause and promote change. However, recommended approaches for advocacy in encephalitis do not exist. Rather, key theoretical elements of a successful advocacy campaign include:

- Develop a deeper understanding of the issue;
- Know who has the power to change matters;
- Decide who the allies and enemies are and involve them;
- Develop a plan with clear advocacy goals and strategies;

- Communicate with the public, stakeholders, and decision makers;
- Educate about vaccines through primary care and community leaders;
- Leverage data regarding encephalitis outcomes to inform priorities in resource-limited settings.

10.3 Implementation status

Assessing the status of encephalitis advocacy is a nuanced task, influenced by a variety of factors including the specific campaign, type of encephalitis, and regional context. Presently, advocacy efforts predominantly centre around preventing vaccine-preventable infectious encephalitis. This encompasses campaigns aimed at JE in Asia, rabies in both Asia and Africa, TBE in Europe, and global initiatives for measles prevention (207).

On the other hand, advocacy campaigns focused on encephalitis diagnosis, treatment, or after-care are often integrated into broader healthcare initiatives. These include global frameworks like the UN Sustainable Development Goals (2015) and are supported by in-country umbrella organisations such as the Neurological Alliance (UK), the National Vector Borne Disease Control Programme (India), or the Vietnam National Immunization program (416). The multifaceted nature of encephalitis advocacy reflects the diverse challenges posed by this condition, necessitating a comprehensive approach that addresses both prevention and management aspects to effectively combat encephalitis.

10.4 Barriers to implementation and discussion

Numerous barriers exist with regards to encephalitis advocacy. There is a lack of data on incidence, prevalence, and cost (human and financial) of encephalitis making it difficult to establish the real burden and acquire quantitative evidence to support advocacy campaigns. This is compounded by existing challenges in data quality related to immunisation coverage in LMICs, wherein data quality is considered poor, with issues such as inflated coverage numerators and inaccurate denominators (417).

Growing vaccine hesitancy in populations due to misinformation affects the success of advocacy campaigns. In the 'Why encephalitis matters?' virtual meeting organised by the WHO and Encephalitis International in 2022, participants highlighted a lack of funding to support global and local advocacy campaigns, and a general lack of importance attributed to encephalitis resulting in it often being omitted from medical training and awareness programmes (329). Furthermore, the nature of the illness and the fact that incidence,

diagnosis, and treatment differ by cause is a barrier to encephalitis advocacy. A widespread lack of public awareness regarding the prevalence of encephalitis, preventive measures, and the severity of its consequences constitutes another barrier to encephalitis advocacy. In some cases, conditions with lesser impacts may receive higher public visibility, leading to disparities in prioritisation and funding across social, financial, healthcare, and political programs and strategies. This discrepancy underscores the critical need for increased education and awareness campaigns to bridge the gap and garner much-needed support for encephalitis advocacy efforts (Table 32).

Recent research has highlighted the imperative to shift the perspective on community health workers (CHWs) from a mere 'temporary solution' to establishing substantive partnerships with both communities and policymakers, focusing on addressing the root causes of structural inequalities (418). Rather than viewing CHWs as a short-term remedy, this paradigm recognises their potential to become integral agents in tackling systemic disparities in LMICs. Such partnerships can create lasting change by working together to transform the underlying structures that perpetuate inequality.

An additional barrier to implementation is that traditional services designed for individuals with neurological disorders in HICs may not be suitable for the needs and resources of LMICs (9). Instead, alternative service provision models that are family-focused and community-based may be more desirable, led by qualified and experienced professionals who can train and supervise local support workers from the community. Overall, in the transition of services from HICs to LMICs, it is crucial to exercise care and consider subtle refinements.

10.5 Gap analysis

Table 32 - Gap analysis for encephalitis advocacy

	Where we are	Where we want to be
Prevention	Encephalitis is not perceived as a travel-related condition and the associated burden is not recognised.	Increase recognition of encephalitis as a travel-related condition and its associated burden
	Vaccines against preventable causes of encephalitis are expensive for travellers.	Need access to affordable vaccines for travellers
	Coverage or implementation of vaccine programmes in endemic areas are insufficient.	Need affordable vaccines and access to information resources about the disease and vaccination in endemic areas, particularly certain LMICs in which particular types of infectious encephalitis are prevalent

	Surveillance strategies and preventive programmes for vector-borne encephalitis (e.g., mosquitos, strained dogs) are insufficient and inadequate. Vaccine hesitancy and anti-vaccine movements may hamper vaccine coverage (9).	Need implementation of global and local surveillance strategies and preventive measures and programmes for vector-borne encephalitis Need a high level of community engagement and widespread communication about vaccine safety and the incidence of encephalitis in vaccinated and unvaccinated population to improve vaccine uptake
Diagnosis and treatment	There is insufficient training on encephalitis in medical school and in some medical professions, encephalitis training does not exist at all.	Need comprehensive and up-to-date medical training
	Guidelines for the management of encephalitis that are recognised by medical councils and organisations do not exist.	Need for management guidelines to be recognised and recommended by medical councils globally
	There is lack of treatment for encephalitis that is free, affordable, and approved by insurance; for example, antivirals are expensive in Senegal (9).	Need for free or affordable treatment or treatment approved by insurance, specifically in LMICs
	There is a lack of biobanking in LMICs as well as associated training (329).	Need for biobanking facilities as well as associated training in LMICs
After-care and support	Services to support families and survivors and information on how to access these services are lacking.	Need for affordable services to support families and survivors and for them to know how to access these services
	Legal frameworks that support the rights of disabled people are often inconsistent or even absent.	Need for legal framework in each country that supports the rights of disabled people Stigma associated with long-term neurological sequalae, particularly in LMICs, need to be considered

LMICs = Low- and middle-income countries

11 Support and after-care for survivors and families

11.1 Introduction

Encephalitis survivors may acquire brain injuries to varying degrees and manifestations. This can make returning to education, work, family, and social life difficult (419). In some cases, encephalitis also increases the risk of death from other causes (420). An acquired brain injury (ABI) after encephalitis is specific to the individual and often hidden, subtle, inconsistent, and lifelong. Affected individuals may look identical to how they were before with effects being cognitive, emotional, behavioural, and social rather than physical (i.e., hidden). In addition, affected individuals may appear to function at the same level as before and with fluctuating

capacity, for example being better on some days more than others (i.e., subtle and inconsistent). A person affected by encephalitis may be perceived to perform better than others that have also been affected by encephalitis, but not as well as they did before the illness (i.e., the impact of encephalitis can be very specific to the individual). If encephalitis occurs in childhood, there is the possibility of a delayed onset of difficulties where the effects of the injury to the brain are only apparent later in life due to the part of the brain affected not yet being fully developed at the time of illness. Consequently, these individuals may be discharged from hospital before the full extent of their disability has been recognised and addressed. As physical disabilities are more rare than cognitive disabilities in encephalitis, affected individuals may not be perceived as disabled by employers, school, services, and the wider public, as their disability may not be immediately visible to others. At the other end of the spectrum some people may need care in their homes or residential care facilities for the rest of their lives.

ABI following encephalitis affects entire families. Families must first come to terms with the illness and its consequences and subsequently find ways to cope. For example, the impact of encephalitis on the lives of three families affected by JE have been described in the following ways: “strange”, “scary”, “devastating”, “shock”, “it is not anything you imagine”, and “this is for life” (262). In addition, the carer role is often assumed by family members and can have a significant impact on physical and psychological health, finances, employment, family relationships, and overall quality of life (421).

Support after encephalitis is needed for both affected individuals and their families. Affected individuals require appropriate, multistage, multidisciplinary, and personalised rehabilitation and/or psychological support to come to terms with the illness and its after-effects, to learn to manage their difficulties, and to re-integrate within social and family life. Families and caregivers also have support needs. Some may be bereaved and require specific bereavement support, while others may need to adjust to and cope with becoming a carer and the resulting change of dynamics within their families. Provision of support and rehabilitation, however, is often suboptimal and even non-existent in some countries where people affected rely mainly on family members to help with daily activities (422). The WHO has recently published the IGAP on epilepsy and other neurological disorders 2022–2031, which expanded on the challenges faced by carers of those with neurological conditions (414). These include stress, financial burden, social isolation, and in cases of a loss, bereavement. These can impact on their health, wellbeing and social relationships.

Despite the evident impact on individual lives, the true burden of disability following encephalitis remains unknown. There is no simple and reliable way of measuring the disability burden, and it is unfamiliar to health and social care providers as well as decision makers. The GBD study estimated 4.8 million DALYs related to encephalitis globally in 2019; encephalitis was the fifth largest contributor to total neurological DALYs in India (230). However, GBD estimates were based on mathematical models that use a large number of data sources of differing quality and data on the distribution and severity of long-term sequelae in survivors were scarce. Survivors of encephalitis face discrimination and stigma associated with their acquired disability. The need to address stigma emerged as part of a main theme from the "Encephalitis as a public health priority" virtual meeting, arguing for improved advocacy and awareness of the effects of encephalitis (329). Article 25 of the UN Convention on the Rights of Persons with Disabilities reinforces the right of persons with disability to attain the highest standard of health care, without discrimination (423). However, this is not always achieved.

Encephalitis is a complex, growing global threat. Some key contributing factors to the global growth of this condition are population density, increasing proximity to animals, communities lacking financial and medical resources and social care support, vaccine hesitancy, and climate change. Consequently, these factors can make encephalitis more prevalent in certain countries and communities. It is challenging to know how to provide individualised support, and if this support is beneficial, particularly in LMICs where the social, medical, and financial cost of encephalitis to countries and individuals is under researched. However, central to improving support pathways is increased knowledge of encephalitis (and its consequences), culturally sensitive approaches to care and support, and ensuring the accessibility of medical, social, and rehabilitative care. A global condition requires a global support response.

Therefore, the disease burden for encephalitis is unequally distributed, experienced disproportionately in LMICs where there are limited resources. This burden is also compounded by a lack of diagnostic testing, treatments, and limited access to neurological care (424). These difficulties and a lack of trained clinicians impact on outcomes (424). Hence, it is vital to strive for a wider understanding of the costs of acute and sequelae care from intersectional perspectives (i.e., medical, financial, societal) to improve the provision of targeted support for LMICs (192).

11.2 Recommended practice

The type of support required following the acute illness is dependent on the type and degree of disability, family and social support network, financial means, age, resilience, provision of

local support, and rehabilitation services culture and education. It is widely recognised that specialist, multi-stage, person-centred, and interdisciplinary rehabilitation is beneficial, and that specialist rehabilitation is highly cost-efficient (425). The needs of each affected individual should ideally be assessed at different stages in their recovery, and support and rehabilitation should be tailored accordingly. Rehabilitation includes not only physical medicine, pharmacology, and nutrition, but also psychology and behaviour, education and counselling, occupational and vocational advice, social and supportive services, architecture and engineering, and other interventions (422). Specifically, neurorehabilitation should aim to optimise functional recovery, disability management, and adaptation to loss and change (426). WHO advocates for community rehabilitation as an addition to existing rehabilitation models and for rehabilitation to look beyond medical needs/care (422).

The WHO IGAP paper outlined targets relating to a global response towards neurological conditions. This includes a target of 75% of countries to include “neurological disorders” in the universal health coverage benefits package by 2031 (414). The action plan also argued for emergency care provision within care pathways, stating that it should be able to respond to those affected, carers, and their family, including minority groups, regardless of geographical location (rural or urban). As carers’ roles can vary on the type of condition and the age of those that they are caring for, it was recommended to involve carers in care planning and policy making, ensuring accessible, evidence-based resources (414).

It is important that disability following encephalitis is addressed not only from a medical perspective (resulting in individual treatment) but also from a social perspective which requires social action to reintegrate the individual into their community. Culturally sensitive education and awareness campaigns aimed at the general public, services, policy makers, and healthcare professionals (especially primary care) are needed to eliminate stigma and discrimination and improve overall quality of life. These awareness campaigns will need a foundation of improved data-sharing processes, to reduce knowledge-gaps, accelerate innovation, and support the capacity of LMICs for research and encephalitis support (414). Once again, this information exchange needs to be an international effort.

As referred to above, elimination of stigma was a key focus of the recent encephalitis WHO publication, which gives the example of India, where most hospitals refuse to admit people with rabies due to the lack of effective cure and stigma (329). This can result in reduced early recognition of certain types of encephalitis, and therefore delayed diagnosis. They highlight encephalitis as a medical *and* social issue and argue for increased awareness among clinicians and policy changers regarding stigma relating to reduced hospital admission. For

family members and loved ones, there is often a lack of closure given the rapid disease progression. In addition, affected families are often alone in their grief because deaths due to rabies are typically sporadic and isolated. Grief counselling services and support groups would be beneficial but are often lacking in LMICs. Hence, innovation in providing support needs to come from speaking directly to people affected by encephalitis and its consequences. Taking a person-centred approach, WHO advocate for the collaboration of multiple stakeholders (e.g., from education, social care, and employment providers) to influence policy and move forward with informed practice to support those affected by encephalitis (including their loved ones) across the life course.

Currently support for families is variable. As aforementioned, families may require specialised bereavement support in the event of loss of life, this needs to take into account different ages, emotional needs, and cultural and religious backgrounds. Support needs of families in which a carer role is adopted should consider all aspects of day-to-day life including financial needs (as government support varies between countries), employment, emotional needs, mourning the loss of the person as they knew them, respite care, and support with daily activities. These activities undertaken to support the affected individual range from practical interventions such as help with eating, washing, and cooking to assistance on how to cope with challenging behaviour and loss of memory. The onus is often placed on family and the community to provide this care. Thus, additional interventions should be widely available for caregivers of individuals affected by encephalitis, as they are for other conditions such as stroke (i.e., psychoeducational interventions focused on coping and problem-solving) or dementia (i.e., educational sessions) (162). The support provided to caregivers is important as it has a strong influence on the management of the affected individual (161). Carer support and protection was described as a priority in the WHO IGAP paper, particularly with calls for financial protection for carers for example through pension provision and flexible working arrangements. Again, support must be culturally sensitive and content-specific, with person-centred training provided (414). This is part of the aim to ensure that those affected by neurological disorders and their carers experience equal rights, to improve their quality of life.

Universal rehabilitation guidelines do not exist, but the World Federation for Neurorehabilitation Position Paper 2015 (426) calls for:

- Long-term, coordinated efforts by governments, non-governmental organisations, international organisations, and other interested partners to facilitate investment in, and the provision of, rehabilitation equipment and the funding of education and training programmes for health professionals.

- The development of a core set of standards to constitute minimum requirements for the establishment of credible neurorehabilitation units.
- Implementation of community-based rehabilitation services with tailored and culturally sensitive education for families and carers.

Key features of support and after-care can include (but are not limited to):

- Provision of accessible information about the illness to enable individuals to understand what happened to them and help them come to terms with the illness.
- Provision of information about recovery so individuals know what to expect and to fill the information-gap in LMICs where social media and communication infrastructure can be limited (427).
- Provision of information on expectations from families/carers following hospital discharge, and management of misinformation (329).
- Provision of practical advice such as who to contact in case of an emergency.
- Provision of information regarding relevant patient organisations, such as Encephalitis International.
- Ensure referrals are in place for follow-up appointments or rehabilitation in the community.
- Ensure social care assessments are in place where there are social care requirements.
- Ensure family doctors/primary-care/general practitioners receive a discharge letter with recommendations for follow-up and referral.
- Ensure transfer to suitable rehabilitation if discharge to home is not possible (e.g., specialised ABI care homes rather than dementia care homes).
- Ensure community rehabilitation if discharge to home is an option.
- Ensure psychological support for affected individuals.
- Ensure psychological support for carers and families.
- Ensure plans are in place for gradual return to work or education.
- Ensure the availability of respite care for carers from caring responsibilities.
- Provide bereavement support.
- Ensure easy access to legal redress for substandard health care
- Ensure presence of national and legal frameworks that embed the rights of disabled people.

11.3 Implementation status

The majority of affected individuals and families in contact with Encephalitis International report inadequate care provision. There are no guidelines for the universal implementation of

support and rehabilitation for people affected by encephalitis and their families/carers. The support received varies considerably depending on location, financial means, and cultural practices. In general, access to support services is often resource-dependent at both a national and individual level. Therefore, not only does the support need to exist, it also has to be accessible. Sultana et al. found that in LMICs, a household affected by encephalitis spends 2-5% of its income on healthcare (192). Most of these costs arose from acute encephalitis management as well as long-term sequelae care. Specifically for patients with JE sequelae, an average of 44%–56% of the household monthly income was spent on healthcare, suggesting a hugely significant expenditure for the families.

Services are more widely available in higher income settings and for wealthier individuals compared to low-resource settings or for individuals living in poverty. Whilst clinicians and healthcare professionals play an important role in support and after-care, it is often families and communities, alongside civil society and faith/community groups, who provide the majority of care needed.

11.4 Barriers to implementation and discussion

Despite improvements in the diagnosis and treatment of encephalitis, information about its after-effects is lacking. The focus is on the acute stage of the illness and affected individuals and their families are often left with little information about effects post-discharge. The lack of knowledge regarding the after-effects of encephalitis combined with the often invisible and subtle changes following some brain injury often results in patients leaving hospital without any follow-up appointment or referral. Thus, these individuals return home and attempt to resume life as before they became unwell, without realising that this is not always possible. They are usually faced with a lack of follow-up support when it is realised that they cannot function as before. Often the ABI is confused with stress, overprotective behaviours of parents in the case of children, and even in cases where there is an understanding family doctor, there are often no services available or there is a long-waiting time.

Reviewing the current health service delivery for autoimmune encephalitis in the Philippines, Pagaling et al. found that out of pocket expenses still make up most of healthcare expenditures, despite government-backed programs (319). There are significant treatment gaps for those with autoimmune encephalitis in the Philippines, including disease recognition, allocation of resources, diagnosis, and ‘prognosis-changing therapeutics’. Treatment gaps such as these mean the long-term management of autoimmune encephalitis is also prohibited by cost and is not easily available.

There is also a lack of rehabilitation services that provide multidisciplinary and personalised treatment plans. Availability of services depend on geographical location; some areas have full provision and others only specific professionals, for example occupational therapists. Neuropsychological services are non-existent in many areas and long waiting lists sometimes delay much-needed intervention. Another barrier to implementation is the nature of the illness itself with various types of encephalitis having different outcomes and affected individuals having different needs. Ideally, rehabilitation for affected individuals would consist of medical, psychological, and social support. The lack of or inadequate communication between health professionals (acute and rehabilitation team), affected individuals, and families/carer-givers is a substantial barrier to implementation. This highlights the importance of the WHO's call for a holistic approach to encephalitis support, including neurorehabilitation, nurses, and occupational/physiotherapists in response to a current lack of interdisciplinary care.

According to WHO (428) current barriers to strengthen and extend rehabilitation in countries include:

- Under-prioritisation by government amongst competing priorities;
- Absence of rehabilitation policies and planning at the national and sub-national levels;
- Limited coordination between ministries of health and social affairs where both are involved in rehabilitation;
- Non-existent or inadequate funding;
- Dearth of evidence of met and unmet rehabilitation needs;
- Insufficient numbers of rehabilitation professionals and lack of skills;
- Absence of rehabilitation facilities and equipment;
- Lack of integration into health systems.

Again, these issues are exacerbated in LMICs, made worse by poor living conditions, lack of sanitation, restricted access to health facilities and running water, overcrowding, and overpopulation (427).

11.5 Gap analysis

Although most issues identified in Table 33 are not encephalitis specific, they are highly relevant to improving support and after-care for survivors and families after an encephalitis diagnosis.

Table 33 - Gap analysis for support and after-care for survivors and families

	Where we are	Where we want to be
Lack of information	Lack of information about expectations following discharge	-Need provision of information at discharge about what to expect
Inexistent /inadequate discharge plans	Discharge plans inadequate without patient participation	-Need agreement on discharge plans between healthcare professionals and affected individual/caregiver. These need to be tailored to family/community circumstances
Lack of follow-up appointment/referrals	Discharge without a follow-up appointment or with extensive waiting time	-Need a timely follow-up appointment to be set-up at discharge
Lack of understanding of ABI following encephalitis by Primary care/family doctor	Doctors often unaware of ABI following encephalitis	-Need to ensure awareness amongst primary care/family doctors of ABI following encephalitis and the existence of services to enhance recovery. This awareness needs to be shared internationally to include LMICs
Lack of services available and/or long waiting times	No community rehabilitation available or long waiting times No support for carers and their families (e.g., family therapy)	-Need multidisciplinary community rehabilitation teams
Lack of support to help with returning to work/education	People advised to return to education/work often resulting in failure	-Need adequate support in place for a phased and gradual return to school/work
Lack of care home specialised in ABI	Older adults recovering from encephalitis sent directly to dementia care homes	-Need adequate provision for rehabilitation of older people
Cost	High cost of health care creates a barrier to accessing the care for those in need	-Need affordable healthcare services -Need to develop similar provision internationally for LMICs, where out-of-pocket expenses are likely to have a higher burden on care givers and family members
Policy and legislation	Inconsistent or absent policies, lack of sanctions for failure to deliver, and voices of people with disabilities are largely silent in critical decisions affecting their lives	-Need stronger policies -Need available services -Need planned improvements for access and inclusion -Need to involve children and adults with disabilities in decisions affecting their lives -Need comprehensive regulatory framework with inclusion of specific objectives regarding the rights of children with disabilities in education, health and social services, and monitoring of the allocation of funds for their implementation
Workplace policy for care givers	Lack of policies in place to help support care givers in their employment	-Need improvement of protective policies such as pension provision and increase in flexible working hours to allow care givers to remain in employment around providing care
Finances	Lack of affordable public or private health financing and insurance, and unequitable access to public health programmes	-Need cover for people with disabilities and measures to make the premiums affordable where private health insurance dominates healthcare financing
Human resources	Limited training on disability for healthcare professionals, limited use of evidence-based guidelines, and limited training on ABI following encephalitis	-Need to integrate education on disability into undergraduate studies and continuing education for all healthcare professionals -Need evidence-based guidelines for assessment and treatment

Data and research	Infrequent inclusion of people with disability in healthcare surveillance Some research exists on needs, barriers, and health outcomes for people with disabilities Limited research looking at recovery and rehabilitation	-Need to include individuals with disabilities, special needs, or developmental retardation in healthcare surveillance -Need more research on the needs, barriers, and health outcomes for people with disabilities -Need more research on the needs of people with encephalitis and their recovery and rehabilitation -Need stronger information and data sharing to LMICs -Need more provision for research in LMICs to increase studies of the impact/cost of encephalitis in these countries
Bereavement	Lack of trained psychosocial support for bereavement	-Need more widely available psychosocial support for bereavement. Psychosocial support needs to be culturally sensitive.
Service delivery	Limited modifications and adjustments made to facilitate health access Variable information, training, and peer support Sporadic use of community-based rehabilitation Lack of targeted interventions based on need	-Need broad range of modifications and adjustments (reasonable accommodation) to facilitate access to healthcare services -Need to empower individuals with disabilities to maximize their health by providing information, training, and peer support -Need detailed responsibilities for all professionals in the health, education, and social protection system developed for the identification and referral of children with disabilities -Need community-based rehabilitation to facilitate access to existing services for disabled people -Need identification of groups that require alternative service delivery models, for example, targeted services or care coordination to improve access to health care

ABI = Acquired brain injury; GP = General practitioner

12 Information

12.1 Introduction

Accurate, up-to-date, and accessible information is essential for managing encephalitis adequately and improving the quality of life of people directly or indirectly affected by this condition. Both professionals and people affected require extensive knowledge about the condition and its effects. However, as needs vary, information must be tailored to the specific characteristics of the audience and their stage of the encephalitis journey. Whilst in hospital, affected individuals and their families need information about the illness and its course. Upon discharge, essential details are needed about recovery, the potential for relapse, the spectrum of after-effects, potential impacts on individual lives, and whom to contact if assistance is required.

Patients may initially present to a primary care practitioner, paramedic, nurse, or emergency personnel before encephalitis is suspected and a neurologist, neuroimmunologist or infectious disease specialist becomes involved. However, in certain regions, even when encephalitis is suspected, patients might not encounter a neurologist. In the Philippines, for example, approximately one neurologist caters to 176,000 adult Filipinos, well below the WHO's recommendation of 1-5 neurologists per 100,000 (319). This underscores the crucial need to integrate encephalitis education into medical school curricula and provide ongoing training for healthcare professionals.

Following discharge, a range of professionals may be directly or indirectly involved, including medical, healthcare, social care, educational, and legal professionals, benefits or disability advisors, and employers. Extensive and accurate information regarding the illness will enable them to provide better input to help improve patient quality of life. Understanding encephalitis is crucial not only when diagnosing patients with the condition but also in addressing preventable forms of encephalitis and providing care for disabilities resulting from it. This includes educating the public and employers about inclusive practices and non-discriminatory approaches towards individuals with disabilities.

In general, there is a dearth of information about encephalitis and its impact among professionals, affected individuals, their families/carers, and the general public. A global survey involving adults from five countries (UK, USA, Germany, India, and Australia) disclosed that a staggering 81% of the worldwide general public lacks awareness about encephalitis (429). Similar lack of public awareness has been reported for LMICs such as Nepal (430). In the IGAP on epilepsy and other neurological disorders for 2022-2031, the WHO states that 'Information systems for neurological disorders are often rudimentary or absent, especially in low-income countries, which complicates data acquisition on the availability and utilization of neurological services and the needs of people with neurological disorders and their carers' (415). In the same report the WHO has stated its global target: for 80% of countries to routinely collect and report on a core set of indicators for neurological disorders through their national health data and information systems at least every three years by 2031.

The lack of information among professionals extends to training. Frackowiak et al. highlighted a case from the UK, illustrating a medical student's experience and arguing that encephalitis is inadequately addressed in undergraduate training, significantly impacting how junior doctors handle encephalitis cases (431). While encephalitis is briefly covered in the

context of meningitis during medical school, crucial aspects such as the urgency of LP, early diagnosis, and prompt treatment to prevent or minimise mortality and disability are often omitted. Despite learning about HSV as a cause of encephalitis, students are not exposed to the multitude of other potential causes, leaving them with the impression that encephalitis is an exceedingly rare condition they are unlikely to encounter. Despite the scarcity of information, the impact of available resources is substantial, as evidenced by quotes from Encephalitis International members who found solace and guidance in the provided information.

In the 'Encephalitis as a public health priority' virtual meeting organised by the WHO and Encephalitis International in 2022, participants highlighted the need for LP in terms of information on how to obtain consent, and training for clinicians as to when LPs are needed, what tests to order, and where to transport the specimen. In the same meeting there was also a strong emphasis on the implementation of biobanks and associated training (329). Experts stressed that comprehensive training should focus on several key aspects: proper techniques for biobanking samples, strategies for securing funding to establish and maintain biobanks, ensuring the continuous functionality of freezers, and implementing measures to prevent sample degradation over time. Additionally, the meeting highlighted the importance of standardizing biobanking protocols across different research centres to facilitate data sharing and collaboration. The same meeting also highlighted the need for increased understanding of autoimmune encephalitis, identification of its biomarkers, and of its neurotropism as well as information pertaining to potential immunomodulatory agents and antivirals, although in certain countries the latter are expensive (9).

12.2 Recommended practice

The provision of appropriate, up-to-date, and accessible information by healthcare and health information systems, along with the dissemination of this information, constitutes a significant component of health literacy. This aspect is crucial in empowering individuals to enhance their health (Table 34) (329). Despite its importance, there is currently no recommended practice for the compilation and dissemination of information related to encephalitis. Given that encephalitis can impact individuals globally, it is imperative that information is tailored to specific audiences, considering factors such as incidence rates, local health systems, economic settings, and cultural backgrounds. It may be necessary to adopt diverse approaches, which should be pilot tested. Involving patients in the development of information and fostering community awareness are essential aspects of this process. Identifying knowledge gaps is equally critical.

Addressing these gaps involves incorporating all types of encephalitis into medical training curricula and subsequent professional development. Furthermore, making widely available professional guidelines and providing free access to professional resources are key strategies for increasing awareness among health professionals, particularly in LMICs (432). These comprehensive measures contribute to a more informed and empowered society in managing and preventing encephalitis.

The 2022 WHO/Encephalitis International stakeholder meeting discussed mechanisms to strengthen countries' capacity to respond to the public health challenge posed by encephalitis and reduce the burden faced by individuals, families, communities, and societies. A key point raised was that in countries where information regarding encephalitis is lacking, social media platforms could prove a helpful tool. A similar argument was outlined in the WHO's IGAP on epilepsy and other neurological disorders for 2022-2031, which also described the need to scale up telemedicine and internet technologies in LMICs and support home-based services (414). In the case of social media, however, a caveat is the danger of misinformation, which may be abated by moderation through professionals knowledgeable about encephalitis. Overall, in LMICs, harnessing the impact of regional, national, and international community networks could be a useful source of support, particularly when non-profit or non-governmental partners such as Encephalitis International work with clinicians and academics to support these groups and networks, and ensure that the provided information is up-to-date, accurate, and on accessible platforms.

Table 34 - Role of encephalitis information resources

Information area	Role
Prevention (infectious encephalitis)	*General public*: Awareness of endemic areas; Likelihood of the condition and severity of the consequences if acquired; Awareness of vaccines and preventive measures; Awareness of climate change impacts on infectious encephalitis; Awareness of symptoms *Travel health professionals*: Likelihood of the condition and severity of consequences if acquired
Diagnosis	*Health professionals*: Awareness of signs and symptoms; Importance of lumbar puncture and scans; awareness of diagnostic guidelines; Information on biobanking
Treatment effects	*Health professionals*: Awareness of timely access to treatment *Affected individuals*: Awareness of expectations and the impact on day-to-day life *General public*: Awareness of acquired brain injury following encephalitis *Health professionals*: Emphasis on the importance of periodic individual assessments; Awareness of brain injury following encephalitis

	Social care professionals: Awareness of brain injury following encephalitis
Recovery and rehabilitation	*Affected individuals*: Awareness of the need for rehabilitation and self-help strategies; Signposting to appropriate services *Families/carers*: Awareness of recovery pathways and the role of rehabilitation; Service signposting for affected individuals and carers *Professionals*: Awareness of rehabilitation after encephalitis and the importance of self-help strategies e.g., Encephalitis International's information booklets for professionals; Service signposting regarding support for carers and family members.
Other information	*Bereaved families*: Service signposting *General public*: Awareness of the condition and resulting brain injury *Families of affected children*: Awareness of immediate and long-term effects following brain injury and brain development; Service signposting *Education professionals*: Awareness of brain injury following encephalitis; Resources for support strategies; Awareness of the impact on families/ carers/ other children

12.3 Implementation status

Global implementation of effective information practice is generally low and varies depending on geographical area, type of encephalitis, and local economic and political priorities (424). Information regarding recovery, rehabilitation, and self-help is mostly non-existent (Table 35). The WHO provides information regarding JE, TBE, and rabies. However, information remains limited regarding other causes. Encephalitis International is the only patient organisation globally that provides information on prevention, diagnosis, treatment, effects, support, and after-care of encephalitis. However, this is not fully adapted for all countries affected by encephalitis.

Table 35 - Implementation status depending on encephalitis type and setting

	High-income country	Low-income country
Infectious		
Vaccine-preventable	Some information depending on the geographical area/hospital type	Little/no information but depends on campaign/outbreaks
Other infectious	Some information depending on the geographical area/hospital type	Little/no information
Autoimmune	Some information depending on the size/speciality of hospital available	Little/no information

12.4 Gap analysis

Table 36 – Gap analysis for provision of information

Issue	Where we are	Where we want to be

Awareness of available vaccines for certain types of encephalitis	Low population awareness of vaccines and presence of vaccine hesitancy/anti-vaccination movement (objections/concerns about safety)	Need high population awareness of and confidence in available vaccines (329)
Awareness of preventive measures for encephalitis apart from vaccination	Low population awareness and confusion over efficacy	Need high population awareness of and confidence in available preventative strategies apart from vaccination including vector control measures
Awareness of the severity of the illness	Low awareness in the general population and amongst travel and health professionals	Need high awareness in the general population and amongst travel and health professionals
Awareness of signs and symptoms of encephalitis among health professionals	Low awareness of signs and symptoms and confusion with psychiatric conditions or alcohol or drug intoxication	Need high awareness of signs and symptoms and differential diagnoses
Increased reporting of encephalitis	Real burden of encephalitis and viral aetiology is poorly described in LMICs (9)	Need improved reporting of encephalitis and improved understanding of global burden
Seeking help	Some reluctance to seek help depending on the local medical system (e.g., private or state)	Need health-seeking behaviours based on the presence of signs and symptoms (424)
	Limited availability of medical services and high cost of transport in low-income countries	Need affordable transport/financial support for transport Need to reduce delay between first signs of encephalitis and hospitalisation (9)
Safety-netting information (advice on potential course of illness and actions to take)	Lack of context/culturally appropriate information	Need culturally appropriate/context suitable safety-netting information readily available
Training of health professionals	All types of encephalitis not included in core training curriculum	Need to include all types of encephalitis in core training curriculum (329)
	Insufficient training /experience on performance of lumbar puncture	Need training/ support in performing a lumbar puncture
	Insufficient training on the effects of encephalitis, particularly neurological sequelae with long-term consequences (424)	Need training on effects of encephalitis
Materials/resources for health professionals	Context/culturally appropriate and condition-specific information not provided	Need culturally appropriate/context suitable and condition-specific materials and resources readily available

	Lack of guidelines for managing encephalitis and its possible effects (433)	Need widely available guidance for managing encephalitis and its effects
Service signposting	Lack of services to signpost to and limited awareness of the need to signpost	Need signposting from health facilities to services available for people with sequelae and their families and for bereavement Need sufficient knowledge on the services needed for different after-effects
Legal redress	Lack of legal framework Lack of knowledge about how/when to seek redress Financial barriers to legal engagement	Need law to allow for legal redress in the cases of poor standard health care and need for citizens to access financial support for legal redress

LMICs = Low- and middle-income countries

13 Conclusion

Encephalitis is a global problem with high death rates and often wreaks devastation on the lives of those affected. The condition does not share the same platforms and awareness among the general public and policy makers as does other comparable conditions such as meningitis and sepsis.

It is likely that encephalitis is more common than many government agencies and policy makers realise. This is in part due to variations in how data are collected and the methodologies used, if indeed it is collected at all in some countries. Surveillance systems for non-vaccine preventable encephalitides often do not exist in many countries and where they do, reporting can be poor.

Many types of encephalitis are vaccine-preventable, or morbidity and mortality can be significantly reduced with early diagnosis and treatment. The outcomes for patients and the economic costs associated with that are also poorly understood. Identification, diagnosis, and treatment are problematic in some countries due to a lack of neurologists, lack of training, lack of access to diagnostics, and lack of access to what are, in some cases, cheap treatments. Prevention is hindered by a lack of vaccination programs in some countries, public confidence is an increasing problem, and variable quality of travel health information to travellers. Much can be done in terms of advocacy around the condition for patients and their families in terms of the training of health, social care, and education professionals; improved after-care and support, and greater awareness of encephalitis as a travel-related condition and the associated preventative strategies that could be accessed. A range of factors affect information for people affected by the condition including availability, accuracy, cultural appropriateness, and signposting.

This report attempts to detail the most important areas for attention in efforts to reduce the incidence, death, and often life-changing disabilities associated with the condition: cause; incidence; morbidity and mortality; economic impact; prevention; diagnosis and treatment; neurology training; surveillance; new and emerging infections; advocacy; support and information for patients.

This report will now be used to commence dialogue with key stakeholders who can influence many of the areas identified such as surveillance and prevention, along with those who can have influence on in-country policy and practice. These discussions will form part of the ongoing international focus and strategy of Encephalitis International. It is recognised that this

report may provide opportunities for some quick wins however real change will require a collaborative approach to ensure that the tools, resources, systems, and commitment to effect real change are in place to mitigate the burdens presented by this too-often devastating disease.

14 Acknowledgements

The authors are extremely grateful to the Marguerite Foundation for their funding of this work and document, and to the Board of Trustees at Encephalitis International who supported the project. The authors also thank Prof David Brown, Dr Sarosh Irani, and Dr Deana Saylor for advice on availability of diagnostic testing and aciclovir use, Rhys Inward for writing the VZV vaccination section, and Praveen Prathapan and Emma Collins for helping to update the last three chapters on advocacy, support, and information. The authors thank the Scientific Advisory Panel and staff team of Encephalitis International whose ongoing work and support continues to contribute to this life-saving, award-winning non-profit.

15 References

1. World Health Organization. Encephalitis: global threats, trends and public health implications. A Technical Brief. [Internet]. Geneva, Switzerland; 2025 [cited 2026 Mar 27]. Available from: https://iris.who.int/server/api/core/bitstreams/8ae7178f-16ec-4ca9-a7b8-4c88ce0fbb10/content

2. Brain Infections Global study [Internet]. [cited 2024 Dec 17]. Available from: https://braininfectionsglobal.tghn.org/

3. Granerod J, Crowcroft NS. The epidemiology of acute encephalitis. Neuropsychol Rehabil. 2007 Oct;17(4–5):406–28. doi:10.1080/09602010600989620 PubMed PMID: 17676528.

4. Whitley RJ. Herpes Simplex Virus Infections of the Central Nervous System. Contin Minneap Minn. 2015 Dec;21(6 Neuroinfectious Disease):1704–13. doi:10.1212/CON.0000000000000243 PubMed PMID: 26633784.

5. Kumar R. Understanding and managing acute encephalitis. F1000Research. 2020;9. doi:10.12688/f1000research.20634.1 PubMed PMID: 32047620; PubMed Central PMCID: PMC6993835.

6. Boucher A, Herrmann JL, Morand P, Buzelé R, Crabol Y, Stahl JP, et al. Epidemiology of infectious encephalitis causes in 2016. Med Mal Infect. 2017 May;47(3):221–35. Located at: PubMed; 28341533. doi:10.1016/j.medmal.2017.02.003

7. Montano SM, Mori N, Nelson CA, Ton TGN, Celis V, Ticona E, et al. Herpes simplex virus encephalitis in Peru: a multicentre prospective study. Epidemiol Infect. 2016 Jun;144(8):1673–8. doi:10.1017/S0950268815003222 PubMed PMID: 26733400.

8. Tique V, Mattar S, Freire M, Illian E, Camargo F, Vergara O, et al. Epidemiological surveillance of herpes viral encephalitis in Cordoba, Colombia. Rev Salud Publica Bogota Colomb. 2016 Aug;18(4):581–91. doi:10.15446/rsap.v18n4.47517 PubMed PMID: 28453063.

9. Kahwagi J, Seye AO, Mbodji AB, Diagne R, Mbengue E hadji, Fall M, et al. Surveillance of Viral Encephalitis in the Context of COVID-19: A One-Year Observational Study among Hospitalized Patients in Dakar, Senegal. Viruses. 2022;14:871.

10. Roshdy WH, Kandeil A, Fahim M, Naguib NY, Mohsen G, Shawky S, et al. Epidemiological characterization of viral etiological agents of the central nervous system infections among hospitalized patients in Egypt between 2016 and 2019. Virol J. 2023 Aug 2;20(1):170. doi:10.1186/s12985-023-02079-y PubMed PMID: 37533069; PubMed Central PMCID: PMC10399032.

11. Granerod J, Tam CC, Crowcroft NS, Davies NWS, Borchert M, Thomas SL. Challenge of the unknown. A systematic review of acute encephalitis in non-outbreak situations. Neurology. 2010 Sep 7;75(10):924–32. Located at: PubMed; 20820004. doi:10.1212/WNL.0b013e3181f11d65

12. Rantalaiho T, Färkkilä M, Vaheri A, Koskiniemi M. Acute encephalitis from 1967 to 1991. J Neurol Sci. 2001 Mar 1;184(2):169–77. Located at: PubMed; 11239952. doi:10.1016/s0022-510x(01)00441-5

13. Child N, Croxson MC, Rahnama F, Anderson NE. A retrospective review of acute encephalitis in adults in Auckland over a five-year period (2005-2009). J Clin Neurosci Off J Neurosurg Soc Australas. 2012 Nov;19(11):1483–5. Located at: PubMed; 22925416. doi:10.1016/j.jocn.2012.03.010

14. Mailles A, Stahl JP. Infectious encephalitis in france in 2007: a national prospective study. Clin Infect Dis Off Publ Infect Dis Soc Am. 2009 Dec 15;49(12):1838–47. doi:10.1086/648419 PubMed PMID: 19929384.

15. Stahl JP, Mailles A, Dacheux L, Morand P. Epidemiology of viral encephalitis in 2011. Med Mal Infect. 2011 Sep;41(9):453–64. doi:10.1016/j.medmal.2011.05.015 PubMed PMID: 21802875.

16. Granerod J, Ambrose HE, Davies NW, Clewley JP, Walsh AL, Morgan D, et al. Causes of encephalitis and differences in their clinical presentations in England: a multicentre, population-based prospective study. Lancet Infect Dis. 2010 Dec;10(12):835–44. doi:10.1016/S1473-3099(10)70222-X PubMed PMID: 20952256.

17. Bitnun A, Ford-Jones EL, Petric M, MacGregor D, Heurter H, Nelson S, et al. Acute childhood encephalitis and Mycoplasma pneumoniae. Clin Infect Dis Off Publ Infect Dis Soc Am. 2001 Jun 15;32(12):1674–84. doi:10.1086/320748 PubMed PMID: 11360206.

18. Christie LJ, Honarmand S, Talkington DF, Gavali SS, Preas C, Pan CY, et al. Pediatric encephalitis: what is the role of Mycoplasma pneumoniae? Pediatrics. 2007 Aug;120(2):305–13. doi:10.1542/peds.2007-0240 PubMed PMID: 17671056.

19. Meyer Sauteur PM, Jacobs BC, Spuesens EBM, Jacobs E, Nadal D, Vink C, et al. Antibody responses to Mycoplasma pneumoniae: role in pathogenesis and diagnosis of encephalitis? PLoS Pathog. 2014 Jun;10(6):e1003983. doi:10.1371/journal.ppat.1003983 PubMed PMID: 24945969; PubMed Central PMCID: PMC4055762.

20. Dubey D, Pittock SJ, Kelly CR, McKeon A, Lopez-Chiriboga AS, Lennon VA, et al. Autoimmune encephalitis epidemiology and a comparison to infectious encephalitis. Ann Neurol. 2018;83(1):166–77. doi:10.1002/ana.25131 PubMed PMID: 29293273; PubMed Central PMCID: PMC6011827.

21. Venkatesan A. Immune-mediated encephalitis for the infectious disease specialist. Curr Opin Infect Dis. 2019 Jun;32(3):251–8. doi:10.1097/QCO.0000000000000546 PubMed PMID: 31021956.

22. O'Connor KC, McLaughlin KA, De Jager PL, Chitnis T, Bettelli E, Xu C, et al. Self-antigen tetramers discriminate between myelin autoantibodies to native or denatured protein. Nat Med. 2007 Feb;13(2):211–7. doi:10.1038/nm1488 PubMed PMID: 17237795; PubMed Central PMCID: PMC3429369.

23. Fujimori J, Takai Y, Nakashima I, Sato DK, Takahashi T, Kaneko K, et al. Bilateral frontal cortex encephalitis and paraparesis in a patient with anti-MOG antibodies. J Neurol Neurosurg Psychiatry. 2017 Jun;88(6):534–6. doi:10.1136/jnnp-2016-315094 PubMed PMID: 28209651.

24. Wang L, ZhangBao J, Zhou L, Zhang Y, Li H, Li Y, et al. Encephalitis is an important clinical component of myelin oligodendrocyte glycoprotein antibody associated demyelination: a single-center cohort study in Shanghai, China. Eur J Neurol. 2019 Jan;26(1):168–74. doi:10.1111/ene.13790 PubMed PMID: 30133068.

25. Pollak T, Al-Diwani A, Lennox B. Neuronal surface autoantibodies, encephalitis, and psychosis: from neurology to psychiatry. Adv Clin Neurosci Rehabil. 17(2):6–10.

26. Alam AM, Easton A, Nicholson TR, Irani SR, Davies NW, Solomon T, et al. Encephalitis: diagnosis, management and recent advances in the field of encephalitides. Postgrad Med J. 2022 Jun 23;postgradmedj-2022-141812. doi:10.1136/postgradmedj-2022-141812 PubMed PMID: 35738892.

27. Kolls BJ, O'Keefe YA, Sahgal AK. Autoimmune Encephalitis: NMDA Receptor Encephalitis as an Example of Translational Neuroscience. Neurother J Am Soc Exp Neurother. 2020 May 11. doi:10.1007/s13311-020-00861-2 PubMed PMID: 32394329.

28. Jones HF, Mohammad SS, Reed PW, Dunn PPJ, Steele RH, Dale RC, et al. Anti-N-methyl-d-aspartate receptor encephalitis in Māori and Pacific Island children in New Zealand. Dev Med Child Neurol. 2017 Jul;59(7):719–24. doi:10.1111/dmcn.13420 PubMed PMID: 28328164.

29. Dalmau J, Tüzün E, Wu H yan, Masjuan J, Rossi JE, Voloschin A, et al. Paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. Ann Neurol. 2007 Jan;61(1):25–36. doi:10.1002/ana.21050 PubMed PMID: 17262855; PubMed Central PMCID: PMC2430743.

30. Hutchinson M, Waters P, McHugh J, Gorman G, O'Riordan S, Connolly S, et al. Progressive encephalomyelitis, rigidity, and myoclonus: a novel glycine receptor antibody. Neurology. 2008 Oct 14;71(16):1291–2. doi:10.1212/01.wnl.0000327606.50322.f0 PubMed PMID: 18852446.

31. Lai M, Hughes EG, Peng X, Zhou L, Gleichman AJ, Shu H, et al. AMPA receptor antibodies in limbic encephalitis alter synaptic receptor location. Ann Neurol. 2009 Apr;65(4):424–34. doi:10.1002/ana.21589 PubMed PMID: 19338055; PubMed Central PMCID: PMC2677127.

32. Lancaster E, Lai M, Peng X, Hughes E, Constantinescu R, Raizer J, et al. Antibodies to the GABA(B) receptor in limbic encephalitis with seizures: case series and characterisation of the antigen. Lancet Neurol. 2010 Jan;9(1):67–76. doi:10.1016/S1474-4422(09)70324-2 PubMed PMID: 19962348; PubMed Central PMCID: PMC2824142.

33. Irani SR, Alexander S, Waters P, Kleopa KA, Pettingill P, Zuliani L, et al. Antibodies to Kv1 potassium channel-complex proteins leucine-rich, glioma inactivated 1 protein and contactin-associated protein-2 in limbic encephalitis, Morvan's syndrome and acquired neuromyotonia. Brain J Neurol. 2010 Sep;133(9):2734–48. doi:10.1093/brain/awq213 PubMed PMID: 20663977; PubMed Central PMCID: PMC2929337.

34. Lancaster E, Martinez-Hernandez E, Titulaer MJ, Boulos M, Weaver S, Antoine JC, et al. Antibodies to metabotropic glutamate receptor 5 in the Ophelia syndrome. Neurology. 2011 Nov 1;77(18):1698–701. doi:10.1212/WNL.0b013e3182364a44 PubMed PMID: 22013185; PubMed Central PMCID: PMC3208954.

35. Dale RC, Merheb V, Pillai S, Wang D, Cantrill L, Murphy TK, et al. Antibodies to surface dopamine-2 receptor in autoimmune movement and psychiatric disorders. Brain J Neurol. 2012 Nov;135(Pt 11):3453–68. doi:10.1093/brain/aws256 PubMed PMID: 23065479.

36. Boronat A, Gelfand JM, Gresa-Arribas N, Jeong HY, Walsh M, Roberts K, et al. Encephalitis and antibodies to dipeptidyl-peptidase-like protein-6, a subunit of Kv4.2 potassium channels. Ann

Neurol. 2013 Jan;73(1):120–8. doi:10.1002/ana.23756 PubMed PMID: 23225603; PubMed Central PMCID: PMC3563722.

37. Petit-Pedrol M, Armangue T, Peng X, Bataller L, Cellucci T, Davis R, et al. Encephalitis with refractory seizures, status epilepticus, and antibodies to the GABAA receptor: a case series, characterisation of the antigen, and analysis of the effects of antibodies. Lancet Neurol. 2014 Mar;13(3):276–86. doi:10.1016/S1474-4422(13)70299-0 PubMed PMID: 24462240; PubMed Central PMCID: PMC4838043.

38. Gresa-Arribas N, Planagumà J, Petit-Pedrol M, Kawachi I, Katada S, Glaser CA, et al. Human neurexin-3α antibodies associate with encephalitis and alter synapse development. Neurology. 2016 Jun 14;86(24):2235–42. doi:10.1212/WNL.0000000000002775 PubMed PMID: 27170573; PubMed Central PMCID: PMC4909558.

39. Zuliani L, Nosadini M, Gastaldi M, Spatola M, Iorio R, Zoccarato M, et al. Management of antibody-mediated autoimmune encephalitis in adults and children: literature review and consensus-based practical recommendations. Neurol Sci Off J Ital Neurol Soc Ital Soc Clin Neurophysiol. 2019 Oct;40(10):2017–30. doi:10.1007/s10072-019-03930-3 PubMed PMID: 31161339.

40. Patel A, Meng Y, Najjar A, Lado F, Najjar S. Autoimmune Encephalitis: A Physician's Guide to the Clinical Spectrum Diagnosis and Management. Brain Sci. 2022 Aug 25;12(9). doi:10.3390/brainsci12091130 PubMed PMID: 36138865; PubMed Central PMCID: PMC9497072.

41. Quan TM, Thao TTN, Duy NM, Nhat TM, Clapham H. Estimates of the global burden of Japanese Encephalitis and the impact of vaccination from 2000-2015. eLife. 2020 May 26;9. doi:10.7554/eLife.51027 PubMed PMID: 32450946.

42. Mackenzie JS, Williams DT, van den Hurk AF, Smith DW, Currie BJ. Japanese Encephalitis Virus: The Emergence of Genotype IV in Australia and Its Potential Endemicity. Viruses. 2022 Nov 9;14(11). doi:10.3390/v14112480 PubMed PMID: 36366578; PubMed Central PMCID: PMC9698845.

43. Riccardi N, Antonello RM, Luzzati R, Zajkowska J, Di Bella S, Giacobbe DR. Tick-borne encephalitis in Europe: a brief update on epidemiology, diagnosis, prevention, and treatment. Eur J Intern Med. 2019/01/22 edn. 2019 Apr;62:1–6. Located at: PubMed; 30678880. doi:10.1016/j.ejim.2019.01.004

44. Camp JV, Nowotny N. The knowns and unknowns of West Nile virus in Europe: what did we learn from the 2018 outbreak? Expert Rev Anti Infect Ther. 2020 Feb;18(2):145–54. Located at: PubMed; 31914833. doi:10.1080/14787210.2020.1713751

45. Lindsey N, Staples J, Lehman J, Fischer M, Centers for Disease Control and Prevention (CDC). Surveillance for human West Nile virus disease - United States, 1999–2008. Vol. 59. 2010;59(2):1–17.

46. Sreenivasan N, Li A, Shiferaw M, Tran CH, Wallace R, Blanton J, et al. Overview of rabies post-exposure prophylaxis access, procurement and distribution in selected countries in Asia and Africa, 2017-2018. Vaccine. 2019/08/27 edn. 2019 Oct 3;37 Suppl 1:A6–13. Located at: PubMed; 31471150. doi:10.1016/j.vaccine.2019.04.024

47. Wambura G, Mwatondo A, Muturi M, Nasimiyu C, Wentworth D, Hampson K, et al. Rabies vaccine and immunoglobulin supply and logistics: Challenges and opportunities for rabies elimination in Kenya. Vaccine. 2019/07/17 edn. 2019 Oct 3;37 Suppl 1:A28–34. Located at: PubMed; 31326251. doi:10.1016/j.vaccine.2019.05.035

48. Warrell MJ, Warrell DA. Rabies and other lyssavirus diseases. Lancet Lond Engl. 2004 Mar 20;363(9413):959–69. doi:10.1016/S0140-6736(04)15792-9 PubMed PMID: 15043965.

49. Tilak R, Kunte R. Scrub typhus strikes back: Are we ready? Med J Armed Forces India. 2019 Jan;75(1):8–17. doi:10.1016/j.mjafi.2018.12.018 PubMed PMID: 30705472; PubMed Central PMCID: PMC6349656.

50. Tarantola A, Goutard F, Newton P, de Lamballerie X, Lortholary O, Cappelle J, et al. Estimating the burden of Japanese encephalitis virus and other encephalitides in countries of the mekong region. PLoS Negl Trop Dis. 2014;8(1):e2533. doi:10.1371/journal.pntd.0002533 PubMed PMID: 24498443; PubMed Central PMCID: PMC3907313.

51. Schibler M, Eperon G, Kenfak A, Lascano A, Vargas MI, Stahl JP. Diagnostic tools to tackle infectious causes of encephalitis and meningoencephalitis in immunocompetent adults in Europe. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2019 Apr;25(4):408–14. doi:10.1016/j.cmi.2018.12.035 PubMed PMID: 30654044.

52. Ellul MA, Benjamin L, Singh B, Lant S, Michael BD, Easton A, et al. Neurological associations of COVID-19. Lancet Neurol. 2020 Sep;19(9):767–83. doi:10.1016/S1474-4422(20)30221-0 PubMed PMID: 32622375; PubMed Central PMCID: PMC7332267.

53. Badenoch JB, Conti I, Rengasamy ER, Watson CJ, Butler M, Hussain Z, et al. Neurological and psychiatric presentations associated with human monkeypox virus infection: A systematic review and meta-analysis. EClinicalMedicine. 2022 Oct;52:101644. doi:10.1016/j.eclinm.2022.101644 PubMed PMID: 36246957; PubMed Central PMCID: PMC9533950.

54. Hoffmann B, Tappe D, Höper D, Herden C, Boldt A, Mawrin C, et al. A Variegated Squirrel Bornavirus Associated with Fatal Human Encephalitis. N Engl J Med. 2015 Jul 9;373(2):154–62. Located at: PubMed; 26154788. doi:10.1056/NEJMoa1415627

55. Wang H, Zhao S, Wang S, Zheng Y, Wang S, Chen H, et al. Global magnitude of encephalitis burden and its evolving pattern over the past 30 years. J Infect. 2022 Jun;84(6):777–87. doi:10.1016/j.jinf.2022.04.026 PubMed PMID: 35452715.

56. Khetsuriani N, Holman RC, Anderson LJ. Burden of encephalitis-associated hospitalizations in the United States, 1988-1997. Clin Infect Dis Off Publ Infect Dis Soc Am. 2002 Jul 15;35(2):175–82. Located at: PubMed; 12087524. doi:10.1086/341301

57. Davison KL, Crowcroft NS, Ramsay ME, Brown DWG, Andrews NJ. Viral encephalitis in England, 1989-1998: what did we miss? Emerg Infect Dis. 2003 Feb;9(2):234–40. Located at: PubMed; 12603996. doi:10.3201/eid0902.020218

58. Granerod J, Cousens S, Davies NWS, Crowcroft NS, Thomas SL. New estimates of incidence of encephalitis in England. Emerg Infect Dis. 2013;19(9):1455–62. Located at: PubMed; 23969035. doi:10.3201/eid1909.130064

59. Trevejo RT. Acute encephalitis hospitalizations, California, 1990-1999: unrecognized arboviral encephalitis? Emerg Infect Dis. 2004 Aug;10(8):1442–9. Located at: PubMed; 15496246. doi:10.3201/eid1008.030698

60. Ishikawa T, Asano Y, Morishima T, Nagashima M, Sobue G, Watanabe K, et al. Epidemiology of acute childhood encephalitis. Aichi Prefecture, Japan, 1984-90. Brain Dev. 1993;15(3):192–7. Located at: PubMed; 8214344. doi:10.1016/0387-7604(93)90064-f

61. Koskiniemi M, Rautonen J, Lehtokoski-Lehtiniemi E, Vaheri A. Epidemiology of encephalitis in children: a 20-year survey. Ann Neurol. 1991 May;29(5):492–7. Located at: PubMed; 1859180. doi:10.1002/ana.410290508

62. Koskiniemi M, Korppi M, Mustonen K, Rantala H, Muttilainen M, Herrgård E, et al. Epidemiology of encephalitis in children. A prospective multicentre study. Eur J Pediatr. 1997 Jul;156(7):541–5. Located at: PubMed; 9243237. doi:10.1007/s004310050658

63. Cizman M, Jazbec J. Etiology of acute encephalitis in childhood in Slovenia. Pediatr Infect Dis J. 1993 Nov;12(11):903–8. Located at: PubMed; 8265278. doi:10.1097/00006454-199311000-00002

64. Kusumi M, Nakashima K, Nakayama H, Takahashi K. Epidemiology of inflammatory neurological and inflammatory neuromuscular diseases in Tottori Prefecture, Japan. Psychiatry Clin Neurosci. 1995 Jun;49(3):169–74. Located at: PubMed; 8612191. doi:10.1111/j.1440-1819.1995.tb02223.x

65. Mailles A, Vaillant V, Stahl JP. Infectious encephalitis in France from 2000 to 2002: the hospital database is a valuable but limited source of information for epidemiological studies. Med Mal Infect. 2007 Feb;37(2):95–102. Located at: PubMed; 17267156. doi:10.1016/j.medmal.2006.11.001

66. Chhour YM, Ruble G, Hong R, Minn K, Kdan Y, Sok T, et al. Hospital-based diagnosis of hemorrhagic fever, encephalitis, and hepatitis in Cambodian children. Emerg Infect Dis. 2002 May;8(5):485–9. Located at: PubMed; 11996683. doi:10.3201/eid0805.010236

67. Rantala H, Uhari M. Occurrence of childhood encephalitis: a population-based study. Pediatr Infect Dis J. 1989 Jul;8(7):426–30. Located at: PubMed; 2755753

68. Nwosu CM, Njeze GE, Opara C, Nwajuaku C, Chukwurah CK. Central nervous system infections in the rainforest zone of Nigeria. East Afr Med J. 2001 Feb;78(2):97–101. Located at: PubMed; 11682955. doi:10.4314/eamj.v78i2.9097

69. Rantakallio P, Leskinen M, von Wendt L. Incidence and prognosis of central nervous system infections in a birth cohort of 12,000 children. Scand J Infect Dis. 1986;18(4):287–94. Located at: PubMed; 3764348. doi:10.3109/00365548609032339

70. Chunsuttiwat S. Japanese encephalitis in Thailand. Southeast Asian J Trop Med Public Health. 1989 Dec;20(4):593–7. Located at: PubMed; 2561716

71. Radhakrishnan K, Thacker AK, Maloo JC, Gerryo SE, Mousa ME. Descriptive epidemiology of some rare neurological diseases in Benghazi, Libya. Neuroepidemiology. 1988;7(3):159–64. Located at: PubMed; 3405368. doi:10.1159/000110150

72. Joshi R, Mishra PK, Joshi D, Santhosh SR, Parida MM, Desikan P, et al. Clinical presentation, etiology, and survival in adult acute encephalitis syndrome in rural Central India. Clin Neurol Neurosurg. 2013 Sep;115(9):1753–61. Located at: PubMed; 23643180. doi:10.1016/j.clineuro.2013.04.008

73. Kupila L, Vuorinen T, Vainionpää R, Hukkanen V, Marttila RJ, Kotilainen P. Etiology of aseptic meningitis and encephalitis in an adult population. Neurology. 2006 Jan 10;66(1):75–80. Located at: PubMed; 16401850. doi:10.1212/01.wnl.0000191407.81333.00

74. Huppatz C, Durrheim DN, Levi C, Dalton C, Williams D, Clements MS, et al. Etiology of encephalitis in Australia, 1990-2007. Emerg Infect Dis. 2009 Sep;15(9):1359–65. Located at: PubMed; 19788802. doi:10.3201/eid1509.081540

75. Barbadoro P, Marigliano A, Ricciardi A, D'Errico MM, Prospero E. Trend of hospital utilization for encephalitis. Epidemiol Infect. 2012 Apr;140(4):753–64. Located at: PubMed; 21733247. doi:10.1017/S0950268811001002

76. Kulkarni MA, Lecocq AC, Artsob H, Drebot MA, Ogden NH. Epidemiology and aetiology of encephalitis in Canada, 1994-2008: a case for undiagnosed arboviral agents? Epidemiol Infect. 2013 Nov;141(11):2243–55. Located at: PubMed; 23148910. doi:10.1017/S095026881200252X

77. Parpia AS, Li Y, Chen C, Dhar B, Crowcroft NS. Encephalitis, Ontario, Canada, 2002-2013. Emerg Infect Dis. 2016 Mar;22(3):426–32. Located at: PubMed; 26890626. doi:10.3201/eid2203.151545

78. Vora NM, Holman RC, Mehal JM, Steiner CA, Blanton J, Sejvar J. Burden of encephalitis-associated hospitalizations in the United States, 1998-2010. Neurology. 2014 Feb 4;82(5):443–51. Located at: PubMed; 24384647. doi:10.1212/WNL.0000000000000086

79. George BP, Schneider EB, Venkatesan A. Encephalitis hospitalization rates and inpatient mortality in the United States, 2000-2010. PloS One. 2014 Sep 5;9(9):e104169–e104169. Located at: PubMed; 25192177. doi:10.1371/journal.pone.0104169

80. Roux A, Houcke S, Sanna A, Mathien C, Mayence C, Gueneau R, et al. Clinical Features, Diagnosis, and Outcome of Encephalitis in French Guiana. Am J Trop Med Hyg. 2019 Feb;100(2):452–9. Located at: PubMed; 30560767. doi:10.4269/ajtmh.18-0308

81. Britton PN, Khoury L, Booy R, Wood N, Jones CA. Encephalitis in Australian children: contemporary trends in hospitalisation. Arch Dis Child. 2016 Jan;101(1):51–6. Located at: PubMed; 26475868. doi:10.1136/archdischild-2015-308468

82. Wickström R, Fowler Å, Bogdanovic G, Bennet R, Eriksson M. Review of the aetiology, diagnostics and outcomes of childhood encephalitis from 1970 to 2009. Acta Paediatr Oslo Nor 1992. 2017 Mar;106(3):463–9. doi:10.1111/apa.13682 PubMed PMID: 27886400.

83. Bodilsen J, Storgaard M, Larsen L, Wiese L, Helweg-Larsen J, Lebech AM, et al. Infectious meningitis and encephalitis in adults in Denmark: a prospective nationwide observational cohort study (DASGIB). Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2018 Oct;24(10):1102.e1-1102.e5. doi:10.1016/j.cmi.2018.01.016 PubMed PMID: 29409994.

84. Kelly TA, O'Lorcain P, Moran J, Garvey P, McKeown P, Connell J, et al. Underreporting of viral encephalitis and viral meningitis, Ireland, 2005-2008. Emerg Infect Dis. 2013;19(9):1428–36. Located at: PubMed; 23965781. doi:10.3201/eid1909.130201

85. Kadambari S, Okike I, Ribeiro S, Ramsay ME, Heath PT, Sharland M, et al. Seven-fold increase in viral meningo-encephalitis reports in England and Wales during 2004-2013. J Infect. 2014 Oct;69(4):326–32. Located at: PubMed; 24887614. doi:10.1016/j.jinf.2014.05.012

86. Pönkä A, Pettersson T. The incidence and aetiology of central nervous system infections in Helsinki in 1980. Acta Neurol Scand. 1982 Nov;66(5):529–35. Located at: PubMed; 7148395. doi:10.1111/j.1600-0404.1982.tb03139.x

87. Henrich TJ, Hutchaleelaha S, Jiwariyavej V, Barbazan P, Nitatpattana N, Yoksan S, et al. Geographic dynamics of viral encephalitis in Thailand. Microbes Infect. 2003 Jun;5(7):603–11. Located at: PubMed; 12787736. doi:10.1016/s1286-4579(03)00100-x

88. Iro MA, Sadarangani M, Goldacre R, Nickless A, Pollard AJ, Goldacre MJ. 30-year trends in admission rates for encephalitis in children in England and effect of improved diagnostics and measles-mumps-rubella vaccination: a population-based observational study. Lancet Infect Dis. 2017 Apr;17(4):422–30. Located at: PubMed; 28259562. doi:10.1016/S1473-3099(17)30114-7

89. Sevilla-Acosta F, Gutiérrez-Mata A, Yock-Corrales A, Bogantes-Ledezma S, Pérez-Corrales C, Camacho-Badilla K. Epidemiology, Etiology and Clinical Aspects of Childhood Acute Encephalitis in a Tertiary Pediatric Hospital in Costa Rica. Pediatr Infect Dis J. 2021 Mar 1;40(3):186–90. doi:10.1097/INF.0000000000002950 PubMed PMID: 33060517.

90. Kim SH, Baek JY, Han M, Lee M, Lim SM, Lee JY, et al. A decrease in the incidence of encephalitis in South Korea during the COVID-19 pandemic: A nationwide study between 2010 and 2021. J Med Virol. 2023 Feb;95(2):e28490. doi:10.1002/jmv.28490 PubMed PMID: 36630084.

91. Lee SJ, Kim JM, Keum HR, Kim SW, Baek HS, Byun JC, et al. Seasonal Trends in the Prevalence and Incidence of Viral Encephalitis in Korea (2015-2019). J Clin Med. 2023 Mar 2;12(5). doi:10.3390/jcm12052003 PubMed PMID: 36902789; PubMed Central PMCID: PMC10003849.

92. Liem B, Anderson NE, Wright SL, Anderson SC, Donnelly J, Austin P, et al. Encephalitis in adults in the Auckland and Northland regions of New Zealand, 2009 to 2018. J Clin Neurosci Off J Neurosurg Soc Australas. 2023 Jan;107:172–7. doi:10.1016/j.jocn.2022.10.024 PubMed PMID: 36494269.

93. Nicolosi A, Hauser WA, Beghi E, Kurland LT. Epidemiology of central nervous system infections in Olmsted County, Minnesota, 1950-1981. J Infect Dis. 1986 Sep;154(3):399–408. Located at: PubMed; 3734490. doi:10.1093/infdis/154.3.399

94. Pohl D, Hennemuth I, von Kries R, Hanefeld F. Paediatric multiple sclerosis and acute disseminated encephalomyelitis in Germany: results of a nationwide survey. Eur J Pediatr. 2007 May;166(5):405–12. Located at: PubMed; 17219129. doi:10.1007/s00431-006-0249-2

95. Leake JAD, Albani S, Kao AS, Senac MO, Billman GF, Nespeca MP, et al. Acute disseminated encephalomyelitis in childhood: epidemiologic, clinical and laboratory features. Pediatr Infect Dis J. 2004 Aug;23(8):756–64. Located at: PubMed; 15295226. doi:10.1097/01.inf.0000133048.75452.dd

96. Jackson AC, Mostaço-Guidolin LC, Sinnock H, Bozat-Emre S, Routledge M, Mahmud SM. Pandemic H1N1 Vaccination and Incidence of Acute Disseminated Encephalomyelitis in Manitoba. Can J Neurol Sci J Can Sci Neurol. 2016 Nov;43(6):819–23. Located at: PubMed; 27608932. doi:10.1017/cjn.2016.291

97. Xiong CH, Yan Y, Liao Z, Peng SH, Wen HR, Zhang YX, et al. Epidemiological characteristics of acute disseminated encephalomyelitis in Nanchang, China: a retrospective study. BMC Public Health. 2014 Feb 4;14:111–111. Located at: PubMed; 24495742. doi:10.1186/1471-2458-14-111

98. Chen Y, Ma F, Xu Y, Chu X, Zhang J. Incidence of acute disseminated encephalomyelitis in the Jiangsu province of China, 2008-2011. Mult Scler J - Exp Transl Clin. 2015 Jul 8;1:2055217315594831–2055217315594831. Located at: PubMed; 28607697. doi:10.1177/2055217315594831

99. Yamaguchi Y, Torisu H, Kira R, Ishizaki Y, Sakai Y, Sanefuji M, et al. A nationwide survey of pediatric acquired demyelinating syndromes in Japan. Neurology. 2016 Nov 8;87(19):2006–15. Located at: PubMed; 27742816. doi:10.1212/WNL.0000000000003318

100. Boesen MS, Magyari M, Born AP, Thygesen LC. Pediatric acquired demyelinating syndromes: a nationwide validation study of the Danish National Patient Register. Clin Epidemiol. 2018 Apr 10;10:391–9. Located at: PubMed; 29692631. doi:10.2147/CLEP.S156997

101. Pavone P, Pettoello-Mantovano M, Le Pira A, Giardino I, Pulvirenti A, Giugno R, et al. Acute disseminated encephalomyelitis: a long-term prospective study and meta-analysis. Neuropediatrics. 2010 Dec;41(6):246–55. Located at: PubMed; 21445814. doi:10.1055/s-0031-1271656

102. de Bruijn MAAM, Bruijstens AL, Bastiaansen AEM, van Sonderen A, Schreurs MWJ, Sillevis Smitt PAE, et al. Pediatric autoimmune encephalitis: Recognition and diagnosis. Neurol Neuroimmunol Neuroinflammation. 2020 Feb 11;7(3):e682. Located at: PubMed; 32047077. doi:10.1212/NXI.0000000000000682

103. Bhatt P, Bray L, Raju S, Dapaah-Siakwan F, Patel A, Chaudhari R, et al. Temporal Trends of Pediatric Hospitalizations with Acute Disseminated Encephalomyelitis in the United States: An Analysis from 2006 to 2014 using National Inpatient Sample. J Pediatr. 2019 Mar;206:26-32.e1. Located at: PubMed; 30528761. doi:10.1016/j.jpeds.2018.10.044

104. VanLandingham M, Hanigan W, Vedanarayanan V, Fratkin J. An uncommon illness with a rare presentation: neurosurgical management of ADEM with tumefactive demyelination in children. Childs Nerv Syst ChNS Off J Int Soc Pediatr Neurosurg. 2010 May;26(5):655–61. Located at: PubMed; 19949803. doi:10.1007/s00381-009-1045-x

105. Hwang J, Chae SA, Lim BC, Choi SA. Incidence of Pediatric Acute Disseminated Encephalomyelitis During the Coronavirus Disease 2019 Pandemic in South Korea. Pediatr Neurol. 2023 Sep;146:44–9. doi:10.1016/j.pediatrneurol.2023.06.009 PubMed PMID: 37429226.

106. de Bruijn MAAM, Leypoldt F, Dalmau J, Lee ST, Honnorat J, Clardy SL, et al. Autoimmune encephalitis. Nat Rev Dis Primer. 2025 Sep 11;11(1):65. doi:10.1038/s41572-025-00650-1 PubMed PMID: 40935848.

107. Campbell GL, Hills SL, Fischer M, Jacobson JA, Hoke CH, Hombach JM, et al. Estimated global incidence of Japanese encephalitis: a systematic review. Bull World Health Organ. 2011 Oct 1;89(10):766-774E. Located at: PubMed; 22084515. doi:10.2471/BLT.10.085233

108. Imam I, Ball S, Wright D, Hanemann CO, Zajicek J. The epidemiology of motor neurone disease in two counties in the southwest of England. J Neurol. 2010 Jun;257(6):977–81. Located at: PubMed; 20094727. doi:10.1007/s00415-009-5448-0

109. Alonso A, Hernán MA. Temporal trends in the incidence of multiple sclerosis: a systematic review. Neurology. 2008 Jul 8;71(2):129–35. Located at: PubMed; 18606967. doi:10.1212/01.wnl.0000316802.35974.34

110. Meningococcal Reference Unit, Gray SJ, Trotter CL, Ramsay ME, Guiver M, Fox AJ, et al. Epidemiology of meningococcal disease in England and Wales 1993/94 to 2003/04: contribution and experiences of the Meningococcal Reference Unit. J Med Microbiol. 2006 Jul;55(Pt 7):887–96. Located at: PubMed; 16772416. doi:10.1099/jmm.0.46288-0

111. Santoro JD, Demakakos P, He S, Kumar S, Murton M, Tennigkeit F, et al. A systematic review of the epidemiology of pediatric autoimmune encephalitis: disease burden and clinical decision-making. Front Neurol. 2024;15:1408606. doi:10.3389/fneur.2024.1408606 PubMed PMID: 39040538; PubMed Central PMCID: PMC11262030.

112. Jmor F, Emsley HCA, Fischer M, Solomon T, Lewthwaite P. The incidence of acute encephalitis syndrome in Western industrialised and tropical countries. Virol J. 2008 Oct 30;5:134–134. Located at: PubMed; 18973679. doi:10.1186/1743-422X-5-134

113. Chen HL, Chang JK, Tang RB. Current recommendations for the Japanese encephalitis vaccine. J Chin Med Assoc JCMA. 2015 May;78(5):271–5. Located at: PubMed; 25841620. doi:10.1016/j.jcma.2014.12.009

114. Rasania SK, Bhalla S, Khandekar J, Pathi S, Matta S, Singh S. Post exposure management of animal bite cases attending a primary health center of Delhi. J Commun Dis. 2004 Sep;36(3):195–8. PubMed PMID: 16509257.

115. Dobler G. Zoonotic tick-borne flaviviruses. Vet Microbiol. 2010 Jan 27;140(3–4):221–8. doi:10.1016/j.vetmic.2009.08.024 PubMed PMID: 19765917.

116. Minta AA, Ferrari M, Antoni S, Portnoy A, Sbarra A, Lambert B, et al. Progress Toward Measles Elimination - Worldwide, 2000-2022. MMWR Morb Mortal Wkly Rep. 2023 Nov 17;72(46):1262–8. doi:10.15585/mmwr.mm7246a3 PubMed PMID: 37971951; PubMed Central PMCID: PMC10684353.

117. World Health Organization. Global Health Estimates 2021: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2021 [Internet]. Geneva, Switzerland; 2024 [cited 2024 Sep 23]. Available from: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death

118. Institute for Health Metrics and Evaluation. [Internet]. Available from: http://ghdx.healthdata.org/gbd-results-tool

119. Beghi E, Nicolosi A, Kurland LT, Mulder DW, Hauser WA, Shuster L. Encephalitis and aseptic meningitis, Olmsted County, Minnesota, 1950-1981: I. Epidemiology. Ann Neurol. 1984 Sep;16(3):283–94. Located at: PubMed; 6148911. doi:10.1002/ana.410160304

120. Fowler A, Stödberg T, Eriksson M, Wickström R. Childhood encephalitis in Sweden: etiology, clinical presentation and outcome. Eur J Paediatr Neurol EJPN Off J Eur Paediatr Neurol Soc. 2008 Nov;12(6):484–90. doi:10.1016/j.ejpn.2007.12.009 PubMed PMID: 18313340.

121. Galanakis E, Tzoufi M, Katragkou A, Nakou I, Roilides E. A prospective multicenter study of childhood encephalitis in Greece. Pediatr Infect Dis J. 2009 Aug;28(8):740–2. doi:10.1097/INF.0b013e318199eff9 PubMed PMID: 19633519.

122. GRINSCHGL G. Virus meningo-encephalitis in Austria. II. Clinical features, pathology, and diagnosis. Bull World Health Organ. 1955;12(4):535–64. PubMed PMID: 14378998; PubMed Central PMCID: PMC2542296.

123. Lohitharajah J, Malavige N, Arambepola C, Wanigasinghe J, Gamage R, Gunaratne P, et al. Viral aetiologies of acute encephalitis in a hospital-based South Asian population. BMC Infect Dis. 2017 Apr 24;17(1):303. doi:10.1186/s12879-017-2403-z PubMed PMID: 28438128; PubMed Central PMCID: PMC5404678.

124. Olsen SJ, Campbell AP, Supawat K, Liamsuwan S, Chotpitayasunondh T, Laptikulthum S, et al. Infectious causes of encephalitis and meningoencephalitis in Thailand, 2003-2005. Emerg Infect Dis. 2015 Feb;21(2):280–9. doi:10.3201/eid2102.140291 PubMed PMID: 25627940; PubMed Central PMCID: PMC4313633.

125. Quist-Paulsen E, Kran AMB, Dunlop O, Wilson J, Ormaasen V. Infectious encephalitis: a description of a Norwegian cohort. Scand J Infect Dis. 2013 Mar;45(3):179–85. doi:10.3109/00365548.2012.719634 PubMed PMID: 23113672.

126. Rathore SK, Dwibedi B, Kar SK, Dixit S, Sabat J, Panda M. Viral aetiology and clinico-epidemiological features of acute encephalitis syndrome in eastern India. Epidemiol Infect. 2014 Dec;142(12):2514–21. doi:10.1017/S0950268813003397 PubMed PMID: 24476571.

127. Schmidt A, Bühler R, Mühlemann K, Hess CW, Täuber MG. Long-term outcome of acute encephalitis of unknown aetiology in adults. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2011 Apr;17(4):621–6. doi:10.1111/j.1469-0691.2010.03276.x PubMed PMID: 20518796.

128. Srey VH, Sadones H, Ong S, Mam M, Yim C, Sor S, et al. Etiology of encephalitis syndrome among hospitalized children and adults in Takeo, Cambodia, 1999-2000. Am J Trop Med Hyg. 2002 Feb;66(2):200–7. doi:10.4269/ajtmh.2002.66.200 PubMed PMID: 12135294.

129. Wong V, Yeung CY. Acute viral encephalitis in children. Aust Paediatr J. 1987 Dec;23(6):339–42. doi:10.1111/j.1440-1754.1987.tb00286.x PubMed PMID: 3435329.

130. Ilias A, Galanakis E, Raissaki M, Kalmanti M. Childhood encephalitis in Crete, Greece. J Child Neurol. 2006 Oct;21(10):910–2. doi:10.1177/08830738060210101701 PubMed PMID: 17005114.

131. Hon KLE, Tsang YCK, Chan LCN, Tsang HW, Wong KYK, Wu YHG, et al. Outcome of Encephalitis in Pediatric Intensive Care Unit. Indian J Pediatr. 2016 Oct;83(10):1098–103. doi:10.1007/s12098-016-2068-4 PubMed PMID: 27053179.

132. Rao S, Elkon B, Flett KB, Moss AFD, Bernard TJ, Stroud B, et al. Long-Term Outcomes and Risk Factors Associated With Acute Encephalitis in Children. J Pediatr Infect Dis Soc. 2017 Mar 1;6(1):20–7. doi:10.1093/jpids/piv075 PubMed PMID: 26553786.

133. Le VT, Phan TQ, Do QH, Nguyen BH, Lam QB, Bach VC, et al. Viral etiology of encephalitis in children in southern Vietnam: results of a one-year prospective descriptive study. PLoS Negl

Trop Dis. 2010 Oct 26;4(10):e854. doi:10.1371/journal.pntd.0000854 PubMed PMID: 21049060; PubMed Central PMCID: PMC2964288.

134. Toudou-Daouda M, Filali-Adib A, Slassi A, Belahsen MF, Souirti Z. Limbic encephalitis: Experience of a moroccan center. Brain Behav. 2019 Jan;9(1):e01177. doi:10.1002/brb3.1177 PubMed PMID: 30474361; PubMed Central PMCID: PMC6346419.

135. Bagdure D, Custer JW, Rao S, Messacar K, Dominguez S, Beam BW, et al. Hospitalized Children With Encephalitis in the United States: A Pediatric Health Information System Database Study. Pediatr Neurol. 2016 Aug;61:58–62. doi:10.1016/j.pediatrneurol.2016.04.014 PubMed PMID: 27353693.

136. Misra UK, Kalita J, Singh RK, Bhoi SK. A Study of Hyponatremia in Acute Encephalitis Syndrome: A Prospective Study From a Tertiary Care Center in India. J Intensive Care Med. 2019 May;34(5):411–7. doi:10.1177/0885066617701422 PubMed PMID: 28393593.

137. Meligy B, Kadry D, Draz IH, Marzouk H, El Baroudy NR, El Rifay AS. Epidemiological Profile of Acute Viral Encephalitis in a Sample of Egyptian Children. Open Access Maced J Med Sci. 2018 Feb 15;6(2):423–9. doi:10.3889/oamjms.2018.103 PubMed PMID: 29531617; PubMed Central PMCID: PMC5839461.

138. Ai J, Xie Z, Liu G, Chen Z, Yang Y, Li Y, et al. Etiology and prognosis of acute viral encephalitis and meningitis in Chinese children: a multicentre prospective study. BMC Infect Dis. 2017 Jul 14;17(1):494. doi:10.1186/s12879-017-2572-9 PubMed PMID: 28705180; PubMed Central PMCID: PMC5513334.

139. Britton PN, Dale RC, Blyth CC, Clark JE, Crawford N, Marshall H, et al. Causes and Clinical Features of Childhood Encephalitis: A Multicenter, Prospective Cohort Study. Clin Infect Dis Off Publ Infect Dis Soc Am. 2019 Aug 1. doi:10.1093/cid/ciz685 PubMed PMID: 31549170.

140. Zhao L, Zhou M, Wang B, Guo J, Chen N, He L. Clinical characteristics and outcome of clinically diagnosed viral encephalitis in southwest China. Neurol Sci Off J Ital Neurol Soc Ital Soc Clin Neurophysiol. 2015 Dec;36(12):2191–7. doi:10.1007/s10072-015-2333-8 PubMed PMID: 26205533.

141. Iro MA, Sadarangani M, Nickless A, Kelly DF, Pollard AJ. A Population-based Observational Study of Childhood Encephalitis in Children Admitted to Pediatric Intensive Care Units in England and Wales. Pediatr Infect Dis J. 2019 Jul;38(7):673–7. doi:10.1097/INF.0000000000002280 PubMed PMID: 30640197.

142. de Blauw D, Bruning AHL, Busch CBE, Kolodziej LM, Jansen NJG, van Woensel JBM, et al. Epidemiology and Etiology of Severe Childhood Encephalitis in The Netherlands. Pediatr Infect Dis J. 2020 Apr;39(4):267–72. doi:10.1097/INF.0000000000002551 PubMed PMID: 32097245.

143. Glaser CA, Gilliam S, Schnurr D, Forghani B, Honarmand S, Khetsuriani N, et al. In search of encephalitis etiologies: diagnostic challenges in the California Encephalitis Project, 1998-2000. Clin Infect Dis Off Publ Infect Dis Soc Am. 2003 Mar 15;36(6):731–42. doi:10.1086/367841 PubMed PMID: 12627357.

144. Milshtein NY, Paret G, Reif S, Halutz O, Grisaru-Soen G. Acute Childhood Encephalitis at 2 Tertiary Care Children's Hospitals in Israel: Etiology and Clinical Characteristics. Pediatr Emerg Care. 2016 Feb;32(2):82–6. doi:10.1097/PEC.0000000000000468 PubMed PMID: 26181499.

145. Andleeb S, Yasir Bari M, Gill I, Urooj S, Nausheen S. Incidence of Encephalitis in the Intensive Care Unit, a Tertiary Care Hospital, Pakistan: A 5-Year Retrospective Study. Turk J Anaesthesiol Reanim. 2020 Aug;48(4):288–93. doi:10.5152/TJAR.2019.62144 PubMed PMID: 32864643; PubMed Central PMCID: PMC7434350.

146. Li Q, Wang R, Xu H, Zhang L, Fu Y, Tian J, et al. Epidemiology and Disease Burden of Hospitalized Children With Viral Central Nervous System Infections in China, 2016 to 2020. Pediatr Neurol. 2023 Jan;138:38–44. doi:10.1016/j.pediatrneurol.2022.09.003 PubMed PMID: 36356470.

147. Chen LW, Olivé-Cirera G, Fonseca EG, Mistieri Simabukuro M, Iizuka T, Armangue T, et al. Very Long-Term Functional Outcomes and Dependency in Children With Anti-NMDA Receptor Encephalitis. Neurol Neuroimmunol Neuroinflammation. 2024 May;11(3):e200235. doi:10.1212/NXI.0000000000200235 PubMed PMID: 38621190; PubMed Central PMCID: PMC11087043.

148. Furuya-Kanamori L, Xu C, Doi SAR, Clark J, Wangdi K, Mills DJ, et al. Comparison of immunogenicity and safety of licensed Japanese encephalitis vaccines: A systematic review and network meta-analysis. Vaccine. 2021 Jul 22;39(32):4429–36. doi:10.1016/j.vaccine.2021.06.023 PubMed PMID: 34175128.

149. Centers for Disease Control and Prevention (CDC). Global rabies: What you should know.

150. Bilinski AM, Fitzpatrick MC, Rupprecht CE, Paltiel AD, Galvani AP. Optimal frequency of rabies vaccination campaigns in Sub-Saharan Africa. Proc Biol Sci. 2016 Nov 16;283(1842). doi:10.1098/rspb.2016.1211 PubMed PMID: 27852799; PubMed Central PMCID: PMC5124087.

151. Khandaker G, Jung J, Britton PN, King C, Yin JK, Jones CA. Long-term outcomes of infective encephalitis in children: a systematic review and meta-analysis. Dev Med Child Neurol. 2016 Nov;58(11):1108–15. doi:10.1111/dmcn.13197 PubMed PMID: 27422743.

152. Rocha ND, de Moura SK, da Silva GAB, Mattiello R, Sato DK. Neurological sequelae after encephalitis associated with herpes simplex virus in children: systematic review and meta-analysis. BMC Infect Dis. 2023 Jan 26;23(1):55. doi:10.1186/s12879-023-08007-3 PubMed PMID: 36703115; PubMed Central PMCID: PMC9878875.

153. Elenga N, Roux A, Cuadro-Alvarez E, Martin E, Kallel H, Defo A. Etiology and prognosis of encephalitis in French Guianese children: a retrospective record-based study. J Infect Public Health. 2020 Jul;13(7):1051–3. doi:10.1016/j.jiph.2020.01.315 PubMed PMID: 32284196.

154. Kim HJ, Cha JH, Kim W, Kim SY, Cho A, Kim H, et al. Clinical features and outcomes of paediatric probable antibody-negative autoimmune encephalitis. Dev Med Child Neurol. 2026 Apr;68(4):549–57. doi:10.1111/dmcn.16456 PubMed PMID: 40751942.

155. The Encephalitis Society. Encephalitis in adults. A guide. 2008 Aug. Report 3rd version.

156. Granerod J, Davies NWS, Ramanuj PP, Easton A, Brown DWG, Thomas SL. Increased rates of sequelae post-encephalitis in individuals attending primary care practices in the United Kingdom: a population-based retrospective cohort study. J Neurol. 2017 Feb;264(2):407–15. doi:10.1007/s00415-016-8316-8 PubMed PMID: 27766471.

157. Butler M, Abdat Y, Zandi M, Michael BD, Coutinho E, Nicholson TR, et al. Mental health outcomes of encephalitis: An international web-based study. Eur J Neurol. 2024

Jan;31(1):e16083. doi:10.1111/ene.16083 PubMed PMID: 37797295; PubMed Central PMCID: PMC11236046.

158. Hansen MA, Samannodi MS, Castelblanco RL, Hasbun R. Clinical Epidemiology, Risk Factors, and Outcomes of Encephalitis in Older Adults. Clin Infect Dis Off Publ Infect Dis Soc Am. 2020 May 23;70(11):2377–85. doi:10.1093/cid/ciz635 PubMed PMID: 31294449.

159. Mailles A, Argemi X, Biron C, Fillatre P, De Broucker T, Buzelé R, et al. Changing profile of encephalitis: Results of a 4-year study in France. Infect Dis Now. 2022 Feb;52(1):1–6. doi:10.1016/j.idnow.2021.11.007 PubMed PMID: 34896660.

160. D'Ippolito M, Aloisi M, Azicnuda E, Silvestro D, Giustini M, Verni F, et al. Changes in Caregivers Lifestyle after Severe Acquired Brain Injury: A Preliminary Investigation. BioMed Res Int. 2018;2018:2824081. doi:10.1155/2018/2824081 PubMed PMID: 30065934; PubMed Central PMCID: PMC6051321.

161. Hooper L, Williams WH, Sarah EW, Chua KC. Caregiver distress, coping and parenting styles in cases of childhood encephalitis. Neuropsychol Rehabil. 2007 Oct;17(4–5):621–37. doi:10.1080/09602010601137054 PubMed PMID: 17676538.

162. Tomlinson AR, Blum RA, Jetté N, Kwon CS, Easton A, Yeshokumar AK. Assessment of care transitions and caregiver burden in anti-NMDA receptor encephalitis. Epilepsy Behav EB. 2020 Jul;108:107066. doi:10.1016/j.yebeh.2020.107066 PubMed PMID: 32375097.

163. Mohamed S, Rosenheck R, Lyketsos CG, Schneider LS. Caregiver burden in Alzheimer disease: cross-sectional and longitudinal patient correlates. Am J Geriatr Psychiatry Off J Am Assoc Geriatr Psychiatry. 2010 Oct;18(10):917–27. doi:10.1097/JGP.0b013e3181d5745d PubMed PMID: 20808108; PubMed Central PMCID: PMC3972419.

164. Hébert R, Bravo G, Préville M. Reliability, validity and reference values of the zarit burden interview for assessing informal caregivers of community-dwelling older persons with dementia. Can J Aging. 2000;19(4):494–507.

165. Carod-Artal FJ, Ferreira Coral L, Trizotto DS, Menezes Moreira C. Burden and perceived health status among caregivers of stroke patients. Cerebrovasc Dis Basel Switz. 2009;28(5):472–80. doi:10.1159/000236525 PubMed PMID: 19752548.

166. Edmond K, Clark A, Korczak VS, Sanderson C, Griffiths UK, Rudan I. Global and regional risk of disabling sequelae from bacterial meningitis: a systematic review and meta-analysis. Lancet Infect Dis. 2010 May;10(5):317–28. doi:10.1016/S1473-3099(10)70048-7 PubMed PMID: 20417414.

167. Tooren HVD, Easton A, Hooper C, Mullin J, Fish J, Carson A, et al. How should we define a 'good' outcome from encephalitis? A systematic review of the range of outcome measures used in the long-term follow-up of patients with encephalitis. Clin Med Lond Engl. 2022 Mar;22(2):145–8. doi:10.7861/clinmed.2021-0505 PubMed PMID: 35197253; PubMed Central PMCID: PMC8966817.

168. Brenner J, Olijslagers SHC, Crijnen YS, de Vries JM, Mandarakas MR, Titulaer MJ. Clinical Outcome Assessments in Encephalitis: A Systematic Review. Neurol Neuroimmunol Neuroinflammation. 2024 Jan;11(1):e200168. doi:10.1212/NXI.0000000000200168 PubMed PMID: 38086078; PubMed Central PMCID: PMC10758981.

169. Cheng HY, Chair SY, Chau JPC. The effectiveness of psychosocial interventions for stroke family caregivers and stroke survivors: a systematic review and meta-analysis. Patient Educ Couns. 2014 Apr;95(1):30–44. doi:10.1016/j.pec.2014.01.005 PubMed PMID: 24485756.

170. Dunkin JJ, Anderson-Hanley C. Dementia caregiver burden: a review of the literature and guidelines for assessment and intervention. Neurology. 1998 Jul;51(1 Suppl 1):S53-60; discussion S65-67. doi:10.1212/wnl.51.1_suppl_1.s53 PubMed PMID: 9674763.

171. Postels DG, Soldatos A, LaRovere KL. Outcomes measures in children after acute central nervous system infections and malaria. Curr Opin Pediatr. 2019 Dec;31(6):756–62. doi:10.1097/MOP.0000000000000823 PubMed PMID: 31693584.

172. Cheng Y, Tran Minh N, Tran Minh Q, Khandelwal S, Clapham HE. Estimates of Japanese Encephalitis mortality and morbidity: A systematic review and modeling analysis. PLoS Negl Trop Dis. 2022 May;16(5):e0010361. doi:10.1371/journal.pntd.0010361 PubMed PMID: 35613183; PubMed Central PMCID: PMC9173604.

173. Kvam KA, Stahl JP, Chow FC, Soldatos A, Tattevin P, Sejvar J, et al. Outcome and Sequelae of Infectious Encephalitis. J Clin Neurol Seoul Korea. 2024 Jan;20(1):23–36. doi:10.3988/jcn.2023.0240 PubMed PMID: 38179629; PubMed Central PMCID: PMC10782093.

174. Michael S, Varley J, Williams R, Bajorek T, Easton A, Irani SR. Criminality in patients with autoimmune encephalitis: A case series. Eur J Neurol. 2024 Apr;31(4):e16197. doi:10.1111/ene.16197 PubMed PMID: 38189625; PubMed Central PMCID: PMC11235586.

175. Piret J, Boivin G. Immunomodulatory Strategies in Herpes Simplex Virus Encephalitis. Clin Microbiol Rev. 2020 Mar 18;33(2). doi:10.1128/CMR.00105-19 PubMed PMID: 32051176; PubMed Central PMCID: PMC7018500.

176. Simon LV, Sandhu DS, Goyal A, Kruse B. Encephalitis, Japanese. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020. PubMed PMID: 29262148.

177. Kumar R, Mathur A, Singh KB, Sitholey P, Prasad M, Shukla R, et al. Clinical sequelae of Japanese encephalitis in children. Indian J Med Res. 1993 Jan;97:9–13. PubMed PMID: 8387460.

178. Taba P, Schmutzhard E, Forsberg P, Lutsar I, Ljøstad U, Mygland Å, et al. EAN consensus review on prevention, diagnosis and management of tick-borne encephalitis. Eur J Neurol. 2017 Oct;24(10):1214-e61. doi:10.1111/ene.13356 PubMed PMID: 28762591.

179. Dacheux L, Delmas O, Bourhy H. Human rabies encephalitis prevention and treatment: progress since Pasteur's discovery. Infect Disord Drug Targets. 2011 Jun;11(3):251–99. doi:10.2174/187152611795768079 PubMed PMID: 21488832.

180. Venkatesan A, Adatia K. Anti-NMDA-Receptor Encephalitis: From Bench to Clinic. ACS Chem Neurosci. 2017 Dec 20;8(12):2586–95. doi:10.1021/acschemneuro.7b00319 PubMed PMID: 29077387.

181. Chi X, Wang W, Huang C, Wu M, Zhang L, Li J, et al. Risk factors for mortality in patients with anti-NMDA receptor encephalitis. Acta Neurol Scand. 2017 Oct;136(4):298–304. doi:10.1111/ane.12723 PubMed PMID: 28028820.

182. Chow C, Dehority W. Long-Term Outcomes in Children Surviving Tropical Arboviral Encephalitis: A Systematic Review. J Trop Pediatr. 2021 May 17;67(2):fmab028. doi:10.1093/tropej/fmab028 PubMed PMID: 34109400.

183. Abboud H, Briggs F, Buerki R, Elkasaby M, BacaVaca GF, Fotedar N, et al. Residual symptoms and long-term outcomes after all-cause autoimmune encephalitis in adults. J Neurol Sci. 2022 Mar 15;434:120124. doi:10.1016/j.jns.2021.120124 PubMed PMID: 34998237.

184. Kvam KA, Stahl JP, Chow FC, Soldatos A, Tattevin P, Sejvar J, et al. Outcome and Sequelae of Autoimmune Encephalitis. J Clin Neurol Seoul Korea. 2024 Jan;20(1):3–22. doi:10.3988/jcn.2023.0242 PubMed PMID: 38179628; PubMed Central PMCID: PMC10782092.

185. Kiyani M, Liu B, Charalambous LT, Adil SM, Hodges SE, Yang S, et al. The longitudinal health economic impact of viral encephalitis in the United States. J Med Microbiol. 2020 Feb;69(2):270–9. doi:10.1099/jmm.0.001153 PubMed PMID: 32040394.

186. Slunge D, Boman A, Studahl M. Burden of Tick-Borne Encephalitis, Sweden. Emerg Infect Dis. 2022 Feb;28(2):314–22. doi:10.3201/eid2802.204324 PubMed PMID: 35075997; PubMed Central PMCID: PMC8798699.

187. Cohen J, Sotoca J, Gandhi S, Yeshokumar AK, Gordon-Lipkin E, Geocadin RG, et al. Autoimmune encephalitis: A costly condition. Neurology. 2019 Feb 26;92(9):e964–72. doi:10.1212/WNL.0000000000006990 PubMed PMID: 30674590.

188. Li A, Gong X, Guo K, Lin J, Zhou D, Hong Z. Direct economic burden of patients with autoimmune encephalitis in western China. Neurol Neuroimmunol Neuroinflammation. 2020 Nov;7(6). doi:10.1212/NXI.0000000000000891 PubMed PMID: 33008922; PubMed Central PMCID: PMC7577530.

189. Griffiths MJ, Lemon JV, Rayamajhi A, Poudel P, Shrestha P, Srivastav V, et al. The functional, social and economic impact of acute encephalitis syndrome in Nepal--a longitudinal follow-up study. PLoS Negl Trop Dis. 2013;7(9):e2383. doi:10.1371/journal.pntd.0002383 PubMed PMID: 24069467; PubMed Central PMCID: PMC3772013.

190. Huong N, Toan N, Khanh T, Thinh L, Nhan L, Minh N, et al. A Cost of Illness Analysis of Children with Encephalitis Presenting to A Major Hospital in Vietnam [Internet]. 2024. Available from: https://doi.org/10.1101/2024.04.24.24306275

191. Nguyen ALT, Slavkovsky R, Phan HT, Nguyen HTT, Vannachone S, Le DH, et al. Estimating the cost of illness of acute Japanese encephalitis and sequelae care in Vietnam and Laos: A cross-sectional study. PLOS Glob Public Health. 2023;3(6):e0001873. doi:10.1371/journal.pgph.0001873 PubMed PMID: 37310946; PubMed Central PMCID: PMC10263309.

192. Sultana R, Slavkovsky R, Ullah MR, Tasnim Z, Sultana S, Khan S, et al. Cost of Acute and Sequelae Care for Japanese Encephalitis Patients, Bangladesh, 2011-2021. Emerg Infect Dis. 2023 Dec;29(12):2488–97. doi:10.3201/eid2912.230594 PubMed PMID: 37987586; PubMed Central PMCID: PMC10683813.

193. Šmit R, Postma MJ. The Burden of Tick-Borne Encephalitis in Disability-Adjusted Life Years (DALYs) for Slovenia. PloS One. 2015;10(12):e0144988. doi:10.1371/journal.pone.0144988 PubMed PMID: 26672751; PubMed Central PMCID: PMC4684505.

194. Labeaud AD, Bashir F, King CH. Measuring the burden of arboviral diseases: the spectrum of morbidity and mortality from four prevalent infections. Popul Health Metr. 2011 Jan 10;9(1):1. doi:10.1186/1478-7954-9-1 PubMed PMID: 21219615; PubMed Central PMCID: PMC3024945.

195. Deng X, Yan R, Li ZQ, Tang XW, Zhou Y, He H. Economic and disease burden of Japanese encephalitis in Zhejiang Province, 2013-2018. PLoS Negl Trop Dis. 2021 Jun;15(6):e0009505. doi:10.1371/journal.pntd.0009505 PubMed PMID: 34153039; PubMed Central PMCID: PMC8248708.

196. Wang X, Su L, Sun S, Hu W, Mu Q, Liang X, et al. Long-Term Neurological Sequelae and Disease Burden of Japanese Encephalitis in Gansu Province, China. Ann Glob Health. 2021;87(1):103. doi:10.5334/aogh.3343 PubMed PMID: 34722167; PubMed Central PMCID: PMC8533657.

197. The burden of neurological disorders across the states of India: the Global Burden of Disease Study 1990-2019. Lancet Glob Health. 2021 Aug;9(8):e1129–44. doi:10.1016/S2214-109X(21)00164-9 PubMed PMID: 34273302; PubMed Central PMCID: PMC8295043.

198. Ding D, Kilgore PE, Clemens JD, Wei L, Zhi-Yi X. Cost-effectiveness of routine immunization to control Japanese encephalitis in Shanghai, China. Bull World Health Organ. 2003;81(5):334–42. PubMed PMID: 12856051; PubMed Central PMCID: PMC2572455.

199. Liu W, Clemens JD, Kari K, Xu ZY. Cost-effectiveness of Japanese encephalitis (JE) immunization in Bali, Indonesia. Vaccine. 2008 Aug 18;26(35):4456–60. doi:10.1016/j.vaccine.2008.06.050 PubMed PMID: 18602436.

200. Greenwood B. The contribution of vaccination to global health: past, present and future. Philos Trans R Soc Lond B Biol Sci. 2014;369(1645):20130433. doi:10.1098/rstb.2013.0433 PubMed PMID: 24821919; PubMed Central PMCID: PMC4024226.

201. Ozawa S, Clark S, Portnoy A, Grewal S, Stack ML, Sinha A, et al. Estimated economic impact of vaccinations in 73 low- and middle-income countries, 2001-2020. Bull World Health Organ. 2017 Sep 1;95(9):629–38. Located at: PubMed; 28867843. doi:10.2471/BLT.16.178475

202. Japanese Encephalitis Vaccines: WHO position paper – February 2015. Releve Epidemiol Hebd. 2015 Feb 27;90(9):69–87. Located at: PubMed; 25726573

203. World Health Organization. Japanese Encephalitis Vaccines: WHO position paper – February 2015 [Internet]. Geneva, Switzerland: World Health Organization; 2015 Feb [cited 2022 Apr 20]. Available from: https://apps.who.int/iris/bitstream/handle/10665/242325/WER9009_69-88.PDF?sequence=1&isAllowed=y

204. Heffelfinger JD, Li X, Batmunkh N, Grabovac V, Diorditsa S, Liyanage JB, et al. Japanese Encephalitis Surveillance and Immunization - Asia and Western Pacific Regions, 2016. MMWR Morb Mortal Wkly Rep. 2017 Jun 9;66(22):579–83. Located at: PubMed; 28594790. doi:10.15585/mmwr.mm6622a3

205. Centers for Disease Control and Prevention (CDC). Japanese encephalitis surveillance and immunization--Asia and the Western Pacific, 2012. MMWR Morb Mortal Wkly Rep. 2013 Aug 23;62(33):658–62. Located at: PubMed; 23965828

206. Im J, Balasubramanian R, Yastini NW, Suwarba IGN, Andayani AR, Bura V, et al. Protecting children against Japanese encephalitis in Bali, Indonesia. Lancet Lond Engl. 2018 Jun 23;391(10139):2500–1. Located at: PubMed; 29976465. doi:10.1016/S0140-6736(18)31191-7

207. Vannice KS, Hills SL, Schwartz LM, Barrett AD, Heffelfinger J, Hombach J, et al. The future of Japanese encephalitis vaccination: expert recommendations for achieving and maintaining optimal JE control. NPJ Vaccines. 2021 Jun 15;6(1):82. doi:10.1038/s41541-021-00338-z PubMed PMID: 34131150; PubMed Central PMCID: PMC8206071.

208. Letson GW, Marfin AA, Mooney J, Minh HV, Hills SL. Impact of vaccination against Japanese encephalitis in endemic countries. PLoS Negl Trop Dis. 2024 Sep;18(9):e0012390. doi:10.1371/journal.pntd.0012390 PubMed PMID: 39226312; PubMed Central PMCID: PMC11398676.

209. Samiak L, Emeto TI. Vaccination and nutritional status of children in Karawari, East Sepik Province, Papua New Guinea. PloS One. 2017 Nov 9;12(11):e0187796–e0187796. Located at: PubMed; 29121088. doi:10.1371/journal.pone.0187796

210. PATH. Four barriers Nepal overcame to introduce Japanese encephalitis vaccines [Internet]. 2018 Oct 26 [cited 2020 Jul 8]. Available from: https://www.path.org/articles/four-barriers-nepal-overcame-introduce-je-vaccines/#:~:text=Decision%2Dmakers%20in%20JE%2Dendemic,and%20need%20for%20technical%20assistance

211. Upreti SR, Janusz KB, Schluter WW, Bichha RP, Shakya G, Biggerstaff BJ, et al. Estimation of the impact of a Japanese encephalitis immunization program with live, attenuated SA 14-14-2 vaccine in Nepal. Am J Trop Med Hyg. 2013 Mar;88(3):464–8. Located at: PubMed; 23358643. doi:10.4269/ajtmh.12-0196

212. Impoinvil DE, Ooi MH, Diggle PJ, Caminade C, Cardosa MJ, Morse AP, et al. The effect of vaccination coverage and climate on Japanese encephalitis in Sarawak, Malaysia. PLoS Negl Trop Dis. 2013 Aug 8;7(8):e2334–e2334. Located at: PubMed; 23951373. doi:10.1371/journal.pntd.0002334

213. Hombach J, Barrett AD, Cardosa MJ, Deubel V, Guzman M, Kurane I, et al. Review on flavivirus vaccine development. Proceedings of a meeting jointly organised by the World Health Organization and the Thai Ministry of Public Health, 26-27 April 2004, Bangkok, Thailand. Vaccine. 2005 Apr 15;23(21):2689–95. Located at: PubMed; 15841565. doi:10.1016/j.vaccine.2004.11.040

214. Wang H, Li Y, Liang X, Liang G. Japanese encephalitis in mainland china. Jpn J Infect Dis. 2009 Sep;62(5):331–6. Located at: PubMed; 19762980

215. Pilz A, Erber W, Schmitt HJ. Vaccine uptake in 20 countries in Europe 2020: Focus on tick-borne encephalitis (TBE). Ticks Tick-Borne Dis. 2023 Jan;14(1):102059. doi:10.1016/j.ttbdis.2022.102059 PubMed PMID: 36410164.

216. Who Publication. Vaccines against tick-borne encephalitis: WHO position paper--recommendations. Vaccine. 2011/07/21 edn. 2011 Nov 8;29(48):8769–70. Located at: PubMed; 21777636. doi:10.1016/j.vaccine.2011.07.024

217. Zavadska D, Odzelevica Z, Karelis G, Liepina L, Litauniece ZA, Bormane A, et al. Tick-borne encephalitis: A 43-year summary of epidemiological and clinical data from Latvia (1973 to 2016). PloS One. 2018 Nov 13;13(11):e0204844–e0204844. Located at: PubMed; 30422984. doi:10.1371/journal.pone.0204844

218. Halsby K, Davidson A, Davis J, Zens K, Dobler G, Pilz A, et al. Incidence of Tick-Borne Encephalitis in Unvaccinated Populations Across Europe (2020-2023). Int J Infect Dis IJID Off Publ Int Soc Infect Dis. 2025 Sep 8;108052. doi:10.1016/j.ijid.2025.108052 PubMed PMID: 40930214.

219. Xing Y, Schmitt HJ, Arguedas A, Yang J. Tick-borne encephalitis in China: A review of epidemiology and vaccines. Vaccine. 2017/01/30 edn. 2017 Mar 1;35(9):1227–37. Located at: PubMed; 28153343. doi:10.1016/j.vaccine.2017.01.015

220. American Clinic Tokyo. Japan's First Approved Vaccine for Tick-Borne Encephalitis (TBE) [Internet]. 2025 May 22 [cited 2025 Sep 25]. Available from: https://www.americanclinictokyo.com/now-available-japans-first-approved-vaccine-for-tick-borne-encephalitis-tbe/

221. Erber W, Schmitt HJ. Self-reported tick-borne encephalitis (TBE) vaccination coverage in Europe: Results from a cross-sectional study. Ticks Tick-Borne Dis. 2018 May;9(4):768–77. doi:10.1016/j.ttbdis.2018.02.007 PubMed PMID: 29501619.

222. Kunze U. Report of the 21st Annual Meeting of the International Scientific Working Group on Tick-Borne Encephalitis (ISW-TBE): TBE - record year 2018. Ticks Tick-Borne Dis. 2020 Jan;11(1):101287. doi:10.1016/j.ttbdis.2019.101287 PubMed PMID: 31522919.

223. Yoshii K, Song JY, Park SB, Yang J, Schmitt HJ. Tick-borne encephalitis in Japan, Republic of Korea and China. Emerg Microbes Infect. 2017 Sep 20;6(9):e82–e82. Located at: PubMed; 28928417. doi:10.1038/emi.2017.69

224. Yoshii K, Takahashi-Iwata I, Shirai S, Kobayashi S, Yabe I, Sasaki H. A Retrospective Epidemiological Study of Tick-Borne Encephalitis Virus in Patients with Neurological Disorders in Hokkaido, Japan. Microorganisms. 2020 Oct 28;8(11). doi:10.3390/microorganisms8111672 PubMed PMID: 33126600; PubMed Central PMCID: PMC7692117.

225. Ohira M, Yoshii K, Aso Y, Nakajima H, Yamashita T, Takahashi-Iwata I, et al. First evidence of tick-borne encephalitis (TBE) outside of Hokkaido Island in Japan. Emerg Microbes Infect. 2023 Dec;12(2):2278898. doi:10.1080/22221751.2023.2278898 PubMed PMID: 37906509; PubMed Central PMCID: PMC10810618.

226. GAVI. New data shows "staggering" increase in measles deaths worldwide [Internet]. 2023 Nov 16 [cited 2025 Sep 25]. Available from: https://www.gavi.org/vaccineswork/new-data-shows-staggering-increase-measles-deaths-worldwide

227. The Encephalitis Society. Measles infection and encephalitis [Internet]. The Encephalitis Society; 2020. Available from: https://www.encephalitis.info/Handlers/Download.ashx?IDMF=6855c790-65a1-4931-b7ea-329ea4ead631

228. World Health Organization. Joint News Release [Internet]. 2019. Available from: https://www.who.int/news-room/detail/05-12-2019-more-than-140-000-die-from-measles-as-cases-surge-worldwide

229. Our World in Data. Vaccination [Internet]. [cited 2024 Sep 23]. Available from: https://ourworldindata.org/vaccination#:~:text=Measles%20vaccine,-Measles%20is%20a&text=You%20can%20switch%20to%20the,that%20figure%20was%20over%2080%25.

230. Wang R, Jing W, Liu M, Liu J. Trends of the Global, Regional, and National Incidence of Measles, Vaccine Coverage, and Risk Factors in 204 Countries From 1990 to 2019. Front Med. 2021;8:798031. doi:10.3389/fmed.2021.798031 PubMed PMID: 35127753; PubMed Central PMCID: PMC8810814.

231. World Health Organization. Measles vaccine coverage [Internet]. [cited 2025 Sep 25]. Available from: https://immunizationdata.who.int/global/wiise-detail-page/measles-vaccination-coverage?CODE=Global&ANTIGEN=MCV1&YEAR=

232. Vanderslott S, Dadonaite B, Roser M. Vaccination [Internet]. OurWorldInData.org; 2020. Available from: https://ourworldindata.org/vaccination

233. Gallup. Wellcome Global Monitor – First Wave Findings. 2019.

234. Vaccine Confidence Project. Vaccine Confidence Project [Internet]. [cited 2025 Oct 2]. Available from: https://www.vaccineconfidence.org/

235. World Health Organization. Measles [Internet]. [cited 2024 Sep 23]. Available from: https://www.who.int/news-room/fact-sheets/detail/measles

236. Co S, Mackenzie I, Shewchuk J. Rabies encephalitis. RadioGraphics. 2015;35:235–8.

237. World Health Organization. WHO guide for rabies pre and post exposure prophylaxis in humans [Internet]. 2014 [cited 2020 Aug 18]. Available from: https://www.who.int/rabies/PEP_Prophylaxis_guideline_15_12_2014.pdf

238. World Health Organization, Global Alliance for Rabies Control, Food and Agriculture Organization of the United Nations, World Organisation for Animal Health. ZERO BY 30: The Global Strategic Plan to end human deaths from dog-mediated rabies by 2030 [Internet]. Geneva, Switzerland; 2018 [cited 2024 Sep 25]. Available from: https://www.who.int/publications/i/item/9789241513838

239. Centers for Disease Control and Prevention (CDC). Rabies status by country [Internet]. [cited 2025 Oct 13]. Available from: https://www.cdc.gov/rabies/country-data/index.html

240. Centers for Disease Control and Prevention (CDC). Vaccine Information Statement. Rabies vaccine: what you need to know [Internet]. 2020 [cited 2020 Aug 18]. Available from: https://www.cdc.gov/vaccines/hcp/vis/vis-statements/rabies.pdf

241. Tran CH, Afriyie DO, Pham TN, Otsu S, Urabe M, Dang AD, et al. Rabies post-exposure prophylaxis initiation and adherence among patients in Vietnam, 2014-2016. Vaccine. 2019/02/02 edn. 2019 Oct 3;37 Suppl 1:A54–63. Located at: PubMed; 30723063. doi:10.1016/j.vaccine.2019.01.030

242. Freire de Carvalho M, Vigilato MAN, Pompei JA, Rocha F, Vokaty A, Molina-Flores B, et al. Rabies in the Americas: 1998-2014. PLoS Negl Trop Dis. 2018 Mar;12(3):e0006271. doi:10.1371/journal.pntd.0006271 PubMed PMID: 29558465; PubMed Central PMCID: PMC5877887.

243. Seetahal JFR, Vokaty A, Vigilato MAN, Carrington CVF, Pradel J, Louison B, et al. Rabies in the Caribbean: A Situational Analysis and Historic Review. Trop Med Infect Dis. 2018 Aug 20;3(3). doi:10.3390/tropicalmed3030089 PubMed PMID: 30274485; PubMed Central PMCID: PMC6160905.

244. Alemayehu T, Oguttu B, Rupprecht CE, Niyas VKM. Rabies vaccinations save lives but where are the vaccines? Global vaccine inequity and escalating rabies-related mortality in low- and middle-income countries. Int J Infect Dis IJID Off Publ Int Soc Infect Dis. 2024 Mar;140:49–51. doi:10.1016/j.ijid.2024.01.008 PubMed PMID: 38232796.

245. Endy TP, Keiser PB, Wang D, Jarman RG, Cibula D, Fang H, et al. Serologic Response of 2 Versus 3 Doses and Intradermal Versus Intramuscular Administration of a Licensed Rabies Vaccine for Preexposure Prophylaxis. J Infect Dis. 2020 Apr 7;221(9):1494–8. doi:10.1093/infdis/jiz645 PubMed PMID: 31802120.

246. Ejemel M, Smith TG, Greenberg L, Carson WC, Lowe D, Yang Y, et al. A cocktail of human monoclonal antibodies broadly neutralizes North American rabies virus variants as a promising candidate for rabies post-exposure prophylaxis. Sci Rep. 2022 Jun 7;12(1):9403. doi:10.1038/s41598-022-13527-0 PubMed PMID: 35672343; PubMed Central PMCID: PMC9174473.

247. Nyasulu PS, Weyer J, Tschopp R, Mihret A, Aseffa A, Nuvor SV, et al. Rabies mortality and morbidity associated with animal bites in Africa: a case for integrated rabies disease surveillance, prevention and control: a scoping review. BMJ Open. 2021 Dec 2;11(12):e048551. doi:10.1136/bmjopen-2020-048551 PubMed PMID: 34857556; PubMed Central PMCID: PMC8640643.

248. Dehal N, Krishan K, Kanchan T, Singh J. Public-funded immunisation: key to varicella control in India. Lancet Lond Engl. 2015 Dec 12;386(10011):2389–90. doi:10.1016/S0140-6736(15)01190-3 PubMed PMID: 26700523.

249. Varicella and herpes zoster vaccines: WHO position paper, June 2014--Recommendations. Vaccine. 2016 Jan 4;34(2):198–9. doi:10.1016/j.vaccine.2014.07.068 PubMed PMID: 26723191.

250. Herlin LK, Hansen KS, Bodilsen J, Larsen L, Brandt C, Andersen CØ, et al. Varicella Zoster Virus Encephalitis in Denmark From 2015 to 2019-A Nationwide Prospective Cohort Study. Clin Infect Dis Off Publ Infect Dis Soc Am. 2021 Apr 8;72(7):1192–9. doi:10.1093/cid/ciaa185 PubMed PMID: 32103249.

251. Persson A, Bergström T, Lindh M, Namvar L, Studahl M. Varicella-zoster virus CNS disease--viral load, clinical manifestations and sequels. J Clin Virol Off Publ Pan Am Soc Clin Virol. 2009 Nov;46(3):249–53. doi:10.1016/j.jcv.2009.07.014 PubMed PMID: 19709927.

252. Wutzler P, Bonanni P, Burgess M, Gershon A, Sáfadi MA, Casabona G. Varicella vaccination - the global experience. Expert Rev Vaccines. 2017 Aug;16(8):833–43. doi:10.1080/14760584.2017.1343669 PubMed PMID: 28644696; PubMed Central PMCID: PMC5739310.

253. Wooding EL, Kadambari S, Warris A. Varicella: is it time for a global vaccination programme? Arch Dis Child. 2025 Jul 18;110(8):586–91. doi:10.1136/archdischild-2024-327593 PubMed PMID: 39978864.

254. Spoulou V, Alain S, Gabutti G, Giaquinto C, Liese J, Martinon-Torres F, et al. Implementing Universal Varicella Vaccination in Europe: The Path Forward. Pediatr Infect Dis J. 2019 Feb;38(2):181–8. doi:10.1097/INF.0000000000002233 PubMed PMID: 30408002.

255. Tam WWS, Chan J, Lo KKH, Lee A, Chan PKS, Chan D, et al. Parental Attitudes and Factors Associated With Varicella Vaccination in Preschool and Schoolchildren in Hong Kong: A Cross-

Sectional Study. Medicine (Baltimore). 2015 Sep;94(36):e1519. doi:10.1097/MD.0000000000001519 PubMed PMID: 26356725; PubMed Central PMCID: PMC4616659.

256. Marziano V, Poletti P, Guzzetta G, Ajelli M, Manfredi P, Merler S. The impact of demographic changes on the epidemiology of herpes zoster: Spain as a case study. Proc Biol Sci. 2015 Apr 7;282(1804):20142509. doi:10.1098/rspb.2014.2509 PubMed PMID: 25761709; PubMed Central PMCID: PMC4375857.

257. Guzzetta G, Poletti P, Merler S, Manfredi P. The Epidemiology of Herpes Zoster After Varicella Immunization Under Different Biological Hypotheses: Perspectives From Mathematical Modeling. Am J Epidemiol. 2016 Apr 15;183(8):765–73. doi:10.1093/aje/kwv240 PubMed PMID: 26994062; PubMed Central PMCID: PMC4832050.

258. Varela FH, Pinto LA, Scotta MC. Global impact of varicella vaccination programs. Hum Vaccines Immunother. 2019;15(3):645–57. doi:10.1080/21645515.2018.1546525 PubMed PMID: 30427766; PubMed Central PMCID: PMC6605725.

259. Lopez AS, Zhang J, Brown C, Bialek S. Varicella-related hospitalizations in the United States, 2000-2006: the 1-dose varicella vaccination era. Pediatrics. 2011 Feb;127(2):238–45. doi:10.1542/peds.2010-0962 PubMed PMID: 21199857; PubMed Central PMCID: PMC4865884.

260. Marano C, Moodley M, Melander E, De Moerlooze L, Nothdurft HD. Perceptions of tick-borne encephalitis risk: a survey of travellers and travel clinics from Canada, Germany, Sweden and the UK. J Travel Med. 2019 Feb 1;26(Suppl 1):S10–6. doi:10.1093/jtm/tay063 PubMed PMID: 30476160; PubMed Central PMCID: PMC6377183.

261. World Health Organization. Japanese encephalitis fact sheet [Internet]. [cited 2020 Nov 24]. Available from: https://www.who.int/en/news-room/fact-sheets/detail/japanese-encephalitis

262. Turtle L, Easton A, Defres S, Ellul M, Bovill B, Hoyle J, et al. 'More than devastating'-patient experiences and neurological sequelae of Japanese encephalitis§. J Travel Med. 2019 Oct 14;26(7). doi:10.1093/jtm/taz064 PubMed PMID: 31504712; PubMed Central PMCID: PMC6792067.

263. Steffen R. Tick-borne encephalitis (TBE) in children in Europe: Epidemiology, clinical outcome and comparison of vaccination recommendations. Ticks Tick-Borne Dis. 2018/09/01 edn. 2019 Jan;10(1):100–10. Located at: PubMed; 30241699. doi:10.1016/j.ttbdis.2018.08.003

264. El-Kurdi R, Rhodes LA, Sauls AD, Selinger R, Schimmelfing JT, Chelminski AN, et al. Assessing barriers to patient acceptance of pharmacist-provided recommendations for international travel. J Am Pharm Assoc JAPhA. 2019 Aug;59(4S):S72–6. doi:10.1016/j.japh.2019.04.021 PubMed PMID: 31248844.

265. Valneva. Valneva's Chikungunya press releases [Internet]. [cited 2024 Oct 2]. Available from: https://valneva.com/category/chikungunya/?post_types=press-release

266. US Food and Drug Administration. FDA Update on the Safety of Ixchiq (Chikungunya Vaccine, Live). FDA Suspends Biologics License: FDA Safety Communication [Internet]. [cited 2025 Oct 2]. Available from: https://www.fda.gov/safety/medical-product-safety-information/fda-update-safety-ixchiq-chikungunya-vaccine-live-fda-suspends-biologics-license-fda-safety?utm

267. Bavarian Nordic. Bavarian Nordic Receives Marketing Authorization in Europe for Chikungunya Vaccine for Persons Aged 12 and Older [Internet]. [cited 2025 Oct 2]. Available from: https://www.bavarian-nordic.com/investor/news/news.aspx?news=7056

268. de la Calle-Prieto F, Arsuaga M, Rodríguez-Sevilla G, Paiz NS, Díaz-Menéndez M. The current status of arboviruses with major epidemiological significance in Europe. Enfermedades Infecc Microbiol Clin Engl Ed. 2024 Nov;42(9):516–26. doi:10.1016/j.eimce.2024.09.008 PubMed PMID: 39505461.

269. Salje H, Alera MT, Chua MN, Hunsawong T, Ellison D, Srikiatkhachorn A, et al. Evaluation of the extended efficacy of the Dengvaxia vaccine against symptomatic and subclinical dengue infection. Nat Med. 2021 Aug;27(8):1395–400. doi:10.1038/s41591-021-01392-9 PubMed PMID: 34168334; PubMed Central PMCID: PMC8364868.

270. Al-Osaimi HM, Kanan M, Marghlani L, Al-Rowaili B, Albalawi R, Saad A, et al. A systematic review on malaria and dengue vaccines for the effective management of these mosquito borne diseases: Improving public health. Hum Vaccines Immunother. 2024 Dec 31;20(1):2337985. doi:10.1080/21645515.2024.2337985 PubMed PMID: 38602074; PubMed Central PMCID: PMC11017952.

271. Haider N, Hasan MN, Onyango J, Asaduzzaman M. Global landmark: 2023 marks the worst year for dengue cases with millions infected and thousands of deaths reported. IJID Reg. 2024 Dec;13:100459. doi:10.1016/j.ijregi.2024.100459 PubMed PMID: 39497753; PubMed Central PMCID: PMC11532885.

272. Stromberg ZR, Fischer W, Bradfute SB, Kubicek-Sutherland JZ, Hraber P. Vaccine Advances against Venezuelan, Eastern, and Western Equine Encephalitis Viruses. Vaccines. 2020 Jun 3;8(2). doi:10.3390/vaccines8020273 PubMed PMID: 32503232.

273. Mahase E. Vaccinating the UK: how the covid vaccine was approved, and other questions answered. BMJ. 2020 Dec 9;371:m4759. doi:10.1136/bmj.m4759 PubMed PMID: 33298577.

274. World Health Organization EC for DC. Tick-borne encephalitis in Europe [Internet]. Available from: https://www.ecdc.europa.eu/sites/portal/files/media/en/healthtopics/vectors/world-health-day-2014/Documents/factsheet-tick-borne-encephalitis.pdf

275. Taylor L, Nel LH. Global Epidemiology of Canine Rabies: Past, Present, and Future Prospects. Vet Med Auckl. 2015;6:361–71.

276. Rocklöv J, Dubrow R. Climate change: an enduring challenge for vector-borne disease prevention and control. Nat Immunol. 2020 May;21(5):479–83. doi:10.1038/s41590-020-0648-y PubMed PMID: 32313242; PubMed Central PMCID: PMC7223823.

277. World Health Organization. Japanese encephalitis: Surveillance standards [Internet]. 2018 [cited 2020 Aug 21]. Available from: https://www.who.int/immunization/monitoring_surveillance/burden/vpd/WHO_SurveillanceVaccinePreventable_10_JE_R2.pdf?ua=1

278. Soman Pillai V, Krishna G, Valiya Veettil M. Nipah Virus: Past Outbreaks and Future Containment. Viruses. 2020 Apr 20;12(4). doi:10.3390/v12040465 PubMed PMID: 32325930; PubMed Central PMCID: PMC7232522.

279. Imai N, Gaythorpe KAM, Abbott S, Bhatia S, van Elsland S, Prem K, et al. Adoption and impact of non-pharmaceutical interventions for COVID-19. Wellcome Open Res. 2020;5:59. doi:10.12688/wellcomeopenres.15808.1 PubMed PMID: 32529040; PubMed Central PMCID: PMC7255913.

280. Balicer RD, Huerta M, Levy Y, Davidovitch N, Grotto I. Influenza outbreak control in confined settings. Emerg Infect Dis. 2005 Apr;11(4):579–83. doi:10.3201/eid1104.040845 PubMed PMID: 15829197; PubMed Central PMCID: PMC3320335.

281. Granerod J. Encephalitis in England: incidence and cause. [London, UK]: London School of Hygiene and Tropical Medicine; 2011.

282. Brown JR, Bharucha T, Breuer J. Encephalitis diagnosis using metagenomics: application of next generation sequencing for undiagnosed cases. J Infect. 2018 Mar;76(3):225–40. doi:10.1016/j.jinf.2017.12.014 PubMed PMID: 29305150; PubMed Central PMCID: PMC7112567.

283. World Health Organization. Fourth WHO Model List of Essential In Vitro Diagnostics [Internet]. Geneva, Switzerland; 2023. Available from: https://www.who.int/teams/health-product-policy-and-standards/assistive-and-medical-technology/medical-devices/selection-access-and-use-in-vitro

284. Waldrop G, Goetz LG, Siddiqi OK, Koralnik IJ, Shah H, Thakur KT. The World Health Organization's Essential Diagnostics List: Diagnostics for neurologic disorders. Neurology. 2019 Oct 8;93(15):680–3. doi:10.1212/WNL.0000000000008247 PubMed PMID: 31591174; PubMed Central PMCID: PMC7010326.

285. McLane HC, Berkowitz AL, Patenaude BN, McKenzie ED, Wolper E, Wahlster S, et al. Availability, accessibility, and affordability of neurodiagnostic tests in 37 countries. Neurology. 2015 Nov 3;85(18):1614–22. doi:10.1212/WNL.0000000000002090 PubMed PMID: 26446063; PubMed Central PMCID: PMC4642148.

286. English M, Esamai F, Wasunna A, Were F, Ogutu B, Wamae A, et al. Assessment of inpatient paediatric care in first referral level hospitals in 13 districts in Kenya. Lancet Lond Engl. 2004 Jun 12;363(9425):1948–53. doi:10.1016/S0140-6736(04)16408-8 PubMed PMID: 15194254.

287. English M, Gathara D, Mwinga S, Ayieko P, Opondo C, Aluvaala J, et al. Adoption of recommended practices and basic technologies in a low-income setting. Arch Dis Child. 2014 May;99(5):452–6. doi:10.1136/archdischild-2013-305561 PubMed PMID: 24482351; PubMed Central PMCID: PMC3995214.

288. Schroeder LF, Elbireer A, Jackson JB, Amukele TK. Laboratory Diagnostics Market in East Africa: A Survey of Test Types, Test Availability, and Test Prices in Kampala, Uganda. PloS One. 2015;10(7):e0134578. doi:10.1371/journal.pone.0134578 PubMed PMID: 26226183; PubMed Central PMCID: PMC4520457.

289. Solomon T, Michael BD, Smith PE, Sanderson F, Davies NWS, Hart IJ, et al. Management of suspected viral encephalitis in adults--Association of British Neurologists and British Infection Association National Guidelines. J Infect. 2012 Apr;64(4):347–73. doi:10.1016/j.jinf.2011.11.014 PubMed PMID: 22120595.

290. Venkatesan A, Tunkel AR, Bloch KC, Lauring AS, Sejvar J, Bitnun A, et al. Case definitions, diagnostic algorithms, and priorities in encephalitis: consensus statement of the international

encephalitis consortium. Clin Infect Dis Off Publ Infect Dis Soc Am. 2013 Oct;57(8):1114–28. doi:10.1093/cid/cit458 PubMed PMID: 23861361; PubMed Central PMCID: PMC3783060.

291. Britton PN, Eastwood K, Paterson B, Durrheim DN, Dale RC, Cheng AC, et al. Consensus guidelines for the investigation and management of encephalitis in adults and children in Australia and New Zealand. Intern Med J. 2015 May;45(5):563–76. doi:10.1111/imj.12749 PubMed PMID: 25955462.

292. Jain P, Prakash S, Khan DN, Garg RK, Kumar R, Bhagat A, et al. Aetiology of acute encephalitis syndrome in Uttar Pradesh, India from 2014 to 2016. J Vector Borne Dis. 2017 Dec;54(4):311–6. doi:10.4103/0972-9062.225835 PubMed PMID: 29460860.

293. Tiwari JK, Malhotra B, Chauhan A, Malhotra H, Sharma P, Deeba F, et al. Aetiological study of viruses causing acute encephalitis syndrome in North West India. Indian J Med Microbiol. 2017 Dec;35(4):529–34. doi:10.4103/ijmm.IJMM_17_180 PubMed PMID: 29405145.

294. Ravi V, Hameed SKS, Desai A, Mani RS, Reddy V, Velayudhan A, et al. An algorithmic approach to identifying the aetiology of acute encephalitis syndrome in India: results of a 4-year enhanced surveillance study. Lancet Glob Health. 2022 May;10(5):e685–93. doi:10.1016/S2214-109X(22)00079-1 PubMed PMID: 35427525.

295. Lee TC, Tsai CP, Yuan CL, Wei CY, Tsao WL, Lee RJ, et al. Encephalitis in Taiwan: a prospective hospital-based study. Jpn J Infect Dis. 2003 Dec;56(5–6):193–9. PubMed PMID: 14695429.

296. Chokephaibulkit K, Kankirawatana P, Apintanapong S, Pongthapisit V, Yoksan S, Kositanont U, et al. Viral etiologies of encephalitis in Thai children. Pediatr Infect Dis J. 2001 Feb;20(2):216–8. doi:10.1097/00006454-200102000-00020 PubMed PMID: 11224846.

297. Mawuntu AHP, Bernadus JBB, Dhenni R, Wiyatno A, Anggreani R, Feliana, et al. Detection of central nervous system viral infections in adults in Manado, North Sulawesi, Indonesia. PloS One. 2018;13(11):e0207440. doi:10.1371/journal.pone.0207440 PubMed PMID: 30444898; PubMed Central PMCID: PMC6239303.

298. Säll O, Thulin Hedberg S, Neander M, Tiwari S, Dornon L, Bom R, et al. Etiology of Central Nervous System Infections in a Rural Area of Nepal Using Molecular Approaches. Am J Trop Med Hyg. 2019 Jul;101(1):253–9. doi:10.4269/ajtmh.18-0434 PubMed PMID: 31162021; PubMed Central PMCID: PMC6609203.

299. Giri A, Arjyal A, Koirala S, Karkey A, Dongol S, Thapa SD, et al. Aetiologies of central nervous system infections in adults in Kathmandu, Nepal: a prospective hospital-based study. Sci Rep. 2013;3:2382. doi:10.1038/srep02382 PubMed PMID: 23924886; PubMed Central PMCID: PMC3737500.

300. El-Amin EO, Elbashir MIH, Elamin OE, Mukhtar Y, Abdo H, Abdul-Rahman I, et al. The underlying aetiologies of coma in febrile Sudanese children. Trans R Soc Trop Med Hyg. 2013 May;107(5):307–12. doi:10.1093/trstmh/trt013 PubMed PMID: 23584374.

301. Tshimangani T, Pongo J, Bodi Mabiala J, Yotebieng M, O'Brien NF. Pediatric Acute Severe Neurologic Illness and Injury in an Urban and a Rural Hospital in the Democratic Republic of the Congo. Am J Trop Med Hyg. 2018 May;98(5):1534–40. doi:10.4269/ajtmh.17-0784 PubMed PMID: 29512478; PubMed Central PMCID: PMC5953377.

302. Bastos MS, Lessa N, Naveca FG, Monte RL, Braga WS, Figueiredo LTM, et al. Detection of Herpesvirus, Enterovirus, and Arbovirus infection in patients with suspected central nervous system viral infection in the Western Brazilian Amazon. J Med Virol. 2014 Sep;86(9):1522–7. doi:10.1002/jmv.23953 PubMed PMID: 24760682.

303. Nelson C, Mori N, Ton T, Zunt J, Kochel T, Romero A, et al. Building a network for multicenter, prospective research of central nervous system infections in South America: Process and lessons learned. eNeurologicalSci. 2018 Dec;13:63–9. doi:10.1016/j.ensci.2018.07.001 PubMed PMID: 30547106; PubMed Central PMCID: PMC6284170.

304. World Health Organization. Baseline country survey on medical devices [Internet]. World Health Organisation; 2010 [cited 2020 May 11]. Available from: https://apps.who.int/iris/bitstream/handle/10665/95785/WHO_HSS_EHT_DIM_11.01_eng.pdf?sequence=1&isAllowed=y

305. World Health Organization. Magnetic resonance imaging units (per million population), total density [Internet]. [cited 2024 Sep 23]. Available from: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/total-density-per-million-population-magnetic-resonance-imaging

306. Statista GmbH. [Internet]. Hamburg, Germany; [cited 2022 Mar 31]. Available from: https://www.statista.com/statistics/282401/density-of-magnetic-resonance-imaging-units-by-country/

307. Jalloul M, Miranda-Schaeubinger M, Noor AM, Stein JM, Amiruddin R, Derbew HM, et al. MRI scarcity in low- and middle-income countries. NMR Biomed. 2023 Dec;36(12):e5022. doi:10.1002/nbm.5022 PubMed PMID: 37574441.

308. Ogbole GI, Adeyomoye AO, Badu-Peprah A, Mensah Y, Nzeh DA. Survey of magnetic resonance imaging availability in West Africa. Pan Afr Med J. 2018;30:240. doi:10.11604/pamj.2018.30.240.14000 PubMed PMID: 30574259; PubMed Central PMCID: PMC6295297.

309. Pan H, Steixner-Kumar AA, Seelbach A, Deutsch N, Ronnenberg A, Tapken D, et al. Multiple inducers and novel roles of autoantibodies against the obligatory NMDAR subunit NR1: a translational study from chronic life stress to brain injury. Mol Psychiatry. 2020 Feb 24. doi:10.1038/s41380-020-0672-1 PubMed PMID: 32089545.

310. Dahm L, Ott C, Steiner J, Stepniak B, Teegen B, Saschenbrecker S, et al. Seroprevalence of autoantibodies against brain antigens in health and disease. Ann Neurol. 2014 Jul;76(1):82–94. doi:10.1002/ana.24189 PubMed PMID: 24853231.

311. Zerche M, Weissenborn K, Ott C, Dere E, Asif AR, Worthmann H, et al. Preexisting Serum Autoantibodies Against the NMDAR Subunit NR1 Modulate Evolution of Lesion Size in Acute Ischemic Stroke. Stroke. 2015 May;46(5):1180–6. doi:10.1161/STROKEAHA.114.008323 PubMed PMID: 25765725.

312. Hammer C, Stepniak B, Schneider A, Papiol S, Tantra M, Begemann M, et al. Neuropsychiatric disease relevance of circulating anti-NMDA receptor autoantibodies depends on blood-brain barrier integrity. Mol Psychiatry. 2014 Oct;19(10):1143–9. doi:10.1038/mp.2013.110 PubMed PMID: 23999527.

313. Irani SR. Autoimmune Encephalitis. Contin Minneap Minn. 2024 Aug 1;30(4):995–1020. doi:10.1212/CON.0000000000001448 PubMed PMID: 39088286.

314. Douma B, Ben Younes T, Benrhouma H, Miladi Z, Zamali I, Rouissi A, et al. Autoimmune Encephalitis in Tunisia: Report of a Pediatric Cohort. J Immunol Res. 2021;2021:6666117. doi:10.1155/2021/6666117 PubMed PMID: 34056010; PubMed Central PMCID: PMC8131150.

315. Saraya AW, Worachotsueptrakun K, Vutipongsatorn K, Sonpee C, Hemachudha T. Differences and diversity of autoimmune encephalitis in 77 cases from a single tertiary care center. BMC Neurol. 2019 Nov 6;19(1):273. doi:10.1186/s12883-019-1501-5 PubMed PMID: 31694559; PubMed Central PMCID: PMC6833261.

316. Wickramasinghe N, Dasanayake D, Malavige N, de Silva R, Chang T. Autoimmune encephalitis in a South Asian population. BMC Neurol. 2021 May 19;21(1):203. doi:10.1186/s12883-021-02232-6 PubMed PMID: 34011309; PubMed Central PMCID: PMC8132416.

317. Nguyen Thi Hoang M, Nguyen Hoan P, Le Van T, McBride A, Ho Dang Trung N, Tran Tan T, et al. First reported cases of anti-NMDA receptor encephalitis in Vietnamese adolescents and adults. J Neurol Sci. 2017 Feb 15;373:250–3. doi:10.1016/j.jns.2017.01.004 PubMed PMID: 28131199; PubMed Central PMCID: PMC5293131.

318. Suthar R, Saini AG, Sankhyan N, Sahu JK, Singhi P. Childhood Anti-NMDA Receptor Encephalitis. Indian J Pediatr. 2016 Jul;83(7):628–33. doi:10.1007/s12098-015-1988-8 PubMed PMID: 26801499.

319. Pagaling GT, Turalde CWR, Jamora RDG. Autoimmune Encephalitis in the Philippines: A Scoping Review on the Treatment Gaps, Challenges, and Current State of Care. Front Neurol. 2022;13:788309. doi:10.3389/fneur.2022.788309 PubMed PMID: 35197921; PubMed Central PMCID: PMC8858951.

320. Vasconcelos G de A, Barreira RM, Antoniollo KENT, Pinheiro AMN, Maia CFR, Alves DMBS, et al. Autoimmune Encephalitis in Latin America: A Critical Review. Front Neurol. 2020;11:606350. doi:10.3389/fneur.2020.606350 PubMed PMID: 33551968; PubMed Central PMCID: PMC7859257.

321. Morillos MB, Borelli WV, Noll G, Piccini CD, Leite MB, Finkelsztejn A, et al. Autoimmune encephalitis in a resource-limited public health setting: a case series analysis. Arq Neuropsiquiatr. 2024 Feb;82(2):1–10. doi:10.1055/s-0044-1779054 PubMed PMID: 38325385; PubMed Central PMCID: PMC10849825.

322. WHO Technical Task Force for “Defeating Meninigitis by 2030". Defeating meningitis by 2030: baseline situation analysis. 2019 Feb.

323. Ayieko P, Ogero M, Makone B, Julius T, Mbevi G, Nyachiro W, et al. Characteristics of admissions and variations in the use of basic investigations, treatments and outcomes in Kenyan hospitals within a new Clinical Information Network. Arch Dis Child. 2016 Mar;101(3):223–9. doi:10.1136/archdischild-2015-309269 PubMed PMID: 26662925; PubMed Central PMCID: PMC4789757.

324. Zida S, Kolia-Diafouka P, Kania D, Sotto A, Foulongne V, Bolloré K, et al. Combined testing for herpes simplex virus and Mycobacterium tuberculosis DNA in cerebrospinal fluid of patients with aseptic meningitis in Burkina Faso, West Africa. J Clin Lab Anal. 2019 Mar;33(3):e22719. doi:10.1002/jcla.22719 PubMed PMID: 30474140; PubMed Central PMCID: PMC6818613.

325. Ahmed SS, Alp E, Ulu-Kilic A, Doganay M. Establishing molecular microbiology facilities in developing countries. J Infect Public Health. 2015 Dec;8(6):513–25. doi:10.1016/j.jiph.2015.04.029 PubMed PMID: 26116452.

326. Samannodi M, Hansen M, Allana A, Hasbun R. Compliance with international guidelines in adults with encephalitis. J Clin Virol Off Publ Pan Am Soc Clin Virol. 2020 Jun;127:104369. doi:10.1016/j.jcv.2020.104369 PubMed PMID: 32315818; PubMed Central PMCID: PMC7194944.

327. The Statistics Portal. Number of magnetic resonance imaging (MRI) units in selected countries as of 2017 (per million population) [Internet]. [cited 2020 May 15]. Available from: https://www.statista.com/statistics/282401/density-of-magnetic-resonance-imaging-units-by-country/

328. Malkin RA. Design of health care technologies for the developing world. Annu Rev Biomed Eng. 2007;9:567–87. doi:10.1146/annurev.bioeng.9.060906.151913 PubMed PMID: 17430083.

329. World Health Organization. Why encephalitis matters? Report of the virtual meeting, 28-29 June 2022 [Internet]. Geneva, Switzerland: World Health Organization; [cited 2023 Mar 13]. Available from: https://apps.who.int/iris/handle/10665/366223

330. Sokhi DS, Bhogal OS. Autoimmune Encephalitis is Recognised as an Important Differential Diagnosis in a Kenyan Tertiary Referral Centre. BMJ Mil Health. 2020 Feb 2. doi:10.1136/jramc-2019-001338 PubMed PMID: 32015184.

331. Erazo R, González J, Quintanilla C, Devaud C, Gayoso C, Toledo X, et al. [Subacute anti-N-methyl-D-aspartate receptor encephalitis. A serie of 13 paediatric cases]. Rev Chil Pediatr. 2016 Dec;87(6):487–93. doi:10.1016/j.rchipe.2016.06.006 PubMed PMID: 27476614.

332. Ghimire P, Khanal UP, Gajurel BP, Karn R, Rajbhandari R, Paudel S, et al. Anti-LGI1, anti-GABABR, and Anti-CASPR2 encephalitides in Asia: A systematic review. Brain Behav. 2020 Aug 12;e01793. doi:10.1002/brb3.1793 PubMed PMID: 32783406.

333. Ganesh A, Wesley SF. Practice Current: When do you suspect autoimmune encephalitis and what is the role of antibody testing? Neurol Clin Pract. 2018 Feb;8(1):67–73. doi:10.1212/CPJ.0000000000000423 PubMed PMID: 29517071; PubMed Central PMCID: PMC5839684.

334. McNerney R. Diagnostics for Developing Countries. Diagn Basel Switz. 2015 May 19;5(2):200–9. doi:10.3390/diagnostics5020200 PubMed PMID: 26854149; PubMed Central PMCID: PMC4665590.

335. Petti CA, Polage CR, Quinn TC, Ronald AR, Sande MA. Laboratory medicine in Africa: a barrier to effective health care. Clin Infect Dis Off Publ Infect Dis Soc Am. 2006 Feb 1;42(3):377–82. doi:10.1086/499363 PubMed PMID: 16392084.

336. World Health Organization. The selection and use of essential medicines, 2025: WHO Model List of Essential Medicines, 24th list [Internet]. [cited 2025 Oct 13]. Available from: https://www.who.int/publications/i/item/B09474

337. Stahl JP, Mailles A. Herpes simplex virus encephalitis update. Curr Opin Infect Dis. 2019 Jun;32(3):239–43. doi:10.1097/QCO.0000000000000554 PubMed PMID: 30921087.

338. Bharucha T, Nashef L, Moran N, Watkins S, Brown D, Zuckerman M. A 9-month retrospective evaluation of the aetiology and management of patients presenting with encephalitis/meningoencephalitis at a South London hospital. Epidemiol Infect. 2020 Feb 5;148:e23. doi:10.1017/S0950268820000047 PubMed PMID: 32019624; PubMed Central PMCID: PMC7026895.

339. Backman R, Foy R, Diggle PJ, Kneen R, Easton A, Defres S, et al. A pragmatic cluster randomised controlled trial of a tailored intervention to improve the initial management of suspected encephalitis. PloS One. 2018;13(12):e0202257. doi:10.1371/journal.pone.0202257 PubMed PMID: 30521521; PubMed Central PMCID: PMC6283633.

340. Mekan SF, Wasay M, Khelaeni B, Saeed Z, Hassan A, Sheerani M. Herpes simplex encephalitis: analysis of 68 cases from a tertiary care hospital in Karachi, Pakistan. JPMA J Pak Med Assoc. 2005 Apr;55(4):146–8. PubMed PMID: 15918625.

341. Ayukawa R, Fujimoto H, Ayabe M, Shoji H, Matsui R, Iwata Y, et al. An unexpected outbreak of Japanese encephalitis in the Chugoku district of Japan, 2002. Jpn J Infect Dis. 2004 Apr;57(2):63–6. PubMed PMID: 15118213.

342. Ngan TTD, Tuyet NT, Hung DT, Cap NT, Nguyen DM, Dat VQ. Clinical characteristics and outcomes of patients with Herpes Simplex Encephalitis in Vietnam: a retrospective study. BMC Infect Dis. 2024 Jun 3;24(1):556. doi:10.1186/s12879-024-09453-3 PubMed PMID: 38831304; PubMed Central PMCID: PMC11149218.

343. Mittal N, Mittal R, Singh S, Godara S. The Availability of Essential Antimicrobials in Public and Private Sector Facilities: A Cross-Sectional Survey in a District of North India. Antibiot Basel Switz. 2024 Jan 29;13(2). doi:10.3390/antibiotics13020131 PubMed PMID: 38391517; PubMed Central PMCID: PMC10886159.

344. Javier Balan D, Bardach A, Palermo C, Alconada T, Sandoval M, Nieto Guevara J, et al. Economic burden of herpes zoster in Latin America: A systematic review and meta-analysis. Hum Vaccines Immunother. 2022 Dec 30;18(7):2131167. doi:10.1080/21645515.2022.2131167 PubMed PMID: 36519226; PubMed Central PMCID: PMC9794010.

345. Kahwagi J. Infectious encephalitis during the second wave of COVID-19: an observational study among hospitalised patients in Dakar, Senegal. Encephalitis Conference: Encephalitis 2021. 2021 Dec 7.

346. Corbell C, Stergachis A, Ndowa F, Ndase P, Barnes L, Celum C. Genital ulcer disease treatment policies and access to acyclovir in eight sub-Saharan African countries. Sex Transm Dis. 2010 Aug;37(8):488–93. doi:10.1097/OLQ.0b013e3181e212e5 PubMed PMID: 20539260.

347. World Health Organization. Atlas: country resources for neurological disorders – 2nd ed. [Internet]. World Health Organization; 2017 [cited 2020 Feb 10]. Available from: https://apps.who.int/iris/bitstream/handle/10665/258947/9789241565509-eng.pdf;jsessionid=BC13F010E798149DEA811941023D68D2?sequence=1

348. Kelly C, Sohal A, Michael BD, Riordan A, Solomon T, Kneen R. Suboptimal management of central nervous system infections in children: a multi-centre retrospective study. BMC Pediatr. 2012 Sep 7;12:145. doi:10.1186/1471-2431-12-145 PubMed PMID: 22958329; PubMed Central PMCID: PMC3443041.

349. Babar ZUD. Forming a medicines pricing policy for low and middle-income countries (LMICs): the case for Pakistan. J Pharm Policy Pract. 2022 Feb 24;15(1):9. doi:10.1186/s40545-022-00413-3 PubMed PMID: 35209945; PubMed Central PMCID: PMC8867617.

350. Pouplin T, Pouplin JN, Van Toi P, Lindegardh N, Rogier van Doorn H, Hien TT, et al. Valacyclovir for herpes simplex encephalitis. Antimicrob Agents Chemother. 2011 Jul;55(7):3624–6. doi:10.1128/AAC.01023-10 PubMed PMID: 21576427; PubMed Central PMCID: PMC3122427.

351. World Health Organization. Global approaches to addressing shortages of essential medicines in health systems. Vol. 30. 2016;30(2):180–5.

352. GBD 2015 Neurological Disorders Collaborator Group. Global, regional, and national burden of neurological disorders during 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Neurol. 2017 Nov;16(11):877–97. Located at: PubMed; 28931491. doi:10.1016/S1474-4422(17)30299-5

353. Kissani N, Liqali L, Hakimi K, Mugumbate J, Daniel GM, Ibrahim EAA, et al. Why does Africa have the lowest number of Neurologists and how to cover the Gap? J Neurol Sci. 2021 Dec 29;434:120119. doi:10.1016/j.jns.2021.120119 PubMed PMID: 34982975.

354. Bassetti CLA, Accorroni A, Arnesen A, Basri HB, Berger T, Berlit P, et al. General neurology: Current challenges and future implications. Eur J Neurol. 2024 Jun;31(6):e16237. doi:10.1111/ene.16237 PubMed PMID: 38545838; PubMed Central PMCID: PMC11236055.

355. Access to Pediatric Neurology Training and Services Worldwide: A Survey by the International Child Neurology Association. Neurology. 2024 Mar 12;102(5):e208125. doi:10.1212/WNL.0000000000208125 PubMed PMID: 38315962; PubMed Central PMCID: PMC11384657.

356. Hillis JM, Berkowitz AL. Neurology Training Worldwide. Semin Neurol. 2018;38(2):135–44. doi:10.1055/s-0038-1647246 PubMed PMID: 29791939.

357. Fong SL, Lim KS, Lim SH, Octaviana F, Tran TC, Thuy Le MA, et al. Education Research: Training of Neurologists in South East Asian Countries: A Cross-Sectional Survey on the Current Neurology Curriculum. Neurol Educ. 2025 Mar;4(1):e200201. doi:10.1212/NE9.0000000000200201 PubMed PMID: 40104779; PubMed Central PMCID: PMC11919386.

358. Khan F, Amatya B, Mannan H, Rathore F. Neurorehabilitation in Developing Countries: Challenges and the Way Forward. Phys Med Rehabil Int. 2(9):1070.

359. Klein A, Berger TC, Hapfelmeier A, Schaffert M, Matuja W, Schmutzhard E, et al. Does the presence of a specialist doctor reduce the burden of disease in people with epilepsy in low-resource settings? A comparison of two epilepsy clinics in rural Tanzania. Epilepsy Behav EB. 2023 Feb;139:109030. doi:10.1016/j.yebeh.2022.109030 PubMed PMID: 36577550.

360. DiBiase RM, Salas RME, Gamaldo CE, Nutakki A, Elicer I, Attarian HP, et al. Training in Neurology: Implementation and Evaluation of an Objective Structured Clinical-Examination Tool for Neurology Postgraduate Trainees in Lusaka, Zambia. Neurology. 2021 Aug 17;97(7):e750–4. doi:10.1212/WNL.0000000000012134 PubMed PMID: 33931541.

361. BMJ Learning. Diagnosis and management of encephalitis.

362. McDonough A, Chishimba L, Chomba M, Zimba S, Mwendaweli N, Asukile M, et al. Neurophobia in Africa: Survey responses from fifteen African countries. J Neurol Sci. 2022 Jan 24;434:120161. doi:10.1016/j.jns.2022.120161 PubMed PMID: 35093723.

363. Public Health England. Notifications of infectious diseases (NOIDs) [Internet]. [cited 2020 Aug 21]. Available from: https://www.gov.uk/government/collections/notifications-of-infectious-diseases-noids#reports

364. Donoso Mantke O, Vaheri A, Ambrose H, Koopmans M, de Ory F, Zeller H, et al. Analysis of the surveillance situation for viral encephalitis and meningitis in Europe. Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull. 2008 Jan 17;13(3). doi:10.2807/ese.13.03.08017-en PubMed PMID: 18445392.

365. Touch S, Grundy J, Hills S, Rani M, Samnang C, Khalakdina A, et al. The rationale for integrated childhood meningoencephalitis surveillance: a case study from Cambodia. Bull World Health Organ. 2009 Apr;87(4):320–4. doi:10.2471/blt.08.052951 PubMed PMID: 19551241; PubMed Central PMCID: PMC2672582.

366. Cavallaro KF, Sandhu HS, Hyde TB, Johnson BW, Fischer M, Mayer LW, et al. Expansion of syndromic vaccine preventable disease surveillance to include bacterial meningitis and Japanese encephalitis: evaluation of adapting polio and measles laboratory networks in Bangladesh, China and India, 2007-2008. Vaccine. 2015 Feb 25;33(9):1168–75. doi:10.1016/j.vaccine.2015.01.004 PubMed PMID: 25597940; PubMed Central PMCID: PMC4830482.

367. Angulo FJ, Halsby K, Davidson A, Ravikumar S, Pilz A, Stark JH, et al. Publicly available surveillance data on tick-borne encephalitis in Europe, 2023. Ticks Tick-Borne Dis. 2024 Aug 12;15(6):102388. doi:10.1016/j.ttbdis.2024.102388 PubMed PMID: 39137541.

368. European Centre for Disease Prevention and Control. Surveillance systems overview for 2022 [Internet]. 2023 [cited 2024 Sep 23]. Available from: https://www.ecdc.europa.eu/en/publications-data/surveillance-systems-overview-2022

369. European Centre for Disease Prevention and Control. Epidemiological situation of tick-borne encephalitis in the European Union and European Free Trade Association countries. Stockholm: ECDC; 2012.

370. Pham QD, Phan LT, Nguyen TPT, Doan QMN, Nguyen HD, Luong QC, et al. An Evaluation of the Rabies Surveillance in Southern Vietnam. Front Public Health. 2021;9:610905. doi:10.3389/fpubh.2021.610905 PubMed PMID: 33996708; PubMed Central PMCID: PMC8116623.

371. Rubeshkumar P, Majella MG, Jahan N, Sakthivel M, Krishnamoorthy Y. Secular trends of rabies in India, 2005-2020: importance of surveillance and implications for elimination strategies. Lancet Reg Health Southeast Asia. 2024 Jan;20:100322. doi:10.1016/j.lansea.2023.100322 PubMed PMID: 38234705; PubMed Central PMCID: PMC10794097.

372. Public Health England. Emerging infections: how and why they arise [Internet]. London, UK: Public Health England; 2019 Feb [cited 2022 Apr 29]. Available from: https://www.gov.uk/government/publications/emerging-infections-characteristics-epidemiology-and-global-distribution/emerging-infections-how-and-why-they-arise

373. Baker RE, Mahmud AS, Miller IF, Rajeev M, Rasambainarivo F, Rice BL, et al. Infectious disease in an era of global change. Nat Rev Microbiol. 2022 Apr;20(4):193–205. doi:10.1038/s41579-021-00639-z PubMed PMID: 34646006; PubMed Central PMCID: PMC8513385.

374. Venkatesan A. Emerging infectious encephalitides. Curr Opin Neurol. 2021 Jun 1;34(3):410–6. doi:10.1097/WCO.0000000000000936 PubMed PMID: 33767094.

375. McEntire CRS, Song KW, McInnis RP, Rhee JY, Young M, Williams E, et al. Neurologic Manifestations of the World Health Organization's List of Pandemic and Epidemic Diseases. Front Neurol. 2021;12:634827. doi:10.3389/fneur.2021.634827 PubMed PMID: 33692745; PubMed Central PMCID: PMC7937722.

376. Bettis AA, L'Azou Jackson M, Yoon IK, Breugelmans JG, Goios A, Gubler DJ, et al. The global epidemiology of chikungunya from 1999 to 2020: A systematic literature review to inform the development and introduction of vaccines. PLoS Negl Trop Dis. 2022 Jan;16(1):e0010069. doi:10.1371/journal.pntd.0010069 PubMed PMID: 35020717; PubMed Central PMCID: PMC8789145.

377. Mailles A, Stahl JP, Bloch KC. Update and new insights in encephalitis. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2017 Sep;23(9):607–13. Located at: PubMed; 28501667. doi:10.1016/j.cmi.2017.05.002

378. Maure C, Khazhidinov K, Kang H, Auzenbergs M, Moyersoen P, Abbas K, et al. Chikungunya vaccine development, challenges, and pathway toward public health impact. Vaccine. 2024 Oct 27;42(26):126483. doi:10.1016/j.vaccine.2024.126483 PubMed PMID: 39467413.

379. Brito Ferreira ML, Militão de Albuquerque M de FP, de Brito CAA, de Oliveira França RF, Porto Moreira ÁJ, de Morais Machado MÍ, et al. Neurological disease in adults with Zika and chikungunya virus infection in Northeast Brazil: a prospective observational study. Lancet Neurol. 2020 Oct;19(10):826–39. doi:10.1016/S1474-4422(20)30232-5 PubMed PMID: 32949543; PubMed Central PMCID: PMC7494308.

380. Cerny T, Schwarz M, Schwarz U, Lemant J, Gérardin P, Keller E. The Range of Neurological Complications in Chikungunya Fever. Neurocrit Care. 2017 Dec;27(3):447–57. doi:10.1007/s12028-017-0413-8 PubMed PMID: 28741102.

381. Teo TH, Her Z, Tan JJL, Lum FM, Lee WWL, Chan YH, et al. Caribbean and La Réunion Chikungunya Virus Isolates Differ in Their Capacity To Induce Proinflammatory Th1 and NK Cell Responses and Acute Joint Pathology. J Virol. 2015 Aug;89(15):7955–69. doi:10.1128/JVI.00909-15 PubMed PMID: 25995257; PubMed Central PMCID: PMC4505608.

382. Gérardin P, Couderc T, Bintner M, Tournebize P, Renouil M, Lémant J, et al. Chikungunya virus-associated encephalitis: A cohort study on La Réunion Island, 2005-2009. Neurology. 2016 Jan 5;86(1):94–102. doi:10.1212/WNL.0000000000002234 PubMed PMID: 26609145.

383. European Centre for Disease Prevention and Control. Chikungunya worldwide overview - Situation update, September 2024 [Internet]. [cited 2024 Nov 18]. Available from: https://www.ecdc.europa.eu/en/chikungunya-monthly

384. Oliveira JRM, Gérardin P, Couderc T, Randrianaivo H, Fritel X, Lecuit M. Chikungunya virus-associated encephalitis: A cohort study on La Réunion Island, 2005-2009. Neurology. 2016 May 24;86(21):2025–6. doi:10.1212/WNL.0000000000002732 PubMed PMID: 27217467.

385. Moreira J, Brasil P, Dittrich S, Siqueria A. Mapping the global landscape of chikungunya rapid diagnostic tests: a scoping review [Internet]. [cited 2022 May 4]. Available from: https://www.medrxiv.org/content/10.1101/2022.01.28.22270018v1.full.pdf

386. World Health Organization. Nipah virus infection [Internet]. [cited 2022 May 3]. Available from: https://www.who.int/health-topics/nipah-virus-infection#tab=tab_1

387. Centers for Disease Control and Prevention (CDC). Nipah Virus [Internet]. [cited 2022 May 3]. Available from: https://www.cdc.gov/vhf/nipah/index.html

388. World Health Organization. NIPAH Baseline Situation Analysis [Internet]. Geneva, Switzerland: World Health Organization; [cited 2022 May 3]. Available from: https://cdn.who.int/media/docs/default-source/documents/health-topics/nipah/who_nipah_baseline_situation_analysis_27jan20188b415c76-8649-4e98-b18f-18c6134f3819.pdf?sfvrsn=8d3de3b2_1&download=true

389. Dhaked RK. Emergence of Nipah Virus: Need More R&D and Public Health Infrastructure [Internet]. Vol. 9. 2018;9(2). Available from: file:///C:/Users/pjks1/Downloads/Emergence_of_Nipah_Virus_Need_More_RD_and_Public_H.pdf

390. Gómez Román R, Tornieporth N, Cherian NG, Shurtleff AC, L'Azou Jackson M, Yeskey D, et al. Medical countermeasures against henipaviruses: a review and public health perspective. Lancet Infect Dis. 2022 Jan;22(1):e13–27. doi:10.1016/S1473-3099(21)00400-X PubMed PMID: 34735799; PubMed Central PMCID: PMC8694750.

391. World Health Organization. WHO Coronavirus (COVID-19) Dashboard [Internet]. [cited 2022 May 3]. Available from: https://covid19.who.int/

392. Siow I, Lee KS, Zhang JJY, Saffari SE, Ng A. Encephalitis as a neurological complication of COVID-19: A systematic review and meta-analysis of incidence, outcomes, and predictors. Eur J Neurol. 2021 Oct;28(10):3491–502. doi:10.1111/ene.14913 PubMed PMID: 33982853; PubMed Central PMCID: PMC8239820.

393. Walton DWA, Thakur KT, Venkatesan A, Breen G, Solomon T, Michael BD. Encephalitis in a Pandemic. Front Neurol. 2021;12:637586. doi:10.3389/fneur.2021.637586 PubMed PMID: 33643210; PubMed Central PMCID: PMC7902878.

394. Koupaei M, Shadab Mehr N, Mohamadi MH, Asadi A, Abbasimoghaddam S, Shekartabar A, et al. Clinical symptoms, diagnosis, treatment, and outcome of COVID-19-associated encephalitis: A systematic review of case reports and case series. J Clin Lab Anal. 2022 Apr 18;e24426. doi:10.1002/jcla.24426 PubMed PMID: 35435264.

395. Shao Z, Feng Y, Zhong L, Xie Q, Lei M, Liu Z, et al. Clinical efficacy of intravenous immunoglobulin therapy in critical ill patients with COVID-19: a multicenter retrospective cohort study. Clin Transl Immunol. 2020;9(10):e1192. doi:10.1002/cti2.1192 PubMed PMID: 33082954; PubMed Central PMCID: PMC7557105.

396. Freire-Álvarez E, Guillén L, Lambert K, Baidez A, García-Quesada M, Andreo M, et al. COVID-19-associated encephalitis successfully treated with combination therapy. Clin Infect Pract. 2020 Oct;7:100053. doi:10.1016/j.clinpr.2020.100053 PubMed PMID: 33163956; PubMed Central PMCID: PMC7604011.

397. Ledford H, Cyranoski D, Van Noorden R. The UK has approved a COVID vaccine - here's what scientists now want to know. Nature. 2020 Dec;588(7837):205–6. doi:10.1038/d41586-020-03441-8 PubMed PMID: 33288887.

398. COVID-19 Vaccine Tracker [Internet]. [cited 2023 Apr 20]. Available from: https://covid19.trackvaccines.org/

399. Ball P. The lightning-fast quest for COVID vaccines - and what it means for other diseases. Nature. 2021 Jan;589(7840):16–8. doi:10.1038/d41586-020-03626-1 PubMed PMID: 33340018.

400. Kaur P, Jain R, Kumar P, Randev S, Guglani V. Clinical Spectrum and Outcome of Acute Encephalitis Syndrome in Children with Scrub Typhus: A Series of Eight Cases from India. Indian J Crit Care Med Peer-Rev Off Publ Indian Soc Crit Care Med. 2020 Sep;24(9):885–7. doi:10.5005/jp-journals-10071-23590 PubMed PMID: 33132580; PubMed Central PMCID: PMC7584842.

401. Banerjee A, Kulkarni S. Orientia tsutsugamushi: The dangerous yet neglected foe from the East. Int J Med Microbiol IJMM. 2021 Jan;311(1):151467. doi:10.1016/j.ijmm.2020.151467 PubMed PMID: 33338890.

402. Garg D, Manesh A. Neurological Facets of Scrub Typhus: A Comprehensive Narrative Review. Ann Indian Acad Neurol. 2021 Dec;24(6):849–64. doi:10.4103/aian.aian_739_21 PubMed PMID: 35359522; PubMed Central PMCID: PMC8965938.

403. Alam A, Agarwal P, Prabha J, Jain A, Kalyan RK, Kumar C, et al. Prediction Rule for Scrub Typhus Meningoencephalitis in Children: Emerging Disease in North India. J Child Neurol. 2020 Oct;35(12):820–7. doi:10.1177/0883073820933148 PubMed PMID: 32580611.

404. Mittal M, Bondre V, Murhekar M, Deval H, Rose W, Verghese VP, et al. Acute Encephalitis Syndrome in Gorakhpur, Uttar Pradesh, 2016: Clinical and Laboratory Findings. Pediatr Infect Dis J. 2018 Nov;37(11):1101–6. doi:10.1097/INF.0000000000002099 PubMed PMID: 29746378.

405. Jamil MD, Hussain M, Lyngdoh M, Sharma S, Barman B, Bhattacharya PK. Scrub typhus meningoencephalitis, a diagnostic challenge for clinicians: A hospital based study from North-East India. J Neurosci Rural Pract. 2015 Dec;6(4):488–93. doi:10.4103/0976-3147.169769 PubMed PMID: 26752890; PubMed Central PMCID: PMC4692003.

406. Prakash Gangwar S, Thangaraj JWV, Zaman K, Vairamani V, Mittal M, Murhekar M. Sequelae Following Acute Encephalitis Syndrome Caused by Orientia Tsutsugamushi. Pediatr Infect Dis J. 2020 May;39(5):e52–4. doi:10.1097/INF.0000000000002595 PubMed PMID: 32301923.

407. Basu S, Saha A, Sarkar S, Sinha MK, Das MK, Datta R, et al. Clinical Profile and Therapeutic Response of Scrub Typhus in Children: A Recent Trend from Eastern India. J Trop Pediatr. 2019 Apr 1;65(2):139–46. doi:10.1093/tropej/fmy027 PubMed PMID: 29800384.

408. Damodar T, Singh B, Prabhu N, Marate S, Gowda VK, Lalitha AV, et al. Association of Scrub Typhus in Children with Acute Encephalitis Syndrome and Meningoencephalitis, Southern India. Emerg Infect Dis. 2023 Apr;29(4):711–22. doi:10.3201/eid2904.221157 PubMed PMID: 36957990; PubMed Central PMCID: PMC10045701.

409. McClymont H, Bambrick H, Si X, Vardoulakis S, Hu W. Future perspectives of emerging infectious diseases control: A One Health approach. One Health Amst Neth. 2022

Jun;14:100371. doi:10.1016/j.onehlt.2022.100371 PubMed PMID: 35075433; PubMed Central PMCID: PMC8770246.

410. Heymann DL, Dar OA. Prevention is better than cure for emerging infectious diseases. BMJ. 2014 Feb 21;348:g1499. doi:10.1136/bmj.g1499 PubMed PMID: 24563451.

411. Centers for Disease Control and Prevention (CDC). One Health [Internet]. [cited 2022 May 3]. Available from: https://www.cdc.gov/onehealth/index.html

412. World Health Organization. Health Promotion Glossary [Internet]. Geneva, Switzerland; 1998 [cited 2020 Nov 18]. Available from: https://www.who.int/healthpromotion/about/HPR%20Glossary%201998.pdf?ua=1

413. Piamonte BLC, Easton A, Wood GK, Davies NWS, Granerod J, Michael BD, et al. Addressing vaccine-preventable encephalitis in vulnerable populations. Curr Opin Neurol. 2023 Jun 1;36(3):185–97. doi:10.1097/WCO.0000000000001158 PubMed PMID: 37078664.

414. World Health Organization. Intersectoral global action plan on Epilepsy and other neurological disorders 2022–2031 [Internet]. Geneva, Switzerland; 2023 [cited 2024 Oct 16]. Available from: https://www.who.int/publications/i/item/9789240076624

415. Grisold W, Freedman M, Gouider R, Guekht A, Lewis S, Medina M, et al. The Intersectoral Global Action Plan (IGAP): A unique opportunity for neurology across the globe. J Neurol Sci. 2023 Jun 15;449:120645. doi:10.1016/j.jns.2023.120645 PubMed PMID: 37062176.

416. Family Medical Practice Vietnam. Japanese encephalitis [Internet]. [cited 2024 Oct 16]. Available from: https://www.vietnammedicalpractice.com/hcmc/en/news/japanese-encephalitis

417. Harrison K, Rahimi N, Danovaro-Holliday MC. Factors limiting data quality in the expanded programme on immunization in low and middle-income countries: A scoping review. Vaccine. 2020 Jun 19;38(30):4652–63. doi:10.1016/j.vaccine.2020.02.091 PubMed PMID: 32446834.

418. Ahmed S, Chase LE, Wagnild J, Akhter N, Sturridge S, Clarke A, et al. Community health workers and health equity in low- and middle-income countries: systematic review and recommendations for policy and practice. Int J Equity Health. 2022 Apr 11;21(1):49. doi:10.1186/s12939-021-01615-y PubMed PMID: 35410258; PubMed Central PMCID: PMC8996551.

419. Easton A. Life after encephalitis: A narrative approach. Oxford, UK: Routledge; 2016.

420. Philpott DCE, Nolan MS, Evert N, Mayes B, Hesalroad D, Fonken E, et al. Acute and Delayed Deaths after West Nile Virus Infection, Texas, USA, 2002-2012. Emerg Infect Dis. 2019 Feb;25(2):256–64. doi:10.3201/eid2502.181250 PubMed PMID: 30667356; PubMed Central PMCID: PMC6346437.

421. Sullivan AB, Miller D. Who is Taking Care of the Caregiver? J Patient Exp. 2015 May;2(1):7–12. doi:10.1177/237437431500200103 PubMed PMID: 28725810; PubMed Central PMCID: PMC5513610.

422. World Health Organization. Neurological disorders: public health challenges [Internet]. Geneva, Switzerland; 2006 [cited 2020 Nov 20]. Available from: https://www.who.int/publications/i/item/9789241563369

423. United Nations. Convention on the Rights of Persons with Disabilities [Internet]. 2006 [cited 2020 Nov 20]. Available from: https://www.un.org/development/desa/disabilities/convention-on-the-rights-of-persons-with-disabilities.html

424. Granerod J, Huang Y, Davies NWS, Sequeira PC, Mwapasa V, Rupali P, et al. Global Landscape of Encephalitis: Key Priorities to Reduce Future Disease Burden. Clin Infect Dis Off Publ Infect Dis Soc Am. 2023 Nov 30;77(11):1552–60. doi:10.1093/cid/ciad417 PubMed PMID: 37436770; PubMed Central PMCID: PMC10686956.

425. Turner-Stokes L, Williams H, Bill A, Bassett P, Sephton K. Cost-efficiency of specialist inpatient rehabilitation for working-aged adults with complex neurological disabilities: a multicentre cohort analysis of a national clinical data set. BMJ Open. 2016 Feb 24;6(2):e010238. doi:10.1136/bmjopen-2015-010238 PubMed PMID: 26911586; PubMed Central PMCID: PMC4769383.

426. World Federation for Neurorehabilitation. Neurorehabilitation in developing countries-time for action. 2015.

427. Cárdenas G, Salgado P, Laura-Foronda E, Popoca-Rodriguez I, Delgado-Hernández RD, Rojas R, et al. Neglected and (re-)emergent infections of the CNS i n low-/middle-income countries. Infez Med. 2021;29(4):513–25. doi:10.53854/liim-2904-3 PubMed PMID: 35146359; PubMed Central PMCID: PMC8805465.

428. Gimigliano F, Negrini S. The World Health Organization 'Rehabilitation 2030: a call for action'. Eur J Phys Rehabil Med. 2017 Apr;53(2):155–68. doi:10.23736/S1973-9087.17.04746-3 PubMed PMID: 28382807.

429. YouGov Plc. 2018.

430. Ghimire S, Dhakal S. Japanese encephalitis: Challenges and intervention opportunities in Nepal. Vet World. 2015 Jan;8(1):61–5. doi:10.14202/vetworld.2015.61-65 PubMed PMID: 27046998; PubMed Central PMCID: PMC4777813.

431. Frackowiak M, Easton A, Michael BD. Encephalitis. Br J Hosp Med Lond Engl 2005. 2019 Apr 2;80(4):C32–4. doi:10.12968/hmed.2019.80.4.C50 PubMed PMID: 30951422.

432. Sharma S, Mishra D, Aneja S, Kumar R, Jain A, Vashishtha VM. Consensus guidelines on evaluation and management of suspected acute viral encephalitis in children in India. Indian Pediatr. 2012 Nov;49(11):897–910. doi:10.1007/s13312-012-0216-0 PubMed PMID: 23255700.

433. Srivastava IN, Van Haren KP. Immunotherapy in Autoimmune Encephalitis: So Many Options, So Few Guidelines. Neurology. 2023 Nov 27;101(22):985–6. doi:10.1212/WNL.0000000000208026 PubMed PMID: 37879941.

16 Appendix

16.1 Methodology appendix

Search terms for:

Cause:
"Encephalitis AND cause"; "encephalitis AND etiology"; "encephalitis AND aetiology"; "encephalitis AND agent"; "encephalitis AND autoimmune"; "encephalitis AND antibody"; "encephalitis AND antibodies"; "encephalitis AND infection"; "encephalitis AND unknown"

Incidence:
"Encephalitis AND incidence"; "encephalitis AND admission rates;" "encephalitis AND epidemiology"; "acute disseminated encephalomyelitis/ADEM and incidence; "autoimmune encephalitis AND incidence"

Morbidity and mortality:
"Encephalitis AND mortality"; "encephalitis AND case-fatality"; "encephalitis AND case fatality"; "encephalitis AND Africa AND mortality"; "encephalitis AND outcome"; "encephalitis AND outcome AND child"; "encephalitis AND sequelae"; "encephalitis AND effect"; "encephalitis AND morbidity"; "encephalitis AND caregiver burden"; "encephalitis AND carer burden"; "Japanese encephalitis/JE AND mortality"; "Japanese encephalitis/JE AND case-fatality"; "Japanese encephalitis/JE AND case fatality"; "Japanese encephalitis/JE AND outcome"; "Japanese encephalitis/JE AND sequelae"; "Japanese encephalitis/JE AND effect"; "Japanese encephalitis/JE AND morbidity"; "herpes/HSV AND mortality"; "herpes/HSV AND case-fatality"; "herpes/HSV AND case fatality"; "herpes/HSV AND outcome"; "herpes/HSV AND sequelae"; "herpes/HSV AND effect"; "herpes/HSV AND morbidity"; "tick-borne encephalitis/TBE AND mortality"; "tick-borne encephalitis/TBE AND case-fatality"; "tick-borne encephalitis/TBE AND case fatality"; "tick-borne encephalitis/TBE AND outcome"; "tick-borne encephalitis/TBE AND sequelae"; "tick-borne encephalitis/TBE AND effect"; "tick-borne encephalitis/TBE AND morbidity"; "rabies AND mortality"; "rabies AND case-fatality"; "rabies AND case fatality"; "rabies AND outcome"; "rabies AND sequelae"; "rabies AND effect"; "rabies AND morbidity"; "acute disseminated encephalomyelitis/ADEM AND mortality"; "acute disseminated encephalomyelitis/ADEM AND case-fatality"; "acute disseminated encephalomyelitis/ADEM AND case fatality"; "acute disseminated encephalomyelitis/ADEM AND outcome"; "acute disseminated encephalomyelitis/ADEM AND sequelae"; "acute disseminated encephalomyelitis/ADEM AND effect"; "acute disseminated encephalomyelitis/ADEM AND morbidity"; "anti-NMDA

encephalitis/NMDA AND mortality"; "anti-NMDA encephalitis/NMDA AND case-fatality"; "anti-NMDA encephalitis/NMDA AND case fatality"; "anti-NMDA encephalitis/NMDA AND outcome"; "anti-NMDA encephalitis/NMDA AND sequelae"; "anti-NMDA encephalitis/NMDA AND effect"; "anti-NMDA encephalitis/NMDA AND morbidity"

Economics/cost and DALYs:
"Encephalitis AND DALY"; "encephalitis AND economic"; "encephalitis AND cost"; "encephalitis AND burden of disease"; "encephalitis AND disease burden"; "encephalitis AND cost effective"

Prevention including vaccine programs, vector control, and epidemic control:
"Encephalitis AND vaccine programs"; "encephalitis AND program"; "Japanese encephalitis AND vaccine"; "Japanese encephalitis AND vaccination"; "Japanese encephalitis AND immunisation;" "Japanese encephalitis AND immunization"; "Tick-borne encephalitis AND vaccine"; "Tick-borne encephalitis AND vaccination"; "Tick-borne encephalitis AND immunisation"; "Tick-borne encephalitis and immunization"; "MMR AND encephalitis"; "measles AND vaccination"; "measles AND immunisation"; "measles AND immunization"; "rabies AND vaccine"; "rabies AND vaccination"; "rabies AND immunisation"; "rabies AND immunization"; "encephalitis AND vector"; "encephalitis AND vector control"; "encephalitis AND prevention"; "encephalitis AND arbovirus"; "encephalitis AND outbreak"; "encephalitis AND outbreak control"; "encephalitis AND epidemic control"; "encephalitis AND control"

Diagnosis:
"Encephalitis AND diag*"; "encephalitis AND lab*"; "encephalitis AND cerebrospinal fluid/CSF"; "encephalitis AND CSF examination"; "encephalitis AND CSF analysis"; "encephalitis AND tests"; "encephalitis AND PCR"; "encephalitis AND molecular*"; "encephalitis AND molecular assay"; "encephalitis AND molecular diag*"; "encephalitis AND nucleic acid test"; "encephalitis AND nucleic acid detection"; "encephalitis AND MRI"; "encephalitis AND MRI availability"; "encephalitis AND MRI use"; "encephalitis AND antibody test"; "encephalitis AND antibody assay"; "autoimmune encephalitis AND diagnostic"; "encephalitis AND autoantibody"; "encephalitis AND essential diagnostic"; "encephalitis AND NMDAR"

Treatment:
"Acyclovir/aciclovir availability"; "acyclovir/aciclovir availability AND encephalitis"; "acyclovir/aciclovir AND Africa"; "acyclovir/aciclovir AND encephalitis"; "acyclovir/aciclovir AND avail*"; "acyclovir/aciclovir AND encephalitis AND Asia"; "acyclovir/aciclovir AND

encephalitis AND Africa"; "encephalitis AND essential medicine"; "encephalitis AND essential medicine AND Africa"

In-country neurologists and access to neurology training:
"Neurologists by country"; "neurology training"; "neurology AND training"; "neurologist"; "neurology presence"; "presence of neurologist"

Surveillance:
"Encephalitis AND surveillance;" "encephalitis AND reporting;" "encephalitis AND report"; "encephalitis AND statistics"; "encephalitis AND routine"; "encephalitis AND monitor"; "encephalitis AND data;" "Japanese encephalitis/JE/JEV AND surveillance;" "Japanese encephalitis/JE/JEV AND reporting;" "Japanese encephalitis/JE/JEV AND report"; "Japanese encephalitis/JE/JEV AND statistics"; "Japanese encephalitis/JE/JEV AND routine"; "Japanese encephalitis/JE/JEV AND monitor"; "Japanese encephalitis/JE/JEV AND data;" "Tick-borne encephalitis/TBE/TBEV AND surveillance;" "Tick-borne encephalitis/TBE/TBEV AND reporting;" "Tick-borne encephalitis/TBE/TBEV AND report"; "Tick-borne encephalitis/TBE/TBEV AND statistics"; "Tick-borne encephalitis/TBE/TBEV AND routine"; "Tick-borne encephalitis/TBE/TBEV AND monitor"; "Tick-borne encephalitis/TBE/TBEV AND data"; "rabies AND surveillance;" "rabies AND reporting;" "rabies AND report"; "rabies AND statistics"; "rabies AND routine"; "rabies AND monitor"; "rabies AND data"

New and emerging infections:
"Encephalitis AND emerging infect*;" "encephalitis AND novel infect*;" "encephalitis AND emerging;" "encephalitis AND re-emerging;" "encephalitis AND new infect*;" "encephalitis AND Nipah;" "encephalitis AND chikungunya;" "encephalitis AND scrub typhus;" "encephalitis AND orientia*;" encephalitis AND bush typhus;" "encephalitis AND covid*;" "encephalitis AND corona*"

16.2 Tables

Table A1 - Details of incidence studies

Study	Date	Country	Continent	Encephalitis type	Age	Incidence per 100,000 (95%CI)
Beghi et al	1950-1981	USA	North America	Viral encephalitis	All	7.4
Rantakallio et al	1966-1983	Finland	Europe	Infectious encephalitis	Children	12.6 (7.86-19.41)
Rantalaiho et al	1967-1991	Finland	Europe	Acute encephalitis	Adult	1.4
Koskiniemi et al	1968-1987	Finland	Europe	Acute encephalitis	Children	8.3 (7.56-9.09)
Wickstrom et al	1970-2009	Sweden	Europe	Encephalitis	Children	7.7
Rantala et al	1973-1987	Finland	Europe	Encephalitis	Children	8.8 (6.7-10.1)
Cizman et al	1979-1991	Slovenia	Europe	Acute encephalitis	Children	6.7 (6.13-7.32)
Iro et al	1979-2011	England	Europe	Encephalitis	Children	5.97 (5.52-6.41)
Ponka et al	1980	Finland	Europe	Encephalitis	All	3.5 (2.06-5.67)
Radhakrishnan et al	1983-1984	Libya	Africa	Encephalitis	Adult	1 (0.32-2.31)
Chunsuttiwat et al	1983-1987	Thailand	Asia	Encephalitis	All	4 (3.83-4.18)
Ishikawa et al	1984-1990	Japan	Asia	Acute encephalitis	Children	3.3 (2.71-3.47)
Kusumi et al	1988-1992	Japan	Asia	Encephalitis	Adult	0.9 (0.37-2.2)
Khetsuriani et al	1988-1997	USA	North America	Encephalitis	All	7.3 (5.6-8.1)
Davison et al	1989-1998	England	Europe	Viral encephalitis	All	1.5 (1.46-1.54)
Trevejo et al	1990-1999	USA	North America	Acute encephalitis	All	4.3 (4.2-4.4)
Huppatz et al	1990-2007	Australia	Oceania	Encephalitis	All	5.2 (4.2-6.7)
Nwosu et al	1991-1993	Nigeria	Africa	Infectious encephalitis	Adult	3.19 (1.28-6.56)
Leake et al	1991-2000	USA	North America	ADEM	Children	0.4 (0.35-0.66)
Pavone et al	1992-2009	Italy	Europe	ADEM	Children	1.1
Koskiniemi et al	1993-1994	Finland	Europe	Acute encephalitis	Children	10.5 (9-12.18)
Heinrich et al	1993-1998	Thailand	Asia	Viral encephalitis	All	6.4
Kulkarni et al	1994-2008	Canada	North America	Encephalitis	All	5.16 (5.09-5.22)
Dubey et al	1995-2015	USA	North America	AIE Infectious encephalitis excluding unknowns	All	0.8 1

Chhour et al	1996-1998	Cambodia	Asia	Encephalitis	Children	0.92 (0.69-1.22)
Pohl et al	1997-1999	Germany	Europe	ADEM	Children	0.07 (0.05-0.1)
Vora et al	1998-2010	USA	North America	Encephalitis	All	6.9
Kupila et al	1999-2003	Finland	Europe	Aseptic encephalitis	Adult	2.2
Barbadoro et al	1999-2005	Italy	Europe	Encephalitis	All	5.88 (5.87-5.89)
Mailles et al	2000-2002	France	Europe	Encephalitis	All	1.9 (1.84-1.96)
George et al	2000-2010	USA	North America	Encephalitis	All	7.3 (7.1-7.6)
Britton et al	2000-2012	Australia	Oceania	Encephalitis	Children	5 (4.6-5.4)
Van Landingham et al	2001-2007	USA	North America	ADEM	Children	0.4
Parpia et al	2002-2013	Canada	North America	Encephalitis	All	4.3 (4.2-4.4)
Kadambari et al	2004-2013	England & Wales	Europe	Viral meningo-encephalitis	All	3.9 (3.74-4.06)
Yamaguchi et al	2005-2007	Japan	Asia	ADEM	Children	0.4 (0.34-0.46)
Kelly et al	2005-2008	Ireland	Europe	Viral encephalitis	All	2.49 (2.31-2.68)
Child et al	2005-2009	New Zealand	Oceania	Encephalitis	>14	0.5
Granerod et al	2005-2009	England	Europe	Encephalitis	All	5.23
Jackson et al	2006-2012	Canada	North America	ADEM	All	0.17 (0.09-0.27)
Bhatt et al	2006-2014	USA	North America	ADEM	Children	0.5 (0.47-0.53)
Joshi et al	2007	India	Asia	AES	Adult	16
Roux et al	2007-2017	French Guiana	South America	Encephalitis	All	4
Xiong et al	2008-2010	China	Asia	ADEM	All	0.31
Chen et al	2008-2011	China	Asia	ADEM	All	0.32
Boesen et al	2008-2015	Denmark	Europe	ADEM	Children	0.54 (0.39-0.75)
Boesen et al	2011-2017	Denmark	Europe	Anti-NMDA Anti-GAD65 Antibody negative but probable AIE	Children	0.07 (0.03-0.17) 0.055 (0.021-0.15) 0.055 (0.021-0.15)
Bodilsen et al	2015-2016	Denmark	Europe	Viral encephalitis	>15	1.4
Marienke et al	2015-2018	Netherlands	Europe	Antibody-mediated AIE ADEM	Children	0.15 (0.095-0.235) 0.25 (0.17-0.35)
Sevilla-Acosta et al.	2017	Costa Rica	North America	Acute encephalitis	Children	3.6
Kim et al	2010-2021	South Korea	Asia	Encephalitis	All	9.48
Lee et al	2015-2019	South Korea	Asia	Encephalitis	All	16.4

Liem et al	2009-2018	New Zealand	Oceania	Encephalitis	Adult	1.1

ADEM = Acute disseminated encephalomyelitis; AES = Acute encephalitis syndrome; AIE = Autoimmune encephalitis; CI = Confidence interval; GAD65 = Glutamate decarboxylase; NMDARE = N-methyl-d-aspartate receptor encephalitis; USA = United States of America

Table A2 – Details of mortality studies

Study	Date	Country	Continent	Encephalitis type	Age	CFR (%)	Raw data CFR
Andleeb et al	2013-2018	Pakistan	Asia	Encephalitis	All	37.3	28/75
Bhatt et al	2006-2014	USA	North America	ADEM	Children	1.7	
Bodilsen et al	2015-2016	Denmark	Europe	Viral encephalitis	Adult >15	5	5/89
Britton et al	2000-2012	Australia	Oceania	Encephalitis	Children	2.6	
Child et al	2005-2009	New Zealand	Oceania	Encephalitis	Adult >14	14	
Davison et al	1989-1998	England	Europe	Viral encephalitis	All	6.5	
Fowler et al	2000-2004	Sweden	Europe	Acute encephalitis	Children	0	0/93
Galanakis et al	2005-2007	Greece	Europe	Encephalitis	Children up to 15	0	0/42
George et al	2000-2010	USA	North America	Encephalitis	All	5.6	
Granerod et al	2005-2008	UK	Europe	Encephalitis	All	12	24/203
Grinschgl et al	1953	Austria	Europe	Viral ME	All	4.6	14/304
Hon et al	2002-2014	Hong Kong	Asia	Encephalitis	Children	>25	≥12/46
Huppatz et al	1990-2007	Australia	Oceania	Encephalitis	All	4.6	
Ilias et al	2000-2004	Greece	Europe	Encephalitis	Children	0	0/18
Ishikawa et al	1984-1990	Japan	Asia	Acute encephalitis	Children	7.8	20/256
Joshi et al	2007	India	Asia	AES	Adult	34.8	n=53
Khetsuriani et al	1988-1997	USA	North America	Encephalitis	All	7.4	
Koskiniemi et al	1968-1987	Finland	Europe	Encephalitis	Children (1mo - 16yr)	3	14/462
Le et al	2004	Vietnam	Asia	Acute encephalitis	Children	29	57/194
Lohitharajah et al	2012-2014	Sri Lanka	Asia	Encephalitis/ME	All	7	7/99
Mailles et al	2007	France	Europe	Encephalitis	All	10	26/253
Beghi et al	1950-1981	USA	North America	Viral encephalitis	All	3.8	
Olsen et al	2003-2005	Thailand	Asia	Encephalitis and ME	All	10	15/149
Quist-Paulsen et al	2000-2009	Norway	Europe	Encephalitis	Adult	7	5/70
Rantalaiho et al	1967-1991	Finland	Europe	Acute encephalitis	Adult	5.6	18/322
Rao et al	2000-2010	USA	North America	Encephalitis	Children <21	5	4/76
Rathore et al	2011-2012	India	Asia	Encephalitis	All	7	37/526

Roux et al	2007-2017	French Guiana	South America	Encephalitis	All	28.7	
Schmidt et al	1992-2004	Switzerland	Europe	Encephalitis of unknown aetiology	All	12.8	5/39
Sevilla-Acosta et al	2017	Costa Rica	North America	Encephalitis	Children	15	6/40
Srey et al	1999-2000	Cambodia	Asia	Encephalitis syndrome	All	22	22/99
Toudou-Daouda et al	2008-2016	Morocco	Africa	Limbic encephalitis	All	9.7	3/31
Vora et al	1998-2010	USA	North America	Encephalitis	All	5.8	
Wong et al	1975-1986	Hong Kong	Asia	Encephalitis	Children <14	28	16/57
de Blauw et al	2003-2013	The Netherlands	Europe	Encephalitis	Children <18	20.8	25/121
Iro et al	2003	England & Wales	Europe	Encephalitis	Children	8.4	87/1031
Zhao et al	2009-2012	China	Asia	Viral encephalitis	All	3.1	34/1107
Britton et al	2013-2016	Australia	Oceania	Encephalitis	Children	4.5	13/287
Ai et al	2009-2012	China	Asia	Viral encephalitis	Children	0.8	2/255
Meligy et al	2015-2016	Egypt	Africa	Viral encephalitis	Children	23	22/96
Wickstrom et al	1970-2009	Sweden	Europe	Encephalitis	Children	3.5	x/408
Misra et al	2014-2016	India	Asia	AES	Children	19	15/79
Bagdure et al	2004-2013	USA	North America	Encephalitis	Children	3	230/7298
Glaser et al	1998-2000	USA	North America	Encephalitis	All	17.1	50/293
Milshtein et al	1999-2009	Israel	Asia	Acute encephalitis	Children	0	0/44
Li et al	2016-2020	China	Asia	Viral encephalitis	Children	0.1	43/39279
Liem et al	2009-2018	New Zealand	Oceania	Encephalitis	Adults ≥15	10.3	14/136

ADEM = Acute disseminated encephalomyelitis; AES = Acute encephalitis syndrome; CFR = Case fatality rate; ME = Meningoencephalitis; UK = United Kingdom; USA = United States of America