UNDERSTANDING AND INTERPRETATION OF THE GLOBAL BURDEN OF DISEASE (GBD) STUDY ESTIMATES ON NEUROLOGICAL DISORDERS

Prof. Valery Feigin

National Institute for Stroke & Applied Neurosciences
Faculty of Health and Environmental Sciences
Auckland University of Technology, New Zealand

18 October 14:45-16:15, Room Hall 520BE

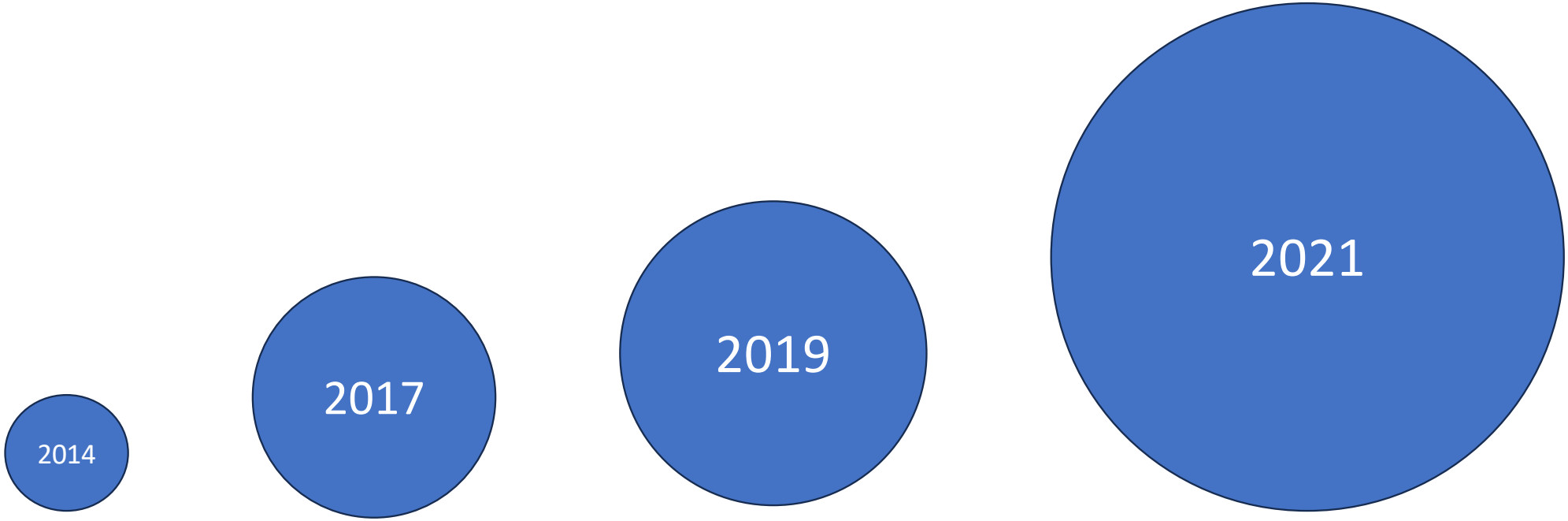
WCN 2023
XXVI WORLD CONGRESS
OF NEUROLOGY

MONTREAL
15 – 19 OCTOBER 2023

Disclosure

- Chair (unpaid) International Advisory Committee of the SAMURAI Study
- Travel support from Moleac Pte Ltd

Evolving GBD coverage of neurological conditions



3 founding members

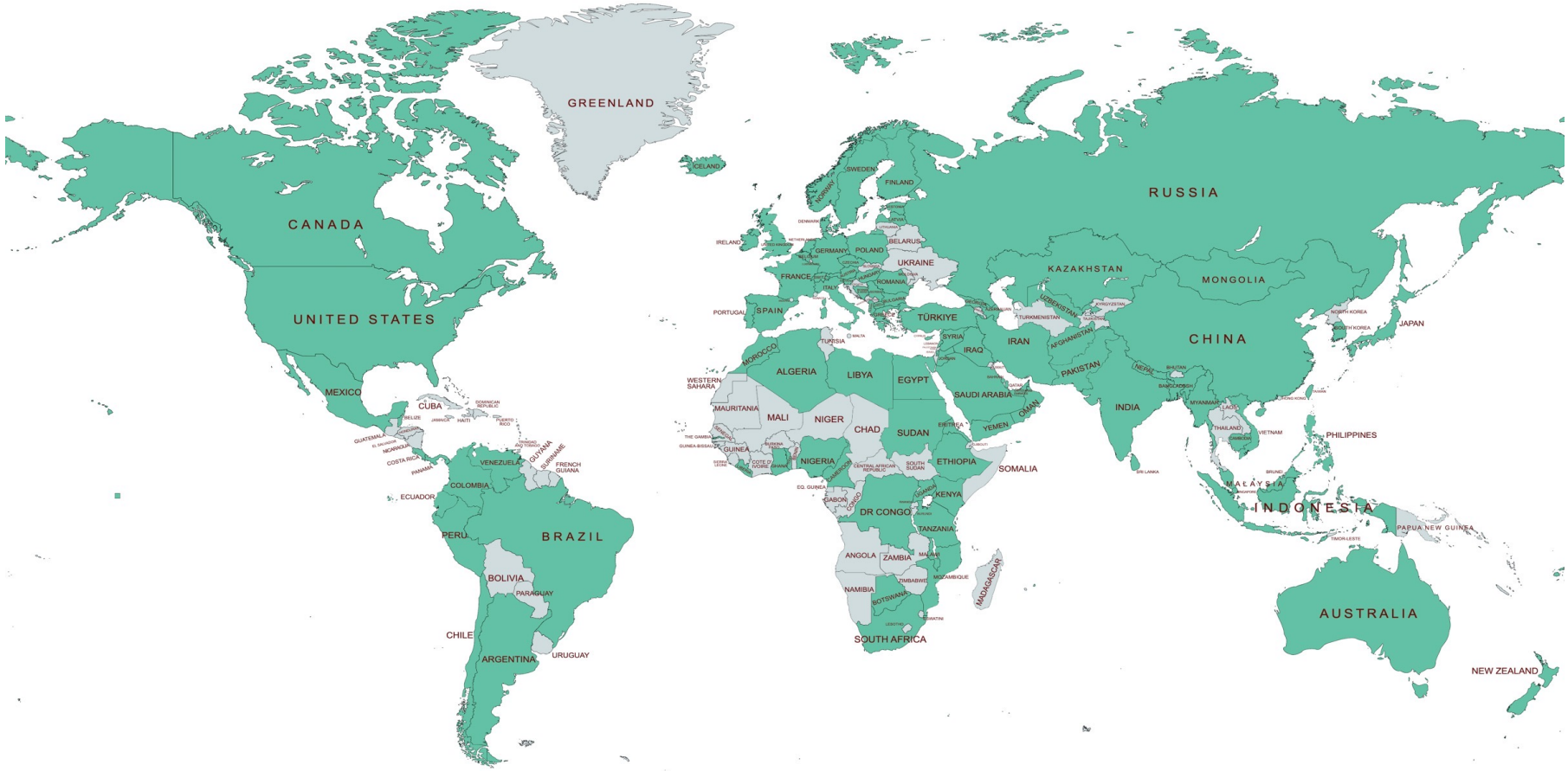
14 neurological conditions

15 neurological conditions

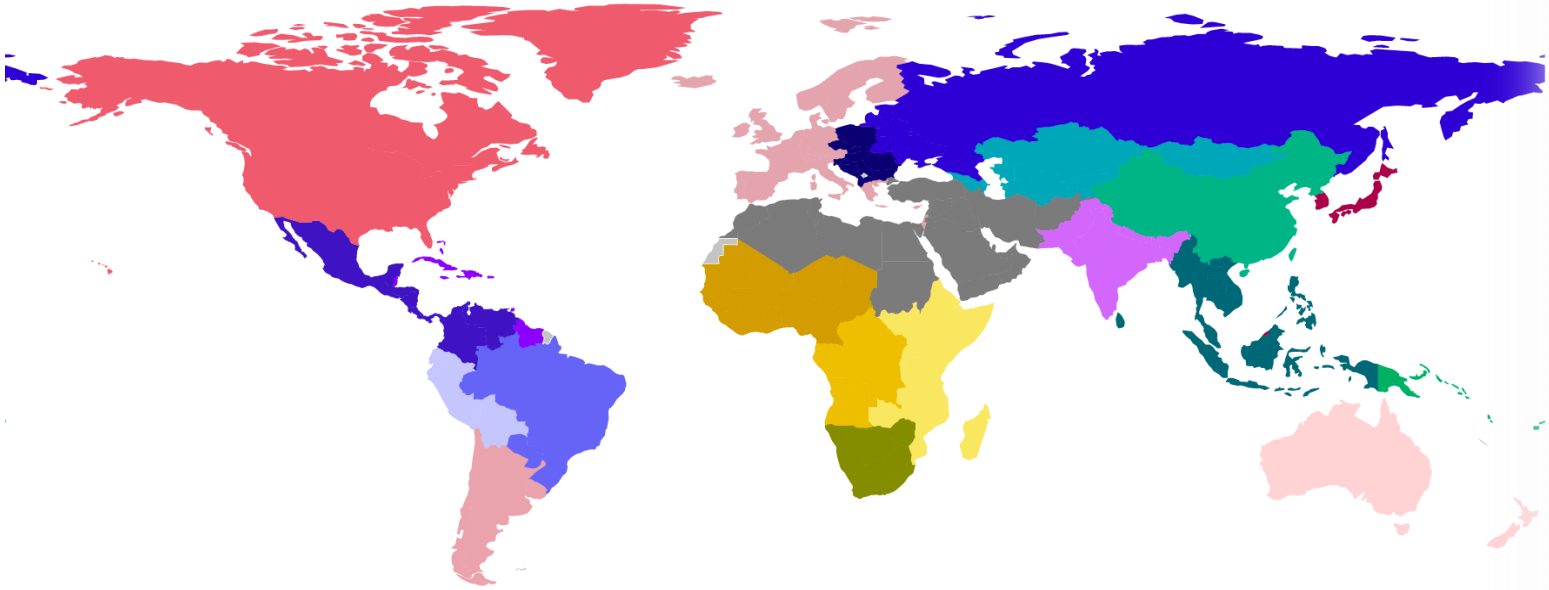
36 neurological conditions

GBD Neurological Collaboration 2021

102 countries, 1750 collaborators



21 GBD REGIONS AND 7 SUPER-REGIONS



High Income
- High-income Asia Pacific
- High-income North America
- Southern Latin America
- Western Europe
- Australasia

Latin America and Caribbean
- Caribbean
- Central Latin America
- Tropical Latin America
- Andean Latin America

Sub-Saharan Africa
- Southern Sub-Saharan Africa
- Western Sub-Saharan Africa
- Central Sub-Saharan Africa
- Eastern Sub-Saharan Africa

North Africa and Middle East
- North Africa and Middle East

Southeast Asia, East Asia, and Oceania
- Southeast Asia
- Oceania
- East Asia

Central Europe, Eastern Europe, and Central Asia
- Central Asia
- Eastern Europe
- Central Europe

South Asia
- South Asia

THE GBD STUDY 2021 NEUROLOGY COLLABORATION GROUP

Subnational estimates available for 20 countries:

- USA
- Poland
- Russia
- NZ (Māori, non- Māori)
- Japan
- Italy
- Norway
- Sweden
- UK
- Mexico
- Brazil
- Iran
- India
- Pakistan
- Indonesia
- Philippines
- Ethiopia
- Kenya
- South Africa
- Nigeria

GLOBAL, REGIONAL, AND NATIONAL BURDEN OF DISORDERS AFFECTING THE NERVOUS SYSTEM, 1990-2021:

a systematic analysis of the Global Burden of Disease Study 2021. Lancet Neurology 2023

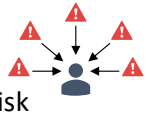
36 disease and injury outcomes

15 previous + **neurodevelopmental conditions in children** (attention-deficit/hyperactivity disorder, autism spectrum disorders, foetal alcohol syndrome, idiopathic developmental intellectual disability, neonatal encephalopathy, neural tube defects, congenital birth defects, Klinefelter syndrome, preterm birth, Down syndrome, other chromosomal abnormalities) **and additional often disabling CNS infections and other conditions** (COVID-19, Zika congenital, syphilis, neonatal sepsis, malaria, neonatal jaundice, rabies)

All available (1990-2021) data sources

population-representative studies, large-scale surveys, censuses, insurance claims, and hospital records that catalogue incidence and prevalence for each condition (**36,000+** incidence, prevalence and other studies for non-fatal models; vital data from **ICD-9** and **ICD-10** codes, verbal autopsy, registry and MoH and other admin data for mortality estimates of 14 fatal conditions)

PAF of disease DALYs



expected decrease in DALYs (YLDs + YLLs) if risk exposure had equalled the theoretical minimum risk exposure level [TMREL] (regression analysis)

Comorbidity correction

to calculate total prevalence of neurological conditions

Analysis

by age, sex, 21 GBD regions, 204 countries (Dismod-MR 2.1 regression analysis for non-fatal estimates; ensemble modeling approach to fatal estimates)

THE GBD STUDY 2021 NEUROLOGY COLLABORATION GROUP

SELECTION

of 36 neurological conditions for GBD 2021

1. Alzheimer's disease and other dementias
2. Attention-deficit/hyperactivity disorder
3. Autism spectrum disorders
4. Encephalitis†
5. Foetal alcohol syndrome
6. Guillain-Barré syndrome†
7. Headache disorders (migraine, tension-type)
8. Idiopathic epilepsy†
9. Idiopathic developmental intellectual disability
10. Meningitis†
11. Motor neuron disease†
12. Multiple sclerosis†
13. Neonatal encephalopathy†
14. Neural tube defects†
15. Nervous system cancer (central nervous system;
16. Neuroblastoma and other peripheral nervous cell tumours)†
17. Neurocysticercosis
18. Other neurological disorders†
19. Parkinson's disease†
20. Traumatic brain injury
21. Rabies†
22. Spinal cord injury
23. Stroke (ischaemic stroke, subarachnoid haemorrhage, intracerebral haemorrhage)†
24. Tetanus†
25. Congenital birth defect
26. COVID-19
27. Down syndrome
28. Echinococcosis (cystic)
29. Klinefelter syndrome
30. Malaria
31. Neonatal jaundice
32. Neonatal sepsis
33. Other chromosomal abnormalities
34. Preterm birth
35. Syphilis (congenital and adult neurosyphilis)
36. Zika virus disease (congenital)

12 conditions with neurological features

CONDITIONS

in other neurological disorders category

ICD-9*

- Cerebral degenerations usually manifest in childhood
- Idiopathic normal pressure hydrocephalus
- Corticobasal degeneration
- Cerebral degeneration in diseases classified elsewhere
- Other cerebral degeneration or unspecified
- Other extrapyramidal disease and abnormal movement disorders
- Spinocerebellar disease
- Other diseases of spinal cord
- Disorders of the autonomic nervous system
- Other demyelinating diseases of central nervous system
- Other and unspecified disorders of the nervous system
- Other or unspecified nerve root and plexus disorders
- Hereditary and idiopathic peripheral neuropathy
- Acute infective polyneuritis
- Polyneuropathy; myoneural disorders (eg, myasthenia gravis, lambert-eaton syndrome)
- Muscular dystrophies and other myopathies
- Neonatal myasthenia gravis

ICD-10*

- Dementia in other diseases classified elsewhere
- Huntington's disease
- hereditary ataxia
- spinal muscular atrophy and related syndromes
- systemic atrophies primarily affecting central nervous system in diseases classified elsewhere
- other degenerative diseases of basal ganglia
- dystonia
- other extrapyramidal and movement disorders
- extrapyramidal and movement disorders in diseases classified elsewhere
- other demyelinating diseases of central nervous system
- inflammatory polyneuropathy (includes fatal outcomes of Guillain-Barré syndrome)
- myasthenia gravis and other myoneural disorders
- primary disorders of muscles (eg, muscular dystrophy)
- disorders of myoneural junction and muscle in diseases classified elsewhere

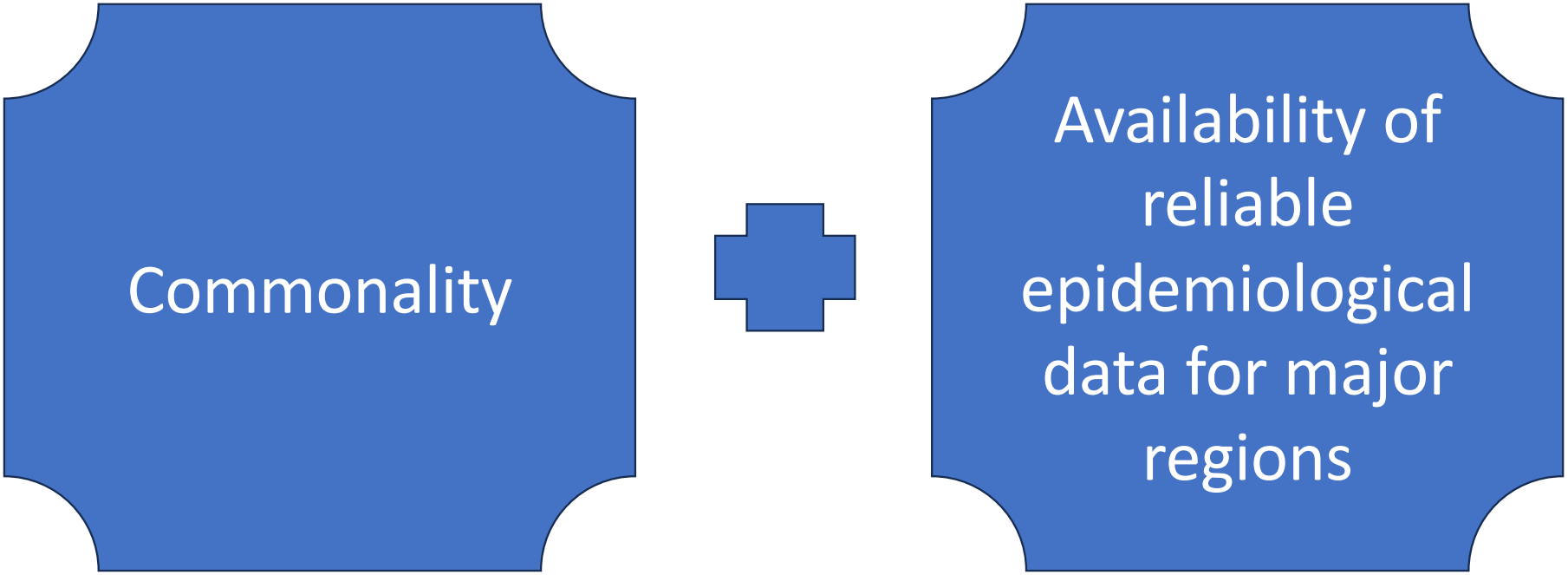
* — Listed conditions correspond to three-digit ICD coding unless four-digit is required to code to an included neurological category

Conditions in other neurological disorders category

- *Listed conditions correspond to three-digit ICD coding unless four-digit is required to code to an included neurological category

ICD-9*	ICD-10*
Cerebral degenerations usually manifest in childhood; idiopathic normal pressure hydrocephalus; corticobasal degeneration; cerebral degeneration in diseases classified elsewhere; other cerebral degeneration or unspecified; other extrapyramidal disease and abnormal movement disorders; spinocerebellar disease; other diseases of spinal cord; disorders of the autonomic nervous system; other demyelinating diseases of central nervous system; other and unspecified disorders of the nervous system; other or unspecified nerve root and plexus disorders; hereditary and idiopathic peripheral neuropathy; acute infective polyneuritis; polyneuropathy; myoneural disorders (eg, myasthenia gravis, Lambert-Eaton syndrome); muscular dystrophies and other myopathies; neonatal myasthenia gravis	Dementia in other diseases classified elsewhere; Huntington's disease; hereditary ataxia; spinal muscular atrophy and related syndromes; systemic atrophies primarily affecting central nervous system in diseases classified elsewhere; other degenerative diseases of basal ganglia; dystonia; other extrapyramidal and movement disorders; extrapyramidal and movement disorders in diseases classified elsewhere; other demyelinating diseases of central nervous system; inflammatory polyneuropathy (includes fatal outcomes of Guillain-Barré syndrome); myasthenia gravis and other myoneural disorders; primary disorders of muscles (e.g., muscular dystrophy); disorders of myoneural junction and muscle in diseases classified elsewhere

Principles of selection



ICD-9 and ICD-10 (fatal) coding for each condition

Condition	ICD-9	ICD-10
Alzheimer's disease and other dementias	290, 291.2, 291.8, 294, 331	F00, F01, F02, F03, G30, G31
Encephalitis	062, 064.9, 139.0, 323	A83-A86.4, B94.1, F07.1, G04-G05.8; G21.3
Idiopathic epilepsy	345	G40, G41
Meningitis	036, 047, 049.9, 320.0-320.3; 320.5-320.89, 321-322.9	A39, A87, D86.81, G00, G03
Motor neuron disease	335	G12
Multiple sclerosis	340	G35
Neonatal encephalopathy due to birth asphyxia and trauma	761.7-761.9, 762, 763, 767, 768; 768.2-768.7, 768.9, 770.1, 779.0-779.2	P01.7, P02, P03, P10, P11, P12, P13, P14, P15, P20, P21, P24, P91
Nervous system cancers*	191, 191.0, 191.1, 191.2, 191.3; 191.4, 191.5, 191.6, 191.7, 191.8; 191.9, 192, 192.0, 192.1, 192.2; 192.3, 192.8, 192.9, 194.3, 194.4; 194‡, 194.0‡, and 194.9‡	C47, C47.0, C47.1, C47.10. C47.11, C47.12, C47.2, C47.20, C47.21, C47.22, C47.3, C47.4; C47.5, C47.6, C47.8; C47.9, C47.90, C70, C70.0, C70.1; C70.5, C70.6, C70.9, C71, C71.0, C71.1; C71.2, C71.3, C71.4, C71.5, C71.6; C71.7, C71.8, C71.9, C72, C72.0, C72.1; C72.2, C72.20, C72.21, C72.22, C72.3, C72.30, C72.31, C72.32, C72.4, C72.40, C72.41, C72.42, C72.5, C72.50, C72.59; C72.8, C72.9, C74‡, C75.1-C75.3
Neural tube defects	740, 741, 742.0	Q00.0-Q00.2; Q01, Q05
Other neurological disorders	330, 331.8, 331.9, 333, 334, 335.3; 336, 337, 341, 349, 349.2, 349.3; 349.8, 353.8, 353.9, 356, 357.0, 357.1, 357.3, 357.4, 357.7, 358; 359, 775.2	F02.2, G10, G11, G12, G12.0, G12.1, G13, G23, G24, G25, G26, G26.0, G36, G37, G61, G70, G71, G73, G90, G95
Parkinson's disease	332, 332.0	F02.3, G20
Rabies	071	A82
Stroke (ischaemic)	433, 434, 435, 437	G45, G46, I63, I65, I66, I67.2-I67.6; 67.5-I67.6, I69.3
Stroke (intracerebral hemorrhage)	431, 432, 437.2	I61, 162, I68.1-I68.2, I69.1-I69.2
Stroke (subarachnoid hemorrhage)	430	I60, I62.0, I67.0-I67.1, I69.0
Tetanus	037-037.9, 771.3, V03.7	A33, A34, A35

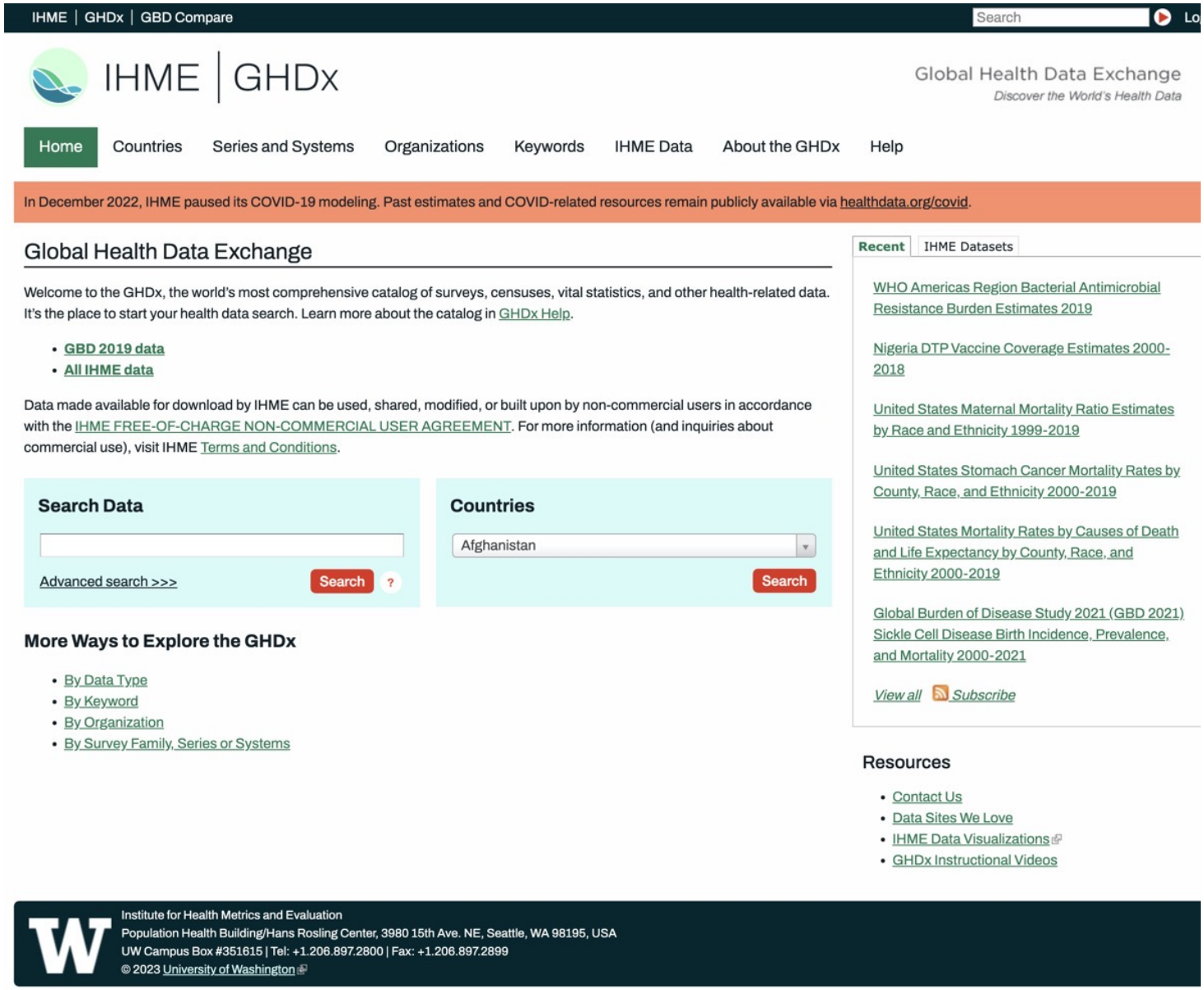
DATA SOURCES

from 1990 to 2021

Data source	How it is used in the GBD
Census or population registry	Denominator, GDP
Vital registration/statistics or sample registration	Causes of death (ICD-9, 10, 11)
Demographic surveillance system	Causes of death
Verbal autopsies	Causes of death
Hospital and Ministry of Health data, WHO databases	Disease incidence and prevalence
Health insurance data	Disease incidence and prevalence
Surveys and disease registries	Incidence, prevalence, risk factors
Morbidity notification data and police records about notifiable infectious diseases or conditions (homicides, injuries etc)	Incidence, prevalence
Published literature (including 'grey' literature) from all possible sources, including PubMed, Scopus etc.	Disease incidence, prevalence, outcomes and risk factors

Data sources

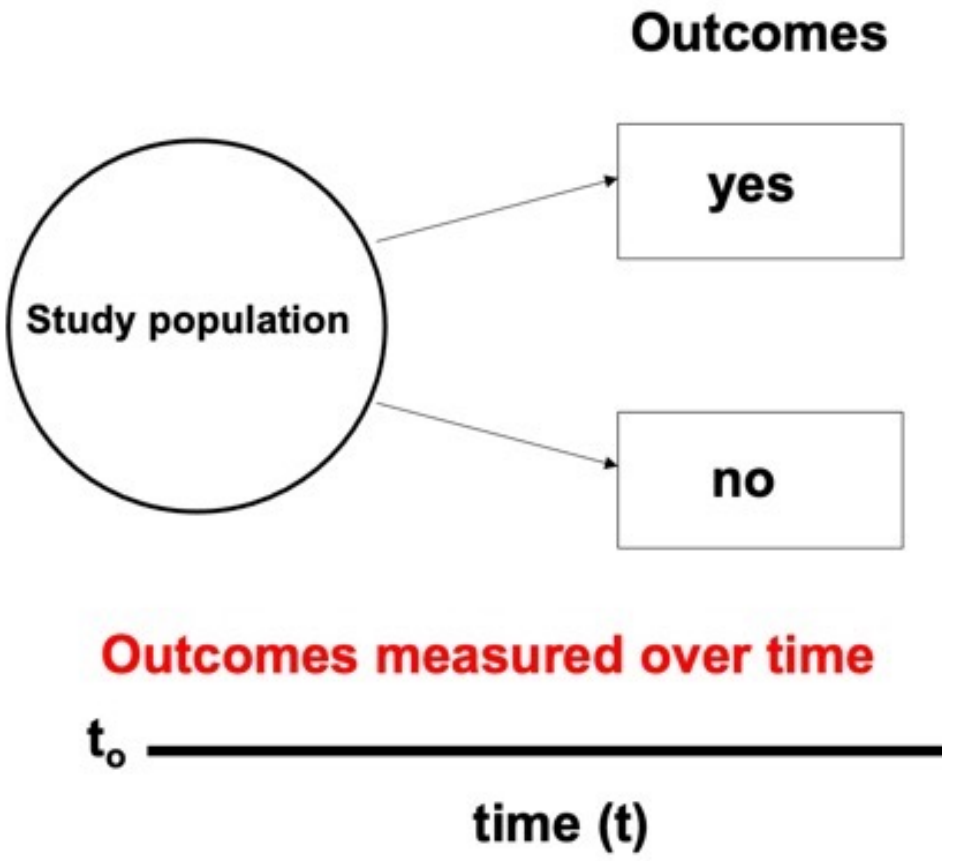
http://ghdx.healthdata.org/



Understanding of basic GBD metrics

- **Incidence**: The number of new cases of a given cause during a given period in a specified population. In GBD, incidence rate is the rate per 100,000 population per year.

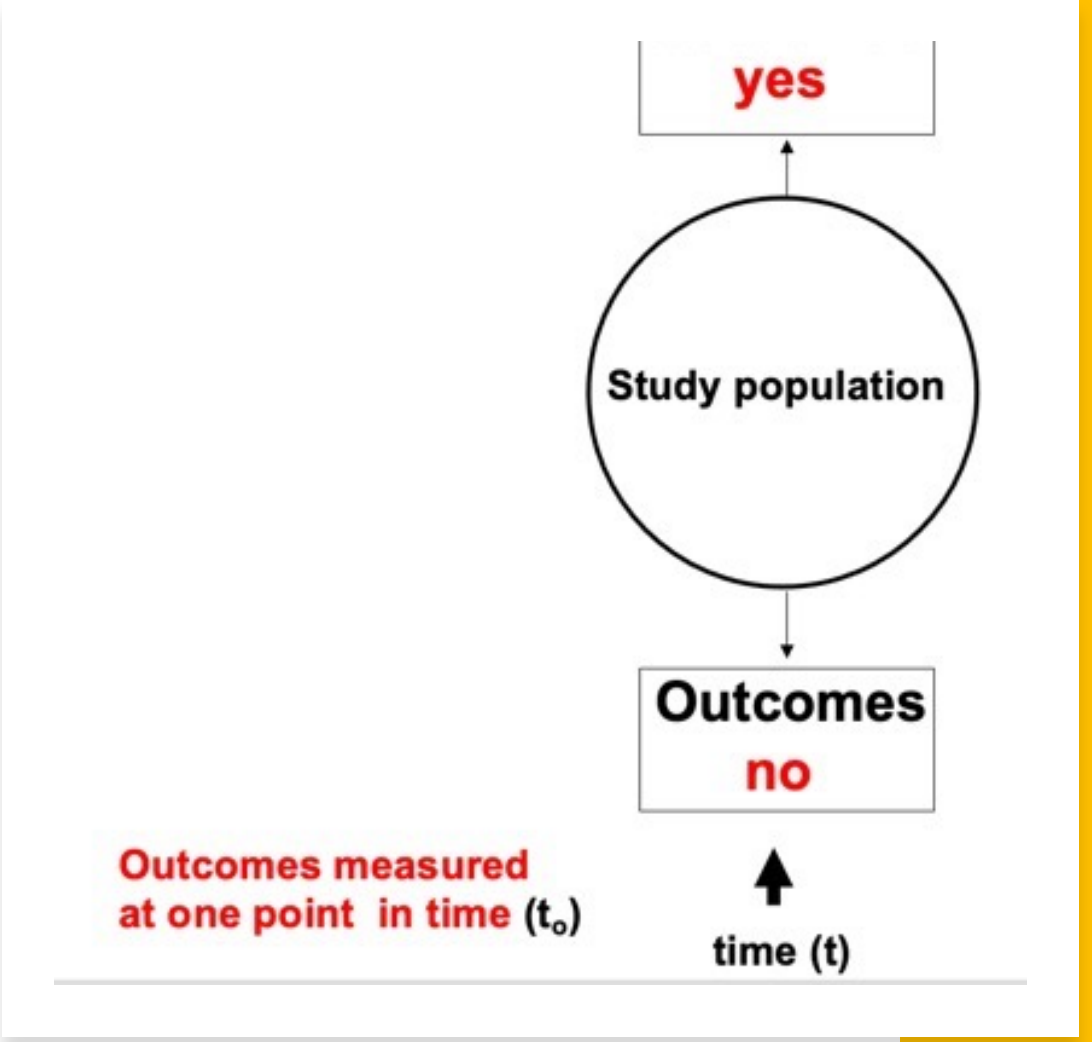
New cases of a disease (nominator) for 1 year / Population (denominator) x 100,000



Understanding of basic GBD metrics

- **Prevalence**: The number of cases of a condition that are present in a specified population at a given time. In GBD, prevalence is the proportion cases of a condition per 100,000 population.

All alive cases of a disease (nominator) at a given time / Population (denominator) x 100,000

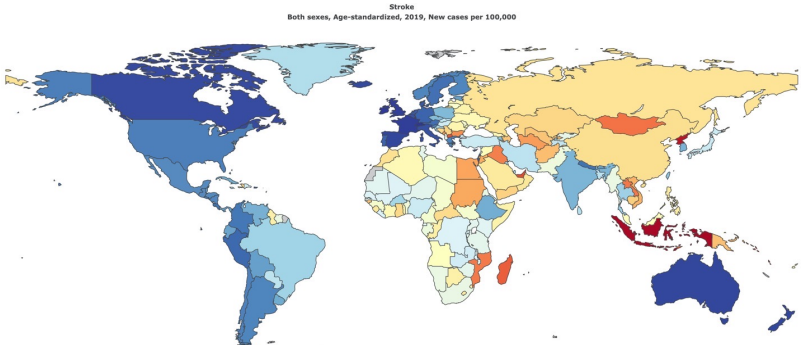


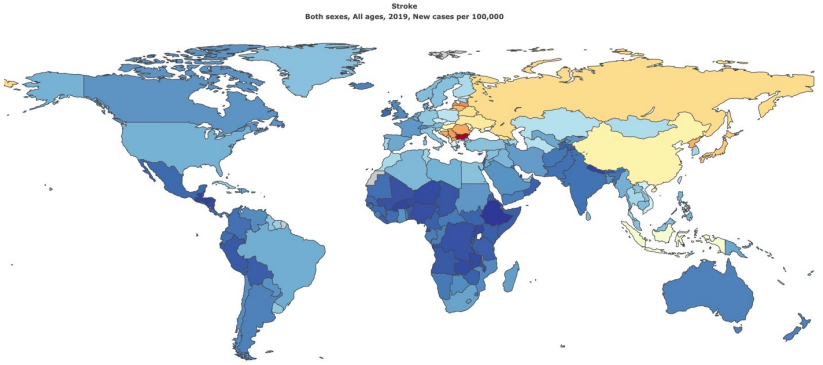
Age-standardised

vs

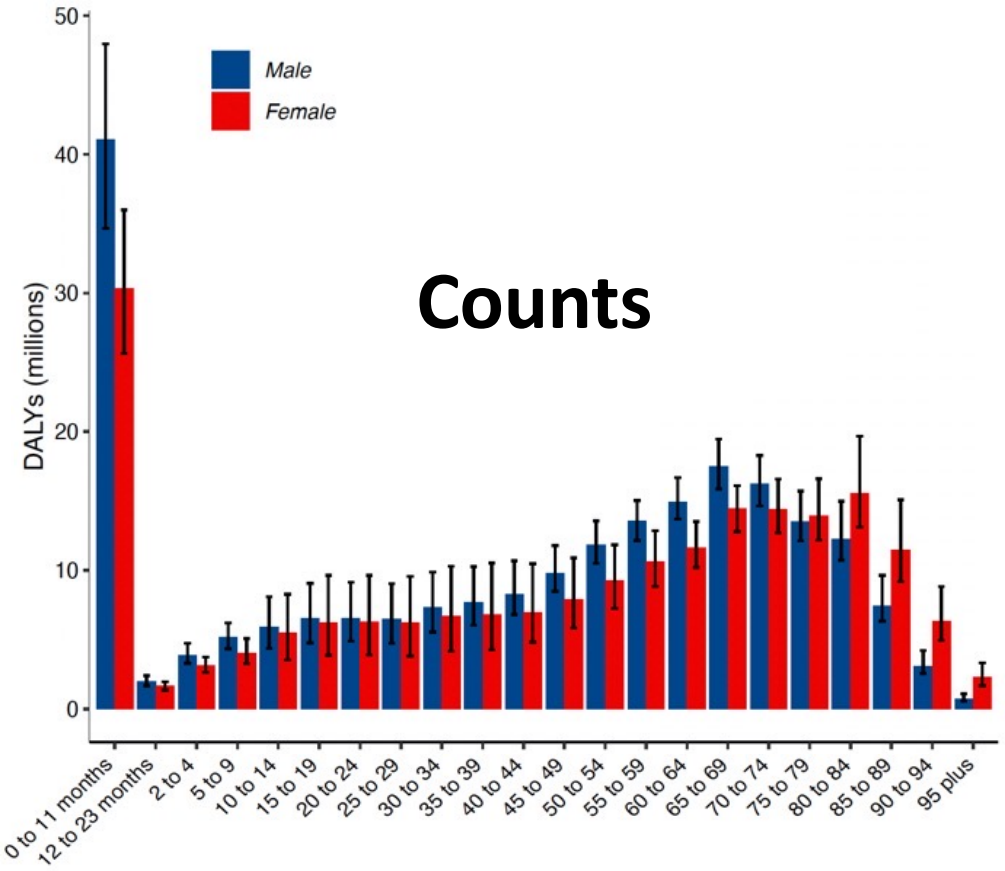
non-standardised rates

Age-standardisation allows comparisons between locations/countries by statistically transforming the age structure of a population to match that of a reference group. In this way, it is possible to adjust for the confounding effects of differences between the populations compared and over time. GBD uses a study-specific set of population weights that were originally derived from the World Health Organization standard and then refined over time to create the GBD population.

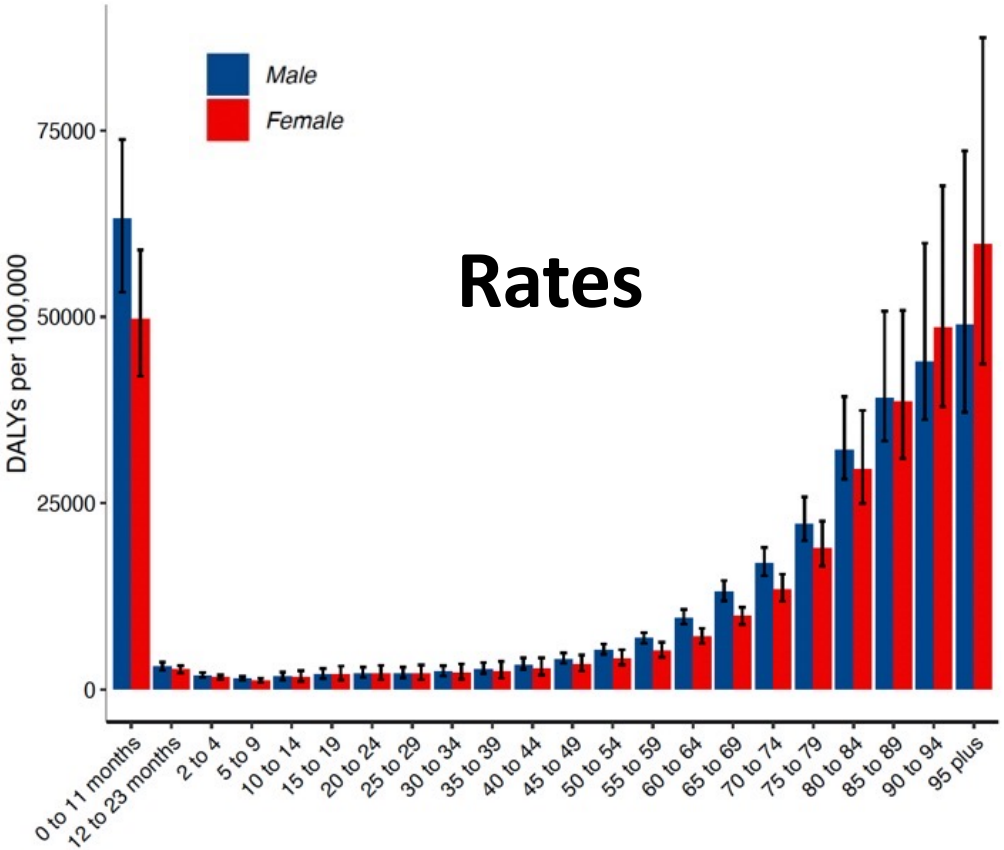




Neurological disorders global age-specific burden in 2021: DALYs counts and rates



Counts



Rates

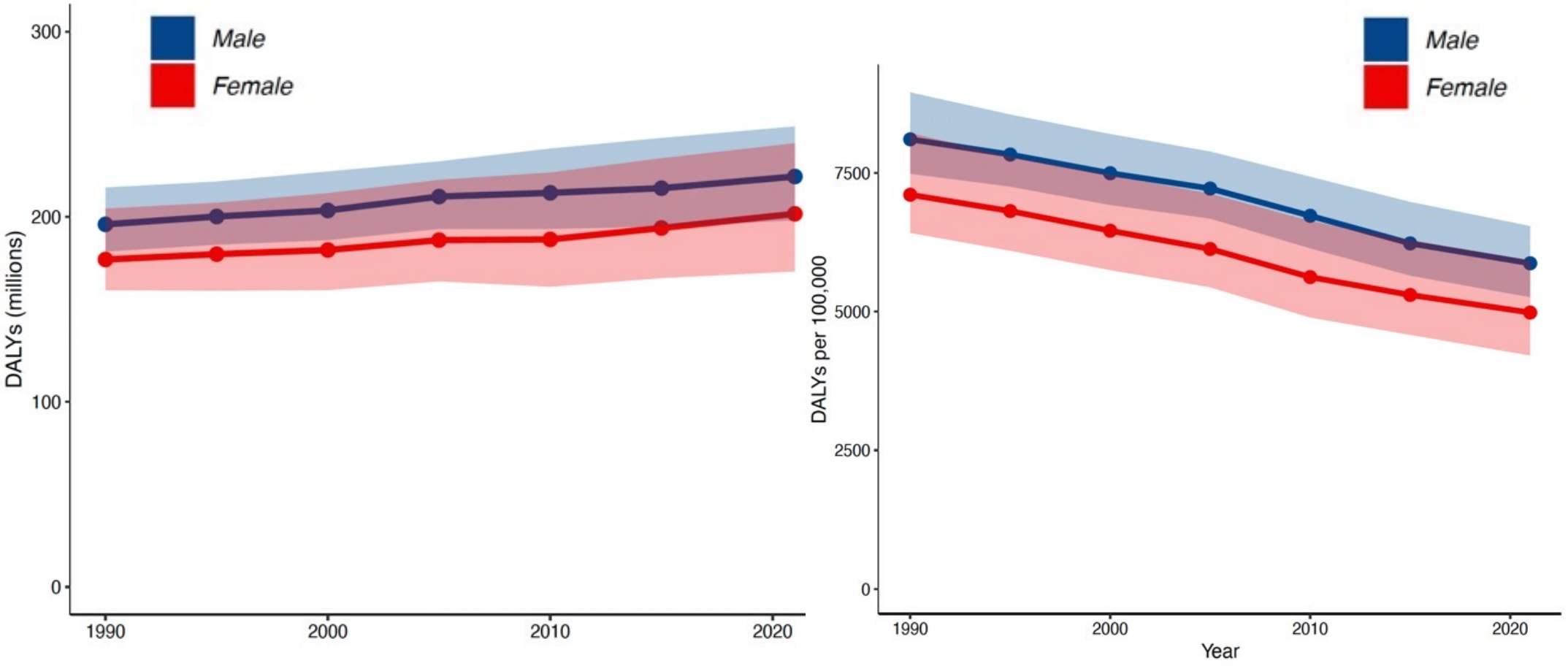
Age-standardised estimates

Age-specific incidence in your population per 100,000 people per year:		Age-specific proportion (%) of the standard (e.g., World) population of the same age groups (weights):		Calculating age-specific incidence rates weighted by the standard:
35-44	20	35-44	12%	35-44 20 x 12 = 240
45-54	30	45-54	11%	45-54 30 x 11 = 330
55-64	40	55-64	8%	55-64 40 x 8 = 320
		Total:	**31%**	**Total:** **890**

Age-standardised rate for your population of 35-64 years

= 890/**31** = 28.7 per 100 000 population

Neurological disorders global burden trends, 1990-2021: DALYs counts and rates by sex



Understanding of basic GBD metrics

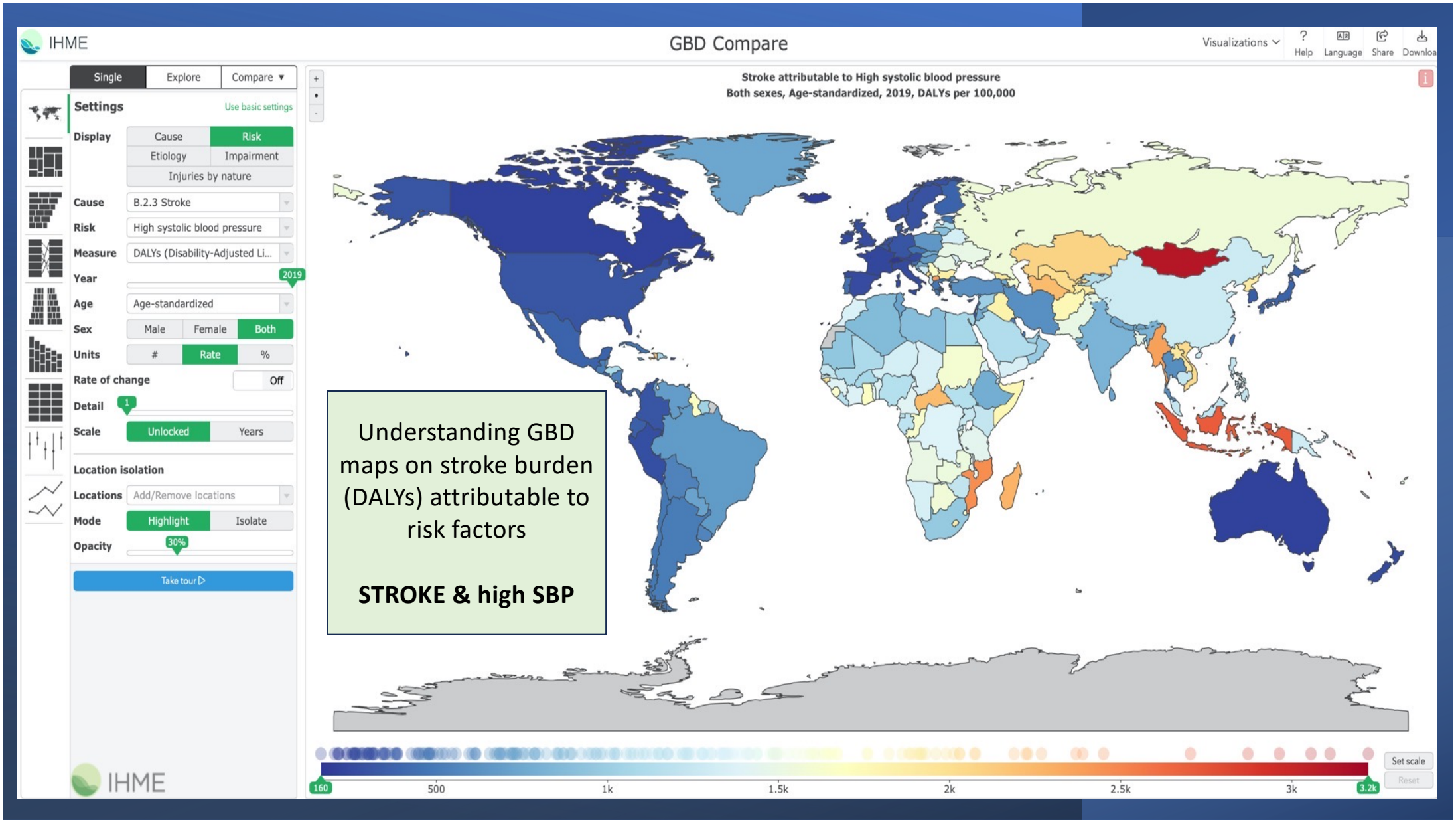
- **Sequela**: A complication of a neurological condition; the level of severity of a condition; health state (e.g., dead/alive)

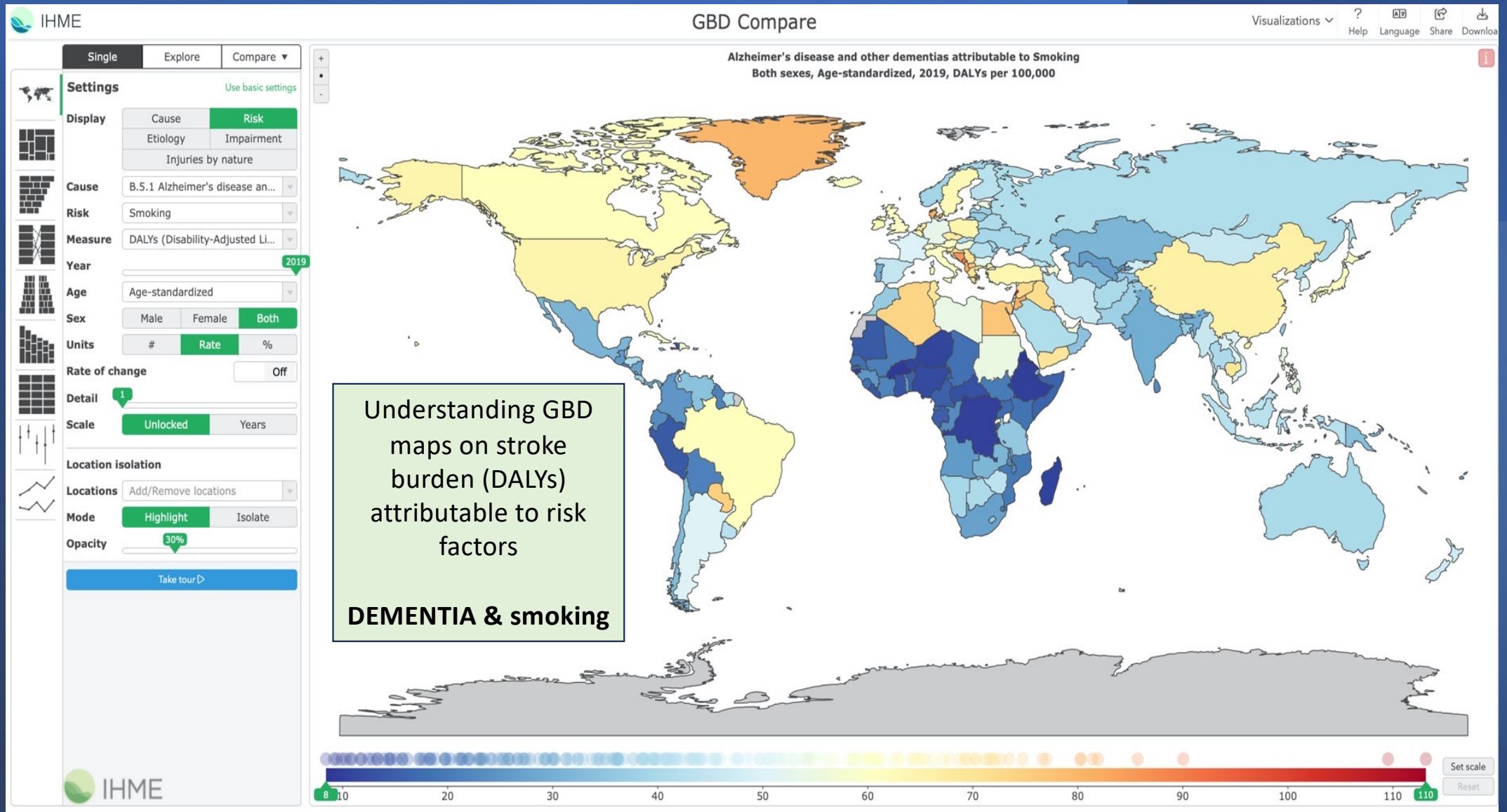
- **95% Uncertainty Interval (UI)**: A range of values that reflects the certainty of an estimate. Larger uncertainty intervals can result from limited data availability, small studies and conflicting data, while smaller uncertainty intervals can result from extensive data availability, large studies and consistent data across different sources.

Understanding of basic GBD metrics

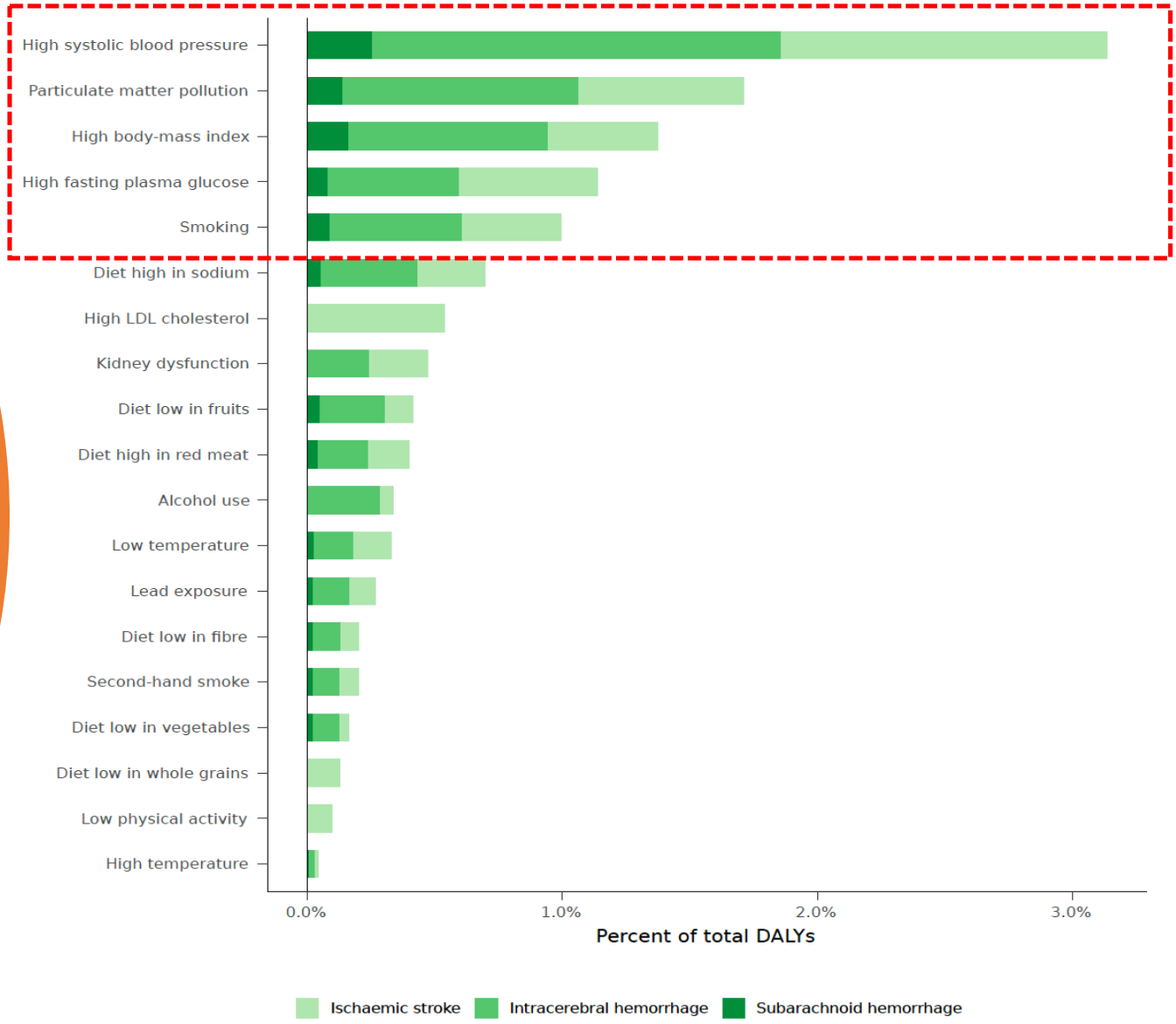
- **Theoretical minimum risk exposure distribution (TMRED):** The prevalence of a risk factor that would confer minimal risk of the outcome on a population (e.g., SBP 114 mmHg).

- **Population-attributable fraction (PAF)**: The proportion of the total burden of a condition estimated to be causally related to the exposure of a population to a risk factor


IHME
GBD Compare
Visualizations
Help
Language
Share
Single
Explore
Compare
Settings
Use basic settings
Display
Cause
Risk
Etiology
Impairment
Injuries by nature
Cause
B.2.3 Stroke
Risk
High systolic blood pressure
Measure
DALYs (Disability-Adjusted Li...
Year
2019
Age
Age-standardized
Sex
Male
Female
Both
Units
#
Rate
%
Rate of change
Off
Detail
1
Scale
Unlocked
Years
Location isolation
Locations
Add/Remove locations
Mode
Highlight
Isolate
Opacity
30%
Take tour
Stroke attributable to High systolic blood pressure
Both sexes, Age-standardized, 2019, DALYs per 100,000
Understanding GBD maps on stroke burden (DALYs) attributable to risk factors
STROKE & high SBP
160
500
1k
1.5k
2k
2.5k
3k
3.2k
Set scale
Reset


IHME
GBD Compare
Visualizations
Help
Language
Share
Downloa
Single
Explore
Compare
Settings
Use basic settings
Display
Cause
Risk
Etiology
Impairment
Injuries by nature
Cause
B.5.1 Alzheimer's disease an...
Risk
Smoking
Measure
DALYs (Disability-Adjusted Li...
Year
2019
Age
Age-standardized
Sex
Male
Female
Both
Units
#
Rate
%
Rate of change
Off
Detail
1
Scale
Unlocked
Years
Location isolation
Locations
Add/Remove locations
Mode
Highlight
Isolate
Opacity
30%
Take tour
IHME
Alzheimer's disease and other dementias attributable to Smoking
Both sexes, Age-standardized, 2019, DALYs per 100,000
Understanding GBD maps on stroke burden (DALYs) attributable to risk factors
DEMENTIA & smoking
8
10
20
30
40
50
60
70
80
90
100
110
Set scale
Reset

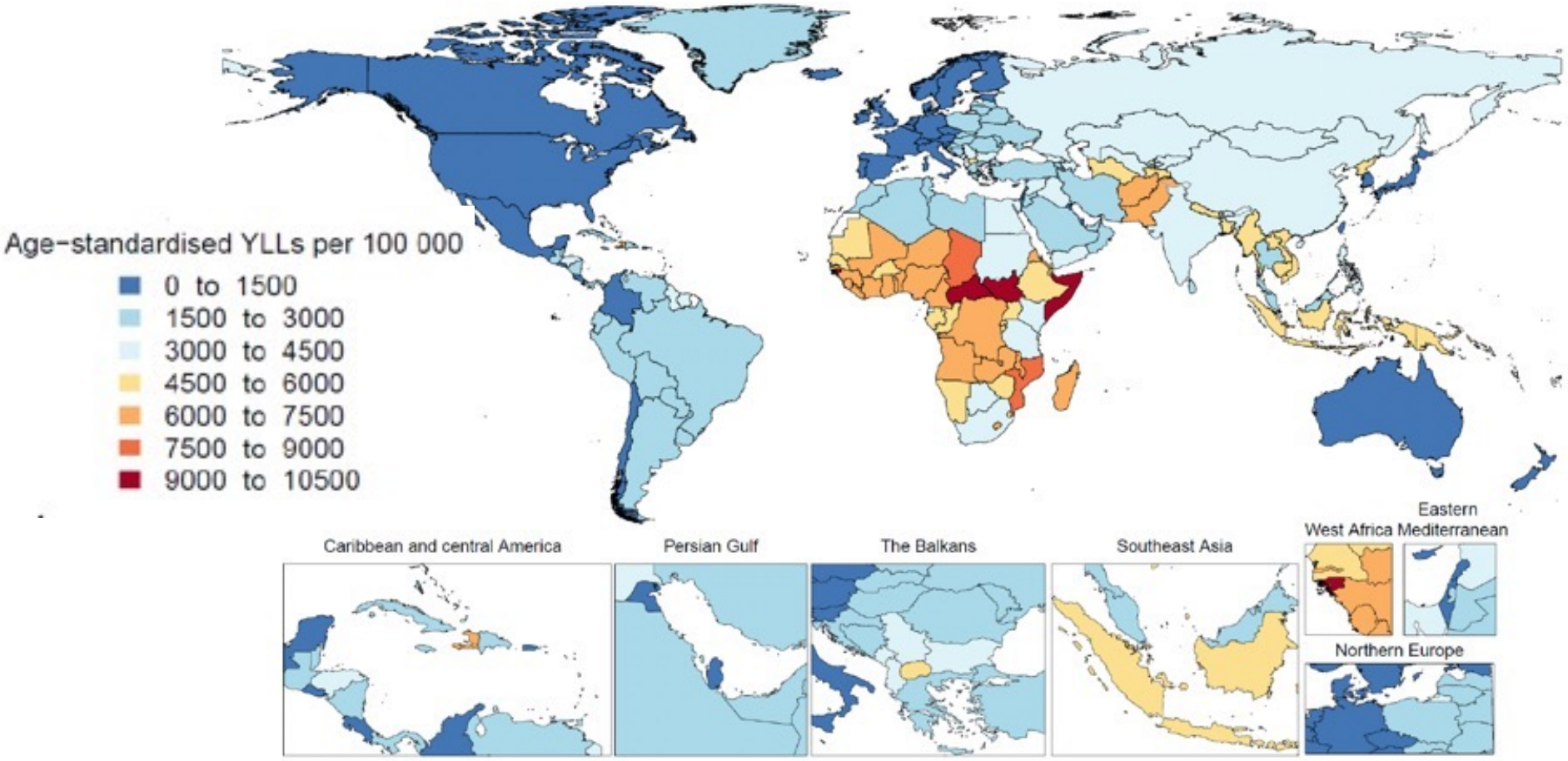
Percentage of DALYs attributable to risk factors by pathological type of stroke for both sexes combined



Years of life lost (YLLs)

- **YLLs** = (number of deaths due to the condition at each age) x (life expectancy at the age at which death occurs)
- Years of life lost due to premature mortality. Example: YLLs due to stroke in Canada in 2019 was over 232,000. It means that 232,000 years of life was lost in Canada due to stroke in 2019
- It reflects a fatal burden of the condition

National age-standardised YLL rates for all neurological conditions combined, 2021



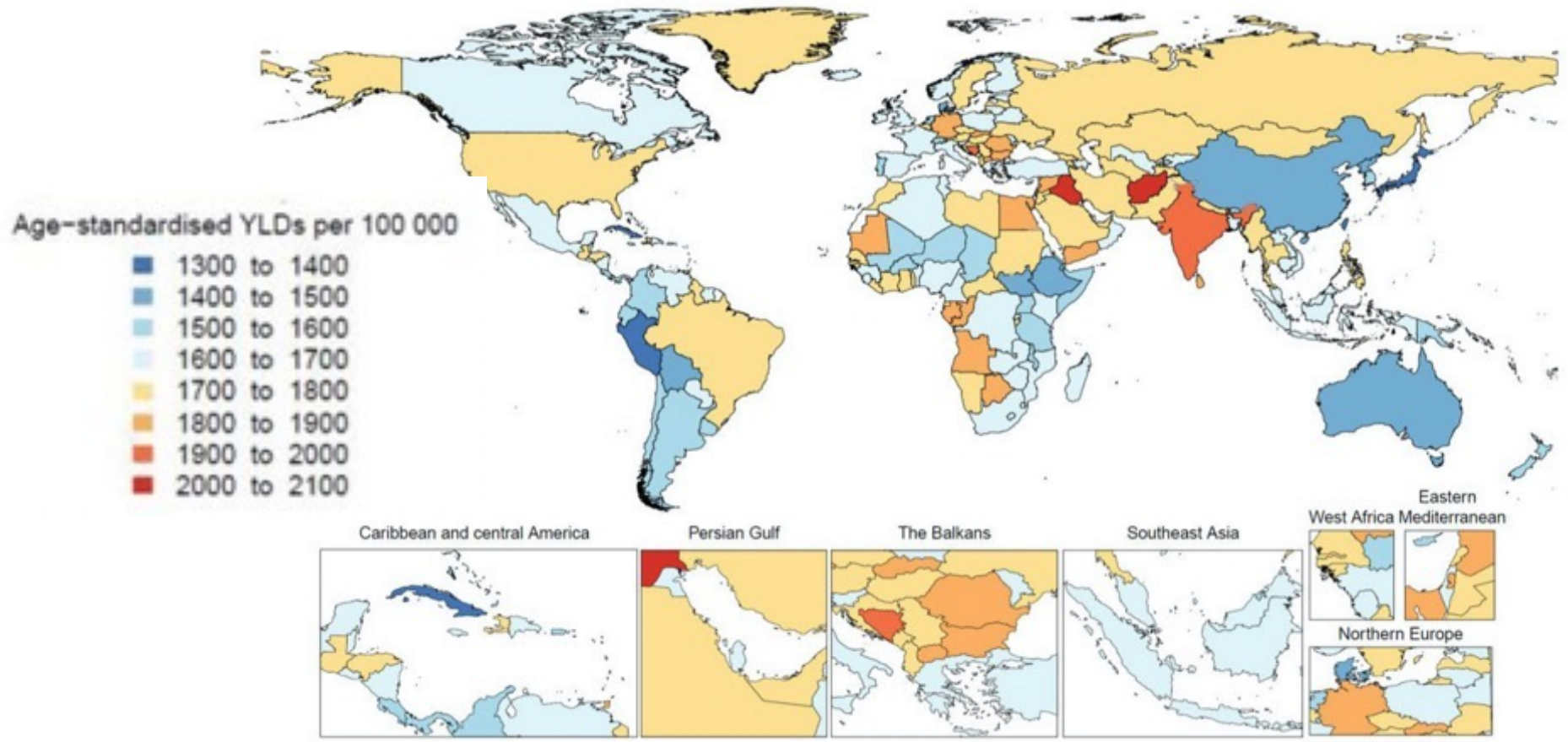
Years lived with disability (YLD)

- **YLD** = (number of prevalent cases of the condition) x (disability weights for the condition) x (average duration of the condition in years until death)

- This includes health loss that may last for only a few days or for a lifetime. For example, YLD due to stroke in Canada in 2019 was almost 97,000. It means that 97,000 years of full health were lost in Canada in 2019 due to stroke.

- It reflects a non-fatal burden of the condition

National age-standardised YLD rates for all neurological conditions combined, 2021



Disability weights

- An estimate of the severity of a health state, measured on a 0–1 scale, where 0 represents no health loss and 1 represents complete health loss (death)

- Derived from a worldwide, cross-cultural study to compare the relative severity of health problems

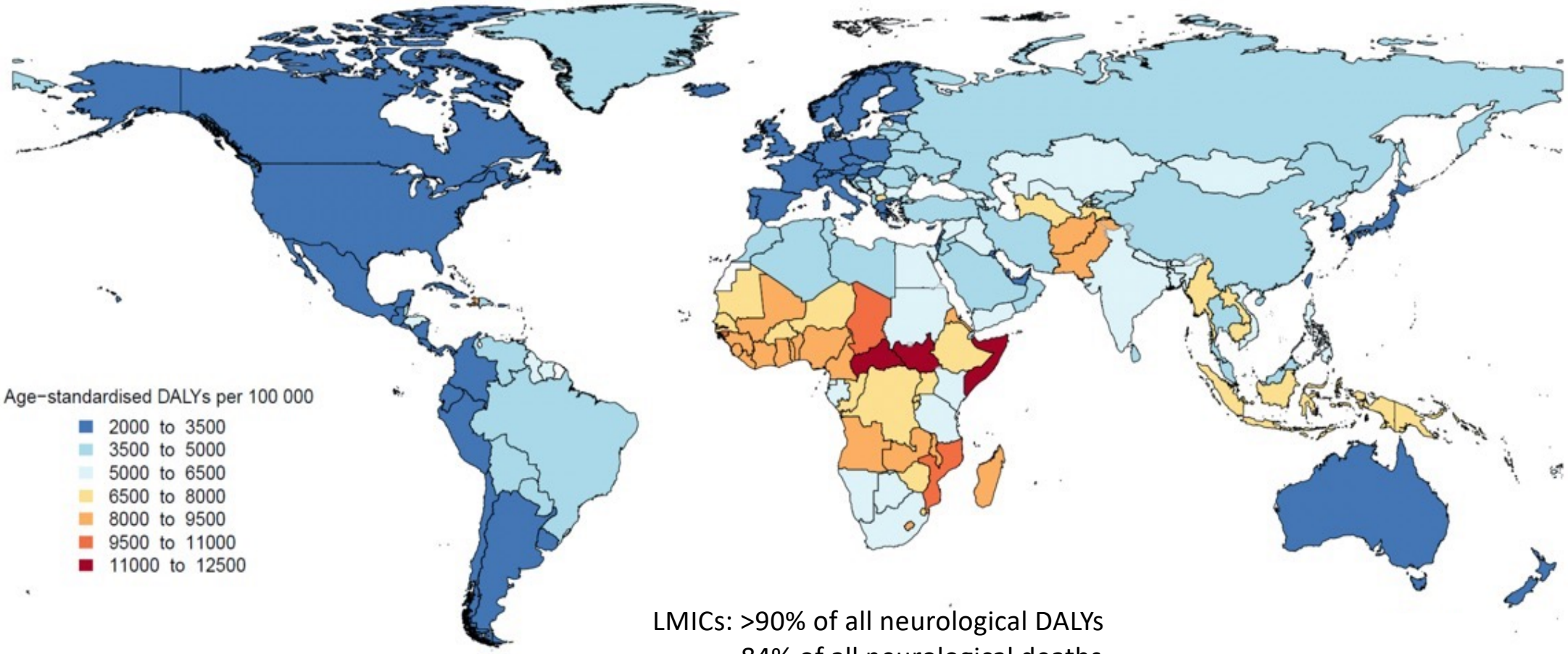
Example of GBD disability weights for selected sequelae of stroke and dementia

Condition	Health state lay description	Disability Weight (95% UI)
Stroke, mild	This person has some difficulty in moving around and some weakness in one hand but is able to walk without help.	0.019 (0.010–0.032)
Stroke, moderate, with no heart failure	This person has some difficulty in moving around and in using the hands for lifting and holding things, dressing, and grooming.	0.070 (0.046–0.099)
Stroke, severe, with no heart failure	Is confined to bed or a wheelchair, has difficulty speaking, and depends on others for feeding, toileting, and dressing.	0.552 (0.377–0.707)
Dementia, mild	This person has some trouble remembering recent events and finds it hard to concentrate and make decisions and plans. They may have slight to moderate difficulty engaging in community affairs, complicated hobbies, and intellectual interests.	0.069 (0.046–0.099)
Dementia, moderate	This person retains highly learned material, but has severe memory problems, is disoriented with respect to time and sometimes place. They are severely impaired in their ability to handle problems and make social judgements. They require assistance with daily activities, and only retain simple chores and hobbies.	0.377 (0.252–0.508)

Disability-adjusted life years (DALYs) lost

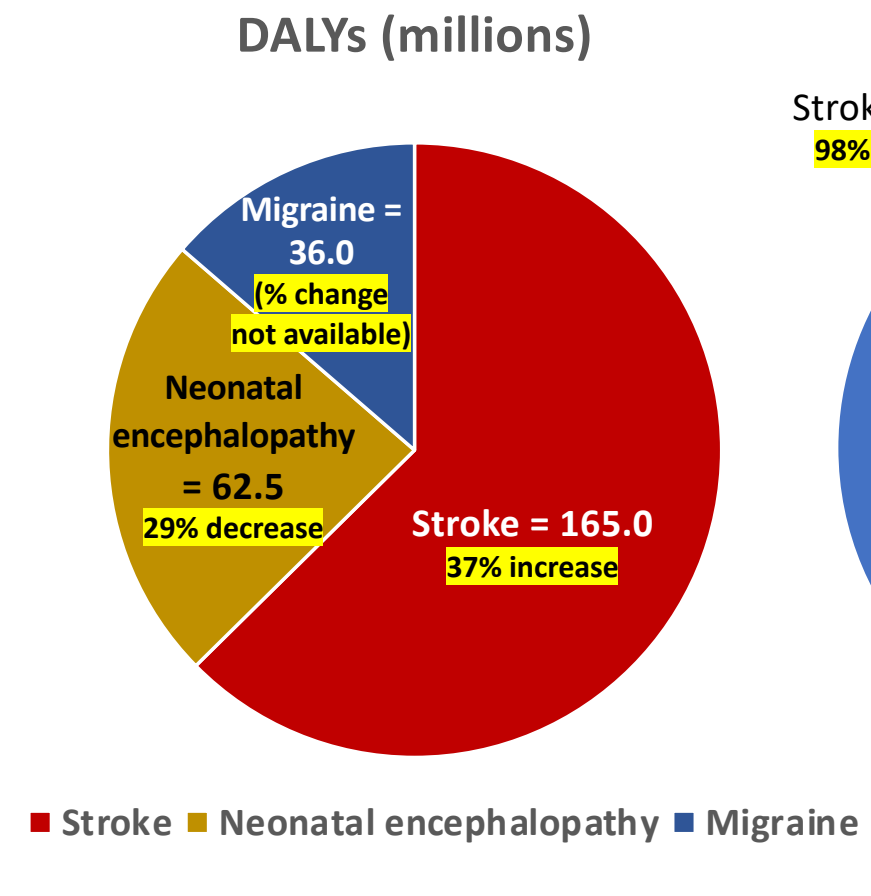
- **DALYs -** Years of healthy life lost to premature death and disability
- **DALYs** = YLL + YLD

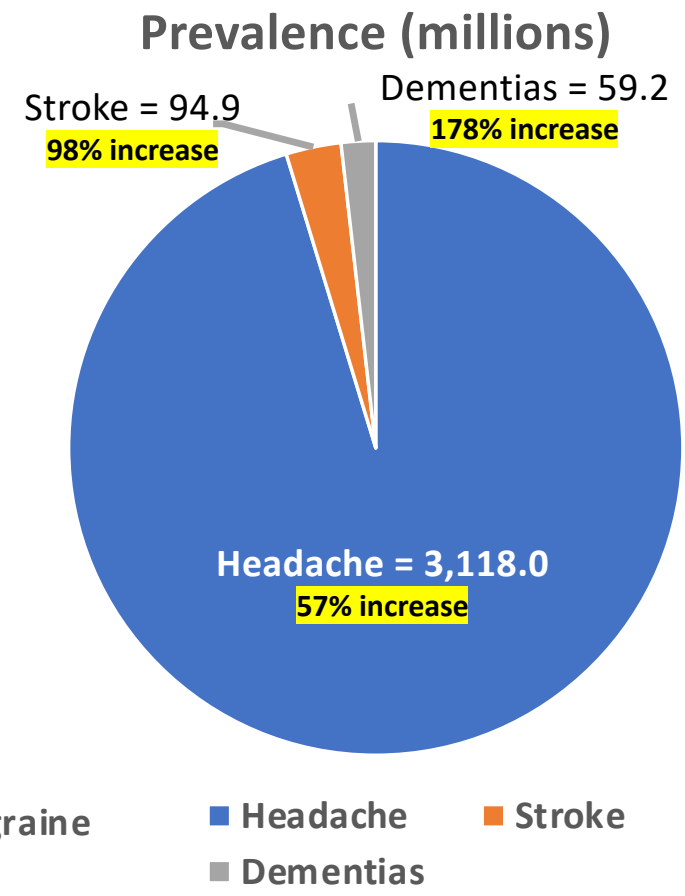
National age-standardised DALY rates for all neurological conditions, 2021

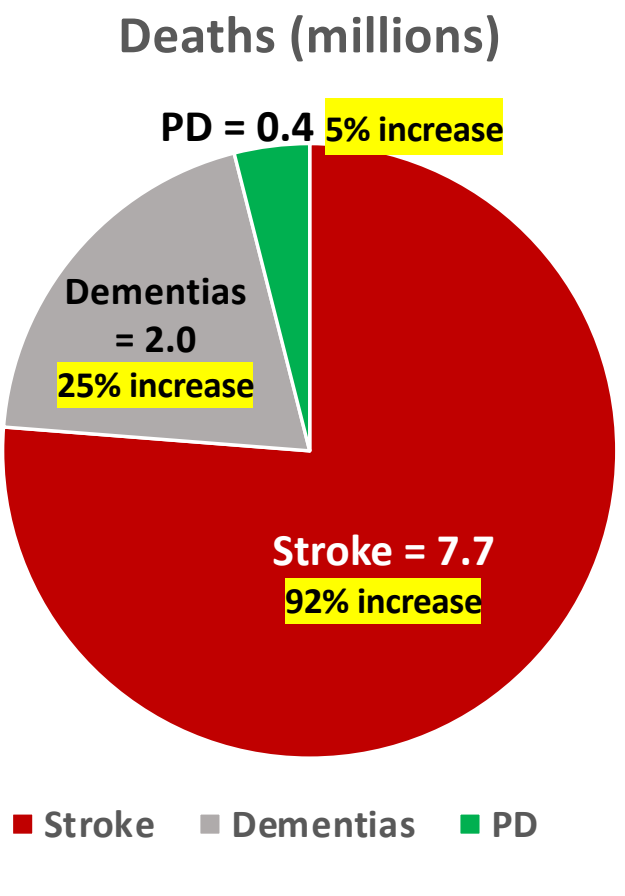


LMICs: >90% of all neurological DALYs
84% of all neurological deaths

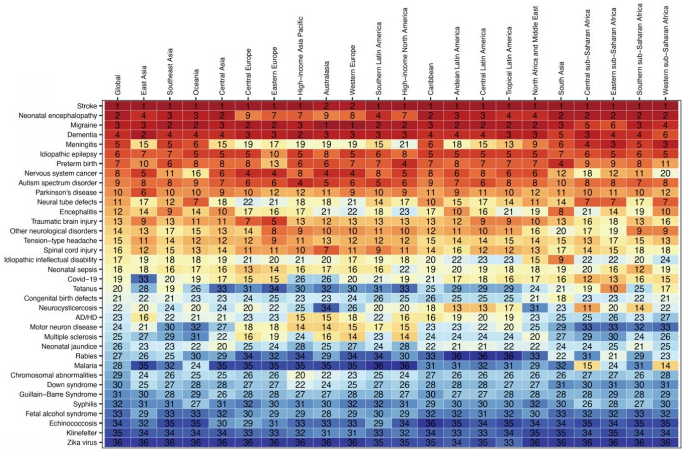
Three diseases contributing most to the global burden of neurological conditions, and % of change from 1990 to 2021 (highlighted)







Top 10 neurological disorders in the world by 21 GBD regions

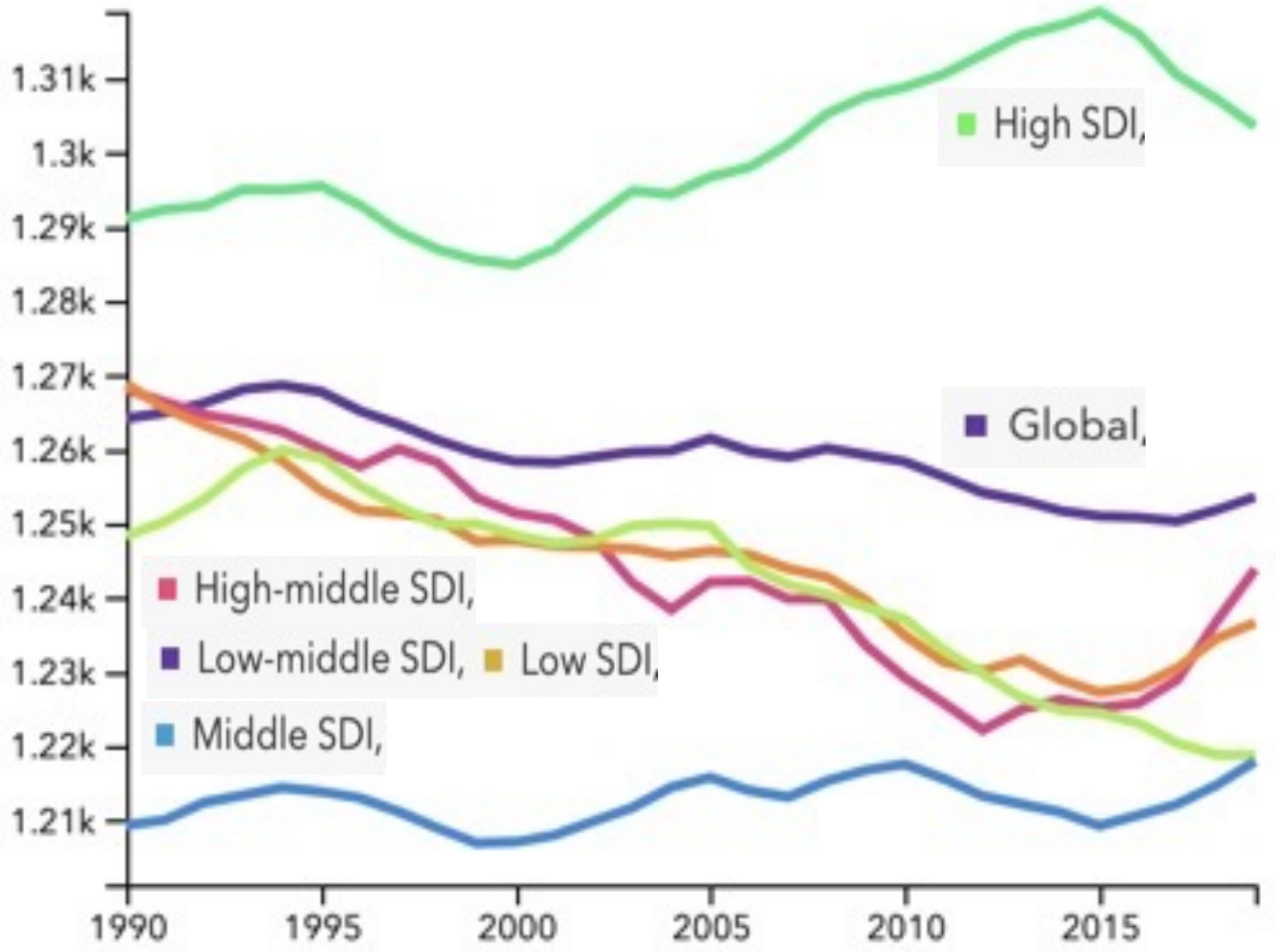


	Global	East Asia	Southeast Asia	Oceania	Central Asia	Central Europe	Eastern Europe	High-income Asia Pacific	Australasia	Western Europe	Southern Latin America	High-income North America	Caribbean	Andean Latin America	Central Latin America	Tropical Latin America	North Africa and Middle East	South Asia	Central sub-Saharan Africa	Eastern sub-Saharan Africa	Southern sub-Saharan Africa	Western sub-Saharan Africa
Neonatal encephalopathy	1	1	1	1	1	1	1	1	2	2	1	1	1	1	1	1	1	1	1	1	1	1
Migraine	2	4	3	3	2	9	7	7	9	8	4	7	2	3	3	4	4	2	2	2	2	2
Meningitis	3	3	2	2	3	2	2	3	1	1	2	2	3	2	2	2	2	3	5	6	3	4
Idiopathic epilepsy	4	2	4	4	4	3	3	2	3	3	3	3	4	4	4	3	3	5	3	4	4	6
Parkinson's disease	5	15	5	6	15	19	17	19	19	19	15	21	6	18	15	13	9	6	4	3	5	3
Stroke	6	7	7	5	5	5	10	5	8	5	6	8	5	5	5	5	5	7	6	5	6	5
Dementia	7	10	6	8	8	8	13	6	6	7	7	4	7	8	7	7	7	4	9	9	8	11
Nervous system cancer	8	5	11	16	6	4	4	8	4	4	8	5	8	6	8	6	6	12	18	12	11	20
Preterm birth	9	8	8	9	7	6	6	4	5	6	5	6	9	7	6	8	8	10	8	8	7	8
Autism spectrum disorder	10	6	10	10	9	10	12	12	11	9	10	9	11	9	11	10	12	11	10	11	10	12

Socio-demographic Index (SDI)

- A summary measure that identifies where countries or other geographic areas sit on the spectrum of development. Expressed on a scale of 0 to 1, SDI is a composite average of the rankings of the incomes per capita, average educational attainment, and fertility rates of all areas in the GBD study.

Age-standardised DALY rates trend of all neurological disorders combined by SDI



Understanding GBD 1990-2021 Study limitations

- Not all common neurological disorders were included (e.g., diabetic neuropathy, restless leg syndrome etc.)
- Not all types of mental disorders included into the group of neurodevelopmental disorders
- Not the whole spectrum of neurological complications associated with COVID-19 was included
- We assumed independence of disabling sequelae when making comorbidity corrections, which can lead to overestimation of the non-fatal burden
- Did not account for deaths associated with TBI and SCI
- General limitations shared by all GBD studies

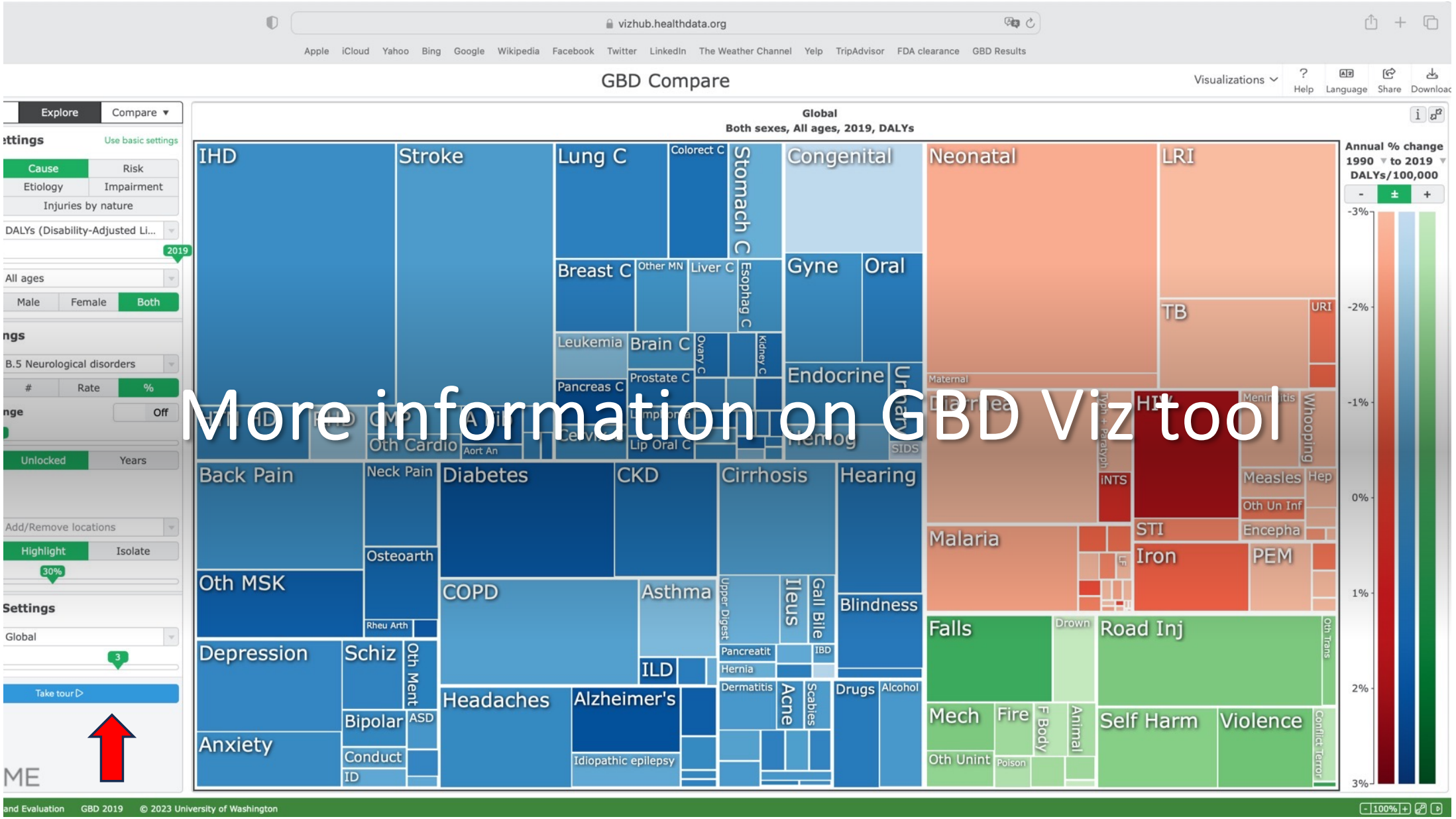
Understanding differences in the same estimates between cycles of GBD publications

Causes of differences

- Implementation of methodological improvements
- Incorporation of new evidence and data (including additional health conditions)

Interpretation of difference

- Latest published estimates overwrite previously published estimates for all previous years


vizhub.healthdata.org
Apple iCloud Yahoo Bing Google Wikipedia Facebook Twitter LinkedIn The Weather Channel Yelp TripAdvisor FDA clearance GBD Results
GBD Compare
Visualizations
Help
Language
Share
Download
Explore
Compare
Use basic settings
Cause
Risk
Etiology
Impairment
Injuries by nature
DALYs (Disability-Adjusted Li...
2019
All ages
Male
Female
Both
B.5 Neurological disorders
#
Rate
%
Off
Unlocked
Years
Add/Remove locations
Highlight
Isolate
30%
Settings
Global
3
Take tour
Global
Both sexes, All ages, 2019, DALYs
Annual % change
1990 to 2019
DALYs/100,000
-3%
-2%
-1%
0%
1%
2%
3%
IHD
Stroke
Lung C
Colorect C
Stomach C
Congenital
Neonatal
LRI
Breast C
Other MN
Liver C
Esophag C
Gyne
Oral
TB
URI
Leukemia
Brain C
Ovary C
Kidney C
Pancreas C
Prostate C
Endocrine
Maternal
Oth Cardio
Aort An
Lip Oral C
SIDS
Back Pain
Neck Pain
Diabetes
CKD
Cirrhosis
Hearing
Osteoarth
Oth MSK
Rheu Arth
COPD
Asthma
ILD
Upper Digest
Ileus
Gall Bile
Pancreatit
Hernia
IBD
Blindness
Depression
Schiz
Oth Ment
Bipolar
ASD
Conduct
ID
Anxiety
Headaches
Alzheimer's
Idiopathic epilepsy
Dermatitis
Acne
Scabies
Drugs
Alcohol
Falls
Drown
Road Inj
Oth Trans
Mech
Fire
F Body
Animal
Oth Unint
Poison
Self Harm
Violence
Conflict Terror
iNTS
Malaria
LF
HIV
STI
Iron
PEM
Measles
Hep
Oth Un Inf
Encepha
Whooping
More information on GBD Viz tool
and Evaluation
GBD 2019
© 2023 University of Washington
100%