Overview, data source, and modeling for Global Burden of Disease 2021

Overview

The Global Burden of Disease (GBD) is a systematic, scientific effort to quantify the comparative magnitude of health loss due to diseases, injuries, and risk factors by age, sex, and geography for specific points in time. The Institute for Health Metrics and Evaluation (IHME) serves as the coordinating center for GBD and affiliated projects. Published in The Lancet, GBD 2021 provides, for the first time, an independent estimation of population for each of 204 countries and territories, and for the globe, using a standardized, replicable approach. It also offers a comprehensive update on fertility and migration.

GBD 2021 incorporates major data additions, improvements, and methodological refinements. Mortality and life expectancy estimates have expanded to a total of 990 locations at the most detailed level. New causes have been added to the fatal and nonfatal cause lists, totaling 369 diseases and injuries. GBD 2021 estimated incidence, prevalence, mortality, years lived with disability (YLDs), years of life lost (YLLs), and disability-adjusted life-years (DALYs) for 23 age groups, males, females, and both sexes combined, across 204 countries and territories, grouped into 21 regions and seven super-regions. The GBD 2021 location hierarchy includes all WHO member states. The GBD disease and injury analytical framework generated estimates for every year from 1990 to 2021. Diseases and injuries were organized into a leveled cause hierarchy from the three broadest causes of death and disability at Level 1 to the most specific causes at Level 4. Within the three Level 1 causes—communicable, maternal, neonatal, and nutritional diseases; noncommunicable diseases; and injuries—there are 22 Level 2 causes, 174 Level 3 causes, and 301 Level 4 causes (including 131 Level 3 causes that are not further disaggregated at Level 4). In total, 364 causes are nonfatal and 286 are fatal.

Data Sources

The GBD estimation process is based on identifying multiple relevant data sources for each disease or injury, including censuses, household surveys, civil registration and vital statistics, disease registries, health service use, air pollution monitors, satellite imaging, disease notifications, and other sources. These data are identified from a systematic review of published studies, searches of government and international organization websites, published reports, primary data sources such as the Demographic and Health Surveys, and datasets contributed by GBD collaborators. A total of 86,249 sources were used in this analysis, including 19,354 sources reporting deaths, 31,499 reporting incidence, 1,973 reporting prevalence, and 26,631 reporting other metrics. Each newly identified and obtained data source is given a unique identifier by a team of librarians and included in the Global Health Data Exchange (GHDx). The GHDx makes publicly available the metadata for each source included in GBD, as well as the data where allowed by the data provider. Additional metadata for each source are available in the online GBD citation tool, GBD Results Tool.

Modeling

For most diseases and injuries, processed data are modeled using standardized tools to generate estimates of each quantity of interest by age, sex, location, and year. There are three main standardized tools: the Cause of Death Ensemble Model (CODEm), Spatiotemporal Gaussian Process Regression (ST-GPR), and DisMod-MR. Previous publications provide more details on these general GBD methods.

CODEm is a highly systematized tool to analyze cause of death data using an ensemble of different modeling methods for rates or cause fractions with varying choices of covariates that perform best with out-of-sample predictive validity testing. DisMod-MR is a Bayesian meta-regression tool that evaluates all available data on incidence, prevalence, remission, and mortality for a disease, enforcing consistency between epidemiological parameters. Previous studies have shown that DisMod-MR can produce robust and valid estimates compared with real surveillance data. ST-GPR is a set of regression methods that borrow strength between locations and over time for single metrics of interest, such as risk factor exposure or mortality rates.

Ref:

- GBD 2021 Diabetes Collaborators. “Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021.” Lancet (London, England) vol. 402,10397 (2023): 203-234. doi:10.1016/S0140-6736(23)01301-6
- GBD 2021 Low Back Pain Collaborators. “Global, regional, and national burden of low back pain, 1990-2020, its attributable risk factors, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021.” The Lancet. Rheumatology vol. 5,6 e316-e329. 22 May. 2023, doi:10.1016/S2665-9913(23)00098-X
- GBD 2021 Sickle Cell Disease Collaborators. “Global, regional, and national prevalence and mortality burden of sickle cell disease, 2000-2021: a systematic analysis from the Global Burden of Disease Study 2021.” The Lancet. Haematology vol. 10,8 (2023): e585-e599. doi:10.1016/S2352-3026(23)00118-7

1. YLD computation

The GBD 2010 DWs were critically dependent on the ways that outcomes were described to survey respondents. Descriptions for health states were designed to balance validity and parsimony, and this approach necessarily meant that some details of different health states had to be omitted. Because lay descriptions were developed collaboratively through individual expert groups organised around a particular set of health issues, some amount of variability in language and detail inevitably occurred. Criticisms and suggestions for improvement came from a number of commentators on the GBD 2010 DWs measurement study. GBD 2013 expanded the list of disease and injury causes and sequelae mapped to 235 unique health states. Additional data for the European Disability Weights Measurement Study were collected between September 23, 2013 and November 11, 2013 in Hungary, Italy, the Netherlands, and Sweden. The initiation of these surveys was connected to a project sponsored by the European Centre for Disease Prevention and Control (the Burden of Communicable Diseases in Europe project). The four selected countries were chosen to be representative of the four regions of Europe (east, south, middle, and north) in terms of age, sex, and education of the respondents. Respondents were recruited from standing internet panels in each country on the basis of quota sampling with reference to age, sex, and education in such a way as to maintain the population representativeness of these characteristics. Eligible participants were 18–65 years old and were preselected in the Netherlands, where the age, sex, and education of respondents were already known, or in the other three countries, invited to participate via a web-link and then selected on

the basis of their individual characteristics. The protocol for the European DWs measurement study followed the protocol that was developed and implemented in the GBD 2010 DWs measurement study. Lay descriptions for some health states that lacked mention of an important symptom or for which consistency of wording across different levels of severity had been noted were reworded. The European DWs measurement study included 255 health states, of which 183 were used in the analyses of GBD 2013. Those 183 consisted of 135 of the 220 health states that were included in the European DWs measurement study with unmodified lay descriptions and 30 from GBD 2010 for which alternative lay descriptions were included. DWs were estimated for additional sequelae that were incorporated into GBD 2013 but had not been included in GBD 2010. Finding high correlation in resulting DW values between the country surveys and the web survey, we analysed the results of all surveys together. We ran probit regression analyses on the answers to the pair-wise comparison questions by using dummies for each health state with a value of 1 for the first state in a pair, –1 for the second state in a pair, and 0 for all states other than the pair. This method formalizes the intuition that if two health states in a pair produce similar health loss, the answers are likely to be evenly split; a pair of health states with very different health loss get many more responses favouring one over the other. The statistical methods infer the distances between values attached to different health states based on the frequencies of responses to the paired comparisons. A second analytic step is needed to anchor the resulting estimates onto the 0–1 DWs scale. We anchored results from the probit regression analysis onto the 0–1 scale by using

population health equivalence data from the GBD 2010 web survey by using a linear regression of the probit coefficients from the analysis of paired comparisons on the logit-transformed DW estimates derived from interval regression of the population health equivalence responses. Using numerical integration, we then estimated mean values for DWs on the natural 0–1 scale. Uncertainty was estimated by bootstrapping with 1000 samples.

The final stage in the estimation of YLDs is a micro-simulation, which adjusts for comorbidity. We refer to this micro-simulation process as "COMO" (for comorbidity correction). For GBD 2019, we estimated the co-occurrence of different diseases by simulating 40,000 individuals in each location-age-sex-year combination as exposed to the independent probability of having any of the sequelae included in GBD 2019 based on disease prevalence. We tested the contribution of dependent and independent comorbidity in the US MEPS data and found that independent comorbidity was the dominant factor even though well-known examples of dependent comorbidity exist, such as clustering of conditions like diabetes and stroke or anxiety and alcohol use disorders. Age was the main predictor of comorbidity such that age-specific micro-simulations accommodated most of the required comorbidity correction. 67 The two components necessary for the computation of YLDs, prevalence of each disease sequelae and DWs, are the two inputs into COMO. The prevalence values are primarily produced by using DisMod-MR 2.1. The DWs have been described earlier in this appendix. The micro-simulation, as performed for each age-sex-location-year, can best be represented as a fourstep process. First, simulants are exposed to

independent probabilities of having each sequela, where the probability is equal to the prevalence estimate. For each simulant, the probability of having a disease sequela is equal to the estimated prevalence from that draw from the uncertainty distribution. Each simulant is determined to have or not have the disease sequelae based on a draw from a binomial distribution. From this simulation, simulants end up having from no to multiple disease sequelae. Second, the DW for each simulant is estimated on the basis of the disease sequelae that they have acquired. The formula for the cumulative DW for a simulant is one minus the multiplicative sum of one minus each DW present

$$Simulant\ DW_l = 1 - \prod_{k=i}^{j} (1 - DW_k)$$

Where:

DW_k is the DW for the k[th] disease sequela that the simulant l has acquired.

Once the simulant DW is computed, the DW attributable to each sequela for the simulant is calculated by using the following formula:

$$ADW_{lk} = \frac{DW_k}{\sum_{k=i}^{k=j} DW_k} * Simulant\ DW_l$$

Where:

ADW_{lk} is the attributable DW for disease sequela k in simulant l

DW_k is the DW for disease sequela k

Simulant DW_l is the DW for simulant l from the combination of all sequelae that they have acquired.

This formula apportions the overall simulant DW to each condition in proportion to the DW of each condition in isolation.

Finally, YLDs per capita in an age-sex-country-year are computed by taking the sum of the attributable DWs for a disease sequela across simulants.

$$YLD\ Rate_k = \frac{\sum_{l=1}^{n} ADW_{lk}}{n}$$

The actual number of YLDs from disease sequela k in an age-sex-location-year is then computed as the YLD rate k times the appropriate age-sex-location-year population. By repeating the simulation process for each age-sex-country-year 1000 times, the uncertainty in the prevalence of each disease sequela and the DW is propagated into the final comorbidity corrected YLD results. We selected 40,000 simulants for each age-sex-location-year group on the basis of simulation testing, which has shown that results are stable for YLDs at this number of simulants even in the younger age groups when prevalence is relatively low. Mean results for YLDs that reflect 40 million simulants (40,000 simulants multiplied by 1000 iterations to capture uncertainty) are very stable in each age-sex-location-year. For any given location-year-age-sex group, sequelae with a prevalence of less than one in 20,000 were excluded from the micro-simulation.

2. DALY calculation

Literature reviews as well as population-based surveys and reports from knee osteoarthritis registries were the main sources of incidence. The DisMod-MR 2.1 model was used to estimate KOA based on age, sex, location and other covariates. Disability weights (DW) range from 0 to 1, where 0 represents health and 1 represents death, and reflect the severity of non-fatal disability caused by a specific disease. The

number of years lived with a disability is calculated by multiplying the DW and the duration of the disability. A disability-adjusted life year (DALY) is the sum of a lost life year and a disability life year. For the decomposition analysis we used the decomposition method developed by Das Gupta to decompose the disability-adjusted life years (DALYs) for osteoarthritis of the knee caused by population ageing, population growth and epidemiological changes.

DALY is calculated as:

$$DALY_{a,g,e,t} = \sum_{k=1}^{20} a_{k,t} * p_t * e_{k,t}$$

Where $DALY_{a,g,e,t}$ represents DALYs number cumulated by population aging, population growth and epidemiologic changes in year t, $a_{k,t}$ is the proportion of population for the age group k at year t, P_t is the population size at year t, and $e_{k,t}$ is represented by DALYs rate for a specific age group k at year t.

3. SDI computation

SDI was originally constructed for GBD 2015 by using the Human Development Index (HDI) methodology, wherein a 0 to 1 index value was determined for each of the original three covariate inputs (TFR in ages 15 to 49 years, EDU15+, and LDI per capita) by using the observed minima and maxima over the estimation period to set the scales. In response to feedback from collaborators and the evolution of the GBD, we have refined the indicator with each GBD cycle. Beginning in GBD 2017, along with our expanded estimation of age-specific fertility, we replaced TFR with TFU25 as one of the three component indices. The TFU25 provides a better measure of women's status in society because it focuses on ages at which childbearing disrupts

the pursuit of education and entrance into the workforce. In addition, we observed that in highly developed countries, the TFU25 has tended to decline consistently over time despite rebounds in TFR driven by increasing fertility at older ages.

Thus, for each covariate input, an index score of 0 represents the minimum level of ea ch covariate input past which selected health outcomes can get no worse, and an index score of 1 represents the maximum level of each covariate input past which selected h ealth outcomes cease to improve. As a composite, a ocation with an SDI of 0 would h ave a theoretical minimum level of sociodemographic development relevant to these h ealth outcomes, and a location with an SDI of 1 (before multiplying by 100 for reporti ng) would have a theoretical maximum level of sociodemographic development relev ant to these health outcomes.

We computed the index scores underlying SDI as follows:

$$I_{cly} = \max\left(\frac{C_{ly} - C_{low}}{C_{high} - C_{low}}, 0.05\right)$$

Where:

I_{cly} is the index for covariate C, location l and year y and is equal to the difference between the value of this covariate in this location year and the lower limit of the covariate divided by the difference between the upper and lower limits for this covariate.

Input data and methodological summary

Case definition

Stroke was defined according to WHO criteria as rapidly developing clinical signs of focal (or less commonly global) disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin (1). Cases of transient ischaemic attack (TIA) were not included.

Acute stroke: Stroke cases are considered acute from the day of incidence of a first-ever stroke through day 28 following the event.

Chronic stroke: Stroke cases are considered chronic beginning 28 days following the occurrence of an event. Chronic stroke includes the late sequelae of an acute stroke and all recurrent stroke events. GBD 2015 adopted this broader definition of chronic stroke than what was used in prior iterations to model acute strokes using only first-ever incident events.

Ischaemic stroke: Ischaemic strokes are characterised by occlusion of blood flow to part of the brain due to hypoperfusion, most commonly due to a thrombus or embolism. It is defined as an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction.

Intracerebral haemorrhage: Intracerebral haemorrhage is characterised by the rupture of a blood vessel resulting in bleeding into the intracerebral part of the brain. It is defined as focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma and results in a clinical stroke.

Subarachnoid haemorrhage: Subarachnoid haemorrhage is characterised as bleeding into the subarachnoid space (the space between the arachnoid membrane and the pia mater of the brain or spinal cord) resulting in a clinical stroke.

The reference definitions for ischaemic stroke and intracerebral haemorrhage were first-ever, subtype-specific stroke, which included subjects who did not survive to hospital admission. For these two subtypes we included, after adjustment, sources which used the following alternate

definitions: 1) sources which included first and recurrent strokes; 2) sources which reported only estimates for all subtypes combined; and 3) sources which included only stroke cases which survived to hospital admission.

The reference definition for subarachnoid haemorrhage was first-ever, subtype-specific stroke, with aneurysmal and non-aneurysmal events combined, which included subjects who did not survive to hospital admission. For subarachnoid haemorrhage, we included, after adjustment for bias, sources which used the following alternate definitions: 1) sources which included first and recurrent strokes; 2) sources which reported only estimates for aneurysmal subarachnoid haemorrhage; and 3) sources which included only stroke cases which survived to hospital admission.

Table 1: ICD codes used for inclusion of hospital and claims data

Stroke subtype	ICD-9	ICD-10
Ischaemic stroke	433-435.9, 437.0-437.1, 437.5-437.8	G45-G46.8, I63-I63.9, I65-I66.9, I67.2-I67.3, I67.5-I67.6, I69.3
Intracerebral haemorrhage	431-432.9, 437.2	I61-I62, I62.1-I62.9, I68.1-I68.2, I69.1-I69.2
Subarachnoid haemorrhage	430-430.9	I60-I60.9, I62.0, I67.0-I67.1, I69.0

Input data

Tables 2a, 2b, and 2c display source count information for non-fatal ischaemic stroke, intracerebral haemorrhage, and subarachnoid haemorrhage, respectively.

Table 2a: Source counts for ischaemic stroke models

Measure	Total sources	Countries with data
Prevalence	123	27
Incidence	348	63
Excess mortality rate	150	48
With-condition mortality rate	16	10

Table 2b: Source counts for intracerebral haemorrhage models

Measure	Total sources	Countries with data
Prevalence	121	26
Incidence	355	62
Excess mortality rate	127	41
With-condition mortality rate	13	9

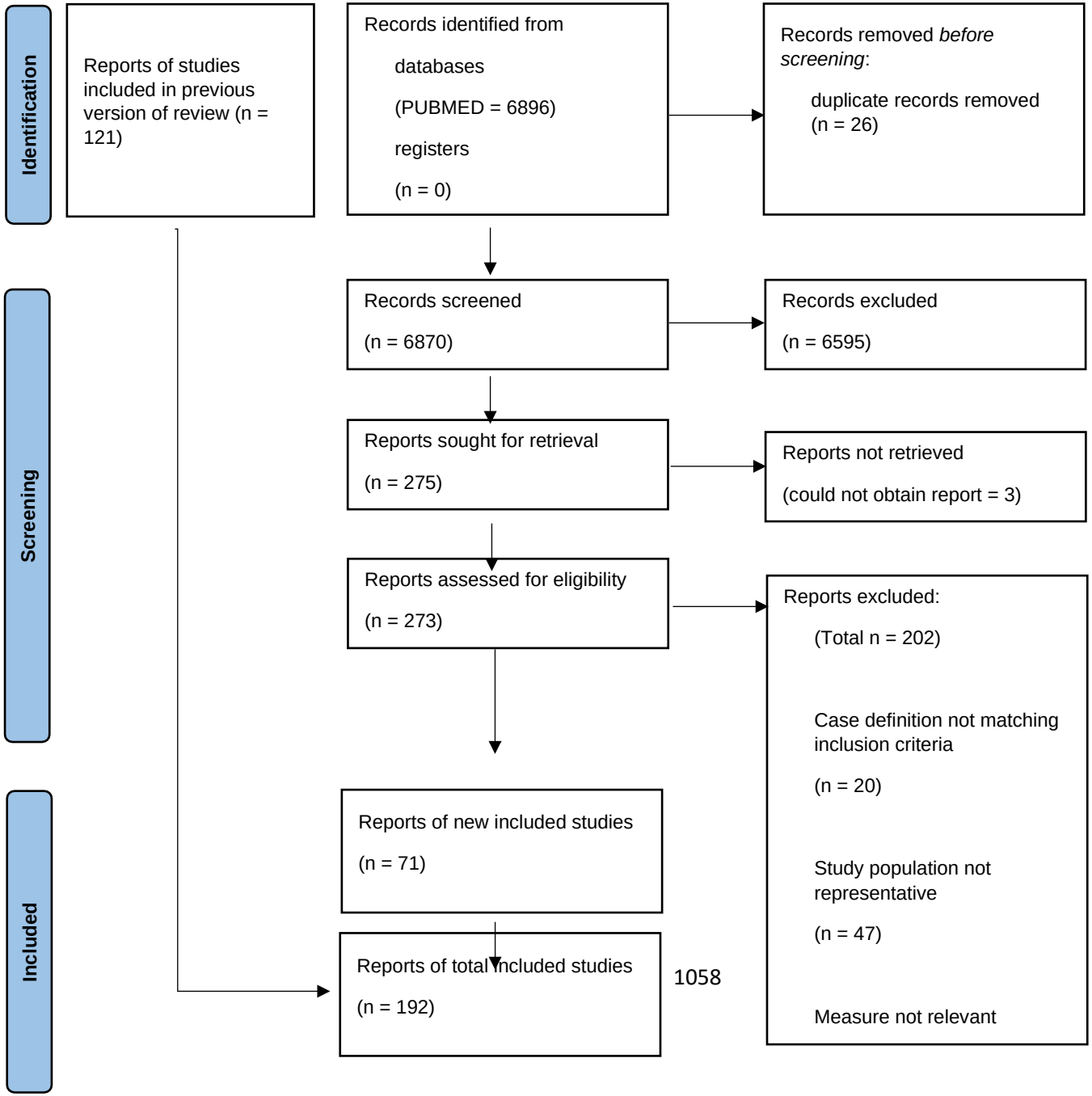
Table 2c: Source counts for subarachnoid haemorrhage models

Measure	Total sources	Countries with data
Prevalence	123	25
Incidence	286	49
Excess mortality rate	88	28
With-condition mortality rate	12	8

A systematic review was performed for stroke models in GBD 2021 in accordance with PRISMA systematic review guidelines. We searched PubMed for our systematic review; the search strings we used and a PRISMA diagram displaying the text review and extraction process are found below:

PubMed: ("stroke"[TIAB] OR "ischemic stroke"[TIAB] OR "ischaemic stroke"[TIAB] OR "cerebral infarction"[TIAB] OR "intracerebral hemorrhage"[TIAB] OR "intracerebral haemorrhage"[TIAB] OR "subarachnoid hemorrhage"[TIAB] OR "subarachnoid haemorrhage"[TIAB]) AND (incidence[TIAB] OR prevalence[TIAB] OR "excess mortality"[TIAB] OR "case fatality"[TIAB] OR "mortality ratio"[TIAB]) AND ("2017/09/01"[PDAT] : "2020/02/25"[PDAT])

Figure 1: PRISMA 2020 flow diagram



In addition to incidence data obtained from the literature reviews for acute stroke, we included inpatient hospital data, adjusted for readmission and primary to any diagnosis using correction factors estimated from claims data in the USA, Poland, Taiwan (province of China), and New Zealand. We excluded data for locations where the datapoints were implausibly low (Viet Nam, the Philippines, India, Nepal, China, Tibet, Kenya, Kyrgyzstan, Chile, Botswana, England, Brazil, Mexico, and Indonesia). For GBD 2021, we split incident unspecified strokes (ICD-10 I64) reported in the hospital data into ischaemic stroke, intracerebral haemorrhage, and subarachnoid haemorrhage according to the proportions of subtype-

specific coded strokes in the inpatient hospital data by source. We also split ICD-10 I62, other and unspecified nontraumatic intracranial haemorrhage, into intracerebral haemorrhage and subarachnoid haemorrhage using the same approach. In addition, we included unpublished stroke registry data for acute ischaemic stroke, acute intracerebral haemorrhage, and acute subarachnoid haemorrhage.

The 30-day case fatality proportion of acute strokes was extracted from the literature and unpublished stroke registries. We expressed 30-day case fatality proportion as a rate (excess mortality rate) using the rate equation $excess\ mortality\ rate = \frac{-\log(1-case\ fatality\ proportion)}{30/365}$. Case fatality proportion was expressed as excess mortality rate under the assumption that death within 30 days of an acute stroke event would be due to the stroke event.[1]

For the chronic stroke models, we included survey data for prevalent stroke. These surveys were identified based on expert opinion and review of major survey series focused on world health that included questions regarding self-reported history of stroke. These surveys reported on the prevalence of all strokes, and we therefore split the prevalence into estimates of subtype-specific stroke prevalence using a custom method described in the modelling strategy section below.

Case fatality proportion of chronic stroke was extracted from the literature and unpublished stroke registries. We expressed case fatality proportion of beyond 30-day acute events as with-condition mortality rate using rate equation $with\ condition\ mortality\ rate = \frac{-\log(1-case\ fatality\ proportion)}{335/365}$ under the assumption that death beyond 30 days may be due to other causes than the index stroke event.[2]

As with many models in GBD, the diversity of data sources available means that we needed to adjust available data to our reference case definition. We thus crosswalked incidence and excess mortality data used in the acute models that did not meet our reference case definitions using MR- BRT, a Bayesian meta-regression tool developed for the GBD. More information on MR-BRT can be found elsewhere in the appendix.

We adjusted datapoints for first and recurrent strokes combined, using data for first strokes only as reference. For ischaemic stroke and intracerebral haemorrhage, we adjusted datapoints that reported all stroke subtypes combined, using as reference studies with subtype-specific information. We also adjusted data which included only persons who survived to hospital admission, using as reference data on both fatal and non-fatal strokes. In addition, we adjusted subtype-specific inpatient clinical informatics data using subtype-specific literature estimates as a reference. These adjustments can be examined more closely in Table 4. The coefficients in Tables 4a, 4b, and 4c below can be used to calculate adjustment factors for alternative definitions. The formula for computing adjustment factors is given in equation 1 below. We included a cubic spline constructed on a standardised age variable (age-scaled) and a sex variable to the crosswalking procedure to adjust for variation by age and sex. With the inclusion of the spline covariate on age, calculating adjustment factors is dependent on what segment of the age spline an adjustment is made; this is shown in tables 3a, 3b, and 3c below.

We split incidence datapoints where the age range was greater than 25 years for all stroke subtypes. Age splitting was based on the global sex-specific age pattern from a single-parameter DisMod model that only included incidence datapoints with less than a 25-year age range.

Equation 1: Calculation of adjustment factors:

$$Estimated\ Reference\ Def = invlogit(logit(Alternative\ Def) - [\sum_{s=0}^{b} Beta_{Alternative\ Def, spline\ basis_s} * Spline\ basis_s(age\_scaled)] - Beta * I(Sex))$$

$I(.)$ = Indicator function, b = Number of spline bases used

No data adjustments were necessary for the chronic stroke models.

Age splines for adjustment factors:
We fit a cubic spline to the standardised age variable (named age_scaled), calculated as:

$$age\ scaled = \frac{(mean\ age\ of\ study - mean(age\ of\ all\ studies))}{standard\ deviation(age\ of\ all\ studies)})$$

We selected knots for the cubic spline on age based on visual inspection of the spline fit to the observed ratios used in computing adjustment factors; see Figures 2a, 2b, and 2c below as examples. The knot placements for the age splines are listed in Table 3. We did not use a spline on age to adjust alternate definitions for subarachnoid haemorrhage incidence or excess mortality rate data for any stroke subtype. The fit of these splines versus the standardised age variable for males and females with the observed logit difference between alternative and reference definitions on the vertical axis are shown in Figures 2a through 2f.

Table 3: Knot placement for age splines

Stroke subtype	Knot placement (age_scaled)	Knot placement (age in years)
Ischaemic stroke	–1.75, –1.00, –0.75, 0.00, 0.75, 1, 1.25	37.9, 49.9, 53.8, 65.7, 77.6, 81.5, 85.5
Intracerebral haemorrhage	–2.95, –1.00, –0.06, 0.85, 1.77	22.1, 51.7, 66.0, 79.8, 93.8

Table 4a: MR-BRT crosswalk adjustment factors for ischaemic stroke

Data input	Measure	Reference or alternate case definition	Gamma	Beta coefficient, logit (95% CI)
First-ever, subtype-specific, fatal and non-fatal events	Incidence	Ref	---	---
Acute first-ever stroke, intercept	Incidence	Alt	0.05	0.34 (0.22 to 0.46)
Acute first-ever stroke, spline_0	Incidence	Alt		–0.30 (–0.50 to –0.10)
Acute first-ever stroke, spline_1	Incidence	Alt		0.01 (–0.07 to 0.09)
Acute first-ever stroke, ages spline_2	Incidence	Alt		–0.12 (–0.17 to –0.07)
Acute first-ever stroke, ages spline_3	Incidence	Alt		–0.19 (–0.25 to –0.14)
Acute first-ever stroke, ages spline_4	Incidence	Alt		0.19 (0.14 to 0.24)
Acute first-ever stroke, ages spline_5	Incidence	Alt		–0.04 (–0.09 to 0.02)
Acute first-ever stroke, ages spline_6	Incidence	Alt		0.07 (0.05 to 0.09)
Acute first-ever stroke, male	Incidence	Alt		0.06 (0.05 to 0.07)
All stroke, intercept	Incidence	Alt		0.33 (0.24 to 0.42)
All stroke, spline_0	Incidence	Alt		0.72 (0.23 to 1.19)
All stroke, spline_1	Incidence	Alt		–0.03 (–0.21 to 0.16)
All stroke, ages spline_2	Incidence	Alt		0.11 (0.01 to 0.22)
All stroke, ages spline_3	Incidence	Alt		–0.46 (–0.60 to –0.32)
All stroke, ages spline_4	Incidence	Alt		0.29

				(0.19 to 0.39)
All stroke, ages spline_5	Incidence	Alt		–0.03 (–0.13 to 0.08)
All stroke, ages spline_6	Incidence	Alt		–0.20 (–0.26 to –0.14)
All stroke, male	Incidence	Alt		–0.09 (–0.12 to –0.07)
Hospital, intercept	Incidence	Alt		–0.08 (–0.20 to 0.03)
Hospital, spline_0	Incidence	Alt		0.57 (0.36 to 0.77)
Hospital, spline_1	Incidence	Alt		0.06 (–0.03 to 0.15)
Hospital, ages spline_2	Incidence	Alt		0.25 (0.20 to 0.30)
Hospital, ages spline_3	Incidence	Alt		0.29 (0.23 to 0.35)
Hospital, ages spline_4	Incidence	Alt		0.02 (–0.03 to 0.08)
Hospital, ages spline_5	Incidence	Alt		0.19 (0.13 to 0.24)
Hospital, ages spline_6	Incidence	Alt		0.03 (0.00 to 0.06)
Hospital, male	Incidence	Alt		–0.11 (–0.12 to –0.10)
Inpatient clinical informatics, intercept	Incidence	Alt		0.50 (0.40 to 0.60)
Inpatient clinical informatics, spline_0	Incidence	Alt		0.40 (0.32 to 0.48)
Inpatient clinical informatics, spline_1	Incidence	Alt		0.06 (0.02 to 0.11)
Inpatient clinical informatics, ages spline_2	Incidence	Alt		0.24 (0.21 to 0.28)

Inpatient clinical informatics, ages spline_3	Incidence	Alt		0.27 (0.24 to 0.31)
Inpatient clinical informatics, ages spline_4	Incidence	Alt		0.16 (0.12 to 0.19)
Inpatient clinical informatics, ages spline_5	Incidence	Alt		0.25 (0.22 to 0.28)
Inpatient clinical informatics, ages spline_6	Incidence	Alt		0.17 (0.15 to 0.18)
Inpatient clinical informatics, male	Incidence	Alt		–0.07 (–0.08 to –0.06)
Acute first-ever stroke, intercept	Excess mortality rate	Alt	0.30	0.05 (–0.20 to 0.30)
Acute first-ever stroke, age_scaled	Excess mortality rate	Alt		–0.23 (–0.25 to –0.21)
Acute first-ever stroke, male	Excess mortality rate	Alt		0.21 (0.19 to 0.23)
All stroke, intercept	Excess mortality rate	Alt		0.54 (0.19 to 0.90)
All stroke, age_scaled	Excess mortality rate	Alt		–0.15 (–0.20 to –0.11)
All stroke, male	Excess mortality rate	Alt		0.14 (0.11 to 0.18)

Figure 2a: Age_scaled spline for adjustment of all stroke to ischaemic stroke incidence data

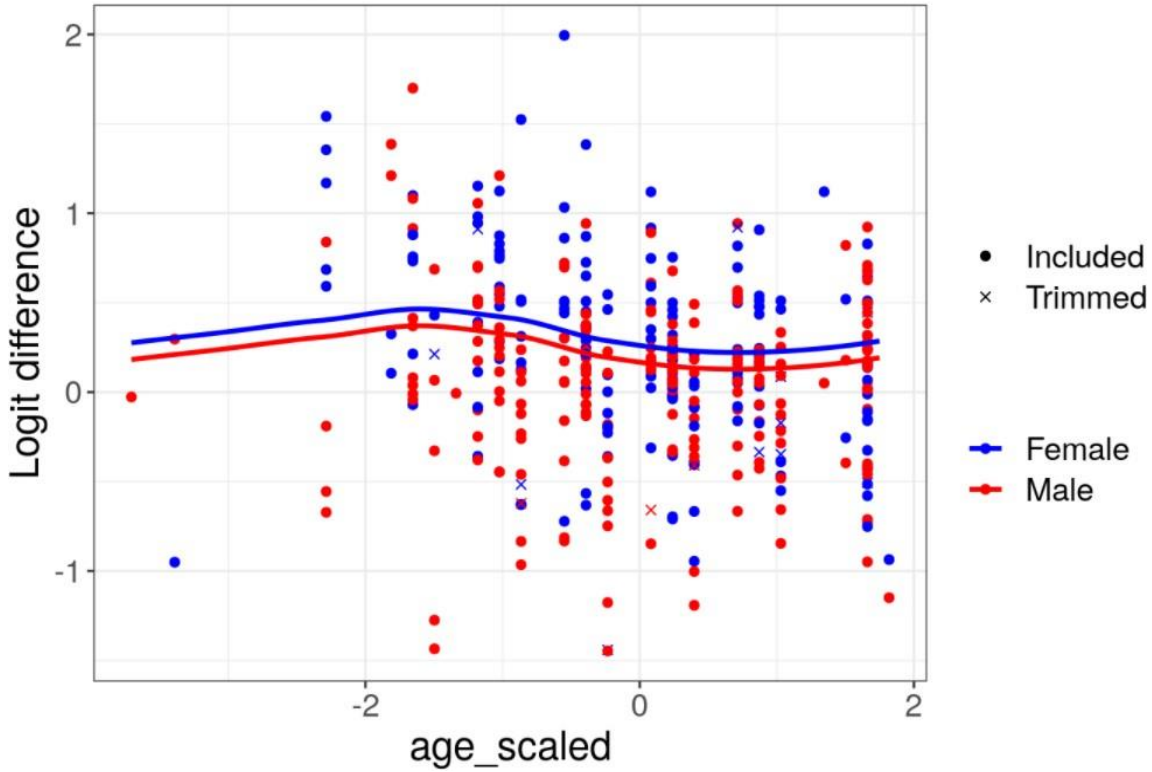


Figure 2b: Age_scaled spline for adjustment of hospital-only ischaemic stroke incidence data

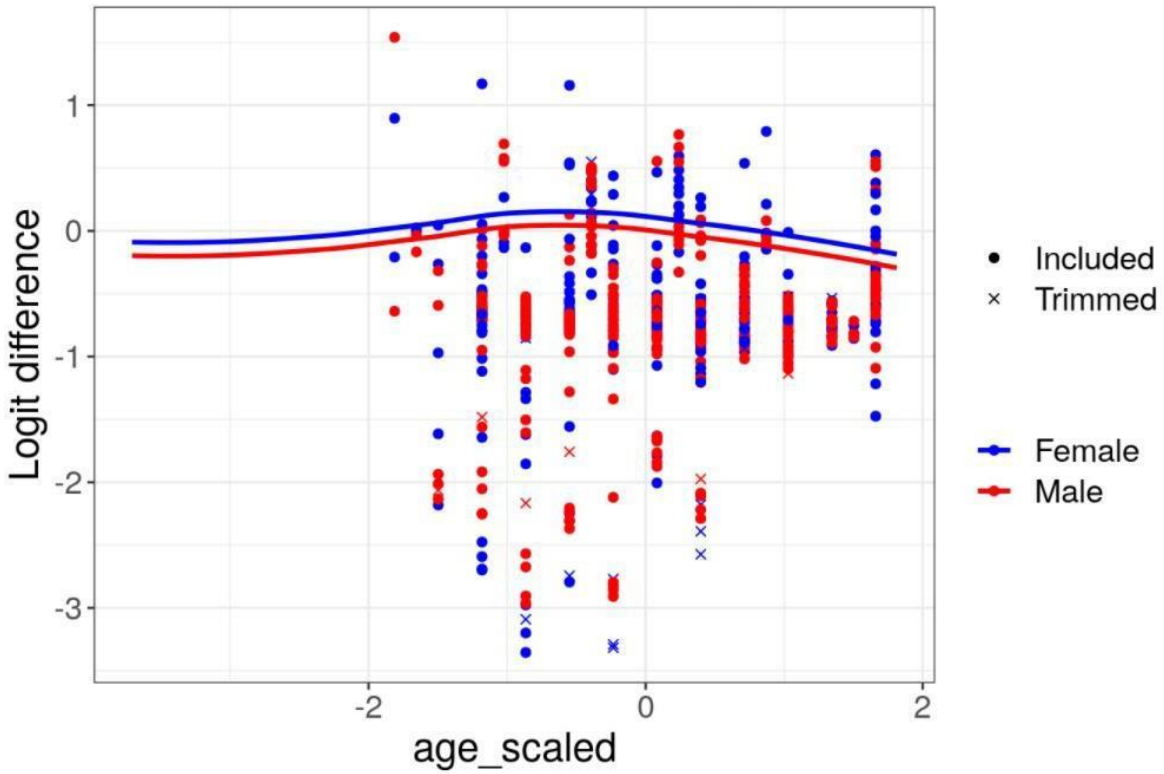


Figure 2c: Age_scaled spline for adjustment of inpatient clinical informatics ischaemic stroke incidence data

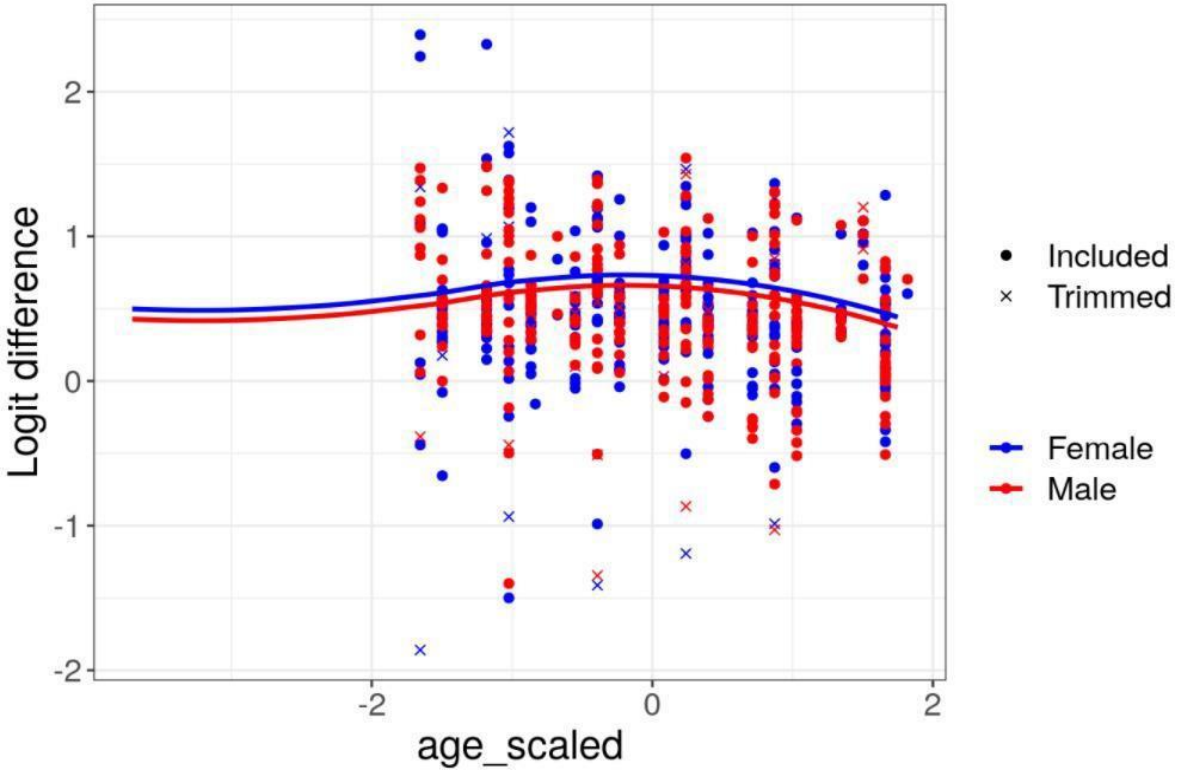


Table 4b: MR-BRT crosswalk adjustment factors for intracerebral haemorrhage

Data input	Measure	Reference or alternate case definition	Gamma	Beta coefficient, logit (95% CI)
First-ever, subtype-specific, fatal and non-fatal events	Incidence	Ref	---	---

Acute first-ever stroke, intercept	Incidence	Alt		–0.07 (–0.23 to 0.09)
Acute first-ever stroke, spline_0	Incidence	Alt		0.01 (–0.10 to 0.11)
Acute first-ever stroke, spline_1	Incidence	Alt		–0.09 (–0.32 to 0.13)
Acute first-ever stroke, ages spline_2	Incidence	Alt		–0.08 (–0.21 to 0.05)
Acute first-ever stroke, ages spline_3	Incidence	Alt		0.11 (–0.01 to 0.22)
Acute first-ever stroke, male	Incidence	Alt		0.15 (0.09 to 0.22)
All stroke, intercept	Incidence	Alt		1.96 (1.83 to 2.08)
All stroke, spline_0	Incidence	Alt		0.07 (0.00 to 0.15)
All stroke, spline_1	Incidence	Alt	0.06	–0.10 (–0.29 to 0.09)
All stroke, ages spline_2	Incidence	Alt		0.25 (0.16 to 0.34)
All stroke, ages spline_3	Incidence	Alt		0.20 (0.12 to 0.29)
All stroke, male	Incidence	Alt		–0.09 (–0.15 to –0.03)
Hospital, intercept	Incidence	Alt		0.11 (–0.01 to 0.23)
Hospital, spline_0	Incidence	Alt		–0.09 (–0.15 to –0.04)
Hospital, spline_1	Incidence	Alt		0.12 (0.01 to 0.23)
Hospital, ages spline_2	Incidence	Alt		0.09 (0.04 to 0.15)
Hospital, ages spline_3	Incidence	Alt		0.07 (0.03 to 0.11)

Hospital, male	Incidence	Alt		–0.04 (–0.07 to –0.01)
Inpatient clinical informatics, intercept	Incidence	Alt		1.01 (0.90 to 1.11)
Inpatient clinical informatics, spline_0	Incidence	Alt		–0.09 (–0.12 to –0.05)
Inpatient clinical informatics, spline_1	Incidence	Alt		0.03 (–0.04 to 0.10)
Inpatient clinical informatics, ages spline_2	Incidence	Alt		–0.07 (–0.11 to –0.04)
Inpatient clinical informatics, ages spline_3	Incidence	Alt		–0.15 (–0.18 to –0.12)
Inpatient clinical informatics, male	Incidence	Alt		0.03 (0.01 to 0.05)
Acute first-ever stroke, intercept	Excess mortality rate	Alt	0.20	0.45 (0.13 to 0.78)
Acute first-ever stroke, age_scaled	Excess mortality rate	Alt		–0.40 (–0.43 to –0.37)
Acute first-ever stroke, male	Excess mortality rate	Alt		–0.01 (–0.04 to 0.02)
All stroke, intercept	Excess mortality rate	Alt		–0.66 (–1.07 to –0.24)
All stroke, age_scaled	Excess mortality rate	Alt		–0.34 (–0.59 to –0.10)
All stroke, male	Excess mortality rate	Alt		0.04 (–0.02 to 0.10)

Figure 2d: Age_scaled spline for adjustment of all stroke to intracerebral haemorrhage incidence data

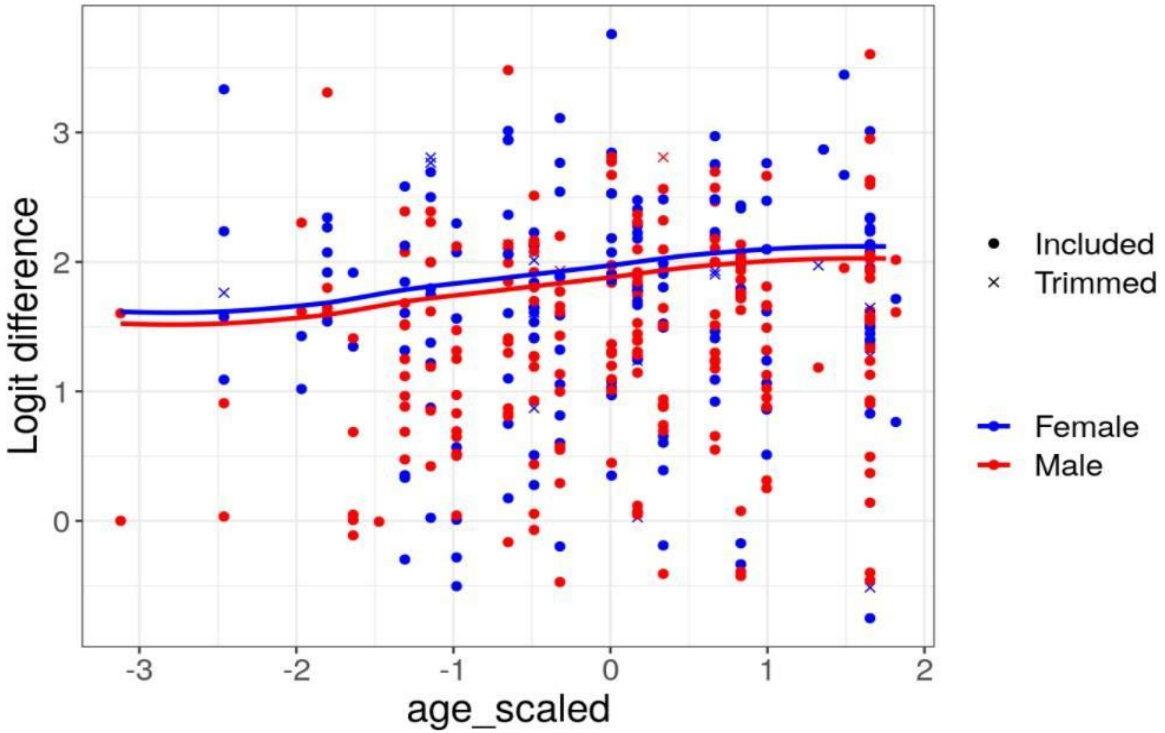


Figure 2e: Age_scaled spline for adjustment of hospital-only intracerebral haemorrhage incidence data

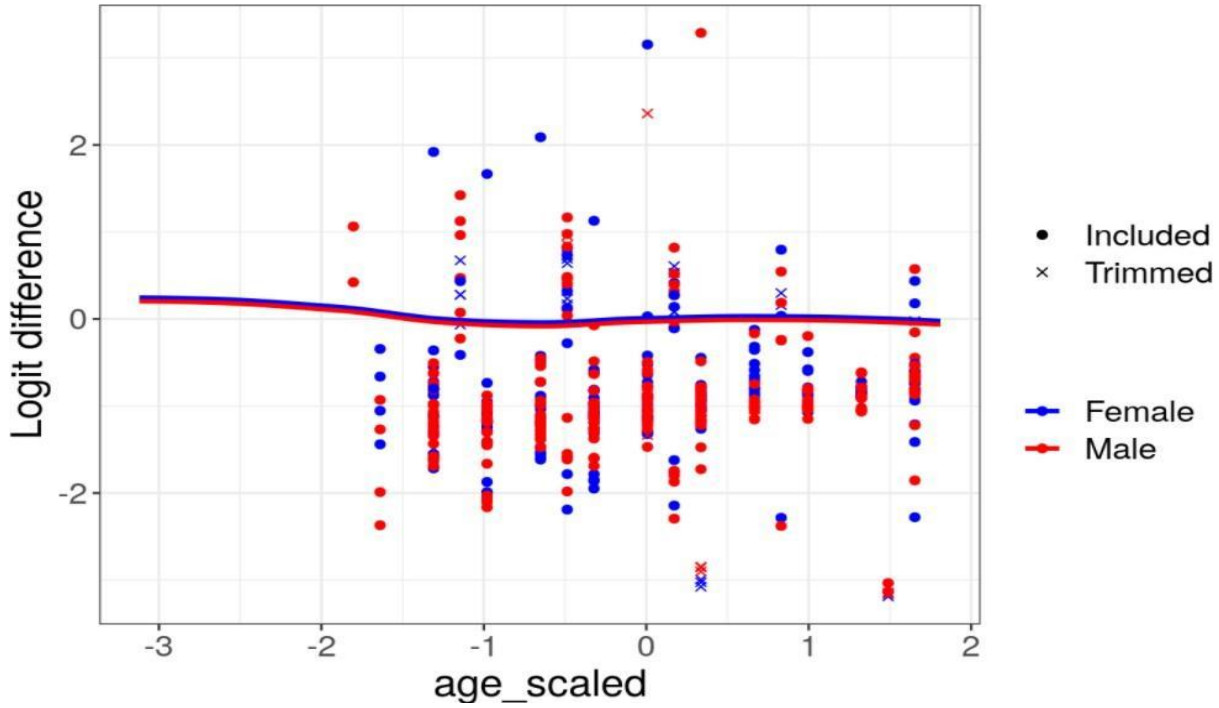


Figure 2f: Age_scaled spline for adjustment of inpatient clinical informatics intracerebral haemorrhage incidence data

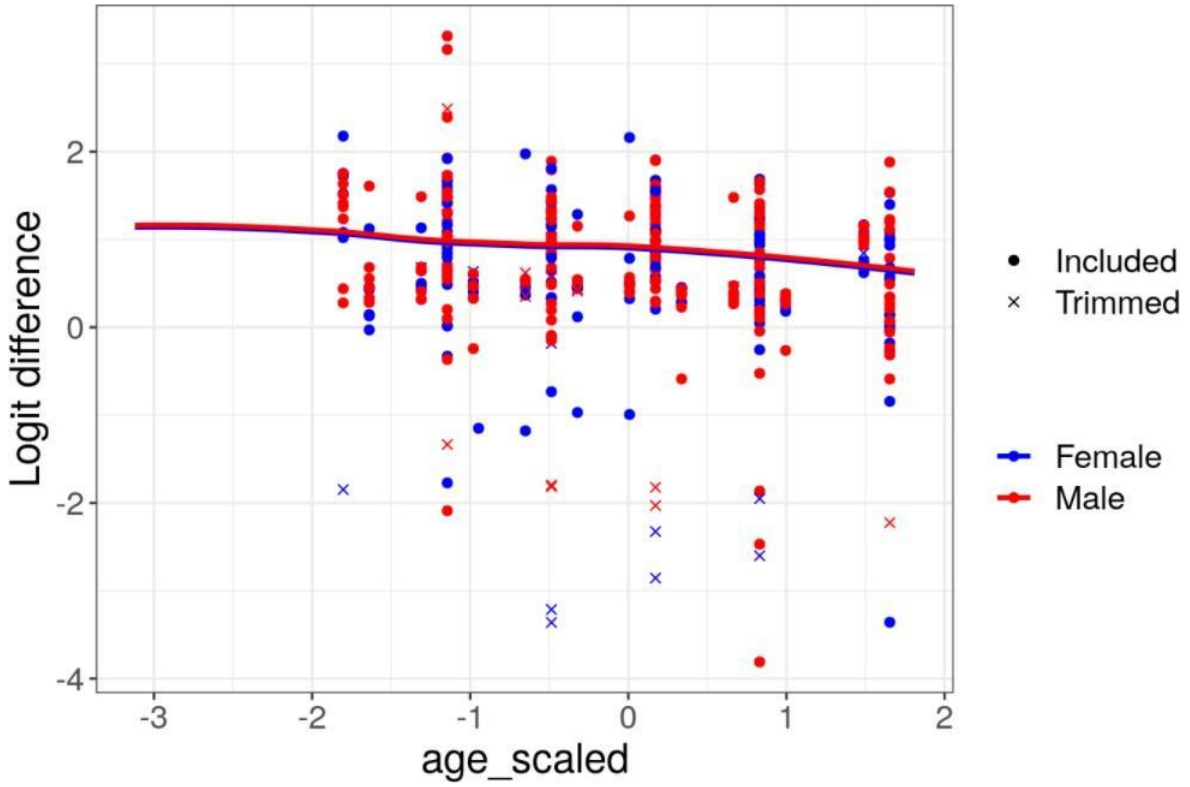


Table 4c: MR-BRT crosswalk adjustment factors for subarachnoid haemorrhage

Data input	Measure	Reference or alternate case definition	Gamma	Beta coefficient, logit (95% CI)

First-ever, subtype-specific, fatal and non-fatal events	Incidence	Ref	---	---
Aneurysmal subarachnoid haemorrhage only, intercept	Incidence	Alt	0.15	–0.08 (–0.27 to 0.10)
Aneurysmal subarachnoid haemorrhage only, age_scaled	Incidence	Alt		–0.15 (–0.17 to –0.12)
Aneurysmal subarachnoid haemorrhage only, male	Incidence	Alt		–0.10 (–0.14 to –0.07)
Acute first-ever stroke, intercept	Incidence	Alt		0.02 (–0.20 to 0.25)
Acute first-ever stroke, age_scaled	Incidence	Alt		–0.02 (–0.08 to 0.04)
Acute first-ever stroke, male	Incidence	Alt		0.05 (–0.03 to 0.14)
Inpatient clinical informatics, intercept	Incidence	Alt		1.11 (0.92 to 1.29)
Inpatient clinical informatics, age_scaled	Incidence	Alt		–0.11 (–0.12 to –0.10)
Inpatient clinical informatics, male	Incidence	Alt		–0.02 (–0.03 to –0.01)

Severity split inputs

The table below illustrates the severity level, lay description, and disability weights for GBD 2021. In previous iterations of GBD, severity splits for stroke were based on the standard approach described elsewhere (3). For GBD 2016, we undertook a review to identify epidemiological literature which reported the degree of disability at 28 days (for acute stroke) or one year (for chronic stroke) using the modified Rankin scale (mRS) and the Mini-Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MoCA). The mRS assesses functional capabilities, whereas the MMSE and MoCA tests provide evaluations of cognitive functioning. We then mapped these measures to the existing GBD categories as indicated in table 5a below. This approach allowed us to include location-specific information and can be updated as more data on functional or cognitive status become available.

We used established cutoffs[3] of the mRS to determine three levels of physical limitation: asymptomatic stroke corresponds to an mRS of 0, mild physical limitations correspond to an mRS of 1 or 2, moderate physical limitations correspond to an mRS of 3, and severe physical limitations correspond to an mRS of 4 or 5. Within the moderate and severe levels of physical limitations, we included categories for those with and without cognitive impairment. This was defined by an MMSE score of less than 24 or a MoCA score of less than 26. In total, this creates six groups of stroke severity (asymptomatic, mild, moderate without cognitive impairment, moderate with cognitive impairment, severe without cognitive impairment, and severe with cognitive impairment). Within these six groups of severity, we further accounted for heart failure due to stroke (stress cardiomyopathy due to acute stroke) and dementia due to stroke as described below.

For GBD 2021, we updated the severity splits for both acute and chronic stroke subtypes to include sequelae leading to controlled, medically managed, mild, moderate, and severe heart failure. The process of estimating heart failure is described elsewhere in the appendix. We also included updates to our chronic stroke model with cognitive impairment to add sequelae of mild, moderate, and severe dementia. The process for estimating dementia is described elsewhere in the appendix. The GBD methods for estimating burden for heart failure and dementia produce estimates of their respective disease burden due to stroke.

For cases of heart failure due to stroke, this involves first estimating the amount of heart failure due to acute stroke and the amount persisting as chronic stroke subtypes. We then split the heart failure due to stroke cases into the stroke severity levels dependent on the mRS and MMSE and MoCA exams as shown in Tables 5a and 5b below. We next split heart failure due to each stroke severity level into the four severity levels for heart failure (controlled, medically managed; mild; moderate; severe).

A similar process accounts for dementia due to stroke cases. In accounting for dementia due to stroke, we assume that dementia due to stroke is a subset of moderate stroke with cognitive impairment and severe stroke with cognitive impairment and adjust only these categories. Unlike heart failure, the GBD estimation process does not produce dementia due to stroke by subtype. We first split the dementia due to stroke cases into stroke subtypes proportionally by the number of estimated chronic stroke subtype cases by age, sex, year, and location. We then assign the dementia due to stroke subtype cases to stroke severity levels 3 and 5 (moderate with cognitive impairment and severe with cognitive impairment respectively) proportionally, with at least 10% of dementia due to stroke cases included in stroke severity level 3 and the remaining 90% of cases included in stroke severity level 5. The proportions of dementia due to stroke severity levels 3 and 5 were determined by expert opinion. If the cases arose that we had more estimated dementia due to severe stroke with cognitive impairment than we did severe stroke with cognitive

impairment cases, the differential number of dementia due to severe stroke cases were added to the moderate stroke with cognitive impairment cases. Finally, the severe and moderate cases of stroke with dementia were further split into severity levels of dementia according to the severity splits described in the appendix section for dementia. Combined disability weights were then assigned to the severity levels of stroke with heart failure and dementia using the standard GBD method for combining disability weights; these are shown in tables 5a and 5b below.

Acute stroke severity splits

Table 5a. Severity distribution, details on the severity levels for acute stroke in GBD 2020 and the associated disability weight (DW) with that severity

Severity level	Lay description	Modified Rankin score	Cognitive status	DW (95% CI)
Stroke, mild	Has some difficulty in moving around and some weakness in one hand, but is able to walk without help.	1	N/A	0.019 (0.010–0.032)
Stroke, moderate, with no heart failure	Has some difficulty in moving around, and in using the hands for lifting and holding things, dressing, and grooming.	2, 3	MoCA ≥26 or MMSE ≥24	0.070 (0.046–0.099)
Stroke, moderate, with controlled, medically managed heart failure	Has some difficulty in moving around, and in using the hands for lifting and holding things, dressing, and grooming. Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities.	2, 3	MoCA ≥26 or MMSE ≥24	0.116 (0.076–0.164)
Stroke, moderate, with mild heart failure	Has some difficulty in moving around, and in using the hands for lifting and holding things, dressing, and grooming. Is short of breath and easily tires with moderate physical	2, 3	MoCA ≥26 or MMSE ≥24	0.109 (0.074–0.154)

	activity, such as walking uphill or more than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort.			
Stroke, moderate, with moderate heart failure	Has some difficulty in moving around, and in using the hands for lifting and holding things, dressing, and grooming. Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity.	2, 3	MoCA ≥26 or MMSE ≥24	0.137 (0.091–0.191)
Stroke, moderate, with severe heart failure	Has some difficulty in moving around, and in using the hands for lifting and holding things, dressing, and grooming. Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems.	2, 3	MoCA ≥26 or MMSE ≥24	0.236 (0.165–0.319)
Stroke, moderate plus cognition problems, with no heart failure	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused.	2, 3	MoCA <26 or MMSE <24	0.316 (0.206–0.437)
Stroke, moderate plus cognition problems, with controlled, medically managed heart failure	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Has been diagnosed with clinical heart failure, a chronic disease	2, 3	MoCA <26 or MMSE <24	0.349 (0.241–0.470)

	that requires medication every day and causes some worry but minimal interference with daily activities.			
Stroke, moderate plus cognition problems, with mild heart failure	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Is short of breath and easily tires with moderate physical activity, such as walking uphill or more than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort.	2, 3	MoCA <26 or MMSE <24	0.344 (0.237–0.464)
Stroke, moderate plus cognition problems, with moderate heart failure	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity.	2, 3	MoCA <26 or MMSE <24	0.365 (0.253–0.487)
Stroke, moderate plus cognition problems, with severe heart failure	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems.	2, 3	MoCA <26 or MMSE <24	0.437 (0.308–0.575)

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.	4, 5	MoCA ≥26 or MMSE ≥24	0.552 (0.377–0.707)
Stroke, severe, with controlled, medically managed heart failure	Is confined to bed or a wheelchair, has difficulty speaking, and depends on others for feeding, toileting, and dressing. Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities.	4, 5	MoCA ≥26 or MMSE ≥24	0.573 (0.408–0.720)
Stroke, severe, with mild heart failure	Is confined to bed or a wheelchair, has difficulty speaking, and depends on others for feeding, toileting, and dressing. Is short of breath and easily tires with moderate physical activity, such as walking uphill or more than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort.	4, 5	MoCA ≥26 or MMSE ≥24	0.570 (0.404–0.720)
Stroke, severe, with moderate heart failure	Is confined to bed or a wheelchair, has difficulty speaking, and depends on others for feeding, toileting, and dressing. Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity.	4, 5	MoCA ≥26 or MMSE ≥24	0.584 (0.417–0.732)
Stroke, severe, with severe heart failure	Is confined to bed or a wheelchair, has difficulty speaking, and depends on others for feeding, toileting, and dressing. Is short of breath and feels tired when at rest. The person avoids	4, 5	MoCA ≥26 or MMSE ≥24	0.630 (0.458–0.777)

	any physical activity, for fear of worsening the breathing problems.			
Stroke, severe plus cognition problems, no heart failure	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things.	4,5	MoCA <26 or MMSE <24	0.588 (0.411–0.744)
Stroke, severe plus cognition problems, controlled, medically managed heart failure	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities.	4,5	MoCA <26 or MMSE <24	0.608 (0.438–0.759)
Stroke, severe plus cognition problems, mild heart failure	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and easily tires with moderate physical activity, such as walking uphill or more than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort.	4,5	MoCA <26 or MMSE <24	0.604 (0.436–0.758)
Stroke, severe plus cognition problems, moderate heart failure	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and easily tires with minimal	4,5	MoCA <26 or MMSE <24	0.617 (0.448–0.768)

	physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity.			
Stroke, severe plus cognition problems, severe heart failure	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems.	4,5	MoCA <26 or MMSE <24	0.659 (0.488–0.808)

Chronic stroke severity splits

Table 5b. Severity distribution, details on the severity levels for chronic stroke in GBD 2020 and the associated disability weight (DW) with that severity

Severity level	Lay description	Modified Rankin score	Cognitive status	DW (95% CI)
Stroke, asymptomatic		0	N/A	N/A
Stroke, mild	Has some difficulty in moving around and some weakness in one hand, but is able to walk without help.	1	N/A	0.019 (0.010–0.032)
Stroke, moderate, with no heart failure	Has some difficulty in moving around, and in using the hands for lifting and holding things, dressing, and grooming.	2, 3	MoCA ≥26 or MMSE ≥24	0.070 (0.046–0.099)
Stroke, moderate, with controlled, medically	Has some difficulty in moving around, and in using the hands for lifting and holding things, dressing, and grooming.	2, 3	MoCA ≥26 or MMSE ≥24	0.082 (0.053–0.118)

managed heart failure	Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities.			
Stroke, moderate, with mild heart failure	Has some difficulty in moving around, and in using the hands for lifting and holding things, dressing, and grooming. Is short of breath and easily tires with moderate physical activity, such as walking uphill or more than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort.	2, 3	MoCA ≥26 or MMSE ≥24	0.108 (0.074–0.154)
Stroke, moderate, with moderate heart failure	Has some difficulty in moving around, and in using the hands for lifting and holding things, dressing, and grooming. Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity.	2, 3	MoCA ≥26 or MMSE ≥24	0.137 (0.091–0.191)
Stroke, moderate, with severe heart failure	Has some difficulty in moving around, and in using the hands for lifting and holding things, dressing, and grooming. Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems.	2, 3	MoCA ≥26 or MMSE ≥24	0.236 (0.165–0.319)
Stroke, moderate plus cognition problems, with no heart failure, with no dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused.	2, 3	MoCA <26 or MMSE <24	0.316 (0.206–0.437)

Stroke, moderate plus cognition problems, with no heart failure, with mild dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. The 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.	2, 3	MoCA <26 or MMSE <24	0.134 (0.091–0.187)
Stroke, moderate plus cognition problems, with no heart failure, with moderate dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. The 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.	2, 3	MoCA <26 or MMSE <24	0.420 (0.295–0.555)
Stroke, moderate plus cognition problems, with no heart failure, with severe dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. The person has complete memory loss, no longer recognizes close family members, and requires help with all daily activities, including personal care.	2, 3	MoCA <26 or MMSE <24	0.487 (0.345–0.628)

Stroke, moderate plus cognition problems, with controlled, medically managed heart failure, with no dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities.	2, 3	MoCA <26 or MMSE <24	0.325 (0.219–0.443)
Stroke, moderate plus cognition problems, with controlled, medically managed heart failure, with mild dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities. The 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.	2, 3	MoCA <26 or MMSE <24	0.145 (0.098–0.207)
Stroke, moderate plus cognition problems, with asymptomatic heart failure, with moderate dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities. The	2, 3	MoCA <26 or MMSE <24	0.427 (0.305–0.561)

	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.			
Stroke, moderate plus cognition problems, with asymptomatic heart failure, with severe dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities. The person has complete memory loss, no longer recognizes close family members, and requires help with all daily activities, including personal care.	2, 3	MoCA <26 or MMSE <24	0.493 (0.354–0.633)
Stroke, moderate plus cognition problems, with mild heart failure, with no dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused.	2, 3	MoCA <26 or MMSE <24	0.344 (0.237–0.464)
Stroke, moderate plus cognition problems, with mild heart failure, with mild dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. The person has some trouble remembering recent events and finds it hard to concentrate and make	2, 3	MoCA <26 or MMSE <24	0.170 (0.117–0.238)

	decisions and plans. They may have slight to moderate difficulty engaging in community affairs, complicated hobbies, and intellectual interests.			
Stroke, moderate plus cognition problems, with mild heart failure, with moderate dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. The 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.	2, 3	MoCA <26 or MMSE <24	0.444 (0.320–0.577)
Stroke, moderate plus cognition problems, with mild heart failure, with severe dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. The person has complete memory loss, no longer recognizes close family members, and requires help with all daily activities, including personal care.	2, 3	MoCA <26 or MMSE <24	0.508 (0.368–0.647)
Stroke, moderate plus cognition problems, with moderate heart failure, with no dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Is short of breath and easily tires with minimal physical activity, such as walking only a short	2, 3	MoCA <26 or MMSE <24	0.365 (0.253–0.487)

	distance. The person feels comfortable at rest but avoids moderate activity.			
Stroke, moderate plus cognition problems, with moderate heart failure, with mild dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity. The 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.	2, 3	MoCA <26 or MMSE <24	0.196 (0.134–0.270)
Stroke, moderate plus cognition problems, with moderate heart failure, with moderate dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity. The 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	2, 3	MoCA <26 or MMSE <24	0.461 (0.334–0.596)

	activities, and only retain simple chores and hobbies.			
Stroke, moderate plus cognition problems, with moderate heart failure, with severe dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity. The person has complete memory loss, no longer recognizes close family members, and requires help with all daily activities, including personal care.	2, 3	MoCA <26 or MMSE <24	0.523 (0.381–0.663)
Stroke, moderate plus cognition problems, with severe heart failure, with no dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems.	2, 3	MoCA <26 or MMSE <24	0.437 (0.308–0.575)
Stroke, moderate plus cognition problems, with severe heart failure, with mild dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems. The person has some trouble remembering recent events and finds it hard to concentrate and make decisions and	2, 3	MoCA <26 or MMSE <24	0.289 (0.206–0.381)

	plans. They may have slight to moderate difficulty engaging in community affairs, complicated hobbies, and intellectual interests.			
Stroke, moderate plus cognition problems, with severe heart failure, with moderate dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems. The 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.	2, 3	MoCA <26 or MMSE <24	0.522 (0.385–0.665)
Stroke, moderate plus cognition problems, with severe heart failure, with severe dementia	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused. Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems. The person has complete memory loss, no longer recognizes close family members, and requires help with all daily activities, including personal care.	2, 3	MoCA <26 or MMSE <24	0.576 (0.428–0.721)

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.	4, 5	MoCA ≥26 or MMSE ≥24	0.552 (0.377–0.707)
Stroke, severe, with asymptomatic heart failure	Is confined to bed or a wheelchair, has difficulty speaking, and depends on others for feeding, toileting, and dressing. Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities.	4, 5	MoCA ≥26 or MMSE ≥24	0.558 (0.389–0.711)
Stroke, severe, with mild heart failure	Is confined to bed or a wheelchair, has difficulty speaking, and depends on others for feeding, toileting, and dressing. Is short of breath and easily tires with moderate physical activity, such as walking uphill or more than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort.	4, 5	MoCA ≥26 or MMSE ≥24	0.570 (0.403–0.72)
Stroke, severe, with moderate heart failure	Is confined to bed or a wheelchair, has difficulty speaking, and depends on others for feeding, toileting, and dressing. Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity.	4, 5	MoCA ≥26 or MMSE ≥24	0.584 (0.417–0.732)
Stroke, severe, with severe heart failure	Is confined to bed or a wheelchair, has difficulty speaking, and depends on others for feeding, toileting, and dressing. Is short of breath and feels tired when at rest. The person avoids	4, 5	MoCA ≥26 or MMSE ≥24	0.630 (0.458–0.777)

	any physical activity, for fear of worsening the breathing problems.			
Stroke, severe plus cognition problems, no heart failure, with no dementia.	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things.	4,5	MoCA <26 or MMSE <24	0.588 (0.411–0.744)
Stroke, severe plus cognition problems, no heart failure, with mild dementia.	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. The 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.	4,5	MoCA <26 or MMSE <24	0.134 (0.091–0.187)
Stroke, severe plus cognition problems, no heart failure, with moderate dementia.	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. The 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.	4,5	MoCA <26 or MMSE <24	0.420 (0.295–0.555)

Stroke, severe plus cognition problems, no heart failure, with severe dementia.	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. The person has complete memory loss, no longer recognizes close family members, and requires help with all daily activities, including personal care.	4,5	MoCA <26 or MMSE <24	0.487 (0.345–0.628)
Stroke, severe plus cognition problems, asymptomatic heart failure, with no dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities.	4,5	MoCA <26 or MMSE <24	0.593 (0.421–0.747)
Stroke, severe plus cognition problems, asymptomatic heart failure, with mild dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities. The 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	4,5	MoCA <26 or MMSE <24	0.588 (0.425–0.734)

	community affairs, complicated hobbies, and intellectual interests.			
Stroke, severe plus cognition problems, asymptomatic heart failure, with moderate dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities. The 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.	4,5	MoCA <26 or MMSE <24	0.719 (0.540–0.856)
Stroke, severe plus cognition problems, asymptomatic heart failure, with severe dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Has been diagnosed with clinical heart failure, a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities. The person has complete memory loss, no longer recognizes close family members, and requires help with all daily activities, including personal care.	4,5	MoCA <26 or MMSE <24	0.750 (0.578–0.882)

Stroke, severe plus cognition problems, mild heart failure, with no dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and easily tires with moderate physical activity, such as walking uphill or more than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort.	4,5	MoCA <26 or MMSE <24	0.605 (0.436–0.758)
Stroke, severe plus cognition problems, mild heart failure, with mild dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and easily tires with moderate physical activity, such as walking uphill or more than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort. The 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.	4,5	MoCA <26 or MMSE <24	0.600 (0.439–0.745)
Stroke, severe plus cognition problems, mild heart failure, with moderate dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and easily tires with moderate physical activity, such as walking uphill or more	4,5	MoCA <26 or MMSE <24	0.727 (0.553–0.861)

	than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort. The 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.			
Stroke, severe plus cognition problems, mild heart failure, with severe dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and easily tires with moderate physical activity, such as walking uphill or more than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort. The person has complete memory loss, no longer recognizes close family members, and requires help with all daily activities, including personal care.	4,5	MoCA <26 or MMSE <24	0.757 (0.589–0.886)
Stroke, severe plus cognition problems, moderate heart failure, with no dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and easily tires with minimal physical activity, such as walking only a short	4,5	MoCA <26 or MMSE <24	0.617 (0.448–0.768)

	distance. The person feels comfortable at rest but avoids moderate activity.			
Stroke, severe plus cognition problems, moderate heart failure, with mild dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity. The 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.	4,5	MoCA <26 or MMSE <24	0.612 (0.450–0.756)
Stroke, severe plus cognition problems, moderate heart failure, with moderate dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity. The 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	4,5	MoCA <26 or MMSE <24	0.735 (0.562–0.868)

	activities, and only retain simple chores and hobbies.			
Stroke, severe plus cognition problems, moderate heart failure, with severe dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity. The person has complete memory loss, no longer recognizes close family members, and requires help with all daily activities, including personal care.	4,5	MoCA <26 or MMSE <24	0.764 (0.596–0.892)
Stroke, severe plus cognition problems, severe heart failure, with no dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems.	4,5	MoCA <26 or MMSE <24	0.659 (0.489–0.808)
Stroke, severe plus cognition problems, severe heart failure, with mild dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems. The person has some trouble remembering recent events and finds it hard to concentrate and make decisions and	4,5	MoCA <26 or MMSE <24	0.655 (0.489–0.794)

	plans. They may have slight to moderate difficulty engaging in community affairs, complicated hobbies, and intellectual interests.			
Stroke, severe plus cognition problems, severe heart failure, with moderate dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems. The 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.	4,5	MoCA <26 or MMSE <24	0.764 (0.593–0.890)
Stroke, severe plus cognition problems, severe heart failure, with severe dementia	Is confined to bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things. Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems. The person has complete memory loss, no longer recognizes close family members, and requires help with all daily activities, including personal care.	4,5	MoCA <26 or MMSE <24	0.790 (0.626–0.910)

Table 6: Data input counts for the estimation process for the custom severity splits

	Acute proportion	Chronic proportion
Site-years (total)	9	16
Number of countries with data	6	13
Number of GBD regions with data (out of 21 regions)	6	7
Number of GBD super-regions with data (out of 7 super-regions)	4	5

The model to split stroke into the six initial severity splits was last updated in GBD 2017. We used DisMod-MR, a Bayesian meta-regression tool, to model the six severity levels, with an independent proportion model for each. The data we used to inform these splits is summarised in table 6. Reports which grouped mRS scores differently than our mapping (eg, 0–2) were adjusted in DisMod by estimating the association between these alternate groupings and our preferred mappings. These statistical associations were used to adjust datapoints to the referent category as necessary. The six models were scaled such that the sum of the proportions for all levels equaled 1.

Modelling strategy

The general approach employed for all of the components of the stroke modelling process is detailed in the bullet points below.

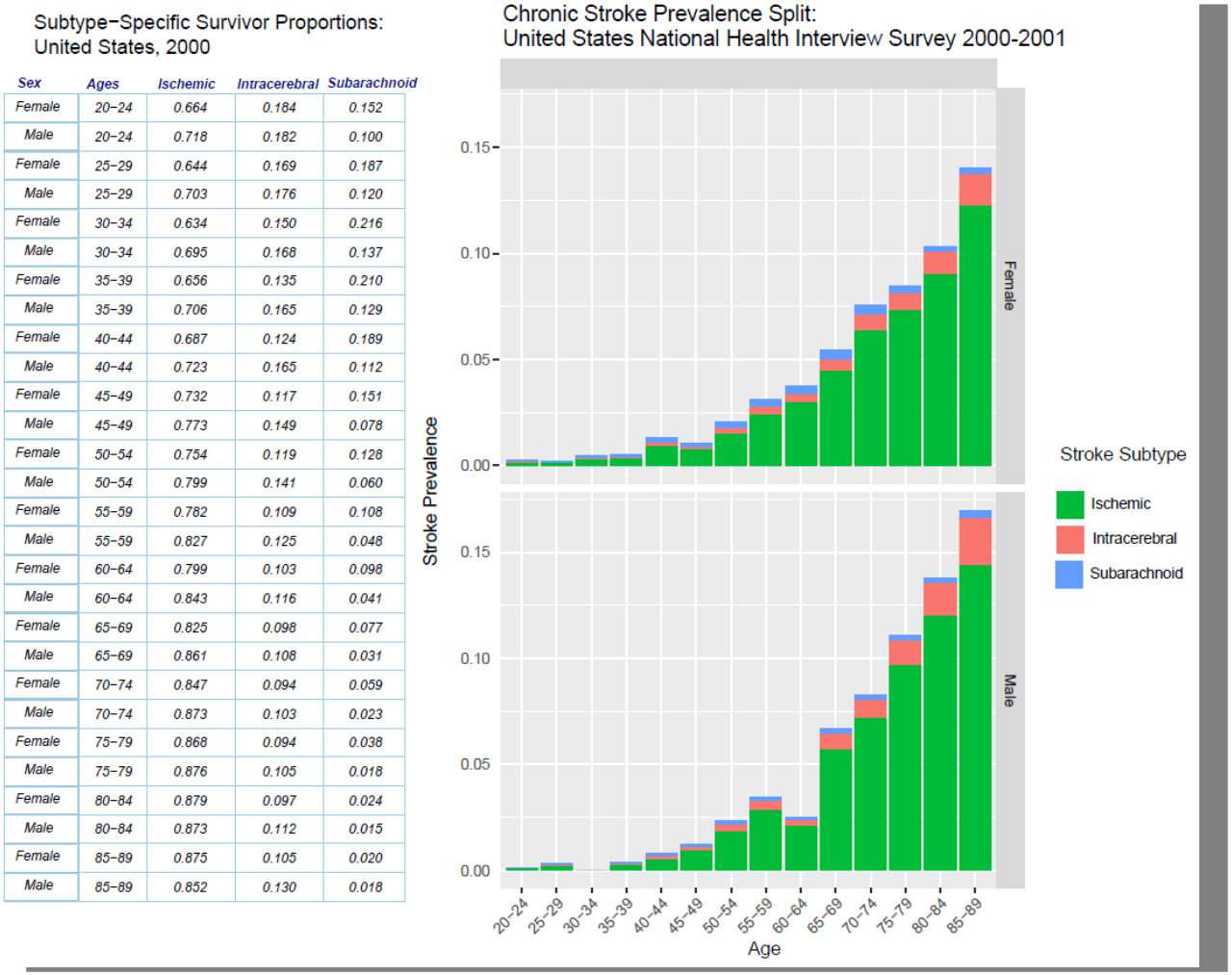
- Datapoints were adjusted from alternative to reference case definitions using estimates from statistical models generated by MR-BRT (discussed elsewhere in the appendix) for the acute models. Coefficients for these crosswalks can be found in Table 2a, 2b, and 2c.
- The GBD summary exposure values (SEV), which are the relative risk-weighted prevalence of exposure, were included as covariates for the ischaemic stroke or intracerebral haemorrhage models as appropriate, and a covariate for country income was used as a country-level covariate for both models (4). Subarachnoid haemorrhage did not include an SEV covariate, but did include a covariate for country income for excess mortality. Coefficients for these covariates can be found in Tables 7a, 7b, 7c for fixed effects located below.
- We used the ratio of acute:chronic cause-specific mortality estimated in DisMod-MR models without cause-specific mortality rate to provide estimates to divide GBD 2020 CoDCorrected stroke deaths into acute and chronic stroke deaths, using the global average for the proportion of acute:chronic stroke mortality. The acute and chronic models were then run using the same incidence, prevalence, and case fatality data as well as the custom cause-specific mortality rates as input data.

- We ran the first-ever acute subtype-specific models with CSMR as derived from CoDCorrect and epidemiological data as described above using DisMod-MR.
- We then calculated the rate of surviving until 28 days after an acute event for all three subtypes using the modelled estimates of excess mortality and incidence from the acute stroke models by age group, sex, year, and location. We then calculated the proportion of subtype-specific stroke survivors by age, sex, year, and location. These proportions were used to split the survey series input data on all stroke prevalence into the three subtypes to enable their use as input data into the chronic stroke DisMod models; Figure 3 shows an example for the USA National Health Interview Survey 2000–2001.

Figure 3: Example of all-stroke prevalence survey split into subtype-specific proportions using proportion of 28-day subtype-specific surviving cases

Subtype−Specific Survivor Proportions:
United States, 2000

Sex	Ages	Ischemic	Intracerebral	Subarachnoid
Female	20–24	0.664	0.184	0.152
Male	20–24	0.718	0.182	0.100
Female	25–29	0.644	0.169	0.187
Male	25–29	0.703	0.176	0.120
Female	30–34	0.634	0.150	0.216
Male	30–34	0.695	0.168	0.137
Female	35–39	0.656	0.135	0.210
Male	35–39	0.706	0.165	0.129
Female	40–44	0.687	0.124	0.189
Male	40–44	0.723	0.165	0.112
Female	45–49	0.732	0.117	0.151
Male	45–49	0.773	0.149	0.078
Female	50–54	0.754	0.119	0.128
Male	50–54	0.799	0.141	0.060
Female	55–59	0.782	0.109	0.108
Male	55–59	0.827	0.125	0.048
Female	60–64	0.799	0.103	0.098
Male	60–64	0.843	0.116	0.041
Female	65–69	0.825	0.098	0.077
Male	65–69	0.861	0.108	0.031
Female	70–74	0.847	0.094	0.059
Male	70–74	0.873	0.103	0.023
Female	75–79	0.868	0.094	0.038
Male	75–79	0.876	0.105	0.018
Female	80–84	0.879	0.097	0.024
Male	80–84	0.873	0.112	0.015
Female	85–89	0.875	0.105	0.020
Male	85–89	0.852	0.130	0.018



- 28-day survivorship data and the post-split prevalence surveys were uploaded into the chronic subtype-specific with CSMR models. These chronic models also use CSMR as derived from CoDCorrect and epidemiological data as described above. Models were evaluated based on expert opinion, comparison with previous iterations, and model fit.

Tables 7a, 7b, 7c below indicate the covariates used by cause in the estimation process, as well as the beta and exponentiated beta values.

Table 7a: Coefficients for covariates used in the acute and chronic ischemic stroke DisMod-MR models

Model	Variable name	Measure	Beta	Exponentiated beta
First-ever acute ischaemic stroke without CSMR	Log-transformed age-standardised SEV scalar: ischaemic stroke	Incidence	0.77 (0.75 to 0.82)	2.17 (2.12 to 2.26)
First-ever acute ischaemic stroke without CSMR	LDI (I$ per capita)	Excess mortality rate	–0.42 (–0.47 to –0.38)	0.65 (0.62 to 0.68)
Chronic ischaemic stroke without CSMR	Log-transformed SEV scalar: ischaemic stroke	Prevalence	0.75 (0.75 to 0.76)	2.12 (2.12 to 2.13)
Chronic ischaemic stroke without CSMR	LDI (I$ per capita)	Excess mortality rate	–0.12 (–0.14 to –0.1)	0.89 (0.87 to 0.90)
First-ever acute ischaemic stroke with CSMR	Log-transformed age-standardised SEV scalar: ischaemic stroke	Incidence	1.25 (1.25 to 1.25)	3.49 (3.47 to 3.49)
First-ever acute ischaemic stroke with CSMR	LDI (I$ per capita)	Excess mortality rate	–0.48 (–0.50 to –0.46)	0.62 (0.61 to 0.63)
Chronic ischaemic stroke with CSMR	Log-transformed SEV scalar: ischaemic stroke	Prevalence	1.16 (1.08 to 1.23)	3.18 (2.94 to 3.42)

Chronic ischaemic stroke with CSMR	LDI (I$ per capita)	Excess mortality rate	–0.45 (–0.49 to –0.42)	0.64 (0.61 to 0.66)

Table 7b: Coefficients for covariates used in the acute and chronic intracerebral haemorrhage DisMod-MR models

Model	Variable name	Measure	Beta	Exponentiated beta
First-ever acute intracerebral haemorrhage without CSMR	Log-transformed SEV scalar: intracerebral Haemorrhage	Incidence	0.78 (0.75 to 0.82)	2.17 (2.12 to 2.28)
First-ever acute intracerebral haemorrhage without CSMR	LDI (I$ per capita)	Excess mortality rate	–0.47 (–0.50 to –0.42)	0.63 (0.61 to 0.65)
Chronic intracerebral haemorrhage without CSMR	Log-transformed SEV scalar: intracerebral haemorrhage	Prevalence	0.77 (0.75 to 0.80)	2.16 (2.12 to 2.22)
Chronic intracerebral haemorrhage without CSMR	LDI (I$ per capita)	Excess mortality rate	–0.13 (–0.18 to –0.10)	0.88 (0.83 to 0.90)
First-ever acute intracerebral haemorrhage with CSMR	Log-transformed SEV scalar: Intracerebral Haemorrhage	Incidence	0.75 (0.75 to 0.76)	2.13 (2.12 to 2.15)
First-ever acute intracerebral haemorrhage with CSMR	LDI (I$ per capita)	Excess mortality rate	–0.29 (–0.32 to –0.24)	0.75 (0.72 to 0.78)
Chronic intracerebral haemorrhage with CSMR	Log-transformed SEV scalar: Intracerebral haemorrhage	Prevalence	1.03 (0.91 to 1.15)	2.79 (2.49 to 3.15)

Chronic intracerebral haemorrhage with CSMR	LDI (I$ per capita)	Excess mortality rate	–0.36 (–0.40 to –0.33)	0.69 (0.67 to 0.72)

Table 7c: Coefficients for covariates used in the acute and chronic subarachnoid DisMod-MR models

Model	Variable name	Measure	Beta	Exponentiated beta
First-ever acute subarachnoid hemorrhage without CSMR	Systolic blood pressure (mmHg)	Incidence	0.03 (0.02 to 0.03)	1.03 (1.02 to 1.03)
First-ever acute subarachnoid haemorrhage without CSMR	LDI (I$ per capita)	Excess mortality rate	–0.47 (–0.50 to –0.42)	0.63 (0.61 to 0.66)
Chronic subarachnoid haemorrhage without CSMR	LDI (I$ per capita)	Excess mortality rate	–0.14 (–0.21 to –0.10)	0.87 (0.81 to 0.90)
First-ever acute subarachnoid haemorrhage with CSMR	LDI (I$ per capita)	Excess mortality rate	–0.30 (–0.48 to –0.11)	0.74 (0.62 to 0.90)

References

[1] Viitanen M, Winblad B, Asplund K. Autopsy-verified causes of death after stroke. *Acta Med Scand*. 1987;222(5):401-8. doi: 10.1111/j.0954-6820.1987.tb10956.x. PMID: 3425392.

[2] Brønnum-Hansen H, Davidsen M, Thorvaldsen P; Danish MONICA Study Group. Long-term survival and causes of death after stroke. *Stroke*. 2001 Sep;32(9):2131-6. doi: 10.1161/hs0901.094253. PMID: 11546907.

[3] Saver JL, Chaisinanunkul N, Campbell BCV, Grotta JC, Hill MD, Khatri P, Landen J, Lansberg MG, Venkatasubramanian C, Albers GW; XIth Stroke Treatment Academic Industry Roundtable. Standardized Nomenclature for Modified Rankin Scale Global Disability Outcomes: Consensus Recommendations From Stroke Therapy Academic Industry Roundtable XI. *Stroke*. 2021 Aug;52(9):3054-3062. doi: 10.1161/STROKEAHA.121.034480. Epub 2021 Jul 29. PMID: 34320814.