Standardised reporting of burden of disease studies: the STROBOD statement

Explanation and elaboration annex

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Annex 1. Glossary and definitions

For the context of the STROBOD statement, we adopt the following definitions:

Burden of disease (BOD) assessment: A study estimating mortality, expressed in Years of Life Lost due to premature mortality (YLL), and/or morbidity, expressed in Years Lost due to Disability (YLD) – also referred to as Years Lived with Disability –, and/or Disability-Adjusted Life Years (DALY) as the sum of YLL and YLD for one or more causes.

Cause: Any factor that contributes to the overall burden of disease in a population. A cause of disease burden can be a disease, an injury, a risk factor, or a hazard.

Disability-Adjusted Life Year (DALY): A summary measure of population health that can be used to quantify health loss due to dying prematurely, and (when applicable) living with certain health consequences of diseases, injuries or risk factors. It is the sum of YLL and YLD; one DALY equals one healthy life year lost.

Disability Weight (DW): A numerical value representing the severity of a health state and ranging from 0 (corresponding to full health) to 1 (corresponding to death). It is a crucial factor when performing YLD calculations as part of a burden of disease assessment.

Disease model: A disease model defines the health outcomes and health states that are causally related to the cause of disease and that are included in the YLD calculations. The health outcomes and health states can be arranged in a sequential order in time using conditional transition probabilities.

Health outcomes: Health outcomes are qualitatively different disease manifestations (e.g. reactive arthritis versus Guillain Barré syndrome).

Health state: Consequences of diseases and injuries that are similar in clinical manifestation but with key differences in severity of symptoms and impact of the disease or injury on functioning; health states are often defined as mild, moderate, severe.

Years of Life Lost due to premature mortality (YLL): The component of the DALY metric that reflects estimates of population health loss from premature mortality. YLL are calculated by multiplying the number of deaths by the remaining life expectancy at the age of death.

Years Lost due to Disability (YLD): The component of the DALY metric that reflects estimates of population loss from time spent in less than optimal health due to disease or injury. YLD for a health outcome/state can be calculated from a prevalence perspective (multiplying prevalence with disability weight) and from an incidence perspective (multiplying incidence with disability weight and duration).

Scenario analysis: A systematic investigation of the effects of changes in structural (model) or methodological (normative) assumptions on burden of disease estimates; sometimes also referred to as sensitivity analysis.

Sensitivity analysis: A systematic investigation of the impact of parameter uncertainty on overall uncertainty; also referred to as variable importance analysis.

Uncertainty Interval (UI): A range of values that is likely to include the true burden of disease estimate. 95% UIs are typically derived as the 2.5th and 97.5th percentiles of the distribution reflecting the joint parameter uncertainty in the burden of disease estimate.

Annex 2. Explanation and elaboration

TITLE

1. Identify the study as a burden of disease assessment by including keywords (e.g., Years of Life Lost, Years Lost due to Disability, Disability-Adjusted Life Years, burden of disease etc), and describe the study setting.

Explanation: It is important to identify a burden of disease (BOD) study from the title, as this will increase transparency and will facilitate retrieval via search engines. Furthermore, identifying the study setting (i.e., cause, reference population, reference period) in the title will strengthen transparency. We encourage authors to use standardized keywords that can be found in the MeSH (Medical Subject Headings) database. The MeSH database helps to find related BOD terms and/or synonyms.

Example 1: *"Measuring disability-adjusted life years (DALYs) due to COVID-19 in Scotland, 2020"* [1]

Example 2: *"Burden of non-communicable diseases in Cyprus, 1990–2017: findings from the Global Burden of Disease 2017 study"* [2]

Cause; Reference population; Reference period; BOD identifier

ABSTRACT

2. Provide a summary of objectives, study setting, methods (including data sources and key methodological design choices used), results (including point estimates and, if applicable, uncertainty intervals), and conclusions.

Explanation: The abstract should include at least one sentence of basic-level introduction to the burden of disease (BOD) field; a brief account of the background and rationale of the work; and the objectives of the study. The abstract must include as much as possible information on the characteristics of your study – i.e. reference population(s), reference year(s) or period(s). The summary paragraph must inform readers whether the BOD study relies on new BOD estimates (referred to as independent BOD study) or on existing BOD estimates (referred to as, e.g. GBD-linked estimates). Major epidemiological data input sources and methodological design choices that were used to estimate the BOD should be clearly

explained. Also, a few sentences putting the main results into general context so it is clear for general readers how the results described in the main document have moved the field forward. Finally, we encourage authors to provide a brief conclusion and potential implications. Please refer to our annotate example below to see how the abstract should be constructed.

Example 1: "*Although the burden of disease in sub-Saharan Africa continues to be dominated by infectious diseases, countries in this region are undergoing a demographic transition leading to increasing prevalence of non-communicable diseases (NCDs). To inform health system responses to these changing patterns of disease, we aimed to assess changes in the burden of NCDs in sub-Saharan Africa from 1990 to 2017. We used data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017 to analyse the burden of NCDs in sub-Saharan Africa in terms of disability-adjusted life-years (DALYs)—with crude counts as well as all-age and age-standardised rates per 100 000 population—with 95% uncertainty intervals (UIs). We examined changes in burden between 1990 and 2017, and differences across age, sex, and regions. We also compared the observed NCD burden across countries with the expected values based on a country's Socio-demographic Index."* [3]

Example 2: *"COVID-19 has affected all countries. Its containment represents a unique challenge for India due to a large population (> 1.38 billion) across a wide range of population densities. Assessment of the COVID-19 disease burden is required to put the disease impact into context and support future pandemic policy development. Here, we present the national-level burden of COVID-19 in India in 2020 that accounts for differences across urban and rural regions and across age groups. Input data were collected from official records or published literature. The proportion of excess COVID-19 deaths was estimated using the Institute for Health Metrics and Evaluation, Washington data. [...] YLL was estimated by multiplying the number of deaths due to COVID-19 by the residual standard life expectancy at the age of death due to the disease. YLD was calculated as a product of the number of incident cases of COVID-19, disease duration and disability weight. [...] The DALY estimations have direct and immediate implications not only for public policy in India, but also internationally given that India represents one sixth of the world's population."* [4]

Study rationale; Aims of the study; Reference population; Reference year; Epidemiological data input sources; major methodological design choices; Conclusion and implications

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INTRODUCTION

3. Present background information to the study, its study aim(s), and its relevance for health policy or practice.

Explanation: This section should explain the background to the study, its aim(s) and objective(s), a summary of the existing literature and why this burden of disease (BOD) assessment is necessary. Authors should describe how this BOD assessment adds value to the existing evidence (e.g., present study's relevance for health policy or practice as well as how it is imbedded in currently available BOD assessement with respect to the topic). The aim(s) of the study should be cleary explained. Adding research questions using bullet points is recommended.

Example 1: *"[…] Both boroughs cover very diverse populations south of the Thames and like many London boroughs there are a range of communities living and working within them. The population structures in general are younger, with both boroughs having higher levels of deprivation although there are pockets of affluence. The populations of the two boroughs have similar health needs […]. The aim of this study was to assess and describe the general burden of disease in the London boroughs of Lambeth and Southwark using the DALY and to assess if this measure supports planning and prioritization of health services [...]"* [5]

Example 2: *"[…] This double burden poses a major threat for LMIC, where the limited financial resources are primarily spent on tackling the problem of ID, often neglecting the problem of NCD. Limited research has been done to identify factors that contribute to the double burden of disease. […] In this ecological study, we assessed the association between gender inequality and the double burden of disease in LMIC. Specifically, is a higher rate of gender inequality associated with a higher occurrence of double burden of disease in LMIC, and does this association differ between men and women?"* [6]

METHODS

Study setting

4. Report for which cause(s) the burden was calculated. Provide a case definition, e.g., in terms of an internationally recognized classification system such as the International Classification of Diseases and Related Health Problems 10th Revision.

Explanation: Accurately report the cause(s) investigated in the burden of disease (BOD) assessment. Include a definition that would allow the reader to identify the same cause in another datasource. Provide a case definition using an internationally recognized classification system such as the International Classification of Diseases and Related Health Problems 10th Revision is highly recommended.

Example 1: *"[…] In the GBD 2019 list of causes, asthma corresponds to the International Classification of Disease 10th revision (ICD-10) codes J45 and J46 and ICD-9 code 493.13,17,18 Asthma was defined as a chronic lung disease involving bronchospasm and shortness of breath due to allergic reactions or hypersensitivity, adjudicated by physician diagnosis and wheezing in the past year […]"* [7]

Example 2: *"[…]The International Classification of Diseases (ICD) 10 codes included in this research were: stroke (G45–G46.8, I60–I63.9, I65–I66.9, I67.0–I67.3, I67.5–I67.6, I68.1–I68.2, I69.0–I69.3), ischemic stroke (G45–G46.8, I63–I63.9, I65–I66.9, I67.2–I67.3, I67.5–I67.6, I69.3), intracerebral hemorrhage (I61–I62, I62.1–I62.9, I68.1–I68.2, I69.1–I69.2), and subarachnoid hemorrhage (I60–I60.9, I62.0, I67.0–I67.1, I69.0)"* [8]

5. Report the reference population and any stratification of the reference population for the burden of disease assessment, i.e., the population for which the burden was calculated. This may include the geographical location (e.g. country or province/state), and whether the general population or a specific subset of the population (e.g., females, adolescents aged 10–19 years etc) was considered.

Explanation: The authors should include information on the characteristicts of the population investigated – geographical location, sex, age, socioeconomic status are all valuable information to characterise the population included. Such information allow readers to determine whether the burden of disease (BOD) assessment is relevant to their own population of interest. In some cases, age and sex can be integrated into one definition, such as adolescents aged 10-19 years or reproductive-age women

(15–49 years). Geographical location(s) should also be defined, for example, with a reference to a country or region or province/state.

Example 1: *"[…] we report updated estimates of the distribution of child deaths by cause in 2010 and time trends of child deaths by cause since 2000."* [9]

Example 2: *"[…] we map annual 2000–2018 geospatial estimates of anemia prevalence in women of reproductive age (15–49 years) across 82 low- and middle-income countries (LMICs), stratify anemia by severity and aggregate results to policy-relevant administrative and national levels.."* [10]

6. Report the reference time period (e.g., year(s), month(s)) of the study. This refers to the time period to which the burden of disease estimates refer.

Explanation: The time period (e.g., year(s), month(s)) for which burden of disease (BOD) estimates are made should be clearly defined by authors. Such information allow readers to determine whether the BOD assessment allows for time period comparisons with their own population of interest.

Example 1: *"[…] We report an increase in NEM from the second half of 2022, associated with high seasonal NPEV activity and increased circulation of CVB3 and CVB4. Cases were clustered in south Wales and south-west England. […]"* [11]

Example 2: *"[…] Based on information from SIVIGILA, we carried out the description and characterization of COVID-19 cases re-ported from March 2020 to August 2021, by age grouped as follows: (0-4, 5-14, 15-29, 30-44, 45-59, 60-69, 70-79 and 80 and +); sex (men and women); ethnicity (1: Indigenous, 2: Gypsies, 3-5: Afro-descendant, 6: Other); municipalities (all municipalities in the department of Nariño) and by the thir-teen administrative sub-regions managed by the department of Nariño (Obando, Occidente, Centro, Guambuyaco, Jua-nambú, La Cordillera, La Sabana, Los Abades, Pacífico Sur, Piedemonte Costero, Río Mayo, Sanquianga and Telembí) […]"* [12]

Epidemiological and demographic input data

7. Report the sources, values, ranges, and, if used, probability distributions for all epidemiological input parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a (supplementary) table to show all epidemiological input parameters and respective sources and assumptions is strongly recommended.

Explanation: In order to calculate Disability-Adjusted Life Years (DALY), several data input sources are required. These can be subdivided into data input sources that inform on fatal cases and data sources that inform on non-fatal cases. Input data that informs on fatal cases include for instance the number of persons that have died from a certain disease in a certain period and region, but it can also refer to a case mortality ratio reported in literature. Data that informs on non-fatal cases include for instance databases with information on incidence or prevalence of the cause of diease under study in a certain period and region, but can also refer to data sources with information on duration of health outcomes or information on the severity level or grading of the cause of disease under study.

Example 1: *"[…] The cause of death was obtained from Statistics Netherlands. Information on disease occurrence (cancer, CHD, CVA, diabetes mellitus, COPD, asthma, Parkinson's disease, rheumatoid arthritis, osteoarthritis, and IBD) was obtained from the National Cancer Registry and the national hospital discharge diagnosis database from the Dutch National Medical Registry. The National Cancer Registry provided information on the type of cancer and the date of histological diagnosis. The national hospital discharge diagnosis database provided the date of diagnosis for CHD, CVA, diabetes mellitus, COPD, asthma, Parkinson's disease, rheumatoid arthritis, osteoarthritis, and IBD […]"* [13]

Example 2: *"[…] Baseline models describing the epidemiology of each specific cause for Australia in 2003 were developed using a range of data sources, methods and assumptions. Typical inputs included prevalence (from surveys), incidence (from disease registers), case fatality (from cohort studies), remission (from cohort and intervention studies), clinical judgement, and information about changes over time in any of these variables […]"* [14]

8. Describe all possible data manipulations, such as bias corrections, data integration steps, or methods to ensure internal consistency of the data inputs.

Explanation: Available epidemiological data typically do not come in a form that make them directly useable for DALY calculations. To ensure accuracy and consistency of the epidemiological input data, a variety of data manipulation techniques may be applied. Bias correction methods aim to correct for

systematic errors in the data. Common correction methods include methods to account for underestimation of prevalence or incidence data, and methods to redistribute of ill-defined deaths. Data integration steps such as meta-analysis or meta-regression can be applied to pool multiple data points for the same parameter into a single estimate. Finally, methods may be applied to ensure internal consistency of the data inputs, such as the use of DisMod [15].

Example 1: *"[…] The Cause of Death Ensemble model (CODEm) was used for deaths due to diabetes mellitus estimation. Deaths in younger age groups are almost exclusively due to type 1 diabetes, while deaths in older ages are primarily due to type 2 diabetes. To account for this age pattern, we set the age range of the diabetes type 1 model to 0-95+ years and the age range of the diabetes type 2 model to 15-95+ years. We used the same covariates in the diabetes type 1 model and diabetes type 2 model as the 0-14 year and 15-95+ year in the overall diabetes models, respectively. There were two unique data manipulation steps that occurred in order to prepare the data as part of the modelling process: (1) We assumed that all deaths <15 years were due to type 1 regardless of the ICD-10 code assigned to the death. We imposed 100% attribution of diabetes mellitus deaths in <15 years to type 1 diabetes mellitus; and (2) ICD-10 diabetes data were reported as type 1, type 2, or unspecified. We developed a regression to estimate the fraction of unspecified diabetes mellitus that was type 1 and type 2. We only used data from 703 country-years to inform the regression. This is because these country-years had more than 50% of the deaths typed to type 1 or type 2 AND at least 70% of type-specific deaths in people >25 years were coded to type 2. Since there was a separate regression to estimate the proportion of type 1 diabetes mellitus and type 2 diabetes mellitus, we scaled the predicted proportions to one. These scaled proportions were then applied to number of deaths coded to unspecified diabetes in each location, year, sex where ICD-10 data was reported. […]"* [16]

Example 2: *"[…] To deal with 'ill-defined codes', we assumed that deaths due to injuries were not likely to be coded as an ill-defined cause; that in adults, ill-defined deaths are more likely to be due to deaths from chronic diseases than from transmissible diseases; and that in children, these deaths are probably due to diseases from Groups I or II. Based on these assumptions all deaths with ill-defined codes in adults were redistributed to Group II and in children to Groups I and II, proportionally to the existing deaths in each age and sex group […]"* [17]

Example 3: "[…] *For several reasons, the number of reported cases, confirmed or otherwise, is only a proportion of actual cases. […] Based on the Thai data and expert opinion, a multiplication factor of 10 was chosen for the 0–15-year-old age group. That is, for each reported case, it was assumed that there were 10 unreported cases. The data from Puerto Rico and expert opinion were used to define a multiplication factor of 27 for all cases among age groups older than 15 years of age."* [18]

9. Report the sources and values of any population data used. If applicable, report the standard population used to calculate age-standardized rates.

Explanation: In order to allow international and temporal comparisons, it is required that burden of disease (BOD) estimates are standardised to adjust for potential differences in population demographic structures. The most common approach to achieve this in BOD assesments is to apply a standard population age-structure to the reference population which is being compared. This requires the computation of age-standardized rates using standard populations such as the 2013 European Standard Population [19] or the World Standard Population [20]. If age-standardized BOD estimates are calculated, the authors should report both the standard population that was applied (e.g. 2013 European Standard Population) as well as the source (e.g. Eurostat).

Example 1: *"[…] Age-adjusted rates across older age-groups were calculated by multiplying age-specific rates by the latest ESP weights for 2013 for each age-group."* [21]

Example 2: *"[…] The results are reported as absolute values as well as crude rates and age-standardized rates per 100 000 population for the year 2017 (European standard population 2013) […]."* [22]

DALY methods

10. Report the age-conditional life expectancy used for calculating Years of Life Lost (i.e., national, regional, or aspirational life tables) or other methods (e.g., potential years of life lost, proportion of premature deaths under a selected age threshold etc).

Explanation: The Years of Life Lost due to premature mortality (YLL) component of DALY is calculated by multiplying the age-sex-location-year specific number of deaths due to a certain cause of disease or injury, by the remaining life expectancy at the age of death. The methdodological design approaches to determine YLL as well as their implications on disease burden estimates have been described elsewhere [23-25].

Example 1: *"[…] Generally, YLL are obtained by multiplying the number of deaths for each cause, sex and age group (N) by optimal life expectancy at the average age at which death occurs (L). In this study, optimal life expectancy is that observed in Japan in 2006."* [26]

Example 2: *"Standard life tables representing the maximum remaining life expectancy at each age, for males and females, were adopted from the GBD study."* [27]

11. Report the perspective taken for calculating Years Lost due to Disability, i.e., incidence or prevalence perspective.

Explanation: The Years Lost due to Disability (YLD) component of DALY takes into account the occurrence (i.e. measured by incidence or prevalence), duration, and severity of a certain cause of disease or injury. Therefore, YLD can be calculated both from a prevalence and an incidence perspective. Prevalence-based YLD is calculated by multiplying the age-sex-location-year specific prevalent cases due to a certain cause of disease or injury, by the disability weight (DW) assigned to this outcome. Incidence-based YLD is calculated by multiplying the age-sex-location-year specific incident cases due to a certain cause of disease or injury, by the duration until remission or death, and the DW assigned to this outcome [23, 28, 29].

Example 1: *"[…] YLDs were derived as the product of the number of new cases, the average duration of the disability and disability weightings for the condition (or disease state). […]"* [30]

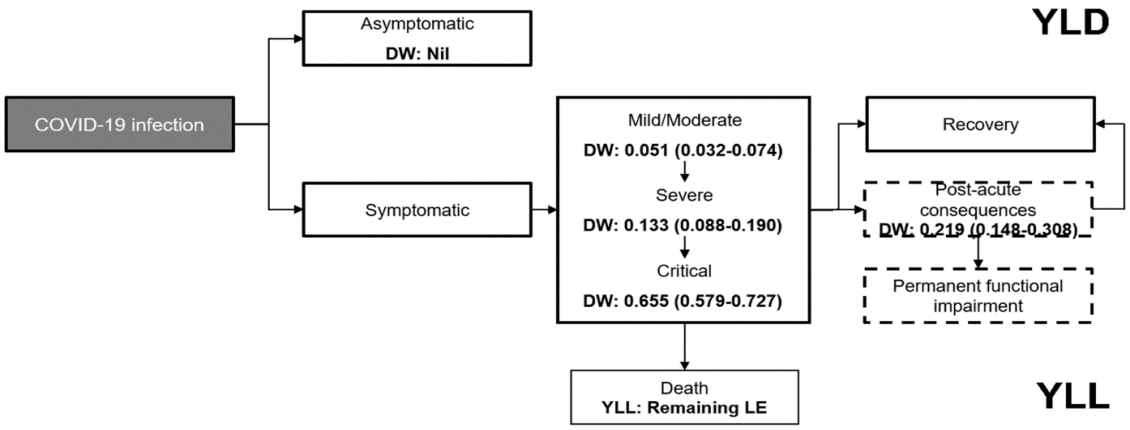
Example 2: *"[…] For most conditions YLD were estimated by multiplying age-specific incidence rates by average duration of each incident case (or, more precisely, of the associated disability until death or recovery) and average disability weight. Only for diabetes mellitus and sense organ disorders YLD were calculated on the basis of prevalence. […]"* [31]

Disease model

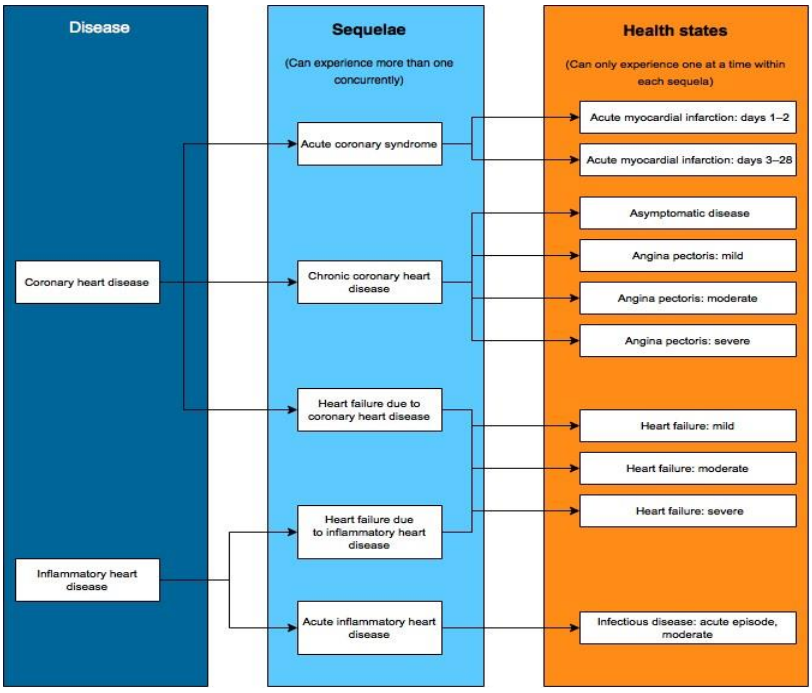
12. Describe the disease model. Present and justify the included health outcomes and health states. Providing a (supplementary) figure visualizing the disease model is strongly recommended.

Explanation: The disease model defines health outcomes that are causally related to the cause and that are included in the Disability-Adjusted Life Year (DALY) calculations. The health outcomes are arranged in a sequential order in time and are consecutively combined by conditional transition probabilities. Not every possible health outcome associated with the cause of disease or risk factor under study will be included in the DALY calculation. The disease model defines health outcomes that are causally related to the disease and that are included in the DALY calculations. The disease model sometimes also presents conditional transition probabilities between the health outcomes.

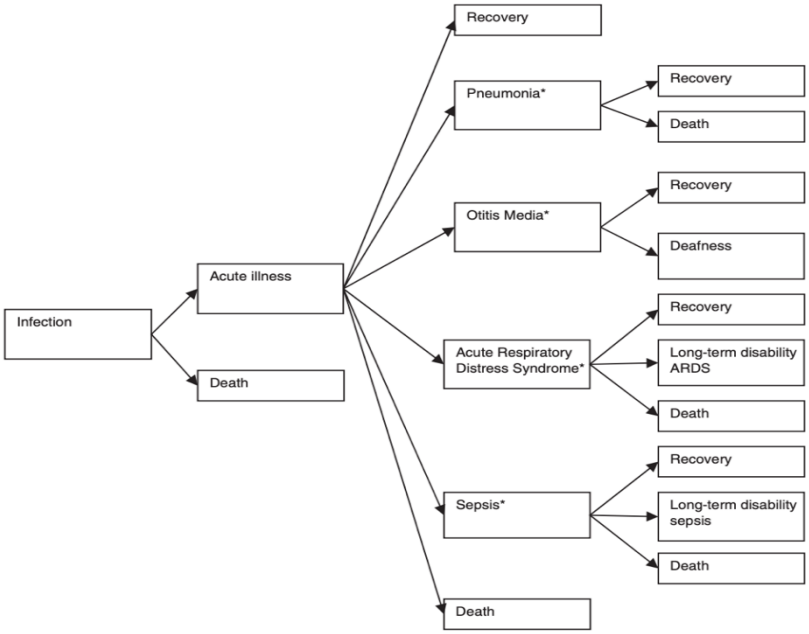
Example 1: *"[…] The DALY accounts for all health states experienced upon infection and is calculated on the basis of a disease model […]"* [32]



Example 2: "*[...] One or more sequelae were defined for each disease in the disease list. Due to the difficulty of assembling data with the granularity and dimensions required for YLD estimation, only sequelae causing significant health loss were included in the conceptual models. An example showing how coronary heart disease and inflammatory heart disease map through sequelae to health states is provided in the figure below […]"* [33]



Example 3: *"[…] The baseline scenario gives the best estimate for health outcomes of the recent pandemic. Besides acute illness, four different complications and their long-term sequelae were included: pneumonia, otitis media, acute respiratory distress syndrome, and sepsis […]"* [34]



13. Report the source(s) and values of the used disability weights. Providing a (supplementary) table depicting the health states, brief lay descriptions, and the numerical values followed by its uncertainty intervals is strongly recommended.

Explanation: Several sources of disability weights (DW) exist; some of them country-specific and other global or regional [35, 36]. Authors should describe here which source/set of DW was used to calculate Years Lost due to Disability (YLD). Citation of the set of DW used should be added. We also encourage authors to provide a (supplementary) table depicting the health states for the cause(s) under study and their brief descriptions (in english) as well as their numerical value followed by its uncertainty intervals.

Example 1: *"[…] all possible combinations of the clinical presentations (acute coronary syndrome, stable angina and heart failure), taken separately or together (seven possible combinations). For each clinical presentation we used the most up-to-date disability weights provided by the GBD study […]"* [37]

Example 2: *"[…] The disability weights used for each health status was derived from the European Disability Weight Study (EDWS) and GBD 2019 […]"* [38]

14. If new disability weights were elicited, provide information on how the health states were described and the elicitation procedures. As a minimum to the latter, describe which valuation technique was used and which reference group and size of the group (also known as panel of judges) evaluated the health states. Providing a supplementary table with a description of the valuation technique and brief lay descriptions used is strongly recommended.

Explanation: Authors should first describe how the health states were depicted. There are two choices to describe the disease: in generic terms or in disease-specific terms. To measure health preferences in disability weights (DW) measurement studies several elicitation methods exist; from pairwise comparison, to visual analogue scale, trade-offs, standard gamble, and population health equivalence (see Example 1). We encourage authors to describe which panel of judges (see Examples 1-3) was used to assess health states as well as its size. Authors should add information about the surveying techniques (e.g. face-to-face interviews, web-based surveys, etc) (see Example 2). Providing a supplementary table with a description of the valuation techniques (and mathematical transformation) used to elicit DW as well as with the health state descriptions included (in english and/or reference language) is strongly recommended (see Example 4). Comprehensive overview of the methodological design choices to derive DW has been described elsewhere [35, 36].

Example 1: *"[…] To elicit health state valuations for the 255 health states, two valuation techniques were used: paired comparison and population health equivalence […]. The panel consisted of members of the general public aged 18 to 65 years from four European countries, namely Hungary, Italy, the Netherlands, and Sweden."* [39]

Example 2: *"[…] We conducted a web-based survey in 2019 to estimate DWs for 231 health states for the Japanese population."* [40]

Example 3: *"[…] In order to explore the possibility of expanding the participants in the survey, we included nurses and oriental medical doctors as well as physicians and medical students (third or fourth grade of a regular course)."* [41]

Example 4: *"[…] We included 206 health states […]. Native speakers with a medical background translated the health states and lay descriptions from the GBD and European DW studies into Chinese. Subsequently, back translation was verified independently by bilingual native speakers. The health states and lay descriptions in English and Chinese are presented in full in the appendix (pp 35–48)."* [42]

15. Report the source(s) and values of the used durations (if applicable). Providing a (supplementary) table depicting the health states and the numerical values followed by its uncertainty intervals is strongly recommended.

Explanation: In order to calculate Years Lost due to Disability (YLD), information on the duration of the included health states is needed, although the type of information is dependent on the approach of the YLD calculaton (prevalence-based or incidence-based). In case of prevalence-based YLD, information of disease duration of health states that last less than 1 year is required (e.g. moderate influenza with a duration of 2 weeks). In case of incidence-based YLD information on both short term and long term/permanent health states (i.e., health states that last one year or longer) is needed. For permanent term health states, the remaining life expectancy at age of onset of the health state is frequently used.

Example 1: *"[…] "Non-fatal cases were given disability weights and durations reflective on the acute nature of the disease and the spectrum of clinical signs. A total of 10% of non-fatal cases were given a DW for dialysis for 1 month followed by a DW of 0.21(SE = 0.04) for severe infection for a further 1 month. For 40% of the non-fatal cases, a DW of 0.21 for a duration of 2 months was given. The remaining 50% of non-fatal cases were given a DW of mean 0.053 (SE = 0.012) for 2 months. Acute lung injury is not one of the unique health states which has a disability weight defined in GBD 2010. Although this sequela occurs in approximately 17% of cases, it is of short duration and therefore likely adequately captured for severe infection."* [43]

Example 2: *"[…] Next, incident YLD was calculated for sex-specific (s) health outcomes by multiplying the number of incidence cases without fatality, with the duration of the disabling condition, and the disability weight specified for a specific health outcome […]. We generated average age-specific durations of lung cancer by Dismod-II software […]"* [44]

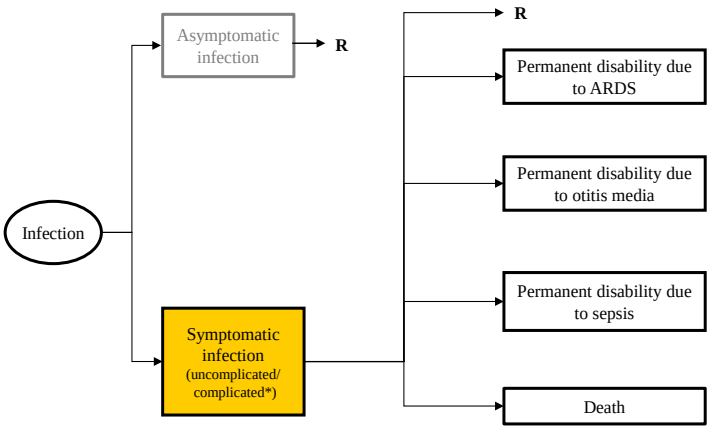
16. Report the source(s) and values of the used conditional probabilities, severity distribution, and/or transition rates. Providing a (supplementary) table depicting the parent/child health outcomes and health states and the numerical values followed by its uncertainty intervals is strongly recommended.

Explanation: A disease model typically comprises a set of health outcomes and health states that are interconnected. In this context, the model can be defined by relationships between "parent" nodes and "child" nodes, with child nodes stemming from parent nodes. The transition from a parent node to a child node is determined by a probability or rate. When the parent-child relationship represents a subset, conditional probabilities specify what portion of the parent node pertains to the child node. For instance,

all cases of diabetes (e.g. type 2) might be split in two mutually exclusive groups, i.e., uncomplicated and complicated cases. In a subsequent step, a subset of the complicated cases may be defined to have diabetic foot ulcer as complication. The term severity distribution is commonly used to represent the set of conditional probabilities used for dividing a parent health state into mutually exclusive severity levels (e.g., mild, moderate, severe). When the parent-child relationship represents a temporal progression (as is common in incidence-based DALY calculations), these relationships are governed by transition rates. In all cases, the parent-child relationships and the corresponding probabilities or rates may be represented in a table, which should also specify the source of the applied values.

Example 1: *"[…] The proportion of individuals with IHF corresponded to 36% of the prevalence of HF estimated by Ceia et al., of which, 41% with NYHA II, 42% NYHA III, and 7% NYHA IV. A DW of 0.06 was considered for IHF. […]"* [45]

Example 2: *"[…] Transitional probabilities describing the flow between consecutive health outcomes were extracted from the literature and validated by disease specialists from the ECDC and RIVM (for more details on outcome trees, disability weights, durations, and transition probabilities see supplementary online material) […]"* [46]



* Complicated health states include Acute Respiratory Distress Syndrome (ARDS), pneumonia, otitis media and sepsis

Health outcome	**Distribution of health states in health outcome**	**Risk to develop that health outcome; *Most likely (range)***	**Sources/ Assumption**
Acute Influenza Infection	Pneumonia: 0.36% Otitis media: 0.65% Sepsis: 0.0097% ARDS: 0.023%	1-2%	Clinical attack rate is set at 1-2% of the total average population in the years 2005-2007. [14] [14] [15] [15]
Permanent disability Acute Respiratory Distress Syndrome (ARDS)		0.023% * 56% = 0.013%	[15-16]

Permanent disability otitis media (deafness)		0.65% * 0.006% = 0.000039%	[1, 14]
Permanent disability sepsis		0.0097% * 82% = 0.00795%	[15, 17]
Death		0 years: 0.00075% 1-4 years: 0.00066% 5-9 years: 0.00031% 10-14 years: 0.00035% 15-19 years: 0.00031% 20-24 years: 0.00043% 25-29 years: 0.0004% 30-34 years: 0.00043% 35-39 years: 0.00098% 40-44 years: 0.0015% 45-49 years: 0.002% 50-54 years: 0.002% 55-59 years: 0.003% 60-64 years: 0.004% 65-69 years: 0.006% 70-74 years: 0.007% 75-79 years: 0.02% 80-84 years: 0.02% +85 years: 0.06%	based on observed mortality in cause of death statistics

Multimorbidity adjustments

17. Report whether or not multimorbidity adjustments were applied to any of the input variables in the estimation of Years Lost due to Disability. If applied, describe which multimorbidity adjustment method was used.

Explanation: Multimorbidity refers to the occurrence of two or more diseases at the same time in the same individual. A variety of methods can be used to correct for multimorbidity when calculating Years Lost due to Disability (YLD – e.g., independent, dependent, multiplicative modeling etc) [47-49]. Examples of these methods are the application of adjusted disability weights (in YLD-calculations).

Example 1: *"[…] YLD, adjusted for comorbidity, was calculated at every time step i as in the following, where Zi is the maximum number of co-existent health states at time step i (which can vary as the prevalence and nature of multimorbidity is time-dependent), ns,i is the number of individuals in state s at time step i, and DWadj,i is the disability weight at time step i adjusted using the multiplicative method (above):*

$$DWadj.i=1-\prod s(1-DWs)$$

To allocate disability among the set of health states experienced by an individual at time i, $DW_{adj,i}$ is proportionally redistributed to these health states:

$$DWadj,s.i=DWadj.i*DWs,i\sum Zs=1DWs,i$$

Adjusted YLD is then calculated as: $YLDadj,i=\sum s=1Zins,i\times DWadj,s,I$ […]" [47]

Example 2: *"[…] Finally, all analyses were based on raw (unadjusted) DWs as well as on DWs that were adjusted for comorbidities. Adjusted DWs were calculated by linear regression analyses, performed in two phases. The DW of one disorder was adjusted for presence of all other comorbid disorders in the sample, plus somatic illnesses that were only available in a subsample of N = 33,178 […]"* [50]

Example 3: *"[…] In order to account for the overlap among these disorders, we used a multiplicative approach to compute comorbidity-adjusted YLD. The prevalence estimates of reporting one, two, or three of this conditions were extrapolated from BHIS for LBP, NKP and OST. Secondly DW were adjusted using the following formula* $1 - \prod i(1 - DWi)$*, with DWi being the disease-specific DW. Considering that LBP, NKP and OST were extrapolated from the same data source, these were considered as interdependent based on the observed correlations. For RHE, we assumed that it was independent of the other health conditions […."* [51]

Social weighting factors

18. Report whether or not age weighting was applied. If applied, describe which parameters were used.

Explanation: Age weighting refers to the practice of attaching different values to life years lived at different ages, with lower weights given to years of healthy life at very young and old ages than for other ages. Comparison of disease burden estimates with or without age-weighting has been examined elsewhere [52].

Example 1: *"[…] Estimates of the burden of disease associated with each respiratory virus were calculated using the DALY formula:*

$$-\left[\frac{DCe^{-\beta a}}{(\beta+r)^2}\left[e^{-(\beta+r)(L)}(1+(\beta+r)(L+a))-(1+(\beta+r)a)\right]\right]$$

where D is the disability weight; C and β are parameters of the age weighting function (parameters of age weighting function used were as for the World Bank study); a is the age at disease onset (mid-range values for each age band were applied); L is the duration of disability, which in case fatalities is the time between age of onset and life expectancy; and r is the social discount rate. The social discount rate using in the Global Burden of Disease study of 0.03 was applied […] [53]

Example 2: *"We did not use time discounting and age weighting."* [54]

Example 3: *"No time discounting was applied, thus future and present disabilities were weighted equally."* [55]

19. Report whether or not time discounting was applied. If applied, describe which discount rate was used.

Explanation: Time discounting refers to the practice as used in many economic analyses to apply a discount rate in the formula to calculate DALY. This discount rate discounts future benefits and converts them into net present-value terms. Usually, the discount rate used in the DALY formula is 3 percent. Comparison of disease burden estimates with or without time-discounting has been examined elsewhere [52].

Example 1: *"[…] DALYs were calculated for each country separately using the disease natural history model for* Campylobacter *spp. presented in Mangen et al. (Mangen et al., 2013). The model was extended to allow for time discounting of the disease burden, a necessity when conducting an economic evaluation […]"* [56]

Example 2: *"[…] The models were then run at 10,000 iterations of the Monte Carlo simulations with and without a 3.5% annual time discount rate […]"* [57]

Uncertainty and scenario analysis

20. Describe any methods used to perform uncertainty and variable importance (sensitivity) analyses. If, for example, Monte Carlo simulations were used, report the number of iterations.

Explanation: Uncertainty analysis, also referred to as uncertainty propagation or probabilistic sensitivity analysis (PSA), allows quantifying the impact of parameter uncertainty on the burden of disease (BOD) estimate. Parameter uncertainty relates to a lack of knowledge on the true value of model parameters. DALY calculations require demographic, epidemiological, and severity parameters, each of which can be uncertain. In general, parameter uncertainty results from sampling error and/or systematic error or bias. In uncertainty analysis, the uncertain parameters are represented by uncertainty distributions. Uncertainty analysis typically uses Monte Carlo simulations, or parametric bootstrap, to sample random values from the specified uncertainty distributions. At each iteration, the sampled values are used to calculate a BOD estimate. The combination of iterations therefore results in a distribution of BOD estimates, reflecting the joint uncertainty in the input parameters. To evaluate which uncertain

parameters contribute most to the uncertainty in the final BOD estimate, variable importance analysis techniques can be applied (sometimes also referred to as sensitivity analysis).

Example 1: *"[…] An uncertainty analysis was done using Monte Carlo simulation […]. The VA cause attribution was validated with the subsample of deaths for which both a medical record and a VA interview were available […]. In this study, the corrected cause profiles were applied to total deaths using proportional mortality by age and sex. The sampling uncertainty of the redistributed causes of death was quantified using Monte Carlo simulation […]."* [58]

Example 2: *"[…]For each death with a non-informative ICD-10 code, the process of redistribution (to informative ICD-10 codes) is repeated 1000 times. This is to represent the variation of different possible causes of death. The 1000 values formed allow for the calculation of an uncertainty interval for each cause of death, within which 95% of the repetitions lie. In summary, the uncertainty interval thus represents the range of death case numbers or YLL within which the true value lies, given the assumptions made."* [59]

21. Describe any scenario analyses that were performed. Present the rationale and the alternative data inputs defining the alternative scenarios.

Explanation: Scenario analyses allow assessing the impact of discrete choices on the burden of disease (BOD) estimates, linked to model or methodological uncertainty. In a secnario analysis, BOD estimates are calculated under different assumptions and compared against the baseline scenario. Scenario analyses are sometimes also referred to as sensitivity analysis. Model uncertainty refers to a lack of knowledge on structural aspects of the BOD estimation. BOD estimations generally follow a disease model or outcome tree. Uncertainty in this disease model may arise when there is insufficient or conflicting evidence on the causal relation of certain symptoms. A second source of model uncertainty can be linked to the epidemiological data used in the DALY calculations. Often the available data come with a lot of restrictions, and several assumptions need to be made to transform these into useable numbers. Whether or not data should be corrected for underreporting or misclassification may for instance become a source of model uncertainty. Methodological uncertainty refers to normative or value choices that need to be made, and for which there is no intrinsically correct choice. As a result, different choices are being made, and contested, in literature. For instance, in the calculation of Years Lost due to Disability (YLD), different methods exist for deriving disability weights (DW), different choices can be made on which population's values to use, and different methods exist for correcting DW for multimorbidity. Likewise, in the calculation of Years of Life Lost due to premature mortality (YLL),

different possibilities exist regarding the choice of the life expectancy table. Whether or not to use social age weighting and/or time discounting is a methodological choice that affects both YLL and YLD.

Example 1: *"[…] by changing life table used as norm: the life table for France in 2001 and the projected life table for France in 2020. […]"* [60]

Example 2: *"[…] The calculations were performed in 8 scenarios that differed from the base case in 1 or more of the following parameters: life-table, discount rate, age weighting, disability weighting, and prevalence of heart failure […]"* [61]

RESULTS

22. Report the point estimates and, if applicable, the uncertainty interval of the burden of disease estimates. Provide both absolute values, crude rates (optional), and age-standardized rates per 100,000 in a table or figure.

Explanation: The resulting burden of disease (BOD) estimates should be reported by their point estimates and, if applicable, their uncertainty intervals. If performed, results of the variable importance analyses can be provided as a tornado plot. In addition to absolute values, it is important to provide crude and age-standardized rates, so that comparison across geographies and time points can be facilitated. As different reference populations can be used to calculate age-standardized rates, it is important to specify which reference was used (see item 9).

Example 1: *"[…] Two years after the first cases of COVID-19 surfaced in Malaysia, there have been 32,063 deaths recorded in the country. Most deaths (31,059 out of 32,063 deaths) occurred in 2021 [...]. We estimated that COVID-19 accounted for 683,903 YLL over the past two years—approximately 21 years lost per person who died of COVID-19, and 1,998 years per 100,000 people […]."* [62]

Example 2: *"[…] In 2002, 8973 female and 9297 male deaths resulted in 267 139 life-years lost (196/1000 persons). [...] In 2002, Estonian population lost 179 222 life-years (131/1000 persons) due to medical conditions and injuries affecting quality of life."* [63]

23. If applicable, report the results of the scenario analyses. Tables and/or figures illustrating findings on the scenario analyses are strongly recommended.

Explanation: The results of the scenario analyses should be presented in such a way that insights can be gained in which choices have the largest influence on the overall result. If a limited number of scenarios were assessed, the results of all scenarios can be presented in a table or graph. If a large number of scenarios were assessed, focus can be laid on the the most extreme scenarios.

Example 1: *"[…] First, increasing the number of positive cases by 50% and 75% led to an increase of 26% (5295) and 39% (5838) of YLD, respectively, as compared to the main results of YLD (4208). This increase led to an estimated 987 827 and 988 370 DALYs, respectively, as compared to the main results of DALYs (986 740). Second, varying the duration from 7 days to 14 days led to an increase of 17% in estimated YLD, from 3484 to 4933. Third, varying the duration for post-acute consequences of COVID-19 or long COVID cases to 84 days and 140 days, it led to an increase of 188% with a total of 11 417 YLDs and 375% with a total of 18 863 YLD, respectively. The duration of 140 days had the highest effect on DALYs (i.e., 1 001 394). […]"* [64]

DISCUSSION

24. Summarise the key study findings and describe how they support the conclusions reached.

Explanation: The interpretation of the burden of disease (BOD) results is an essential component when reporting DALY. General readers and policymakers can benefit from the authors' interpretation of the results in light of the existing evidence. Thus, the authors can discuss the implication of the final BOD results in context of existing research.

Example 1: *[…] The current study investigated the burden of female breast cancer in MENA and its attributable risk factors by age and socioeconomic development, and found a substantial increase in the burden of this disease over the last three decades. Compared with the global values in 1990 and 2019, the MENA region had lower age-standardised DALY rates in almost all age group except those aged between 35 and 55 years old. Furthermore, the age-standardised death rate increased with advancing age, while the DALY rates peaked in the 55–59 age group. There was a positive association between the burden of female breast cancer and SDI, while high-fasting plasma glucose accounted for the largest attributable burden. […] to evaluate the effects of health policies on the burden of breast cancer in the*

individual countries of this region and to estimate its burden for the coming decades, which could be useful information for healthcare authorities." [65]

25. Discuss how the findings fit within current knowledge. Discuss potential implications for public health practice. Compare the results with those of other studies, and discuss methodological design differences, if relevant.

Explanation: The authors can discuss the evidence prior to the study; points like how the resulting burden of disease (BOD) estimates fit within the current knowledge and what does this BOD assessment adds (i.e., added value over to what is already known) can clearly be discussed. The authors should include a discussion of the implication of the study for public health practice or policy and/or for future research in the BOD field. Finally, comparisons with existing BOD assessments and differences in methods can also be discussed.

Example 1: *"[…] Data from a mental health survey done in Australia has informed the severity distribution for anxiety disorders in GBD since GBD 2010. […]. The addition of region-specific severity distributions for anxiety disorders greatly increases the precision in burden estimates for non-high-income countries and potentially shifts the burden rankings for anxiety disorders for these regions. Furthermore, we distinguish the non-fatal burden of anxiety disorders that have been averted from the proportion that could be avoided and that which cannot be treated with existing treatments, thereby providing a roadmap for clinicians, public health practitioners, and policy makers to translate GBD findings into actionable results. This method could also be applied to other causes of burden in GBD to increase the precision of burden estimates and aid resource allocation by avoidable burden."* [66]

26. Discuss strengths and limitations, and the generalisability of the study findings. If applicable, discuss the results of the uncertainty and scenario analyses.

Explanation: A discussion of the strengths and limitations of the performed burden of disease (BOD) assessment should be added. This can include a description of the nature and/or quality of data sources used; methodological design choices used to quantify Years of Life Lost due to premature mortality and/or Years Lost due to Disability; and important assumptions made with regard to how they impact the resulting BOD results. Limitions should also be discussed in the light of the scenario or sensitivity analyses, e.g. indicating the level of robustness.

Example 1: *"[…] A limitation of this study is the availability of local epidemiological information for a number of important conditions. This would impact on YLD burden estimation. Local incidence or*

prevalence data by gender and age were relatively complete for some diseases such as cancers and certain notifiable infectious diseases, but for a number of other key diseases, such as Alzheimer's disease and other dementias, osteoarthritis, adult -onset hearing loss and chronic obstructive pulmonary disease, the detailed information required was unavailable or generally limited. Information on the distribution of disease severity for conditions such as angina, heart failure, schizophrenia, adult-onset hearing loss, Alzheimer's disease and other dementias, asthma, vision disorders and chronic obstructive pulmonary disease were similarly scarce. […] Another issue relevant to the precision of our estimates is the inability to adjust for comorbidities in the SBoD study to account for individuals who simultaneously experience multiple conditions […]." [67]

OPEN SCIENCE

27. Make the source code or computational model(s) available as supporting information or via a dedicated open access repository (e.g., GitHub).

Explanation: Providing access to the source code or computational model(s) used in the burden of disease (BOD) assessment is essential for transparency and reproducibility. This allow researchers not only to validate findings, but also to build upon existing disease burden work, as well as to ensure the reliability of results. By making such sources publicly available through open-access repositories (e.g., GitHub), we promote collaborative and open science, fostering trust and accountability in the BOD research community while accelarting the pace of discovery.

Example 1: *"Data are available in a public, open access repository (ghdx.healthdata.org). The data that support the findings of this study are available from the corresponding author upon reasonable request."* [68]

Example 1: *"The R scripts and inputs for the mapping and redistributions are available via GitHub (https://github.com/sciensanogit/BeBOD and https://github.com/sciensanogit/SEYLL2019). All estimates presented in this manuscript can be explored via https://burden.sciensano.be/shiny/mortality2019. […]."* [69]

28. Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support or any potential conflict(s) of interest of the study contributor(s) in accordance with the journal policy.

Explanation: Authors should be transparent in reporting the role of the funding source. All sources of funding should be declared as an acknowledgment or under a separate sub-heading. The role of study funder(s), if any, in identification, study design, data collection, data analysis, interpretation of burden of disease (BOD) results, in the writing of the manuscript, and decision to submit the BOD study for publication should be stated. Also, authors must disclose any conflict of interests (e.g., financial and/or personal relationships, academic competition, or intellectual beliefs etc). A conflict of interest form can be completed using the ICMJE guidelines and submitted based on the journal's requirements.

Example 1: *"The funder of the study had no role in study design, data collection, analysis, and interpretation, or writing of the report."* [70]

Example 2: *"P.K. was a speaker/consultant for Novartis, Roche and ValenzaBio. M.M. is or recently was a speaker and/or advisor for and/or has received research funding from Astria, Allakos, Alnylam, Amgen, Aralez, ArgenX, AstraZeneca, BioCryst, Blueprint, Celldex, Centogene, CSL Behring, Dyax, FAES, Genentech, GIInnovation, GSK, Innate Pharma, Kalvista, Kyowa Kirin, Leo Pharma, Lilly, Menarini, Moxie, Novartis, Pfizer, Pharming, Pharvaris, Roche, Sanofi/Regeneron, Shire/Takeda, Third Harmonic Bio, UCB and Uriach. All other authors declare no competing interests."* [71]

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