World Health Organization

International Labour Organization

TECHNICAL REPORT WITH DATA SOURCES AND METHODS

WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury, 2000–2016

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WHO/ILO joint estimates of the work-related burden of disease and injury, 2000-2016: technical report with data sources and methods

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LIST OF ABBREVIATIONS

CI	confidence interval
CRA	Comparative Risk Assessment
DALY	disability-adjusted life year
GATHER	Guidelines for accurate and transparent health estimates reporting
ILO	International Labour Organization
SDG	Sustainable Development Goal
UN	United Nations
UR	uncertainty range
WHO	World Health Organization

EXECUTIVE SUMMARY

The World Health Organization (WHO) and International Labour Organization (ILO) have produced their first WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury (WHO/ILO Joint Estimates), within the established methodological framework of the global Comparative Risk Assessment. These estimates include exposure to occupational risk factors and burden of disease attributable to exposure to occupational risk factors.

Attributable burdens of disease have been estimated for 41 pairs of occupational risk factor and health outcome (i.e. disease or injury, referred to as "cause" elsewhere). For 39 established pairs, population attributable fractions were extracted from the published literature and applied to the disease burden envelopes provided by WHO Global Health Estimates. For burden of disease, the numbers of attributable deaths and disability-adjusted life years lost were estimated.

Based on a series of systematic reviews and meta-analyses conducted for the WHO/ILO Joint Estimates, the production of estimates for several additional pairs of occupational risk factor and health outcome has been considered. The bodies of evidence on the occupational risk factor of long working hours and the health outcomes of ischaemic heart disease and stroke met pre-specified criteria for quality of evidence and strength of evidence, and WHO and the ILO have produced estimates for these pairs. Exposure to long working hours was estimated using a three-model approach, followed by calculation of the population attributable fractions and ultimately the attributable burden of disease.

This Technical Report presents the analytical framework, data sources and methods of the WHO/ILO Joint Estimates; the full set of these inter-agency estimates is reported in the separate Global Monitoring Report. All estimates of burden of disease were produced at the country, regional and global levels, and are disaggregated by sex and age group. The estimates were reported according to the *Guidelines for accurate and transparent health estimates reporting* (GATHER). It is anticipated that these estimates will improve understanding of the work-related burden of disease, and provide a base for policy and practice in occupational and workers' health and safety, nationally, regionally and globally.

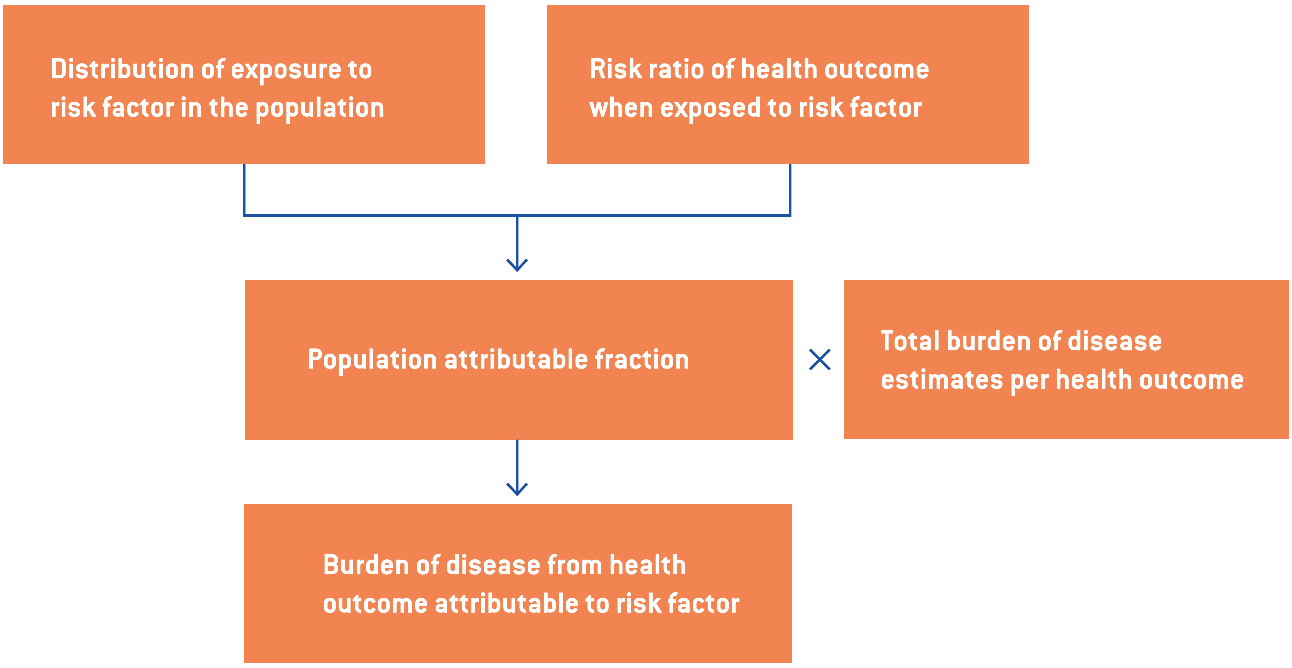
1. INTRODUCTION

To achieve the Sustainable Development Goals (SDGs) and meet the aims of the 2030 United Nations (UN) Agenda *(1)*, the World Health Organization (WHO) and the International Labour Organization (ILO) have developed the WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury (WHO/ILO Joint Estimates). These estimates are required to monitor progress towards the goals and agenda in relation to occupational and workers' health and safety, and to plan and implement actions to prevent work-related burden of disease. For the first time, these two UN Specialized Agencies have together produced estimates of the exposure to occupational risk factors (as defined by Ezzati et al. *(2)* and WHO *(3)*) and the resulting burden of disease attributable to these factors, for the period 2000–2016. Consistent with the terminology and classification of the overarching analytical framework (Ezzati et al. *(2)*), the term "burden of disease" refers to the combined burdens of three types of health outcomes, namely communicable diseases, non-communicable diseases and injuries. This work builds on previous initiatives *(4–15)*. In this Technical Report, we describe the analytical framework, data sources and methods used to produce the WHO/ILO Joint Estimates for both established and recently added pairs of occupational risk factor and health outcome.

1.1. Estimate production

All WHO/ILO Joint Estimates are produced within the framework of the global Comparative Risk Assessment (CRA), and could provide an additional indicator for occupational and workers' health and safety as well as monitoring progress towards the SDGs (16). The CRA conceptual framework is a web of hierarchically organized risk factors and health outcomes (referred to as "causes" by Ezzati et al. (2)) that contribute to health loss (e.g. loss of life or of years lived without disability) (2), enabling the quantification of exposure to defined risk factors and the burden of disease from a specific health outcome attributable to these risk factors (17). Combining information on prevalence of exposure to a defined risk factor with information about the increased risk of the incidence of or mortality from a defined health outcome among people exposed to the risk factor allows the calculation of the population attributable fraction for this pair of risk factor and health outcome (i.e. the proportional reduction in death or disease from this health outcome that would occur if exposure to the risk factor were removed or reduced to a counterfactual exposure distribution) (Fig. 1).

FIGURE 1
COMPARATIVE RISK ASSESSMENT METHOD FOR BURDEN OF DISEASE ESTIMATION



In collaboration with partners, WHO developed the CRA methodology in the late 1990s *(2)* and has successfully used this methodology to estimate work-related burden of disease *(4, 18)*. The methodology is established to the point that it is applied to produce several SDG indicators that are endorsed by the UN Statistical Commission (e.g. SDG indicators 3.9.1, 3.9.2 and 3.9.3, mortality rate attributed to: household and ambient air pollution; unsafe water, unsafe sanitation and lack of hygiene; and unintentional poisoning, respectively). In producing the WHO/ILO Joint Estimates, WHO and the ILO have implemented this method jointly to estimate the work-related burden of disease attributable to selected occupational risk factors; this approach has enabled comparability and consistency between methods and estimates of exposure to risk factors and of burden of disease, across risk factors and health outcomes, and over time. The WHO/ILO Joint Estimates were produced with theoretical minimum risk exposure, using counterfactual exposure distribution (the exposure distribution that results in minimum population risk) *(17)* as the basis of comparison. All WHO/ILO Joint Estimates are reported in adherence with the *Guidelines for accurate and transparent health estimates reporting* (GATHER) *(19)* (Annex 1). This ensures transparency in the reporting of data sources, methods and results, along dedicated and agreed technical reporting guidelines specifically for health estimates. WHO consulted its Member States on the estimates in March 2020 and July 2020. The estimates were produced in September 2020.

1.2. Pairs of occupational risk factor and health outcome

The WHO/ILO Joint Estimates currently cover a total of 41 pairs of occupational risk factor and health outcome: 39 previously established pairs and another two recently added pairs, for which the exposure and the burden of disease had not previously been estimated.

1.3. Disaggregation by WHO region, sex and age

Geographically, the WHO/ILO Joint Estimates are reported at the levels of country and region, and globally. The six regions used are those classified by WHO (African Region, Region of the Americas, South-East Asia Region, European Region, Eastern Mediterranean Region and Western Pacific Region). As estimates are reported disaggregated by country, they can be combined to produce estimates for other geographic regions, such as the five ILO-classified regions, or non-geographically defined regions, such as the World Bank income groups.

The estimates of exposure to occupational risk factors are reported for 194 countries, but burden of disease estimates only for the 183 of these with populations greater than 90 000 in 2015 *(20)*. Burden of disease estimates, and hence attributable burdens of disease, could not be produced for 11: Andorra, Cook Islands, Dominica, Marshall Islands, Monaco, Nauru, Niue, Palau, Saint Kitts and Nevis, San Marino and Tuvalu.

All estimates are produced fully disaggregated by two socioeconomic variables: sex and age group. For the variable sex, estimates were produced for the three categories of both sexes, females and males. For the variable age group, estimates were produced for 18 groups (≥ 15, 15–19, 20–24, ..., 90–94 and ≥ 95 years). These disaggregations of the estimates enable monitoring of inequalities in burden of disease by sex and age group, both between and within countries. This fulfils the call to "leave no one behind" in the SDGs, and in sustainable development more broadly (1).

2. OCCUPATIONAL RISK FACTOR AND HEALTH OUTCOME PAIRS

2.1. Established pairs

Estimates for 39 established pairs of occupational risk factor and health outcome (Table 1) were produced by determining the burden of disease using existing data and established WHO and ILO methodologies (Section 3.1 and 4.1) *(2, 21, 22)*.

2.2. Recently added pairs

The feasibility of producing estimates for several additional pairs of occupational risk factor and health outcome, identified by WHO and the ILO in consultation with individual experts at the beginning of the interagency work on the WHO/ILO Joint Estimates *(26)*, has been investigated and considered. Domains, and specific selection criteria within each domain, were developed to systematically prioritize pairs of occupational risk factor and health outcome (Table 2). Scoping reviews of the evidence base were conducted for these potential additional pairs to assess (i) the availability of global data on exposure to the occupational risk factor and (ii) the existing systematic review and meta-analytic evidence of the effect of exposure to the occupational risk factor on the health outcome. The application of these criteria identified 16 prioritized additional pairs of risk factor and health outcome for further consideration through evidence review and synthesis.

Supported by more than 220 individual experts in 35 countries, WHO and the ILO then conducted a series of systematic reviews and meta-analyses of the evidence for these prioritized pairs for burden of disease estimation (for an overview see Pega et al. *(27)*). To ensure that these systematic reviews and meta-analyses were tailored to fulfil the specific evidence and data needs of the WHO/ILO Joint Estimates, and that any estimates obtained were based on the latest and entire bodies of evidence currently available, all systematic reviews and meta-analyses followed peer-reviewed pre-published protocols *(28–37)* and were conducted and reported along WHO and ILO standards for such evidence syntheses *(38–45)*.

TABLE 1
ESTABLISHED PAIRS OF OCCUPATIONAL RISK FACTOR AND HEALTH OUTCOME

	Risk factor[a]	Health outcome[b]
1	Occupational exposure to asbestos	Trachea, bronchus and lung cancers
2	Occupational exposure to asbestos	Ovary cancer
3	Occupational exposure to asbestos	Larynx cancer
4	Occupational exposure to asbestos	Mesothelioma
5	Occupational exposure to arsenic	Trachea, bronchus and lung cancers
6	Occupational exposure to benzene	Leukaemia
7	Occupational exposure to beryllium	Trachea, bronchus and lung cancers
8	Occupational exposure to cadmium	Trachea, bronchus and lung cancers
9	Occupational exposure to chromium	Trachea, bronchus and lung cancers
10	Occupational exposure to diesel engine exhaust	Trachea, bronchus and lung cancers
11	Occupational exposure to formaldehyde	Nasopharynx cancer
12	Occupational exposure to formaldehyde	Leukaemia
13	Occupational exposure to nickel	Trachea, bronchus and lung cancers
14	Occupational exposure to polycyclic aromatic hydrocarbons	Trachea, bronchus and lung cancers
15	Occupational exposure to silica	Trachea, bronchus and lung cancers
16	Occupational exposure to sulphuric acid	Larynx cancer
17	Occupational exposure to trichloroethylene	Kidney cancer
18	Occupational asthmagens	Asthma
19	Occupational particulate matter, gases and fumes	Chronic obstructive pulmonary disease
20	Occupational noise	Other hearing loss
21	Occupational injuries[c]	Pedestrian road injuries
22	Occupational injuries[c]	Cyclist road injuries
23	Occupational injuries[c]	Motorcyclist road injuries
24	Occupational injuries[c]	Motor vehicle road injuries
25	Occupational injuries[c]	Other road injuries
26	Occupational injuries[c]	Other transport injuries
27	Occupational injuries[c]	Poisoning by carbon monoxide
28	Occupational injuries[c]	Poisoning by other means
29	Occupational injuries[c]	Falls
30	Occupational injuries[c]	Fire, heat and hot substances
31	Occupational injuries[c]	Drowning
32	Occupational injuries[c]	Unintentional firearm injuries
33	Occupational injuries[c]	Other exposure to mechanical forces
34	Occupational injuries[c]	Pulmonary aspiration and foreign body in airway
35	Occupational injuries[c]	Foreign body in other body part
36	Occupational injuries[c]	Non-venomous animal contact
37	Occupational injuries[c]	Venomous animal contact
38	Occupational injuries[c]	Other unintentional injuries
39	Occupational ergonomic factors	Back and neck pain

[a] Defined as per the Global Burden of Disease Study classification *(25)*.
[b] Defined as per the burden of disease classification of the WHO Global Health Estimates *(26)* with the exception of injuries, which are defined as per Global Burden of Disease Study classification *(25)*.
[c] Throughout this report the term "Occupational injuries" is used as defined by Ezzati et al. *(2, 3)* to represent an occupational risk factor within the framework of the global Comparative Risk Assessment. This definition differs from that adopted by the 1982 Thirteenth International Conference of Labour Statisticians *(27)*, and was revised by the 1998 Sixteenth International Conference of Labour Statisticians *(28)* to mean "any personal injury, disease or death resulting from an occupational accident".

TABLE 2

DOMAINS AND CRITERIA FOR SELECTING ADDITIONAL PAIRS OF OCCUPATIONAL RISK FACTOR AND HEALTH OUTCOME FOR THE CONSIDERATION OF ESTIMATE PRODUCTION

Domain	Criterion
Large burden of disease	Prioritize pairs of occupational risk factor and health outcome that our crude estimates suggest accrue a larger burden of disease (threshold: ≥ 6000 deaths or ≥ 30 000 DALYs) compared with others
Existing data on exposed population and effect estimate	Prioritize occupational risk factors for which both a global database (ideally disaggregated by country, sex, age group, industry and level of exposure) of the exposed population and a relative effect estimate exist over those without such data
Existing systematic review evidence	Prioritize pairs of occupational risk factor and health outcome that our scoping review suggests have at least some prior systematic review evidence with strong relative effect estimates over pairs for which evidence has not yet been systematically reviewed; relative effect estimates (for example, risk ratios, odds ratios and hazard ratios) are considered strong if they are derived through meta-analysis from multiple high-quality studies, such as randomized controlled trials or prospective cohort studies
Scientific consensus on causality	Prioritize pairs of occupational risk factor and health outcome that have a relatively high-quality body of supporting theoretical and empirical evidence on causality over pairs with a relatively low-quality body of such evidence; crucial supporting evidence includes evidence of a causal effect of the risk factor on the outcome, as well as on the causal pathways (or mechanisms) through which the risk factor affects the outcome, including key mediating factors (especially for more distal risk factors)
Included in existing WHO or ILO methodology	Prioritize pairs of occupational risk factor and health outcome that have already been included in the WHO/ILO methodologies over those that have not
Large public interest or knock-on effect	Prioritize pairs of occupational risk factor and health outcome that are of greater current public interest or have larger knock-on effects (e.g. effects on health workers that threaten health care provision) over those of lesser public interest or without any knock-on effects
Preventable occupational risk factor	Prioritize more easily preventable pairs of occupational risk factor and health outcome over those that are less easily preventable

DALYs, disability-adjusted life years; ILO, International Labour Organization; WHO, World Health Organization.

In order to harmonize the systematic reviews and to ensure consistency, WHO and the ILO: convened 48 coordination meetings with all lead reviewers; convened two face-to-face meetings with individual experts; provided several training workshops to build capacity of participating individual experts in conducting the specific systematic reviews along the agreed standards; established a Working Group of systematic review methodologists to strengthen global capacity for evidence synthesis for work-related burden of disease estimation; and, supported by individual experts, developed novel systematic review tools *(46)*. An overview of all systematic reviews and a description of all innovations developed for this series is available elsewhere *(27)*.

The occupational risk factor of interest in four systematic reviews and meta-analyses was exposure to long working hours (here defined as ≥ 55 hours/week) (Table 3). Following the pre-published protocols *(28–31)*, studies of the effect of exposure to long working hours on the risk of stroke, ischaemic heart disease, depressive disorder and alcohol use disorder were subject to systematic review and their reported estimates were included in meta-analyses *(38–41)* (Table 4).

WHO and the ILO selected the pairs of occupational risk factor and health outcome with an evidence base (as presented in the systematic reviews and meta-analyses) that the organizations judged sufficient for the production of official burden of disease estimates *(2, 48)*. Using Navigation Guide ratings *(49)*, the body of evidence had to have been judged to be either of “high quality” or “moderate quality" (Table 5) and the strength of the evidence had to have been rated as "sufficient evidence for harmfulness" (Table 6) *(48)*. The organizations then selected the "best" effect estimate (risk ratios for morbidity versus mortality) based on strength of evidence ratings *(48)*. If there was any evidence for fatal or non-fatal events of the health outcome rated as "sufficient evidence for harmfulness", this was selected as the "best" estimate. In the event that both fatal and non-fatal events had the same rating, estimates for fatal events were prioritized.

TABLE 3
DEFINITION OF RISK FACTOR, RISK FACTOR LEVELS AND THEORETICAL MINIMUM RISK EXPOSURE LEVEL FOR EXPOSURE TO LONG WORKING HOURS

Occupational risk factor	Definition	Levels (hours per week)	Theoretical minimum risk exposure level
Exposure to long working hours[a]	Working > 40 hours per week, that is, exceeding the standard working hours (35–40 hours per week)	(i) 35–40 (ii) 41–48 (iii) 49–54 (iv) ≥ 55	Standard working hours defined as 35–40 hours per week

[a] The ILO defines long working hours as > 48 hours per week, based on the Hours of Work (Industry) Convention, 1919 (No. 1) and Hours of Work (Commerce and Offices) Convention, 1930 (No. 30), which set the general standard of 48 hours of work per week.

TABLE 4
SYSTEMATIC REVIEWS AND META-ANALYSES ON THE EFFECT OF EXPOSURE TO LONG WORKING HOURS ON VARIOUS HEALTH OUTCOMES

Exposure to long working hours (hours per week)	No. studies in meta-analysis (no. participants)	Risk ratio[a] (95% CI)	Quality of evidence (see Table 5)	Strength of evidence of human data (see Table 6)	Evidence sufficient to proceed to estimation *(47)*
Ischaemic heart disease *(39)*					
41–48	20 (312 209)	0.98 (0.91–1.07)	Low	Inadequate evidence of harmfulness	No
49–54	18 (308 405)	1.05 (0.94–1.17)	Low	Inadequate evidence of harmfulness	No
≥ 55	22 (339 680)	1.17 (1.05–1.31)	Moderate	Sufficient evidence of harmfulness	Yes
Stroke *(38)*					
41–48	12 (265 937)	1.01 (0.91–1.12)	Low	Inadequate evidence of harmfulness	No
49–54	17 (275 181)	1.13 (1.00–1.28)	Moderate	Limited evidence of harmfulness	No
≥ 55	7 (162 644)	1.35 (1.13–1.61)	Moderate	Sufficient evidence of harmfulness	Yes
Depressive disorder *(31)*					
41–48	8 (49 392)	1.03 (0.90–1.17)	Low	Inadequate evidence of harmfulness	No
49–54	8 (49 392)	1.04 (0.95–1.13)	Low	Inadequate evidence of harmfulness	No
≥ 55	17 (91 142)	1.05 (0.96–1.14)	Low	Inadequate evidence of harmfulness	No
Alcohol use disorder *(40)*					
41–48	0 (0)	–	Low	Inadequate evidence of harmfulness	No
49–54	0 (0)	–	Low	Inadequate evidence of harmfulness	No
≥ 55	0 (0)	–	Low	Inadequate evidence of harmfulness	No

CI, confidence interval.
[a] Calculated for the effect of the category of exposure to long working hours on the health outcome, compared with the minimum risk exposure level, defined as working 35–40 hours per week (standard working hours).

TABLE 5

NAVIGATION GUIDE QUALITY OF EVIDENCE RATINGS *(49)*

Quality of evidence rating	Definition
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

TABLE 6

NAVIGATION GUIDE STRENGTH OF EVIDENCE RATINGS *(49)*

Strength of evidence rating	Definition
Sufficient evidence of harmfulness	The available evidence usually includes consistent results from well designed, well conducted studies, and the conclusion is unlikely to be strongly affected by the results of future studies; for human evidence a positive relationship is observed between exposure and outcome where chance, bias and confounding can be ruled out with reasonable confidence.
Limited evidence of harmfulness	The available evidence is sufficient to determine the effects of the exposure, but confidence in the estimate is constrained by factors such as: the number, size or quality of individual studies; confidence in the effect; or inconsistency of findings across individual studies. As more information becomes available, the observed effect could change and this change may be large enough to alter the conclusion. For human evidence, a positive relationship is observed between exposure and outcome where chance, bias and confounding cannot be ruled out with reasonable confidence.
Inadequate evidence of harmfulness	Studies permit no conclusion about a toxic effect. The available evidence is insufficient to assess effects of the exposure because of the limited number or size of studies, the low quality of individual studies or inconsistency of findings across individual studies. More information may allow an estimation of effects.
Evidence of lack of harmfulness	The available evidence includes consistent results from well designed, well conducted studies, and the conclusion is unlikely to be strongly affected by the results of future studies. For human evidence, more than one study showed no effect on the outcome of interest at the full range of exposure levels that humans are known to encounter, where bias and confounding can be ruled out with reasonable confidence. The conclusion is limited to the age at exposure and/or other conditions and levels of exposure studied.

According to the above-described criteria for proceeding to estimation, WHO and the ILO have been able to calculate the burdens of disease for the category of exposure to long working hours of ≥ 55 hours per week and the health outcomes of stroke and ischaemic heart disease (see last column in Table 4). Estimates for these two pairs are also provided in the accompanying Global Monitoring Report *(26)* as well as a dedicated scientific journal article *(48)*.

3. DATA SOURCES

In this section, we report the various input data sources used to produce the WHO/ILO Joint Estimates for the established pairs, as well as the two recently added pairs (ischaemic heart disease and stroke attributable to exposure to long working hours). The input databases and sources are summarized in Table 7.

3.1. Established pairs

For the 39 established pairs of occupational risk factor and health outcome included in this estimation (Table 1), WHO and the ILO derived the population attributable fractions (disaggregated by country, sex and age group) from the Global Burden of Disease Study *(23)* and total disease burden envelopes from the WHO Global Health Estimates *(3)*. Each established pair's attributable burden of disease was then estimated using the CRA framework *(2)*.

3.2. Recently added pairs

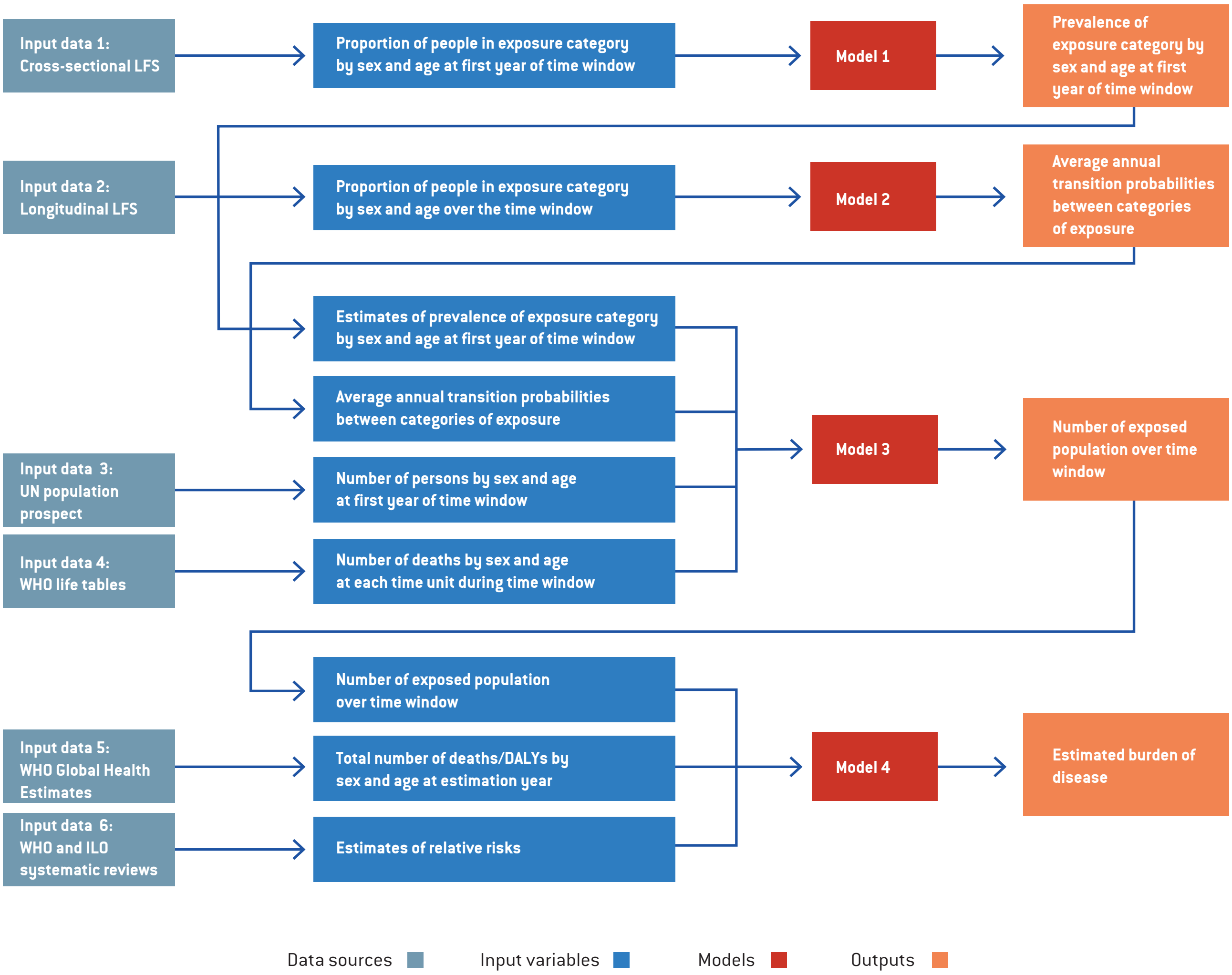
The WHO/ILO Joint Estimates on exposure to long working hours are produced primarily from global databases. The sources, availability, and coverage by country, area or territory and population of the data in these exposure databases on long working hours are described in detail below and depicted in Fig. 2.

TABLE 7
SUMMARY OF THE MAIN DATA SOURCES USED AS INPUTS

Database/estimates	Content	Source
WHO/ILO global cross-sectional and longitudinal databases of working hours	Prevalence of exposure to long working hours by exposure level (41–48, 49–54 and ≥ 55 hours per week), country/area/territory, sex and age group	Labour Force Surveys, Gallup surveys
UN population prospects	No. people by country, sex and age group	UN estimates
WHO life tables	Probability of dying by country, sex and age group	WHO estimates
WHO total disease burden envelope by health outcome	No. DALYs and deaths by country, health outcome, sex and age group	WHO estimates

DALYs, disability-adjusted life years; ILO, International Labour Organization; UN, United Nations; WHO, World Health Organization.

FIGURE 2
FLOW CHART SHOWING HOW DATA SOURCES, INPUT DATA AND MODELS WERE COMBINED TO PRODUCE MODEL OUTPUTS AND BURDEN ESTIMATES



Source: Pega et al. *(48)*.

3.2.1. Exposure

(a) Cross-sectional database

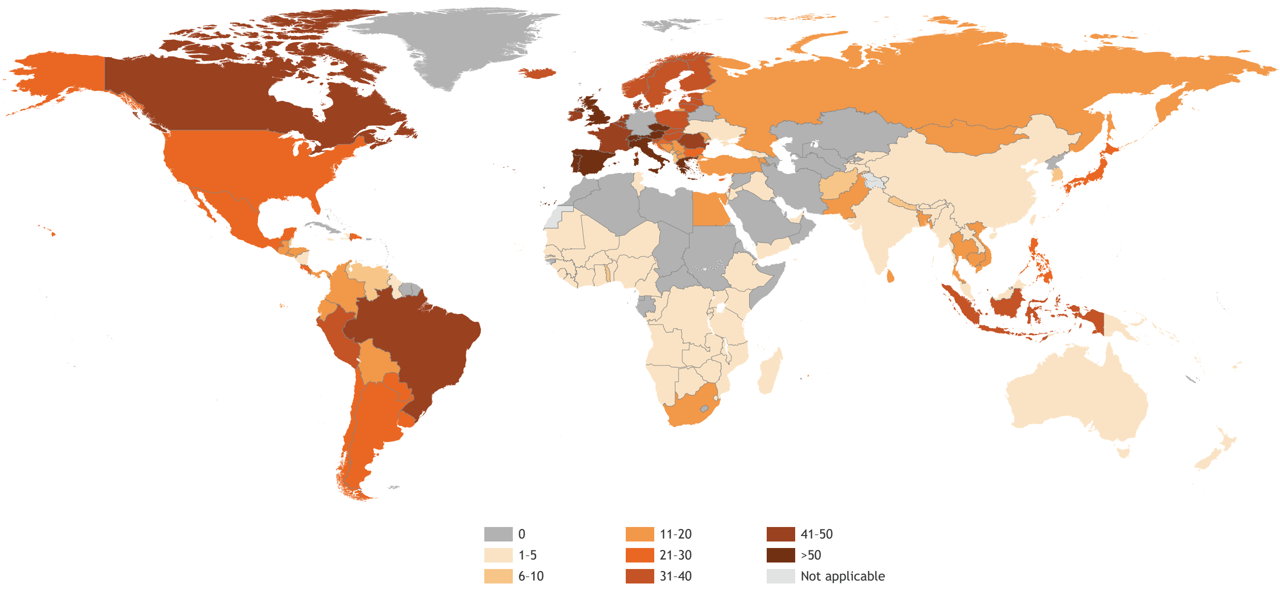
The WHO/ILO Global Cross-Sectional Working Hours Database includes 467 million observations from 2324 surveys conducted in 154 countries, areas and territories between 1 January 1976 and 31 December 2018 (Table 8), the majority of which are official household surveys (mainly Labour Force Surveys). Data from at least one survey are available for 77.4% (154/199) of the countries, areas and territories. Data are available for at least half of the countries, areas and territories within each region (Table 8). The number of surveys in the database by country, area and territory is presented in Fig. 3 and the number of surveys by country, area and territory grouped within region over time for the period 1976–2018 is shown in Fig. 4. Aggregate data are openly available to browse via the ILOSTAT web portal (https://ilostat.ilo.org), and fully disaggregated data for a country are available to the responsible national statistical office and other government agencies upon request. A more detailed description of the database, including all source surveys, is provided elsewhere (see Pega et al. *(48)*).

TABLE 8
NUMBER OF SURVEYS AND NUMBER AND PERCENTAGE OF COUNTRIES, AREAS AND TERRITORIES COVERED IN THE WHO/ILO GLOBAL CROSS-SECTIONAL WORKING HOURS DATABASE BY REGION AND GLOBALLY

	WHO region[a]						Global
	African Region	Region of the Americas	South-East Asia Region	European Region	Eastern Mediterranean Region	Western Pacific Region	
No. countries, areas and territories	47	36	11	53	22	30	199
No. surveys	135	437	96	1435	66	155	2324
No. countries, areas and territories with ≥ 1 survey (% of countries, areas and territories)	37 (78.7%)	24 (66.7%)	10 (90.9%)	45 (84.9%)	11 (50.0%)	27 (90.0%)	154 (77.4%)

[a] See Annex 2 for listing of countries, areas and territories within regions.

FIGURE 3
MAP OF COUNTRIES, AREAS AND TERRITORIES WITH DATA (COLOURS) AND WITHOUT DATA (GREY) IN THE WHO/ILO GLOBAL CROSS-SECTIONAL WORKING HOURS DATABASE



The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury
Map Production: WHO GIS Centre for Health, DNA/DDI

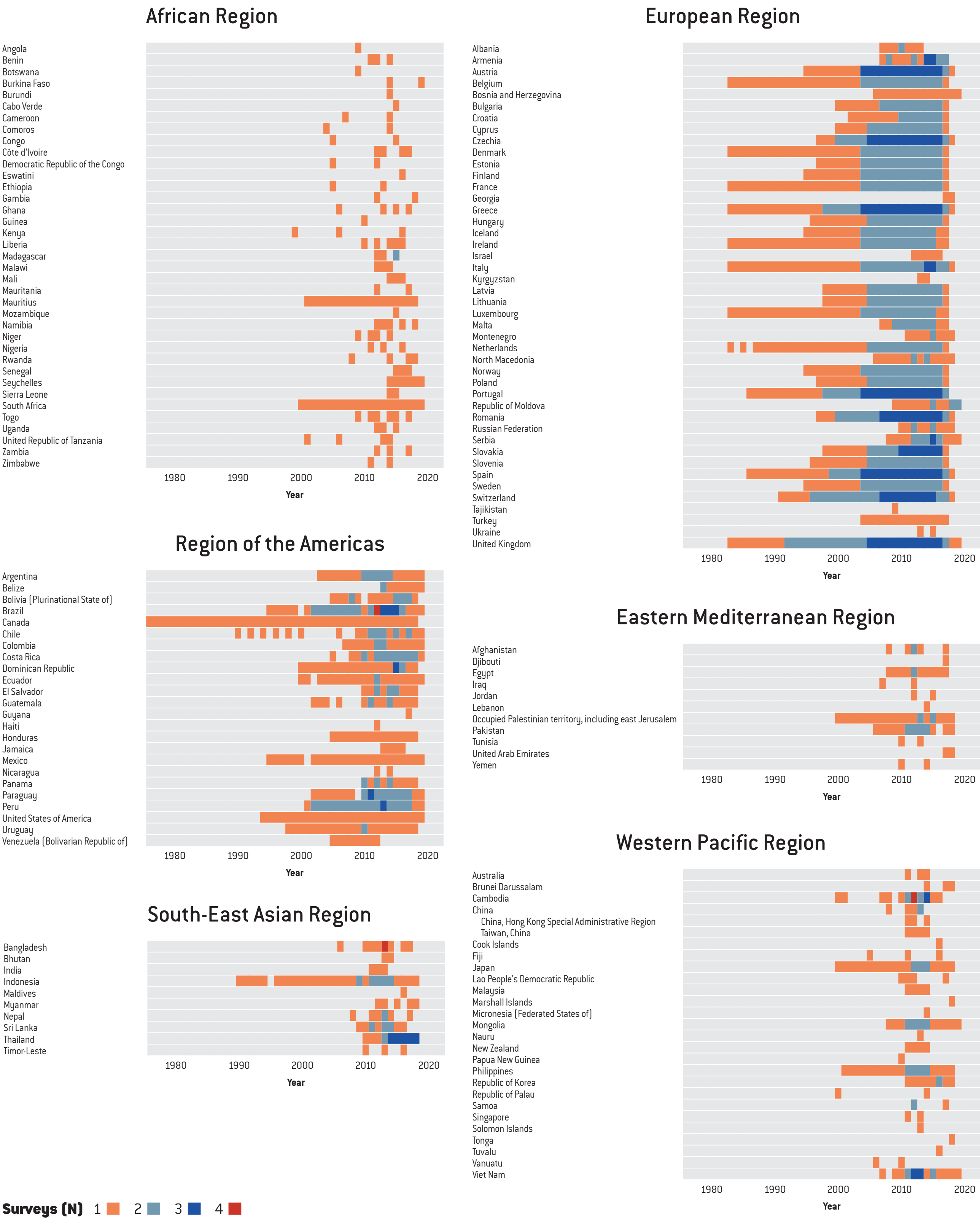
World Health Organization

(b) Longitudinal database

The WHO/ILO Global Longitudinal Working Hours Database was also established specifically for the WHO/ILO Joint Estimates. The database comprises 143 million observations from 739 quarterly datasets of Labour Force Surveys conducted in 15 countries between 1 January 2000 and 31 December 2018. These quarterly survey datasets use sample rotation to ensure sample overlaps, with measures taken repeatedly from the same survey participants over consecutive years.

FIGURE 4

TIME AND COUNTRY, AREA AND TERRITORY DISTRIBUTION OF THE NUMBER OF SURVEYS IN THE WHO/ILO GLOBAL CROSS-SECTIONAL WORKING HOURS DATABASE GROUPED BY REGION



Because microdata do not include individual participant identifiers, data were probabilistically linked longitudinally using matching by household number, household sequence number, sex and year of birth. These were all official surveys conducted by national statistical offices and originally shared by countries with the ILO or European Commission Directorate Eurostat (https://ec.europa.eu/eurostat). A more detailed description of the database, including all source surveys, is provided elsewhere (see Pega et al. *(48)*).

3.2.2. Effect estimates

Risk ratios for the effect of exposure to long working hours on ischaemic heart disease and stroke were sourced from the literature using systematic reviews and meta-analyses *(38, 39)*. Table 4 summarizes the bodies of evidence from systematic reviews and meta-analyses of studies with estimates of the effect of long working hours on four different health outcomes, reporting the effect of long working hours on each health outcome by three different risk factor categories. For the two recently added pairs considered in this report, systematic reviews found sufficient evidence of harmfulness at the exposure level of ≥ 55 hours per week on both ischaemic heart disease and stroke.

3.2.3. Total burden of disease envelopes

Estimates of the total numbers of deaths (Annexes 3 and 4) and DALYs as a result of ischaemic heart disease and stroke for the years 2000, 2010 and 2016 were sourced from the WHO Global Health Estimates *(3)*. The total number of deaths by disease, sex and age group were available for 2016 for the 183 countries with populations larger than 90 000 in the year 2015. These estimates are openly available to browse via the WHO Global Health Observatory webpage (https://www.who.int/data/gho).

3.2.4. Other data sources

(a) UN population estimates

Estimates of the total populations by country, year, sex and age group for the years 1950–2018 were sourced from the UN global population estimates *(50)*.

(b) WHO life tables

Estimates of probability of death by country, year, sex and age group were sourced from WHO life tables *(51)*.

4. ESTIMATION METHODS

4.1. Established pairs

We followed the CRA framework *(2)* to estimate the burden of disease attributable to exposure to occupational risk factors. We derived population attributable fractions (disaggregated by sex and age group) for the 39 established pairs of occupational risk factor and health outcome (Table 1) from the Global Burden of Disease Study. The estimates from which these population attributable fractions were calculated are openly available (http://ghdx.healthdata.org/). WHO and the ILO calculated point estimates of population attributable fractions from the Global Burden of Disease Study estimates as the attributable number of deaths or DALYs as a fraction of the total number of deaths or DALYs, by country, sex, age and health outcome for the years 2000, 2010 and 2016 as:

$$PAF_P = \frac{aBOD_{P,GBD}}{BOD_{0,GBD}} \qquad (1)$$

where PAF is the population attributable fraction, aBOD is the attributable burden of disease (number of deaths or DALYs) and BOD is the burden of disease envelope (total number of deaths or DALYs). The subscript P indicates variables relating to the numbers of deaths or DALYs resulting from a particular health outcome attributable to that occupational risk factor, for each cohort defined by country, sex and age group (attributable burden of disease for the specific risk factor). The subscript 0 indicates the numbers of deaths or DALYs resulting from a particular health outcome, for each cohort defined by country, sex and age group (total disease burden envelope).

For each pair, point estimates of the respective WHO/ILO attributable burden of disease estimates were calculated by multiplying the WHO/ILO Global Health Estimates of the total numbers of deaths and DALYs by the corresponding population attributable fraction separately for each cohort defined by country, sex, age and health outcome for the years 2000, 2010 and 2016, that is:

$$aBOD_P = BOD_{0,GHE} \times PAF_P \qquad (2)$$

where $BOD_{0,GHE}$ represents the burden of disease envelope defined by International Statistical Classification of Diseases and Related Health Problems (version 10) codes in the Global Health Estimates *(3)* in terms of numbers of deaths or DALYs.

The 95% uncertainty ranges (URs) for $aBOD_P$ were calculated assuming that it follows a normal distribution with expected value $\mathcal{E}$ equal to the point estimate and variance (var) calculated as:

$$\text{var}(\text{aBOD}) = \text{var}(\text{BOD})\text{var}(\text{PAF}) + \text{var}(\text{BOD})[\mathcal{E}(\text{PAF})]^2\text{var}(\text{PAF})[\mathcal{E}(\text{BOD})]^3 \quad (3)$$

where it is assumed that PAF and BOD are independent random variables. In this case, the upper and lower URs are defined as $\mathcal{E}(\text{aBOD}) \pm z^*\sqrt{\text{var}(\text{aBOD})}$, where z^* is the critical value calculated from the inverse of the cumulative distribution function of the standard normal distribution at 0.025.

4.2. Additional pairs

To produce these estimates, data were required on the number of workers exposed to long working hours, as well as the risk ratio of exposure at the hazardous level (here defined as ≥ 55 hours per week) compared with exposure to the theoretical minimum risk exposure level (here defined as 35–40 hours per week). We estimated the number of the exposed population using multilevel models *(52)*. Measures of exposure to long working hours were taken primarily from global databases of national official surveys, and the models contributed the percentage of the population (disaggregated by country, sex and age group; Annex 5) exposed to working ≥ 55 hours per week. Our estimates of exposure were combined with estimates of the risk ratios to generate the population attributable fractions for long working hours and each of the health outcomes of ischaemic heart disease and stroke, which were then used to estimate the attributable burden of disease *(48)*. We made several modelling assumptions based on available evidence (Table 9), described in the following. A more detailed description of the estimation models for the recently added pairs is provided elsewhere *(48)*.

4.2.1. Exposure to long working hours

A three-model approach was developed to estimate the exposure to long working hours (Annex 5) *(48)*. Model 1 estimated the prevalence of exposure to long working hours using a multilevel model. Model 2 calculated the transition probabilities between exposure categories during the time window of the exposure. Finally, Model 3 was a microsimulation model used to estimate the exposed population during the time window.

(a) Model 1: Multilevel model

An established multilevel model was used that predicts prevalence over time for a particular geographical region *(52)*. WHO has used this model regularly to estimate exposure to environmental risk factors such as air pollution *(64)* and water sanitation and hygiene *(65)*. The UN Statistical Commission considers this method to be established, and has approved it for producing several SDG indicators, including 3.9.1, 3.9.2 and 3.9.3 (https://unstats.un.org/unsd/statcom). In the microsimulation model, these estimates were used as the first set of input data (Input Data 1).

For each year during 1980–2016, for each population defined by country, sex and age group, we produced estimates of the proportion of the population in each exposure category (i). We modelled Input Data 1 using the following multilevel model (Model 1):

$$\text{Proportion}_i = A_i + B_i t \quad (4)$$

where Proportion_i is the proportion of the population in exposure category i in a given group defined by country/area/territory, sex and age group, and t is the survey year. The intercept A_i and slope B_i of t, dependent on Proportion_i, are calculated using a multilevel model with sex and age as fixed effects, and sex and age as random effects, nested in the countries, areas and territories within the region (with regions treated independently). Because Proportion_i was strongly non-linearly dependent on age, we linearized age by fifth-order orthogonal polynomials to prevent collinearity.

For exposure to long working hours, direct measures are available in the WHO/ILO global databases, as described in Section 3.2.1. These provided the proportion of survey participants within the predefined categories of working hours (including ≥ 55 hours per week) that people in a group defined by country, sex and age group were exposed to, allowing exposure to be modelled directly.

(b) Model 2: Transition probabilities

Based on the methodology developed by Eurostat, pseudo-longitudinal data were derived from the European Union (EU) Labour Force Surveys by matching data from the annually overlapping samples, averaging over the four quarters per year, for the years 2010–2018. Because of the absence of personal identifiers, matching was based on household number, household sequence number, sex and year of birth. Longitudinal weights were derived by scaling the available target year weights to represent the correct labour market status (labour market inactive versus working) by sex and 10-year age group *(66)*. The aggregated transition matrix for labour market status was then ranked to match initial and target year margins (with the exception of initial year inactivity status).

TABLE 9
MODELLING ASSUMPTIONS AND THEIR EVIDENCE BASE

Assumption in main analysis (sensitivity analyses)	Explanation and example	Evidence base
Lag time (*a*) of 10 years (8 and 12 years)	For an outcome event in year *t*, the exposure is assumed to have occurred in the lag year (year *t*–*a*) For example, burden of disease in 2016 is attributable to exposure 10 years earlier, with the lag year being 2006	Theoretically, lag time varies according to the mechanism via which long working hours are associated with ischaemic heart disease and stroke, that is, either: directly (exposure has a direct effect on pathophysiology); indirectly (exposure impacts risk factors for ischaemic heart disease and/or stroke); as a trigger (exposure triggers events that lead to ischaemic heart disease and/or stroke events); and/or as a prognostic factor (exposure affects prognosis of coronary heart disease or cerebrovascular disease) *(53, 54)*. If direct and indirect effects are the dominant mechanisms, then lag time could be < 10 years; if exposure acts as a trigger or a prognostic factor, 10 years would be too long. If all four mechanisms contribute to risk of cardiovascular disease, an average lag of 10 years is an appropriate assumption. Previous examples of the use of lag times of around 10 years include: (i) in WHO/ILO systematic reviews and meta-analyses on ischaemic heart disease and stroke *(38, 39)*; (ii) mean follow-up times in previous large systematic reviews and individual studies of around 9 and 8 years for ischaemic heart disease and stroke, respectively *(55, 56)*; (iii) an incubation period of at least 10 years for coronary heart disease *(57)*; and (iv) according to evidence from the CONSTANCES Cohort Study in France, only a lag time of ≥ 10 years was found to increase odds ratios of ischaemic heart disease and stroke *(58, 59)*.

TABLE 9 (CONTINUED)

MODELLING ASSUMPTIONS AND THEIR EVIDENCE BASE

Assumption in main analysis (sensitivity analyses)	Explanation and example	Evidence base
Time window of exposure (*b*) of 10 years (8 and 12 years)	Rather than occurring in year *t*–*a* only, exposure occurs in any year during a "critical" time window of length *b*, and exposure within any year in this time window can still cause the disease outcome in year *t* For example, to estimate burden of disease in 2016, we model exposure over a 10-year time window	As mentioned above, the four potential mechanisms *(53, 54)* are likely to have different lag times; a time window of exposure around the lag year accounts for some of this variability. Previous occupational burden of disease studies have also estimated exposure over a time window (60, 61). Evidence suggests that exposure (sometimes measured cumulatively) to long working hours during this 10-year time window contributes to a significant increase in cardiovascular disease incidence (57–59).
Spacing of the time window (*b*) symmetrically around the lag year	The time window of the exposure is equally spaced around the "lag year" of the average lag period (year *t*–*a*), so that the time window of exposure is defined as from year *t*–*a*–(*b*/2) to year *t*–*a*+(*b*/2) For example, to estimate burden of disease in 2016, we model exposure over the time window of 2001–2010	As mentioned above, the four potential mechanisms *(53, 54)* are likely to have different lag times; with the exception of the trigger mechanism, symmetrical spacing of the time window around the lag year is a reasonable assumption. If all four mechanisms contribute, symmetrical spacing is the most appropriate model. This is common practice in studies estimating burden of disease attributable to exposure to occupational risk factors; for example, a report on the burden of occupational cancer in the United Kingdom of Great Britain and Northern Ireland estimated the "peak latency" period for their outcomes of interest and spaced the time window of exposure symmetrically around this point (61).
The highest exposure category in any year over the time window of exposure (the most common exposure category)	For each worker, the highest exposure category they had in any year over the time window is assigned as their exposure category over the window For example, during 2001–2010, worker A was exposed to ≥ 55 hours work per week in 2001 and 2002, and to 49–54 hours work per week in 2003–2011; we therefore assign worker A the exposure category of ≥ 55 hours per week	For diseases with long latency periods, which is possible for cardiovascular disorders, once the disease process has started, the worker continues to be at risk even if exposure levels are reduced. The assignment of the highest level of exposure observed over the time window is in line with assumptions made by other studies focusing on the effect of long working hours and ischaemic heart disease and stroke (55, 56, 58, 59, 62, 63).
The "best" effect estimate	For estimating numbers of deaths and DALYs and for all cohorts defined by country, sex, and age group, we assigned the same "best" effect estimate	There is no evidence for effect modification by country (or WHO region), sex or age group in the subgroup analyses in the WHO/ILO systematic reviews *(38, 39)*; we therefore assigned the pooled effect estimate from the main analysis. This is the same approach used in previous WHO burden of disease studies (21). We systematically selected the "best" effect estimate, based on the pre-specified criteria (see Section 2.2). This is based on prioritizing mortality over morbidity and relatively higher strength of evidence over lower strength of evidence (Section 2.2 and Table 4).

Source: Pega et al. (16).

We estimated average transition probabilities between exposure categories of long working hours by running a weighted multinomial logit regression model, including sex and a function of age as regressors, and using a matched sample of all available longitudinal data. We then used fractional polynomials with automated model selection in Stata version 14 (StataCorp LLC, College Station, United States of America) to model age for each separate regression run for exposure categories $h_0, h_1, \ldots, h_5$ (where the six categories refer to labour market inactive and working hours categories 0–35, 35–40, 41–48, 49–54 and ≥ 55 hours per week). From the coefficients estimated, we derived predicted probabilities of transitioning between exposure categories by group defined by sex and age group. Including age as a continuous function allowed strength to be borrowed from the distribution of age, in order to estimate age groups with limited numbers of observations. The final estimates, particularly for the highest and lowest age groups, are therefore driven by the choice of function.

For each population group defined by country, sex and age group, we estimated the probability (P_j) of transitioning from long working hours exposure category *i* in year *t* to exposure category *i* in year *t* + 1. Here, *j* denotes one of the *n* possible transitions from one of the exposure categories in year *t* to a specific exposure category in year *t* + 1. We adopted methods developed by Eurostat for calculating these transition probabilities *(66)*. Using Input Data 2, we scaled the survey weights for the target year (year *t* + 1) to represent the correct labour market status by country, sex and age group for the initial year (year *t*) and the target year. We then adjusted the complete sample in the target year to match margins for labour market status in both years, using iterative raking by sex. We did not match the exposure category *i* = 0 (labour market inactive) for the initial year. Input Data 2 was modelled using the multinomial logit regression model (Model 2):

$$P_j = \frac{\exp\left(\beta_j X_j\right)}{1 + \sum_{\alpha} \exp\left(\beta_{\alpha} X_j\right)} \qquad (5)$$

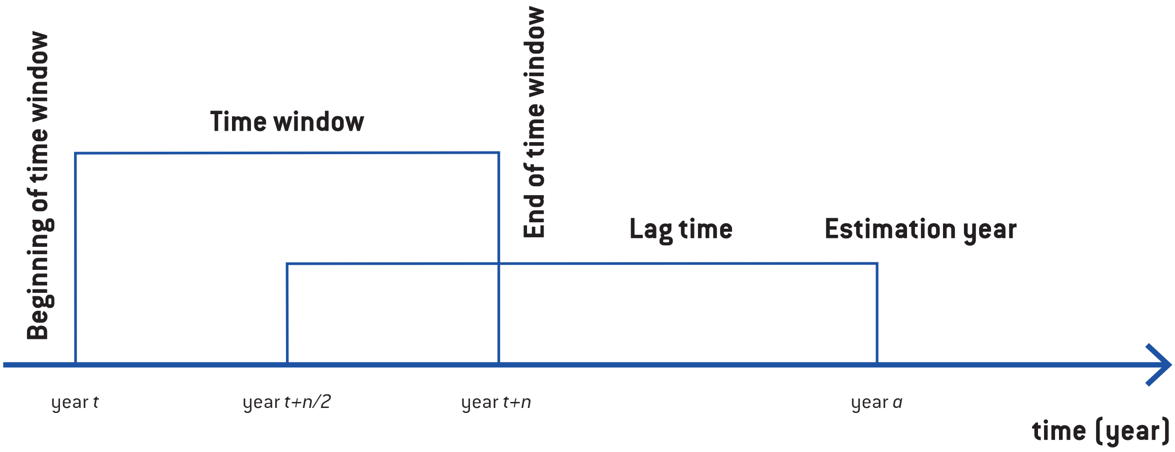
where β_j is the set of regression coefficients describing the longitudinal weights associated with transition *j*; X_j is a set of explanatory variables (sex and age as a fractional polynomial with maximal permitted degree of four associated with transition *j*); and the summation (index α) encompasses all possible transitions *j* (except the transition from *i* = 0 in year *t* to *i* = 0 in year *t* + 1, which was chosen as a pivot outcome).

By modelling transition probabilities, we derived 15 900 transition probabilities for the 15 countries for which we hold data (listed in supplementary tables S3 and S5 of Pega et al. *(48)*) using Input Data 2. In addition, by modelling quarterly EU Labour Force Surveys data using transition probabilities, Eurostat derived 31 104 transition probabilities covering 27 countries and shared these transition probabilities with WHO and the ILO. For populations defined by country, sex and age group for which P_i could not be calculated (because the required longitudinal data were unavailable), P_i was imputed. The imputed P_i was the mean of all transition probabilities of the population defined by the same sex and age in the region, weighted by the number of observations contributing to the transition probabilities.

(c) Model 3: Microsimulation

A time window is the period in which an exposure can lead to health loss in the estimation year *(67)*. As an example, we seek to estimate the burden of disease at year *a* that is attributable to past exposure to a risk factor. For this, we require estimates of the number of people exposed to the risk factor, at a particular level of exposure, throughout the time window (year *t* – (*b*/2) to year *t* + (*b*/2)). The known or assumed lag time is year *t* + (*b*/2) to year *a*. We then seek to estimate the number of people exposed to the risk factor at the highest level of exposure during the time window (Fig. 5).

FIGURE 5
DEFINITION OF TIME WINDOW OF EXPOSURE. ADAPTED FROM PEGA ET AL. *(48)*.



For each population defined by country, sex and age group, we estimated the proportion (Proportion$_k$) of the population in each exposure category throughout the time window (year $t - (b/2)$ to year $t + (b/2)$). We defined k as the highest exposure category i in any year in the time window. Based on advice from the WHO/ILO Technical Advisory Group, we assumed burden of ischaemic heart disease and stroke in the estimation year could be the result of exposure to (hazardous) working hours during a time window of 5–15 years before the estimation year. For example, to estimate burden for the year 2016, we assume that the time window of exposure was 2001–2010.

We used microsimulation, a method for generating micro-level estimates by combining individual- and aggregate-level datasets, and initiated a synthetic population for each country. We used input data on the probability of dying for the synthetic cohort to ensure representative sex and age distribution during the first year of the time window (i.e. estimation year minus 15 years), as well as the estimates output from the multilevel model to probabilistically assign each individual to a specific exposure category (i) in the first year. Using transition probabilities for each year over the entire time window, transitions from one exposure category to another were stochastically modelled to estimate each synthetic individual's working hours category in each year. Using transition probabilities over the time window (Input Data 4), from the first year of the time window to the estimation year, each individual was stochastically assigned to the states of "dead" or "alive". All synthetic individuals that reached the state "dead" before the estimation year were censored. Using this microsimulation method, Proportion$_k$ is derived using the model (Model 3):

$$\text{Proportion}_k = \frac{\sum_{l=1,\ldots,n} \delta_{k,\max}(S_l)}{n} \qquad (6)$$

where the summation runs through individuals "alive" in the estimation year; δ_k,max is the Kronecker delta function; S_l is the sequence of the lth individual of all working hours categories (i) in each year in the time window; and max denotes the highest i that the lth individual experiences in the sequence assigned.

4.2.2. Burden of disease

As for the established pairs, the CRA framework *(2)* was used to estimate the burden of disease attributable to exposure to occupational risk factors. We estimated the proportional reduction in death or disease that would occur if exposure was reduced to a level with a minimum risk (i.e. working 35–40 hours per week), while other conditions remain unchanged.

(a) Population attributable fractions

We calculated population attributable fractions (Annexes 6 and 7) using prevalence estimates from the WHO/ILO global working hours databases for the recently added pairs of exposure to long working hours and both ischaemic heart disease and stroke, using estimates output from the microsimulation model (Model 3) and risk ratios for the exposure categories. To produce the attributable burdens of ischaemic heart disease and stroke for the risk factor of exposure to long working hours, we applied the estimation model:

$$\mathrm{PAF} = \frac{\sum_{k=1}^{n} \mathrm{Proportion}_k \left(\mathrm{RR}_k - 1\right)}{\sum_{k=1}^{n} \mathrm{Proportion}_k \left(\mathrm{RR}_k - 1\right) + 1} \qquad (7)$$

where $\mathrm{Proportion}_k$ is the proportion of the population in working hours category k; RR_k is the risk ratio for the exposure category k; and n is the total number of long working hours categories.

(b) Applying population attributable fractions to total disease burden envelopes

Applying the population attributable fraction (Annexes 6 and 7) to the total mortality burden of the health outcome provides the total number of deaths from the disease or injury that can be attributed to the occupational risk factor. The population attributable fractions calculated for each additional pair of occupational risk factor and health outcome were applied to the total disease burden envelopes for the health outcome from the WHO Global Health Estimates for the years 2000–2016 *(3)*.

4.2.3. Uncertainty range calculations

When estimating the attributable burden of disease for selected occupational risk factors, several risks of bias and/or errors may exist, such as risk of selection bias, statistical error, or risk of confounding of underlying input parameters. A large body of literature exists regarding the estimation of statistical uncertainty of an estimate, which is itself a function of existing estimates.

We calculated uncertainty ranges for exposure, death and DALY estimates using bootstrapping *(68)*. One hundred estimates of prevalence were produced with starting parameters sampled independently from normal distributions, with the median equal to the corresponding point estimate and uncertainty ranges taken from those of the prevalence estimates per year. The 2.5% and 97.5% quantiles of the resulting random deviates of the exposures were then calculated and assigned as the lower and upper limits of the uncertainty range, respectively *(48)*.

4.2.4. Sensitivity analyses

We performed the following sensitivity analyses to test our assumptions (Annex 8): (i) we reduced the lag time to 8 years (2003–2012); (ii) we increased the lag time to 12 years (1999–2008); (iii) we reduced the time window for the exposure to 8 years (2002–2009); (iv) we increased the time window to 12 years (2000–2011); and (v) we assigned the long working hours category with the largest number of years in the time window (censoring years spent in labour market inactivity) *(48)*.

4.3. Inequalities in work-related burden of disease

To consider differences in the occupational burden of disease between regions, sexes and age groups, we used the number of deaths or DALYs per 100 000 population (i.e. death or DALY rate) for all regions, both sexes and for people of working age (≥ 15 years) as the reference. As an absolute measure of inequality, for each death rate and DALY rate for each category of region, sex and age group, we then calculated the difference from the reference rate (global rate) *(58)*. As a relative measure of inequality, we also calculated the rate ratios as the fraction of the reference rate for each death rate and DALY rate, for each category *(69)*.

5. DISCUSSION

The WHO/ILO Joint Estimates have several strengths and limitations which should be considered when interpreting the estimates.

5.1. Strengths

These official estimates of work-related burden of disease have been produced jointly by the UN Specialized Agencies for health and labour, improving partnerships for development and policy coherence across sectors.

The exposure estimates were generated from large cross-sectional and longitudinal databases of direct exposure measurements collected primarily by producers of official statistics in countries, areas and territories. This is the largest exposure database for any occupational risk factor (comprising over 2300 official surveys, primarily Labour Force Surveys, and covering 77.4% (154/199) of the countries, areas and territories with at least one survey). These data are likely to be of high quality as they are produced primarily by national statistics offices using national statistical standards; once provided to WHO and the ILO, they are harmonized to international statistical standards.

The estimates of burden of disease are generated using risk ratios calculated in tailor-made systematic reviews and meta-analyses of the latest bodies of evidence that were comprehensive, transparent and synthesized with the latest systematic review methods. The production of these WHO/ILO reviews was also supported by a large number of individual experts.

The WHO/ILO Joint Estimates make use of new and improved modelling methods, including microsimulation models to estimate exposure over a time window using the longitudinal data of direct exposure. This is a versatile and flexible modelling approach for producing complex occupational exposure estimates that make use of official data produced by countries, areas and territories.

Finally, the estimates of burden of disease are produced at the country, regional and global levels. They are also fully disaggregated by sex and age group, honouring the central premise of the SDGs to reduce inequalities *(1)*. The estimates provide the basis for designing, planning, costing, implementing and evaluating actions to prevent work-related burden of disease, with a focus on improving population health and health equity among workers, both within and across sectors.

5.2. Limitations

As for all estimates, several assumptions have been made during their modelling (Table 9). However, all assumptions have been transparently reported as stipulated in the GATHER guidelines *(19)* (Annex 1). The modelling assumptions are based on the best current evidence, but some assumptions may change as additional evidence becomes available and the evidence base improves.

The estimates are not disaggregated by some important factors, such as occupation, industrial section and migration status. As more data become available, this additional disaggregation can be considered and added as appropriate, if and when feasible.

6. CONCLUSIONS

The WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury (WHO/ILO Joint Estimates) provide a new approach for generating estimates of loss of life and health from exposure to occupational risk factors, the relative importance of different occupational risk factors and health outcomes leading to death or disability, global regional patterns, trends over time, and inequalities by sex and age group within and between countries. These estimates are obtained in several ways, from the use of large cross-sectional and longitudinal data, to new and innovative evidence synthesis and statistical modelling approaches that add accuracy to these estimates. This estimation cycle has benefited from the contributions of a large number of individual experts and a variety of data sources to calculate the burden of disease for the included pairs. The resulting estimates (as well as the processes undergone, methods developed and experience gained) can help advance understanding of the work-related burden of disease at the national, regional and global levels for the period 2000–2016, and its distribution by sex and age group. These estimates provide the base for policy and practice in occupational and workers' health and safety nationally, regionally and globally.

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ANNEXES

ANNEX 1.
GATHER (GUIDELINES FOR ACCURATE AND TRANSPARENT HEALTH ESTIMATES REPORTING) CHECKLIST OF INFORMATION THAT SHOULD BE INCLUDED IN NEW REPORTS OF GLOBAL HEALTH ESTIMATES

Item no.	Checklist item	Page no.
Objectives and funding		
1	Define the indicator(s), populations (including age, sex and geographic entities) and time period(s) for which estimates were made.	Abstract, 3
2	List the funding sources for the work.	Abstract, 3
Data inputs: for all data inputs from multiple sources that are synthesized as part of the study		
3	Describe how the data were identified and how the data were accessed.	8
4	Specify the inclusion and exclusion criteria. Identify all ad hoc exclusions.	–
5	Provide information on all included data sources and their main characteristics. For each data source used, report reference information or contact name/institution, population represented, data collection method, year(s) of data collection, sex and age range, diagnostic criteria or measurement method, and sample size, as relevant.	8
6	Identify and describe any categories of input data that have potentially important biases (e.g. based on characteristics listed in item 5).	10
Data inputs: for data inputs that contribute to the analysis but were not synthesized as part of the study		
7	Describe and give sources for any other data inputs.	Table 7; Sections 3.2.3 and 3.2.4
Data inputs: for all data inputs		
8	Provide all data inputs in a file format from which data can be efficiently extracted (e.g. a spreadsheet rather than a PDF), including all relevant meta-data listed in item 5. For any data inputs that cannot be shared because of ethical or legal reasons, such as third-party ownership, provide a contact name or the name of the institution that retains the right to the data.	https://www.who.int/teams/environment-climate-change-and-health/monitoring/who-ilo-joint-estimates
Data analysis		
9	Provide a conceptual overview of the data analysis method. A diagram may be helpful.	7–10
10	Provide a detailed description of all steps of the analysis, including mathematical formulae. This description should cover, as relevant, data cleaning, data pre-processing, data adjustments and weighting of data sources, and mathematical or statistical model(s).	8–9
11	Describe how candidate models were evaluated and how the final model(s) were selected.	8–9
12	Provide the results of an evaluation of model performance, if done, as well as the results of any relevant sensitivity analysis.	10, Annex 7
13	Describe methods for calculating uncertainty of the estimates. State which sources of uncertainty were, and were not, accounted for in the uncertainty analysis.	9–10
14	State how analytic or statistical source code used to generate estimates can be accessed.	Pega et al. *(1)*, supplementary file 2

Item no.	Checklist item	Page no.
Results and discussion		
15	Provide published estimates in a file format from which data can be efficiently extracted.	https://www.who.int/teams/environment-climate-change-and-health/monitoring/who-ilo-joint-estimates
16	Report a quantitative measure of the uncertainty of the estimates (e.g. uncertainty intervals).	10–13
17	Interpret results in light of existing evidence. If updating a previous set of estimates, describe the reasons for changes in estimates.	14
18	Discuss limitations of the estimates. Include a discussion of any modelling assumptions or data limitations that affect interpretation of the estimates.	14–15

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1. Pega F, Nafradi B, Momen NC, Ujita Y, Streicher KN, Pruss-Ustun AM, et al. Global, regional, and national burdens of ischemic heart disease and stroke attributable to exposure to long working hours for 194 countries, 2000-2016: A systematic analysis from the WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury. Environ Int. 2021:106595. https://doi.org/10.1016/j.envint.2021.106595 PMID:34011457

ANNEX 2.
COUNTRIES, AREAS AND TERRITORIES INCLUDED WITHIN THE DIFFERENT REGIONS

WHO region	Countries, areas and territories included in regional grouping
African Region (47)	Algeria; Angola; Benin; Botswana; Burkina Faso; Burundi; Cabo Verde; Cameroon; Central African Republic; Chad; Comoros; Congo; Côte d'Ivoire; Democratic Republic of the Congo; Equatorial Guinea; Eritrea; Eswatini; Ethiopia; Gabon; Gambia; Ghana; Guinea; Guinea-Bissau; Kenya; Lesotho; Liberia; Madagascar; Malawi; Mali; Mauritania; Mauritius; Mozambique; Namibia; Niger; Nigeria; Rwanda; Sao Tome and Principe; Senegal; Seychelles; Sierra Leone; South Africa; South Sudan; Togo; Uganda; United Republic of Tanzania; Zambia; Zimbabwe
Region of the Americas (36)	Antigua and Barbuda; Argentina; Bahamas; Barbados; Belize; Bolivia (Plurinational State of); Brazil; Canada; Chile; Colombia; Costa Rica; Cuba; Dominica[a]; Dominican Republic; Ecuador; El Salvador; Grenada; Guatemala; Guyana; Haiti; Honduras; Jamaica; Mexico; Nicaragua; Panama; Paraguay; Peru; Puerto Rico[a,b]; Saint Kitts and Nevis[a]; Saint Lucia; Saint Vincent and the Grenadines; Suriname; Trinidad and Tobago; United States of America; Uruguay; Venezuela (Bolivarian Republic of)
South-East Asia Region (11)	Bangladesh; Bhutan; Democratic People's Republic of Korea; India; Indonesia; Maldives; Myanmar; Nepal; Sri Lanka; Thailand; Timor-Leste
European Region (53)	Albania; Andorra[a]; Armenia; Austria; Azerbaijan; Belarus; Belgium; Bosnia and Herzegovina; Bulgaria; Croatia; Cyprus; Czechia; Denmark; Estonia; Finland; France; Georgia; Germany; Greece; Hungary; Iceland; Ireland; Israel; Italy; Kazakhstan; Kyrgyzstan; Latvia; Lithuania; Luxembourg; Malta; Monaco[a]; Montenegro; Netherlands; North Macedonia; Norway; Poland; Portugal; Republic of Moldova; Romania; Russian Federation; San Marino[a]; Serbia; Slovakia; Slovenia; Spain; Sweden; Switzerland; Tajikistan; Turkey; Turkmenistan; Ukraine; United Kingdom; Uzbekistan
Eastern Mediterranean Region (22)	Afghanistan; Bahrain; Djibouti; Egypt; Iran (Islamic Republic of); Iraq; Jordan; Kuwait; Lebanon; Libya; Morocco; occupied Palestinian territory, including east Jerusalem[b]; Oman; Pakistan; Qatar; Saudi Arabia; Somalia; Sudan; Syrian Arab Republic; Tunisia; United Arab Emirates; Yemen
Western Pacific Region (30)	Australia; Brunei Darussalam; Cambodia; China; China, Hong Kong Special Administrative Region[b]; Taiwan, China[b]; Cook Islands[a]; Fiji; Japan; Kiribati; Lao People's Democratic Republic; Malaysia; Marshall Islands[a]; Micronesia (Federated States of); Mongolia; Nauru[a]; New Zealand; Niue[a]; Palau[a]; Papua New Guinea; Philippines; Republic of Korea; Samoa; Singapore; Solomon Islands; Tokelau[a]; Tonga; Tuvalu[a]; Vanuatu; Viet Nam

[a] WHO/ILO Joint Estimates not calculated because population was < 90 000 in 2015 or because of a lack of disease burden envelope.
[b] No burden of disease calculated.

ANNEX 3.

NUMBER OF DEATHS FROM ISCHAEMIC HEART DISEASE IN 2000, 2010 AND 2016, AND MEAN PERCENTAGE CHANGE FOR 2000–2010, 2010–2016 AND 2000–2016, BY WHO REGION AND SEX, 183 COUNTRIES

WHO region	Both sexes						Males						Females					
	No. deaths (95% UR)			Percent change (95% UR)			No. deaths (95% UR)			Percent change (95% UR)			No. deaths (95% UR)			Percent change (95% UR)		
	2000	2010	2016	2000-2010	2010-2016	2000-2016	2000	2010	2016	2000-2010	2010-2016	2000-2016	2000	2010	2016	2000-2010	2010-2016	2000-2016
African Region	371 397 (361 067 to 381 726)	440 276 (428 238 to 452 313)	511 583 (494 976 to 528 190)	18.6 (14.0 to 23.2)	16.2 (11.4 to 21.1)	37.8 (31.9 to 43.9)	186 494 (179 551 to 193 438)	218 127 (209 950 to 226 304)	254 673 (243 270 to 266 075)	17.0 (10.9 to 23.4)	16.8 (10 to 23.8)	36.6 (28.8 to 44.9)	184 902 (177 255 to 192 550)	222 149 (213 314 to 230 983)	256 910 (244 836 to 268 985)	20.1 (13.5 to 27.2)	15.7 (8.6 to 22.8)	38.9 (30.3 to 48.0)
Region of the Americas	1 082 451 (1 062 748 to 1 102 153)	1 019 442 (1 003 076 to 1 035 809)	1 091 057 (1 072 147 to 1 109 968)	-5.8 (-8.1 to -3.5)	7.0 (4.5 to 9.5)	0.8 (-1.6 to 3.4)	554 605 (541 967 to 567 243)	544 727 (533 581 to 555 872)	602 473 (588 817 to 616 130)	-1.8 (-4.7 to 1.3)	10.6 (7.2 to 14.2)	8.6 (5.2 to 12.1)	527 846 (512 730 to 542 961)	474 716 (462 730 to 486 701)	488 584 (475 503 to 501 665)	-10.1 (-13.4 to -6.5)	2.9 (-0.8 to 6.8)	-7.4 (-11.0 to -3.7)
South-East Asia Region	1 288 839 (1 225 507 to 1 352 171)	1 840 810 (1 752 591 to 1 929 029)	2 232 827 (2 109 956 to 2 355 698)	42.8 (33.3 to 53.0)	21.3 (12.7 to 30.5)	73.2 (61.2 to 86.5)	739 596 (687 907 to 791 285)	1 067 877 (995 836 to 1 139 919)	1 326 192 (1 224 099 to 1 428 284)	44.4 (30.8 to 5 9.3)	24.2 (12.4 to 37.6)	79.3 (61.5 to 98.9)	549 244 (512 649 to 585 839)	772 933 (722 015 to 823 850)	906 635 (838 266 to 975 005)	40.7 (28.1 to 54.6)	17.3 (5.9 to 30.1)	65.1 (49.2 to 82.5)
European Region	2 586 293 (2 558 722 to 2 613 865)	2 482 974 (2 454 508 to 2 511 439)	2 342 222 (2 311 315 to 2 373 128)	-4.0 (-5.5 to -2.5)	-5.7 (-7.3 to -4.0)	-9.4 (-11.0 to -7.9)	1 221 191 (1 204 364 to 1 238 018)	1 171 248 (1 154 455 to 1 188 041)	1 102 244 (1 084 448 to 1 120 040)	-4.1 (-6.0 to -2.1)	-5.9 (-7.9 to -3.9)	-9.7 (-11.6 to -7.8)	1 365 103 (1 343 261 to 1 386 944)	1 311 726 (1 288 742 to 1 334 710)	1 239 978 (1 214 708 to 1 265 247)	-3.9 (-6.2 to -1.7)	-5.5 (-8.0 to -2.9)	-9.2 (-11.5 to -6.8)
Eastern Mediterranean Region	573 168 (557 611 to 588 725)	722 549 (702 898 to 742 201)	833 643 (808 225 to 859 061)	26.1 (21.3 to 31.0)	15.4 (10.7 to 20.1)	45.4 (39.6 to 51.7)	325 365 (312 994 to 337 736)	410 344 (394 716 to 425 972)	471 885 (451 782 to 491 988)	26.1 (19.6 to 33.0)	15.0 (8.5 to 21.6)	45.0 (36.9 to 53.6)	247 803 (238 370 to 257 236)	312 205 (300 291 to 324 120)	361 758 (346 203 to 377 313)	26.0 (19.4 to 33.0)	15.9 (9.4 to 22.7)	46.0 (37.9 to 54.3)
Western Pacific Region	1 097 552 (1 040 616 to 1 154 488)	1 919 192 (1 810 143 to 2 028 241)	2 390 467 (2 234 783 to 2 546 152)	74.9 (61.9 to 88.3)	24.6 (14.2 to 36.0)	117.8 (100.2 to 136.4)	558 580 (518 335 to 598 826)	946 060 (871 710 to 1 020 410)	1 179 459 (1 073 590 to 1 285 327)	69.4 (52.2 to 88.5)	24.7 (10.5 to 40.7)	111.2 (88.0 to 137.0)	538 972 (498 697 to 579 247)	973 132 (893 359 to 1 052 905)	1 211 009 (1 096 862 to 1 325 156)	80.6 (61.9 to 101.1)	24.4 (9.4 to 41.3)	124.7 (98.3 to 152.5)

UR, uncertainty range.
Source: WHO Global Health Estimates

ANNEX 4.

NUMBER OF DEATHS FROM STROKE IN 2000, 2010 AND 2016, AND MEAN PERCENTAGE CHANGE FOR 2000–2010, 2010–2016 AND 2000–2016, BY WHO REGION AND SEX, 183 COUNTRIES

	Both sexes						Males						Females					
	No. deaths (95% UR)			Percent change (95% UR)			No. deaths (95% UR)			Percent change (95% UR)			No. deaths (95% UR)			Percent change (95% UR)		
WHO region	2000	2010	2016	2000-2010	2010-2016	2000-2016	2000	2010	2016	2000-2010	2010-2016	2000-2016	2000	2010	2016	2000-2010	2010-2016	2000-2016
African Region	288 864 (281 103 to 296 626)	325 119 (316 587 to 333 652)	365 790 (354 413 to 377 167)	12.6 (8.2 to 17.0)	12.5 (8.0 to 17.3)	26.6 (21.4 to 31.9)	124 422 (119 801 to 129 043)	139 376 (134 237 to 144 515)	158 704 (151 713 to 165 696)	12.0 (6.4 to 18.2)	13.9 (7.4 to 20.5)	27.6 (20.5 to 35.0)	164 442 (158 206 to 170 678)	185 743 (178 932 to 192 555)	207 086 (198 111 to 216 061)	13.0 (7.2 to 19.1)	11.5 (5.4 to 18.0)	25.9 (18.9 to 33.3)
Region of the Americas	436 764 (429 104 to 444 424)	408 744 (402 120 to 415 369)	434 666 (426 750 to 442 582)	-6.4 (-8.6 to -4.2)	6.3 (3.8 to 9.0)	-0.5 (-2.9 to 2.1)	196 897 (192 505 to 201 289)	188 842 (184 849 to 192 835)	203 926 (199 119 to 208 733)	-4.1 (-7.0 to -1.1)	8.0 (4.6 to 11.5)	3.6 (0.3 to 7.0)	239 868 (233 592 to 246 144)	219 903 (214 617 to 225 188)	230 740 (224 451 to 237 029)	-8.3 (-11.5 to -5.0)	4.9 (1.3 to 8.8)	-3.8 (-7.4 to -0.1)
South-East Asia Region	952 324 (907 457 to 997 190)	1 132 818 (1 082 432 to 1 183 205)	1 247 157 (1 185 283 to 1 309 032)	19.0 (11.5 to 26.9)	10.1 (2.8 to 17.4)	31.0 (22.5 to 40.3)	490 775 (459 137 to 522 413)	598 346 (562 147 to 634 544)	675 665 (629 650 to 721 679)	21.9 (11.7 to 33.4)	12.9 (3.1 to 23.6)	37.7 (24.9 to 50.8)	461 548 (429 736 to 493 360)	534 473 (499 423 to 569 523)	571 493 (530 127 to 612 858)	15.8 (5.1 to 27.3)	6.9 (-3.3 to 18.0)	23.8 (12.1 to 36.8)
European Region	1 329 767 (1 312 118 to 1347416)	1 109 316 (1 094 351 to 1 124 282)	985 952 (970 561 to 1 001 343)	-16.6 (-18.1 to -15.0)	-11.1 (-13.0 to -9.3)	-25.9 (-27.4 to -24.4)	524 747 (515 775 to 533 718)	455 507 (447 780 to 463 234)	410 060 (402 234 to 417 887)	-13.2 (-15.2 to -11.1)	-10.0 (-12.2 to -7.7)	-21.9 (-23.8 to -19.8)	805 020 (789 822 to 820 219)	653 809 (640 993 to 666 625)	575 892 (562 639 to 589 144)	-18.8 (-21.0 to -16.6)	-11.9 (-14.5 to -9.2)	-28.5 (-30.6 to -26.3)
Eastern Mediterranean Region	245 021 (237 111 to 252 930)	293 154 (283 716 to 302 592)	323 368 (311 564 to 335 171)	19.6 (14.4 to 25.3)	10.3 (5.1 to 15.9)	32.0 (25.8 to 38.5)	122 734 (116 903 to 128 565)	144 991 (138 358 to 151 623)	159 750 (151 514 to 167 985)	18.1 (10.7 to 26.2)	10.2 (2.9 to 18.2)	30.2 (21.3 to 39.6)	122 287 (116 941 to 127 632)	148 163 (141 448 to 154 878)	163 618 (155 162 to 172 074)	21.2 (13.7 to 29.1)	10.4 (3.1 to 18.3)	33.8 (25.0 to 43.3)
Western Pacific Region	1 869 988 (1 755 720 to 1 984 256)	2 134 255 (2 005 039 to 2 263 470)	2 390 356 (2 227 107 to 2 553 604)	14.1 (4.7 to 24.5)	12.0 (2.4 to 22.8)	27.8 (16.7 to 39.8)	965 226 (879 782 to 1 050 669)	1 115 956 (1 018 178 to 1 213 734)	1 266 693 (1 142 081 to 1 391 306)	15.6 (2.2 to 30.8)	13.5 (-0.4 to 29.5)	31.2 (14.7 to 49.5)	904 762 (828 891 to 980 634)	1 018 299 (933 823 to 1 102 774)	1 123 662 (1 018 202 to 1 229 123)	12.6 (0.1 to 26.8)	10.4 (-2.6 to 25.0)	24.2 (9.2 to 41.2)

UR, uncertainty range.
Source: WHO Global Health Estimates

ANNEX 5.

PROPORTION OF POPULATION EXPOSED TO LONG WORKING HOURS (≥ 55 HOURS PER WEEK) FOR 2000, 2010 AND 2016, AND MEAN PERCENTAGE CHANGE FOR 2000–2010, 2010–2016 AND 2000–2016, BY WHO REGION AND SEX, 183 COUNTRIES

	Both sexes						Males						Females					
	No. deaths (95% UR)			Percent change (95% UR)			No. deaths (95% UR)			Percent change (95% UR)			No. deaths (95% UR)			Percent change (95% UR)		
WHO region	2000	2010	2016	2000–2010	2010–2016	2000–2016	2000	2010	2016	2000–2010	2010–2016	2000–2016	2000	2010	2016	2000–2010	2010–2016	2010–2016
African Region	17.3 (16.9 to 17.7)	13.5 (13.3 to 13.6)	11.4 (11.2 to 11.5)	−22.3 (−24.2 to −20.4)	−15.6 (−17.3 to −13.9)	−34.4 (−36.1 to −32.6)	21.5 (20.9 to 22.1)	17.4 (17.1 to 17.7)	15.3 (15.0 to 15.6)	−18.9 (−21.4 to −16.2)	−12.4 (−14.6 to −10.1)	−28.9 (−31.3 to −26.5)	13.3 (12.8 to 13.7)	9.6 (9.4 to 9.8)	7.5 (7.3 to 7.7)	−27.7 (−30.4 to −24.7)	−21.5 (−24.1 to −18.8)	−43.2 (−45.6 to −40.8)
Region of the Americas	8.8 (8.7 to 8.9)	7.3 (7.2 to 7.4)	6.4 (6.3 to 6.6)	−17.2 (−19.0 to −15.4)	−12.1 (−14.9 to −9.2)	−27.2 (−29.3 to −25.1)	13.2 (13.1 to 13.4)	10.8 (10.6 to 11.0)	9.4 (9.1 to 9.7)	−18.4 (−20.2 to −16.5)	−12.9 (−16.0 to −9.8)	−28.9 (−31.1 to −26.7)	4.6 (4.5 to 4.8)	4.0 (3.8 to 4.1)	3.6 (3.4 to 3.8)	−14.3 (−18.5 to −10.0)	−9.8 (−15.9 to −3.6)	−22.7 (−27.3 to −17.9)
South-East Asia Region	11.5 (10.5 to 12.5)	11.7 (11.0 to 12.3)	11.7 (10.8 to 12.5)	1.4 (−8.6 to 12.8)	0.1 (−9.2 to 10.0)	1.5 (−9.5 to 13.9)	17.9 (16.2 to 19.6)	18.2 (17.0 to 19.3)	18.1 (16.5 to 19.6)	1.5 (−9.2 to 14.1)	−0.4 (−10.8 to 10.7)	1.1 (−11.0 to 14.8)	4.9 (3.9 to 5.9)	4.9 (4.2 to 5.6)	5.0 (4.2 to 5.8)	0.8 (−21.2 to 31.3)	2.2 (−18.0 to 26.8)	3.0 (−19.7 to 35.1)
European Region	4.6 (4.6 to 4.6)	3.9 (3.9 to 4.0)	3.5 (3.5 to 3.6)	−14.8 (−16.1 to −13.6)	−9.8 (−11.4 to −8.1)	−23.1 (−24.5 to −21.8)	7.5 (7.4 to 7.5)	6.2 (6.1 to 6.2)	5.4 (5.3 to 5.5)	−17.5 (−18.9 to −15.9)	−11.9 (−13.9 to −9.9)	−27.3 (−28.8 to −25.7)	2.0 (2.0 to 2.0)	1.9 (1.8 to 1.9)	1.8 (1.8 to 1.9)	−6.5 (−8.8 to −4.1)	−3.5 (−6.3 to −0.7)	−9.8 (−12.3 to −7.3)
Eastern Mediterranean Region	9.8 (9.6 to 10.0)	10.7 (10.5 to 10.9)	11.4 (11.1 to 11.6)	9.4 (5.9 to 13.0)	5.9 (2.8 to −9.2)	15.9 (12.0 to 20.0)	17.4 (17.0 to 17.9)	19.5 (19.1 to 20.0)	21.0 (20.5 to 21.5)	12.1 (8.4 to 16.0)	7.5 (4.0 to 11.0)	20.4 (16.2 to 24.8)	1.8 (1.7 to 1.9)	1.3 (1.3 to 1.4)	1.0 (1.0 to 1.1)	−26.4 (−32.5 to −19.5)	−21.3 (−27.3 to −15.0)	−42.1 (−47.3 to −36.3)
Western Pacific Region	3.9 (3.5 to 4.4)	5.9 (5.5 to 6.4)	8.4 (7.8 to 9.0)	51.7 (32.1 to 74.9)	42.0 (27.8 to 57.9)	115.4 (88.7 to 148.3)	4.5 (3.9 to 5.2)	7.4 (6.6 to 8.1)	11.1 (10.1 to 12.1)	62.8 (37.6 to 95.8)	50.6 (32.1 to 72.0)	145.2 (107.9 to 192.5)	3.3 (2.6 to 3.9)	4.4 (3.9 to 5.0)	5.7 (5.0 to 6.3)	36.0 (8.6 to 74.9)	27.6 (7.7 to 51.7)	73.5 (39.9 to 120.4)

UR, uncertainty range.

ANNEX 6.

POPULATION ATTRIBUTABLE FRACTIONS FOR ISCHAEMIC HEART DISEASE DEATHS AND DALYS ATTRIBUTABLE TO EXPOSURE TO LONG WORKING HOURS (≥ 55 HOURS PER WEEK) FOR 2000, 2010 AND 2016, AND MEAN PERCENTAGE CHANGE FOR 2000–2010, 2010–2016 AND 2000–2016, BY WHO REGION AND SEX , 183 COUNTRIES

	Both sexes						Males						Females					
	PAF (%) (95% UR)			Percent change (95% UR)			PAF (%) (95% UR)			Percent change (95% UR)			PAF (%) (95% UR)			Percent change (95% UR)		
WHO region	2000	2010	2016	2000–2010	2010–2016	2000–2016	2000	2010	2016	2000–2010	2010–2016	2000–2016	2000	2010	2016	2000–2010	2010–2016	2000–2016
Deaths																		
African Region	3.4 (3.2 to 3.6)	3.3 (3.1 to 3.6)	3.3 (3.1 to 3.5)	−2.4 (−10.8 to 6.7)	−0.6 (−9.7 to 9.4)	2.9 (−11.7 to 6.9)	4.6 (4.2 to 4.9)	4.6 (4.2 to 4.9)	4.6 (4.2 to 5.0)	0.0 (−11.0 to 12.6)	0.6 (−11.0 to 13.5)	0.6 (−11.3 to 13.7)	2.3 (2.1 to 2.5)	2.1 (1.9 to 2.3)	2.1 (1.8 to 2.3)	−5.8 (−17.8 to 8.4)	−3.5 (−16.9 to 11.8)	−9.1 (−21.6 to 5.0)
Region of the Americas	2.2 (2.0 to 2.3)	2.3 (2.1 to 2.5)	2.3 (2.1 to 2.5)	6.0 (−5.8 to 18.9)	0.5 (−10.4 to 12.4)	6.4 (5.2 to 19.5)	3.6 (3.3 to 4.0)	3.7 (3.4 to 4.1)	3.6 (3.3 to 3.9)	1.7 (−11.2 to 16.0)	−2.9 (−14.8 to 10.4)	−1.2 (−13.6 to 13.4)	0.6 (0.5 to 0.7)	0.7 (0.6 to 0.7)	0.7 (0.6 to 0.8)	10.5 (−3.6 to 26.9)	4.8 (−8.0 to 19.3)	15.8 (1.2 to 33.1)
South-East Asia Region	7.2 (6.2 to 8.4)	7.2 (6.1 to 8.3)	7.2 (6.0 to 8.4)	−0.2 (−19.9 to 24.5)	0.7 (−20.4 to 24.9)	−0.9 (−20.9 to 23.7)	9.3 (7.5 to 11.2)	9.3 (7.6 to 11.2)	9.2 (7.4 to 11.1)	0.0 (−24.7 to 33.2)	−1.0 (−25.8 to 32.0)	−1.0 (−26.2 to 32.8)	4.4 (3.5 to 5.3)	4.3 (3.4 to 5.1)	4.1 (3.3 to 5.0)	−2.4 (−26.5 to 29.9)	−3.9 (−28.9 to 28.7)	−6.2 (−30.7 to 26.1)
European Region	1.8 (1.6 to 1.9)	1.6 (1.4 to 1.7)	1.4 (1.3 to 1.5)	−11.5 (−21.0 to −1.2)	−8.2 (−18.0 to 2.5)	18.7 (−27.1 to −9.6)	3.1 (2.8 to 3.4)	2.7 (2.4 to 2.9)	2.5 (2.3 to 2.7)	−12.6 (−23.6 to −0.3)	−8.0 (−19.5 to 4.9)	−19.6 (−29.4 to −8.4)	0.6 (0.5 to 0.6)	0.6 (0.5 to 0.6)	0.5 (0.5 to 0.6)	−6.1 (−20.5 to 0.4)	−7.9 (−21.7 to 8.9)	−13.5 (−26.0 to 1.4)
Eastern Mediterranean Region	6.0 (5.5 to 6.5)	5.7 (5.2 to 6.2)	5.5 (5.0 to 6.1)	−5.1 (−16.5 to 7.8)	−2.5 (−14.9 to 11.4)	7.5 (−19.2 to 5.4)	8.4 (7.5 to 9.3)	8.1 (7.2 to 9.0)	7.9 (7.0 to 8.9)	−3.6 (−17.9 to 12.9)	−1.7 (−16.6 to 15.9)	−5.3 (−19.7 to 11.4)	2.9 (2.5 to 3.2)	2.6 (2.3 to 2.9)	2.4 (2.1 to 2.8)	−10.7 (−24.7 to 5.5)	−4.8 (−20.4 to 13.5)	−15.0 (−28.6 to 0.7)
Western Pacific Region	3.3 (2.8 to 3.8)	2.8 (2.4 to 3.3)	2.7 (2.3 to 3.2)	−14.5 (−30.9 to 5.6)	−2.9 (−23.2 to 22.9)	−17.0 (−33.9 to 3.2)	4.4 (3.6 to 5.2)	3.7 (3.0 to 4.5)	3.6 (2.8 to 4.4)	−14.6 (−35.6 to 13.8)	−3.8 (−30.4 to 30.8)	−17.8 (−39.8 to 9.8)	2.2 (1.7 to 2.6)	1.9 (1.5 to 2.4)	1.9 (1.4 to 2.4)	−11.5 (−35.7 to 20.1)	−1.4 (−30.9 to 39.1)	−12.7 (−38.4 to 20.2)
DALYs																		
African Region	3.8 (3.6 to 4.0)	3.8 (3.6 to 4.0)	3.9 (3.7 to 4.1)	0.1 (−6.7 to 7.4)	1.0 (−5.7 to 8.3)	1.2 (−5.5 to 8.3)	5.0 (4.7 to 5.3)	5.1 (4.8 to 5.4)	5.1 (4.8 to 5.5)	1.6 (−7.0 to 11.1)	1.6 (−6.7 to 10.9)	3.3 (−5.2 to 12.7)	2.4 (2.3 to 2.6)	2.4 (2.2 to 2.5)	2.3 (2.2 to 2.5)	−2.3 (−11.8 to 8.3)	−1.3 (−11.1 to 9.3)	−3.6 (−12.8 to 6.9)
Region of the Americas	3.3 (3.0 to 3.6)	3.4 (3.2 to 3.7)	3.4 (3.1 to 3.7)	4.8 (−6.2 to 17.6)	−1.4 (−11.4 to 9.9)	3.4 (−7.9 to 15.7)	4.9 (4.4 to 5.3)	5.0 (4.5 to 5.4)	4.8 (4.4 to 5.2)	2.1 (−10.3 to 16.6)	−3.3 (−14.7 to 9.6)	−1.2 (−13.4 to 12.5)	1.0 (0.9 to 1.1)	1.1 (1.0 to 1.2)	1.1 (1.0 to 1.2)	7.2 (−5.3 to 21.9)	1.3 (−10.1 to 14.1)	8.5 (−4.2 to 23.2)
South-East Asia Region	8.3 (7.2 to 9.4)	8.4 (7.3 to 9.6)	8.5 (7.3 to 9.7)	1.6 (−15.8 to 23.0)	0.6 (−16.9 to 21.7)	2.2 (−15.9 to 23.6)	10.1 (8.4 to 11.8)	10.2 (8.5 to 11.9)	10.2 (8.4 to 12.0)	0.9 (−20.6 to 27.8)	0.0 (−22.1 to 28.0)	0.9 (−21.5 to 29.3)	5.5 (4.5 to 6.4)	5.6 (4.6 to 6.6)	5.5 (4.5 to 6.5)	1.5 (−20.8 to 29.7)	−1.2 (−22.9 to 27.4)	0.3 (−22.1 to 28.4)
European Region	2.6 (2.4 to 2.8)	2.4 (2.2 to 2.6)	2.3 (2.1 to 2.5)	−8.9 (−18.7 to 1.7)	−4.1 (−13.7 to 6.8)	−12.7 (−21.4 to −2.4)	3.9 (3.5 to 4.2)	3.5 (3.2 to 3.8)	3.4 (3.1 to 3.7)	−9.2 (−20.0 to 3.3)	−4.2 (−15.3 to 8.5)	−13.0 (−23.3 to −1.3)	0.9 (0.8 to 1.0)	0.9 (0.8 to 1.0)	0.8 (0.8 to 0.9)	−4.1 (−17.2 to 11.3)	−3.3 (−16.2 to 12.1)	−7.2 (−19.4 to 7.1)
Eastern Mediterranean Region	6.9 (6.4 to 7.4)	6.8 (6.3 to 7.4)	6.9 (6.3 to 7.4)	−0.7 (−10.8 to 10.5)	0.2 (−10.7 to 12.5)	−0.5 (−10.9 to 10.9)	9.1 (8.3 to 9.9)	9.1 (8.2 to 10.0)	9.2 (8.3 to 10.0)	−0.1 (−12.7 to 13.8)	0.6 (−12.7 to 15.7)	0.6 (−12.1 to 15.0)	3.6 (3.2 to 3.9)	3.4 (3.0 to 3.7)	3.3 (3.0 to 3.7)	−5.1 (−17.6 to 9.0)	−1.5 (−15.5 to 14.5)	−6.6 (−19.5 to 7.9)
Western Pacific Region	4.8 (4.2 to 5.3)	4.3 (3.8 to 4.9)	4.3 (3.7 to 4.9)	−9.4 (−24.5 to 7.6)	−1.3 (−19.2 to 20.2)	−10.6 (−25.8 to 7.6)	6.0 (5.1 to 6.9)	5.5 (4.6 to 6.4)	5.4 (4.4 to 6.4)	−8.6 (−27.7 to 15.1)	−1.7 (−23.7 to 25.5)	−10.1 (−30.1 to 13.6)	3.3 (2.7 to 3.8)	3.0 (2.4 to 3.6)	3.0 (2.4 to 3.6)	−8.2 (−30.1 to 18.4)	−0.1 (−24.9 to 33.5)	−8.3 (−30.2 to 19.8)

DALYs, disability-adjusted life years; PAF, population attributable fraction; UR, uncertainty range.

ANNEX 7.

POPULATION ATTRIBUTABLE FRACTIONS FOR STROKE DEATHS AND DALYS ATTRIBUTABLE TO EXPOSURE TO LONG WORKING HOURS (≥ 55 HOURS PER WEEK) FOR 2000, 2010 AND 2016, AND MEAN PERCENTAGE CHANGE FOR 2000–2010, 2010–2016 AND 2000–2016, BY WHO REGION AND SEX , 183 COUNTRIES

	Both sexes						Males						Females					
	PAF (%) (95% UR)			Percent change (95% UR)			PAF (%) (95% UR)			Percent change (95% UR)			PAF (%) (95% UR)			Percent change (95% UR)		
WHO region	2000	2010	2016	2000–2010	2010–2016	2000–2016	2000	2010	2016	2000–2010	2010–2016	2000–2016	2000	2010	2016	2000–2010	2010–2016	2000–2016
Deaths																		
African Region	6.2 (5.9 to 6.5)	6.3 (5.9 to 6.6)	6.3 (5.9 to 6.7)	0.9 (−6.5 to 9.0)	0.6 (−7.4 to 8.9)	1.5 (6.4 to 10.2)	8.6 (8.0 to 9.3)	8.8 (8.2 to 9.5)	9.0 (8.3 to 9.7)	2.6 (−7.7 to 13.9)	1.4 (−9.4 to 13.1)	4.0 (−7.1 to 16.1)	4.4 (4.0 to 4.7)	4.3 (4.0 to 4.7)	4.2 (3.9 to 4.6)	−1.3 (−12.0 to 10.6)	−1.7 (−13.2 to 10.9)	−3.0 (−14.4 to 9.6)
Region of the Americas	4.5 (4.2 to 4.8)	4.4 (4.1 to 4.7)	4.2 (3.9 to 4.5)	−2.7 (−11.7 to 7.1)	−3.6 (−12.0 to 5.7)	6.2 (−14.7 to 3.1)	8.0 (7.3 to 8.6)	7.5 (6.9 to 8.1)	7.2 (6.6 to 7.7)	−5.2 (−15.4 to 6.4)	−5.0 (−14.8 to 6.3)	−9.9 (−19.7 to 1.3)	1.6 (1.5 to 1.8)	1.6 (1.5 to 1.8)	1.6 (1.5 to 1.7)	−0.1 (−11.5 to 12.5)	−2.6 (−13.1 to 9.2)	−2.7 (−13.6 to 9.5)
South-East Asia Region	12.6 (11.1 to 14.1)	12.7 (11.3 to 14.1)	12.8 (11.3 to 14.3)	0.7 (−14.7 to 18.9)	0.6 (−14.5 to 18.3)	1.3 (−14.9 to 20.4)	17.0 (14.4 to 19.8)	17.1 (14.7 to 19.6)	17.1 (14.5 to 19.8)	0.5 (−18.7 to 24.4)	−0.2 (−19.5 to 23.2)	0.3 (−19.8 to 25.7)	7.9 (6.5 to 9.3)	7.7 (6.4 to 9.1)	7.6 (6.4 to 9.0)	−2.1 (−24.2 to 26.3)	−1.0 (−23.0 to 25.8)	−3.0 (−24.0 to 24.5)
European Region	2.8 (2.6 to 3.0)	2.7 (2.5 to 2.9)	2.5 (2.3 to 2.6)	−5.2 (−14.7 to 5.3)	−7.5 (−16.1 to 1.9)	12.4 (−20.9 to −2.5)	5.2 (4.7 to 5.8)	4.9 (4.5 to 5.3)	4.5 (4.1 to 4.9)	−7.1 (−19.0 to 6.4)	−7.9 (−18.5 to 3.8)	−14.5 (−25.0 to −2.2)	1.2 (1.1 to 1.3)	1.1 (1.0 to 1.2)	1.0 (0.9 to 1.1)	−8.0 (−20.3 to 6.3)	−9.2 (−20.3 to 3.7)	−16.5 (−27.2 to −3.4)
Eastern Mediterranean Region	10.4 (9.5 to 11.4)	9.8 (8.9 to 10.6)	9.5 (8.6 to 10.4)	−6.2 (−17.1 to 6.1)	2.3 (−14.1 to 11.1)	−8.4 (−19.7 to 4.5)	15.1 (13.4 to 16.9)	14.5 (12.9 to 16.2)	14.2 (12.6 to 15.9)	−4.4 (−18.4 to 12.7)	−1.8 (−16.9 to 15.0)	−6.1 (−20.6 to 11.1)	5.7 (5.0 to 6.3)	5.1 (4.5 to 5.8)	5.0 (4.3 to 5.6)	−9.1 (−23.6 to 7.5)	−3.5 (−19.7 to 16.0)	−12.3 (−26.8 to 4.5)
Western Pacific Region	6.1 (5.2 to 7.2)	6.0 (5.0 to 6.9)	6.0 (5.0 to 7.1)	−3.1 (−23.3 to 22.3)	0.7 (−20.8 to 27.0)	−2.4 (−24.0 to 24.1)	7.6 (6.0 to 9.4)	7.2 (5.7 to 8.8)	7.2 (5.6 to 9.0)	−5.4 (−31.2 to 30.5)	−0.6 (−29.2 to 38.6)	−6.0 (−33.0 to 30.6)	4.5 (3.6 to 5.6)	4.6 (3.6 to 5.6)	4.7 (3.6 to 5.8)	0.3 (−27.5 to 37.6)	2.1 (−27.5 to 41.6)	2.4 (−26.9 to 42.6)
DALYs																		
African Region	6.8 (6.5 to 7.1)	7.0 (6.7 to 7.2)	7.1 (6.8 to 7.3)	2.6 (−2.7 to 8.1)	1.3 (−4.0 to 6.9)	4.0 (−1.5 to 9.8)	9.3 (8.8 to 9.7)	9.6 (9.1 to 10.0)	9.8 (9.3 to 10.2)	3.3 (−3.7 to 10.9)	2.0 (−5.0 to 9.3)	5.4 (−1.9 to 13.2)	4.7 (4.5 to 5.0)	4.8 (4.5 to 5.1)	4.8 (4.5 to 5.0)	1.4 (−6.1 to 9.3)	−0.5 (−8.3 to 7.9)	0.9 (−7.0 to 9.5)
Region of the Americas	6.2 (5.8 to 6.6)	5.9 (5.6 to 6.3)	5.8 (5.4 to 6.1)	−3.9 (−12.0 to 4.8)	−2.9 (−10.6 to 5.5)	−6.7 (−14.3 to 1.9)	9.9 (9.1 to 10.7)	9.4 (8.8 to 10.1)	9.1 (8.4 to 9.7)	−4.8 (−14.4 to 6.2)	−4.0 (−13.2 to 6.3)	−8.6 (−17.7 to 1.7)	2.5 (2.3 to 2.7)	2.4 (2.3 to 2.6)	2.4 (2.2 to 2.5)	−3.2 (−13.0 to 7.8)	−2.7 (−12.0 to 7.5)	−5.9 (−15.0 to 4.1)
South-East Asia Region	14.4 (13.1 to 15.7)	14.7 (13.5 to 16.0)	14.9 (13.6 to 16.2)	2.1 (−10.2 to 15.9)	1.2 (−10.5 to 14.6)	3.3 (−9.2 to 17.4)	18.1 (16.0 to 20.3)	18.4 (16.3 to 20.4)	18.4 (16.4 to 20.5)	1.3 (−13.9 to 19.2)	0.5 (−14.5 to 18.2)	1.8 (−13.8 to 19.2)	10.1 (8.7 to 11.5)	10.2 (8.8 to 11.5)	10.2 (8.9 to 11.5)	0.9 (−17.0 to 23.0)	0.1 (−17.1 to 19.9)	1.1 (−16.7 to 21.5)
European Region	4.1 (3.8 to 4.4)	4.0 (3.7 to 4.2)	3.8 (3.6 to 4.1)	−2.6 (−11.8 to 7.7)	−3.8 (−12.2 to 5.6)	−6.3 (−14.9 to 3.3)	6.7 (6.0 to 7.3)	6.4 (5.8 to 6.9)	6.1 (5.6 to 6.5)	−4.5 (−15.4 to 8.4)	−4.5 (−15.0 to 7.2)	−8.8 (−19.3 to 3.1)	1.9 (1.7 to 2.1)	1.8 (1.6 to 1.9)	1.7 (1.6 to 1.9)	−4.0 (−15.9 to 9.7)	−3.3 (−14.3 to 8.9)	−7.2 (−18.4 to 6.1)
Eastern Mediterranean Region	11.7 (10.9 to 12.5)	11.5 (10.7 to 12.2)	11.5 (10.7 to 12.2)	−2.0 (−10.5 to 7.4)	0.2 (−8.7 to 9.8)	−1.8 (−10.5 to 8.0)	16.3 (14.9 to 17.6)	16.2 (14.9 to 17.6)	16.3 (14.9 to 17.7)	−0.5 (−11.8 to 12.0)	0.6 (−10.7 to 13.6)	0.1 (−11.0 to 12.9)	6.9 (6.3 to 7.6)	6.6 (6.0 to 7.2)	6.6 (6.0 to 7.2)	−4.6 (−16.4 to 8.6)	−0.8 (−12.8 to 13.3)	−5.4 (−16.9 to 7.6)
Western Pacific Region	8.6 (7.5 to 9.6)	8.5 (7.4 to 9.5)	8.6 (7.4 to 9.8)	−1.1 (−16.9 to 17.9)	1.3 (−16.5 to 22.0)	0.1 (−17.1 to 20.6)	10.4 (8.6 to 12.2)	10.1 (8.4 to 11.8)	10.1 (8.3 to 12.0)	−2.4 (−23.5 to 24.3)	0.3 (−22.2 to 29.0)	−2.0 (−24.4 to 26.3)	6.5 (5.3 to 7.7)	6.6 (5.3 to 7.8)	6.7 (5.4 to 8.1)	1.0 (−21.8 to 31.0)	2.6 (−21.9 to 34.9)	3.6 (−20.8 to 35.0)

DALYs, disability-adjusted life years; PAF, population attributable fraction; UR, uncertainty range.

ANNEX 8.

RESULTS FROM SENSITIVITY ANALYSES FOR DEATHS AND DALYS ATTRIBUTABLE TO EXPOSURE TO LONG WORKING HOURS (95% UNCERTAINTY RANGES), 183 COUNTRIES, FOR THE YEAR 2016

Sensitivity analysis	Ischaemic heart disease		Stroke	
	No. deaths (95% UR)	No. DALYs (millions) (95% UR)	No. deaths (95% UR)	No. DALYs (millions) (95% UR)
Main analysis	346 753 (319 658 to 373 848)	10.66 (9.87 to 11.44)	398 441 (369 826 to 427 056)	12.60 (11.82 to 13.39)
Reduced lag time to 8 years (2003–2012)	324 346 (298 508 to 350 185)	10.22 (9.46 to 10.97)	368 317 (342 619 to 394 015)	11.95 (11.22 to 12.68)
Increased lag time to 12 years (1999–2008)	376 814 (347 892 to 405 735)	11.18 (10.37 to 11.99)	439 169 (406 739 to 471 600)	13.43 (12.57 to 14.28)
Reduced time window of exposure to 8 years (2002–2009)	307 329 (282 867 to 331 792)	9.51 (8.80 to 10.22)	351 911 (326 800 to 377 022)	11.21 (10.51 to 11.91)
Increased time window of exposure to 12 years (2000–2011)	386 339 (356 810 to 415 868)	11.713 (10.88 to 12.54)	446 171 (414 058 to 478 284)	13.93 (13.07 to 14.80)
Assigned most common exposure category over time window (restricted to years in labour market activity)	179 360 (166 755 to 191 966)	5.01 (4.70 to 5.31)	219 517 (203 999 to 235 034)	6.47 (6.06 to 6.88)

UR, uncertainty range.

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