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Estimating the global incidence of traumatic brain injury

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OBJECTIVE Traumatic brain injury (TBI)—the "silent epidemic"—contributes to worldwide death and disability more than any other traumatic insult. Yet, TBI incidence and distribution across regions and socioeconomic divides remain unknown. In an effort to promote advocacy, understanding, and targeted intervention, the authors sought to quantify the case burden of TBI across World Health Organization (WHO) regions and World Bank (WB) income groups.

METHODS Open-source epidemiological data on road traffic injuries (RTIs) were used to model the incidence of TBI using literature-derived ratios. First, a systematic review on the proportion of RTIs resulting in TBI was conducted, and a meta-analysis of study-derived proportions was performed. Next, a separate systematic review identified primary source studies describing mechanisms of injury contributing to TBI, and an additional meta-analysis yielded a proportion of TBI that is secondary to the mechanism of RTI. Then, the incidence of RTI as published by the Global Burden of Disease Study 2015 was applied to these two ratios to generate the incidence and estimated case volume of TBI for each WHO region and WB income group.

RESULTS Relevant articles and registries were identified via systematic review; study quality was higher in the high-income countries (HICs) than in the low- and middle-income countries (LMICs). Sixty-nine million (95% CI 64–74 million) individuals worldwide are estimated to sustain a TBI each year. The proportion of TBIs resulting from road traffic collisions was greatest in Africa and Southeast Asia (both 56%) and lowest in North America (25%). The incidence of RTI was similar in Southeast Asia (1.5% of the population per year) and Europe (1.2%). The overall incidence of TBI per 100,000 people was greatest in North America (1299 cases, 95% CI 650–1947) and Europe (1012 cases, 95% CI 911–1113) and least in Africa (801 cases, 95% CI 732–871) and the Eastern Mediterranean (897 cases, 95% CI 771–1023). The LMICs experience nearly 3 times more cases of TBI proportionally than HICs.

CONCLUSIONS Sixty-nine million (95% CI 64–74 million) individuals are estimated to suffer TBI from all causes each year, with the Southeast Asian and Western Pacific regions experiencing the greatest overall burden of disease. Head injury following road traffic collision is more common in LMICs, and the proportion of TBIs secondary to road traffic col-

ABBREVIATIONS AFR = African Region; AMR-L = Region of the Americas–Latin America; AMR-US/Can = Region of the Americas–United States and Canada; EMR = Eastern Mediterranean Region; EUR = European Region; GBD = Global Burden of Disease; GBD 2015 = GBD Study 2015; HI = head injury; HIC = high-income country; IHME = Institute for Health Metrics and Evaluation; LIC = low-income country; LMICs = low- and middle-income countries; MIC = middle-income country; MOI = mechanism of injury; P(RTI) = probability that a member of the population will sustain an RTI annually; P(RTI|TBI) = probability that TBI is secondary to RTI; P(TBI|RTI) = probability that an RTI will lead to a TBI; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RTI = road traffic injury; RTI_{TOTAL} = total number of RTIs in a country annually; $RTI \cap TBI$ = intersection of RTI_{TOTAL} and TBI_{TOTAL}; SEAR = Southeast Asian Region; TBI = traumatic brain injury; TBI_{TOTAL} = total number of TBI cases in a region annually; WB = World Bank; WHO = World Health Organization; WPR = Western Pacific region; $\cap$ = intersection of 2 events; | = conditional on 1 event.

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lision is likewise greatest in these countries. Meanwhile, the estimated incidence of TBI is highest in regions with higher-quality data, specifically in North America and Europe.

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KEYWORDS epidemiology; global; incidence; prevalence; traumatic brain injury; volume; worldwide

Traumatic brain injury (TBI), often referred to as the "silent epidemic,"[208,253] remains a growing public health concern and represents the greatest contributor to death and disability globally among all trauma-related injuries.[206] Previous studies from the United States and New Zealand have estimated approximately 500–800 new cases of TBI per 100,000 people each year.[83,209] However, estimates of the TBI burden from low- and middle-income countries (LMICs) are scarce. A large survey-based study in 8 LMICs identified a lifetime prevalence of TBI from < 1% (China) to nearly 15% (Mexico and Venezuela) of the studied population, with most estimates approximating those from high-income countries (HICs).[134] Efforts to identify reliable epidemiological data on the incidence of and the disability and mortality from TBI in resource-poor settings are still needed.

Road traffic collisions are a significant source of TBI.[24,161,216,231,257,259] Using national registries, population-based literature, and statistical modeling, the Global Burden of Disease (GBD) Study 2015 (GBD 2015)[116] estimated the incidence of road traffic injuries (RTIs) in countries worldwide. By understanding the relationship between RTI and TBI, the incidence of TBI can be estimated. Because the interaction between RTI and TBI probably differs across regions of various populations, regulations, and infrastructures, a region-specific estimate of this relationship is essential to ensure accurate TBI estimates.

Beyond a fundamental disparity in quality data, a majority of the global population resides in LMICs, underscoring the need for reliable estimates of the TBI burden in resource-poor settings. In this comprehensive review, we provide estimates for TBI across geographic regions and income groups to deliver a global estimate of the volume and burden of TBI worldwide.

Methods

Overview

Incidence figures and overall disease volume were calculated from literature reviews, national registries, the GBD initiative, and the World Bank (WB). A similar methodology of estimating the frequency of traumatic injuries in LMICs has been described elsewhere.[4,149] A flowchart illustrates the contribution of relevant data sources and a stepwise progression in our methodology (Fig. 1). Initially, the incidences of RTI in different countries were obtained from the Institute for Health Metrics and Evaluation (IHME) GBD dataset. The incidences of RTIs were converted to population-based rates, that is, P(RTI), which represents the proportion of RTIs in a given population (that is, the probability that a person living in a country will sustain an RTI in a year; Fig. 1 II). By multiplying P(RTI) by the country population, we were able to obtain the RTI_{TOTAL}, representing the total number of RTIs in a country annually (Fig. 1 III):

$$RTI_{TOTAL} = P(RTI) \times \text{Population}.$$

We next sought to obtain the number of patients who had sustained a TBI or head injury (HI) from total RTIs, represented by $RTI \cap TBI$ (that is, the intersection of RTI_{TOTAL} and TBI_{TOTAL}; Fig. 1). To this end, we conducted a systematic review and meta-analysis of studies reporting the proportion of RTIs that had resulted in TBIs in different WHO regions and income groups. This proportion is expressed as a probability value, P(TBI|RTI), that is, the proportion sustaining TBI after RTI (Fig. 1 IV):

$$P(TBI|RTI) = \frac{RTI \cap TBI}{RTI_{TOTAL}}.$$

By multiplying the RTI_{TOTAL} by P(TBI|RTI), we obtained the total number of patients who sustained TBI after RTI (Fig. 1 V):

$$RTI \cap TBI = RTI_{TOTAL} \times P(TBI|RTI)$$

$$RTI \cap TBI = RTI_{TOTAL} \times \frac{RTI \cap TBI}{RTI_{TOTAL}}.$$

Understanding that traffic collisions are one of many TBI mechanisms of injury (MOIs), we sought the proportion of TBIs that are caused by RTIs. Accordingly, we conducted another systematic review and meta-analysis, this time to quantify the proportion of TBIs with RTI as the MOI in different WHO regions and income groups. This proportion is expressed as a probability value, P(RTI|TBI), that is, the proportion of TBIs secondary to RTIs (Fig. 1 VI):

$$P(RTI|TBI) = \frac{RTI \cap TBI}{TBI_{TOTAL}}.$$

Multiplying $RTI \cap TBI$ by the inverse of P(RTI|TBI) and thereby accounting for the non-RTI causes of TBI, we obtained the total number of TBI cases annually in different WHO regions and income groups (Fig. 1 VIII):

$$TBI_{TOTAL} = \frac{RTI \cap TBI}{P(RTI|TBI)}$$

$$TBI_{TOTAL} = \frac{RTI \cap TBI}{\frac{RTI \cap TBI}{TBI_{TOTAL}}}$$

$$TBI_{TOTAL} = RTI \cap TBI \times \frac{TBI_{TOTAL}}{RTI \cap TBI}.$$

A more detailed explanation of our methodology is outlined below.

Incidence of RTIs

To identify the proportion of the population that sus-

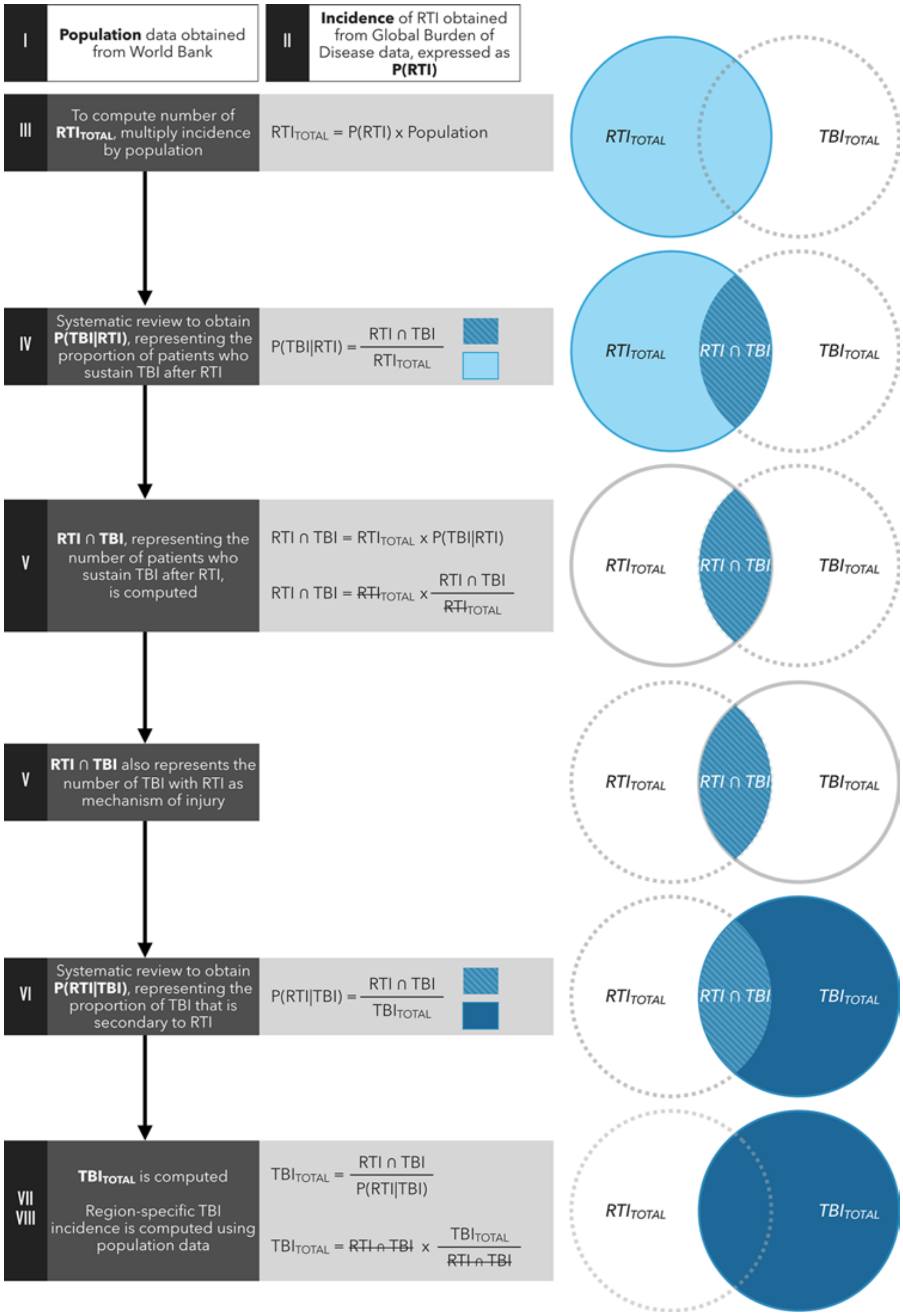

FIG. 1. Methodology flow diagram. P(RTI) = probability that a member of the population will sustain an RTI annually; P(RTI|TBI) = probability that a TBI is secondary to an RTI; P(TBI|RTI) = probability that an RTI will lead to TBI; RTI_{TOTAL} = total cases of RTI, with or without TBI; RTI∩TBI = intersection of RTIs and TBIs, thus representing either the number of RTIs that lead to TBI or the number of TBIs secondary to RTIs; TBI_{TOTAL} = total cases of TBI, whether the mechanism is an RTI or a non-RTI. Figure is available in color online only.

tains an RTI every year, we obtained and extracted relevant data on the incidence of RTI from the IHME GBD dataset by using the open-access site vizhub.healthdata.org/epi/.[116] Region-specific data sources included the World Health Organization (WHO) regional office, ministries of health, and so forth, while mixed-effects-modeled IHME GBD data were excluded. Regions not recognized by the WB or the WHO were excluded (for example, Tibet). In a few instances, the incidence for only one sex was provided; therefore, to maintain uniformity and generalizability, incidence data that included male and female sex were selected for analysis over incidence data for just one

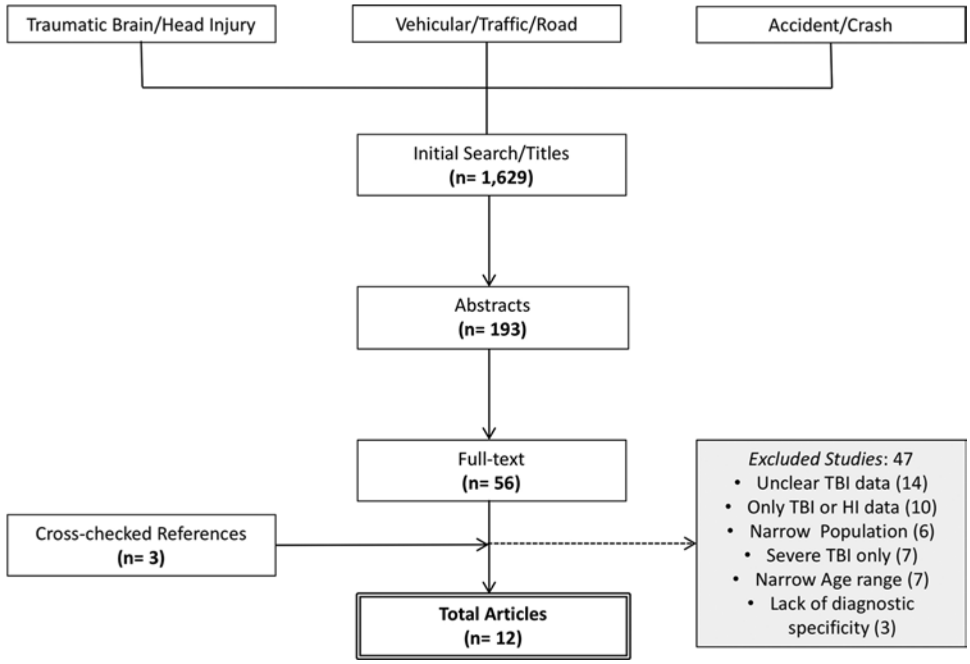

FIG. 2. PRISMA diagram for P(TBI|RTI): quantifying the proportion of RTIs that include TBI.

sex. Incremental age and sex values were averaged, and mean incidence values were estimated for each country. Each incidence value was expressed as the probability that a person living in a country would sustain an RTI annually [P(RTI); Fig. 1 II and III].

The total number of RTIs (RTI_{TOTAL}) per WHO region and WB income group was calculated as the product of the WB 2015 population metadata[260] and the GBD RTI data. The WB metadata are modeled figures to project population changes over time.

Proportion of RTIs Causing TBIs

The probability of sustaining a TBI after an RTI is represented by P(TBI|RTI). This is equal to the ratio of RTIs with TBI to all RTI cases with or without TBI in a population (Fig. 1 IV). To identify this proportion, a systematic literature search of PubMed was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for studies reporting the proportion of RTIs resulting in TBI or HI (Fig. 2).[173] The aim of the search was to comprehensively identify population- and hospital-based studies quantifying the injuries resulting from traffic accidents. Thus, a series of searches were performed to capture a wide range of relevant studies to calculate the proportion of TBIs or HIs resulting from the primary event of an RTI. A full description of search parameters, as well as inclusion and exclusion criteria, can be found in the *Appendix*. Briefly, search terms included “traffic accident,” “vehicular crash,” “vehic* accident,” “brain injury,” and “head injury.” Our search focused on “accident” as opposed to “crash” or “collision” because most epidemiological studies on road injuries have historically followed this notation convention until recently, when studies began to shift to more objective terminology. Thus, our use of “vehicular crash” was an attempt to capture more recent studies using this new convention. Articles were included if epidemiological data categorized the types of injuries sustained from RTIs and if the proportion of RTIs resulting in HI or brain injury was discernible. Studies that included only TBI or HI and those that only reported a certain severity of injury (for example, severe TBI only) were excluded to minimize selection bias. Two reviewers (A.R., S.G.) and a single arbiter (M.C.D.) conducted this search.

Next, we conducted a search of governmental traffic injury registries that reported HIs. The Organisation for Economic Co-operation and Development (OECD) Health Statistics report (“Injuries in Road Traffic Accidents 2016”) and citation information from the IHME GBD data on road injury incidence were queried.[116] Registries from 15 different countries were screened: United States, United Kingdom, Canada, Mexico, Brazil, Australia, New Zealand, Taiwan, China, India, South Africa, Belgium, Chile, France, Italy. A single registry (United Kingdom) yielded compatible information on HI and was incorporated into the model with the peer-reviewed study data.

Study results were then pooled using MedCalc software version 15.1 to conduct a meta-analysis. Data were pooled with inverse probability random-effects weighting to estimate the proportion of RTIs resulting in TBI, represented by P(TBI|RTI) for each WB income group and WHO region.

The number of cases of RTI that resulted in TBI, represented by $RTI \cap TBI$, was calculated as the product of RTI_{TOTAL} and P(TBI|RTI) for all WHO regions and WB income groups (Fig. 1 V).

Traumatic Brain Injury MOI

Another systematic literature review and meta-analysis

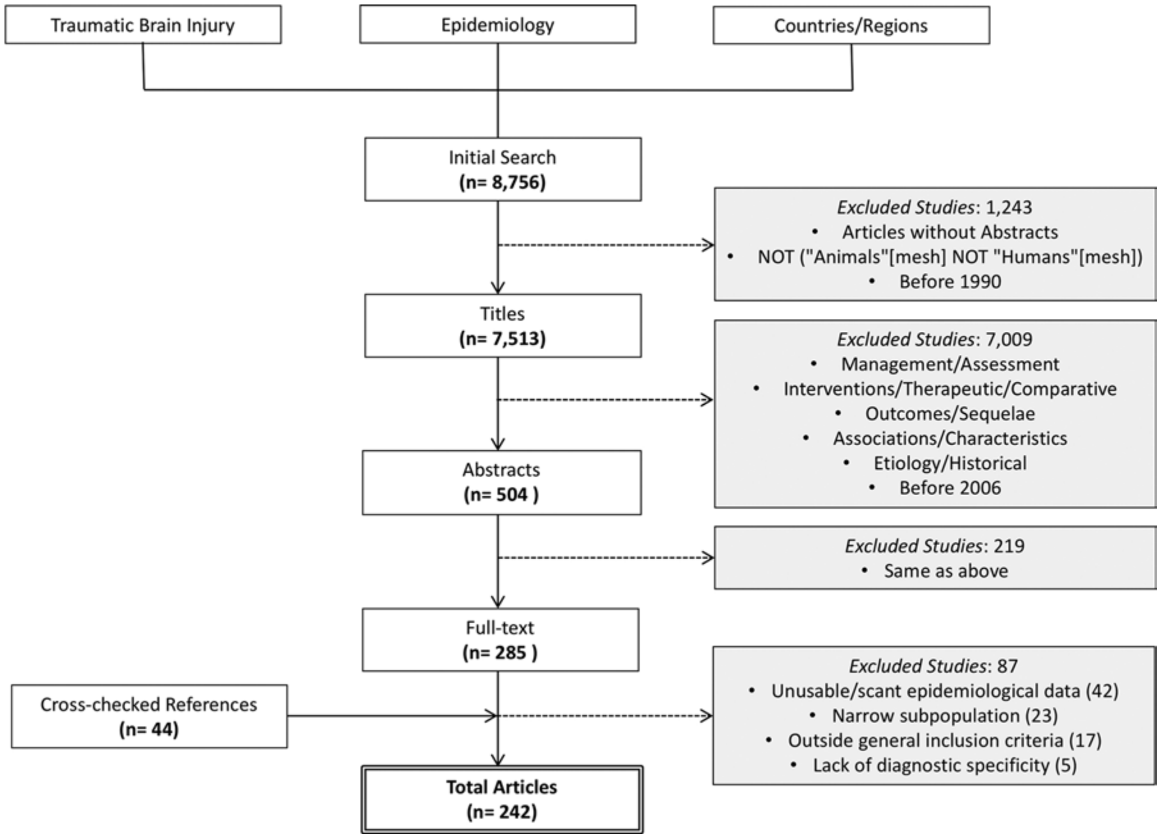

FIG. 3. PRISMA diagram for MOIs: quantifying the proportion of TBIs secondary to RTIs [P(RTI|TBI)].

was conducted to estimate the relative distribution and proportions of MOI for TBI. The goal was to calculate the proportion of TBI cases that were attributable to RTI, represented by P(RTI|TBI), or the probability that TBI resulted from RTI as a mechanism. This is equal to the ratio of TBI caused by RTI to TBI from all causes in a population (Fig. 1 VI).

Following the PRISMA guidelines,[173] we searched the PubMed and Cochrane Database of Systematic Reviews to identify studies reporting country-specific epidemiological data on TBI MOI. A full list of search terms and the search methodology can be found in the *Appendix*, and a detailed breakdown of the article screening process is illustrated in Fig. 3. In summary, MeSH and title/abstract terms were included to maximize the inclusion of studies related to TBI epidemiology (incidence, prevalence, burden, mortality, and so forth) published in countries recognized by the WB. Given the scope of this review, 4 reviewers (A.R., M.P., R.E.B., Y.C.H.) and 1 arbiter (M.C.D.) screened the articles, while 5 investigators extracted relevant data from source articles (A.R., R.E.B., M.P., Y.C.H., M.C.D.). The methodological quality of individual studies was scored on a 6-point scale from lowest (0 = small sample size, hospital based) to highest (5 = large, ideal population based) to allow quality comparisons among regions and income groups.[238] As described by Feigin et al.,[82] less rigorous study quality was permitted for studies from LMICs, from which data would otherwise be unavailable.

Mechanism of injury studies were first selected based on completeness of data (that is, the sum of individual MOI cases equaled the total number of TBI cases reported). Studies were then reviewed for study design and subject selection; studies reporting incidence within a population that could be extended beyond a hospital (that is, at least the regional level) were included for data analysis. Mechanism of injury studies were excluded if they had narrow selection criteria (only pediatric patients, only severe TBI, and so forth).

Incidence of TBIs

The total number of TBI cases from all MOIs (TBI_{TOTAL}) in a population annually was computed by dividing the number of TBI cases secondary to RTI (RTI∩TBI) by the proportion of TBIs caused by RTIs [P(RTI|TBI); Fig. 1 VII]. The WB population data and TBI_{TOTAL} were then used to calculate the incidence of TBI in a given population [P(TBI); Fig. 1 VIII]. The calculations for confidence intervals are outlined in the Supplement.

Severity of Injury

Finally, we sought to characterize the distribution of mild, moderate, and severe TBI. Studies identified in the systematic review for MOI (*Methods, Traumatic Brain Injury MOI*) were queried for the reporting of TBI severity. Population-based studies categorizing TBI severity with Glasgow Coma Scale scores of mild (13–15), moderate

TABLE 1. Proportion, incidence, and volume of TBI worldwide by WB income group and WHO region

	I	II	III	IV	V	VI		VII	VIII	
Group	Population	P(RTI)	RTI_{TOTAL}	P(TBI|RTI)	RTI∩TBI	P(RTI|TBI)	TBI_{TOTAL}	95% CI	TBI Incidence (cases per 100,000 people)	95% CI
LMIC	6,160,384,080	0.01308	80,577,165	0.344	27,727,408	0.555	49,954,794	30,597,109–69,312,478	811	497–1125
HIC	1,188,267,169	0.01300	15,448,795	0.289	4,464,702	0.249	17,903,925	8,963,471–26,844,378	1507	754–2259
AFR	990,267,592	0.01292	12,798,416	0.344	4,404,063	0.555	7,934,534	7,247,018–8,622,050	801	732–871
AMR-L	634,315,984	0.01368	8,677,844	0.335	2,906,427	0.504	5,765,538	4,840,302–6,690,774	909	763–1055
AMR-US/Can	357,270,594	0.01121	4,004,087	0.289	1,157,181	0.249	4,640,418	2,323,192–6,957,645	1299	650–1947
EMR	648,060,427	0.01300	8,425,138	0.330	2,783,097	0.479	5,814,715	4,999,254–6,630,175	897	771–1023
EUR	916,755,857	0.01201	11,007,015	0.310	3,416,926	0.368	9,278,934	8,354,033–10,203,834	1012	911–1113
SEAR	1,928,530,522	0.01529	29,484,574	0.344	10,145,937	0.555	18,279,321	15,387,571–21,171,070	948	798–1098
WPR	1,873,450,273	0.01405	26,331,186	0.336	8,853,523	0.511	17,312,953	14,746,696–19,879,210	924	787–1061
Global	7,348,651,249						69,026,412	64,213,245–73,839,580	939	874–1005

AFR = African Region; AMR-L = Region of the Americas–Latin America; AMR-US/Can = Region of the Americas–United States and Canada; EMR = Eastern Mediterranean Region; EUR = European Region; HIC = high-income country; LMICs = low- and middle-income countries; P(RTI) = probability that a member of the population will sustain an RTI annually; P(RTI|TBI) = probability that TBI is secondary to RTI; P(TBI|RTI) = probability that RTI will lead to TBI; RTI = road traffic injury; RTI_{TOTAL} = total cases of RTI, with or without TBI; RTI∩TBI = intersection of RTIs and TBIs, thus representing either the number of RTIs that lead to TBI or the number of TBIs with RTI as the mechanism of injury; SEAR = Southeast Asia Region; TBI = traumatic brain injury; TBI_{TOTAL} = total cases of TBI, whether mechanism is RTI or non-RTI; WPR = Western Pacific Region.

(9–12), and severe (3–8) were extracted. Severity distribution values were pooled using random-effects inverse weighting meta-analysis in accordance with the methodology and reasoning outlined above (*Methods, Proportion of RTIs Causing TBIs*). From these data, the proportion of different TBI severities was calculated and multiplied by the total TBI incidence to arrive at an estimated incidence of mild, moderate, and severe TBI across geographic regions and income brackets.

Results

Incidence of RTIs

A total of 66 countries were represented in the GBD RTI mean incidence rate data, including all 7 WHO regions—African Region (AFR) = 20 countries, Region of the Americas–Latin America (AMR-L) = 6 countries, Region of the Americas–United States and Canada (AMR-US/Can) = 1 country, Eastern Mediterranean Region (EMR) = 8 countries, European Region (EUR) = 18 countries, Southeast Asian Region (SEAR) = 6 countries, Western Pacific Region (WPR) = 7 countries—and all WB income groups (high = 16, middle = 40, low = 10). The annual incidence is displayed as a proportion of the population [P(RTI)] and was highest in the SEAR (1.5%) and lowest in the AMR-US/Can (1.1%; Table 1). Despite differences in the proportion of motor vehicle users across WHO regions, there was relatively minimal variability in the risk of RTI.

Proportion of RTIs Resulting in TBI

A total of 12 large RTI studies reporting data on the proportion of HIs or TBIs were identified.[9,29,36,46,65,103,149,170,203,216,229,249] Five WHO regions were represented: AFR = 5 studies (4 countries), AMR-L = 0 studies, AMR-US/Can = 1 study, EMR = 0 studies, EUR = 2 studies (2 countries), SEAR = 2 studies (1 country), WPR = 2 studies (2 countries). All income groups were also represented (studies: HIC = 3, middle-income country [MIC] = 6, low-income country [LIC] = 3). Methodology, sample size, and cohort characteristics for each study can be found in Supplemental Table S1. The pooled proportion of RTIs and TBIs for each region and income group is listed in Table 1. The greatest P(TBI|RTI) was found in the AFR and SEAR (34%), whereas AMR-US/Can (29%) had the lowest proportion. This equated to 4,404,063 TBI cases related to RTI in AFR and 1,157,181 in AMR-US/Can. Despite having an equivalent or lower P(TBI|RTI) than in the AFR, the SEAR and WPR carry the greatest absolute caseload of TBIs secondary to RTIs, at 10.1 and 8.9 million new cases each year, respectively.

Traumatic Brain Injury MOI and Injury Severity

The systematic review to describe TBI epidemiology and to quantify TBI MOI yielded more than 240 full-text articles from an initial 8756 titles.[1–3,5–8,10–23,25–28,30–35,37,38,40–44,47–64,67,69–78,83,85–99,101,102,104,106–115,117–148,150–169,171,172,174–194,196–202,204,205,207,209–215,217–219,221–228,230–237,239–248,250–252,255–258,261–267] The search process is illustrated in detail in Fig. 3, while the full account of included articles with relevant epidemiological data is listed in Supplemental Table S2. Beyond epidemiological data, the brain injury character-

TABLE 2. Characteristics and overview of TBI severity studies

Parameter	Country	WHO Region	Income Level	Sample Size (no.)	Severity Index	Severity (% injuries)		
						Mild	Moderate	Severe
Authors & Year								
Selassie et al., 2014	US	AMR-US/Can	High	33,695	AIS	45.7	19.63	34.67
Bener et al., 2011	Qatar	EMR	High	1,952	GCS	82.94	9.528	7.53
Siman-Tov et al., 2016	Israel	EUR	High	2,419	GCS	72.59	9.384	18.02
Szarpak & Madziała, 2011	Poland	EUR	High	1,031	GCS	82.44	10.18	7.37
Ji et al., 2015	China	WPR	Middle	195,189	Other	78.87	18.51	2.62
Chiu et al., 2007	Taiwan	WPR	Middle	1,474	GCS	82.7	8.82	8.48
Chiu et al., 2007	Taiwan	WPR	Middle	5,754	GCS	87.46	5.89	6.64
Overall estimate				241,514		81.02	11.04	7.95

AIS = Abbreviated Injury Scale; GCS = Glasgow Coma Scale.

istics, patient demographics, and study setting and design were captured in a comprehensive database of the most relevant TBI studies worldwide over the last decade. After further filtering by study population, injury setting, completeness of data, and broad/representative subject selection, we identified 10 studies reporting on 11 unique cohorts (1 study[52] counted twice) that provided representative TBI mechanism distributions (Supplemental Table S3).[18,33,52,112,114,129,144,185,187,252] Five WHO regions (unique cohorts: AFR = 3, AMR-US/Can = 1, EMR = 2, EUR = 2, WPR = 3) and 2 WB income groups (HIC = 4, MIC = 7) were represented. The pooled proportion [P(RTI|TBI)] for each income group and WHO region is listed in Table 1. The P(RTI|TBI) was lowest in the AMR-US/Can (25%) and highest in the SEAR and AFR (56% each).

A total of 6 studies, comprising 7 distinct cohorts, were incorporated into the severity of injury estimate (4 WHO regions).[33,52,125,218,228,240] Mild TBI accounted for 81.02% of injuries, moderate TBI for 11.04%, and severe TBI for 7.95% (Table 2).

Worldwide Incidence and Volume of TBI

The incidence of TBI was highest in the AMR-US/Can (1299 cases per 100,000 people, 95% CI 650–1947) and EUR (1012 cases per 100,000 people, 95% CI 911–1113) and lowest in the AFR (801 cases per 100,000 people, 95% CI 732–871; Table 1). Extrapolating onto regional populations, the greatest volume of TBI annually was observed in the SEAR (18.3 million) and WPR (17.3 million; Fig. 4).

The global incidence of all-cause, all-severity TBI is estimated at 939 cases per 100,000 people (95% CI 874–1005); thus, an estimated 69.0 million (95% CI 64.2–73.8 million) people worldwide will suffer TBI each year (Table 1). Mild TBI affects approximately 740 cases per 100,000 people, or a total of 55.9 million people each year, whereas 5.48 million people are estimated to suffer severe TBI each year (73 cases per 100,000 people).

Discussion

In this report, we have amassed a comprehensive overview of global TBI, with a focus on quantifying injury incidence and volume. Our model estimates that between 64 and 74 million new cases of TBI will occur worldwide each year. While the incidence of TBI was highest in the AMR-US/Can and EUR, the greatest overall burden of TBI is seen in the SEAR and WPR.

Estimates provided here are generally higher than those in previous efforts to quantify the volume of TBI. In 2010, it was estimated that 1.7 million people in the United States sustain a TBI each year,[45] far fewer than our estimate of 4.6 million in the United States and Canada. However, the former report primarily examined individuals presenting to an emergency department for care and thus probably underestimated the overall population burden of TBI. Indeed, many patients who sustain a mild TBI (sports concussions, falls, low-velocity RTI) probably never seek medical attention. Zhang et al. estimated that up to 1650 adolescents per 100,000 patients suffer a concussion each year—a figure that does not include the many other types and severities of HI.[264] Preliminary results from the 2010 GBD Project[39] suggested that the global incidence rate of TBI was 200 cases per 100,000 people per year, equating to approximately 15 million persons affected. For comparison, an estimated 3.8 million new cases of human immunodeficiency virus, 287 million cases of malaria, and 8.8 million cases of tuberculosis will develop each year.[116] In terms of other common conditions causing neurological morbidity and mortality, recent estimates suggest that each year there are 16.9 million new cases of stroke and 30 million new cases of central nervous system infection.[82] Contextualizing their figure of 15 million new cases, the GBD Project authors acknowledged the uncertainty of their estimate and that it was "a likely underestimate" because they had used hospital- and emergency department–based studies. The updated GBD study (GBD 2015) used here provides more accurate figures for RTI, and our ratio estimates are based on more recent TBI studies. Furthermore, the higher prevalence of mild TBI in our estimate probably explains some of these disparities.

In calculating the incidence figures herein, we relied on RTI data from the IHME since reliable, population-based incidence figures for TBI in the majority of LMICs were unavailable—both in the literature and via national registries. Relative ratios of TBI occurrence, as well as the contribution of RTI to overall TBI, obtained via systematic review and meta-analysis are subject to multiple sources of bias. Any small difference or inaccuracy in the TBI/RTI

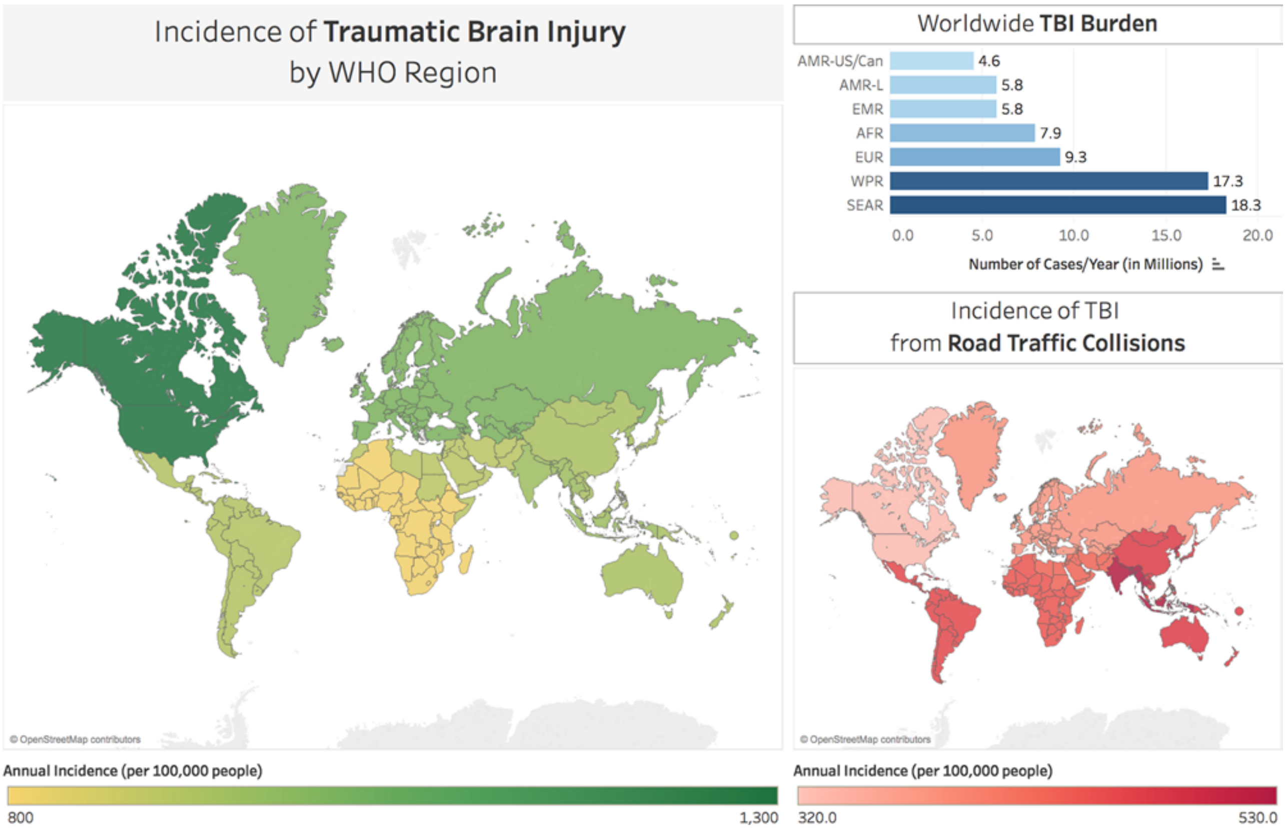

FIG. 4. Map showing incidence of TBI (cases per 100,000 people) by WHO region (*left*). Bar graph (*upper right*) indicating the estimated volume of TBI annually across WHO regions. Map (*lower right*) showing incidence of TBI (cases per 100,000 people) secondary to traffic collisions by WHO region. Regarding maps, reproduced with permission from OpenStreetMap Contributors, CC BY-SA 2.0 (http://www.openstreetmap.org/copyright). Figure is available in color online only.

ratio is compounded when applied to P(RTI) and regional populations. For example, in this model, a low P(RTI|TBI) will boost regional TBI incidence because incidence is calculated from the product of P(RTI) and the inverse of P(RTI|TBI). The incidence of TBI in the AMR-US/Can probably stands as an outlier in part for this very reason. While also relatively high, the EUR incidence (1012 cases per 100,000 people) is somewhat diluted by MICs, in which less robust, hospital-derived data tend to produce lower overall TBI incidence rates because some cases of mild TBI are never reported. The lower TBI incidence in the AFR is probably explained in part by lower-quality road traffic data from member countries, as well as by the overwhelming contribution of RTIs to TBI. In this model, the contribution of all other MOIs (recreation, falls, assault, and so forth) is incorporated indirectly by the inverse proportion of TBIs from RTIs (Fig. 1).

Nevertheless, several observations lending credence to our estimates warrant elaboration. First, our meta-regression suggests that P(TBI|RTI) is highest in the AFR (34%) and SEAR (34%) and lowest in the AMR-US/Can (29%). This is an intuitive finding given the abundance of traffic regulations and safety laws in places like the United States relative to many LICs.[52,203] Additionally, RTI refers to injuries sustained not only by motorists, but also by pedestrians and cyclists. A dearth of sidewalks and traffic lights and poor helmet compliance among cyclists and motorcyclists in LMICs probably translate to a higher rate of HI following RTI.[66,100,220] Moreover, inadequate on-board safety technology or overcapacity vehicles can compound an otherwise trivial collision. The single collision of a cargo truck full of unrestrained occupants in LMICs can result in dozens of cases of TBI—a scenario not frequently observed in most HICs.

Second, we found that P(RTI|TBI) was lowest in the AMR-US/Can (25%) and highest in the SEAR (56%) and AFR (56%). A larger proportion of studies from the SEAR and AFR represented hospital-based analyses relative to studies from regions with a predominance of HICs (Supplemental Table S2). As a result, TBI presenting to hospitals in LMICs likely overrepresented high-severity injuries, which are known to be associated with road traffic collisions more than other MOIs.[5,185,187,252] Furthermore, in many HICs, in which life expectancy exceeds that in LMICs, injury secondary to falls, especially in the elderly, tends to dilute the overall mechanistic proportion of TBI; our results suggest that this phenomenon may exist.[18,112]

Mild TBI occurs with far greater frequency than moderate or severe TBI—nearly 10-fold the burden of both moderate and severe injury. When establishing health care priorities in the setting of limited resources, some may dismiss this mild TBI burden as being of nominal consequence. However, the disabling effects of even mild TBI probably translate into economic, societal, and quality of life detriments. Nearly a quarter of patients describe disabling symptoms several months after injury.[195,268] And despite the normalization of neuropsychological and functional scales by 1 year, half of TBI victims report 3 or more persistent posttraumatic symptoms.[68]

The volume and extent of our literature review attempts not only to address our stated hypotheses, but also to aid researchers interested in exploring these hypotheses further. The tremendous amount of data found within these studies cannot possibly be summarized in a single paper; instead, highlights and major patterns are described in the text and tables. Readers are encouraged to consult the Supplemental Tables to gain a more granular understanding of the nature of TBI in regions around the world. Supplemental Table S2 is organized by WHO region and country to serve as a quick reference for the interested reader and those seeking an understanding of the data available in—and absent from—the literature.

Limitations and Future Directions

The conclusions of this report must be examined in the context of our study design. First, all TBI estimates were modeled after the GBD estimates for RTI. Therefore, assumptions or errors made in the GBD methodology would be carried over into these estimates. Second, by nature of the data available from the literature, we assumed uniform disease susceptibility across age groups and sexes. We also assumed that member countries of a particular WHO region or WB income group share the same injury incidence and proportion. The gold-standard alternative to this limitation is a series of large, population-based sampling studies conducted in every representative population worldwide; the feasibility and cost of such an effort is problematic, though no less important.

Next, the literature reviews and meta-analyses conducted to obtain RTI and TBI relative ratios rely on heterogeneous and often biased study designs. Naturally, a topic as broad as TBI yields results from non-uniform populations, thereby making aggregations and direct comparisons challenging. For example, in the latter systematic review, some studies only examined severe TBI[84,243,257] and some only reported on TBI in young[188,194,197,241,243,245,254,258,265] or elderly[48,49,134,225] cohorts. Combining epidemiological data across disparate cohorts risks misrepresentation of the disease burden and volume. Moreover, the methodological quality from LMICs was, on average, lower than that from HICs; the TBI estimates from HICs may be more reliable than those from LMICs. This limitation is inherent to most global epidemiological surveys, wherein data derive from sources of disparate quality. Lastly, even basic discrepancies, such as differing definitions of TBI or conflicting injury severity scores, encountered across studies may have influenced our results.

Despite the limitations of this model and its underlying methodology, justification for its use resides in the scientific estimation of TBI burden in countries and regions in which data are otherwise entirely unavailable. Our aim of estimating the volume of TBI on a global scale in a transparent and quantitative fashion has been realized, albeit with the aforementioned considerations. Concrete estimates of TBI with region and income-level specificity are provided.

A tremendous burden—approximately 69 million cases—of TBI can be expected each year. The vast majority of this burden affects populations in LMICs, in which adequate health care resources are often either inaccessible or nonexistent. Examining the disease burden between regions and comparing against available resources allow identification of such deficits in existing health care coverage. More robust research, especially in LMICs where high-quality data are deficient, is essential for a targeted campaign. A logical first step in this effort is the establishment of an international TBI registry to improve our understanding of the nature and scope of TBI worldwide. Such a registry should be intuitive, secure, electronic, transferable across heterogeneous institutional informational technologies, and free. While there are multiple such platforms available, we have extensive experience with REDCap[105] (Research Electronic Data Capture, Vanderbilt University) and its successful application in international data collection for clinical neurosurgery in LMICs. Secondarily—and concurrently—a series of targeted, community-based epidemiological surveys of representative populations would allow for the generation of more reliable incidence and mortality figures for TBI in low-resource settings. Ultimately, curbing the silent epidemic of TBI will require a multipronged effort toward public awareness, safety legislation and enforcement, injury prevention campaigns, health care capacity strengthening, and community-based efforts to promote recovery and rehabilitation.

Conclusions

Each year an estimated 69 million individuals will suffer a TBI, the vast majority of which will be mild (81%) and moderate (11%) in severity. Per capita, the highest annual incidence of all-cause TBI is observed in the AMR-US/Can and EUR (1299 and 1012 cases per 100,000 people, respectively). Taking into account regional populations, however, the greatest burden of HIs is in the SEAR (18.3 million) and WPR (17.3 million). The health care systems in LMICs encounter nearly 3 times as many total TBIs than those in HICs. These estimates are limited by relatively low-quality data from LMICs and suggest the need for more robust and accurate injury reporting. The global disparity in health care between regions with fewer resources and a high disease burden and those with greater assets and a lower burden deserves attention and action.

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Appendix

Search Terms for Incidence of TBI From RTI

A series of 4 search parameters were used in PubMed (1, 2, 4) and PubMed Central (3):

1) “vehicular accident”[ti] OR “traffic accident”[ti]

Titles: 631; Abstracts reviewed: 50; Full texts reviewed: 8

2) (“vehicular accidents” AND “traumatic brain injury”) OR

("traffic accident" AND "traumatic brain injury") OR ("road accident" AND "traumatic brain injury") OR ("vehicular crash" AND "traumatic brain injury")

Titles: 88; Abstracts reviewed: 10; Full texts reviewed: 5

3) (vehicular accidents AND "traumatic brain injury") OR (traffic accident AND "traumatic brain injury") OR (road accident AND "traumatic brain injury") OR (vehicular crash AND "traumatic brain injury")

Titles: 565; Abstracts reviewed: 50; Full texts reviewed: 7

4) road traffic accidents[tiab] AND (injury[tiab] OR injuries[tiab] OR trauma[tiab] OR traumas[tiab] OR traumatic[tiab]) AND (brain[tiab] OR head[tiab])

Titles: 345; Abstracts reviewed: 83; Full texts reviewed: 36

Abstracts were selected if content was suggestive of an epidemiological study that categorized types of injuries sustained from RTIs. Full texts were selected if the abstract stated or suggested that the study contained the proportion of RTIs leading to HIs or TBIs. Final articles were included if the study provided sufficient information to calculate a proportion of TBI or HI. Articles were excluded for the following reasons:

1) Included causes of HI other than RTIs
2) Entire study population had HI or TBI
3) Sample size under 100
4) Studies conducted before 2000
5) Head injury cases unclear to decipher
6) Strict conditions of HI cases examined (for example, severe or mild cases only)

Search Terms for TBI Mechanism of Injury and Severity Distribution

((("epidemiology" [Subheading] OR "Epidemiology"[MeSH] OR epidemiology[tiab] OR epidemiological[tiab] OR population[tiab] OR population-based[tiab] OR inciden*[tiab] OR prevalen*[tiab] OR burden OR ratio[tiab] OR DALY[tiab] OR "disability adjusted life year*"[tiab] OR YLL[tiab] OR "years of life lost"[tiab] OR YLD[tiab] OR "years lost to disability"[tiab] or "years lost due to disability"[tiab] OR ratio[tiab] OR QALY[tiab] OR "quality adjusted life year*"[tiab]))

AND

("Head Injuries, Penetrating"[MeSH] OR "Head Injuries, Closed"[MeSH] OR "Brain Injuries"[MeSH] OR "Intracranial Hemorrhage, Traumatic"[MeSH] OR brain injur*[tiab] OR head injur*[tiab]))

AND

("Africa"[MeSH] OR "Asia"[MeSH] OR "Central America"[MeSH] OR "Developing Countries"[MeSH] OR "Geographical Locations Category"[MeSH] OR "Internationality"[MeSH] OR "Latin America"[MeSH] OR "South America"[MeSH] OR "Dominican Republic"[tiab] OR "Principe"[tiab] OR "Puerto Rico"[tiab] OR "Sao Tome"[tiab] OR "Saudi Arabia"[tiab] OR "Sierra Leone"[tiab] OR "Virgin Islands"[tiab] OR Afghanistan*[tiab] OR Africa*[tiab] OR Albania*[tiab] OR Algeria*[tiab] OR America*[tiab] OR Andorra*[tiab] OR Angola*[tiab] OR Antarct*[tiab] OR Antigua*[tiab] OR Arab Emirate*[tiab] OR Argentin*[tiab] OR Armenia*[tiab] OR Aruba*[tiab] OR Asia*[tiab] OR Atlantic[tiab] OR Australia*[tiab] OR Austria*[tiab] OR Azerbaijan*[tiab] OR Azores Islands[tiab] OR Baham*[tiab] OR Bahra*[tiab] OR Bangladesh*[tiab] OR Barbad*[tiab] OR Barbuda*[tiab] OR Barthelemy[tiab] OR Barthélemy[tiab] OR Belarus*[tiab] OR Belgi*[tiab] OR Belize[tiab] OR Bengali[tiab] OR Benin*[tiab] OR Bermuda*[tiab] OR Bhutan*[tiab] OR Bissau[tiab] OR 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OR Qatar*[tiab] OR Romania*[tiab] OR Russia*[tiab] OR Rwanda*[tiab] OR Saint Lucia[tiab] OR Saint Vincent[tiab] OR Samoa*[tiab] OR San Marino[tiab] OR Sao Tome[tiab] OR Senegal*[tiab] OR Serbia*[tiab] OR Seychelles[tiab] OR Sierra Leone*[tiab] OR Singapore[tiab] OR Slovakia*[tiab] OR Slovenia*[tiab] OR Solomon[tiab] OR Solomon Island*[tiab] OR Somalia*[tiab] OR South [tiab] OR Spain[tiab] OR Sri Lanka[tiab] OR Sudan*[tiab] OR Suriname*[tiab] OR Swaziland*[tiab] OR Swed*[tiab] OR Switzerland[tiab] OR Syria*[tiab] OR Taiwan[tiab] OR Tajik*[tiab] OR Tanzania*[tiab] OR Thai*[tiab] OR third world countr*[tiab] OR third world nation*[tiab] OR Timor Leste[tiab] OR Timor*[tiab] OR Tobago[tiab] OR Togo*[tiab] OR Tonga*[tiab] OR Trinidad*[tiab] OR Tunisia*[tiab] OR Turkey[tiab] OR Turkish[tiab] OR Turkmen*[tiab] OR Turks[tiab] OR Tuvalu*[tiab] OR Uganda*[tiab] OR Ukrain*[tiab] OR under developed countr*[tiab] OR under developed nation*[tiab] OR underdeveloped nation*[tiab] OR underdeveloped nation*[tiab] OR United Kingdom[tiab] OR United States[tiab] OR Uruguay[tiab] OR Uzbeki*[tiab] OR Vanuatu*[tiab] OR Vatican[tiab] OR Venezuela*[tiab] OR Viet nam*[tiab] OR Vietnam*[tiab] OR Vincent[tiab] OR West[tiab] OR West Bank[tiab] OR Yemen*[tiab] OR Zambia*[tiab] OR Zimbabw*[tiab])

NOT

("Animals"[MeSH] NOT "Humans"[MeSH])

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