**Summary**

**Background** Gastro-oesophageal reflux disease is a common chronic ailment that causes uncomfortable symptoms and increases the risk of oesophageal adenocarcinoma. We aimed to report the burden of gastro-oesophageal reflux disease in 195 countries and territories between 1990 and 2017, using data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017.

**Methods** We did a systematic review to identify measurements of the prevalence of gastro-oesophageal reflux disease in geographically defined populations worldwide between 1990 and 2017. These estimates were analysed with DisMod-MR, a Bayesian mixed-effects meta-regression tool that incorporates predictive covariates and adjustments for differences in study design in a geographical cascade of models. Fitted values for broader geographical units inform prior distributions for finer geographical units. Prevalence was estimated for 195 countries and territories. Reports of the frequency and severity of symptoms among individuals with gastro-oesophageal reflux disease were used to estimate the prevalence of cases with no, mild to moderate, or severe to very severe symptoms at a given time; these estimates were multiplied by disability weights to estimate years lived with disability (YLD).

**Findings** Data to estimate gastro-oesophageal reflux disease burden were scant, totalling 144 location-years (unique measurements from a year and location, regardless of whether a study reported them alongside measurements for other locations or years) of prevalence data. These came from six (86%) of seven GBD super-regions, 11 (52%) of 21 GBD regions, and 39 (20%) of 195 countries and territories. Mean estimates of age-standardised prevalence for all locations in 2017 ranged from 4408 cases per 100,000 population to 14,035 cases per 100,000 population. Age-standardised prevalence was highest (>11,000 cases per 100,000 population) in the USA, Italy, Greece, New Zealand, and several countries in Latin America and the Caribbean, north Africa and the Middle East, and eastern Europe; it was lowest (<7000 cases per 100,000 population) in the high-income Asia Pacific, east Asia, Iceland, France, Denmark, and Switzerland. Global prevalence peaked at ages 75–79 years, at 18,820 (95% uncertainty interval [95% UI] 13,770–24,000) cases per 100,000 population. Global age-standardised prevalence was stable between 1990 and 2017 (8791 [95% UI 7772–9834] cases per 100,000 population in 1990 and 8819 [7781–9863] cases per 100,000 population in 2017, percentage change 0.3% [−0.3 to 0.9]), but all-age prevalence increased by 18.1% (15.6–20.4) between 1990 and 2017, from 7859 (6905–8851) cases per 100,000 population in 1990 to 9283 (8189–10,400) cases per 100,000 population in 2017. YLDs increased by 67.1% (95% UI 63.5–70.3) between 1990 and 2017, from 3.60 million (1.93–6.12) in 1990 to 6.01 million (3.22–10.19) in 2017.

**Interpretation** Gastro-oesophageal reflux disease is common worldwide, although less so in much of eastern Asia. The stability of our global age-standardised prevalence estimates over time suggests that the epidemiology of the disease has not changed, but the estimates of all-age prevalence and YLDs, which increased between 1990 and 2017, suggest that the burden of gastro-oesophageal reflux disease is nonetheless increasing as a result of ageing and population growth.

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or both. Why some individuals have more frequent or severe symptoms or complications of reflux than others is poorly understood, but obesity, hiatal hernias, alcohol, smoking, and various foods and medications have been reported as risk factors. A positive association with age has been observed in many—but not all—studies.

Gastro-oesophageal reflux disease syndromes include typical reflux (defined by heartburn, regurgitation, or both, and sometimes accompanied by belching, water brash, or nausea), angina-mimicking chest pain, and extra-oesophageal symptoms such as chronic cough and chronic laryngitis. Complications of gastro-oesophageal reflux disease include oesophageal inflammation, stricture, ulceration, perforation, metaplasia (ie, Barrett’s oesophagus), and oesophageal adenocarcinoma. 

Associations of varying strength have been detected between reflux beyond the oesophagus and outcomes such as dental erosion, difficulty controlling concurrent asthma, and increased risk of laryngopharyngeal carcinoma.

Lifestyle changes to reduce reflux of stomach contents, such as weight loss and eating smaller meals, are commonly recommended (eg, by treating physicians and in practice guidelines written by professional organisations and committees) and moderately supported by evidence. Often, however, effective control of symptoms requires the use of acid-suppressing medications, such as proton-pump inhibitors. Long-term use of proton-pump inhibitors has been associated with adverse outcomes such as loss of bone-mineral density and increased occurrence of enteric and pulmonary infections. Surgical or endoscopic procedures to reduce reflux are done in selected medication-dependent or refractory cases. Health-care systems and individuals incur economic costs for physician visits, medications, and procedures.

Objective measures such as oesophageal pH monitoring or endoscopy can be used to diagnose gastro-oesophageal reflux disease or its effect on oesophageal mucosa, but these procedures are invasive and can miss cases with fluctuating course. Multiple expert groups have endorsed the use of clinical history and response to therapy in making a clinical diagnosis. Multiple symptom-based questionnaires have been developed for use in population-based research, and prevalence studies have mainly been carried out with this approach.

Several systematic reviews have been published in the past two decades describing the incidence and prevalence of gastro-oesophageal reflux disease. The methodology of systematic reviews, however, limits comparisons across geography and time to those geographies and times for which reported studies exist, and does not quantitatively account for differences in study design. Eusebi and colleagues did a meta-analysis of gastro-oesophageal reflux disease, which produced global and regional pooled estimates of disease prevalence and explored features of study designs that might explain inter-study heterogeneity, but did not use information about these design features to adjust the

Research in context

Evidence before this study
The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) has not estimated the burden of health loss due to gastro-oesophageal reflux disease. Two previous systematic reviews and one previous meta-analysis evaluated the prevalence of gastro-oesophageal reflux disease and its geographical variation. These studies suggested that the prevalence of this disease around the world ranged from 2.5% to 33.1%, and that prevalence was lower in east Asia and southeast Asia. One systematic review suggested that prevalence increased after 1995. The designs of these studies did not quantitatively account for the effect that differences in study design might have on study results, and only provided estimates of prevalence for the small number of countries where original studies have been done or for broadly defined regions, and did not estimate the burden of gastro-oesophageal reflux disease in terms of years lived with disability (YLDs) or other composite measures of health loss.

Added value of this study
GBD 2017 provides the first comprehensive estimates of global, regional, and country-specific prevalence and non-fatal health loss due to gastro-oesophageal reflux disease for 195 countries and territories, from 1990 to 2017, using patterns observed in data from different locations, ages, and times to produce the best possible estimates both where data are available and where they are not. GBD 2017 incorporated more data sources on the prevalence of gastro-oesophageal reflux disease than previous systematic reviews and meta-analyses, and used a modelling approach that adjusted for the effects of non-standard study designs on prevalence data. Even after these adjustments, GBD 2017 generally confirmed the findings reported in previous studies with regard to the range of gastro-oesophageal reflux disease prevalence seen worldwide and the finding that prevalence is lower in countries in east Asia and in the high-income Asia Pacific, but it did not find a global increase in the prevalence of gastro-oesophageal reflux disease after accounting for population ageing.

Implications of all the available evidence
Gastro-oesophageal reflux disease is common and increasing due to population ageing. Health-care systems should be prepared to address the needs of increasing numbers of patients with gastro-oesophageal reflux disease. In some locations, there might be an increase in the prevalence of gastro-oesophageal reflux disease beyond the increase due to age, but more research is required to determine whether this is true and, if so, what factors are driving this increase and what interventions might decrease the burden of gastro-oesophageal reflux disease.
contribution of non-standard studies to pooled estimates. Furthermore, the chronicity of gastro-oesophageal reflux disease and the fact that it can cause persistent or episodic symptoms of varying severity make it important to move beyond estimations of incidence and prevalence, and to quantify the severity and duration of health loss it causes. The Global Burden of Disease research framework uses meta-regression methods to synthesise data from published studies to make estimates for 195 countries and territories worldwide from 1990 to the present, and expresses the relative health loss due to more than 350 diseases and injuries in common terms that facilitate comparisons. Here, we report results from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017, the first iteration of GBD to estimate non-fatal health loss due to gastro-oesophageal reflux disease.

Methods
Overview
The overall objectives, methods, and organisation of GBD 2017 have been previously reported. Methods relevant to estimating the burden of gastro-oesophageal reflux disease are summarised here and described further in the appendix (pp 1–8).

For our analysis, individuals with heartburn, regurgitation, or both, at least once weekly over a 12-month recall period, were defined as having gastro-oesophageal reflux disease. This definition was chosen over the consensus-group-recommended definition of mild symptoms occurring at least twice a week or moderate to severe symptoms occurring at least weekly because of greater data availability, and is consistent with a previously published meta-analysis. Individuals who had oesophageal complications (eg, ulceration or metaplasia) without symptoms, whose sole symptom of gastro-oesophageal reflux was chest pain without typical reflux symptoms, or who had reflux primarily as a trigger or exacerbating factor in respiratory or head and neck diseases (eg, chronic cough or dental erosion) were not included. This strategy avoids double-counting disability already attributed to other underlying diseases modelled in GBD.

Prevalence estimation
Data inputs for estimating the prevalence of gastro-oesophageal reflux disease included epidemiological studies of gastrointestinal illness published in peer-reviewed journals and identified in a systematic review via PubMed, and data from the US National Health Interview Surveys. Search terms and other details of the systematic review are provided in the appendix (pp 1–3). A complete set of unadjusted input data included in the model can be downloaded from the GBD 2017 Data Resources website. Extracted data from studies with acceptable but non-preferred designs were marked with study-level covariates to allow for estimation of fixed effects due to study characteristics in our global meta-regression analysis (described later).

Gastro-oesophageal reflux disease data were analysed with a Bayesian mixed-effects meta-regression framework, DisMod-MR 2.1, developed for GBD non-fatal estimation processes, which has been previously described in detail and is summarised here. Estimates are made by fitting a series of models, each of which serves to generate a Bayesian prior distribution for a subsequent model. At each step, DisMod assumes a compartmental disease model with three states—susceptible, diseased, and dead—with transition between states determined by incidence, remission, excess mortality due to disease, and other-cause mortality. These disease parameters are modelled with an offset log-normal data likelihood function, and a system of age-integrated differential equations are solved to ensure internal consistency among disease parameters.

The first model in the DisMod series is a global mixed-effect model, which uses all data from both sexes, all locations, and all years, and estimates coefficients for fixed effects for sex, study design characteristics, and predictive covariates, and random effects for each of the seven GBD super-regions. The next step is to fit separate mixed-effects models for each year, sex, and super-region, each of which re-estimates the fixed effect coefficients and estimates random effects for each GBD region within that super-region; the Bayesian prior distribution for each super-region-level model is based on the distribution estimated by the initial global model with the fixed effects and the random effect for that super-region. This method is repeated to fit separate mixed-effects models specific to sex, year, and region, using the preceding super-region model and the random effect for the region to determine the Bayesian prior, and estimating random effects for countries. This approach is again repeated to fit separate models specific to sex, year, and country, using the preceding regional model and the random effect for the country to determine the Bayesian prior. For 15 countries, an additional round of models is fit for subnational units (such as states or provinces), each deriving its Bayesian prior from its country model and a pseudo-random effect based on the average ratio of observed subnational data to country-model predictions. This algorithm for developing prior distributions for subnational models is sensitive to data in age groups that have low estimated values in the country-level fit, which can cause the model to ignore the preponderance of the data; in these cases, data for the affected age groups in the subnational locations are excluded.

As mentioned, the DisMod framework estimates fixed effects for study design characteristics; these study-level fixed effects reflect the association observed in input data between study design characteristics and measured disease parameters, and they serve to adjust for measurement bias due to non-reference study designs.
Fixed effects are also estimated for predictive covariates; these reflect the association observed between that covariate and disease input data and serve to help estimate disease parameters in locations with scarce or absent input data. To be considered as a predictive covariate, a factor must have a demonstrated association with disease in non-GBD studies, and valid estimates of the distribution of that factor must exist for all GBD locations and estimation years available to use as DisMod inputs. The association between a predictive covariate and disease parameters need not be causal to serve this purpose. Candidate predictive covariates found to have null or highly uncertain coefficients in preliminary models do not improve estimates, so they are left out of the final model for parsimony.

Ultimately, final estimates for national or subnational locations reflect local data, adjusted for study design characteristics, if local data are present, and reflect prior distributions from broader geographical units and the influence of predictive covariates if no local data are available. Estimates from the finest level of geography are later aggregated to make final estimates for the broader geographical units. Uncertainty intervals are taken as the 2.5th and 97.5th percentiles of the posterior distribution.

Parameters used in DisMod for gastro-oesophageal reflux disease were as follows: excess mortality was assumed a priori to be 0, and remission prior was set to 0–2–0–5 cases per person-year. Incidence was forced to 0 from birth to age 5 years, and after this age prior was set to 0–0–0–2 cases per person-year. We included study-level covariates for alternative recall periods, for alternative minimum symptom frequencies, for the use of a score-based case definition that synthesised the severity, number, and frequency of symptoms, for the use of a case definition based on a single cardinal reflux symptom (regurgitation only), for studies in which the representativeness of the sample was considered questionable, and for data extracted from a report from a national survey, rather than a peer-reviewed publication. We considered location-level covariates for mean body-mass index (BMI), smoking prevalence, mean alcohol consumption, and the Healthcare Access and Quality Index, but these covariates were non-predictive in preliminary models, so they were not retained in the final model.

**Estimation of years lived with disability**

Years lived with disability (YLDs) synthesise the frequency and non-fatal health consequences of a disease. YLD estimation in GBD begins by estimating the point prevalence, specific to year, age, sex, and location, of specific health states that can result from the disease, generally at different levels of severity. Each of
| Country                  | Cases (95% UI) | Age-standardised prevalence per 100 000 population (95% UI) | Cases (95% UI) | Age-standardised prevalence per 100 000 population (95% UI) | Percentage change in age-standardised prevalence, 1990–2017 |
|--------------------------|----------------|-------------------------------------------------------------|----------------|-------------------------------------------------------------|----------------------------------------------------------|
| **Global**               |                |                                                              |                |                                                             |                                                          |
| Central Europe, eastern Europe, and central Asia |                |                                                              |                |                                                             |                                                          |
| Central Asia            | 6 394 907      | (5 583 352 to 7 177 563)                                    | 8 790 6        | (7 771 5 to 9 834 2)                                        |                                                          |
| Armenia                 | 352 696        | (309 406 to 398 280)                                        | 987 80         | (961 1 to 1 013 8)                                         |                                                          |
| Azerbaijan              | 697 858        | (596 2 787 384)                                             | 1 087 61       | (1 062 0 to 1 113 2)                                        |                                                          |
| Georgia                 | 641 764        | (573 487 to 7 389 651)                                      | 987 36         | (960 5 to 1 014 1)                                         |                                                          |
| Kazakhstan              | 1 639 153      | (1 482 763 to 1 906 743)                                    | 2 025 117      | (1 988 6 to 2 061 651)                                     |                                                          |
| Kyrgyzstan              | 396 352        | (347 972 to 471 070)                                        | 2 186 27       | (1 965 2 to 2 407 2)                                        |                                                          |
| Mongolia                | 105 785        | (92 949 to 118 621)                                          | 3 457 51       | (2 896 2 to 4 018 8)                                        |                                                          |
| Tajikistan              | 413 349        | (361 725 to 470 714)                                        | 8 444 122      | (7 391 4 to 9 614 29)                                      |                                                          |
| Turkmenistan            | 299 365        | (260 810 to 340 823)                                        | 527 679        | (461 060 to 596 888)                                        |                                                          |
| Uzbekistan              | 1 689 598      | (1 480 911 to 1 931 215)                                    | 3 228 360      | (2 909 666 to 3 774 888)                                   |                                                          |
| Central Europe          | 1 368 238      | (1 148 232 to 1 641 575)                                    | 1 435 221      | (1 276 673 to 1 616 908)                                   |                                                          |
| Albania                 | 260 352        | (225 294 to 295 366)                                        | 2 056 54       | (1 732 524 to 2 374 498)                                   |                                                          |
| Bosnia and Herzegovina  | 439 944        | (385 200 to 500 245)                                        | 2 928 83       | (2 507 672 to 3 349 041)                                   |                                                          |
| Bulgaria                | 999 730        | (878 178 to 1 126 907)                                      | 9 151 65       | (8 081 113 to 10 277 715)                                  |                                                          |
| Croatia                 | 542 018        | (475 567 to 613 473)                                        | 8 285 94       | (7 141 6 to 10 490 6)                                      |                                                          |
| Czech Republic          | 1 111 875      | (983 317 to 1 250 751)                                      | 13 347 26      | (11 780 9 to 1 499 650)                                    |                                                          |
| Hungary                 | 1 133 724      | (991 109 to 1 273 814)                                      | 1 200 586      | (1 052 677 to 1 349 429)                                   |                                                          |
| North                   | 179 217        | (167 638 to 178 946)                                        | 2 499 56       | (2 129 700 to 2 923 218)                                   |                                                          |
| Montenegro              | 60 782         | (53 290 to 68 863)                                          | 7 3077         | (6 443 to 8 232)                                           |                                                          |
| Poland                  | 4 121 732      | (3 614 649 to 4 630 101)                                    | 11 679 65      | (10 680 7 to 13 679 58)                                    |                                                          |
| Romania                 | 2 453 724      | (2 118 210 to 2 718 890)                                    | 2 988 1        | (2 846 4 to 3 130 48)                                      |                                                          |
| Serbia                  | 997 193        | (878 033 to 1 129 595)                                      | 1 070 416      | (945 234 to 1 202 930)                                     |                                                          |
| Slovakia                | 529 557        | (465 432 to 597 995)                                        | 2 664 82       | (2 585 386 to 3 060 346)                                   |                                                          |
| Slovenia                | 254 302        | (218 240 to 242 437)                                        | 2 928 1        | (2 812 9 to 3 047 68)                                      |                                                          |

(Table continues on next page)
| Country                  | 1990 Cases (95% UI) | 1990 Age-standardised prevalence per 100 000 population (95% UI) | 2017 Cases (95% UI) | 2017 Age-standardised prevalence per 100 000 population (95% UI) | Percentage change in age-standardised prevalence between 1990 and 2017 |
|--------------------------|---------------------|---------------------------------------------------------------|---------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| Eastern Europe           | 37 730 687          | 12 622 0 (11 229 5 to 14 143 0)                              | 34 376 933          | 12 618 8 (11 223 3 to 14 138 4)                               | 0%                                                            |
| Belarus                  | 1 489 446           | 15 550 9 (13 102 7 to 17 813 1)                               | 1 556 424           | 12 551 2 (11 097 6 to 14 182 6)                               | 0%                                                            |
| Lithuania                | 531 993             | 13 072 7 (11 620 1 to 14 710 4)                               | 590 825             | 13 176 8 (11 672 9 to 14 687 1)                               | 0·8%                                                          |
| Moldova                  | 577 391             | 12 550 0 (11 0 49 0 to 14 89 2 2)                             | 579 476             | 12 551 5 (11 0 97 8 to 14 187 3)                               | 0%                                                            |
| Russia                   | 21 439 973          | 12 493 1 (11 118 2 to 13 951 4)                               | 23 453 080          | 12 501 5 (11 126 5 to 13 971 0)                               | 0·1%                                                          |
| Ukraine                  | 8 045 735           | 12 975 7 (11 539 4 to 14 591 5)                               | 7 714 495           | 12 976 0 (11 536 9 to 14 591 8)                               | 0%                                                            |
| High income Asia         | 94 282 055          | 8889 8 (7686 5 to 9917 5)                                     | 130 784 112         | 93 444 5 (8271 2 to 10 426 2)                                 | 5·1% (3·3 to 6·9)                                              |
| Australia                | 1 965 726           | 873 1 (772 9 to 974 4)                                        | 3 007 914           | 86 783 (7681 3 to 9609 0)                                     | -0·6% (0·8 to -0·5)                                            |
| New Zealand              | 474 428             | 12 741 7 (11 255 1 to 14 393 9)                               | 697 329             | 12 745 7 (11 269 5 to 14 394 5)                               | 0%                                                            |
| Pacific                  | 9 665 737           | 4859 3 (4260 0 to 5445 7)                                     | 13 420 425          | 6 815 3 (4 635 4 to 7 973 9)                                  | 6·8% (4·2 to 10·5)                                             |
| Brunei                   | 11 549              | 5604 4 (4934 7 to 6 319 3)                                    | 24 969              | 5 577 8 (4 912 0 to 6 295 9)                                  | -0·5% (0·6 to -0·3)                                            |
| Japan                    | 6 716 173           | 4371 1 (3824 9 to 4928 2)                                     | 8 450 935           | 4 840 7 (3 852 5 to 5 975 7)                                  | 0·7% (0·6 to 0·8)                                              |
| Singapore                | 220 335             | 6667 7 (5824 8 to 75 684 6)                                   | 475 987            | 681 5 7 (5 397 3 to 6 768 5)                                  | 1·8% (1·7 to 6·2)                                              |
| South Korea              | 2 717 470           | 6 269 0 (5 570 0 to 7 057 5)                                  | 4 961 715           | 6841 5 (6 140 3 to 7 501 0)                                   | 7·6% (1·1 to 16·6)                                             |
| High income North America| 37 381 801          | 11 708 9 (10 346 6 to 12 171 4)                               | 55 883 266          | 12 346 1 (10 975 4 to 13 857 6)                               | 5·4% (1·7 to 9·3)                                              |
| Canada                   | 3 347 774           | 10 074 9 (8 827 1 to 11 271 9)                                | 4 703 994           | 10 076 2 (8 829 7 to 11 274 4)                               | 0% (0·0 to 0·1)                                                |
| Greenland                | 6094                | 10 095 6 (9 621 3 to 12 286 9)                                | 7 514              | 10 889 0 (9 606 9 to 12 280 0)                                | -0·2% (0·4 to 0·1)                                             |
| USA                      | 342 277 096         | 11 888 2 (10 502 3 to 13 327 0)                               | 5 117 800           | 12 608 2 (11 205 8 to 14 166 5)                               | 6·1% (1·9 to 10·3)                                             |
| Southern Latin America   | 5 166 628           | 10 745 2 (9 446 4 to 12 101 4)                                | 7 895 164           | 10 742 8 (9 445 5 to 12 097 9)                                | 0% (0·0 to 0·0)                                                |
| Argentina                | 3 472 219           | 10 744 2 (9 445 3 to 12 100 2)                                | 5 185 67            | 10 743 4 (9 445 9 to 12 099 3)                                | 0% (0·0 to 0·0)                                                |
| Chile                    | 1 329 485           | 10 745 743                                                    | 2 259 677           | 10 739 8 (9 444 3 to 12 092 7)                                | -0·1% (0·0 to 0·1)                                             |
| Uruguay                  | 363 715             | 10 745 6 (9 447 8 to 12 101 5)                                | 436 480            | 10 748 8 (9 450 7 to 12 106 9)                                | 0% (0·0 to 0·0)                                                |

(Table continues on next page)
| Country          | 1990       | 2017       | Percentage change in age-standardised prevalence between 1990 and 2017 |
|------------------|------------|------------|---------------------------------------------------------------------|
| Western Europe   | 840.7      | 859.5      | 1.2% (-0.1 to 3.3)                                                   |
| Andorra          | 839.9      | 839.2      | -0.1% (-0.2 to 0.1)                                                  |
| Austria          | 984.9      | 984.4      | 0% (0-0.1)                                                           |
| Belgium          | 803.9      | 818.9      | 1.9% (-2.1 to 6.5)                                                   |
| Cyprus           | 829.4      | 828.9      | -0.2% (-0.2 to 0)                                                    |
| Denmark          | 712.7      | 690.5      | -3.1% (-9.2 to 1.2)                                                  |
| Finland          | 825.9      | 824.9      | 2.1% (-2.6 to 7.1)                                                   |
| France           | 698.0      | 698.0      | 0% (-0.1 to 0.1)                                                     |
| Germany          | 696.4      | 728.5      | 5.5% (+0.6 to 16.2)                                                  |
| Greece           | 1297.0     | 1297.9     | 0% (0-0.1)                                                           |
| Iceland          | 542.7      | 551.7      | 1.7% (-2.6 to 6)                                                     |
| Ireland          | 839.2      | 839.4      | 0% (-0.1 to 0.1)                                                     |
| Israel           | 710.4      | 731.0      | 0% (-0.1 to 0.1)                                                     |
| Italy            | 1109.2     | 1109.3     | 0% (-0.1 to 0.1)                                                     |
| Luxembourg       | 839.4      | 839.2      | 0% (-0.2 to 0.1)                                                     |
| Malta             | 839.2      | 839.3      | 0% (-0.2 to 0.1)                                                     |
| Netherlands      | 754.1      | 754.0      | 0% (-0.1 to 0.1)                                                     |
| Norway           | 766.4      | 779.2      | 1.7% (-1.7 to 4.8)                                                   |
| Portugal         | 821.8      | 821.9      | 0% (0-0.1)                                                           |
| Spain            | 802.6      | 802.6      | 0% (0-0.1)                                                           |
| Sweden           | 921.3      | 980.1      | 6.4% (2.1 to 11.6)                                                   |
| Switzerland      | 771.6      | 664.0      | 0% (-0.1 to 0.1)                                                     |
| UK               | 853.8      | 992.0      | 1.6% (-1.5 to 5.1)                                                   |
| Latin America    | 1296.5     | 1288.9     | -0.6% (-1.6 to 0.4)                                                  |
| Andean Latin America | 1268.9  | 1268.3     | 0% (-0.1 to 0.1)                                                     |
| Bolivia          | 1268.2     | 1268.2     | 0% (0-0.1)                                                           |

(Table continues on next page)
| Country          | Cases (95% UI) | Age-standardised prevalence per 100 000 population (95% UI) | Cases (95% UI) | Age-standardised prevalence per 100 000 population (95% UI) | Percentage change in age-standardised prevalence between 1990 and 2017 |
|------------------|----------------|-------------------------------------------------------------|----------------|-------------------------------------------------------------|---------------------------------------------------------------|
| Ecuador          | 984,351        | 12,682.9                                                    | 2,062,720      | 12,682.2                                                    | 0%                                                            |
| Peru             | 2,150,754      | 12,682.9                                                    | 4,139,252      | 12,682.2                                                    | 0%                                                            |
| Caribbean        | 3,991,532      | 12,682.9                                                    | 6,277,903      | 12,683.0                                                    | 0%                                                            |
| Antigua and      | 749            | 12,682.4                                                    | 12,936         | 12,682.0                                                    | 0%                                                            |
| Barbuda          | 629,103        | 11,167.9 to 14,257.0                                        | 11,409.0 to 14,580 | 11,166.3 to 14,258.6                                      | 0%                                                            |
| The Bahamas      | 28,921         | 12,682.6                                                    | 52,211         | 12,682.8                                                    | 0%                                                            |
| Barbados         | 34,005         | 12,682.6                                                    | 47,091         | 12,682.9                                                    | 0%                                                            |
| Belize           | 16,515         | 12,681.3                                                    | 45,096         | 12,683.3                                                    | 0%                                                            |
| Bermuda          | 8677           | 12,682.6                                                    | 11,187         | 12,682.2                                                    | 0%                                                            |
| Cuba             | 1,420,211      | 12,681.4                                                    | 1,844,304      | 12,683.6                                                    | 0%                                                            |
| Dominica         | 8456           | 12,681.2                                                    | 9926           | 12,683.4                                                    | 0%                                                            |
| Dominican Republic| 710,149       | 12,681.9                                                    | 1,322,819      | 12,683.3                                                    | 0%                                                            |
| Grenada          | 16,676         | 12,681.0                                                    | 15,811         | 12,683.7                                                    | 0%                                                            |
| Guyana           | 7,113          | 12,682.9                                                    | 91,162         | 12,683.7                                                    | 0%                                                            |
| Haiti            | 595,300        | 12,682.4                                                    | 128,410        | 12,683.6                                                    | 0%                                                            |
| Jamaica          | 252,206        | 12,682.5                                                    | 377,853        | 12,682.9                                                    | 0%                                                            |
| Puerto Rico      | 465,500        | 12,682.7                                                    | 594,095        | 12,682.9                                                    | 0%                                                            |
| Saint Lucia      | 13,799         | 12,682.4                                                    | 25,659         | 12,683.2                                                    | 0%                                                            |
| Saint Vincent    | 11,076         | 12,681.1                                                    | 15,994         | 12,683.4                                                    | 0%                                                            |
| and the          |                |                                                             |                |                                                            |                                                              |
| Grenadines       |                |                                                             |                |                                                            |                                                              |
| Suriname         | 42,715         | 12,684.1                                                    | 76,193         | 12,682.7                                                    | 0%                                                            |
| Trinidad and     | 1,356,196      | 12,682.9                                                    | 208,364        | 12,683.2                                                    | 0%                                                            |
| Tobago           | 1,048,878      | 12,682.9                                                    | 184,208        | 12,683.2                                                    | 0%                                                            |
| Virgin Islands   | 11,234         | 12,682.1                                                    | 16,639         | 12,683.2                                                    | 0%                                                            |
| Central Latin     | 16,202,918     | 12,901.9                                                    | 32,927,601     | 12,901.7                                                    | 0%                                                            |
| America          | (14,490,377)   | (14,430,5 to 14,518.0)                                      | (29,125,287 to 37,092,301) | (14,433,0 to 14,518.0)                                      | (0 to 0.1)                                                    |
| Colombia         | 3,838,979      | 12,682.7                                                    | 6,718,862      | 12,682.2                                                    | 0%                                                            |
| Costa Rica       | 315,341        | 12,680.0                                                    | 643,481        | 12,682.8                                                    | 0%                                                            |
| El Salvador      | 502,274        | 12,682.4                                                    | 761,814        | 12,682.5                                                    | 0%                                                            |
| Guatemala        | 689,797        | 12,682.9                                                    | 1,846,653      | 12,683.1                                                    | 0%                                                            |

(Table continues on next page)
|           | 1990 | 2017 | Percentage change in age-standardised prevalence between 1990 and 2017 |
|-----------|------|------|------------------------------------------------------------------|
|           | Cases (95% UI) | Age-standardised prevalence per 100 000 population (95% UI) | Cases (95% UI) | Age-standardised prevalence per 100 000 population (95% UI) |
| (Continued from previous page) | | | | |
| Honduras | 393 181 | 12 682 8 | 1 007 462 | 12 682 6 |
| Mexico | 9 462 821 | 13 119 0 | 16 678 596 | 13 119 3 |
| Nicaragua | 219 914 | 12 682 5 | 737 071 | 12 683 3 |
| Panama | 255 097 | 12 683 3 | 505 780 | 12 683 3 |
| Venezuela | 1 891 125 | 12 682 9 | 4 028 482 | 12 682 9 |
| Tropical Latin America | 16 898 751 | 13 152 4 | 31 295 753 | 12 958 9 |
| Brazil | (14 716 683 to 19 258 614) | (13 956 9 to 14 827 0) | (27 528 37 to 35 334 444) | (11 348 2 to 14 600 6) |
| Paraguay | 299 068 | 13 021 6 | 842 300 | 12 021 6 |
| North Africa and Middle East | 30 409 759 | 11 977 8 | 68 737 046 | 12 008 5 |
| Afghanistan | 866 025 | 11 910 9 | 2 484 705 | 11 894 7 |
| Algeria | 2 171 467 | 11 895 3 | 4 877 477 | 11 897 1 |
| Bahrain | 34 061 | 11 824 | 204 219 | 11 813 5 |
| Egypt | 5 809 584 | 11 895 4 | 10 119 981 | 11 891 0 |
| Iran | 5 001 252 | 12 351 3 | 11 052 904 | 12 365 1 |
| Iraq | 1 400 026 | 11 887 5 | 4 177 739 | 11 888 3 |
| Jordan | 27 1457 | 10 863 8 | 1 011 184 | 10 821 9 |
| Kuwait | 189 295 | 11 833 1 | 577 936 | 11 875 4 |
| Lebanon | 365 936 | 11 904 5 | 952 420 | 11 892 0 |
| Libya | 352 363 | 11 864 1 | 815 503 | 11 888 0 |
| Morocco | 2 381 645 | 11 901 6 | 4 308 151 | 11 899 2 |
| Palestine | 155 922 | 11 906 3 | 458 141 | 11 891 5 |
| Oman | 169 998 | 11 810 6 | 577 981 | 11 785 3 |
| Qatar | 50 998 | 11 772 7 | 388 768 | 11 753 4 |
| Saudi Arabia | 1 606 688 | 11 599 5 | 5 270 480 | 14 934 5 |
| Sudan | 1 667 811 | 11 904 5 | 3 527 829 | 11 908 6 |
| Syria | 992 553 | 11 894 2 | 1 869 431 | 11 895 6 |
| Tunisia | 812 012 | 11 900 3 | 1 507 001 | 11 902 3 |

(continued from next page)
### Articles

| Region                  | 1990 (Continued from previous page) | 2017 | Percentage change in age-standardised prevalence between 1990 and 2017 |
|------------------------|-------------------------------------|------|---------------------------------------------------------------------|
|                        | Cases (95% UI) | Age-standardised prevalence per 100 000 population (95% UI) | Cases (95% UI) | Age-standardised prevalence per 100 000 population (95% UI) |                                                      |
|                        | (Continued from previous page) | | | |                                                      |
| Turkey                 | 5610 (409) | 11 627 3 | | 10 364 102 | | 0.7% (-3.0 to 4.7) |
| United Arab Emirates   | 202 (16) | 11 774 0 | | 1 483 707 | | -0.1% (-4.0 to 2.0) |
| Yemen                  | 975 454 (852 148 to 1 115 838) | 11 897 0 | | 2 633 288 | | 0% (-0.1 to 0.1) |
| Samoa                  | 6542 (751 to 7 329 513) | 7 780 9 | | 125 641 877 (109 874 703 to 14 166 532) | 7 626 3 | | -2.0% (-8.8 to 1.2) |
| South Asia             | Bangladesh | 3 892 280 (5 086 564 to 7 466 810) | 8 100 8 | | 11 129 522 (10 392 671 to 13 146 219) | 8 104 5 | | 0% (-0.2 to 0.2) |
|                        | Bhutan     | 3 014 15 (26 154 to 34 504) | 7 751 7 | | 68 868 | | 0% (-0.2 to 0.2) |
|                        | India      | 4 282 902 (45 742 767 to 59 502 412) | 6 794 8 | | 98 695 062 (86 507 971 to 111 701 091) | 7 555 9 | | -2.5% (-6.5 to 1.5) |
|                        | Nepal      | 105 570 (919 017 to 1 399 947) | 7 716 3 | | 2 035 175 (1 777 735 to 2 391 353) | 7 716 5 | | 0% (-0.2 to 0.2) |
|                        | Pakistan   | 5 788 273 (5 050 852 to 6 549 723) | 7 712 7 | | 12 913 254 (11 215 751 to 14 697 558) | 7 716 8 | | 0% (-0.1 to 0.1) |
|                        |            | 108 018 49 (93 904 101 to 123 102 854) | 682 5 | | 175 090 32 (153 995 489 to 196 638 213) | 684 2 | | -0.3% (0.0 to 0.6) |
| Southeast Asia, east Asia, and Oceania | East Asia | 78 509 585 (68 321 008 to 89 300 084) | 654 8 | | 121 776 73 (106 423 295 to 136 940 451) | 653 1 | | 0.3% (-0.6 to 0.1) |
|                        | China      | 74 123 916 (64 440 571 to 84 473 388) | 666 4 | | 115 635 108 (100 599 950 to 129 193 020) | 648 9 | | -0.4% (-0.7 to 0.1) |
|                        | North Korea | 1 415 675 (1 238 275 to 1 608 966) | 7 095 0 | | 2 153 622 (1 897 013 to 2 433 680) | 7 101 7 | | 0.1% (-0.1 to 0.3) |
|                        | Taiwan (Province of China) | 1 662 905 (1 464 259 to 1 864 376) | 8 11 6 | | 2 608 24 (2 283 352 to 2 933 327) | 8 557 3 | | 5.4% (-0.0 to 11.8) |
|                        | Oceania    | 265 844 (355 046 to 418 897) | 7 564 4 | | 7 183 28 (6 788 215 to 9 050 548) | 7 545 4 | | 0% (-0.1 to 0.0) |
|                        | American Samoa | 28 48 | 7 560 8 | | 3 832 | | 7 562 3 | | 0% (-0.2 to 0.2) |
|                        | Federated States of Micronesia | 5 44 | 7 564 8 | | 6 976 | | 7 640 0 | | 0% (-0.0 to 0.0) |
|                        | Fiji       | 4 694 | 7 563 1 | | 6 675 2 | | 7 654 2 | | 0% (-0.1 to 0.1) |
|                        | Guam       | 4 965 | 7 569 1 | | 11 450 0 (10 314 0 to 14 493 0) | 7 559 6 | | 0% (-0.2 to 0.1) |
|                        | Kiribati   | 4 465 | 7 567 0 | | 13 423 | | 7 594 6 | | 0% (-0.1 to 0.1) |
|                        | Marshall Islands | 2 189 | 7 566 1 | | 3 223 2 (4 423 8) | 7 564 6 | | 0% (-0.1 to 0.1) |
|                        | Northern Mariana Islands | 7 43 | 7 575 6 | | 3 886 | | 7 660 0 | | 0% (-0.1 to 0.1) |
|                        | Papua New Guinea | 226 468 | 7 565 9 | | 5 58 4 68 | | 7 648 4 | | 0% (-0.1 to 0.1) |
|                        | Samoa      | 9 07 | 7 567 4 | | 12 365 | | 7 660 0 | | 0% (-0.1 to 0.1) |
|                        | Solomon Islands | 16 956 | 7 566 6 | | 3 74 4 | | 7 653 5 | | 0% (-0.1 to 0.1) |
|                        | Tonga      | 5 435 | 7 559 4 | | 6 848 | | 7 652 8 | | 0% (-0.1 to 0.1) |
|                        |            | (475 3 to 6 272) | (667 8 to 5 815 0) | | (599 7 to 7 756) | | (666 5 to 5 822 3) | | (0.0 to 0.2) |

(Table continues on next page)
| Region                  | Cases (95% UI) | Age-standardised prevalence per 100,000 population (95% UI) | Cases (95% UI) | Age-standardised prevalence per 100,000 population (95% UI) | Percentage change in age-standardised prevalence between 1990 and 2017 |
|-------------------------|----------------|-------------------------------------------------------------|----------------|-------------------------------------------------------------|---------------------------------------------------------------|
| Vanuatu                 | 8052           | (6979 to 9128)                                             | 17392          | (15184 to 19896)                                           | 0% (-0.1 to 0.1)                                              |
| Southeast Asia          | 29145          | (25328 to 33729)                                           | 52832          | (46066 to 59422)                                           | -0.1% (-0.1 to 0)                                             |
| Cambodia                | 534682         | (462237 to 614523)                                         | 112312         | (983024 to 1218230)                                        | 0.1% (-0.1 to 0.3)                                            |
| Indonesia               | 11878970       | (10303277 to 1363368)                                      | 20837890       | (18259685 to 23735645)                                     | 0% (0 to 0.1)                                                 |
| Laos                    | 222941         | (1951710 to 256072)                                        | 465242         | (405810 to 534147)                                         | 0% (-0.1 to 0.1)                                              |
| Malaysia                | 1080504        | (939298 to 1241568)                                        | 3264050        | (2071205 to 2680115)                                       | 0% (-0.2 to 0.7)                                              |
| Maldives                | 10930          | (9474 to 12543)                                            | 6954           | (31918 to 42835)                                           | 0% (0 to 0)                                                   |
| Mauritius               | 77469          | (67487 to 88573)                                           | 115778         | (102035 to 130232)                                         | 0% (0 to 0)                                                   |
| Myanmar                 | 2477119        | (2154301 to 283551)                                        | 399030         | (3507395 to 4511431)                                       | 0% (-0.1 to 0.1)                                              |
| Philippines             | 3609380        | (3255032 to 4145211)                                       | 7098335        | (6201752 to 8085339)                                       | 0% (-0.1 to 0.1)                                              |
| Sri Lanka               | 1155324        | (1007932 to 1232357)                                       | 1790553        | (1577425 to 2106251)                                       | 0% (-0.2 to 0.1)                                              |
| Seychelles              | 4789           | (4324 to 5613)                                             | 8576           | (7540 to 9696)                                             | 0% (0 to 0.1)                                                 |
| Thailand                | 3956064        | (344819 to 453742)                                         | 667799         | (5861268 to 7514335)                                       | 0% (0 to 0)                                                   |
| East Timor              | 42549          | (36712 to 49364)                                           | 75927          | (66294 to 86448)                                           | 0% (-0.1 to 0.1)                                              |
| Vietnam                 | 4059573        | (3532963 to 4655972)                                       | 787828         | (6924407 to 8906273)                                       | 0% (-0.1 to 0.2)                                              |
| Sub-Saharan Africa      | 33882466       | (28818455 to 37656551)                                     | 72356270       | (62882341 to 82538296)                                     | 0% (-0.1 to 0.1)                                              |
| Central sub-            | 3624034        | (3147653 to 4133745)                                       | 8416692        | (7475758 to 9601950)                                       | 0% (-0.1 to 0.1)                                              |
| Saharan Africa          | 99727          | (8796 to 11058)                                            | 99720          | (8798 to 11063)                                            | 0% (-0.1 to 0.1)                                              |
| Angola                  | 99754          | (8978 to 11068)                                            | 183208         | (1590905 to 2092591)                                       | 0% (-0.2 to 0)                                                |
| Central African Republic| 185824        | (161348 to 212145)                                         | 343986         | (298810 to 391890)                                         | 0% (-0.1 to 0.2)                                              |
| Congo                   | 163056         | (141551 to 186013)                                         | 395815         | (344838 to 449769)                                         | 0% (-0.1 to 0.1)                                              |
| Democratic Republic of  | 2499114        | (2171223 to 2848156)                                       | 506905         | (4872711 to 6397127)                                       | 0% (-0.2 to 0.2)                                              |
| the Congo               | 99722          | (8974 to 11054)                                            | 99733          | (8978 to 11073)                                            | 0% (-0.2 to 0.2)                                              |
| Equatorial              | 27965          | (24295 to 31543)                                           | 91065          | (78663 to 105171)                                          | 0% (-0.3 to 0.3)                                              |
| Guinea                  | 27965          | (24295 to 31543)                                           | 91065          | (78663 to 105171)                                          | 0% (-0.3 to 0.3)                                              |
| Gabon                   | 99722          | (8976 to 11059)                                            | 99720          | (8798 to 11125)                                            | 0% (-0.2 to 0.2)                                              |
| Eastern sub-            | 12294679       | (1067097 to 1404118)                                       | 26995872       | (2147580 to 3095077)                                       | 0% (0 to 0.1)                                                 |
| Saharan Africa          | 101499         | (8978 to 11068)                                            | 101545         | (88016 to 11070)                                           | 0% (-0.2 to 0.2)                                              |
| Burundi                 | 355257         | (308934 to 406605)                                         | 726783         | (631557 to 832364)                                         | 0% (-0.2 to 0.3)                                              |
| Comoros                 | 30327          | (26321 to 34544)                                           | 60321          | (52823 to 68115)                                           | 0% (-0.1 to 0.1)                                              |

(Table continues on next page)
| Articles |
|---------------------------------|
| 1990 | 2017 | Percentage change in age-standardised prevalence between 1990 and 2017 |
| **Cases (95% UI)** | **Age-standardised prevalence per 100 000 population (95% UI)** | **Cases (95% UI)** | **Age-standardised prevalence per 100 000 population (95% UI)** | **(Continued from previous page)** |
| **Djibouti** | 32 391 | 99768 | 95 574 | 99 786 | 0% | (-0·1 to 0·1) |
| **Eritrea** | 178 175 | 99707 | 422 713 | 99702 | 0% | (-0·1 to 0·1) |
| **Ethiopia** | 2 341 820 | 10 4401 | 71 248 84 | 10 441 | 0% | (-0·1 to 0·1) |
| **Kenya** | 1 456 981 | 10 4396 | 3 691 026 | 10 439 | 0% | (-0·1 to 0·1) |
| **Malawi** | 786 364 | 997 67 | 1 796 418 | 997 64 | 0% | (-0·1 to 0·1) |
| **Madagascar** | 2 679 142 | 451 740 | (93 552 to 544 81) | 997 5 | 0% | (-0·1 to 0·1) |
| **Malawi** | 39 752 | 997 82 | (389 4 to 1116 2) | 997 06 | 0% | (-0·1 to 0·1) |
| **Mozambique** | 1 665 221 | 997 72 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Rwanda** | 465 665 | 997 27 | (232 to 1115 2) | 997 06 | 0% | (-0·1 to 0·1) |
| **Somalia** | 451 740 | 997 5 | (94 575 to 127 368) | 997 06 | 0% | (-0·1 to 0·1) |
| **South Sudan** | 39 752 | 997 82 | (389 4 to 1116 2) | 997 06 | 0% | (-0·1 to 0·1) |
| **Tanzania** | 1 665 221 | 997 72 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Uganda** | 917 646 | 997 47 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Zambia** | 489 142 | 997 06 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **South Africa** | 1 417 764 | 997 06 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Botswana** | 88 663 | 997 4 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Botswana** | 88 663 | 997 4 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Lesotho** | 130 771 | 997 27 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Namibia** | 1 000 196 | 997 47 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **South Africa** | 1 417 764 | 997 06 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Zimbabwe** | 658 888 | 997 9 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Western sub-Saharan Africa** | 13 050 989 | 997 5 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Benin** | 300 081 | 997 27 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Burkina Faso** | 601 123 | 997 19 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Cameroun** | 683 204 | 997 06 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Cape Verde** | 2 459 335 | 997 06 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Chad** | 386 159 | 997 06 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |
| **Côte d’Ivoire** | 781 980 | 997 06 | (879 7 to 1116 3) | 997 06 | 0% | (-0·1 to 0·1) |

(The table continues on the next page.)
these disease states corresponds to one of a set of health states for which disability weights have been derived from population-based surveys. Health states describe the consequences of disease or injury in terms relevant to an individual's life, such as loss of function and pain or other symptoms. The disability weights for these health states range from 0 to 1, with 0 representing perfect health and 1 representing death. Prevalent cases in each health state are multiplied by the disability weight of that health state to calculate YLDs. In a microsimulation process, all health states for all diseases are assigned to simulants according to their point-prevalence specific to year, age, sex, and location, assuming independent probability. For simulants assigned health states for multiple diseases, YLDs are adjusted with a multiplicative function of the disability weights. YLDs due to all health states range from 0 to 1, with 0 representing no disability and 1 representing perfect health.

The prevalence of health states for gastro-oesophageal reflux disease symptoms as the proportions of cases in each of the GBD 2017 gastro-oesophageal reflux disease severities was calculated for the pooled total cases, along with standard errors based on a simple proportion model. Many studies also report the frequency of gastro-oesophageal reflux disease symptoms as the proportions of cases in each of a set of mutually exclusive and collectively exhaustive frequency categories. Examples of frequency categories include 2–6 days per week, and daily; 1–3 days per week, 4–6 days, and 0–1 days per week.

Table: Prevalence of gastro-oesophageal reflux disease in 1990 and 2017 for both sexes and all locations, with percentage change

| Country            | 1990 Cases | 1990 Age-standardised prevalence per 100,000 population | 2017 Cases | 2017 Age-standardised prevalence per 100,000 population | Percentage change in age-standardised prevalence between 1990 and 2017 |
|--------------------|------------|--------------------------------------------------------|------------|-------------------------------------------------------|-------------------------------------------------------------------|
| The Gambia         | 62,614     | 9974.4                                                 | 150,031    | 9974.4                                                 | 0%                                                                |
| Ghana              | 1,018,657  | (88,046 to 1,110,600)                                  | 2,404,418  | (87,981 to 1,117,9)                                    | 0%                                                                |
| Guinea             | 427,099    | 9974                                                  | 803,402    | 9973.6                                                 | 0%                                                                |
| Guinea-Bissau      | 63,239     | (59,230 to 67,230)                                    | 127,114    | (66,982 to 111,163)                                    | 0%                                                                |
| Liberia            | 127,277    | 9971                                                  | 229,522    | 9976.1                                                 | 0%                                                                |
| Mali               | 571,001    | (496,150 to 645,898)                                  | 1,281,127  | (87,992 to 1,116,7)                                    | 0%                                                                |
| Mauritania         | 1,415,78   | 9973.5                                                | 2,83,014   | 9973.8                                                 | 0%                                                                |
| Niger              | 481,801    | (418,426 to 549,732)                                  | 1,224,640  | (87,952 to 1,116,0)                                    | 0%                                                                |
| Nigeria            | 6,382,642  | (5,562,220 to 7,242,068)                              | 13,84,601  | (87,982 to 1,115,8)                                    | 0%                                                                |
| São Tomé and Príncipe | 8,049 | (7,025 to 9,092)                                      | 15,560     | (87,978 to 1,116,4)                                    | 0%                                                                |
| Senegal            | 485,760    | 9973.9                                                | 1,062,457  | 9973.4                                                 | 0%                                                                |
| Sierra Leone       | 268,422    | 9974.6                                                | 561,252    | 9975.3                                                 | 0%                                                                |
| Togo               | 224,534    | (194,807 to 257,389)                                  | 563,399    | 9972                                                   | 0%                                                                |

The super-regions North Africa and the Middle East and South Asia each contain only one region, which bears the same name, so these rows are not repeated. 95% UI=95% uncertainty interval.
per week, and daily; and so on. For each study, 1000 proportion draws were generated for each frequency category with a beta distribution. These proportion draws were multiplied by the assumed mean days per week symptomatic for the category (the midpoint of the range) to produce draws of the number of days per week symptomatic that were contributed by cases in that category, and these draws for proportion-weighted means were summed across categories to estimate days per week symptomatic for all cases in the study. Means and SDs of these draws were combined in a meta-analysis, and the final mean and SD were divided by seven to estimate the proportion of cases that were symptomatic on a given day, with uncertainty.

Data about severity and frequency were too sparse to adjust meta-analyses for person, place, or time, so the same pooled proportions were applied to all combinations of year, age, sex, and location.

Because a single distribution of severity and frequency was applied to calculate YLDs for all years, ages, sexes, and locations, all variation in YLDs is driven by variation in prevalence. Because fatalities related to gastro-oesophageal reflux disease are attributed to other underlyng causes of death (eg, oesophageal carcinoma), no years of life lost (YLLs) are directly estimated for gastro-oesophageal reflux disease and disability-adjusted life-years (DALYs) are equal to YLDs.

Final estimates of prevalence and YLDs were specific to year, age, sex, and location. These estimates were weighted and aggregated by the age-sex distribution of the population in the location and year to which the estimates applied to produce all-age estimates. The same year-age-sex-location-specific estimates were adjusted to the GBD reference population by direct methods as previously described to produce age-standardised estimates.

The percentage change in estimates between 1990 and 2017 was estimated by calculating the percentage change between pairs of 1000 draws from the bootstrap distributions of estimates for each year, then finding the mean and 25th and 975th ordered values of the resulting combined distribution.

At the recommendation of GBD network collaborators, as a post-hoc analysis, final age-standardised YLD rate estimates were plotted against GBD estimates of Socio-demographic Index and their relationships modelled with reduced cubic splines.

We documented each step of the GBD 2017 estimation processes, as well as data sources, in accordance with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement.

Role of the funding source
The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of
the report. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results
In our systematic review, we found 112 studies that met the inclusion criteria. Four studies used diagnostic codes to identify cases in administrative data, two studies used self-reported diagnosis, and the remainder were surveys that used symptom-based questionnaires: 27 studies used the GBD case-definition for gastro-oesophageal reflux disease, and 79 studies used one of more than 50 alternatives that differed in recall period, minimum symptom frequency, defining symptoms, or manner of scoring. Combined with data from a household survey, this strategy provided 144 location-years of prevalence data and 406 prevalence datapoints; six datapoints in young age groups in subnational locations were excluded to avoid over-estimation of pseudorandom effects, as described above. Data for the model were from six (86%) of seven GBD super-regions, 11 (52%) of 21 GBD regions, and 39 (20%) of 195 countries and territories (figure 1). No data were found for southeast Asia, Oceania, central Asia, the Caribbean, Andean Latin America, central Latin America, or any region of sub-Saharan Africa. Data counts such as these for all diseases are found in the disease-specific summaries in the methods appendix of the GBD 2017 paper on non-fatal disease burden estimation.

The estimates of age-standardised prevalence of gastro-oesophageal reflux disease for all countries and territories in GBD 2017 are presented in the table.

Mean estimates of age-standardised prevalence of gastro-oesophageal reflux disease for all locations in 2017 ranged from 4408 per 100 000 population in Japan to 14035 cases per 100 000 population in Saudi Arabia (table). Geographical variation in the age-standardised prevalence of gastro-oesophageal reflux disease in 2017 is shown in figure 2. Standardised for age, gastro-oesophageal reflux disease was most prevalent in the USA, Italy, Greece, New Zealand, and several countries in Latin America and the Caribbean (excluding southern Latin America), north Africa and the Middle East, and eastern Europe, at more than 11 000 cases per 100 000 population. Age-standardised prevalence was lowest in high-income Asia Pacific, east Asia, Iceland, France, Denmark, and Switzerland, at less than 7000 cases per 100 000 population. The ratio of age-standardised prevalence among males versus females was 1·0 globally in both 1990 and 2017, ranging from 0·98 to 1·00 across super-regions. Prevalence increased with age, peaking at age 75–79 years overall and for both sexes (18 820 [95% UI 13 770–24 000] cases per 100 000 population for both sexes combined; illustrated for each sex separately in figure 3).

The global age-standardised prevalence of gastro-oesophageal reflux disease was stable over time, at 8791 (95% UI 7772 to 9834) cases per 100 000 population in 1990 and 8819 (7781 to 9863) cases per 100 000 population in 2017, with a percentage change of 0·3% (–0·3 to 0·9).

The percentage change in age-standardised prevalence was also small, with an uncertainty interval that includes zero for all GBD regions except for high-income North America, where estimates increased by 5·4% (1·7 to 9·3), high-income Asia Pacific, where estimates increased by 6·8% (4·2 to 10·5), and Australasia, where estimates decreased by 0·6% (0·5 to 0·8). Without age standardisation, however, global all-age prevalence increased by 18·1% (15·6 to 20·4) between 1990 and 2017, from 7859 (6905 to 8851) cases per 100 000 population in 1990 to 9283 (8189 to 10 400) cases per 100 000 population in 2017. A larger increase between 1990 and 2017 was seen in the global count of prevalent cases—from 424 million (372 to 477) in 1990 to 709 million (626 to 795) in 2017, a change of 67·2% (63·8 to 70·6).

YLDs due to gastro-oesophageal reflux disease for all locations estimated in GBD 2017 are shown in the table in the appendix (pp 12–20). Globally, gastro-oesophageal reflux disease was responsible for 3·60 million (95% UI 3·22–10·19) YLDs in 1990. By 2017, this had increased to 6·8% (4·2 to 10·5). The percentage change in age-standardised prevalence was also small, with an uncertainty interval that includes zero for all GBD regions except for high-income North America, where estimates increased by 5·4% (1·7 to 9·3), high-income Asia Pacific, where estimates increased by 6·8% (4·2 to 10·5), and Australasia, where estimates decreased by 0·6% (0·5 to 0·8). Without age standardisation, however, global all-age prevalence increased by 18·1% (15·6 to 20·4) between 1990 and 2017, from 7859 (6905 to 8851) cases per 100 000 population in 1990 to 9283 (8189 to 10 400) cases per 100 000 population in 2017. A larger increase between 1990 and 2017 was seen in the global count of prevalent cases—from 424 million (372 to 477) in 1990 to 709 million (626 to 795) in 2017, a change of 67·2% (63·8 to 70·6).

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non-fatal health loss by other conditions by use of a tree map on the GBD Compare Online Hub. An increase in total YLDs over time was seen across all GBD regions, as shown in figure 4.

All-age YLD rates also increased globally, from 67 (95% UI 36 to 113) per 100,000 population in 1990 to 79 (42 to 133) per 100,000 population in 2017, an increase of 18·0% (15·5 to 20·2), and increased in each GBD super-region (data not shown). Age-standardised YLD rates, however, remained stable across that period, at 74 (40 to 126) per 100,000 population in 1990 and 75 (40 to 127) per 100,000 population in 2017, representing a 0·6% (–0·2 to 1·2) change. As seen for age-standardised prevalence, age-standardised YLD rates did not change significantly between 1990 and 2017 in most GBD regions; exceptions were high-income North America (5·3% [1·7 to 9·3]), high-income Asia Pacific (6·8% [4·1 to 10·6]), and eastern sub-Saharan Africa (0·7% [0·2 to 1·1]).

Geographical variation in age-standardised YLD rates reflects variation in prevalence. YLD rates by age also reflect variation in prevalence, with a peak rate at ages 75–79 years globally (appendix p 10). No relationship was seen between age-standardised gastro-oesophageal reflux disease YLD rate and Socio-demographic Index (appendix p 11).

Discussion
We estimated a global increase in total YLDs due to gastro-oesophageal reflux disease between 1990 and 2017, and in YLD rates in populations, but stable YLD rates when standardised to a reference age distribution. This discrepancy between a stable age-standardised YLD rate but rising all-age YLD rate over time reflects higher prevalence in older age groups and the ageing of the global population over time.13 Age-standardised prevalence of gastro-oesophageal reflux disease is estimated to be highest in the USA, Italy, New Zealand, and countries in Latin America and the Caribbean (excluding southern Latin America), north Africa and the Middle East, and eastern Europe, and lowest in high-income Asia Pacific, east Asia, and some countries in western Europe. In contrast to the global trend and most other regions, high-income North America and high-income Asia Pacific showed increases in the age-standardised YLD rate due to gastro-oesophageal reflux disease between 1990 and 2017. In these regions there could be factors contributing to increasing gastro-oesophageal reflux disease burden beyond just demographic changes. However, additional factors contributing to the changing burden in these two regions and factors associated with spatial variation in gastro-oesophageal reflux disease prevalence were not identified here. The fact that

Figure 4: Years lived with disability due to gastro-oesophageal reflux disease for all GBD regions, 1990–2017
GBD=Global Burden of Diseases, Injuries, and Risk Factors Study.
established risk factors of high BMI, alcohol, and smoking were not predictive in our model raises the question of whether spatial and temporal variation in these results is driven more by measurement error than by underlying epidemiology.

Our results are largely consistent with previous systematic reviews and one meta-analysis of gastro-oesophageal reflux disease, reporting prevalence estimates ranging from approximately 10% to 30% in the USA and the Middle East and from 3% to 8% in east Asian countries. Our regional estimates are similar to the regional pooled estimates in the meta-analysis of Eusebi and colleagues, with higher estimates in the Americas and the Middle East, and lower estimates for Asia, although GBD 2017 estimates were generally lower than Eusebi and colleagues’ estimates for near-equivalent geographies. A noteworthy difference is that Eusebi and colleagues estimated very high prevalence in South Asia, 22.1% (95% CI 11.5–35.0), well above the GBD estimate of 7.0% (95% CI 6.2–8.0), but very similar estimates in southeast Asia (7.4% vs 8.1%). These differences are likely to be due to the fact that Eusebi and colleagues did not adjust for variations in study design; more than half of the 106 studies included in Eusebi and colleagues’ regional estimates had at least one study design characteristic that would have prompted adjustment in the GBD 2017 modelling approach. These differences are consistent with Eusebi and colleagues’ finding of a lower global prevalence estimate based on only a subset of studies that met a more stringent case definition. The systematic review by El-Serag and colleagues also noted higher estimates of gastro-oesophageal reflux disease prevalence for studies published in 1995–2009 compared to studies published before 1995, although it did not report a temporal difference over time for studies published after 1995. Similarly, GBD 2017 prevalence estimates rose between 1990 and 2017, but this rise is largely attenuated with age standardisation, which is not addressed by El-Serag and colleagues. Eusebi and colleagues did not test temporal trends.

Our analysis has several limitations. The first and most important limitation is scarce input data and absence of data for many locations. Prevalence data for modelling gastro-oesophageal reflux disease total 144 location-years, similar to many chronic diseases, such as migraine headache (124 location-years of prevalence data), but substantially lower than better-studied diseases such as diabetes (2340 location-years of prevalence data). Scarcity of data restrict the precision of estimates for all locations. The absence of data for particular locations requires estimates for those locations to be determined by regional, super-regional, and global estimates. Our estimation of YLDs from prevalence data is also limited by scarce data about the distribution of symptom severity and frequency, and the resulting assumption that these distributions are the same across years, age groups, sexes, and locations. Additional data will be sought in future rounds of GBD, and additional population-based studies of gastro-oesophageal reflux disease prevalence, severity, and symptom frequency should be done, particularly in locations with few or no data.

A second data limitation is that input studies use heterogeneous study designs and are subject to potential biases that are only partially overcome in the DisMod modelling framework. Estimating fixed effects for study design characteristics in successive mixed-effects models essentially corrects for potential study-design biases on the basis of ecological comparisons, and cannot fully adjust for variation in study design if certain designs are preferentially used in some years and locations more than others. In future rounds, we should use pre-modelling adjustments for bias that use internal comparisons of case definitions from validation studies or inter-study comparisons of design features between studies that are well matched in location and time. With additional data and improved pre-modelling data adjustments, associations between gastro-oesophageal reflux disease prevalence data and established risk factors such as high BMI, obesity, and smoking should be re-evaluated, to see whether they can further strengthen predictions in data-sparse locations. Since data on gastro-oesophageal reflux disease are taken primarily from surveys, sometimes with low response rates, that were focused on gastrointestinal symptoms and potentially influenced by commercial interest, future rounds of GBD should seek data from general household surveys with high response rates, and consider adjustments to data from surveys that announce a focus on gastrointestinal symptoms (which might bias participation), have poor response rates, or are commercially sponsored.

A third limitation is that our case definition required an individual to have typical reflux symptoms at least weekly for 12 months. This definition is consistent with a published meta-analysis and similar to expert group recommendations for population-based research on gastro-oesophageal reflux disease, but might miss individuals who have appreciable symptoms over shorter periods of time, those who have atypical symptoms, and those who have asymptomatic mucosal injury and risk of complications. Future rounds of GBD should estimate burden due to these additional presentations of the disease. Conversely, symptom-based definitions might include individuals with similar symptoms not due to reflux of stomach contents, such as those with functional dyspepsia. Differences might exist in the association between symptoms and findings on diagnostic studies by location. Validation studies in representative populations should be done to estimate the predictive value of symptom-based questionnaires compared to more comprehensive and specific case definitions.

Finally, health loss due to conditions for which gastro-oesophageal reflux disease is a risk factor (such as oesophageal carcinoma) is accounted for in separate GBD estimates, but the relationship to gastro-oesophageal reflux disease should be made more explicit in future.
rounds to fully account for the effect of this disease on human health.

Our study has several strengths. We have incorporated more prevalence data sources than previously published systematic reviews and one previous meta-analysis. More importantly, GBD 2017 is, to our knowledge, the first study to apply methods of meta-regression to estimate the prevalence of gastro-oesophageal reflux disease, which offers several advantages. Rather than qualitatively assessing the differences in study design that might explain differences in estimates of epidemiological measures from diverse sources, we have accounted quantitatively for many of these important differences using fixed effects for study-level covariates. Rather than reporting estimates only for age groups, years, and locations for which prevalence data have been collected, we have generated estimates for all age groups, years, and locations, incorporating information from adjacent age groups, years, and locations to calculate the best possible prevalence estimates where no data are available. Although estimates for locations without data are less certain, they provide policy makers and other stakeholders with the best available knowledge about the possible extent of this problem, and a tool by which to gauge the value of further research on this disease relative to expenditures in other areas.

The choice of time period for GBD, 1990–2017, also offers the chance to observe trends in gastro-oesophageal reflux disease epidemiology during a period of increasing obesity prevalence. An association between obesity and gastro-oesophageal reflux disease has been observed in previous studies, suggesting that gastro-oesophageal reflux disease might rise in the 1990–2017 period. The fact that we did not see a rise in age-standardised prevalence of gastro-oesophageal reflux disease in this period does not undermine the association reported in these studies, which were done at the individual level, and could be due to data or modelling limitations (as discussed previously); it could also imply the existence of other risk factors with a large influence on global gastro-oesophageal reflux disease occurrence.

Finally, GBD 2017 is the first study to move beyond measuring gastro-oesophageal reflux disease occurrence to estimating the relative burden that gastro-oesophageal reflux disease imposes in terms of YLDs, facilitating comparison with the burden of other diseases and injuries.

In conclusion, GBD 2017 identifies gastro-oesophageal reflux disease as an important cause of non-fatal health loss, which is increasing because of its association with age and the ageing of the global population. Our estimates also show an increase in prevalence after age standardisation for some locations, but variation in age-standardised prevalence was not associated with known risk factors and might be due to measurement error we could not adjust for with current data and methods. These findings indicate that health-care systems need to be prepared to address the needs of increasing numbers of patients with gastro-oesophageal reflux disease. Further studies are needed to identify useful public health interventions. Given the costs and adverse outcomes associated with symptomatic treatment for gastro-oesophageal reflux disease (such as pulmonary infection and loss of bone-mineral density associated with long-term proton-pump inhibitor use) and the increased risk of oesophageal carcinoma in people with gastro-oesophageal reflux disease, additional large, high-quality studies of gastro-oesophageal reflux disease prevalence are needed to verify these findings. Further research is required to identify more modifiable risk factors for gastro-oesophageal reflux disease, and to develop more effective interventions to modify its established risk factors and its relationship to oesophageal carcinoma.
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Contributors
M A Dirac prepared the first draft. S Safiri and R Malekzadeh reviewed the earliest draft and provided critical feedback. All other authors provided important feedback and edits to finalise the manuscript. M A Dirac did the systematic review, did all modelling and analysis, and prepared tables and figures. D Tsoi assisted with the systematic review. S Safiri provided additional tables and figures. M Naghavi provided overall guidance. All other authors provided data, reviewed results, provided guidance on methodology, and reviewed the manuscript.

Declaration of interests
S I James reports grants from Sanofi Pasteur, outside the submitted work. All other authors declare no competing interests.

Data sharing
To download the data used in these analyses, please visit the Global Health Data Exchange.

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