# Estimation of the global prevalence of dementia in 2019 and 📵 🦒 📵 forecasted prevalence in 2050: an analysis for the Global **Burden of Disease Study 2019**





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### Summary

Background Given the projected trends in population ageing and population growth, the number of people with dementia is expected to increase. In addition, strong evidence has emerged supporting the importance of potentially modifiable risk factors for dementia. Characterising the distribution and magnitude of anticipated growth is crucial for public health planning and resource prioritisation. This study aimed to improve on previous forecasts of dementia prevalence by producing country-level estimates and incorporating information on selected risk factors.

Methods We forecasted the prevalence of dementia attributable to the three dementia risk factors included in the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019 (high body-mass index, high fasting plasma glucose, and smoking) from 2019 to 2050, using relative risks and forecasted risk factor prevalence to predict GBD risk-attributable prevalence in 2050 globally and by world region and country. Using linear regression models with education included as an additional predictor, we then forecasted the prevalence of dementia not attributable to GBD risks. To assess the relative contribution of future trends in GBD risk factors, education, population growth, and population ageing, we did a decomposition analysis.

Findings We estimated that the number of people with dementia would increase from 57.4 (95% uncertainty interval 50.4-65.1) million cases globally in 2019 to 152.8 (130.8-175.9) million cases in 2050. Despite large increases in the projected number of people living with dementia, age-standardised both-sex prevalence remained stable between 2019 and 2050 (global percentage change of 0.1% [-7.5 to 10.8]). We estimated that there were more women with dementia than men with dementia globally in 2019 (female-to-male ratio of 1.69 [1.64-1.73]), and we expect this pattern to continue to 2050 (female-to-male ratio of 1.67 [1.52-1.85]). There was geographical heterogeneity in the projected increases across countries and regions, with the smallest percentage changes in the number of projected dementia cases in high-income Asia Pacific (53% [41-67]) and western Europe (74% [58-90]), and the largest in north Africa and the Middle East (367% [329-403]) and eastern sub-Saharan Africa (357% [323-395]). Projected increases in cases could largely be attributed to population growth and population ageing, although their relative importance varied by world region, with population growth contributing most to the increases in sub-Saharan Africa and population ageing contributing most to the increases in east Asia.

Interpretation Growth in the number of individuals living with dementia underscores the need for public health planning efforts and policy to address the needs of this group. Country-level estimates can be used to inform national planning efforts and decisions. Multifaceted approaches, including scaling up interventions to address modifiable risk factors and investing in research on biological mechanisms, will be key in addressing the expected increases in the number of individuals affected by dementia.

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### Introduction

A growing body of evidence from North America and Europe suggests a decreasing trend in dementia incidence, potentially due to increases in educational attainment and improvements in the management of cardiovascular disease and its risk factors. 1-3 It remains unclear whether these trends will continue into the future or whether they extend to other geographical areas, with previous work in Japan and China suggesting increases in age-specific prevalence, which is a function of disease incidence and

duration.<sup>4,5</sup> However, all estimates agree that the absolute number of people affected by dementia will show large increases over time. 6-9 Globally, the number of people affected by dementia was estimated to have increased by 117% (95% uncertainty interval [UI] 114-121) between 1990 and 2016, largely due to population ageing.<sup>10</sup>

Demographic analyses suggest that these patterns are driven by decreases in fertility coupled with increases in life expectancy, which together lead to large changes in the age structure of the population (larger numbers of

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### Research in context

### Evidence before this study

Global efforts to summarise the prevalence and burden of dementia, including the World Dementia Report and the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD), can serve to guide resource allocation and health policy decision making. Additionally, projections of future dementia burden are essential to guide health system planning and inform research funding decisions. We searched PubMed on Oct 23, 2020, using the search terms ["dementia" OR "alzheim\*"] AND ["forecast" OR "project\*"] AND "prevalence." Of 635 articles published in English, three reported on global estimates of projected prevalence for dementia or Alzheimer's disease and 30 reported on countryspecific estimates. The three studies that calculated global estimates either assumed a constant prevalence and applied population estimates to calculate the effect of changing demographics, or used macrosimulation techniques to estimate prevalence on the basis of transition probabilities for incidence, progression of disease, and mortality. However, none of the available global studies included comprehensive country-level estimates, nor did they consider the potential effects of trends in exposure to known dementia risk factors.

### Added value of this study

This study leveraged country-specific estimates of dementia prevalence from the GBD study to project dementia prevalence globally, by world region, and at the country level. Furthermore, we incorporated information on projected trends in exposure to known dementia risk factors to understand how trends in risk factors might affect the projected number of individuals

with dementia, and did decomposition analysis to understand the drivers of forecasted changes. Our estimates of age-standardised prevalence remained stable between 2019 and 2050 (percentage change of 0.1% [95% uncertainty interval -7.5 to 10.8]), whereas the number of individuals estimated to have dementia increased considerably, from 57.4 (50.4-65.1) million cases in 2019 to 152.8 (130.8-175.9) million cases in 2050. Although we projected increases in the estimated number of individuals with dementia in every country, there was considerable variation, with the highest projected increases in regions of north Africa and the Middle East, and eastern sub-Saharan Africa.

### Implications of all the available evidence

Due to increases in population growth and population ageing, huge increases in the number of individuals affected by dementia can be expected in 2050. Given that there are currently no available disease-modifying therapies, appropriate emphasis should be placed on efforts to address known modifiable risk factors. Multimodal interventions have shown some success in delaying the rate of cognitive decline and present a promising approach to risk reduction and dementia prevention. Simultaneously, it will be necessary to plan for the expected increases in the utilisation of health and social care services and to expand resources to support caregivers of individuals with dementia. Finally, continued resources should be directed towards better understanding and characterising disease mechanisms, with the goal of developing effective therapeutic agents.

people at the oldest ages than was the case historically).<sup>11,12</sup> These changes, along with largely stable age-specific prevalence estimates and population growth, lead to large increases in the number of people affected by dementia. Given that these demographic trends are expected to continue into the future, the number of people with dementia will continue to rise.<sup>10</sup>

Additionally, evidence has emerged supporting the importance of potentially modifiable risk factors for dementia. The 2020 update to the Lancet Commission on dementia prevention, intervention, and care highlighted the evidence for 12 modifiable risk factors for dementia: low education, hypertension, hearing impairment, smoking, midlife obesity, depression, physical inactivity, diabetes, social isolation, excessive alcohol consumption, head injury, and air pollution.13 Addressing these factors through public health interventions is a pathway towards reducing disease prevalence, and future changes in modifiable risk factors might influence the trajectory of trends in age-specific prevalence. Studies have hypothesised that education and the prevalence and treatment of cardiovascular disease might be key in explaining previous and future trends in dementia prevalence.14,15 Therefore, incorporating the potential effect of changes

in risk factors should be a key component of any forecast of dementia prevalence.

The increases over time in the number of people affected by dementia accentuate the importance of not only quantifying the current burden of dementia, but also generating forecasts of the prevalence of dementia to allow for informed policy decisions, health system planning, and allocation of resources. Previous efforts to forecast the prevalence of dementia have largely either been country-specific or have predicted future global cases by simply applying global prevalence estimates to population projections. <sup>16-19</sup> Other work has applied macrosimulation techniques, using estimates of incidence, progression, and mortality, although the data requirements to fit these models are large while the evidence base for such data is sparse. <sup>20</sup>

This Article aims firstly to improve and expand on previous forecasting estimates by incorporating the estimated effect of future changes in selected modifiable risk factors and projecting dementia prevalence until 2050 globally, as well as by world region and country, and secondly to decompose the drivers of changes in dementia prevalence. This Article was produced as part of the Global Burden of Diseases, Injuries, and Risk

Factors Study (GBD) Collaborator Network and in accordance with the GBD Protocol.

### Methods

### Overview and definitions

The category of dementia, as described in this Article, is referred to under the name Alzheimer's disease and other dementias in GBD 2019. General GBD methods can be found in the GBD 2019 summary papers and in the appendix (pp 10–11). 12,21,22 The overall GBD protocol and data visualisation tools can be found online. This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER), 23 and a completed GATHER checklist is available in the appendix (pp 3–4). Flow charts summarising the methodology for the estimation of dementia prevalence from 1990 to 2019 and the projection of dementia prevalence to 2050 are available in the appendix (pp 5–6).

### Prevalence data

The reference case definitions for the estimation of dementia prevalence in the GBD studies were from the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III, DSM-III-R, DSM-IV, or DSM-5, or the International Classification of Diseases (ICD)-8, ICD-9, or ICD-10, assigned by study clinicians in representative surveys.24,25 Additional data collected using different definitions or ascertainment methods were included and were adjusted to account for bias due to differences in study characteristics. In GBD 2019, the prevalence of dementia was adjusted downwards to account for dementia that is caused by other clinical diseases (eg, clinical stroke, Parkinson's disease, Down syndrome, and traumatic brain injury).26 This correction ensures that the GBD cause list is mutually exclusive. However, dementia as described in this Article does not include this correction, because the future total burden of all dementias is of policy relevance and has been the focus of previous forecasting efforts. Therefore, estimates presented in this Article will not align with those presented in the online tools. The data sources used in this study were identified through systematic review (appendix pp 12-13) and can be downloaded from the Global Health Data Exchange.

We used a Bayesian meta-regression model, MR-BRT (Meta-Regression–Bayesian Regularised Trimmed), <sup>27</sup> to estimate the sex ratio from sex-specific data and applied this ratio to split data only reported for both sexes combined (34 studies). Additionally, we age-split data with an age range greater than 20 years using the global age pattern, estimated from all data available in narrow age bins (61 studies). To adjust for bias by study definition or characteristics, we used MR-BRT to estimate a network meta-regression model of the bias between the reference case definition and alternative criteria. This modelling framework allows for the inclusion of evidence on the association between

different alternative methods rather than limiting the analysis to data on direct comparisons between the reference criteria and each alternative criterion. We modelled the bias associated with studies that used clinical records for diagnosis, studies that used algorithms to classify dementia cases, studies that applied the National Institute on Aging–Alzheimer's Association diagnostic criteria, studies that used general practice records (eg, electronic medical records for diagnosis), and studies that used the 10/66 diagnostic algorithm.<sup>28,29</sup> We also adjusted for bias in US medical claims data but, because there was evidence of differential bias by age, we used a separate model with a spline on age to appropriately make this adjustment (appendix p 14).

### Estimation of prevalence from 1990 to 2019

used Disease Modelling Meta-Regression (DisMod-MR) 2.1,30 a Bayesian compartmental model widely used in GBD non-fatal modelling, to generate initial estimates of dementia prevalence. This model ensures consistency between the different parameters (ie, prevalence, incidence, remission, mortality) by enforcing associations in a set of differential equations. We assumed zero remission and no incidence before 40 years of age given that dementia is a progressive, chronic disease and is extremely rare before this age.31,32 The Bayesian modelling framework allows for the estimation of prevalence in locations with little or no data by leveraging information from covariates as well as priors based on the model fit from the previous higher level of the location hierarchy (ie, the prior for a specific country would be based on the model fit for the region). In locations with high-quality data for both prevalence and incidence, we found that the data on incidence combined with mortality estimates implied a higher prevalence than that observed in the data. Given that dementia incidence is probably measured with less precision because of the gradual onset of disease, we chose to retain prevalence data in our models and exclude data on incidence to improve the estimation of prevalence in this model. Although the measurement of prevalent dementia is not without error, because of the higher average disease severity among prevalent cases than among incident cases, measurement error is probably lower among prevalent cases. In this model, we used covariates of smoking prevalence and average years of education in the population aged 15 years and older to help to guide the model estimation in locations with poor-quality data or no data. We set priors on the value of the education parameter on the basis of the results of a literature meta-analysis on the relative risk of dementia for each additional year of education (appendix p 15). This prevalence model used literature data on mortality to guide initial estimates of dementia mortality, and estimates from this model served as inputs to the mortality modelling process (appendix pp 16–19).

See Online for appendix
For GBD protocol and data
visualisation tools see
http://www.healthdata.org/
qbd/2019

For the **Global Health Data Exchange** see http://ghdx.
healthdata.org/

After estimating mortality due to dementia, we ran a second DisMod-MR 2.1 model to calculate final prevalence estimates. This model included the same settings as the first model but excluded literature data on mortality and included our GBD dementia mortality estimates.

### Risk factor forecasts

We initially included the three risk factors (high bodymass index [BMI], high fasting plasma glucose, and smoking) for which sufficient evidence exists to merit inclusion as risk factors for dementia in GBD 2019. 22,33-35 However, various other risk factors have also been proposed for dementia and we tested the association between dementia prevalence and risk factor prevalence for other risks that were included in the 2020 Lancet Commission report<sup>13</sup> and are quantified within the GBD framework (low physical activity, high systolic blood pressure, low education, alcohol use, and air pollution). To quantify risk factors other than education, we used the summary exposure value (SEV), which is a risk-weighted prevalence of a given risk factor exposure, first developed for GBD 2015.36 The SEVs range from 0 to 1, with a value of 0 indicating that there is no risk (or no protection for protective risk factors) in a population and a value of 1 indicating that the entire population is at maximum risk.

To forecast SEVs from 2019 to 2050, we calculated the annualised rate of change in logit SEV for each location, age, sex, and past year. We then estimated future annualised rates of change by calculating a weighted mean of prior annualised rates over the time series. A recency weighting parameter altered how much weight is given to more recent trends versus older trends. This parameter was selected using out-of-sample predictive validity holding out the last 10 years of data available. Forecasts for this period were then used to calculate the root-mean square error, which informed the selection of weights. To reduce the effect of extreme trends in long-range forecasts, we implemented caps at the 5th and 95th percentiles of logit SEVs.

We forecasted years of education (up to a maximum of 18 years of education) using similar methods, but assumed that education does not change after 25 years of age and held education forecasts constant after 25 years of age within a given location-sex-specific birth cohort to prevent implausible within-cohort changes. These methods have been previously used in GBD forecasting papers on cause-specific mortality, and additional details can be found in these papers. <sup>37,38</sup>

# Forecasting dementia prevalence attributable to GBD risk factors

We forecasted the combined effect of the three GBD risk factors by calculating a risk factor scalar that describes the proportion of prevalence attributable to GBD risk factors. To calculate our risk factor scalar, we first estimated the population attributable fractions (PAFs) for each risk factor, using past and forecasted SEVs from 1990 to 2050

and relative risks describing the association between each risk factor and dementia, from GBD 2019.<sup>22</sup> We then estimated the joint PAF for the three risk factors, taking into account potential mediation between the interrelated risk factors. Finally, we calculated scalars specific to each forecasted year, location, age group, and sex as:

$$Scalar = \frac{1}{1 - PAF}$$

Additional details on the calculation of PAFs, risk factor mediation, and scalars can be found in the appendix (pp 21–22) or in previous GBD forecasting papers.<sup>37,38</sup>

# Forecasting dementia prevalence not attributable to GBD risk factors

We then forecasted GBD risk-deleted prevalence, calculated as the total prevalence divided by the risk factor scalar. To select the additional risk factors to include in our forecasting model, we evaluated the association between each risk factor that was both quantified within the GBD framework and included in the 2020 Lancet Commission report<sup>13</sup> (low physical activity, high systolic blood pressure, low education, alcohol use, and air pollution) and dementia prevalence (logit-transformed). We used sexstratified models, controlling for 5-year age group and world region. We decided to include covariates for which the estimated association with dementia prevalence in both men and women was significant and in the same direction as the effect reported in the Lancet Commission report.<sup>13</sup> On the basis of these criteria, we added education as a covariate in our forecasting model (appendix p 23).

We used linear regression to forecast logit-transformed GBD risk-deleted prevalence, using sex-stratified models. We included covariates for 5-year age group (reference: 40–44 years), world region (reference: Andean Latin America; appendix p 61), and education (in years), as shown in the equation below depicting the linear regression models:

$$\begin{split} & \text{Logit(prevalence)}_{\text{sex}} = \beta_0 + \beta_1 \times \text{Education} + \sum_{i=2}^{12} \beta_i \\ & \times \text{Age group}_i + \sum_{i=13}^{33} \beta_i \times \text{Region}_i + \varepsilon \end{split}$$

Because our input data on prevalence and risk factors were themselves estimates, we ran 1000 models to incorporate uncertainty from our inputs. Each model used one draw from the distribution of each input to our forecasting model. Finally, to account for trends unexplained by our covariates, we fit a random walk model (autoregressive integrated moving average [ARIMA<sub>(0,10)</sub>]) to the residuals of our regression models and added forecasts of these residuals to our estimated forecasts.

### Final prevalence forecasts

We calculated the total forecasted prevalence as the product of our forecasted prevalence not attributable to GBD risk factors and the forecasted risk factor scalar. To ensure continuity between past and future means and UIs, we intercept-shifted the forecasted draws of logit-transformed prevalence. We calculated the number of projected cases of dementia by multiplying prevalence forecasts with population forecasts, as calculated for the GBD population forecasting paper.<sup>38</sup>

### Decomposition of forecasts

To quantify the drivers of changes in the number of individuals with dementia, we estimated the relative contribution of population growth, population age structure, changes due to changes in GBD risk factor prevalence, and changes due to changes in education. For this decomposition analysis, we used methods developed by Das Gupta,<sup>39</sup> which summarise the contribution of various factors to observed changes by algebraically isolating the standardised impact of each contributing multiplicative factor.

# Quantification of SDI aggregates, age-standardisation, and uncertainty

Socio-demographic Index (SDI) is a composite indicator of total fertility rate, mean years of education in individuals older than 15 years, and lag-distributed income per capita.<sup>12</sup> Countries were assigned to an SDI quintile on the basis of their estimated values on these indicators in 2019, and these designations were used to produce aggregated estimates of dementia prevalence by SDI quintile. We calculated age-standardised rates using the GBD world population standard.12 We propagated uncertainty through all components of the analysis by sampling 1000 draws at each stage of our estimation process. UIs were defined as the 25th and 975th values of the ordered draws. A difference in two quantities was defined as significant if the 95% UI of the difference did not include zero. For our analyses, we used Stata (versions 13.1 and 15.1), Python (versions 3.6.2 and 3.6.8), and R (versions 3.4.2 and 3.5.0).

### Role of the funding source

The study funders had no role in study design, data collection, data analysis, data interpretation, or the writing of the manuscript.

### Results

We estimated a global percentage change in age-standardised both-sex dementia prevalence between 2019 and 2050 of 0.1% (95% UI -7.5 to 10.8), indicating that the global age-sex-specific prevalence of dementia is expected to remain stable. Dementia prevalence was higher in women than in men and increased with age, doubling about every 5 years until 85 years of age in both 2019 and 2050 (figure 1). In 2050, the prevalence of dementia in men globally was forecasted to be 0.5% (95% UI 0.4 to 0.7) among those aged 40–69 years, 6.5% (5.3 to 8.0) among those aged 70–84 years, and

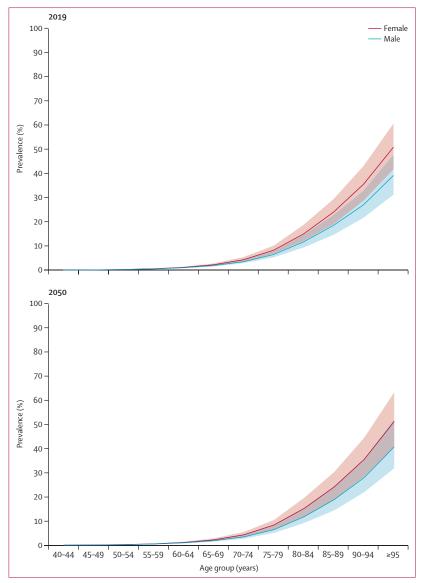


Figure 1: Global prevalence of dementia (with 95% uncertainty intervals) by age group and sex in 2019 and 2050

23.5% (19.1 to 29.2) among those aged 85 years and older. In women, the global forecast was projected to be 0.6% (0.5 to 0.8) among those aged 40–69 years, 8.5% (7.0 to 10.4) among those aged 70–84 years, and 30.5% (25.0 to 36.8) among those aged 85 years and older (figure 1).

In comparison, we estimated a much larger percentage change in all-age dementia prevalence between 2019 and 2050 (117% [95% UI 100–133]) due to population ageing, and an even larger percentage change in the all-age numbers of prevalent cases (166% [148–185]), due to a combination of population ageing and population growth (figure 2). In 2019, there were an estimated 57·4 (95% UI 50·4–65·1) million individuals living with dementia globally. We estimated that this number would increase

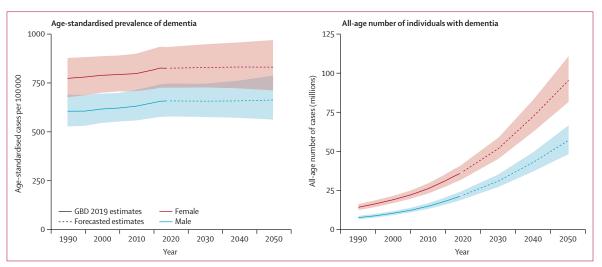


Figure 2: Estimated trends in the global age-standardised dementia prevalence (A) and all-age number of cases (B), with 95% uncertainty intervals, 2019–50 GBD=Global Burden of Diseases, Injuries, and Risk Factors Study.

to  $83\cdot2$  ( $73\cdot0-94\cdot6$ ) million individuals in 2030,  $116\cdot0$  ( $100\cdot7-132\cdot1$ ) million individuals in 2040, and  $152\cdot8$  ( $130\cdot8-175\cdot9$ ) million individuals living with dementia in 2050 (table). We estimated that there were more women with dementia than men with dementia globally in 2019 (female-to-male ratio of  $1\cdot69$  [ $1\cdot64-1\cdot73$ ]), and we expect this pattern to continue to 2050 (female-to-male ratio of  $1\cdot67$  [ $1\cdot52-1\cdot85$ ]).

The percentage change between 2019 and 2050 in total number of dementia cases was highest for the low SDI quintile (330% [95% UI 295 to 362]) and lowest for the high-middle SDI quintile (113% [93 to 134]) and high SDI quintile (140% [117 to 160]). The percentage change in age-standardised rates between 2019 and 2050 was also highest for the low SDI quintile (8 · 2% [0 · 5 to 19 · 8]). The low-middle SDI quintile (1 · 3% [-6 · 9 to 12 · 4]) had the lowest percentage change in age-standardised rates. However, the observed differences between SDI quintiles in percentage change in age-standardised rates were not significant (table).

When examining further patterns of percentage change in the number of projected dementia cases by country or world region, there was evidence of large variability in the projected increases. Although there were increases for every country, the smallest increases were projected in high-income Asia Pacific (53% [95% UI 41–67]) and western Europe (74% [58–90]), whereas the largest estimated increases were in north Africa and the Middle East (367% [329–403]) and eastern sub-Saharan Africa (357% [323–395]; figure 3; table).

The decomposition of percentage change in projected dementia cases indicated a fairly small overall effect of changing prevalence, which included an increase in prevalence due to GBD risk factors for all regions except high-income Asia Pacific, and a decrease in prevalence due to the added effect of trends in education in this analysis. The increases attributable to GBD risk factors

in most regions included the effects of increases in BMI and fasting plasma glucose, as well as less clear trends in smoking. Declines in dementia prevalence due to GBD risk factors in high-income Asia Pacific stem from expected declines in risk factor prevalence in this region. However, these effects were overwhelmed by changes due to population ageing and growth. Although at the global level population ageing and population growth contributed about equally to forecasted increases in dementia prevalence, we observed different patterns at the regional level. Whereas population growth is predicted to drive most of the increases in dementia prevalence in sub-Saharan Africa, population growth contributes to a much lesser extent in east Asia and western Europe. In central Europe, eastern Europe, and high-income Asia Pacific, anticipated declines in populations serve to partly counteract the effect of population ageing. Although population ageing is expected to lead to increases in projected dementia cases in every region, the largest projected increases due to population ageing are observed in east Asia, and north Africa and the Middle East (figure 4).

### Discussion

Most of the projected increase in the numbers of people living with dementia can be attributed to population ageing and population growth, although the relative contribution of these two factors varied across GBD world regions. By contrast, we found that country-level projected changes in age-specific or age-standardised dementia prevalence attributable to changes over time in risk factor prevalence were fairly small. In most regions, increases in age-standardised dementia prevalence due to increases in the prevalence of GBD risk factors, including BMI, fasting plasma glucose, and smoking, were counterbalanced with decreases in age-standardised prevalence due to increases in average educational attainment.

	Number of cases	Percentage change		
	2019	2050	Counts	Age-standardised rate
Global	57394906 (50380728 to 65059424)	152 811 943 (130 760 492 to 175 873 110)	166% (148 to 185)	0·1% (-7·5 to 10·8)
Low SDI	1216893 (1060042 to 1393547)	5 227 425 (4 488 746 to 6 092 498)	330% (295 to 362)	8·2% (0·5 to 19·8)
Low-middle SDI	4 452 767 (3 889 055 to 5 074 679)	15 086 525 (12 932 740 to 17 576 030)	239% (210 to 268)	1·3% (-6·9 to 12·4)
Middle SDI	10 091 960 (8 801 589 to 11 532 222)	34514380 (29282762 to 40178089)	242% (215 to 271)	7·1% (-1·6 to 19·0)
High-middle SDI	9 259 873 (8 039 014 to 10 636 963)	19700344 (16583929 to 23011962)	113% (93 to 134)	1.5% (-5.1 to 9.9)
High SDI	32 373 413 (28 631 545 to 36 610 092)	77 559 727 (65 787 984 to 90 463 680)	140% (117 to 160)	2·8% (-5·7 to 14·0)
Central Asia	436 494 (378 705 to 502 096)	1501050 (1254725 to 1773782)	244% (206 to 280)	10·3% (0·9 to 23·0)
Armenia	31 890 (27 501 to 36 767)	69 994 (55 443 to 87 569)	119% (84 to 161)	11.6% (1.5 to 24.0)
Azerbaijan	52 070 (45 063 to 59 823)	195 210 (152 079 to 242 269)	275% (208 to 344)	12.6% (1.8 to 27.0)
Georgia	46 291 (39 650 to 53 463)	78 458 (53 756 to 107 641)	70% (22 to 126)	10·7% (1·3 to 22·8)
Kazakhstan	107 698 (93 064 to 123 939)	356 674 (285 733 to 435 149)	231% (181 to 287)	9.8% (-0.1 to 22.2)
Kyrgyzstan	28 171 (24 481 to 32 273)	105 987 (85 565 to 130 209)	276% (220 to 338)	1.8% (-5.3 to 10.2)
Mongolia	10 986 (9548 to 12 630)	53 692 (41 881 to 66 919)	389% (300 to 487)	5·4% (-2·0 to 14·9)
Tajikistan	29 261 (25 457 to 33 337)	135 868 (109 121 to 167 616)	364% (293 to 436)	5·2% (-5·3 to 19·4)
Turkmenistan	22 117 (19 151 to 25 329)	96 861 (77 795 to 117 753)	338% (268 to 409)	10.0% (-1.6 to 24.9)
Uzbekistan	, ,			14·3% (2·5 to 30·5)
	108 010 (94 263 to 123 838)	408 306 (307 806 to 515 406)	278% (196 to 357)	
Central Europe	1969 960 (1700 079 to 2274 491)	3586187 (2939018 to 4280177)	82% (60 to 107)	1.4% (-5.1 to 9.6)
Albania	36 079 (31 092 to 41 597)	86733 (66 420 to 110 254)	141% (89 to 200)	8.5% (-0.4 to 19.3)
Bosnia and Herzegovina	48 081 (41 437 to 56 056)	92167 (72773 to 116 388)	92% (59 to 130)	7·7% (-2·7 to 20·9)
Bulgaria	135 285 (116 074 to 156 914)	185719 (145 989 to 230 430)	37% (14 to 63)	-0·1% (-7·2 to 7·7)
Croatia	83 429 (71 139 to 97 166)	129 479 (101 243 to 158 966)	55% (32 to 82)	0.8% (-7.7 to 11.2)
Czech Republic	192748 (164883 to 223173)	379 742 (313 505 to 453 786)	97% (72 to 126)	3·4% (-4·4 to 12·8)
Hungary	183 870 (157 845 to 213 183)	295 379 (238 639 to 361 018)	61% (38 to 85)	-1·5% (-8·1 to 6·0)
Montenegro	8247 (7088 to 9583)	14870 (11535 to 18690)	80% (50 to 115)	5·3% (-2·9 to 15·2)
North Macedonia	28 279 (24 324 to 32 878)	75 147 (62 224 to 89 882)	166% (133 to 205)	7·0% (-1·7 to 18·2)
Poland	663 408 (573 431 to 766 171)	1323739 (1052220 to 1608391)	100% (70 to 132)	-1.6% (-8.6 to 6.8)
Romania	341195 (291477 to 395164)	577 177 (466 820 to 696 706)	69% (47 to 93)	3·3% (-5·1 to 12·8)
Serbia	129 117 (110 961 to 149 416)	178 262 (142 370 to 222 173)	38% (18 to 60)	3·2% (-5·0 to 13·1)
Slovakia	77 185 (66 652 to 89 480)	163 037 (132 519 to 195 206)	111% (84 to 142)	1·2% (-5·5 to 9·0)
Slovenia	43 038 (36 793 to 50 186)	84735 (69 330 to 101 544)	97% (73 to 122)	2·9% (-4·1 to 11·3)
Eastern Europe	2 907 654 (2 509 228 to 3 349 800)	5591863 (4403039 to 6883544)	92% (58 to 127)	3·1% (-2·5 to 9·8)
Belarus	137 286 (117 896 to 158 209)	245 114 (193 199 to 303 605)	79% (47 to 111)	2·8% (-4·1 to 10·9)
Estonia	26710 (22672 to 31012)	48 807 (37 612 to 61 074)	83% (50 to 122)	7.7% (-0.5 to 18.1)
Latvia	38 907 (33 450 to 45 208)	57 136 (42 067 to 74 344)	47% (13 to 85)	3·7% (-3·6 to 12·7)
Lithuania	56 244 (47 804 to 65 483)	81 237 (63 019 to 101 071)	44% (19 to 70)	0·2% (-6·1 to 7·3)
Moldova	46 924 (40 603 to 54 020)	119 453 (94 246 to 149 879)	155% (107 to 207)	8.8% (-0.2 to 20.3)
Russia	1 949 811 (1 679 013 to 2 243 097)	4032 617 (3 036 325 to 5 108 853)	107% (62 to 155)	4·0% (-2·3 to 11·2)
Ukraine	651773 (559 460 to 754347)	1007 499 (775 208 to 1304 708)	55% (24 to 91)	-1·4% (-6·6 to 4·1)
Australasia	414 288 (361 823 to 472 380)	945 658 (780 004 to 1117 118)	128% (105 to 153)	0.3% (-8.0 to 10.5)
		796 702 (656 789 to 944 398)		- ,
Australia Now Zooland	348 673 (304 883 to 398 147)		128% (104 to 153)	-0.2% (-8.5 to 9.9)
New Zealand	65 616 (56 674 to 75 685)	148 956 (121 688 to 177 915)	127% (103 to 155)	1.0% (-7.2 to 11.3)
High-income Asia Pacific	4839076 (4175048 to 5562598)	7 421 319 (6 290 211 to 8 711 763)	53% (41 to 67)	-10·9% (-16·4 to -4·3
Brunei	1574 (1374 to 1795)	7317 (6133 to 8717)	365% (314 to 420)	-7·3% (-15·6 to 2·3)
Japan	4117308 (3528130 to 4752471)	5 237 201 (4 376 503 to 6 191 162)	27% (16 to 39)	-8·3% (-14·7 to -1·7)
South Korea	671 288 (593 383 to 759 915)	1954016 (1649586 to 2318128)	191% (157 to 229)	-12·2% (-19·5 to -4·1
Singapore	48 906 (43 164 to 55 374)	222784 (187231 to 264640)	356% (303 to 413)	-5·1% (-13·5 to 5·5)

	Number of cases	Percentage change		
	2019	2050	Counts	Age-standardised rat
(Continued from p	previous page)			
High-income North America	5 856 696 (5 417 356 to 6 362 004)	11 830 056 (10 436 624 to 13 286 322)	102% (83 to 122)	0·5% (-8·5 to 12·1)
Canada	587 364 (513 628 to 665 177)	1308143 (1092204 to 1555797)	123% (98 to 151)	-2·4% (-11·8 to 10
Greenland	439 (382 to 508)	1447 (1174 to 1740)	229% (186 to 277)	4·1% (-4·7 to 16·0
USA	5 2 6 8 8 9 3 (4 8 9 8 9 4 3 to 5 7 1 4 1 4 0)	10 520 259 (9 316 869 to 11777 173)	100% (80 to 120)	0·7% (-8·5 to 12·5
Southern Latin America	634348 (546426 to 731042)	1468705 (1203709 to 1775598)	131% (106 to 160)	4·0% (-5·0 to 15·9
Argentina	412 268 (354 720 to 473 783)	892 180 (726 352 to 1078 782)	116% (89 to 147)	4·3% (-5·5 to 16·8
Chile	174 921 (151 480 to 201 357)	491 617 (399 004 to 604 396)	181% (144 to 222)	2·4% (-6·2 to 14·
Uruguay	47 160 (40 364 to 54718)	84842 (66762 to 105314)	80% (52 to 111)	7·7% (-2·5 to 21·2
Western Europe	7860682 (6799340 to 9053849)	13 642 589 (11 417 565 to 16 153 469)	74% (58 to 90)	-1·6% (-8·4 to 7·7
Andorra	1066 (926 to 1220)	2897 (2376 to 3463)	172% (143 to 200)	0.0% (-7.7 to 10.0
Austria	146 391 (125 797 to 168 938)	309 629 (250 432 to 372 437)	111% (89 to 137)	8-4% (-0-8 to 20-
Belgium	190 477 (161 979 to 220 869)	330 572 (272 158 to 399 548)	73% (58 to 93)	-4·5% (-12·2 to 5·
Cyprus	14143 (12108 to 16320)	38 840 (31 358 to 47 469)	175% (139 to 215)	-1·1% (-8·3 to 7·8
Denmark	81 923 (70 840 to 93 957)	137 508 (112 574 to 166 054)	68% (48 to 91)	-6·5% (-15·2 to 4·
Finland	97 549 (83 238 to 113 043)	154 002 (126 428 to 184 870)	58% (40 to 79)	-1·5% (-9·3 to 8·3
France	1203439 (1032014 to 1392214)	2191307 (1809791 to 2657863)	82% (62 to 102)	1.8% (-7.1 to 13.
Germany	1691221 (1477093 to 1944181)	2796783 (2168685 to 3527605)	65% (35 to 101)	1.8% (-6.5 to 13.
Greece	206 366 (174 643 to 240 487)	298 617 (237 117 to 371 264)	45% (24 to 67)	-1·7% (-10·6 to 9·
Iceland	4222 (3646 to 4842)	10 019 (8368 to 11 863)	137% (115 to 163)	-3·0% (-12·5 to 7·
Ireland	53 932 (46 375 to 62 488)	142 416 (119 268 to 170 671)	164% (136 to 195)	-1·5% (-11·1 to 11
Israel	85 869 (74 010 to 99 187)	210 339 (173 516 to 250 735)	145% (120 to 171)	-2·2% (-10·7 to 7·2
Italy	1487368 (1270750 to 1726466)	2316951 (1895878 to 2770019)	56% (41 to 73)	-5·2% (-12·4 to 3·
Luxembourg	6583 (5708 to 7534)	16 797 (13 947 to 19 856)	155% (131 to 183)	1.2% (-9.0 to 13.
Malta	6651 (5714 to 7728)	11 674 (9515 to 14 061)	76% (53 to 100)	-2·4% (-10·2 to 7·
Netherlands	277 262 (241 522 to 316 994)	493 122 (414 048 to 591 597)	78% (58 to 99)	-6·3% (-14·3 to 3·
Norway	75 301 (65 103 to 86 442)	149 264 (123 996 to 176 637)	98% (80 to 118)	-4·8% (-10·6 to 1·
Portugal	200 994 (171 278 to 233 809)	351 504 (284 708 to 420 991)	75% (55 to 97)	-0·7% (-8·5 to 9·4
Spain	826 686 (734 234 to 937 050)	1516523 (1290677 to 1764312)	83% (67 to 101)	-4·4% (-12·5 to 7·2
Sweden	153 805 (132 692 to 176 783)	249 290 (208 673 to 298 769)	62% (46 to 79)	-2·3% (-9·8 to 7·4
Switzerland	142 105 (121 551 to 164 647)	307 925 (255 333 to 365 367)	117% (99 to 138)	0·3% (-7·4 to 9·7
UK	907 331 (784 009 to 1 045 033)	1592475 (1320026 to 1912805)	75% (58 to 95)	-2·4% (-11·7 to 9·
Andean Latin America	328 296 (287 528 to 373 369)	1150 562 (958 542 to 1376 098)	250% (208 to 294)	7·8% (-0·9 to 19·
Bolivia	43 829 (38 130 to 50 090)	136 892 (112 902 to 164 437)	212% (172 to 260)	6·5% (-2·4 to 18·
Ecuador	87769 (76 477 to 100 216)	268 822 (211 958 to 329 156)	206% (160 to 255)	5·9% (-3·1 to 17·3
Peru	196 699 (172 549 to 224 224)	744 847 (599 223 to 902 865)	279% (222 to 338)	8-8% (-0-7 to 22-2

Our estimate for the global number of dementia cases in 2050 is similar to previous estimates from the World Alzheimer Report 2019 (152 million cases), 40 but much higher than previous estimates of the forecasted global prevalence from work done by Brookmeyer and colleagues (106.8 million cases [95% UI 47.2–221.2]). 20 The estimates from Brookmeyer and colleagues were only for Alzheimer's disease, which constitutes a subset of the total prevalence of dementia, and therefore it is expected that these estimates would be lower than the ones presented here. Due to the high prevalence of mixed pathologies among dementia cases and potential

unknown differences in the distribution of underlying causes of dementia across geographical locations, the larger total dementia category is more relevant for the global study of dementia.<sup>41</sup>

Consistent with previous reports, 10,17 we estimated that there were more women with dementia than men with dementia in 2019, and our analysis indicated that this pattern would continue in 2050. These patterns exist despite the larger prevalence of vascular risks in men than in women, suggesting potentially strong counteracting mechanisms driving these inequities. Although the sex difference can be explained in part by higher life

Antigua and Barbuda The Bahamas 1920 (1) Barbados 3023 (2) Belize 1366 (2) Bermuda 865 (7) Cuba 116 055 (2) Dominica 574 (4) Dominican 51735 (4) Cuba 128 (5) Dominican 51735 (4) Dominican 1058 (5) Guyana 2805 (7) Haiti 26 215 (7) Jamaica 17 937 (7) Puerto Rico 51 313 (4) Saint Lucia 1217 (7) Saint Vincent 830 (7) Saint Vincent 830 (7) Trinidad and 10 194 (8) Tobago Virgin Islands 10 39 (8) Central Latin 1336 442 (7) America Colombia 36 9 422 (7) Costa Rica 32 637 (7) El Salvador 36 675 (7) Guatemala 60 721 (8) Honduras 32 371 (7) Mexico 596 202 (8) Nicaragua 28 540 (7) Panama 26 527 (7)	256 420 to 331 563) 516 to 673)	2050	Counts	Age-standardised rate
Caribbean         291 809 (2)           Antigua and Barbuda         592 (5)           The Bahamas         1920 (3)           Barbados         3023 (3)           Belize         1366 (3)           Bermuda         865 (7)           Cuba         116 055 (3)           Dominica         574 (4)           Dominican         51735 (4)           Republic         Grenada         1058 (5)           Guyana         2805 (3)           Haiti         26 215 (2)           Jamaica         17 937 (3)           Puerto Rico         51 313 (4)           Saint Lucia         1217 (3)           Saint Vincent and the Grenadines         300 (7)           Suriname         3070 (2)           Trinidad and Tobago         10 194 (8)           Virgin Islands         1039 (8)           Central Latin         1336 442 (3)           America         Colombia         36 942 (2)           Costa Rica         32 637 (3)           El Salvador         36 675 (3)           Guatemala         60 721 (5)           Honduras         32 371 (2)           Mexico         596 202 (5)           Nicaragua         28 540 (2) <th></th> <th></th> <th></th> <th>Age-staridardiscu rate</th>				Age-staridardiscu rate
Antigua and Barbuda The Bahamas 1920 (3 Barbados 3023 (3 Belize 1366 (3 Bermuda 865 (7 Cuba 116 055 (3 Dominica 574 (4 Dominican 51735 (4 Bermuda 2805 (3 Haiti 26 215 (3 Jamaica 17 937 (3 Jamaica 17 937 (3 Saint Lucia 1217 (3 Saint Vincent and the Grenadines Suriname 3070 (7 Trinidad and Tobago Virgin Islands 103 (4 (4 (2 Karbusta) 13 (4 (4 (4 (4 (4 (4 Karbusta) 13 (4 (4 (4 (4 (4 (4 (4 (4 (4 (4 (4 (4 (4				
Barbuda The Bahamas 1920 (1) Barbados 3023 (2) Belize 1366 (3) Belize 1366 (5) Bermuda 865 (7) Cuba 116 055 (2) Dominica 574 (4) Dominican 51735 (4) Republic Grenada 1058 (9) Guyana 2805 (2) Haiti 26 215 (2) Jamaica 17 937 (2) Puerto Rico 51 313 (4) Saint Lucia 1217 (1) Saint Vincent 830 (7) and the Grenadines Suriname 3070 (2) Trinidad and 10 194 (8) Tobago Virgin Islands 1039 (8) Central Latin 1336 442 (2) America Colombia 369 422 (3) Costa Rica 32 637 (2) El Salvador 36 675 (3) Guatemala 60 721 (5) Honduras 32 371 (2) Mexico 596 202 (5) Nicaragua 28 540 (2) Panama 26 527 (2)	516 to 673)	744761 (619 430 to 885 112)	155% (126 to 186)	2·0% (-5·7 to 11·9)
Barbados 3023 (2 Belize 1366 (2 Bermuda 865 (2 Cuba 116 055 (3 Dominica 574 (4 Dominican 51735 (4 Republic Grenada 1058 (5 Guyana 2805 (2 Haiti 26 215 (2 Jamaica 17 937 (2 Jamaica 17937 (3 Saint Lucia 1217 (3 Saint Vincent 830 (7 and the Grenadines Suriname 3070 (2 Trinidad and 10 194 (8 Tobago Virgin Islands 1039 (8 Central Latin 1336 442 (3 America 26 25 (2 Costa Rica 32 637 (3 El Salvador 36 675 (3 Guatemala 60 721 (5 Honduras 32 371 (3 Mexico 596 202 (5 Nicaragua 28 540 (3 Panama 26 527 (3		1815 (1497 to 2163)	207% (174 to 245)	8.8% (-0.1 to 20.1)
Belize 1366 (2 Bermuda 865 (7 Cuba 116 055 (2) Dominica 574 (4 Dominican 51735 (4 Republic Grenada 1058 (5 Guyana 2805 (2) Haiti 26 215 (2) Jamaica 17 937 (2) Puerto Rico 51 313 (4 Saint Lucia 1217 (2) Saint Vincent 830 (7 and the Grenadines Suriname 3070 (2) Trinidad and 10 194 (8) Tobago Virgin Islands 1039 (8) Central Latin 1336 442 (2) America 26 26 27 (2) El Salvador 36 675 (2) Guatemala 60 721 (5) Honduras 32 371 (2) Mexico 596 202 (5) Nicaragua 28 540 (2) Panama 26 527 (2)	1685 to 2183)	6268 (5081 to 7683)	226% (180 to 277)	2·9% (-4·5 to 12·2)
Bermuda 865 (7 Cuba 116 055 (2 Dominica 574 (4 Dominican 51735 (4 Republic Grenada 1058 (9 Guyana 2805 (2 Haiti 26 215 (7 Jamaica 17 937 (7 Puerto Rico 51 313 (4 Saint Lucia 1217 (1 Saint Vincent 830 (7 and the Grenadines Suriname 3070 (7 Trinidad and 10 194 (8 Trinidad and 10 194 (8 Tobago Virgin Islands 1336 442 (7 America Colombia 369 422 (3 Costa Rica 32 637 (7 El Salvador 36 675 (3 Guatemala 60 721 (9 Honduras 32 371 (7 Mexico 596 202 (9 Nicaragua 28 540 (7 Panama 26 527 (7)	2619 to 3476)	5731 (4693 to 6990)	89% (66 to 114)	-0·2% (-6·3 to 7·8)
Cuba 116 055 (2 Dominica 574 (4 Dominican 574 (4 Dominican 51735 (4 Republic Grenada 1058 (5 Guyana 2805 (2 Haiti 26 215 (2 Jamaica 17 937 (2 Puerto Rico 51 313 (4 Saint Lucia 1217 (2 Saint Vincent and the Grenadines Suriname 3070 (2 Trinidad and 10 194 (8 Tobago Virgin Islands 1039 (8 Central Latin 1336 442 (2 America 26 26 27 (2 El Salvador 36 675 (3 Guatemala 60 721 (5 Guatemala 60 721 (5 Honduras 32 371 (2 Mexico 596 202 (5 Nicaragua 28 540 (2 Panama 26 527 (2)	1193 to 1547)	6213 (5027 to 7505)	355% (293 to 420)	7·5% (-1·4 to 19·8)
Dominica 574 (4 Dominican 51735 (4 Republic Grenada 1058 (5 Guyana 2805 (2 Haiti 26 215 (2 Jamaica 17 937 (3 Puerto Rico 51 313 (4 Saint Lucia 1217 (3 Saint Vincent and the Grenadines Suriname 3070 (3 Trinidad and 10 194 (8 Tobago Virgin Islands 1039 (8 Central Latin 1336 442 (3 America 26 32 (3) Costa Rica 32 637 (3 El Salvador 36 675 (3) Guatemala 60 721 (5) Honduras 32 371 (3) Mexico 596 202 (5) Nicaragua 28 540 (3) Panama 26 527 (3)	750 to 994)	2066 (1723 to 2437)	139% (113 to 166)	2·4% (-4·7 to 9·9)
Dominican Republic  Grenada  1058 (s Guyana  2805 (2 Haiti  26 215 (2 Jamaica  Puerto Rico  Saint Lucia  Saint Vincent and the Grenadines  Suriname  Trinidad and Tobago  Virgin Islands  Central Latin  America  Colombia  Costa Rica  El Salvador  Guatemala  Honduras  Mexico  Panama  51735 (4 2805 (2) 28540	102 392 to 131 211)	259 547 (206 790 to 320 644)	124% (89 to 165)	-1·9% (-10·3 to 8·1)
Republic  Grenada 1058 (s. Guyana 2805 (c. Guyana 2805 (c. Jamaica 17937 (c. Jamaica 17937 (c. Jamaica 1217 (c. Saint Lucia 1217 (c. Saint Vincent and the Grenadines Suriname 3070 (c. Trinidad and Tobago Virgin Islands 10194 (c. Jamaica 1336 442 (c. Jamaica 133	497 to 658)	999 (834 to 1194)	74% (56 to 94)	6-3% (-3-0 to 18-6)
Guyana 2805 (2  Haiti 26 215 (2  Jamaica 17 937 (2)  Puerto Rico 51 313 (4  Saint Lucia 1217 (2  Saint Vincent and the Grenadines  Suriname 3070 (2  Trinidad and Tobago  Virgin Islands 10 194 (8  Central Latin 1336 442 (2  America 26 32 (3)  Costa Rica 32 637 (2  El Salvador 36 675 (3)  Guatemala 60721 (8)  Honduras 32 371 (2  Mexico 596 202 (8)  Nicaragua 28 540 (2)  Panama 26 527 (2)	45 434 to 58 660)	149 178 (119 437 to 184399)	188% (143 to 239)	7·3% (-4·1 to 22·6)
Haiti 26215 (2) Jamaica 17937 (2) Puerto Rico 51313 (4) Saint Lucia 1217 (2) Saint Vincent and the Grenadines Suriname 3070 (2) Trinidad and 10194 (3) Tobago Virgin Islands 1039 (4) Central Latin 1336 442 (2) America Colombia 369 422 (3) Costa Rica 32 637 (2) El Salvador 36 675 (3) Guatemala 60721 (5) Honduras 32 371 (2) Mexico 596 202 (5) Nicaragua 28 540 (2) Panama 26 527 (2)	900 to 1239)	1743 (1417 to 2102)	65% (46 to 86)	6·4% (-2·9 to 18·3
Jamaica 17 937 (2) Puerto Rico 51313 (4) Saint Lucia 1217 (2) Saint Vincent and the Grenadines Suriname 3070 (2) Trinidad and 10 194 (8) Tobago Virgin Islands 1036 442 (2) America Colombia 36 9 422 (3) Costa Rica 32 637 (3) El Salvador 36 675 (3) Guatemala 60 721 (5) Honduras 32 371 (2) Mexico 596 202 (5) Nicaragua 28 540 (2) Panama 26 527 (3)	2448 to 3179)	8799 (6635 to 11290)	214% (143 to 293)	9·8% (0·4 to 22·1)
Puerto Rico 51313 (4) Saint Lucia 1217 (7) Saint Vincent and the Grenadines Suriname 3070 (7) Trinidad and 10 194 (8) Tobago Virgin Islands 1036 442 (7) America Colombia 369 422 (7) Costa Rica 32 637 (7) Guatemala 60 721 (8) Honduras 32 371 (7) Mexico 596 202 (8) Panama 26 527 (7)	22 676 to 30 173)	83761 (67 453 to 102 671)	219% (171 to 274)	0·4% (-5·5 to 7·7)
Saint Lucia 1217 (2 Saint Vincent and the Grenadines Suriname 3070 (2 Trinidad and 10 194 (8) Tobago Virgin Islands 1036 442 (2) America Colombia 36 9 422 (3) Costa Rica 32 637 (3) El Salvador 36 675 (3) Guatemala 60 721 (5) Honduras 32 371 (2) Mexico 596 202 (5) Nicaragua 28 540 (2) Panama 26 527 (3)	15 630 to 20 448)	40 797 (30 753 to 52 364)	127% (81 to 177)	2·9% (-6·4 to 15·6
Saint Vincent and the Grenadines  Suriname 3070 (2  Trinidad and 10 194 (8  Tobago Virgin Islands 1336 442 (3  America Colombia 369 422 (3  Costa Rica 32 637 (3  El Salvador 36 675 (3  Guatemala 60 721 (9  Honduras 32 371 (2  Mexico 596 202 (9  Nicaragua 28 540 (2  Panama 26 527 (3	44 429 to 58 540)	105 338 (84 370 to 127 371)	105% (75 to 142)	5·1% (-2·7 to 14·3)
and the Grenadines  Suriname  3070 (2  Trinidad and Tobago  Virgin Islands  1036 442 (3  America  Colombia  369 422 (3  Costa Rica  El Salvador  Guatemala  Honduras  Mexico  See 202 (5  Nicaragua  Panama  300 (2)  300 (3)  300 (	1058 to 1396)	3314 (2693 to 3984)	172% (139 to 209)	1.6% (-5.6 to 11.4
Trinidad and Tobago Virgin Islands 10 194 (8 10 194) Virgin Islands 10 199 (8 10 194) Central Latin 1336 442 (1 194) America Colombia 36 9 422 (1 194) Costa Rica 32 637 (1 194) El Salvador 36 675 (1 194) Guatemala 60 721 (8 194) Honduras 32 371 (1 194) Mexico 596 202 (8 194) Panama 26 527 (1 194)	723 to 954)	1921 (1550 to 2373)	131% (97 to 170)	10.6% (0.3 to 24.4)
Tobago Virgin Islands 1039 (8 Central Latin America Colombia Costa Rica El Salvador Guatemala Honduras Mexico Sp6 202 (9 Nicaragua Panama 1036 442 (1) 136 142 (1) 136 142 (1) 136 142 (1) 136 142 (1) 137 142 (	2673 to 3508)	8843 (6838 to 11139)	188% (137 to 250)	6·3% (-4·3 to 19·5
Central Latin     1336 442 (3)       America     369 422 (3)       Colombia     369 422 (3)       Costa Rica     32 637 (3)       El Salvador     36 675 (3)       Guatemala     60 721 (5)       Honduras     32 371 (2)       Mexico     596 202 (5)       Nicaragua     28 540 (2)       Panama     26 527 (2)	8906 to 11 620)	29 968 (22 350 to 38 589)	194% (126 to 267)	3.0% (-4.7 to 11.5)
America  Colombia 369 422 (3  Costa Rica 32 637 (3  El Salvador 36 675 (3  Guatemala 60721 (5  Honduras 32 371 (7  Mexico 596 202 (5  Nicaragua 28 540 (7  Panama 26 527 (7)	899 to 1192)	1680 (1367 to 2052)	62% (39 to 87)	8-3% (-0-4 to 19-5
Costa Rica 32 637 (2 El Salvador 36 675 (3 Guatemala 60721 (5 Honduras 32 371 (2 Mexico 596 202 (5 Nicaragua 28 540 (2 Panama 26 527 (2	1166 913 to 1523738)	4532279 (3777 037 to 5372 328)	239% (202 to 277)	1.7% (-5.6 to 10.6
El Salvador 36 675 (3 Guatemala 60721 (5 Honduras 32 371 (2 Mexico 596 202 (5 Nicaragua 28 540 (2 Panama 26 527 (3	321 596 to 420 670)	1375 881 (1099 923 to 1666 047)	272% (219 to 333)	3·1% (-5·5 to 13·9)
Guatemala 60721 (£ Honduras 32371 (£ Mexico 596 202 (£ Nicaragua 28540 (£ Panama 26527 (£	28 575 to 37 017)	114 227 (92 564 to 137 653)	250% (200 to 299)	2·4% (-6·1 to 13·0
Honduras 32371 (2 Mexico 596 202 (5 Nicaragua 28 540 (2 Panama 26 527 (2	31 852 to 42 157)	88 198 (68 336 to 110 623)	140% (92 to 190)	8-4% (-1-2 to 21-8)
Mexico         596 202 (5           Nicaragua         28 540 (2           Panama         26 527 (2	52 642 to 70 077)	238 013 (187 528 to 296 739)	292% (221 to 366)	12·2% (0·9 to 28·0)
Nicaragua 28 540 (2 Panama 26 527 (2	28 168 to 37 050)	109 116 (89 822 to 133 872)	237% (190 to 288)	5·2% (-3·9 to 17·3)
Panama 26 527 (2	519 647 to 681 934)	1843 049 (1507 097 to 2231 411)	209% (168 to 256)	-2·2% (-9·1 to 5·5)
	25 020 to 32 451)	116 953 (96 199 to 138 362)	310% (262 to 361)	6.6% (-3.1 to 18.8
Vanaruala 153345 (1	23 122 to 30 302)	99 043 (79 933 to 120 285)	273% (221 to 331)	12·0% (-1·3 to 29·2)
veriezueia 153 345 (J	134 849 to 173 312)	547798 (429 118 to 673 874)	257% (193 to 325)	1·3% (-7·3 to 12·2)
Tropical Latin 1887784 (1 America	1663243 to 2140431)	5786 996 (4830 039 to 6888 937)	207% (167 to 251)	-1.6% (-10.6 to 8.9
Brazil 1849 981 (1	1630321 to 2097631)	5 666 116 (4722 302 to 6738 480)	206% (166 to 251)	-1·9% (-11·0 to 8·6
Paraguay 37 803 (3	32 992 to 43 043)	120 880 (95 942 to 150 443)	220% (162 to 285)	-0.4% (-10.0 to 11.1

expectancy in women than in men, previous evidence also suggests potential sex differences in the biological mechanisms that underlie Alzheimer's disease.<sup>42,43</sup>

We predicted that population ageing and population growth will drive enormous increases in the number of individuals affected by dementia both regionally and globally. The consequences of these increases are compounded by the high societal and monetary costs of the disease. Given the current absence of available effective disease-modifying treatments for dementia, immediate efforts to reduce these projected increases will need to target disease prevention through

interventions for modifiable risk factors. 46,47 Our analysis suggested that there would not be large changes in age-specific dementia prevalence due to changes in risk factor prevalence, based on the continuation of previous trends in the population-level exposure to educational attainment, BMI, fasting plasma glucose, and smoking. However, interventions that alter the expected trends in risk factor prevalence might reduce the expected future prevalence of dementia. Results from the 2020 update to the *Lancet* Commission on dementia prevention, intervention, and care suggest that up to 40% of dementia prevalence might be preventable through interventions

	Number of cases			
	2019	2050	Counts	Age-standardised rate
(Continued from pre	evious page)			
North Africa and Middle East	2 962 640 (2 583 925 to 3 377 445)	13 832 847 (11 816 689 to 15 945 101)	367% (329 to 403)	5·4% (-3·5 to 17·2)
Afghanistan	55734 (48 041 to 64 424)	288 376 (237 496 to 350 721)	417% (350 to 485)	18·1% (5·5 to 34·9)
Algeria	250 509 (216 675 to 286 620)	1118 628 (928 381 to 1318 929)	347% (298 to 399)	9·3% (-3·2 to 25·0)
Bahrain	5126 (4500 to 5832)	60 650 (50 530 to 71 633)	1084% (927 to 1243)	1·2% (-8·1 to 11·4
Egypt	305 675 (270 740 to 346 640)	1530167 (1228884 to 1858374)	401% (321 to 482)	10·5% (-1·8 to 26·6
Iran	524457 (455729 to 600 058)	2 188 336 (1 826 920 to 2 598 034)	317% (274 to 369)	7·3% (-2·8 to 19·5
Iraq	159 548 (138 599 to 182 752)	1050756 (881154 to 1225100)	559% (483 to 643)	-5·7% (-13·3 to 3·5
Jordan	37 373 (32 500 to 43 146)	232 594 (186 892 to 281 471)	522% (437 to 606)	1.6% (-8.4 to 13.2
Kuwait	18 001 (15 760 to 20 412)	171 121 (143 406 to 200 674)	850% (754 to 946)	0.4% (-8.4 to 10.9
Lebanon	45 952 (40 149 to 52 642)	187 024 (158 959 to 219 882)	307% (269 to 351)	11·5% (0·4 to 25·3)
Libya	29 286 (25 486 to 33 426)	128 595 (100 400 to 161 805)	339% (264 to 418)	-0.5% (-10.9 to 12
Morocco	225 682 (196 500 to 260 413)	826 320 (675 460 to 989 097)	266% (220 to 312)	11·0% (-1·0 to 27·2
Oman	11 965 (10 398 to 13 630)	124 803 (104 609 to 149 126)	943% (812 to 1080)	5.6% (-6.8 to 22.1
Palestine	16 173 (14 130 to 18 487)	79 811 (65 643 to 95 431)	393% (334 to 454)	1·1% (-9·0 to 14·1
Qatar	4201 (3665 to 4814)	85 046 (69 847 to 101 841)	1926% (1624 to 2235)	2·2% (-7·8 to 12·8
Saudi Arabia	85735 (74 923 to 97 360)	855760 (714919 to 1021030)	898% (789 to 1016)	9·4% (-2·3 to 23·3
Sudan	115705 (100 676 to 132 536)	633 251 (521 059 to 754 760)	447% (383 to 511)	15·7% (2·1 to 33·0)
Syria	85 971 (74 907 to 98 724)	366 323 (296 122 to 440 646)	326% (264 to 388)	-2·4% (-10·8 to 7·4
Tunisia	95 059 (82 275 to 109 286)	329 849 (259 371 to 402 301)	247% (195 to 308)	6.0% (-5.3 to 19.8
Turkey	803590 (696792 to 918286)	3 031 455 (2 477 722 to 3 603 133)	277% (229 to 330)	0.5% (-9.4 to 11.3
United Arab Emirates	11711 (10 166 to 13 478)	221 672 (174 599 to 283 193)	1795% (1382 to 2265)	0·7% (-9·9 to 12·9
Yemen	75 189 (65 552 to 86 510)	309 394 (231 977 to 390 266)	311% (216 to 395)	6.5% (-2.7 to 18.5
outh Asia	4876300 (4220657 to 5599132)	15 070 552 (12 509 797 to 17 939 166)	209% (176 to 245)	6·2% (-2·9 to 19·3
Bangladesh	570 899 (496 938 to 659 613)	2 020 081 (1 650 451 to 2 447 563)	254% (205 to 304)	3·7% (-4·7 to 15·3
Bhutan	2588 (2244 to 2970)	11668 (9759 to 13719)	351% (302 to 403)	9·2% (-0·7 to 24·0
India	3843118 (3329923 to 4414367)	11 422 692 (9 367 149 to 13 833 711)	197% (160 to 238)	6·4% (-3·6 to 20·4
Nepal	85 635 (74 287 to 98 355)	265 658 (216 849 to 320 886)	210% (169 to 259)	4·0% (-7·8 to 19·6
Pakistan	374 060 (326 782 to 429 775)	1350453 (1083452 to 1668674)	261% (205 to 317)	2·7% (-6·5 to 15·8
ast Asia	15 801 493 (13 821 683 to 18 083 556)	47 361 122 (38 293 892 to 56 536 958)	200% (161 to 235)	4.0% (-6.0 to 17.0
China	15 330 045 (13 401 824 to 17 569 373)	45 538 093 (36 763 912 to 54 489 693)	197% (159 to 233)	3·7% (-6·6 to 16·9
North Korea	192152 (166006 to 223420)	415 335 (323 416 to 531 013)	116% (78 to 165)	-7·0% (-12·5 to -0·
Taiwan (province of China)	279 296 (255 558 to 305 494)	644733 (547 990 to 755 399)	131% (101 to 161)	-5·7% (-14·4 to 4·0
)ceania	21822 (19048 to 24912)	84753 (69511 to 101441)	288% (237 to 341)	3.8% (-2.9 to 13.2
American Samoa	191 (166 to 220)	622 (509 to 753)	226% (188 to 268)	4·0% (-3·5 to 13·2
Fiji	3125 (2719 to 3563)	8107 (6268 to 10 222)	159% (109 to 215)	2·3% (-6·1 to 12·8
Guam	1044 (909 to 1194)	2980 (2420 to 3619)	185% (145 to 230)	6·7% (-1·2 to 16·4
Kiribati	255 (221 to 293)	772 (617 to 967)	203% (157 to 260)	2·1% (-5·6 to 12·7
Marshall Islands	108 (94 to 124)	417 (325 to 522)	285% (214 to 362)	9·5% (0·4 to 21·3)
Federated States of Micronesia	281 (245 to 320)	904 (728 to 1090)	222% (176 to 269)	3·1% (-5·2 to 13·9
Northern Mariana Islands	246 (215 to 279)	1147 (932 to 1381)	366% (303 to 436)	3.6% (-4.1 to 13.4
Papua New Guinea	13 460 (11717 to 15 447)	55 964 (44 852 to 68 164)	316% (251 to 383)	3·9% (-3·2 to 13·7
Samoa	692 (602 to 799)	1658 (1318 to 2050)	139% (102 to 183)	-0·2% (-8·4 to 9·5)
Solomon Islands	1276 (1116 to 1466)	4549 (3702 to 5521)	256% (210 to 305)	6.9% (-2.5 to 19.5
Tonga	447 (388 to 515)	1059 (872 to 1276)	137% (107 to 167)	2·9% (-5·6 to 13·5
Vanuatu	696 (602 to 805)	1903 (1565 to 2282)	174% (139 to 207)	6.8% (-2.0 to 18.5
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	Number of cases		Percentage change	
	2019	2050	Counts	Age-standardised rates
(Continued from pre	evious page)			
Southeast Asia	3 126 758 (2 736 119 to 3 566 647)	10 574 716 (9 000 551 to 12 307 479)	238% (207 to 269)	4·0% (-4·6 to 17·2)
Cambodia	55 230 (47 880 to 63 067)	207 476 (173 504 to 246 671)	276% (235 to 320)	7.0% (-4.4 to 22.9)
Indonesia	987 673 (860 373 to 1126 148)	3399 285 (2 879 466 to 3 994 398)	244% (210 to 280)	7·3% (-3·0 to 21·5)
Laos	19 370 (16 867 to 22 070)	87 292 (72 799 to 104 356)	351% (304 to 400)	10·7% (-0·9 to 26·4)
Malaysia	142 172 (124 189 to 163 480)	495 842 (411 045 to 596 328)	249% (207 to 293)	1.5% (-8.3 to 13.7)
Maldives	1703 (1480 to 1948)	11135 (9290 to 13157)	554% (486 to 635)	4·8% (-6·0 to 19·8)
Mauritius	9833 (8638 to 11249)	27 056 (21706 to 33 294)	175% (131 to 223)	2·7% (-7·4 to 14·8)
Myanmar	228 825 (200 081 to 262 541)	726358 (598 408 to 865 404)	217% (182 to 259)	2·5% (-8·4 to 17·6)
Philippines	328 852 (286 204 to 375 815)	969 025 (770 021 to 1223 981)	195% (142 to 251)	-1.8% (-8.9 to 7.1)
Seychelles	607 (528 to 691)	1598 (1312 to 1915)	163% (135 to 196)	-0.7% (-10.2 to 10.3)
Sri Lanka	146778 (127 955 to 168 267)	475 050 (374 248 to 599 464)	224% (166 to 289)	6.9% (-3.6 to 21.3)
Thailand	670 047 (590 205 to 759 861)	2391672 (1973 046 to 2864 142)	257% (207 to 311)	2·1% (-8·0 to 15·7)
Timor-Leste	4036 (3480 to 4639)	12 124 (9963 to 14 527)	201% (160 to 244)	3·2% (-4·9 to 14·5)
Vietnam	531 633 (462 526 to 604 039)	1756 890 (1459 362 to 2079 348)	230% (194 to 266)	3·1% (-7·0 to 17·1)
Central sub- Saharan Africa	228 263 (198 193 to 261 421)	985 553 (792 176 to 1 192 065)	332% (262 to 402)	3·4% (-3·8 to 13·0)
Angola	46 598 (40 335 to 53 877)	250 926 (204 456 to 306 412)	439% (357 to 520)	8-3% (-1-5 to 22-3)
Central African Republic	8207 (7177 to 9434)	24731 (17314 to 34890)	201% (115 to 306)	-1·2% (-7·6 to 6·8)
Congo (Brazzaville)	11 538 (10 409 to 12 751)	47 842 (35 289 to 64 009)	315% (210 to 431)	1.9% (-8.1 to 14.1)
DR Congo	153 708 (133 011 to 176 719)	626 362 (471 561 to 787 957)	308% (220 to 396)	1·1% (-6·8 to 10·4)
Equatorial Guinea	2416 (2086 to 2778)	14438 (11553 to 17658)	498% (399 to 600)	8.0% (-2.7 to 22.2)
Gabon	5796 (5033 to 6680)	21 254 (17 326 to 25 715)	267% (218 to 317)	6·7% (-4·1 to 20·9)
Eastern sub- Saharan Africa	659 471 (575 759 to 755 115)	3 011 820 (2 579 860 to 3 508 755)	357% (323 to 395)	7·5% (-0·4 to 19·3)
Burundi	14791 (12 946 to 16 923)	57 936 (43 752 to 73 814)	292% (212 to 380)	-1.6% (-6.6 to 3.8)
Comoros	2074 (1810 to 2389)	6757 (5201 to 8596)	226% (161 to 299)	-1·1% (-8·0 to 6·8)
Djibouti	2085 (1821 to 2383)	11 937 (9646 to 14 655)	473% (382 to 571)	9·2% (-1·1 to 23·1)
Eritrea	7666 (6628 to 8826)	34 048 (25 632 to 44 102)	344% (244 to 457)	-0.5% (-7.5 to 8.4)
Ethiopia	174 023 (150 855 to 200 051)	945 224 (796 227 to 1112 239)	443% (387 to 501)	8-9% (0-9 to 21-5)
Kenya	86 815 (75 493 to 99 319)	361 042 (299 955 to 429 552)	316% (272 to 365)	3·7% (-5·1 to 15·3)
Madagascar	37 380 (32 571 to 43 031)	159725 (122 529 to 205 672)	327% (237 to 425)	1.8% (-6.2 to 11.6)
Malawi	36 636 (31 524 to 42 617)	132 360 (105 569 to 160 851)	261% (206 to 320)	6·7% (-1·9 to 18·8)
Mozambique	43 083 (37 458 to 49 507)	181519 (145133 to 225 939)	321% (248 to 392)	11·8% (1·3 to 26·5)
Rwanda	24705 (21 429 to 28 401)	124755 (101 000 to 150739)	405% (330 to 483)	4·8% (-4·0 to 17·2)
Somalia		62 012 (45 851 to 80740)	185% (120 to 259)	-1·1% (-6·0 to 4·3)
	21758 (18783 to 25194)	,	, , , , , , , , , , , , , , , , , , , ,	
South Sudan	14107 (12290 to 16137)	69 983 (53 255 to 87 649)	396% (297 to 498)	11·4% (3·3 to 21·4)
Uganda	58 045 (50 363 to 66 863)	273 221 (225 592 to 330 531)	371% (303 to 440)	10.0% (-0.9 to 24.5)
Tanzania	110 250 (97 219 to 124 082)	469767 (393 407 to 556 700)	326% (272 to 383)	8.9% (-1.4 to 23.4)
Zambia	26 055 (22 661 to 29 816)	119 644 (96 970 to 144 675)	359% (296 to 431)	3.6% (-4.6 to 14.6)
Southern sub- Saharan Africa	291518 (253 868 to 333 957)	830 974 (652 402 to 1050 035)	185% (133 to 243)	1·7% (-6·2 to 11·4)
Botswana	6737 (5847 to 7720)	26 873 (21 406 to 33 078)	299% (235 to 364)	6.0% (-5.7 to 19.8)
Eswatini	2416 (2087 to 2806)	6950 (5149 to 9148)	188% (121 to 264)	0.7% (-7.4 to 10.1)
Lesotho	5312 (4591 to 6097)	10726 (7577 to 14607)	102% (47 to 169)	10·2% (-1·1 to 24·4)
Namibia	7738 (6686 to 8923)	25 993 (20 376 to 32 595)	236% (172 to 308)	0·1% (-7·9 to 9·7)
South Africa	241 937 (210 294 to 277 409)	680 045 (514 016 to 882 003)	181% (121 to 250)	1·0% (-7·3 to 11·1)
Zimbabwe	27 377 (23 716 to 31 626)	80 386 (52 705 to 111 531)	194% (100 to 295)	2·4% (-6·8 to 13·1)
			(Table	e continues on next page)

	2019	2050	Counts	Age-standardised rat
		2050	Counts	Age-standardised rat
Continued from p	revious page)			
Vestern sub- Jaharan Africa	663 109 (580 172 to 757 219)	2 971 613 (2 479 440 to 3 541 678)	348% (292 to 404)	8-2% (0-1 to 19-1)
Benin	17 550 (15 411 to 20 147)	76 035 (63 139 to 90 660)	333% (279 to 389)	7·9% (-2·0 to 20·5
Burkina Faso	33793 (29276 to 38647)	136726 (113069 to 164640)	305% (252 to 360)	13·2% (3·7 to 27·1)
Cape Verde	2546 (2197 to 2927)	8324 (6959 to 9857)	227% (192 to 267)	12·2% (-0·7 to 29·2
Cameroon	41181 (35745 to 47 081)	172 812 (138 989 to 210 888)	320% (255 to 389)	5·8% (-3·2 to 17·2
Chad	20 134 (17 569 to 23 061)	75 448 (59 705 to 93 987)	275% (204 to 347)	9·4% (1·3 to 20·1)
Côte d'Ivoire	34 438 (30 002 to 39 416)	178 367 (143 742 to 216 796)	418% (342 to 489)	8.5% (0.1 to 19.9)
The Gambia	3796 (3280 to 4390)	12887 (10686 to 15460)	240% (199 to 281)	6-9% (-2-2 to 19-6
Ghana	57 276 (49 942 to 65 600)	240708 (199701 to 288 987)	320% (271 to 375)	15·0% (2·2 to 31·4)
Guinea	21227 (18 523 to 24 293)	61 087 (50 105 to 73 039)	188% (151 to 222)	10.8% (2.4 to 21.7)
Guinea-Bissau	2271 (1981 to 2619)	9487 (7644 to 11 487)	318% (258 to 377)	5·9% (-1·5 to 15·8
Liberia	7084 (6171 to 8125)	31 859 (24 087 to 40 485)	350% (253 to 441)	7·6% (-2·5 to 21·4
Mali	31 455 (27 298 to 36 114)	138 631 (114 835 to 166 676)	341% (286 to 400)	11·9% (3·2 to 23·7)
Mauritania	8404 (7354 to 9634)	34368 (28252 to 41619)	309% (258 to 367)	8.8% (0.6 to 19.3
Niger	26 476 (23 097 to 30 336)	122 138 (97 425 to 150 149)	362% (286 to 440)	8·2% (1·7 to 17·2)
Nigeria	300 332 (262 100 to 341 329)	1462514 (1169996 to 1804298)	387% (300 to 473)	7·1% (-2·1 to 18·0
São Tomé and Príncipe	418 (362 to 480)	1535 (1259 to 1850)	267% (220 to 324)	11·1% (-0·1 to 26·1
Senegal	29 539 (25 705 to 33 689)	107 492 (88 966 to 129 398)	264% (219 to 310)	7·7% (-0·3 to 18·2
Sierra Leone	12 993 (11 252 to 14 966)	45 849 (37 580 to 55 292)	253% (203 to 303)	6·9% (-2·0 to 20·0
Togo	12 196 (10 648 to 13 964)	55318 (44644 to 66974)	354% (287 to 425)	4·9% (-3·9 to 16·3
I=Socio-demograpl	nic Index.			

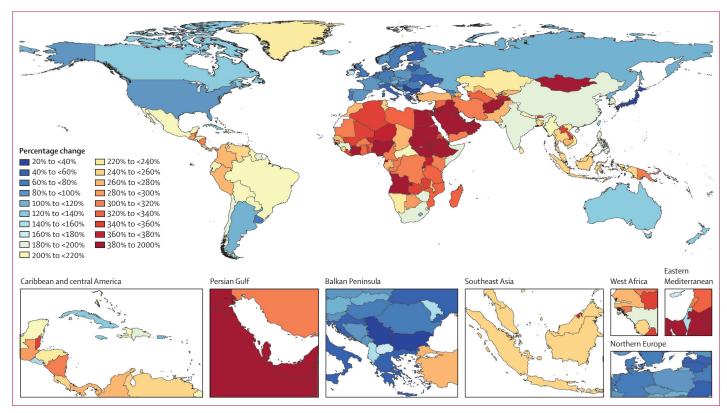
targeting modifiable risk factors.<sup>13</sup> This conclusion suggests that large changes in the exposure distributions of modifiable risk factors (ie, decreases in harmful risk factors and increases in protective factors) have the potential to considerably change our forecasted estimates and reduce the future burden of disease.

The 2019 guidelines on dementia risk reduction from WHO further highlight potential interventions that might help to reduce the projected increases in dementia prevalence.<sup>48</sup> However, these guidelines focus primarily on individual-level interventions. Our results indicate that there are differences in the estimated change in agestandardised prevalence rates across SDI quintiles, and suggest that structural inequalities must also be addressed to tackle the observed disparities.

Our estimates can be used to plan for increases in the anticipated resources and support that will be needed by individuals with dementia and their caregivers in the future. Currently, many shortcomings exist in the identification, treatment, and care of individuals with dementia globally. Lower diagnosis rates in low-income settings than in high-income settings and gaps in the availability of resources for the management of neuropsychiatric symptoms of dementia will be important to address.<sup>49–51</sup> Evidence suggests that hospitalisation rates are higher among those with dementia than among

those without dementia, and health systems need to be prepared for the expected increases in service use that will accompany increases in the number of people with dementia.52 High rates of comorbidity with many other chronic diseases further complicate the care required for individuals with dementia and underscore the need to appropriately plan for the health-care needs of this population.53 Furthermore, although large gaps currently exist in the availability of quality end-of-life care for individuals with dementia, such care can positively affect both individuals with dementia and their caregivers. 54,55 Therefore, efforts should be made to provide these services and scale up available resources to meet the needs of individuals with dementia in the future. The effect on the increasing numbers of caregivers that will be needed to support growing numbers of people with dementia should also be considered, and evidence-based interventions to support caregivers should be part of any comprehensive plan to address increases in dementia prevalence.56

Our study had some limitations. The methodology for forecasting prevalence due to GBD risk factors using PAFs relies on the assumptions of the PAF calculation—in particular, the assumption that risks examined are causally related to dementia. To the extent that the estimated relative risks reflect non-causal increases or



 $\textit{Figure 3:} \ Percentage \ change \ between \ 2019 \ and \ 2050 \ in \ all-age \ number \ of \ individuals \ with \ dementia \ by \ country$ 

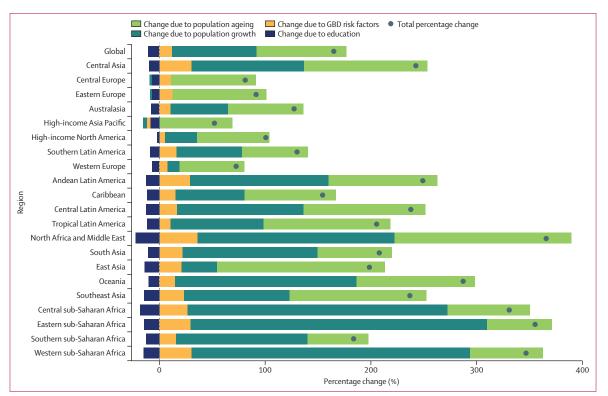


Figure 4: Decomposition of percentage change in the number of individuals with dementia between 2019 and 2050 globally and by world region GBD=Global Burden of Diseases, Injuries, and Risk Factors Study.

decreases in risk, this assumption might be violated. Our estimates of dementia prevalence from the GBD study are based on sparse and heterogeneous data because of the absence of standardised methodologies for measuring dementia in population-based studies.10 When no data existed, we relied on the Bayesian framework of the DisMod-MR 2.1 and assumed that prevalence could be explained using regional estimates of prevalence adjusted by covariate values. Although there is no available gold standard to which we can judge the validity of our estimates, our global estimates are very similar to those from other efforts, such as the World Alzheimer Report.40 Furthermore, some of the geographical heterogeneity observed could be due to methodological differences in prevalence studies, even though we attempted to adjust for studies using different methodologies and different definitions of dementia. Due to the heterogeneity in prevalence data over time, we did not allow observed time trends to affect our forecasted time trends in the future, because this could have induced spurious trends caused by changes in diagnostic procedures over time. Instead, our future time trends are based solely on expected trends in risk factor prevalence, as well as trends in population ageing and growth. Further investments in high-quality epidemiological studies are required to better estimate trends over time in dementia incidence and prevalence as well as geographical variation in dementia prevalence. This observed heterogeneity in prevalence data, in combination with high correlations between GBD risk factors and other dementia risk factors, could have had a role in our ability to detect a significant association between risk factors of dementia that are not currently included in the GBD study and GBD risk-deleted dementia prevalence by country. This limited the number of risk factors we could include as predictors of future dementia prevalence as well as the risk factors we could include in the decomposition analysis showing the effect of risks on future prevalence. The number of risk factors we tested for inclusion was additionally limited to include only those risk factors that were included in the 2020 Lancet Commission report and are part of the GBD comparative risk assessment framework. 13,22 Despite this limitation. we were able to include risks for which large changes in the prevalence of exposure are expected, including BMI, educational attainment, and fasting plasma glucose. 57-59 These risks are of most importance to future forecasts, which will only be affected by the exclusion of risk factors if the future exposure to a given risk is expected to change. However, future efforts should seek to incorporate more risks within GBD, which would allow us to include additional risk factors without relying on the estimation of the ecological association between risk exposure prevalence and dementia prevalence.

We also assumed that the maximal educational attainment was 18 years of education and that educational attainment was constant after the age of 25 years, as higher

levels of education are probably not consequential for most health outcomes quantified in the GBD project. However, continued education throughout the life course might convey a greater protective benefit for dementia.60 Furthermore, our exposure estimates for high BMI are based on the distribution of BMI in a population at a specific timepoint, but the evidence for BMI as a risk factor suggests that midlife BMI is most important. Therefore, future efforts should consider lagging BMI exposure to capture the risk-outcome association in forecasts more accurately. Additionally, this study focused on the overall prevalence of dementia because of a scarcity of globally relevant data on the decomposition of the broader dementia category into clinical subtypes. It is possible that clinical subtypes, such as vascular dementia, might have different underlying associations with dementia risk factors, which could affect our results. However, evidence suggesting a large overlap of neuropathologies across clinical subtypes calls into question the precision or even utility of clinical subtype designations.41,61 Our study also focused on the estimation of dementia prevalence, as the estimation of the numbers of individuals with dementia is of direct relevance for public health planning efforts. However, the estimation of future dementia incidence is also useful and should be the topic of future investigations.

Despite these limitations, this study improves on previous global forecasts of dementia in several important ways. First, drawing on the strength of the countrylevel estimates from GBD 2019, we were able to produce estimates of projected prevalence by country, world region, and SDI quintile, whereas previous studies have been restricted to global and regional estimates. Second, we used country-level forecasts of four different risk factors that have been shown to be associated with dementia, and the observed association between these risks and dementia prevalence from 1990 to 2019, to incorporate changes in prevalence that would be due to changes in these risk factors. Third, we were able to quantify through decomposition analysis the relative contribution of changes in GBD risk factors, changes in education, changes in population growth, and changes in population ageing.

The country-level specificity of our estimates will allow policy makers and decision makers to understand the expected increases in the number of individuals with dementia and the drivers of these increases in a given geographical setting. This information might be helpful for public health planning efforts, particularly as they relate to scaling up the availability of resources required to meet the needs of individuals with dementia and their caregivers. Furthermore, the projected increases in the number of people with dementia, due largely to population growth and population ageing, underscore the crucial need for research focused on the discovery of disease-modifying treatments, effective low-cost interventions, and novel modifiable risk factors for the prevention or delay of disease onset.

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Please see the appendix (pp 5–7) for more detailed information about individual author contributions to the research, divided into the following categories: managing the estimation or publication process; writing the first draft of the manuscript; primary responsibility for applying analytical methods to produce estimates; primary responsibility for seeking, cataloguing, extracting, or cleaning data; designing or coding figures and tables; providing data or critical feedback on data sources; development of methods or computational machinery; providing critical feedback on methods or results; drafting the manuscript or revising it critically for important intellectual content; and managing the overall research enterprise. The corresponding author had final responsibility for the decision to submit for publication.

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#### Data sharing

Citations for the data used in the study can be accessed from the Global Health Data Exchange (http://internal-ghdx.healthdata.org/). Access to the data is also provided as a data use agreements permit.

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#### References

- Wolters FJ, Chibnik LB, Waziry R, et al. Twenty-seven-year time trends in dementia incidence in Europe and the United States: the Alzheimer Cohorts Consortium. Neurology 2020; 95: e519–31.
- 2 Matthews FE, Stephan BCM, Robinson L, et al. A two decade dementia incidence comparison from the Cognitive Function and Ageing Studies I and II. Nat Commun 2016; 7: 11398.
- 3 Satizabal CL, Beiser AS, Chouraki V, Chêne G, Dufouil C, Seshadri S. Incidence of dementia over three decades in the Framingham Heart Study. N Engl J Med 2016; 374: 523–32.
- 4 Dodge HH, Buracchio TJ, Fisher GG, et al. Trends in the prevalence of dementia in Japan. *Int J Alzheimers Dis* 2012; 2012: 956354.
- Wu Y-T, Ali G-C, Guerchet M, et al. Prevalence of dementia in mainland China, Hong Kong and Taiwan: an updated systematic review and meta-analysis. *Int J Epidemiol* 2018; 47: 709–19.
- 6 Alzheimer's Disease International, Wimo A, Ali G-C, et al. World Alzheimer report 2015. The global impact of dementia: an analysis of prevalence, incidence, cost and trends. Sept 21, 2015. https://www.alz.co.uk/research/world-report-2015 (accessed April 8, 2018).
- 7 Li S, Yan F, Li G, et al. Is the dementia rate increasing in Beijing? Prevalence and incidence of dementia 10 years later in an urban elderly population. Acta Psychiatr Scand 2007; 115: 73–79.
- 8 Larson EB, Yaffe K, Langa KM. New insights into the dementia epidemic. N Engl J Med 2013; 369: 2275–77.
- 9 Catindig J-AS, Venketasubramanian N, Ikram MK, Chen C. Epidemiology of dementia in Asia: insights on prevalence, trends and novel risk factors. J Neurol Sci 2012; 321: 11–16.
- Nichols E, Szoeke CEI, Vollset SE, et al. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019; 18: 88–106.
- 11 Lutz W, Sanderson W, Scherbov S. The coming acceleration of global population ageing. *Nature* 2008; 451: 716–19.
- 12 Wang H, Abbas KM, Abbasifard M, et al. Global age-sex-specific fertility, mortality, healthy life expectancy (HALE), and population estimates in 204 countries and territories, 1950–2019: a comprehensive demographic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; 396: 1160–203.
- 13 Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the *Lancet* Commission. *Lancet* 2020; 396: 413–46.
- 14 Langa KM, Larson EB, Crimmins EM, et al. A comparison of the prevalence of dementia in the United States in 2000 and 2012. JAMA Intern Med 2017; 177: 51–58.
- 15 Skoog I, Börjesson-Hanson A, Kern S, et al. Decreasing prevalence of dementia in 85-year olds examined 22 years apart: the influence of education and stroke. Sci Rep 2017; 7: 6136.
- 16 Jorm AF, Dear KBG, Burgess NM. Projections of future numbers of dementia cases in Australia with and without prevention. Aust N Z J Psychiatry 2005; 39: 959–63.
- 17 Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. Alzheimers Dement 2013; 9: 63–75.
- 18 Matthews KA, Xu W, Gaglioti AH, et al. Racial and ethnic estimates of Alzheimer's disease and related dementias in the United States (2015–2060) in adults aged ≥65 years. Alzheimers Dement 2019; 15: 17–24.
- 19 Hebert LE, Weuve J, Scherr PA, Evans DA. Alzheimer disease in the United States (2010–2050) estimated using the 2010 census. *Neurology* 2013; 80: 1778–83.
- 20 Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi HM. Forecasting the global burden of Alzheimer's disease. Alzheimers Dement 2007; 3: 186–91.

- 21 Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; 396: 1204–22.
- 22 Murray CJL, Aravkin AY, Zheng P, et al. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; 396: 1223–49.
- 23 Stevens GA, Alkema L, Black RE, et al. Guidelines for accurate and transparent health estimates reporting: the GATHER statement. *Lancet* 2016; 388: e19–23.
- 24 American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 5th edn. Washington, DC: American Psychiatric Association, 2013.
- 25 WHO. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization, 1992.
- 26 GBD 2019 Dementia Collaborators. The burden of dementia due to Down syndrome, Parkinson's disease, stroke, and traumatic brain injury: a systematic analysis for the Global Burden of Disease Study 2019. Neuroepidemiology 2021; 55: 286–96.
- 27 Zheng P, Aravkin A, Barber R, Sorensen R, Murray C. Trimmed constrained mixed effects models: formulations and algorithms. *J Comput Graph Stat* 2021; 30: 544–56.
- 28 McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984; 34: 939–44.
- 29 Prince M, Acosta D, Chiu H, Scazufca M, Varghese M. Dementia diagnosis in developing countries: a cross-cultural validation study. *Lancet* 2003; 361: 909–17.
- 30 Flaxman AD, Vos T, Murray CJL. An integrative metaregression framework for descriptive epidemiology. Seattle, WA: University of Washington Press, 2015.
- 31 Vieira RT, Caixeta L, Machado S, et al. Epidemiology of early-onset dementia: a review of the literature. Clin Pract Epidemiol Ment Health 2013; 9: 88–95.
- 32 Jicha GA, Carr SA. Conceptual evolution in Alzheimer's disease: implications for understanding the clinical phenotype of progressive neurodegenerative disease. J Alzheimers Dis 2010; 19: 253–72.
- Anstey KJ, von Sanden C, Salim A, O'Kearney R. Smoking as a risk factor for dementia and cognitive decline: a meta-analysis of prospective studies. Am J Epidemiol 2007; 166: 367–78.
- 34 Pedditzi E, Peters R, Beckett N. The risk of overweight/obesity in mid-life and late life for the development of dementia: a systematic review and meta-analysis of longitudinal studies. Age Ageing 2016; 45: 14–21.
- 35 Crane PK, Walker R, Hubbard RA, et al. Glucose levels and risk of dementia. N Engl J Med 2013; 369: 540–48.
- 36 Forouzanfar MH, Afshin A, Alexander LT, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016; 388: 1659–724.
- 37 Foreman KJ, Marquez N, Dolgert A, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories. *Lancet* 2018; 392: 2052–90.
- 38 Vollset SE, Goren E, Yuan C-W, et al. Fertility, mortality, migration, and population scenarios for 195 countries and territories from 2017 to 2100: a forecasting analysis for the Global Burden of Disease Study. *Lancet* 2020; 396: 1285–306.
- 39 Das Gupta P. A general method of decomposing a difference between two rates into several components. *Demography* 1978; 15: 99–112.
- 40 Alzheimer's Disease International. World Alzheimer Report 2019: attitudes to dementia. Sept 1, 2019. https://www.alzint.org/u/ WorldAlzheimerReport2019.pdf (accessed Feb 2, 2021).
- 41 Schneider JA, Arvanitakis Z, Bang W, Bennett DA. Mixed brain pathologies account for most dementia cases in communitydwelling older persons. *Neurology* 2007; 69: 2197–204.
- 42 Hohman TJ, Dumitrescu L, Barnes LL, et al. Sex-specific association of apolipoprotein E with cerebrospinal fluid levels of Tau. JAMA Neurol 2018; 75: 989–98.

- 43 Koran MEI, Wagener M, Hohman TJ. Sex differences in the association between AD biomarkers and cognitive decline. *Brain Imaging Behav* 2017; 11: 205–13.
- 44 Wimo A, Jönsson L, Bond J, Prince M, Winblad B, Alzheimer's Disease International. The worldwide economic impact of dementia 2010. Alzheimers Dement 2013; 9: 1–11.
- 45 Wimo A, Guerchet M, Ali G-C, et al. The worldwide costs of dementia 2015 and comparisons with 2010. Alzheimers Dement 2017; 13: 1-7
- 46 Cummings JL, Morstorf T, Zhong K. Alzheimer's disease drug-development pipeline: few candidates, frequent failures. Alzheimers Res Ther 2014; 6: 37.
- 47 Waite LM. Treatment for Alzheimer's disease: has anything changed? Aust Prescr 2015; 38: 60–63.
- 48 WHO. Risk reduction of cognitive decline and dementia: WHO guidelines. Geneva: World Health Organization, 2019.
- 49 Livingston G, Sommerlad A, Orgeta V, et al. Dementia prevention, intervention, and care. *Lancet* 2017; 390: 2673–734.
- 50 Ferri CP, Jacob KS. Dementia in low-income and middle-income countries: different realities mandate tailored solutions. PLoS Med 2017; 14: e1002271.
- 51 Connolly A, Gaehl E, Martin H, Morris J, Purandare N. Underdiagnosis of dementia in primary care: variations in the observed prevalence and comparisons to the expected prevalence. *Aging Ment Health* 2011; 15: 978–84.
- 52 Phelan EA, Borson S, Grothaus L, Balch S, Larson EB. Association of incident dementia with hospitalizations. *JAMA* 2012; 307: 165–72.

- 53 Bunn F, Burn A-M, Goodman C, et al. Comorbidity and dementia: a scoping review of the literature. BMC Med 2014; 12: 192.
- 54 Blasi ZV, Hurley AC, Volicer L. End-of-life care in dementia: a review of problems, prospects, and solutions in practice. *J Am Med Dir Assoc* 2002; 3: 57–65.
- 55 Shega JW, Hougham GW, Stocking CB, Cox-Hayley D, Sachs GA. Patients dying with dementia: experience at the end of life and impact of hospice care. J Pain Symptom Manage 2008; 35: 499–507.
- 56 Gilhooly KJ, Gilhooly MLM, Sullivan MP, et al. A meta-review of stress, coping and interventions in dementia and dementia caregiving. BMC Geriatr 2016; 16: 106.
- 57 Cho NH, Shaw JE, Karuranga S, et al. IDF Diabetes Atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res Clin Pract* 2018; 138: 271–81.
- 58 Goujon A, Samir KC, Speringer M, et al. A harmonized dataset on global educational attainment between 1970 and 2060—an analytical window into recent trends and future prospects in human capital development. J Demogr Economics 2016; 82: 315–63.
- 59 Jaacks LM, Vandevijvere S, Pan A, et al. The obesity transition: stages of the global epidemic. *Lancet Diabetes Endocrinol* 2019; 7: 231–40.
- 60 Hatch SL, Feinstein L, Link BG, Wadsworth MEJ, Richards M. The continuing benefits of education: adult education and midlife cognitive ability in the British 1946 birth cohort. J Gerontol B Psychol Sci Soc Sci 2007; 62: S404–14.
- 61 Kovacs GG, Alafuzoff I, Al-Sarraj S, et al. Mixed brain pathologies in dementia: the BrainNet Europe consortium experience. Dement Geriatr Cogn Disord 2008; 26: 343–50.