1	Dia	betes and all-cause mortality among middle-aged and older adults in
2	С	hina, England, Mexico, rural South Africa, and the United States: A
3		population-based study of longitudinal aging cohorts
4		
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- 41 epidemiology
- 42

# 43 **ARTICLE HIGHLIGHTS**

#### 44 Why did we undertake this study?

45 We aimed to address the need for comparable estimates of all-cause mortality among

- 46 people with diabetes in diverse global settings.
- 47

# 48 What is the specific question(s) we wanted to answer?

- 49 How does diabetes impact all-cause mortality among middle-aged and older adults
- 50 (aged 51 years or greater) in China, England, Mexico, rural South Africa, and the United
- 51 States?
- 52

#### 53 What did we find?

- 54 Middle-aged and older adults with diabetes had higher all-cause mortality than people
- 55 without diabetes in all countries. Relative mortality differences ranged from mortality
- rate ratios of 1.53 in the United States to 2.02 in Mexico. Absolute mortality differences
- 57 ranged from mortality rate differences (per 1,000 person-years) of 11.9 in England to

58 24.6 in South Africa.

59

# 60 What are the implications of our findings?

There is an urgent need to implement clinical and public health interventions to improvediabetes outcomes globally.

# 63 ABSTRACT

Objective: There is a need for comparable worldwide data on the impact of diabetes on
 mortality. This study assessed diabetes and all-cause mortality among middle-aged and
 older adults in five countries.

67

68 **Research Design and Methods:** We analyzed adults aged 51 years or older followed between 2010 and 2020 from population-based cohorts in China, England, Mexico, rural 69 70 South Africa, and the United States. Diabetes was defined by self-report or an elevated 71 diabetes blood-based biomarker meeting the clinical criteria for diabetes. All-cause mortality was assessed through linkages or informant interviews. We used Poisson 72 73 regression models to estimate mortality rate ratios and mortality rate differences, comparing people with diabetes to those without diabetes. Models were adjusted for 74 age, gender, education, smoking status, body mass index, and economic status. 75 76 77 **Results:** We included 29,397 individuals, of whom 4,916 (16.7%) died during the study period. The median follow-up time ranged from 4.6 years in South Africa to 8.3 years in 78 79 China. The adjusted all-cause mortality rate ratios for people with diabetes versus those without diabetes ranged from 1.53 (95% CI: 1.39-1.68) in the United States to 2.02 80 81 (95% CI: 1.34-3.06) in Mexico. The adjusted mortality rate differences (per 1,000 82 person-years) for people with diabetes versus those without diabetes ranged from 11.9 83 (95% CI: 4.8-18.9) in England to 24.6 (95% CI: 12.2-37.0) in South Africa. 84

- 85 Conclusions: Diabetes was associated with increased all-cause mortality in population-
- 86 based cohorts across five diverse countries. There is an urgent need to implement
- 87 clinical and public health interventions to improve diabetes outcomes globally.

#### 88 INTRODUCTION

More than half a billion people worldwide are living with diabetes.<sup>1,2</sup> By 2050, this 89 number will increase to 1.2 billion people.<sup>1</sup> Given the epidemiology of diabetes, it is 90 91 crucial to understand how it impacts long-term health outcomes such as mortality in diverse populations worldwide. All-cause mortality among people with diabetes at the 92 93 population level is a key metric in the World Health Organization (WHO) global diabetes monitoring framework.<sup>3</sup> The WHO recommends monitoring diabetes mortality because it 94 95 is inherently significant to patients and policymakers, modifiable through evidence-96 based interventions, and amenable to standardized assessment methods.<sup>3</sup> 97 98 While diabetes has long been associated with increased mortality in high-income 99 countries,<sup>4-6</sup> contemporary and cross-national estimates of this association have been 100 limited by several factors. First, there is a paucity of data on diabetes and mortality from 101 low- and middle-income countries where most people with diabetes live, and this is 102 especially true for middle-aged or older adults who are often understudied in these 103 settings.<sup>7</sup> Second, temporal declines in all-cause mortality in high-income countries 104 have been observed in recent decades, so updated data are needed.<sup>8</sup> Third, population 105 data on diabetes and mortality are often not comparable across settings due to 106 differences in sample selection, case definitions, and mortality ascertainment.<sup>7</sup> These 107 limitations pose challenges for accurately assessing the global burden of diabetes and 108 monitoring diabetes policy responses.

110 To address these gaps, this study aimed to evaluate the association between diabetes

and all-cause mortality among middle-aged and older adults with diabetes using recent

112 data from comparable population-based aging cohorts in five diverse countries.

113

#### 114 **RESEARCH DESIGN AND METHODS**

#### 115 Study design and sample

116 We conducted a longitudinal analysis of population-based aging cohorts in five

117 countries: China (China Health and Retirement Longitudinal Study [CHARLS]),<sup>9</sup>

118 England (English Longitudinal Study of Ageing [ELSA]),<sup>10</sup> Mexico (Mexican Health and

Aging Study [MHAS]),<sup>11</sup> rural South Africa (Health and Aging in Africa: A Longitudinal

120 Study of an INDEPTH Community in South Africa [HAALSI]),<sup>12</sup> and the United States

121 (Health and Retirement Study [HRS]).<sup>13</sup> These cohorts are part of the HRS International

122 Family of Studies, a network of longitudinal aging studies with similar sampling designs,

123 eligibility, and assessment methods.<sup>14</sup> The cohort inclusion criteria for this analysis were

(1) availability of baseline and follow-up data from 2010 to 2020 and (2) collection of a

125 blood-based diabetes biomarker at the baseline wave during this period. We chose

126 2010 to 2020 as our period of interest to maximize comparability between cohorts. With

127 one exception, the included cohorts were nationally representative of each country's

middle-aged and older population. The exception was the South Africa cohort, which

129 was representative of rural communities in sub-Saharan Africa. See Appendix 1 for

130 details on the years of data collection and censoring by cohort.

Due to minor differences in the lower end of age eligibility between cohorts, we excluded individuals younger than 51 at baseline to ensure comparability. We also excluded respondents without follow-up information, with no available blood-based diabetes biomarker, or with missing data on prior diabetes diagnosis, gender, education, economic status, smoking status, BMI, or survey weights. In the South Africa cohort, we excluded individuals with missing human immunodeficiency virus (HIV) status. Appendix 2 shows participant flow diagrams for each cohort including numbers lost to follow-up.

139

#### 140 **Definition of diabetes**

We defined diabetes as either (1) a history of self-reported diagnosis by a physician or 141 142 health care worker or (2) an elevated blood-based biomarker meeting clinical criteria for 143 diabetes.<sup>15,16</sup> We used HbA1c ≥6.5% (48 mmol/mol) as the biomarker threshold in all 144 countries except China and South Africa where we used fasting blood glucose ≥126 mg/dL (7.0 mmol/L) or random blood glucose ≥200 mg/dL (11.1 mmol/L). In China, 145 146 plasma glucose was assessed using an enzymatic colorimetric test (92% of individuals were fasting). In the South African cohort, capillary glucose was assessed using a point-147 148 of-care analyzer (24% of individuals were fasting). In England, HbA1c was assessed 149 using venous blood samples. In Mexico, HbA1c was assessed using a point-of-care analyzer certified by the National Glycohemoglobin Standardization Program.<sup>17</sup> In the 150 151 United States, HbA1c was assessed using dried blood spots converted to whole blood equivalent values.<sup>18</sup> Relevant question text and biomarker details are provided in 152 153 Appendix 3-4.

#### 155 Mortality ascertainment

156 All-cause mortality was captured in England by linking to the National Health Service Central Register (latest available data from April 2018). In other cohorts, all-cause 157 158 mortality was captured during interviews with respondents' spouses or other informants. 159 In all cohorts, the month and year of death were available. If the date of death was 160 unknown, it was estimated as the midpoint between waves in which an individual was 161 known to be alive and had died. We measured survival time in years from the baseline 162 interview as defined in this study to death, loss to follow-up, or the end of the follow-up 163 period (May 2018 in England and December 2019 in the other countries), whichever came first. 164

165

#### 166 Statistical analysis

Analyses were conducted within each cohort and accounted for survey weights and 167 168 sampling design when available. We first calculated the overall and age-stratified 169 diabetes prevalence at baseline. In calculating overall prevalence, we age-standardized to the WHO standard population. We then used Poisson regression with an offset for 170 171 log-transformed person-years and robust standard errors to estimate differences in 172 mortality rates among people with diabetes versus those without diabetes. Poisson 173 models give similar results to Cox models when there are shorter follow-up intervals and 174 have the advantage of directly estimating event rates.<sup>19,20</sup> Both relative (mortality rate 175 ratios) and absolute (mortality rate and mortality rate differences) measures are 176 reported. Mortality rates and mortality rate differences are presented as the number of 177 deaths per 1,000 person-years.

We used prior evidence to develop a directed acyclic graph showing our conceptual 178 179 model of the relationship between diabetes and mortality (Appendix 5).<sup>21</sup> We adjusted 180 for baseline covariates, including age (51-59 years, 60-69 years, and  $\geq$ 70 years). 181 gender (women vs. men), education (less than upper secondary, upper secondary and 182 vocational, and tertiary), smoking status (current vs. not current smoker), BMI categories (underweight: BMI < 18.5 kg/m<sup>2</sup>; normal weight: 18.5-24.9 kg/m<sup>2</sup>; overweight: 183 25.0-29.9 kg/m<sup>2</sup>; obese:  $\geq$  30.0 kg/m<sup>2</sup>), and economic status (tertiles). Economic status 184 185 was defined as the annual income of the individual and their co-residing spouse or 186 dependent children in high-income countries (England and the United States) and the annual household per-capita consumption in upper-middle-income countries (China, 187 188 Mexico, and South Africa). Per-capita consumption is the preferred measure of living standard derived from surveys in developing countries.<sup>22</sup> In the South African cohort, we 189 190 also adjusted for HIV status, given the high prevalence (23%) and known mortality association in this population.<sup>23</sup> Models were run in the overall sample and by gender. 191 192 We estimated differences in mortality rates among people with no diabetes, diagnosed 193 diabetes, and undiagnosed diabetes. Analyses were performed using Stata version 194 18.0.

195

#### 196 Sensitivity analyses

We conducted three sensitivity analyses. First, we assessed the consistency of our findings using Cox proportional hazards regression models. Second, we estimated the association between diabetes and mortality using a slightly more restrictive epidemiological diabetes definition of either (1) the self-reported use of a glucose-

201	lowering medication or (2) an elevated biomarker meeting clinical criteria for
202	diabetes. <sup>24,25</sup> Finally, we performed an analysis without the adjustment for BMI
203	categories given the potentially bidirectional relationship between diabetes and BMI.
204	
205	Data availability and ethics
206	This study was deemed exempt from institutional ethics approval at the University of
207	Michigan (HUM00256096). Data included in this study are publicly available for all
208	cohorts except for mortality data for ELSA. Details on accessing data can be found at
209	the Gateway to Global Aging Data website (https://g2aging.org/).
210	
211	RESULTS
212	Survey and respondent characteristics
213	Table 1 presents survey and respondent characteristics for the five cohorts. The final
214	sample included 6,251 individuals in China, 4,819 in England, 1,717 in Mexico, 3,411 in
215	South Africa, and 13,199 in the United States. Of the 29,397 total individuals, 4,916
216	(16.7%) died during the study period. The median follow-up time ranged from 4.6
217	(interquartile range [IQR]: 4.4-4.8) years in South Africa to 8.3 (IQR: 8.2-8.4) years in
218	China. There were 191,782 total person-years of follow-up in the cohorts (China: 48,122
219	person-years; England: 24,536 person-years; Mexico: 11,192 person-years; South
220	Africa: 14,722 person-years; and United States: 93,210 person-years).
221	
222	There was considerable cross-country variation in some respondent characteristics, as
223	illustrated in Table 1. For example, while nine-tenths of individuals in China (89.9%

224 [95% CI: 88.2-91.4]), Mexico (88.8% [95% CI: 85.9-91.2]), and South Africa (93.3%

- [95% CI: 92.4-94.1]) had less than an upper secondary education, most individuals in
- 226 England (69.2% [95% CI: 67.5-70.8]) and the United States (86.1% [95% CI: 84.7-87.4])
- had an upper secondary education or greater. Current smoking ranged from 8.4% (95%
- 228 CI: 7.5-9.3) in South Africa to 31.0% (95% CI: 28.6-33.6) in China. The prevalence of
- individuals who were obese ranged from 4.5% (95% CI: 3.9-5.3) in China to 43.3%
- 230 (95% CI: 42.3-44.4) in the United States.
- 231

#### 232 Diabetes prevalence

233 The age-standardized prevalence of diabetes was highest in Mexico (37.4% [95% CI:

234 33.4-41.5], followed by the United States (21.8% [95% CI: 20.8-22.8]), China (15.7%

235 [95% CI: 14.3-17.2]), South Africa (12.1% [95% CI: 11.1-13.3]), and England (11.7%

[95% CI: 10.6-13.0]). Figure 1 shows the age-specific prevalence of diabetes by cohort

at baseline. Among individuals with diabetes, the age-standardized proportion of those

with diabetes who reported a prior diabetes diagnosis ranged from 46.4% (95% CI:

42.1-50.7) in China to 86.1% (95% CI: 84.1-87.9) in the United States (Table 1).

240

#### 241 Mortality rates

Adjusted all-cause mortality rates (per 1,000 person-years) are presented in Figure 2

and Appendix 6. In each cohort, mortality rates were higher among people with diabetes

- than those without diabetes. Across the cohorts, mortality rates among people with
- diabetes were highest in South Africa (57.5 [95% CI: 45.5-69.5]), followed by the United

246	States (39.2 [95% CI: 36.1-42.4]), China (95% CI: 35.5 [95% CI: 28.6-42.4]), England
247	(28.8 [95% CI: 22.1-35.6]), and Mexico (29.0 [95% CI: 19.0-39.0]).

248

#### 249 Mortality rate ratios and mortality rate differences

The adjusted overall all-cause mortality rate ratios for people with diabetes versus those without diabetes ranged from 1.53 (95% CI: 1.39-1.68) in the United States to 2.02

**č** 

252 (95% CI: 1.34-3.06) in Mexico (Figure 3A). The adjusted mortality rate differences (per

253 1,000 person-years) for people with diabetes versus those without diabetes ranged from

254 11.9 (95% CI: 4.8-18.9) in England to 24.6 (95% CI: 12.2-37.0) in South Africa. No

significant differences were observed in adjusted mortality rate ratios or adjusted

256 mortality rate differences by sex in cohorts. Mortality rate ratios appeared to decrease in

older age groups in the cohorts from England and the United States (Appendix 7).

258

Figure 3B shows results when the diabetes classification was separated by diagnosed 259 260 or undiagnosed status, compared to no diabetes. In general, there appeared to be a 261 tendency among people diagnosed with diabetes to have higher mortality than people 262 with undiagnosed diabetes. However, these differences were statistically significant only 263 in Mexico where people with diagnosed diabetes compared to undiagnosed diabetes 264 had an adjusted mortality rate ratio of 1.95 (95% CI: 1.11-3.43), corresponding to an 265 adjusted mortality rate difference of 22.6 (95% CI: -7.3-52.4) deaths per 1,000 person-266 years (Appendix 8).

267

### 269 Sensitivity analyses

270 The results of the first sensitivity analysis using Cox proportional hazards regression 271 models (Appendix 9) were generally consistent with the main results using Poisson 272 regression models. In the second sensitivity analysis using the slightly more restrictive 273 epidemiological diabetes definition of either the use of a glucose-lowering medication (in 274 place of self-reported diagnosis) or an elevated biomarker, we observed a slightly 275 higher point estimate for the adjusted mortality rate ratios in the China cohort (1.86 vs. 276 1.79) and slightly lower adjusted mortality rate ratios in the Mexico cohort (1.84 vs. 2.02; 277 Appendix 10). The third sensitivity analysis removing adjustment for BMI had the effect of slightly attenuating the mortality rate ratios and mortality rate differences compared to 278 279 the main analysis (Appendix 11).

280

#### 281 CONCLUSIONS

In this study of middle-aged and older adults followed between 2010 and 2020 from 282 283 population-based cohorts in five diverse countries (four of which were nationally 284 representative), we found that people with diabetes consistently had higher all-cause 285 mortality than people without diabetes. Relative mortality differences were similar 286 across cohorts, ranging from mortality rate ratios of 1.53 (95% CI: 1.39-1.68) in the 287 United States to 2.02 (95% CI: 1.34-3.06) in Mexico. Absolute mortality differences had 288 more variation across cohorts, ranging from mortality rate differences (per 1,000 289 person-years) of 11.9 (95% CI: 4.8-18.9) in England to 24.6 (95% CI: 12.2-37.0) in 290 South Africa. These findings using recent and comparable data highlight the immense 291 burden of diabetes around the world, particularly in low- and middle-income country

settings such as rural South Africa and Mexico where the absolute mortality impact of
 diabetes appears greatest. These are also settings where diabetes care is thought to be
 least robust.<sup>3,26,27</sup>

295

296 Many prior studies assessing the association between diabetes and all-cause mortality 297 have been conducted in high-income countries and among younger age groups.<sup>3,7,8</sup> 298 Large-scale meta-analyses in the last two decades have reported relative mortality 299 differences among people with diabetes, as compared to those without diabetes, that are generally similar to findings in our study.<sup>4,6,28,29</sup> However, these meta-analyses 300 301 primarily included non-representative cohorts from high-income countries, limiting 302 population inferences globally. A multi-country analysis from 1995 to 2016 in 16 303 countries provides updated evidence of a reduction in all-cause mortality among people 304 with diagnosed diabetes, but data were only available from high-income countries.<sup>8</sup> The 305 Prospective Urban Rural Epidemiology study reported greater absolute mortality among 306 people with diabetes in middle-income and low-income countries, as compared to people with diabetes in high-income countries.<sup>5</sup> While studies on diabetes-related 307 308 mortality previously have been performed in each of the countries included in our 309 analysis,<sup>30-36</sup> our study uniquely compares diabetes-related mortality in multiple 310 countries using similar methods across the entire continuum of middle-aged and older 311 adults. Individuals in this age range are sometimes excluded from population-based 312 studies worldwide. However, they have the highest diabetes prevalence and require 313 comprehensive clinical management to prevent diabetes complications.

315 An important secondary finding in our study was the tendency of higher mortality among 316 people with diagnosed diabetes compared to undiagnosed diabetes. This finding was 317 most marked in Mexico and South Africa. Many-though not all-prior high-quality 318 population-based studies have reported similar findings.<sup>5,30-32,37</sup> We hypothesize that the 319 greater mortality among people with previously diagnosed compared to undiagnosed 320 diabetes likely reflects a selection effect related to diabetes severity and/or diabetes 321 duration. Diabetes patients with the highest disease severity or progression are most 322 likely to experience symptoms, to seek a diagnosis in the health care system, and, 323 despite obtaining a diagnosis, to die. This selection effect may be most salient in countries at lower income levels where the proportion of adults with diabetes who are 324 325 diagnosed is as low as 20%, compared to 80% or greater in some high-income 326 countries such as the United States.<sup>3</sup>

327

What are the policy implications emerging from this work? The higher absolute mortality 328 329 rates in South Africa and Mexico suggest that people with diabetes in these countries 330 experience challenges accessing quality diabetes care. There is an urgent need to 331 scale up evidence-based interventions to manage diabetes and its associated 332 cardiovascular risk factors, particularly in low- and middle-income countries where 333 societies are aging, absolute diabetes mortality is highest, and the population with diabetes is rapidly growing.<sup>2</sup> Evidence from Sweden shows that people with diabetes 334 335 who are appropriately managed and achieve risk factor control have little or no excess mortality compared to those without diabetes.<sup>38</sup> Yet only 10% of people with diabetes in 336 337 low- and middle-income countries receive comprehensive diabetes management

aligned with guidelines.<sup>26</sup> In the coming decades, diabetes will cause a staggering
degree of premature mortality unless health systems are strengthened to improve
diabetes care.<sup>1</sup> The WHO Global Diabetes Compact is a crucial international effort to
stimulate improvements in equitable, affordable, and quality care for people with
diabetes.<sup>1,3</sup> A key pillar of these efforts is the inclusion of stakeholders from the public
and private sectors, as well as individuals with lived experiences of diabetes.

344

345 Our study has several limitations. First, our analysis did not include people aged 50 346 years or younger. Younger populations with diabetes tend to have high diabetes mortality compared to young populations without diabetes.<sup>30-32</sup> Our results should not be 347 348 generalized to entire populations or young populations. Still, they can be generalized to populations aged 51 years or older, which represent approximately two-thirds of people 349 with diabetes worldwide.<sup>2</sup> Second, differences in the blood-based diabetes biomarkers 350 351 collected in each cohort (e.g., glucose versus HbA1c) may contribute to slightly different 352 phenotypes of individuals classified as having undiagnosed diabetes.<sup>39,40</sup> This limitation could decrease the comparability of estimates across cohorts. Third, our study lacks 353 354 data on cause-specific mortality, preventing us from distinguishing between 355 microvascular and macrovascular patterns of death among individuals with diabetes. 356 Fourth, the South African cohort was not nationally representative, though it is 357 representative of a rural community like many others in sub-Saharan Africa. Finally, 358 while this analysis used data from a geographically and economically diverse set of 359 countries, the included cohorts may not fully represent populations with diabetes 360 worldwide. In particular, none of the cohorts were drawn from low- or lower-middle-

income countries. Estimating diabetes mortality in these settings is an important area offuture research.

- In summary, we observed that diabetes was consistently associated with increased all-
- 365 cause mortality across five diverse settings, and absolute diabetes mortality was
- 366 particularly high in low- and middle-income countries where systems of care for
- 367 diabetes are known to be weaker. The findings reinforce the need to implement clinical
- 368 and public health interventions to improve diabetes outcomes in countries worldwide.

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# 392 Conflict of Interest

- 393 D.F. and JM.-G. have received consultant fees from the World Health Organization for
- 394 activities relating to global diabetes monitoring.
- 395

# 396 Author Contributions and Guarantor Statement

- H.G., J.M.-G., and D.F. conceived the idea for this study. H.G. conducted the statistical
- analysis. H.G. and D.F. wrote the first draft of the manuscript with substantial revisions
- 399 from J.M.-G. H.G. and P.Z. verified the underlying data. Y.S.Z. and P.Z. provided
- 400 analytic support. All authors provided crucial input on multiple iterations of the
- 401 manuscript. D.F. had full access to the data except the ELSA mortality data; due to
- 402 privacy regulations, these data were restricted in access to P.Z. D.F. is the guarantor of
- 403 this work and, as such, takes responsibility for the integrity of the data and the accuracy
- 404 of the data analysis.

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518 Table 1: Survey and respondent characteristics

	China (CHARLS)	England (ELSA)	Mexico (MHAS)	South Africa (HAALSI)	United States (HRS)
Survey characteristics					
Years of data collection (baseline to endline)	2011 to 2019	2012 to 2018	2012 to 2019	2014 to 2019	2010 to 2019
Sample size, n	6,251	4,819	1,717	3,411	13,199
Deaths, n	968	400	206	510	2,832
Follow-up time (years), median (IQR)	8.3 (8.2-8.4)	5.5 (5.2-5.7)	7.1 (7.1-7.2)	4.6 (4.4-4.8)	7.5 (6.2-9.0)
Respondent characteristics					
Age (years), median (IQR)	61 (56-68)	64 (57-72)	63 (56-70)	65 (57-73)	63 (57-72)
Women, % (95% CI)	50.2 (47.8-52.6)	50.9 (49.4-52.3)	55.2 (50.8-59.6)	53.7 (52.0-55.4)	54.1 (53.3-54.9)
Education, % (95% CI)					
Less than upper secondary	89.9 (88.2-91.4)	30.8 (29.3-32.5)	88.8 (85.9-91.2)	93.3 (92.4-94.1)	13.9 (12.7-15.4)
Upper secondary and vocational	8.2 (7.3-9.2)	50.7 (49.0-52.4)	3.4 (2.1-5.6)	4.3 (3.7-5.0)	58.7 (56.9-60.4)
Tertiary	1.9 (0.9-3.9)	18.4 (17.1-19.9)	7.7 (5.9-10.1)	2.4 (1.9-2.9)	27.4 (25.5-29.4)
Current smoker, % (95% CI)	31.0 (28.6-33.6)	13.7 (12.5-15.0)	16.9 (12.9-21.8)	8.4 (7.5-9.3)	14.9 (13.8-16.0)
BMI, % (95% CI)					
<18.5 (Underweight)	7.5 (6.7-8.3)	0.9 (0.6-1.3)	0.9 (0.4-1.8)	5.6 (4.9-6.5)	1.0 (0.8-1.3)
18.5-24.9 (Normal)	61.0 (58.6-63.4)	26.4 (25.0-28.0)	26.0 (21.8-30.7)	36.5 (34.9-38.1)	20.8 (20.0-21.7)
25.0-29.9 (Overweight)	27.0 (24.6-29.5)	41.8 (40.2-43.5)	38.0 (34.0-42.2)	28.3 (26.9-29.9)	34.8 (33.8-35.8)
≥30 (Obese)	4.6 (3.9-5.3)	30.8 (29.3-32.4)	35.1 (31.0-39.5)	29.6 (28.0-31.1)	43.3 (42.3-44.4)
Diabetes (diagnosed and undiagnosed), % (95% CI)*	15.7 (14.3-17.2)	11.7 (10.6-13.0)	37.4 (33.4-41.5)	12.1 (11.1-13.3)	21.8 (20.8-22.8)
Diagnosed among all with	46.4 (42.1-50.7)	76.1 (69.3-81.7)	53.6 (47.2-59.9)	57.8 (52.5-62.9)	86.1 (84.1-87.9)

520

\*Values are age-standardized to the WHO standard population among adults aged 50 years and older. CHARLS=China 521 Health and Retirement Longitudinal Study. ELSA=English Longitudinal Study of Ageing. HAALSI=Health and Aging in

522 Africa: A Longitudinal Study of an INDEPTH Community in South Africa. HRS=Health and Retirement Study.

523 IQR=Interquartile range. MHAS=Mexican Health and Aging Study.





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526 Diabetes was defined among individuals self-reporting a previous diabetes diagnosis or those with an

527 elevated biomarker (hemoglobin A1c ≥6.5% [48 mmol/mol], fasting plasma glucose ≥126 mg/dL [7.0
 528 mmol/L], or random capillary glucose ≥200 mg/dL [11.1 mmol/L]). The vertical error bars represent 95%

529 Cls.



#### 530 Figure 2: Adjusted all-cause mortality rates by cohort

Mortality rates are presented as the number of deaths per 1,000 person-years. The vertical error bars
represent 95% CIs. Estimates were derived using Poisson regression models with an offset for logtransformed person-years and robust standard errors and adjusted for age, gender, education, smoking
status, body mass index, and economic status. Models in South Africa also adjusted for HIV status.
CHARLS=China Health and Retirement Longitudinal Study. ELSA=English Longitudinal Study of Ageing.

537 HAALSI=Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa.

538 HRS=Health and Retirement Study. MHAS=Mexican Health and Aging Study.

# Figure 3: Adjusted all-cause mortality rate ratios and mortality rate differences 540

541 Panel A: Overall and by gender

Country			Mortality rate ratio			Mortality rate difference
China (CHARLS)						
Women		_ <b></b>	2.06 (1.53 - 2.76)			16.7 (7.8 - 25.7)
Men		— <b>•</b> —	1.52 (1.18 - 1.96)			12.5 (3.8 - 21.2)
Overall			1.79 (1.45 - 2.22)		-	15.7 (8.7 - 22.7)
England (ELSA)						
Women			1.88 (1.20 - 2.94)		_ <b></b>	12.7 (1.6 - 23.7)
Men		_ <b>_</b>	1.54 (1.11 - 2.15)		<b></b>	10.8 (1.5 - 20.2)
Overall			1.70 (1.30 - 2.22)		-	11.9 (4.8 - 18.9)
Mexico (MHAS)						
Women			2.00 (1.16 - 3.43)		_ <b></b>	12.8 (2.1 - 23.6)
Men			2.01 (1.13 - 3.58)		<b>—</b> •—	17.0 (-0.0 - 33.9)
Overall			2.02 (1.34 - 3.06)			14.7 (4.9 - 24.4)
South Africa (HAALSI)						
Women		_ <b></b>	1.78 (1.27 - 2.49)			17.7 (5.2 - 30.2)
Men		_ <b>_</b>	1.72 (1.26 - 2.35)			- 32.4 (9.6 - 55.2)
Overall			1.75 (1.39 - 2.20)			24.6 (12.2 - 37.0)
United States (HRS)						
Women		-	1.58 (1.43 - 1.76)		•	13.6 (10.0 - 17.1)
Men			1.49 (1.30 - 1.70)			13.9 (9.1 - 18.8)
Overall		+	1.53 (1.39 - 1.68)		+	13.6 (10.5 - 16.7)
	0.5	1 2	4	-20	0 20 40	60
	Me	ortality rate ratio		M	lortality rate difference	•

# 543 Panel B: By diagnosed vs. undiagnosed



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Mortality rate differences are presented as the number of deaths per 1,000 person-years. The horizontal error
bars represent 95% CIs. Estimates were derived using Poisson regression models with an offset for logtransformed person-years and robust standard errors and adjusted for age, gender, education, smoking status,
body mass index, and economic status. Models in South Africa also adjusted for HIV status. CHARLS=China
Health and Retirement Longitudinal Study. ELSA=English Longitudinal Study of Ageing. HAALSI=Health and
Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa. HRS=Health and Retirement
Study. MHAS=Mexican Health and Aging Study.







