APPENDIX

To calibrate the model, the NSDUH data was fitted across three MDE states and five age groups (18–25, 26–34, 35–49, 50–64, ≥65 years) for a total of 15 distinct groups for males and females. The Davidon–Fletcher-Powell optimization algorithm was used to search for parameter estimates that minimize the sum of squared differences between the model and the NSDUH data for the years 2005–2017.

While children are excluded from the data sources, the model simulates individuals from birth until death, with onset of depression occurring as early as age 12 years. (Note: The NSDUH MDE survey questions differ between youth and adults, and are not comparable for combined analysis.[1]) The simulated population begins in 1900, with new births and deaths each year, so that the model achieves observed population and depression patterns by 2005.

The NSDUH data showed a significant increase in past year MDE among adults ages 18–25 years in recent years,[2,3] and this appeared in lifetime MDE prevalence estimates in 2016 and 2017 (Appendix Figure 1). Calibration was performed in two steps: (1) estimate model parameters for first MDE incidence and under-reporting by calibrating to survey data 2005–2015; (2) using these parameters, estimate a scaling factor that increases first MDE incidence probabilities to fit data for females and males ages 18–25 years and identify the start year of the increase to achieve the best fit. Results from this two-step process are reported for 2017 in the main manuscript. Results using estimates from step 1 (prior to the increase in lifetime MDE prevalence) appear in Appendix Figures 4 and 5. using the 'Bhat' and 'splines' packages in R.[4,5]

After calibration, model estimates for lifetime MDE prevalence by age group without recall error adjustment corresponded closely to the NSDUH data (Appendix Figure 1). Appendix Figure 2 shows a comparison after recall error adjustment, where individuals with recall error in the model are categorized as never MDE. Lifetime MDE prevalence decreased slightly with each successive age group, before dropping dramatically for the oldest age group. In NSDUH, for all age groups except for ages ≥65 years, lifetime MDE prevalence ranged from 16.4% to 25.0% for females, and 9.0% to 14.6% for males, with upper end estimates representing 18–25 year olds in 2017 (Appendix Figure 1). Lifetime prevalence was markedly lower in the oldest age group, with point estimates ranging from 5.7% to 9.9% for females, and from 2.8% to 5.5% for males. By 2017, prevalence among females was 24.5% for 18–25 year olds, 19.7% for 26–34 year olds, 18.9% for 35–49 year olds, 18.0% for 50–64 year olds, and 9.5% for ages ≥65 years. For males, lifetime MDE prevalence was 15.0% for 18–25 year olds, 12.2% for 26–34 year olds, 12.7% for 35–49 year olds, 10.7% for 50–64 year olds, and 5.3% for those aged ≥65 years in 2017.

Model estimates for each age group were relatively stable from 2005–2015, with <0.1% absolute changes in prevalence over the 11-year period prior to the subsequent 2016–2017 increase. To capture recent trends in MDE prevalence among young adults, incidence probabilities were increased three-fold in the model beginning in 2016. An estimated 2.5X and 3.8X increase was applied to all female and male first MDE incidence probabilities for the years 2016 and 2017 (not shown in Figure 2). If the current trend of rising MDE incidence among young adults continues, it is unclear what impact this would have on the likelihood of recall error going forward as these individuals enter older age groups. Results are presented for the adult

population only; other research using NSDUH indicates that the MDE prevalence increase occurred earlier and at ages <18 years.[3]

For sensitivity analysis, we used Latin hypercube sampling for parameter space exploration with the 'pse' package in R.[6,7] This method efficiently samples across parameter distributions to cover the full range of all parameter value combinations. The user specifies the distribution and initial values for each parameter, as well as the total number of sample points to use. A total of 200 parameter combinations were sampled, with each run re-fitting and re-estimating splines coefficients for MDE incidence probabilities and age group-specific under-reporting probabilities. For recovery and recurrence parameters, we sampled values from a uniform distribution range that halved (50% decrease) and doubled (100% increase) base estimates. Values for the relative risk of mortality associated with ever having a MDE were sampled from a normal distribution (RR=1.71, SD=0.092).[8]

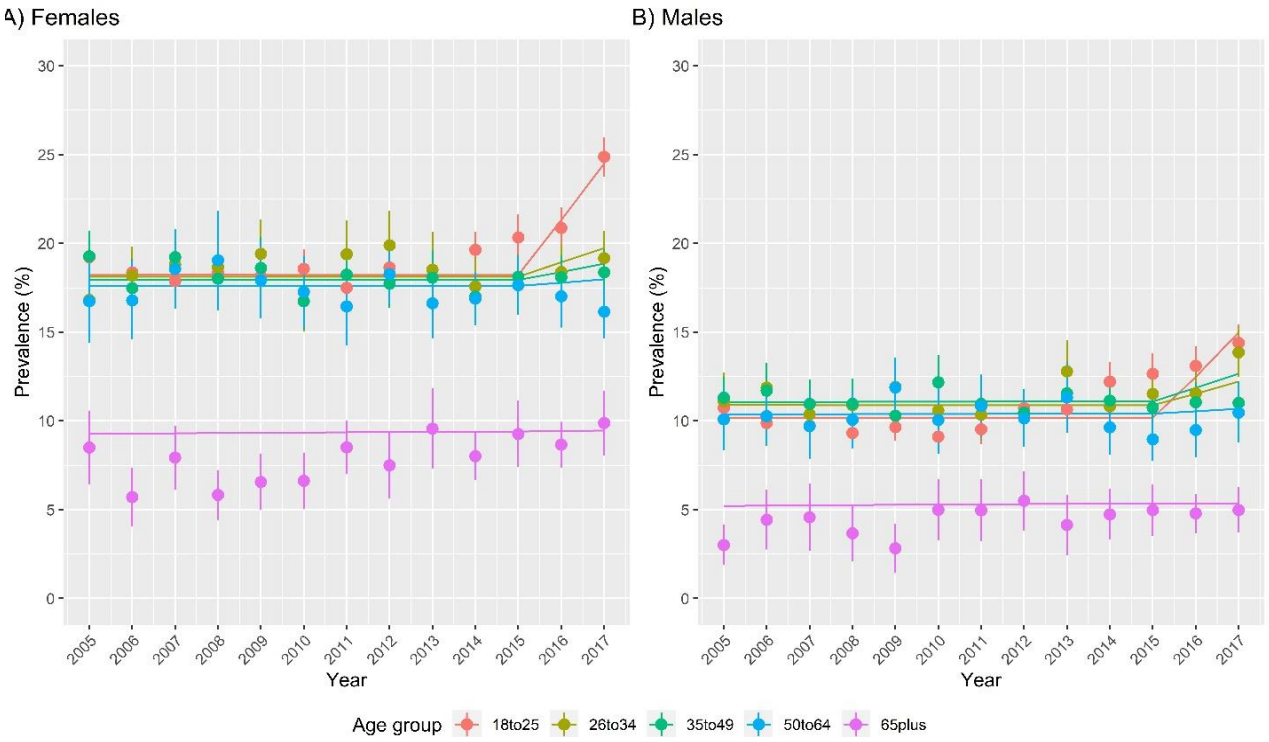
R code for the model structure, calibration, and sensitivity analysis are available online: https://github.com/jamietam/dep-model-AJPM.

Appendix Table 1. Model Parameters

Parameter	Model estimates
First MDE incidence probabilities	Age at onset of MDE incidence for females ages ≥22 years and males age ≥29 years in the Baltimore-ECA cohort study.[9] Cubic natural splines for MDE incidence with knots at ages 13 and 18 years were used to estimate probabilities among females ages 12–21 years and males ages 12–28 years. This extends previously reported curves for age at MDE onset to include youth and young adults,[9] and ensures that the model produces accurate estimates by age 18 years. The splines are given three degrees of freedom with knots at age 13 and 18 years. To account for the recent increase among young adults, scaling factors were estimated during calibration and applied to annual probabilities in 2016 and 2017.
MDE recovery probabilities	Annual probability of recovery calculated from 85% cumulative recovery from first MDE over 10 years in the Baltimore-ECA cohort study.[10] Annual probability $= 1 - (1 - Cumulative\ Incidence)^{(1/Duration\ in\ Years)} = 1 - (1 - 0.85)^{(1/10)} = 0.173$).
MDE recurrence probabilities	Annual probability of recurrence calculated from 45% cumulative recurrence after first MDE over 10 years in the Baltimore-ECA cohort study.[10] Annual probability $= (1 - (1 - 0.45)^{(1/10)} = 0.058)$.
Annual probability of death	Age, sex, and birth-cohort specific death probabilities from the Human Mortality Database, which relies on information from the National Vital Statistics System.[11]
Relative risk of mortality for lifetime history of MDEs	Pooled relative risk of mortality for people with lifetime history of major depression (RR=1.71, 95% CI=1.54, 1.90) estimated from a meta-analysis of 43 studies.[8] This estimate is nearly identical to another systematic review estimate.[12]

MDE, major depressive episode; ECA, Epidemiological Catchment Area.

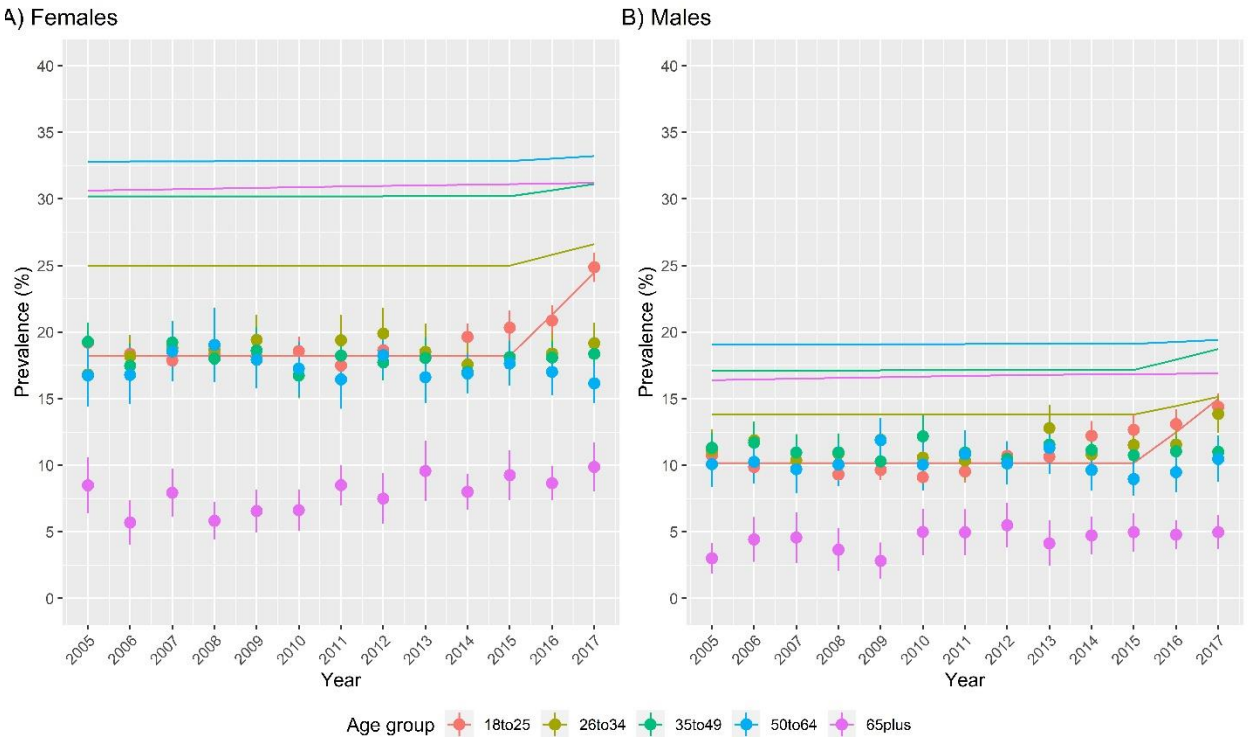
Appendix Figure 1. Lifetime MDE prevalence by age group without recall error adjustment, U.S., 2005–2017.



Notes: Horizontal lines represent model estimates for each age group without recall error adjustment, where individuals who under-report are categorized as never MDE; Dots with vertical lines represent National Survey on Drug Use and Health data for each age group and their corresponding 95% CIs.

MDE, major depressive episode.

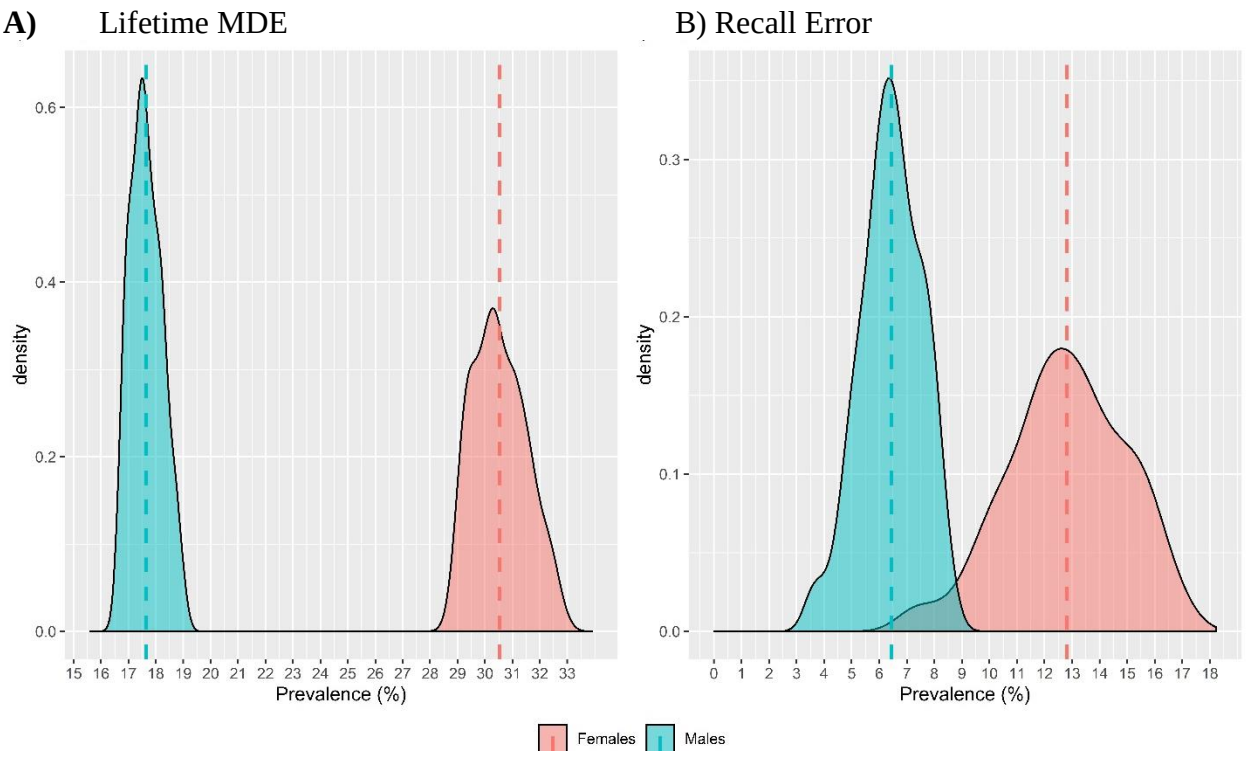
Appendix Figure 2. Lifetime MDE prevalence by age group with recall error adjustment, U.S., 2005–2017.



Notes: Horizontal lines represent model estimates for each age group with recall error adjustment, where individuals who under-report are categorized as former MDE; Dots with vertical lines represent National Survey on Drug Use and Health data for each age group and their corresponding 95% CIs.

MDE, major depressive episode.

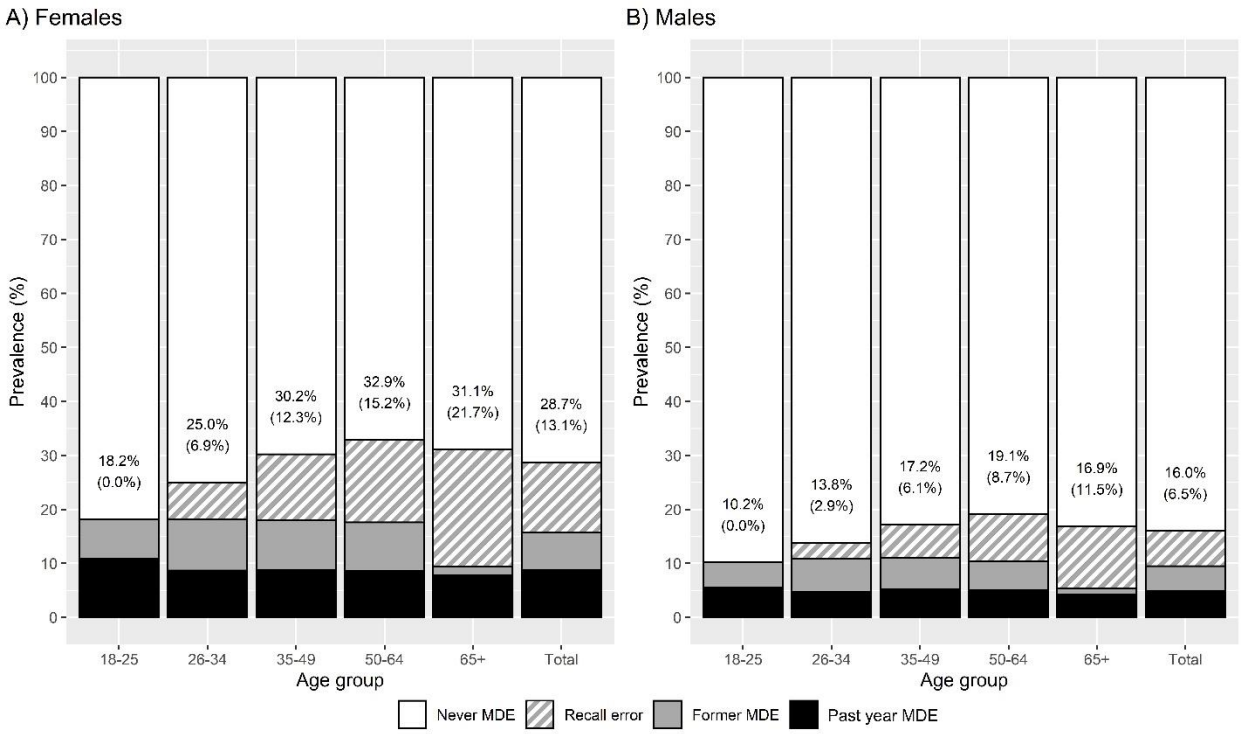
Appendix Figure 3. Uncertainty distributions of lifetime MDE prevalence and recall error, adults ages 18–99 years, 2017.



Notes: Red = Females; Blue = Males; Vertical dashed line = mean value; (A) Latin hypercube sampling results for lifetime MDE prevalence with 95% of values for females between 29.0% and 32.5% and for males between 16.7% and 18.8% among males; (B) Latin hypercube sampling results for the proportion of adults with former MDE that under-report lifetime MDEs, with 95% of estimates from 8.1%–16.5% for females and from 4.0%–8.3% for males.

MDE, major depressive episode.

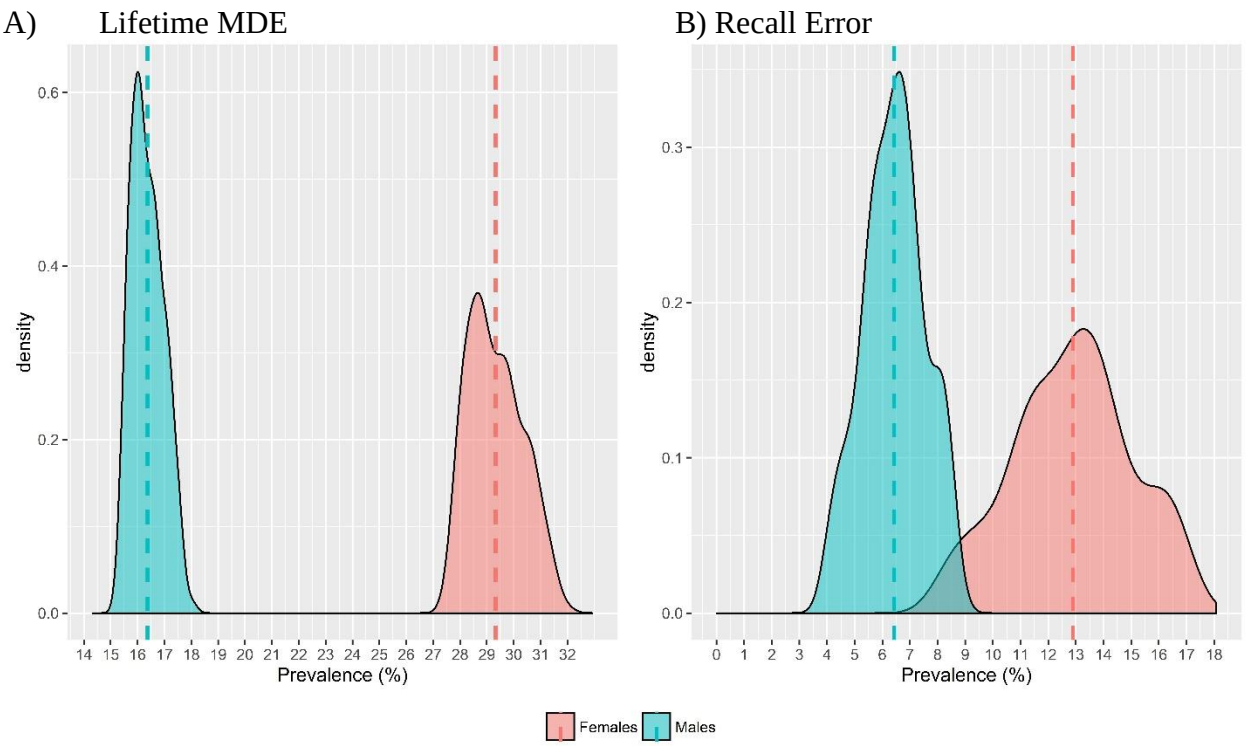
Appendix Figure 4. Adult lifetime MDE prevalence by age group with recall error adjustment, 2015.



Notes: Distribution of the adult population with past year MDE (black), former MDE (gray), former MDE with recall error (diagonal hatching pattern), and never MDE (white). Numbers represent the percent of individuals with lifetime MDE. Numbers in parentheses represent the percent of individuals with recall error who fail to report lifetime MDE.

MDE, major depressive episode.

Appendix Figure 5. Uncertainty distributions of lifetime MDE prevalence and recall error, adults ages 18–99 years, 2015.



Notes: Red = Females; Blue = Males; Vertical dashed line = mean value; (A) Latin hypercube sampling results for lifetime MDE prevalence with 95% of values for females between 27.8% and 31.3% and for males between 15.4% and 17.6% among males; (B) Latin hypercube sampling results for the proportion of adults with former MDE that under-report lifetime MDEs, with 95% of estimates from 8.6%–16.9% for females and from 4.2%–8.5% for males.

MDE, major depressive episode.

APPENDIX REFERENCES

1. Center for Behavioral Health Statistics and Quality. 2016 National Survey on Drug Use and Health: Methodological Summary and Definitions. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2017.
2. Center for Behavioral Health Statistics and Quality. 2017 National Survey on Drug Use and Health: Detailed Tables. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2018.
3. Twenge JM, Cooper AB, Joiner TE, Duffy ME, Binau SG. Age, period, and cohort trends in mood disorder indicators and suicide-related outcomes in a nationally representative dataset, 2005–2017. *J Abnorm Psychol*. 2019;128(3):185–199. https://doi.org/10.1037/abn0000410.
4. Leubeck G, Meza R. Bhat: General likelihood exploration. R package version 0.9-10. 2013.
5. R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2015.
6. McKay MD, Beckman RJ, Conover WJ. A comparison of three methods for selecting values of input variables in the analysis of output from a computer code. *Technometrics*. 1979;21(2):239–245. https://doi.org/10.1080/00401706.1979.10489755.
7. Chalom A, de Prado PIKL. pse: Parameter Space Exploration with Latin Hypercubes. R package version 0.4.5. http://CRAN.R-project.org/package=pse. Published 2016.
8. Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. *JAMA Psychiatry*. 2015;72(4):334–341. https://doi.org/10.1001/jamapsychiatry.2014.2502.
9. Eaton WW, Anthony JC, Gallo J, et al. Natural history of diagnostic interview schedule / DSM-IV major depression: the Baltimore Epidemiologic Catchment Area follow-up. *Arch Gen Psychiatry*. 1997;54(11):993–999. https://doi.org/10.1001/archpsyc.1997.01830230023003.
10. Eaton WW, Shao H, Nestadt G, Lee BH, Bienvenu OJ, Zandi P. Population-based study of first onset and chronicity in major depressive disorder. *Arch Gen Psychiatry*. 2008;65(5):513–520. https://doi.org/10.1001/archpsyc.65.5.513.
11. Human Mortality Database. www.mortality.org. Accessed November 26, 2017.
12. Eaton WW, Martins SS, Nestadt G, Bienvenu OJ, Clarke D, Alexandre P. The burden of mental disorders. *Epidemiol Rev*. 2008;30:1–14. https://doi.org/10.1093/epirev/mxn011.