BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Direct estimates of disability-adjusted life years lost due to stroke from a community-based study of 91,417individuals in rural Gadchiroli, India

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-028695
Article Type:	Research
Date Submitted by the Author:	19-Dec-2018
Complete List of Authors:	Sudharsanan, Nikkil; Harvard University T H Chan School of Public Health, Center for Population and Development Studies Deshmukh, Mahesh; Society for Education Action and Research in Community Health Kalkonde, Yogeshwar; Society for Education Action and Research in Community Health, Public Health
Keywords:	Neurology < INTERNAL MEDICINE, EPIDEMIOLOGY, Stroke < NEUROLOGY, PUBLIC HEALTH

SCHOLARONE™
Manuscripts

Direct estimates of disability-adjusted life years lost due to stroke from a community-based study of 91,417individuals in rural Gadchiroli, India

Nikkil Sudharsanan[1], Mahesh Deshmukh[2], Yogeshwar Kalkonde[2],

[1]Center for Population and Development Studies, Harvard T.H. Chan School of Public Health, Boston, MA, USA

[2]Society for Education, Action and Research in Community Health (SEARCH), Gadchiroli, Maharashtra, India

Address for correspondence:

Yogeshwar Kalkonde, M.D., M.Sc.

SEARCH, PO and District Gadchiroli,

Maharashtra, India 422605

Phone: +91-7138- 255407

Fax: +91 – 7138-255411

Email: yogesh_kalkonde@searchforhealth.ngo

Word count-4943

Short title: Stroke burden in rural Gadchiroli, India

Figures-2

Key words: stroke, burden, DALY, prevalence, mortality, rural, India

Abstract

Objective: Estimating the burden of diseases is an important way to identify healthcare priorities. Stroke is emerging as a public health priority in India. A majority of Indians live in rural areas but estimates of the disease burden due to stroke for rural India do not exist. In this study we directly estimated disability-adjusted life years (DALYs) lost due to stroke using unique population-level data in rural Gadchiroli, India.

Methods: Stroke mortality and stroke prevalence were estimated in two separate population-studies conducted in a demographic surveillance site in Gadchiroli. Stroke mortality was estimated in 86 villages from 2011 to 2013, where cause of death was determined using verbal autopsies. The prevalence of stroke was estimated in 39 of the 86 villages in 2014 using a house-to-house survey. These data were used to estimate years of life lost (YLLs), years of life lost due to disability (YLDs),and DALYs lost due to stroke in a mid-term population of 91,417 individuals in year 2012.

Results: 229 stroke deaths occurred in two years in a population of 94,154 individuals. There were 175 stroke survivors in a population of 45,053.Anestimated 2,984 DALYs were lost due to stroke per 100,000 person-years (2,821 among women and 3,142 among men). Years of life lost (YLL) accounted for 95.6% of the DALYs lost. Close to two thirds (62%) of the total DALYs lost due to stroke were at premature ages between 30 and 70 years.

Conclusions: This first direct estimate of DALYs lost due to stroke in rural India revealed a high burden of stroke with high YLLs and a significant burden at premature ages. Preventive and curative services need to be urgently developed and the burden of stroke needs to be tracked in rural India.

Keywords: stroke, DALYs, disability, mortality, rural India.

Strengths and limitations of this study

- While a majority of India's population lives in rural areas, very little population-level data are available on the disease burden due to stroke. This is the first study to directly estimate the burden of stroke in rural India.
- The study shows a very high burden for both men and women in the rural area of Gadchiroli district of India.
- This study uses rare verbal autopsy-based cause of death and population stroke prevalence data from a long-running demographic surveillance site.
- A limitation of this study is that the stroke mortality and stroke prevalence data are from adjacent (2011-2013 and 2014) but non-overlapping periods.
- Diagnosis of stroke was made using verbal autopsies and validated clinical diagnosis method as very few patients had brain imaging.

Introduction

Stroke is the second leading cause of death and disability globally[1–3]. In 2016, stroke accounted for 10.1% of all deaths and 4.8% of all disability adjusted life years (DALYs) lost[1].Stroke in India has important global implications-14% of global DALYs lost due to stroke occur in India[4]. According to modeled estimates in the Global Burden of Disease (GBD) study, stroke was the fifth leading cause of DALYs lost[5].The GBD study also found substantial heterogeneity across states, with the highest burden of stroke in the states of West Bengal, Assam, Odisha, and Chhattisgarh, and substantially lower levels in Mizoram, Sikkim, and Delhi[4].Given that health policy decisions are often made at state and local levels, these results call attention to the importance of sub-national stroke burden estimates for identifying which specific parts of the country need better preventive and curative stroke services.

One of the most important sub-national distinctions in India is between urban and rural areas. Two thirds of India's population (and 12% of world's population) lives in rural areas where health services are often not available, especially specialty care for individuals that have already experienced a stroke[6].Compared to urban areas, patterns of non-communicable disease (NCD)risk factors also tend to be less pronounced in rural areas[7–9], potentially leading to the belief that stroke and other NCDs are primarily a problem of urbanizing city centers. Therefore, an important open question is whether stroke, a disease associated with urbanizing city centers, is an important public health problem in rural areas as well.

Unfortunately, most of the existing studies of stroke in India do not shed light on the burden of stroke among the 890 million individuals living in rural parts of India [10]. The GBD studies, for example, do not provide estimates separately for urban and rural areas. Using data from a rural surveillance site in Andhra Pradesh, Joshi et al. (2006) found that stroke was a leading cause of death between the years 2003 and 2004;Kalkonde et al. (2015) used data from rural Maharashtra and similarly concluded that stroke was the leading cause of death between 2011 and 2013[11,12].While these studies provided a rare insight into the importance of stroke in rural areas, policy efforts are generally focused on diseases that carry a large burden of avertable life years lost, which the previous two studies did not estimate.

In this study, we provide one of the first direct estimates of the combined morbidity and mortality burden of stroke – measured through DALYs lost – in a demographic surveillance site in rural India. We directly estimated DALYs using rare sources of local census, population-representative stroke prevalence, and verbal-autopsy-based cause of death data from the Gadchiroli demographic surveillance site in rural Maharashtra, India. We measured both the overall burden of stroke and also determined how the burden varies across age and sex and whether the burden is primarily driven by stroke mortality or morbidity.

Methods

Study setting

The study was conducted in Gadchiroli district of India which has a population of 1,072,942 individuals, the majority of whom live in rural areas (89%). More than one third of individuals in the district (38.3%) are considered "scheduled tribes," India's tribal demographic group[13]. Based on data collected by the Indian government, Gadchiroli falls in the bottom 101 of India's

718 districts in terms of development and is classified by the government as a "backwards district"[14].

All data are from a rural demographic surveillance site monitored by the Society for Education, Action and Research in Community Health (SEARCH), a non-governmental organization working in the Gadchiroli district of Maharashtra, India since 1986. SEARCH identifies health priorities of the community it works with through research and develops and tests healthcare interventions to address these priorities. SEARCH operates a demographic surveillance system in 86 villages in Gadchiroli with routine population censuses and a constantly updated enumeration of births and deaths that occur within the site. As of 2011, the surveillance site had a population of 94,154 individuals.

Estimation of mortality due to stroke

The details of the method used to estimate stroke mortality including sample size estimation have been previously published[12]. Briefly, in the 86 villages where SEARCH works all birth and deaths are reported at the village level by a resident community health worker to SEARCH staff. Within 2-4 weeks of a reported death, trained surveyors collected information on the deceased using a well-validated verbal autopsy tool. This information was then reviewed by two separate physicians who independently assigned cause of death; conflicting causes of death were reconciled between coders with a third coder adjudicating the cause of death if the two coders continued to disagree. For this study, we used data on all deaths between April 1st, 2011 to March 31st, 2013.

Estimation of the prevalence of stroke survivors

The prevalence of stroke was estimated from a three-stage population-based survey of 45,053 individuals living in 39 of the 86 site villages conducted between January and May of 2014. Details of the sample size calculations, sampling method, participant recruitment and non-participation have been published previously[15]. Briefly, trained surveyors conducted a house-to-house survey to screen for symptoms of stroke using a well-validated questionnaire. A trained physician evaluated individuals who screened-positive to diagnose stroke and doubtful cases were evaluated by a neurologist.

Calculation of DALYs

DALYs lost due to stroke were estimated as the sum of years of life lost (YLL) from stroke and years of life lost due to disability (YLD) due to stroke[16]. Years of life lost due to stroke were estimated for the 2011-2013 period by multiplying the number of deaths from stroke at each age by the remaining life expectancy in the GBD standard life table at that age and then summing across all ages. In sensitivity analyses, we used the Indian National Life Table for rural Maharashtra to determine how YLLs vary based on different survival assumptions.

To estimate YLDs due to stroke, we first calculated the age-specific prevalence of stroke for five-year age groups between the ages 0 and 85+ from the cross-sectional survey conducted in 2014. Next, age-specific population estimates were calculated for the 2011-2013 period by using the census conducted by SEARCH in 2005 and 2015 to first calculate age-specific growth rates and then projecting the age-specific counts of individuals in 2005 forward to 2012 (mid-period population for 2011-2013 which was 91,417) using the estimated age-specific growth rates. We then multiplied the age-specific stroke prevalence rates by the age-specific population counts in 2012 to estimate the expected number of individuals with stroke for the period. To estimate YLDs, we then multiplied the number of expected cases of stroke by a disability weight of 0.266 based on prior studies of the burden of stroke [17]and summed across all ages. In sensitivity analyses, we used a range of potential disability weights for stroke and found no substantive change to our conclusions.

Finally, DALYs were calculated as the sum of YLL and YLD expressed per 100,000 person-years lived. Based on the recommendations of the 2010 GBD and 2013 WHO GBD studies, we did not use age weights or other methods of discounting in estimating DALYs [18,19].

Ethical approval

The data used in this study were from previous studies to estimate stroke mortality and prevalence. These studies were approved by the Institutional Ethical Committee of SEARCH[15,20]. The procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2000.

Patient and Public Involvement

Patients and the public were not involved in the study design, data analysis, or writing of the manuscript. Community health workers aided in the data collection by reporting deaths within the surveillance site to SEARCH staff and in screening of individuals in the study population to assess the prevalence of stroke. Findings of the study will be shared with the study population through a community awareness programme.

Results

Table 1 presents stroke mortality rate, stroke deaths, and YLLs due to stroke overall and separately by sex and age. Overall, there were 229 stroke deaths between 2011 and 2013, corresponding to a stroke mortality rate of 125.3 per 100,000 person years, 5216.2 absolute YLLs lost, and 2583.0 YLLs lost per 100,000 person years. YLLs lost were slightly higher for men compared to women (2966.3 for men compared to 2737.2 for women). The majority of stroke deaths occurred between ages 65 and 80, with the largest amount of YLLs occurring among those aged 65 to 70. Stroke mortality rates and YLLs per 100,000person years, however, were highest at ages above 75 for both women and men.

Table 2 presents stroke prevalence, expected stroke cases, and YLDs due to stroke overall and separately by sex and age. Overall, there were 901.5 expected cases of stroke per 100,000 person years between 2011 and 2013, corresponding to a stroke prevalence of 388.4 per 100,000 person years, 239.8 absolute YLD, and 131.2 YLDs per 100,00 person years. The morbidity burden of stroke was much higher for men: men had a stroke prevalence of 519.4, 162.6 YLDs, and 176 YLDs per 100,000 person years compared to a stroke prevalence of 255.1, 75.6 YLDs, and 83.6 YLDs per 100,000 person years for women. For both women and men, the morbidity burden of stroke is clustered above the age of 50.

Figure 1 graphs DALYs due to stroke per 100,000 person years by age-group, separately for women and men. Total DALYs lost due to stroke were 2,984 per 100,000 person years with a higher burden among men (3,142 per 100,000person years) relative to women (2,812 per

100,000person years). For both women and men, the rate of DALYs lost due to stroke increased steadily over age to a peak between ages 75 and 85. However, 62% of total DALYs lost due to stroke occurred prematurely between ages 30 and 70. The vast majority of DALYs for both women and men were due to YLLs, with small contributions from YLDs (3.0% for women, 5.6% for men).

Figure 2 compares the rate of DALYs lost due to stroke estimated in Gadchiroli to the national and global DALYs lost due to stroke from the GBD study[4]. The estimated rate of DALYs lost due to stroke in Gadchiroli is higher than all the states in the GBD study with the closest estimate in West Bengal (2821). Our estimate is closer to estimate for the neighbouring state of Chhattisgarh (2142) than the state of Maharashtra (1341), where Gadchiroli is located.

Discussion

In this first estimation of DALYs lost due to stroke in rural India using directly estimated inputs, we found a very high burden of stroke in the rural, Gadchiroli district, of Maharashtra, India. Importantly, the majority of DALYs lost occurred at relatively young ages between 30 and 70, revealing a large premature burden of stroke. We found moderate sex differences in the burden of stroke with a slightly higher burden among men compared to women, driven primarily by a greater number of YLLs due to stroke among men. For both women and men, more than 95% of the total disease burden was due to YLLs, indicating a high level of stroke mortality in Gadchiroli.

Our estimate of DALYs due to stroke per 100,000 person years was higher than the Indian state-specific estimates published in a recent GBD study [4].As the GBD estimates are heavily modeled based on scarce data, extrapolated using multiple indirect sources of information, and are based on predictive models built with data from other contexts, it is possible that the GBD estimate of the burden of stroke in India could be underestimated[21]. However, higher estimates in our study could also be due to geographical differences within India and lack of healthcare services in Gadchiroli leading to excessive mortality. Furthermore, estimates for rural areas of India are not available separately in the GBD study, where the majority of India's population lives and where there are significant challenges to healthcare delivery. Therefore, in this context our study provides a value addition and highlights a need to monitor the stroke burden in rural India. Beyond the GBD, our results are difficult to directly compare to other studies due to a paucity of DALY estimates from other parts of India, particularly rural India, as well as other low- and middle-income countries. To our knowledge, in India, there is only one other population-based study that has estimated DALYs lost due to stroke using directly estimated inputs, and this study was based in an urban city center. Banerjee et al. (2013) used data from city of Kolkata and estimated that 795.6 DALYs per 100,000 person-years lived were lost due to stroke[22]. The large difference between our estimate is partly driven by the choice of life table used in the calculation of DALYs. Banerjee et al. used Indian life tables to calculate DALYs where the life expectancies are lower compared to those in the GBD 2010 life tables. However, in sensitivity analyses, we found that even when using the rural Indian life tables, we estimated a substantially higher burden of DALYs lost due to stroke (1,842 per 100,000 person-years lived), though the magnitude of this difference reduced substantially. Maredzea et al. (2015) estimated DALYs lost due to stroke in rural South Africa using a prevalence-based method similar to ours

[23]. Based on data from the Agincourt cohort in rural South Africa, the authors estimated that 2,156 DALYs were lost due to stroke per 100,000 person-years—closer in magnitude to our estimate[23].Additionally, we found that the contribution of YLD to DALYs was only about 5% (4.4%), compared to around 25% in the study by Banerjee et al. and 8.7% in the study by Maredzea et. al. This indicates that stroke mortality is potentially much higher in Gadchiroli compared to these other contexts. Although there is only one study estimating DALYs due to stroke in India, our results are broadly consistent with a small number of studies documenting a high incidence and mortality rate from stroke in specific Indian sub-populations [11,12,24–27].Similarly, the high burden of stroke in Gadchiroli is consistent with recent nationally-representative evidence that finds high levels of stroke mortality in eastern states, such as Chhattisgarh, that are geographically adjacent to Gadchiroli, and have similar levels of development and healthcare services[28].Lack of access to healthcare and poor prevention and treatment of stroke are the likely important reasons for this pattern. As hypertension is the most important risk factor for stroke[29], undetected, untreated and uncontrolled hypertension could be the driver of stroke in Gadchiroli.

The major strength of our study is the direct estimation of DALYs based on mortality and prevalence data on stroke from a demographic surveillance site. Both the stroke prevalence and mortality data were conducted using validated instruments with rare cause of death data for a large population [12,15]. Such a method provides estimates that more closely represent actual disease conditions than those obtained using indirect methods. We also used the new methods for DALY estimation recommended by the GBD 2010 study[1], allowing for a consistent comparison of DALYs due to stroke across populations and time. The study also has some limitations. The mortality and prevalence data were from non-overlapping periods. The mortality data were from years 2011-2013 while the prevalence data were obtained in 2014. However, since the study was conducted in the same population pool, we believe that the difference in the time period is unlikely to significantly affect the estimation of DALYs. We used a single disability weight of 0.266 for stroke disability. While using different disability weights based on the level of disability due to stroke is recently being proposed by the GBD study group, we believe that given the smaller proportion of YLDs (4.4%) in the DALYs in our study, the method used in this estimation is unlikely to significantly affect the estimation of DALYs. As brain imaging is not readily available in this region we could not assess DALYs due to ischemic and hemorrhagic strokes separately. Also, our study may not be completely representative of rural India as different rural regions of India might have different access to healthcare, which will affect the overall risk of having a stroke, disability and the mortality due to stroke.

Our study shows a high, underappreciated burden of stroke in a rural area of India and has important implications for health policy. It also highlights a need to monitor the stroke burden in rural areas of India where very little data are available and people remain vulnerable to preventable mortality. This would be essential to track progress towards the Sustainable Development Goals adopted in a United Nations General Assembly in 2015 which calls for one-third reduction in premature mortality because of non-communicable diseases by2030[30].At a systems level, identifying, testing, and scaling different ways of delivering preventive and curative health services for stroke, particularly controlling high blood pressure, the leading risk factor for stroke[31],in rural, resource-constrained environments in Gadchiroli and other parts of India will be essential.

Authors' Contributions

Conceived the study- YK; Analysed data- NS, MD, YK; Wrote the manuscript- NS, YK; Revised the draft critically for intellectual content-YK, NS, AB.

Data Sharing

No additional data available.

Funding

SEARCH was supported by the John D. and Catherine T. MacArthur Foundation. Dr. Sudharsanan received support from "Penn Indian re-SEARCH, a collaboration for High-Impact Health and Demographic Research", Global Engagement Fund, University of Pennsylvania.

Competing interests

None

Acknowledgements

We thank Drs.Vikram Sahane, Jyoti Puthran, Sujay Kakarmath and Vaibhav Agavane and the field supervisors of SEARCH for technical assistance. We thank people of Gadchiroli for their support in conducting these studies.

References

1 Hay SI, Abajobir AA, Abate KH, *et al.* Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for

195 countries and territories, 1990--2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017;**390**:1260–344.

2 Bennett DA, Krishnamurthi R V., Barker-Collo S, *et al.* The global burden of ischemic stroke: Findings of the GBD 2010 study. *Glob Heart* 2014;**9**:107–12. doi:10.1016/j.gheart.2014.01.001

3 Naghavi M, Abajobir AA, Abbafati C, *et al.* Global, regional, and national age-sex specific mortality for 264 causes of death, 1980--2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017;**390**:1151–210.

4 Prabhakaran D, Jeemon P, Sharma M, *et al.* The changing patterns of cardiovascular diseases and their risk factors in the states of India: the Global Burden of Disease Study 1990–2016. *Lancet Glob Heal* Published Online First: 2018. doi:10.1016/S2214-109X(18)30407-8

5 Dandona L, Dandona R, Kumar GA, *et al.* Nations within a nation: variations in epidemiological transition across the states of India, 1990--2016 in the Global Burden of Disease Study. *Lancet* 2017;**390**:2437–60.

6 Balarajan Y, Selvaraj S, Subramanian S V. Health care and equity in India. *Lancet* 2011;**377**:505–15.

7 Geldsetzer P, Manne-Goehler J, Theilmann M, *et al.* Geographic and sociodemographic variation of cardiovascular disease risk in India: A cross-sectional study of 797,540 adults. *PLoS Med* 2018;**15**:e1002581.

8 Chadha SL, Gopinath N, Shekhawat S. Urban-rural differences in the prevalence of coronary heart disease and its risk factors in Delhi. *Bull World Health Organ* 1997;**75**:31.

9 Thankappan KR, Shah B, Mathur P, *et al.* Risk factor profile for chronic non-

communicable diseases: results of a community-based study in Kerala, India. *Indian J Med Res* 2010;**131**:53.

10 World Bank. *World Development Indicators, 2017*. Washington, DC: 2017.

11 Joshi R, Cardona M, Iyengar S, *et al.* Chronic diseases now a leading cause of death in rural India--mortality data from the Andhra Pradesh Rural Health Initiative. *Int J Epidemiol* 2006;**35**:1522–9. doi:10.1093/ije/dyl168

12 Kalkonde Y V, Deshmukh MD, Sahane V, *et al.* Stroke Is the Leading Cause of Death in Rural Gadchiroli, India: A Prospective Community-Based Study. *Stroke* 2015;**46**:1764–8. doi:10.1161/STROKEAHA.115.008918

13 2011 C of I. District Census Handbook Gadchiroli. 2011.

14 NITI Ayog. Transformation of Aspirational Districts Baseline Rankings and Real-Time Monitoring Dashboard. New Delhi: 2018.

15 Kalkonde Y V., Sahane V, Deshmukh MD, *et al.* High Prevalence of Stroke in Rural Gadchiroli, India: A Community-Based Study. *Neuroepidemiology* 2016;**46**:235–9. doi:10.1159/000444487

16 Murray CJ. Quantifying the burden of disease: the technical basis for disability-adjusted life years. *Bull World Health Organ* 1994;**72**:429.

17 WHO. Global burden of disease 2004 update: disability weights for diseases and conditions. 2008.

18 WHO methods and data sources for global burden of disease estimates 2000-2011.

19 Murray CJL, Vos T, Lozano R, *et al.* Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet (London, England)* 2012;**380**:2197–223.

doi:10.1016/S0140-6736(12)61689-4

20 Kalkonde Y V., Deshmukh MD, Sahane V, *et al.* Stroke Is the Leading Cause of Death in Rural Gadchiroli, India: A Prospective Community-Based Study. *Stroke* 2015;**46**:1764–8. doi:10.1161/STROKEAHA.115.008918

21 Gakidou E, Afshin A, Abajobir AA, *et al.* Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990--2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017;**390**:1345–422.

22 Banerjee TK, Dutta S, Ray BK, *et al.* Disease burden of stroke in Kolkata, India: derivation of disability-adjusted life years by a direct method. *Neuroepidemiology* 2013;**41**:88–93.

23 Maredza M, Bertram MY, Tollman SM. Disease burden of stroke in rural South Africa: An estimate of incidence, mortality and disability adjusted life years. *BMC Neurol* 2015;**15**. doi:10.1186/s12883-015-0311-7

24 Gajalakshmi V, Lacey B, Kanimozhi V, *et al.* Body-mass index, blood pressure, and cause-specific mortality in India: a prospective cohort study of 500 810 adults. *Lancet Glob Heal* 2018;**6**:e787–94. doi:10.1016/S2214-109X(18)30267-5

25 Ray BK, Hazra A, Ghosal M, *et al.* Early and delayed fatality of stroke in Kolkata, India: results from a 7-year longitudinal population-based study. *J Stroke Cerebrovasc Dis* 2013;**22**:281–9. doi:10.1016/j.jstrokecerebrovasdis.2011.09.002

26 Pandian JD, Singh G, Kaur P, *et al.* Incidence, short-term outcome, and spatial distribution of stroke patients in Ludhiana, India. *Neurology* 2016;**86**:425–33. doi:10.1212/WNL.0000000000002335

27 Dalal PM, Malik S, Bhattacharjee M, *et al.* Population-based stroke survey in Mumbai, India: Incidence and 28-day case fatality. *Neuroepidemiology* 2008;**31**:254–61. doi:10.1159/000165364

28 Ke C, Gupta R, Xavier D, *et al.* Divergent trends in ischaemic heart disease and stroke mortality in India from 2000 to 2015: a nationally representative mortality study. *Lancet Glob Heal* 2018;**6**:e914--e923.

29 Collins R, Peto R, MacMahon S, *et al.* Blood pressure, stroke, and coronary heart disease: part 2, short-term reductions in blood pressure: overview of randomised drug trials in their epidemiological context. *Lancet* 1990;**335**:827–38.

30 United Nations. The Sustainable Development Goals Report 2018. New York: 2018.

31 O'Donnell MJ, Chin SL, Rangarajan S, *et al.* Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. *Lancet* 2016;**388**:761–75.

Table 1: Estimated age- and sex-specific distribution of stroke deaths, stroke mortality, and years of life lost (YLLs)[a] due to stroke between 2011-2013

Age group	Men				Women				Total			
	Stroke mortality rate (per 100,000)	Stroke deaths	YLLs	YLLs (per 100,000)	Stroke mortality rate (per 100,000)	Stroke deaths	YLLs	YLLs (per 100,000)	Stroke mortality rate (per 100,000)	Stroke deaths	YLLs	YLLs (per 100,000)
0-4	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0
4-9	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0
10-14	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0
15-19	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0
20-24	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0
25-29	12.0	1	61.4	733.9	0.0	0	0.0	0.0	6.2	1	61.4	383.5
30-34	0.0	0	0.0	0.0	29.3	2	108.9	1596.1	14.5	2	108.9	788.0
35-39	13.5	1	51.5	694.8	14.3	1	51.5	735.1	13.9	2	103.1	714.4
40-44	67.0	4	186.6	3126.0	0.0	0	0.0	0.0	33.3	4	186.6	1550.8
45-49	65.5	4	167.2	2737.4	85.1	5	209.0	3559.3	75.1	9	376.2	3140.2
50-54	200.4	9	333.5	7423.2	160.5	7	259.4	5945.7	180.7	16	592.8	6695.3
55-59	263.9	11	356.2	8545.6	138.3	5	161.9	4477.3	205.5	16	518.1	6655.7
60-64	302.1	8	222.5	8401.8	275.5	10	278.1	7661.2	286.7	18	500.6	7973.6
65-69	702.6	24	559.0	16363.0	553.9	22	512.4	12899.8	622.6	46	1071.3	14501.1
70-74	850.0	17	321.8	16090.5	1091.5	21	397.5	20661.6	968.4	38	719.3	18331.8
75-79	2252.3	20	296.0	33333.3	2394.1	26	384.8	35432.8	2330.3	46	680.8	34488.3
80-84	3208.6	12	131.9	35262.0	1181.1	6	65.9	12980.3	2040.8	18	197.8	22428.6
85+	2755.9	7	53.5	21055.1	1898.7	6	45.8	14506.3	2280.7	13	99.3	17424.6
Total	127.7	118	2740.9	2966.3	122.7	111	2475.3	2737.2	125.3	229	5216.2	2853.0

[a]YLLs were calculated using the life expectancy used in the GBD 2010 study

Table 2: Estimated age- and sex-specific distribution of stroke cases, stroke prevalence[a], and years of life lost due to disability (YLDs)[b] due to stroke between 2011-2013

	Men				Women				Total			
Age group	Stroke prevalence per 100,000	Expected stroke cases	YLDs	YLDs per 100,000	Stroke prevalence per 100,000	Expected stroke cases	YLDs	YLDs per 100,000	Stroke prevalence per 100,000	Expected stroke cases	YLDs	YLDs per 100,000
0-4	0.0	0.00	0.0	0.0	61.1	4.56	1.2	16.3	[illegible]	4.48	1.2	7.9
5-9	0.0	0.00	0.0	0.0	0.0	0.00	0.0	0.0	0.0	0.00	0.0	0.0
10-14	44.5	3.33	0.9	11.8	0.0	0.00	0.0	0.0	[illegible]	3.34	0.9	6.1
15-19	0.0	0.00	0.0	0.0	36.9	3.39	0.9	9.8	[illegible]	3.38	0.9	4.9
20-24	47.3	4.40	1.2	12.6	0.0	0.00	0.0	0.0	[illegible]	4.46	1.2	6.7
25-29	106.4	8.90	2.4	28.3	56.8	4.34	1.2	15.1	[illegible]	13.20	3.5	21.9
30-34	121.7	8.52	2.3	32.4	173.6	11.85	3.2	46.2	[illegible]	20.50	5.5	39.5
35-39	54.3	4.03	1.1	14.4	51.6	3.62	1.0	13.7	[illegible]	7.63	2.0	14.1
40-44	397.9	23.75	6.3	105.8	127.8	7.75	2.1	34.0	[illegible]	31.32	8.3	69.2
45-49	210.4	12.85	3.4	56.0	153.1	8.99	2.4	40.7	[illegible]	21.93	5.8	48.7
50-54	721.6	32.42	8.6	192.0	681.8	29.74	7.9	181.4	[illegible]	62.22	16.5	186.9
55-59	1522.2	63.45	16.9	404.9	634.5	22.94	6.1	168.8	[illegible]	85.33	22.7	291.6
60-64	3270.2	86.60	23.0	869.9	1154.4	41.90	11.1	307.1	[illegible]	133.05	35.4	563.7
65-69	4812.8	164.41	43.7	1280.2	1068.7	42.45	11.3	284.3	[illegible]	206.57	54.9	743.8
70-74	4000.0	80.00	21.3	1064.0	3876.0	74.57	19.8	1031.0	[illegible]	154.40	41.1	1046.7
75-79	6508.9	57.80	15.4	1731.4	1485.1	16.13	4.3	395.0	[illegible]	74.49	19.8	1003.8
80-84	10769.2	40.28	10.7	2864.6	2381.0	12.10	3.2	633.3	[illegible]	53.28	14.2	1606.7
85+	8163.3	20.73	5.5	2171.4	0.0	0.00	0.0	0.0	3846.2	21.92	5.8	1023.1
Total	519.4	611.45	162.6	176.0	255.1	284.33	75.6	83.6	[illegible]	901.50	239.8	131.2

[a]Prevalence rate was calculated from a subsample of individuals surveyed in 2014 and then applied to the overall 2012 population counts to estimate expected cases of stroke.
[b]YLD's are calculated using a disability weight of 0.266 for stroke

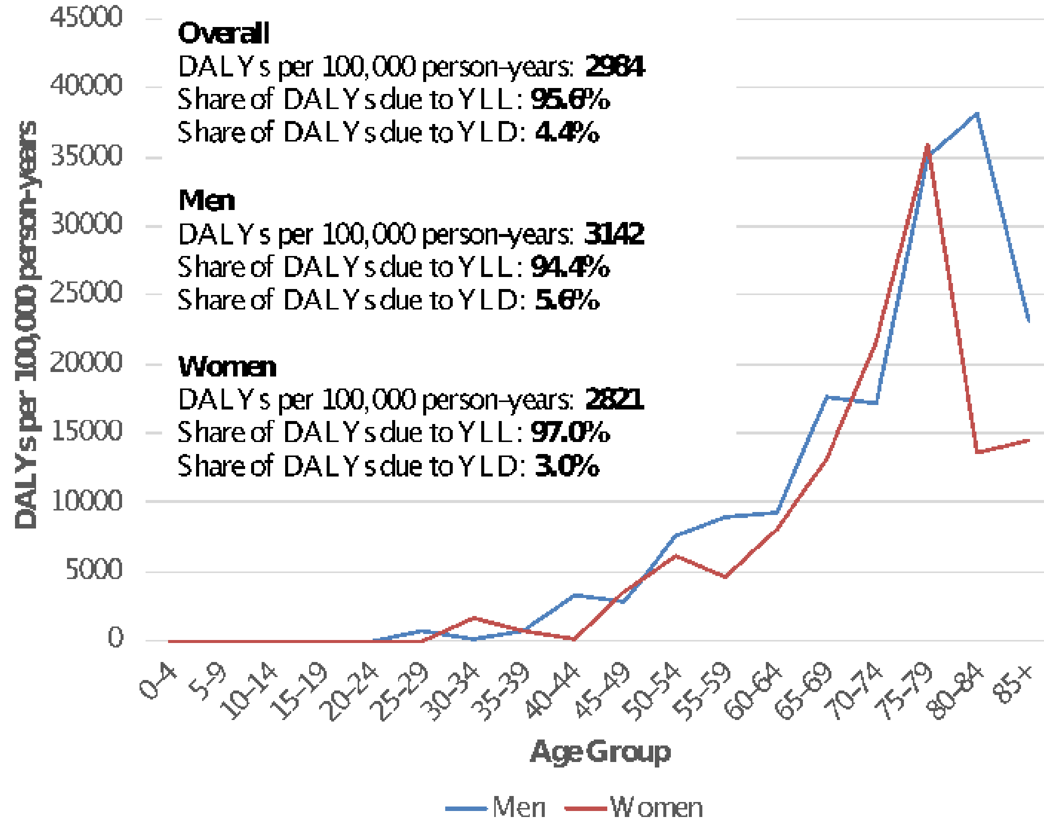


Figure 1 Age-specific rate of DALYs(a)(b) lost due to stroke per 100,000 person-years for men and women, Gadchiroli, 2011-2013.
(a) DALYs were estimated as the sum of years of life lost (YLLs) and years of life lost due to disability (YLD) due to stroke.
(b) YLLs were estimated using the 2010 GBD standard life table.

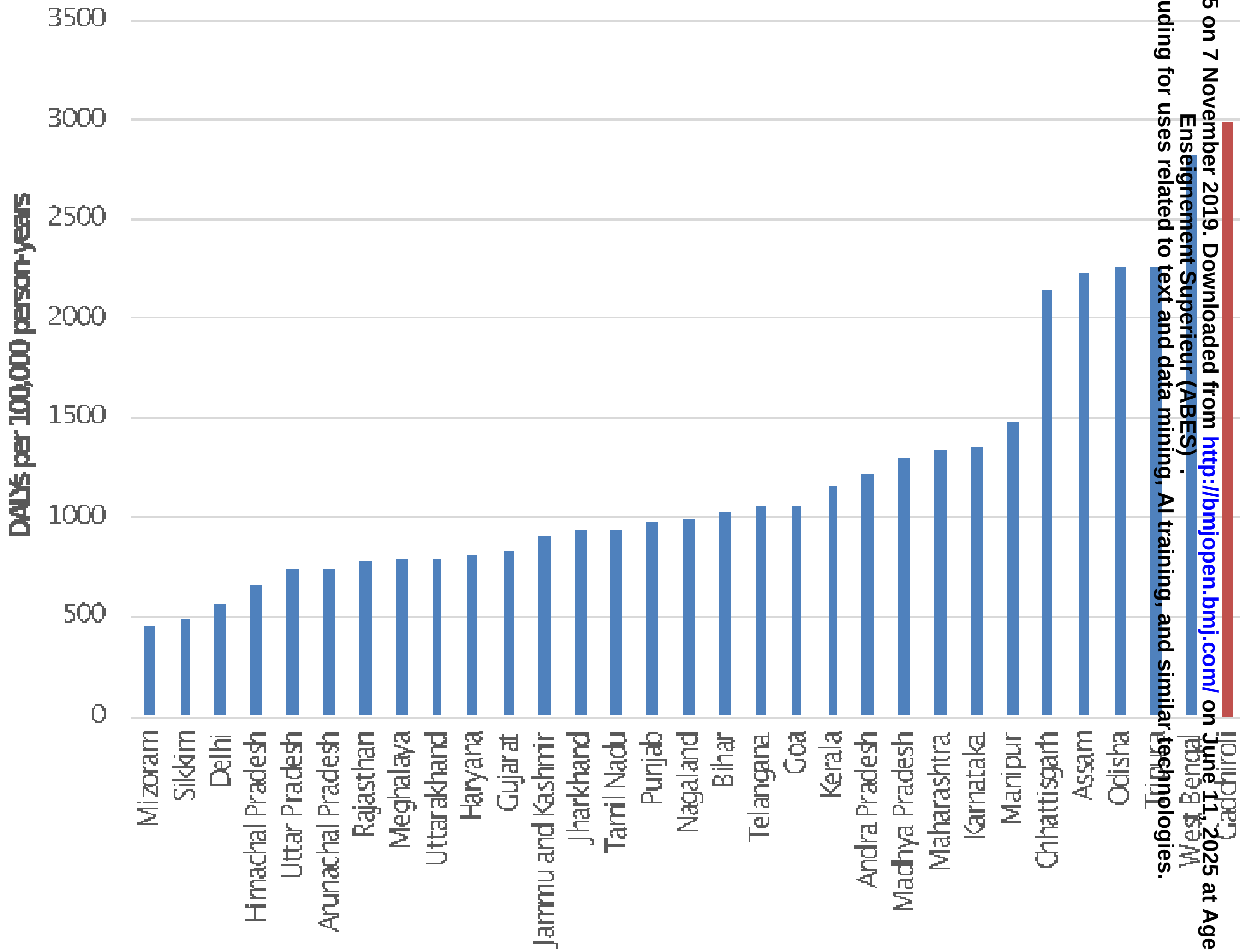


Figure 2 Total DALYs lost due to stroke per 100,000 for Gadchiroli[(a)] and for each Indian state[(b)]
[(a)]The Gadchiroli estimate is from the present study and is for the 2011-2013 period.
[(b)]Indian state estimates are from the 2016 GBD study [5].

Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cross sectional reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	#3	State specific objectives, including any prespecified hypotheses	5
Study design	#4	Present key elements of study design early in the paper	6-7
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	6
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7, 12
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	6-7

Bias	#9	Describe any efforts to address potential sources of bias	12
Study size	#10	Explain how the study size was arrived at	6
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	7-8
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	7-8
	#12b	Describe any methods used to examine subgroups and interactions	7-8
	#12c	Explain how missing data were addressed	7
	#12d	If applicable, describe analytical methods taking account of sampling strategy	7
	#12e	Describe any sensitivity analyses	7
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	8-9
	#13b	Give reasons for non-participation at each stage	6
	#13c	Consider use of a flow diagram	N/A
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	N/A
	#14b	Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	8-9
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-9
	#16b	Report category boundaries when continuous variables were categorized	N/A
	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	N/A

Key results	#18	Summarise key results with reference to study objectives	10
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	12
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	10-12
Generalisability	#21	Discuss the generalisability (external validity) of the study results	12
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

BMJ Open

Direct estimates of disability-adjusted life years lost due to stroke in rural India: A cross-sectional observational study of a demographic surveillance site in rural Gadchiroli, India

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-028695.R1
Article Type:	Research
Date Submitted by the Author:	12-Jul-2019
Complete List of Authors:	Sudharsanan, Nikkil; Harvard University T H Chan School of Public Health, Center for Population and Development Studies; Heidelberg University, Heidelberg Institute of Global Health Deshmukh, Mahesh; Society for Education Action and Research in Community Health Kalkonde, Yogeshwar; Society for Education Action and Research in Community Health, Public Health
Primary Subject Heading:	Global health
Secondary Subject Heading:	Neurology
Keywords:	Neurology < INTERNAL MEDICINE, EPIDEMIOLOGY, Stroke < NEUROLOGY, PUBLIC HEALTH

SCHOLARONE™
Manuscripts

Direct estimates of disability-adjusted life years lost due to stroke in rural India: A cross-sectional observational study of a demographic surveillance site in rural Gadchiroli, India

Nikkil Sudharsanan[1,2], Mahesh Deshmukh[3], Yogeshwar Kalkonde[3] (Corresponding author)

[1]Heidelberg Institute of Global Health, Heidelberg University, Heidelberg, Germany

[2]Center for Population and Development Studies, Harvard T.H. Chan School of Public Health, Boston, MA, USA

[3]Society for Education, Action and Research in Community Health (SEARCH), Gadchiroli, Maharashtra, India

Address for correspondence:

Yogeshwar Kalkonde, M.D., M.Sc.

SEARCH, PO and District Gadchiroli,

Maharashtra, India 422605

Phone: +91-7138- 255407

Fax: +91 – 7138-255411

Email: yvkalkonde@gmail.com

Word count-4,010

Short title: Stroke burden in rural Gadchiroli, India

Figures-2

Key words: stroke, burden, DALY, prevalence, mortality, rural, India

Abstract

Objective: To directly estimate disability-adjusted life years (DALYs) lost due to stroke in rural Gadchiroli, India and measure the contribution of mortality and disability to total DALYs lost.

Design: Cross-sectional descriptive study using population census, vital registration, and stroke prevalence data.

Setting: A demographic surveillance site of 86 villages in Gadchiroli, a rural district in Maharashtra, India.

Participants: Population counts and mortality information were drawn from a census and vital registration system covering a population of approximately 94,154 individuals; stroke prevalence information was based on a door-to-door evaluation of all 45,053 individuals from 39 of the 86 villages in the surveillance site.

Primary outcome measures: Years of life lost (YLL), years lived with disability (YLD), and DALYs lost due to stroke.

Results: There were 229 stroke deaths among the total population of 94,154 individuals and 175 stroke survivors among the sub-population of 45,053 individuals. An estimated 2,984 DALYs were lost due to stroke per 100,000 person-years with a higher burden among men compared to women (3,142 vs. 2,821 DALYs). Over three fourths (80%) of the total DALYs lost due to stroke were between ages 30 and 70. Years of life lost (YLL) accounted for 95.6% of total DALYs lost.

Conclusions: There was a high burden of stroke in rural Gadchiroli with a significant burden at premature ages. These results reveal a substantial need for both surveillance and improved preventive and curative services for stroke in rural India.

Keywords: stroke, DALYs, disability, mortality, rural India.

Strengths and limitations of this study

- The major strength of this study design is that it was based on census, verbal autopsy-based mortality surveillance, and stroke prevalence data from a long-running demographic surveillance site. This allowed us to provide direct, unmodeled, estimates of DALYs lost due to stroke.
- A limitation of this study was the lack of brain imaging and therefore inability to distinguish the contribution of ischemic and hemorrhagic stroke to the total DALYs lost due to stroke.
- The study data are also from a single district of India and may not be representative of all of rural India.

Introduction

Stroke is the third leading cause of death and disability globally (1). In 2017, stroke accounted for an estimated 11.0% of all deaths and 5.3% of all disability adjusted life years (DALYs) lost (1,2). Stroke in India has important global implications since an estimated 13.3% of global DALYs lost due to stroke occur in India. Within India, stroke was the sixth leading cause of DALYs lost in 2017 based on modeled estimates from the Global Burden of Disease (GBD) study (1). The GBD study also found substantial heterogeneity across states, with the highest burden of stroke in the states of West Bengal, Assam, Odisha, and Chhattisgarh, and substantially lower levels in Mizoram, Sikkim, and Delhi (3). Given that health policy decisions are often made at state levels, these results call attention to the importance of sub-national stroke burden estimates for identifying which specific parts of the country need better preventive and curative stroke services.

One of the most important sub-national distinctions in India is between urban and rural areas. Two thirds of India's population -- which is 12% of the world's population -- lives in rural areas (4) where health services are often not available, especially specialty care for individuals that have already experienced a stroke (5). Compared to urban areas, patterns of non-communicable disease (NCD) risk factors also tend to be less pronounced in rural areas (6,7), potentially leading to the belief that stroke and other NCDs are primarily a problem of urbanizing city centers. Therefore, an important open question is whether stroke, a disease associated with urbanizing city centers, is an important public health problem in rural areas as well.

Existing studies find high stroke mortality among the 890 million individuals living in rural parts of India (8–11). Using data from a rural surveillance site in Andhra Pradesh, Joshi et al. (2006) found that stroke was a leading cause of death between the years 2003 and 2004; Kalkonde et al. (2015) used data from rural Maharashtra and similarly concluded that stroke was the leading cause of death between 2011 and 2013 (8,11). Based on data from the Million Deaths Study, Ke et al. (2018) found that stroke mortality rates were higher in rural, than in urban, India (9). While these studies provided an important insight into the importance of stroke mortality in rural areas, policy efforts are generally focused on diseases that carry a large burden of avertable life years lost, the combination of morbidity and premature mortality due to stroke, which the previous studies did not estimate.

In this study, we provide direct estimates of the disease burden of stroke -- measured through DALYs lost -- in a demographic surveillance site in rural India. We directly estimated DALYs lost using rare sources of local census, population-representative stroke prevalence, and verbal-autopsy-based cause of death data from the Gadchiroli demographic surveillance site in rural Maharashtra, India for the years 2011-2013. We measured both the overall burden of stroke and also determined how the burden varies across age and sex and whether the burden is primarily driven by stroke mortality or morbidity.

Methods

Study setting

All data were from a rural demographic surveillance site monitored by the Society for Education, Action and Research in Community Health (SEARCH), a non-governmental organization working in the Gadchiroli district of Maharashtra, India since 1986. As of the last national census in 2011, Gadchiroli had a population of 1,072,942 individuals, the majority of whom live in rural areas (89%). More than one third of individuals in the district (38.3%) are considered "scheduled tribes," India's tribal demographic group (12). Based on data collected by the Indian government, Gadchiroli falls in the bottom 101 of India's 718 districts in terms of development and is classified by the government as an "aspirational district" (13). SEARCH operates a demographic surveillance system in 86 villages in Gadchiroli with routine population censuses conducted every 10 years, 5 years after the national censuses. There is also a continuous enumeration of births and deaths that occur within the site with annual updating of the population register. As of 2011, the surveillance site had a population of 94,154 individuals. Data from census, mortality surveillance and studies on stroke mortality and prevalence were obtained directly from SEARCH.

Estimation of mortality due to stroke

The details of the method used to estimate stroke mortality including sample size estimation have been previously published (8). Briefly, SEARCH operates a community-based demographic surveillance system where all births and deaths within the surveillance site are reported at the village level by a resident community health worker (CHW) to SEARCH staff. The data on causes of death was collected prospectively between April 1st, 2011 and March 31st, 2013.

Within 2-4 weeks of a reported death, trained surveyors collected information on the deceased using a well-validated verbal autopsy tool (14). This information was then reviewed by two physicians who independently assigned cause of death; conflicting causes of death were reconciled between coders with a third coder adjudicating the cause of death if the two coders continued to disagree. Both physician coders agreed on the diagnosis of stroke in 92.6% of stroke deaths and adjudication by a third physician was needed in 7.4% of deaths.

Estimation of the prevalence of stroke survivors

The prevalence of stroke was estimated from a three-stage population-based screening of all 45,053 individuals living in 39 of the 86 site villages conducted between January and May of 2014. Details of the sample size calculations, data collection method, participant recruitment and non-participation have been published previously (15). Briefly, trained surveyors went house-to-house to screen for symptoms of stroke using a well-validated questionnaire which was used in prior population-based studies in India for estimating stroke prevalence (16). The questionnaire was translated into the local language (Marathi) and was validated for the Gadchiroli population using a neurologist's clinical diagnosis as the gold standard. The questionnaire had a sensitivity of 86% and specificity of 99% (15). The questionnaire had six questions: did anyone in the family ever have a) weakness on one side of the body?, b) numbness on one side of the body?, c) drooping of one side of face? or d) slurring of speech. If the respondent had any of these, they were asked whether these symptoms were e) sudden in onset and f) lasted more than 24 hours. If the respondent had one or more of the first four symptoms and if the symptoms were sudden in onset and lasted more than 24 hours, that individual was referred to the physician for further evaluation. Diagnosis of stroke was made by the study physician using WHO's clinical definition of stroke as a focal (or at times global) neurological impairment of sudden onset, and lasting >24 hours, and of presumed vascular origin. Clinical diagnosis alone was used when no supporting documents were available irrespective of whether the patient had any residual neurodeficit at the time of evaluation by the physician. Doubtful cases were evaluated by the study neurologist (YK).

Estimation of population in 2012

We estimated the age-specific population for 2012 (the mid-period population for the 2011-2013 period over which mortality data were collected) based on censuses conducted in the Gadchiroli surveillance site in 2005 and 2015. To do so, we first calculated age-specific annual growth rates over the 10-year intercensal period and then applied these growth rates to the 2005 initial population to estimate age-specific counts of individuals in 2012.

Calculation of DALYs

DALYs lost due to stroke were estimated as the sum of years of life lost (YLL) from stroke and years lived with disability (YLD) due to stroke. YLL due to stroke were estimated for the 2011-2013 period by multiplying the number of deaths from stroke at each age by the remaining life expectancy in the 2017 GBD reference life table at that age and then summing across all ages (17). In sensitivity analyses, we used the Indian National Life Table for rural Maharashtra to determine how YLLs vary based on different survival assumptions.

To estimate YLD due to stroke, we first calculated the age-specific prevalence of stroke for five-year age groups between the ages 0 and 85+ from the cross-sectional evaluation conducted in

2014. We then multiplied the age-specific stroke prevalence rates by the age-specific population counts in 2012 to estimate the expected number of individuals with stroke for the period. We then multiplied the number of expected cases of stroke by a disability weight of 0.07 -- drawn from the 2017 GBD Disability Weights for long-term stroke of moderate severity (18) -- and summed across all ages.

Finally, DALYs were calculated as the sum of YLL and YLD expressed per 100,000 person-years lived. Based on the recommendations of the 2017 GBD study, we did not use age weights or other methods of discounting in estimating DALYs (1). We also did not apply any inclusion or exclusion criteria to the input data.

Sensitivity analyses

Since our data did not allow us to assess the severity of disability due to stroke, we had to assign a uniform single weight to all survivors in the calculation of DALYs (18). We therefore conducted sensitivity analyses to determine how much influence this assignment of a single disability weight had on our conclusions. To do this, we re-estimated our main analyses using the minimum (0.019) and maximum (0.588) disability weights for stroke given as part of the 2017 GBD study (18).

Ethical approval

The data used in this study were from previous studies to estimate stroke mortality and prevalence. These studies were approved by the Institutional Ethical Committee of SEARCH

(8,15). The procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2000.

Patient and Public Involvement

SEARCH has been working with people in these 86 villages for more than 30 years to monitor their health priorities, develop and test solutions, and provide village-based treatments of selected ailments through its CHWs. The current and previous studies have identified stroke as a leading public health problem in these villages and SEARCH is testing a community-based intervention to reduce stroke deaths. For this study, patients and the public were not involved in the study design, data analysis, or writing of the manuscript. CHWs of SEARCH were involved in the data collection.

Study checklist

We have provided the GATHER checklist and information on GATHER items as supplementary files (Supplementary File 1).

Results

Table 1 presents stroke mortality rate, stroke deaths, and YLL due to stroke. There were 229 stroke deaths between 2011 and 2013, corresponding to a stroke mortality rate of 125.3 per 100,000 person-years, 5,545.4 absolute YLL, and 3,033.0 YLL per 100,000 person-years. YLL per 100,000 person-years were slightly higher for men compared to women (3,148.4 for men compared to 2,915.2 for women). The majority of stroke deaths occurred between ages 65 and 80, with the largest amount of YLL occurring among those aged 65 to 70. Stroke mortality rates and YLL per 100,000 person-years, however, were highest at ages above 75 for both women and men.

Table 2 presents stroke prevalence, expected stroke cases, and YLD due to stroke. Overall, there were 901.5 expected cases of stroke per 100,000 person-years between 2011 and 2013, corresponding to a stroke prevalence of 388.4 per 100,000 person-years, 63.1 absolute YLD, and 34.5 YLD per 100,000 person-years. The morbidity burden of stroke was much higher for men: men had a stroke prevalence of 519.4, 42.8 YLD, and 46.3 YLD per 100,000 person-years compared to a stroke prevalence of 255.1, 19.9 YLDs, and 22.0 YLD per 100,000 person-years for women. For both women and men, the morbidity burden of stroke is clustered above the age of 50.

Figure 1 graphs DALYs due to stroke per 100,000 person-years by age-group. Total DALYs lost due to stroke were 3,068 per 100,000 person-years with a higher burden among men relative to women (3,195 vs 2,937 per 100,000 person-years). For both women and men, the rate of DALYs lost due to stroke increased steadily over age to a peak between ages 75 and 85. However, 80%

of total DALYs lost due to stroke occurred prematurely between ages 30 and 70. The vast majority of DALYs for both women and men were due to YLL, with small contributions from YLD (0.7% for women, 1.5% for men).

Figure 2 compares the rate of DALYs lost due to stroke estimated in Gadchiroli to the national and global DALYs lost due to stroke from the GBD study (3). The estimated rate of DALYs lost due to stroke in Gadchiroli is higher than all the states in the GBD study with the closest estimate in West Bengal (2,821). Our estimate is closer to estimate for the neighbouring state of Chhattisgarh (2,142) than the state of Maharashtra (1,341), where Gadchiroli is located.

Table 3 presents the sensitivity of DALYs lost and the share of DALYs due to YLD to the choice of disability weight. When the maximum disability weight for stroke is used to estimate YLD, total DALYs per 100,000 increases to 3,323 (3,537 for men and 3,100 for women) and an 8.7% contribution from YLD. Using the minimum disability for stroke has a minor effect on our main estimates, reducing DALYs per 100,000 from 3,068 to 3,042 and the contribution of YLD from 1.1% to 0.3%.

All results are attached in spreadsheet form as per the GATHER checklist (Supplementary File 2).

Discussion

We found a very high burden of DALYs lost due to stroke in the rural, Gadchiroli district, of Maharashtra, India. Importantly, the majority of DALYs lost occurred at relatively young ages between 30 and 70, revealing a large premature burden of stroke. We found slightly higher burden among men compared to women, driven primarily by a greater number of YLL due to stroke among men. For both women and men, more than 98% of the total disease burden was due to YLL, indicating a high level of stroke mortality in Gadchiroli.

Our estimate of DALYs due to stroke per 100,000 person-years was higher than the Indian state-specific estimates published in a recent GBD study (3). As the GBD estimates are heavily modeled based on scarce data, extrapolated using multiple indirect sources of information, and are based on predictive models built with data from other contexts, it is possible that the GBD estimate of the burden of stroke in India could be an underestimate. However, higher estimates in our study could also be due to geographical differences within India and lack of healthcare services in Gadchiroli leading to excessive mortality. Furthermore, estimates for rural areas of India are not available separately in the GBD study, where the majority of India's population lives, and where there are significant challenges to healthcare delivery. Therefore, in this context our study provides a value addition and highlights a need to monitor the stroke burden in rural India. Beyond the GBD, our results are difficult to directly compare to other studies due to a paucity of DALY estimates from other parts of India, particularly rural India, as well as other low- and middle-income countries. To our knowledge, in India, there is only one other population-based study that has estimated DALYs lost due to stroke directly, and this study was based in an urban city center. Banerjee et al. (2013) used data from city of Kolkata and estimated that 795.6 DALYs per 100,000 person-years lived were lost due to stroke (19). The large difference between our estimate is partly driven by the choice of life table used in the calculation of DALYs. Banerjee et al. used Indian life tables to calculate DALYs where the life expectancies are lower compared to those in the 2017 GBD reference life tables. However, in sensitivity analyses, we found that even when using the rural Indian life tables, we estimated a substantially higher burden of DALYs lost due to stroke (1,842 per 100,000 person-years lived), though the magnitude of this difference reduced substantially. Maredzea et al. (2015) estimated DALYs lost due to stroke in rural South Africa using a prevalence-based method similar to ours (20). Based on data from the Agincourt cohort in rural South Africa, the authors estimated that 2,156 DALYs were lost due to stroke per 100,000 person-years—closer in magnitude to our estimate. Additionally, we found that the contribution of YLD to DALYs in our study was less than 2% (1.1%), compared to around 25% in the study by Banerjee et al. and 8.7% in the study by Maredzea et. al. This indicates that stroke mortality is potentially much higher in Gadchiroli compared to these other contexts. Our results are broadly consistent with a number of studies documenting a high incidence and mortality rate from stroke in specific Indian sub-populations (8–11,21–24). Similarly, the high burden of stroke in Gadchiroli is consistent with recent nationally-representative evidence that finds high levels of stroke mortality in eastern states, such as Chhattisgarh, that are geographically adjacent to Gadchiroli, and have similar levels of development and healthcare services (9). Lack of access to healthcare and poor prevention and treatment of stroke are the likely important reasons for this pattern. As hypertension is the most important risk factor for stroke (25,26), undetected, untreated, and uncontrolled hypertension could be the driver of stroke in Gadchiroli.

The major strength of our study is the direct estimation of DALYs based on mortality and prevalence data on stroke from a demographic surveillance site. Both the stroke prevalence and mortality data were conducted using validated instruments with rare cause of death data for a large population. Such a method provides estimates that more closely represent actual disease conditions than those obtained using indirect methods. We also used the new methods for DALY estimation recommended by the GBD 2017 study (1), allowing for a consistent comparison of DALYs due to stroke across populations and time.

The study also has some limitations. We had to estimate the population in 2012 based on census data from 2005 and 2015, potentially leading to inaccurate measures of person-years lived. However, our estimates would only have substantial bias if there was a sudden in- or out-migration of individuals into the surveillance site which was not the case based on decadal growth rates. The mortality and prevalence data were from non-overlapping periods. The mortality data were from years 2011-2013 while the prevalence data were obtained in 2014. Therefore, we had to estimate the number of stroke survivors during the 2011-2013 period by applying the 2014 age-specific prevalence rates to the population counts for 2011-2013. However, since the study was conducted in the same population pool, we believe that the difference in the time period is unlikely to significantly affect the estimation of DALYs. We used a single disability weight of 0.07 for stroke disability. While the GBD study group proposes using different disability weights based on the level of disability due to stroke, we believe that given the smaller proportion of YLDs (1.1%) in the DALYs in our study, the method used in this estimation is unlikely to significantly affect the estimation of DALYs. Indeed, our sensitivity analyses reveal that even if all stroke survivors were assigned the most severe stroke disability weight from the 2017 GBD study, the absolute number of DALYs lost only increases slightly and the share of DALYs due YLDs is still less than 10%.

As brain imaging is not readily available in this region we could not assess DALYs lost due to ischaemic and haemorrhagic strokes separately. In the Trivandrum stroke registry from the state of Kerala, 82% patients from rural areas had ischaemic stroke while the remainder had haemorrhagic stroke (10). Relatively recent data from Ludhiana population-based stroke registry from rural Punjab found that 63% of strokes were ischaemic while 36% were haemorrhagic (27). Stroke patients from our study are likely to have a proportion of haemorrhagic strokes similar or higher than that reported by the Ludhiana stroke registry given high early mortality in our study area where 46% of stroke deaths occurred within first month after onset of stroke symptoms (8). Also, our study may not be completely representative of rural India as different rural regions of India might have different access to healthcare, which will affect the overall risk of having a stroke, disability and the mortality due to stroke. Lastly, causes of death were assigned based on verbal autopsies rather than medically certified causes of death. Therefore, there is a chance that stroke deaths were misclassified or missed. However, India does not have a comprehensive vital registration system, so verbal autopsies, which have high sensitivity (≥ 75%) and specificity (>90%) in diagnosing stroke (28,29), provide the only source of information on causes of death in resource poor setting like Gadchiroli.

Our study shows a high, underappreciated burden of stroke in a rural area of India and has important implications for health policy. It also highlights a need to monitor the stroke burden in rural areas of India where very little data are available and people remain vulnerable to preventable mortality. This would be essential to track progress towards the Sustainable Development Goals adopted in a United Nations General Assembly in 2015 which calls for one-third reduction in premature mortality because of non-communicable diseases by 2030 (30). At a systems level, identifying, testing, and scaling different ways of delivering preventive and curative health services for stroke, particularly controlling high blood pressure, the leading risk factor for stroke (26), in rural, resource-constrained environments in Gadchiroli and other parts of India will be essential.

Authors' Contributions

Conceived the study- YK; Analysed data- NS, MD, YK; Wrote the manuscript- NS, YK; Revised the draft critically for intellectual content-YK, NS.

Data Sharing

No additional data available.

Funding

SEARCH was supported by the John D. and Catherine T. MacArthur Foundation. Dr. Sudharsanan received support from "Penn Indian re-SEARCH, a collaboration for High-Impact Health and Demographic Research", Global Engagement Fund, University of Pennsylvania.

Competing interests

None

Acknowledgements

We thank Drs. Vikram Sahane, Jyoti Puthran, Sujay Kakarmath and Vaibhav Agavane and the field supervisors of SEARCH for technical assistance. We thank people of Gadchiroli for their support in conducting these studies.

References

1. Kyu HH, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. 2018;392(10159):1859–1922.

2. Roth GA, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. 2018;392(10159):1736–1788.

3. Dandona L, Dandona R, Kumar GA, Shukla D, Paul VK, Balakrishnan K, et al. Nations within a nation: variations in epidemiological transition across the states of India, 1990–2016 in the Global Burden of Disease Study. The Lancet. 2017;390(10111):2437–2460.

4. United Nations Department of Economic and Social Affairs, Population Division. World Urbanization Prospects: The 2018 Revision. 2018.

5. Bhandari L, Dutta S. Health infrastructure in rural India. India Infrastruct Rep. 2007;265–271.

6. Geldsetzer P, Manne-Goehler J, Theilmann M, Davies JI, Awasthi A, Vollmer S, et al. Diabetes and hypertension in India: a nationally representative study of 1.3 million adults. JAMA Intern Med. 2018;178(3):363–372.

7. Geldsetzer P, Manne-Goehler J, Theilmann M, Davies JI, Awasthi A, Danaei G, et al. Geographic and sociodemographic variation of cardiovascular disease risk in India: A cross-sectional study of 797,540 adults. PLoS Med. 2018;15(6):e1002581.

8. Kalkonde YV, Deshmukh MD, Sahane V, Puthran J, Kakarmath S, Agavane V, et al. Stroke is the leading cause of death in rural Gadchiroli, India: a prospective community-based study. Stroke. 2015;46(7):1764–1768.

9. Ke C, Gupta R, Xavier D, Prabhakaran D, Mathur P, Kalkonde YV, et al. Divergent trends in ischaemic heart disease and stroke mortality in India from 2000 to 2015: a nationally representative mortality study. Lancet Glob Health. 2018;6(8):e914–e923.

10. Sridharan SE, Unnikrishnan J, Sukumaran S, Sylaja P, Nayak SD, Sarma PS, et al. Incidence, types, risk factors, and outcome of stroke in a developing country: the Trivandrum Stroke Registry. Stroke. 2009;40(4):1212–1218.

11. Joshi R, Cardona M, Iyengar S, Sukumar A, Raju CR, Raju KR, et al. Chronic diseases now a leading cause of death in rural India—mortality data from the Andhra Pradesh Rural Health Initiative. Int J Epidemiol. 2006;35(6):1522–1529.

12. 2011 Census of India. District Census Handbook Gadchiroli. 2011.

13. NITI Ayog. Transformation of Aspirational Districts Baseline Rankings and Real-Time Monitoring Dashboard. New Delhi; 2018.

14. SRS Collaborators of the RGI-CGHR. Prospective Study of Million Deaths in India: Technical Document No VIII: Health Care Professional's Manual For Assigning Causes of

Death Based on RHIME Reports [Internet]. University of Toronto; 2011 Mar. Available from: www.cghr.org/mds

15. Kalkonde YV, Sahane V, Deshmukh MD, Nila S, Mandava P, Bang A. High prevalence of stroke in rural Gadchiroli, India: a community-based study. Neuroepidemiology. 2016;46(4):235–239.

16. Gourie-Devi M, Gururaj G, Satishchandra P. Neuroepidemiology in Developing Countries: Manual for Descriptive Studies. National Institute of Mental Health and Neuro Sciences; 1994.

17. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2017 (GBD 2017) Reference Life Table. Seattle, United States: Institute for Health Metrics and Evaluation (IHME); 2018.

18. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2017 (GBD 2017) Disability Weights. Seattle, United States: Institute for Health Metrics and Evaluation (IHME); 2018.

19. Banerjee TK, Dutta S, Ray BK, Ghosal M, Hazra A, Chaudhuri A, et al. Disease burden of stroke in Kolkata, India: derivation of disability-adjusted life years by a direct method. Neuroepidemiology. 2013;41(2):88–93.

20. Maredza M, Bertram MY, Tollman SM. Disease burden of stroke in rural South Africa: an estimate of incidence, mortality and disability adjusted life years. BMC Neurol. 2015;15(1):54.

21. Gajalakshmi V, Lacey B, Kanimozhi V, Sherliker P, Peto R, Lewington S. Body-mass index, blood pressure, and cause-specific mortality in India: a prospective cohort study of 500 810 adults. Lancet Glob Health. 2018;6(7):e787–e794.

22. Ray BK, Hazra A, Ghosal M, Banerjee T, Chaudhuri A, Singh V, et al. Early and delayed fatality of stroke in Kolkata, India: results from a 7-year longitudinal population-based study. J Stroke Cerebrovasc Dis. 2013;22(4):281–289.

23. Pandian JD, Singh G, Kaur P, Bansal R, Paul BS, Singla M, et al. Incidence, short-term outcome, and spatial distribution of stroke patients in Ludhiana, India. Neurology. 2016;86(5):425–433.

24. Dalal P, Malik S, Bhattacharjee M, Trivedi N, Vairale J, Bhat P, et al. Population-based stroke survey in Mumbai, India: incidence and 28-day case fatality. Neuroepidemiology. 2008;31(4):254.

25. Collins R, Peto R, MacMahon S, Godwin J, Qizilbash N, Hebert P, et al. Blood pressure, stroke, and coronary heart disease: part 2, short-term reductions in blood pressure: overview of randomised drug trials in their epidemiological context. The Lancet. 1990;335(8693):827–838.

26. O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. The Lancet. 2016;388(10046):761–75.

27. Kaur P, Verma SJ, Singh G, Bansal R, Paul BS, Singla M, et al. Stroke profile and outcome between urban and rural regions of Northwest India: Data from Ludhiana population-based stroke registry. Eur Stroke J. 2017;2(4):377–384.

28. Kumar R, Thakur J, Rao B, Singh M, Bhatia S, others. Validity of verbal autopsy in determining causes of adult deaths. Indian J Public Health. 2006;50(2):90.

29. Yang G, Rao C, Ma J, Wang L, Wan X, Dubrovsky G, et al. Validation of verbal autopsy procedures for adult deaths in China. Int J Epidemiol. 2005;35(3):741–748.

30. United Nations. The Sustainable Development Goals Report 2018. New York; 2018.

Table 1: Estimated age- and sex-specific stroke mortality, stroke deaths, and years of life lost (YLL)[a] due to stroke between 201[illegible]-201[illegible]

	Men				Women				Total			
Age group	Stroke mortality rate (per 100,000)	Stroke deaths	YLL	YLL (per 100,000)	Stroke mortality rate (per 100,000)	Stroke deaths	YLL	YLL (per 100,000)	Stroke mortality rate (per 100,000)	Stroke deaths	YLL	YLL (per 100,000)
0-4	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0
4-9	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0
10-14	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0
15-19	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0
20-24	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0
25-29	12.0	1	63.2	754.9	0.0	0	0.0	0.0	6.2	1	63.2	394.4
30-34	0.0	0	0.0	0.0	29.3	2	116.4	1706.0	14.5	2	116.4	842.2
35-39	13.5	1	53.3	718.3	14.3	1	53.3	759.9	13.9	2	106.5	738.5
40-44	67.0	4	193.5	3241.9	0.0	0	0.0	0.0	33.3	4	193.5	1608.3
45-49	65.5	4	174.0	2848.5	85.1	5	217.5	3703.7	75.1	9	391.5	3267.7
50-54	200.4	9	348.3	7754.4	160.5	7	270.9	6211.0	180.7	16	619.2	6994.0
55-59	263.9	11	373.8	8968.4	138.3	5	169.9	4698.9	205.5	16	543.7	6985.0
60-64	302.1	8	234.5	8856.7	275.5	10	293.2	8075.9	286.7	18	527.7	8405.2
65-69	702.6	24	593.6	17377.9	553.9	22	544.2	13699.9	622.6	46	1137.8	15400.5
70-74	850.0	17	345.5	17272.8	1091.5	21	426.7	22179.8	968.4	38	772.2	19678.8
75-79	2252.3	20	321.9	36248.8	2394.1	26	418.5	38531.8	2330.3	46	740.3	37504.8
80-84	3208.6	12	146.2	39083.2	1181.1	6	73.1	14386.9	2040.8	18	219.3	24859.0
85+	2755.9	7	61.5	24196.0	1898.7	6	52.7	16670.3	2280.7	13	114.1	20023.8
Total	127.7	118	2909.1	3148.4	122.7	111	2636.3	2915.2	125.3	229	5545.4	3033.0

[a]YLL were calculated using the 2017 GBD reference life table.

Table 2: Estimated age- and sex-specific stroke prevalence[a], and years lived with disability (YLD)[b] due to stroke between 2011-201[illegible]

Age group	Men: Stroke Prevalence rate per 100,000	Men: Expected stroke cases	Men: YLD	Men: YLD per 100,000	Women: Stroke prevalence rate per 100,000	Women: Expected stroke cases	Women: YLD	Women: YLD per 100,000	Total: Stroke Prevalence rate per 100,000	Total: Expected stroke cases	Total: YLD	Total: YLD per 100,000
0-4	0.0	0.0	0.0	0.0	61.1	4.6	0.3	4.3	29.6	4.5	0.3	2.1
5-9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
10-14	44.5	3.3	0.2	3.1	0.0	0.0	0.0	0.0	23.0	3.3	0.2	1.6
15-19	0.0	0.0	0.0	0.0	36.9	3.4	0.2	2.6	18.3	3.4	0.2	1.3
20-24	47.3	4.4	0.3	3.3	0.0	0.0	0.0	0.0	25.1	4.5	0.3	1.8
25-29	106.4	8.9	0.6	7.5	56.8	4.3	0.3	4.0	82.4	13.2	0.9	5.8
30-34	121.7	8.5	0.6	8.5	173.6	11.8	0.8	12.2	148.3	20.5	1.4	10.4
35-39	54.3	4.0	0.3	3.8	51.6	3.6	0.3	3.6	52.9	7.6	0.5	3.7
40-44	397.9	23.7	1.7	27.9	127.8	7.7	0.5	8.9	260.3	31.3	2.2	18.2
45-49	210.4	12.8	0.9	14.7	153.1	9.0	0.6	10.7	183.0	21.9	1.5	12.8
50-54	721.6	32.4	2.3	50.5	681.8	29.7	2.1	47.7	709.7	62.2	4.4	49.2
55-59	1522.2	63.4	4.4	106.6	634.5	22.9	1.6	44.4	1096.2	85.3	6.0	76.7
60-64	3270.2	86.6	6.1	228.9	1154.4	41.9	2.9	80.8	2119.3	133.1	9.3	148.4
65-69	4812.8	164.4	11.5	336.9	1068.7	42.4	3.0	74.8	2796.1	206.6	14.5	195.7
70-74	4000.0	80.0	5.6	280.0	3876.0	74.6	5.2	271.3	3934.9	154.4	10.8	275.4
75-79	6508.9	57.8	4.0	455.6	1485.1	16.1	1.1	104.0	3773.6	74.5	5.2	264.2
80-84	10769.2	40.3	2.8	753.8	2381.0	12.1	0.8	166.7	6040.3	53.3	3.7	422.8
85+	8163.3	20.7	1.5	571.4	0.0	0.0	0.0	0.0	3846.2	21.9	1.5	269.2
Total	519.4	611.4	42.8	46.3	255.1	284.3	19.9	22.0	388.4	901.5	63.1	34.5

[a]Prevalence rate was calculated from a subsample of individuals surveyed in 2014 and then applied to the overall 2012 population counts to estimate expected cases of stroke.
[b]YLD are calculated using a disability weight of 0.07 for stroke

Table 3: Sensitivity of DALYs per 100,000 and share of DALYS due to YLD to stroke disability weights

	Original stroke disability weight (0.07)[a]	Lowest stroke disability weight (0.019)[b]	Highest stroke disability weight (0.588)[c]
Total	3068	3042	3323
Share due to YLD	1.1%	0.3%	8.7%
Men	3195	3161	3537
Share due to YLD	1.5%	0.4%	11.0%
Women	2937	2921	3100
Share due to YLD	0.7%	0.2%	6.0%

[a]This is the disability weight for long-term stroke survivors of moderate severity in the 2017 GBD list of disability weights
[b]This is the lowest disability weight across stroke categories in the 2017 GBD list of disability weights
[c]This is the highest disability weight across stroke categories in the 2017 GBD list of disability weights

Figure Legends

Figure 1: Age-specific rate of DALYs lost due to stroke per 100,000 person-years, 2011-2013, Gadchiroli, India.

Figure 2: Comparison of total DALYs lost due to stroke per 100,000 person-years to published state-level estimates from the 2016 Global Burden of Disease Study.

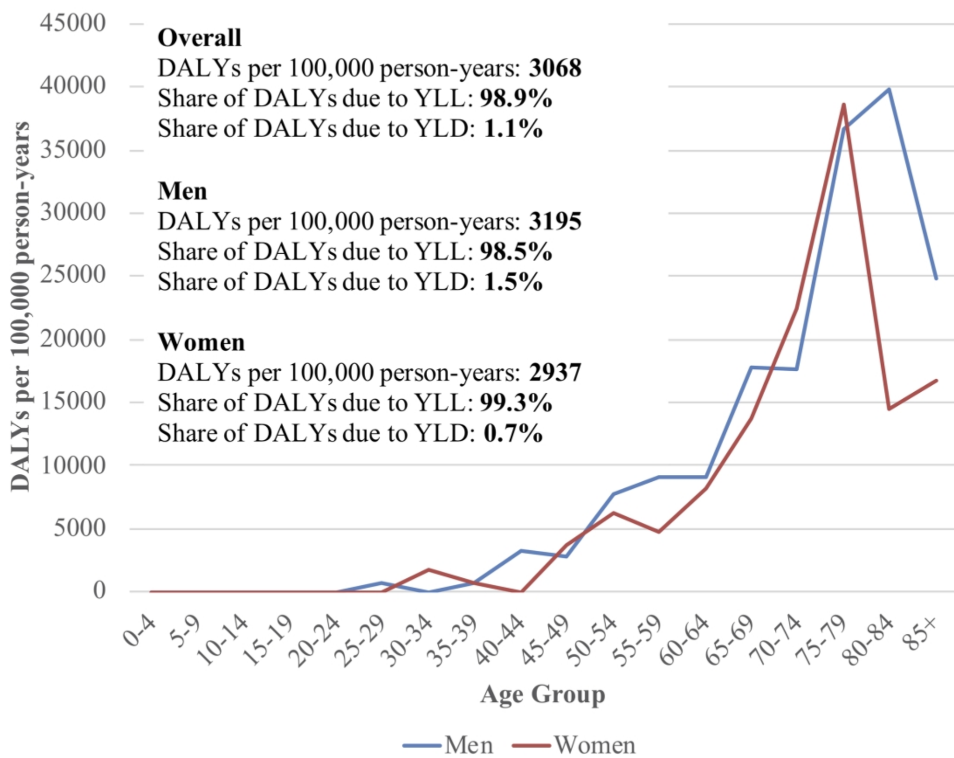


Figure 1: Age-specific rate of DALYs lost due to stroke per 100,000 person-years, 2011-2013, Gadchiroli, India.

186x145mm (300 x 300 DPI)

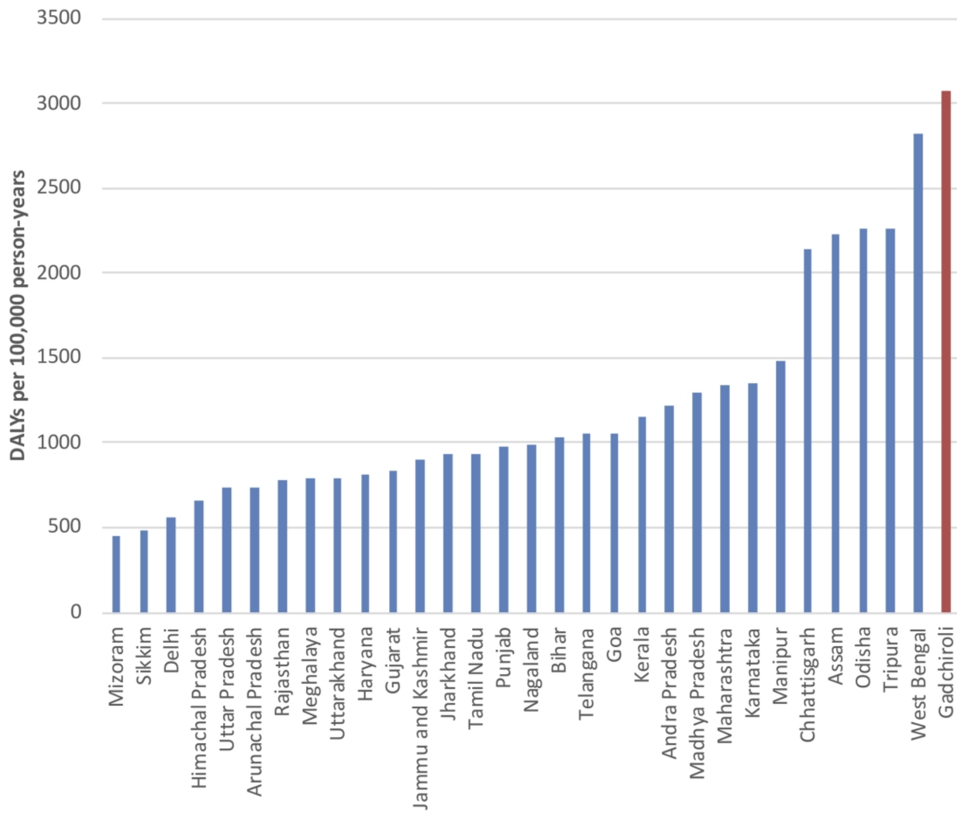


Figure 2: Comparison of total DALYs lost due to stroke per 100,000 person-years to published state-level estimates from the 2016 Global Burden of Disease Study.

189x156mm (300 x 300 DPI)

Gather Appendix

5. Provide information on all included data sources and their main characteristics. For each data source used, report reference information or contact name/institution, population represented, data collection method, year(s) of data collection, sex and age range, diagnostic criteria or measurement method, and sample size, as relevant.

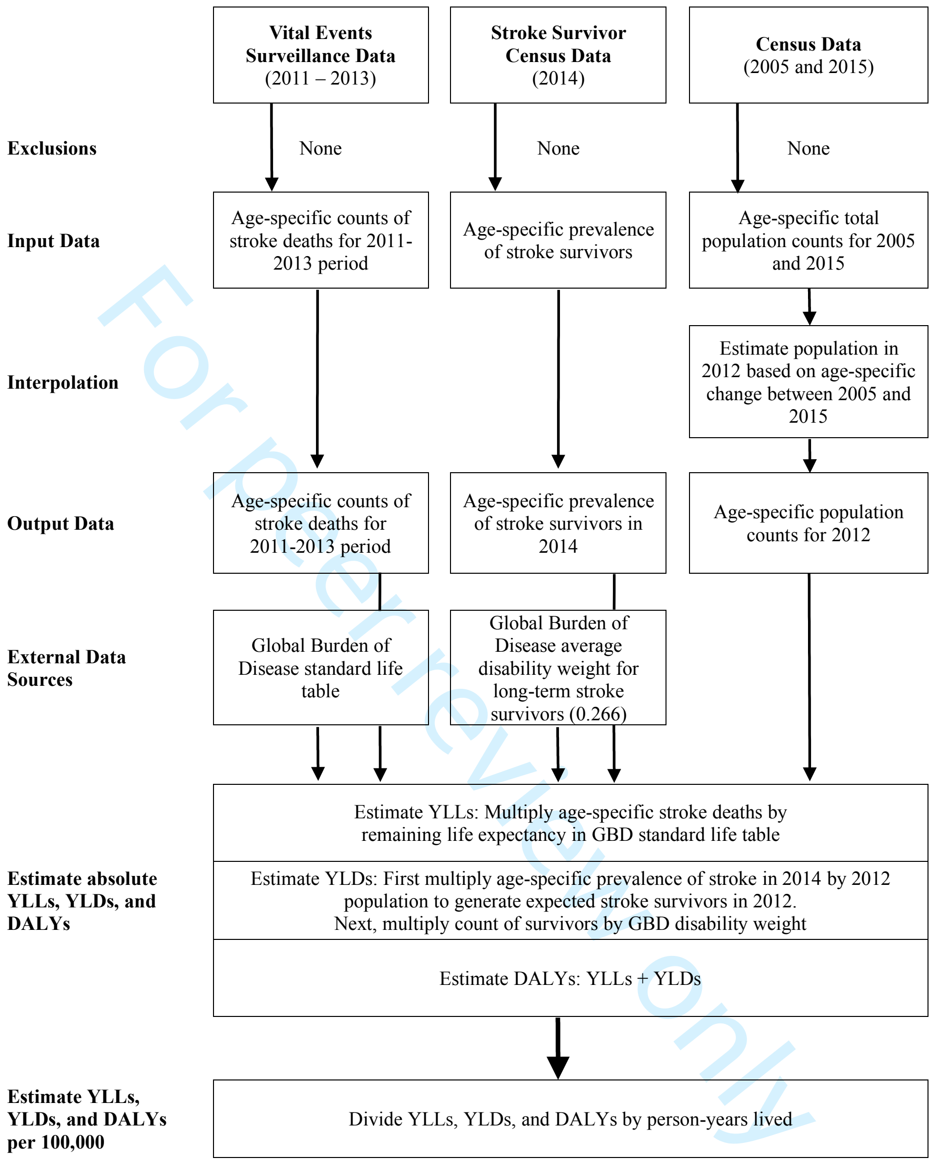
Data Source	Collecting Institution	Population Represented	Data collection method	Years of data collection	Age and sex representation
Gadchiroli surveillance site population census	SEARCH	All individuals living in the 86 villages that form the Gadchiroli surveillance site	House to house enumeration in 2005 and 2015.	2005 and 2015	Both sexes and all ages
Gadchiroli vital event registry	SEARCH	All individuals living in the 86 villages that form the Gadchiroli surveillance site	All births and deaths are reported to the research team by the community health workers of SEARCH who are residents of the village. Annual house to house cross-survey is conducted to find out any missing births and deaths.	Continuously between 2011 and 2013	Both sexes and all ages
Gadchiroli stroke prevalence data	SEARCH	All individuals living in 39 of the 86 villages that form the Gadchiroli surveillance site	We conducted a three-stage screening. First, a house to house survey of all individuals living in 39 villages was done by trained surveyors using a validated screening questionnaire. Those who	2014	Both sexes and all ages

			screened positive were evaluated by a trained physician in the second phase. Doubtful cases were evaluated by the study neurologist in the third phase.		

8. Provide all data inputs in a file format from which data can be efficiently extracted, including all relevant meta-data listed in item 5. For any data inputs that cannot be shared because of ethical or legal reasons, such as third-party ownership, provide a contact name or the name of the institution that retains the right to the data.

Input data could not be shared due to ethical reasons as the consent of the participant at the time of data collection did not include a clause to share deidentified data with third parties.

9. Provide a conceptual overview of the data analysis method. A diagram may be helpful.



10. Provide a detailed description of all steps of the analysis, including mathematical formulae. This description should cover, as relevant, data cleaning, data pre-processing, data adjustments and weighting of data sources, and mathematical or statistical model(s).

Data cleaning

Data were checked for any missing variables and outliers during data cleaning phase. Missing or incorrect information was recollected from the field.

Data pre-processing

We conducted two data pre-processing actions: estimating the number of individuals alive at each age in 2012 based on the 2005 and 2012 censuses and estimating the number of individuals with stroke in 2012 based on the 2014 data.

To estimate the number of number of individuals alive in 2012, we first estimated the age-specific growth rates of the population between 2005 and 2015 using the following expression

$$r_i = \ln\left(\frac{N_i(2015)}{N_i(2005)}\right) * \frac{1}{10}$$

where r_i is the age-specific growth rate, $N_i(2015)$is the number of people in age group i in 2015 and $N_i(2005)$is the number of people in age group i in 2005. We then estimated the population in 2012 by age group as:

$$N_i(2012) = N_i(2005)e^{r_i 7}$$

Second, our estimates of stroke survivors came from a census of 45,053 individuals from 39 of the 86 villages in the surveillance site in the year 2014. To estimate the number of stroke survivors in 2012 in the overall population, we multiplied the age-specific prevalence rates from the 2014 data by the 2012 age-specific population counts.

Mathematical models

We estimated DALYs directly using the following equations:

$$YLL = \sum_{i:0,85,5} D_i * LE_i$$

where $D_i$is the number of stroke deaths in five-year age group i, and LE_i is life expectancy at age group i from the 2017 GBD reference life table.

$$YLD = \sum_{i:0,85,\,5} S_i * DW$$

where s_i are the number of stroke survivors in age group i and DW is the disability weight for stroke. After calculating both YLLs and YLDs, we calculated DALYS as

$$DALYs = YLL + YLD$$

13. Describe methods for calculating uncertainty of the estimates. State which sources of uncertainty were, and were not, accounted for in the uncertainty analysis.

Our study has three input data sources: information on counts of individuals from a population census, information on counts of deaths due to stroke from continuous population surveillance system, and information on the number of stroke survivors from a population screening of 39 of surveillance site villages. Since all three of the input sources are from census or complete population surveillance records, they do not carry with them a sampling uncertainty. This is in contrast to GBD estimates, which are based on predictions and extrapolations from statistical models rather than census data and thus carry substantial uncertainty and need to be reported with uncertainty intervals. For this reason, we do not have a measure of uncertainty around our estimate.

There are two sources of non-sampling uncertainty that we have not explicitly accounted for: uncertainty in the estimates of people alive in 2012 and uncertainty in the true number of individuals with stroke in 2012. For both these sources of uncertainty, it is not clear which direction the bias may go nor how to account for this uncertainty quantitatively. We believe that the magnitude of error introduced by these two sources of uncertainty is minor however, for the following reasons. First, our estimates of number of people alive by age group in 2012 would only produce large errors if there were sudden in or out migration events between 2005 and 2015. Second, our estimates of stroke survivors would only introduce error if the prevalence rates of stroke changed drastically between 2012 and 2014, which we believe is unlikely.

14. State how analytic or statistical source code used to generate estimates can be accessed.

We have uploaded a spreadsheet that contains generates our estimates with the submission of the manuscript.

15. Provide published estimates in a file format from which data can be efficiently extracted.

We have uploaded our tables in a spreadsheet format with the submission of the manuscript.

Years of life lost

	Males			
Age group	Stroke deaths	YLL GBD	YLL WHO	YLL SRS
0	0	0.00	0.00	0.00
5	0	0.00	0.00	0.00
10	0	0.00	0.00	0.00
15	0	0.00	0.00	0.00
20	0	0.00	0.00	0.00
25	1	63.16	64.60	44.80
30	0	0.00	0.00	0.00
35	1	53.27	54.68	36.00
40	4	193.47	198.92	126.80
45	4	173.99	179.24	109.60
50	9	348.33	359.28	211.50
55	11	373.80	385.72	216.70
60	8	234.53	242.00	129.60
65	24	593.63	611.76	314.40
70	17	345.46	354.54	178.50
75	20	321.89	329.40	166.00
80	12	146.17	149.82	80.40
85+	7	61.46	63.49	37.80
Total	118	2909.147501	2993.43	1652.1

	Females					Age group
Age group	Stroke deaths	YLL GBD	YLL WHO	YLL SRS		Age group
0	0	0.00	0.00	0.00		0
5	0	0.00	0.00	0.00		5
10	0	0.00	0.00	0.00		10
15	0	0.00	0.00	0.00		15
20	0	0.00	0.00	0.00		20
25	0	0.00	0.00	0.00		25
30	2	116.41	119.26	80.80		30
35	1	53.27	54.68	36.00		35
40	0	0.00	0.00	0.00		40
45	5	217.48	224.05	137.00		45
50	7	270.92	279.44	164.50		50
55	5	169.91	175.33	98.50		55
60	10	293.16	302.50	162.00		60
65	22	544.16	560.78	288.20		65
70	21	426.74	437.96	220.50		70
75	26	418.46	428.22	215.80		75
80	6	73.09	74.91	40.20		80
85+	6	52.68	54.42	32.40		85+
Total	111	2636.27609	2711.535	1475.9		Total

Total			
Stroke deaths	YLL GBD	YLL WHO	YLL SRS
0	0.00	0.00	0.00
0	0.00	0.00	0.00
0	0.00	0.00	0.00
0	0.00	0.00	0.00
0	0.00	0.00	0.00
1	63.16	64.60	44.80
2	116.41	119.26	80.80
2	106.54	109.35	72.00
4	193.47	198.92	126.80
9	391.47	403.29	246.60
16	619.25	638.72	376.00
16	543.71	561.04	315.20
18	527.68	544.50	291.60
46	1137.79	1172.54	602.60
38	772.20	792.49	399.00
46	740.34	757.62	381.80
18	219.26	224.73	120.60
13	114.14	117.91	70.20
229	5545.42359	5704.965	3128

Years lived with disability

	Males				
Age group	Expected cases of stroke	Disability Weight	YLD		Age group
0	0.0	0.07	0.0		0
5	0.0	0.07	0.0		5
10	3.3	0.07	0.2		10
15	0.0	0.07	0.0		15
20	4.4	0.07	0.3		20
25	8.9	0.07	0.6		25
30	8.5	0.07	0.6		30
35	4.0	0.07	0.3		35
40	23.7	0.07	1.7		40
45	12.8	0.07	0.9		45
50	32.4	0.07	2.3		50
55	63.4	0.07	4.4		55
60	86.6	0.07	6.1		60
65	164.4	0.07	11.5		65
70	80.0	0.07	5.6		70
75	57.8	0.07	4.0		75
80	40.3	0.07	2.8		80
85+	20.7	0.07	1.5		85+
Total	611.4		42.8		Total

Females			Total		
Expected cases of	Disability Weight	YLD	Age group	Expected cases of	Disability Weight
4.6	0.07	0.3	0	4.5	0.07
0.0	0.07	0.0	5	0.0	0.07
0.0	0.07	0.0	10	3.3	0.07
3.4	0.07	0.2	15	3.4	0.07
0.0	0.07	0.0	20	4.5	0.07
4.3	0.07	0.3	25	13.2	0.07
11.8	0.07	0.8	30	20.5	0.07
3.6	0.07	0.3	35	7.6	0.07
7.7	0.07	0.5	40	31.3	0.07
9.0	0.07	0.6	45	21.9	0.07
29.7	0.07	2.1	50	62.2	0.07
22.9	0.07	1.6	55	85.3	0.07
41.9	0.07	2.9	60	133.1	0.07
42.4	0.07	3.0	65	206.6	0.07
74.6	0.07	5.2	70	154.4	0.07
16.1	0.07	1.1	75	74.5	0.07
12.1	0.07	0.8	80	53.3	0.07
0.0	0.07	0.0	85+	21.9	0.07
284.3		19.9	Total	901.5	

YLD
0.3
0.0
0.2
0.2
0.3
0.9
1.4
0.5
2.2
1.5
4.4
6.0
9.3
14.5
10.8
5.2
3.7
1.5
63.1

YLL, YLD, and DALYs per 100,000

	Males				
Age group	YLL GBD/100,000	YLL WHO/100,000	YLL SRS/100,000	YLD/100,00	DALY GBD/100,000
0	0.0	0	0	0.0	0
5	0.0	0	0	0.0	0
10	0.0	0	0	3.1	3
15	0.0	0	0	0.0	0
20	0.0	0	0	3.3	3
25	754.9	772	536	7.5	762
30	0.0	0	0	8.5	9
35	718.3	737	485	3.8	722
40	3241.9	3333	2125	27.9	3270
45	2848.5	2935	1794	14.7	2863
50	7754.4	7998	4708	50.5	7805
55	8968.4	9254	5199	106.6	9075
60	8856.7	9139	4894	228.9	9086
65	17377.9	17909	9204	336.9	17715
70	17272.8	17727	8925	280.0	17553
75	36248.8	37095	18694	455.6	36704
80	39083.2	40059	21497	753.8	39837
85+	24196.0	24996	14882	571.4	24767
Total	3148.4	3240	1788	46.3	3195

DALY WHO/100,000	DALY SRS/100,000	Age group	YLL GBD/100,000	YLL WHO/100,000
0	0	0	0.0	0
0	0	5	0.0	0
3	3	10	0.0	0
0	0	15	0.0	0
3	3	20	0.0	0
780	543	25	0.0	0
9	9	30	1706.0	1748
741	489	35	759.9	780
3361	2153	40	0.0	0
2949	1809	45	3703.7	3816
8049	4759	50	6211.0	6406
9361	5306	55	4698.9	4849
9368	5123	60	8075.9	8333
18246	9541	65	13699.9	14118
18007	9205	70	22179.8	22763
37550	19149	75	38531.8	39431
40813	22251	80	14386.9	14746
25567	15453	85+	16670.3	17222
3286	1834	Total	2915.2	2998

Females				
YLL SRS/100,000	YLD/100,00	DALY GBD/100,000	DALY WHO/100,000	DALY SRS/100,000
0	4.3	4	4	4
0	0.0	0	0	0
0	0.0	0	0	0
0	2.6	3	3	3
0	0.0	0	0	0
0	4.0	4	4	4
1184	12.2	1718	1760	1196
514	3.6	764	784	517
0	8.9	9	9	9
2333	10.7	3714	3826	2344
3771	47.7	6259	6454	3819
2724	44.4	4743	4893	2768
4463	80.8	8157	8414	4544
7256	74.8	13775	14193	7331
11460	271.3	22451	23034	11732
19871	104.0	38636	39535	19975
7913	166.7	14554	14913	8080
10253	0.0	16670	17222	10253
1632	22.0	2937	3020	1654

	Total				
Age group	YLL GBD/100,000	YLL WHO/100,000	YLL SRS/100,000	YLD/100,00	DALY GBD/100,000
0	0.0	0	0	2.1	2
5	0.0	0	0	0.0	0
10	0.0	0	0	1.6	2
15	0.0	0	0	1.3	1
20	0.0	0	0	1.8	2
25	394.4	403	280	5.8	400
30	842.2	863	585	10.4	853
35	738.5	758	499	3.7	742
40	1608.3	1654	1054	18.2	1626
45	3267.7	3366	2058	12.8	3280
50	6994.0	7214	4247	49.2	7043
55	6985.0	7208	4049	76.7	7062
60	8405.2	8673	4645	148.4	8554
65	15400.5	15871	8156	195.7	15596
70	19678.8	20196	10168	275.4	19954
75	37504.8	38380	19341	264.2	37769
80	24859.0	25480	13673	422.8	25282
85+	20023.8	20686	12316	269.2	20293
Total	3033.0	3120	1711	34.5	3068

DALY WHO/100,000	DALY SRS/100,000
2	2
0	0
2	2
1	1
2	2
409	286
873	595
762	503
1672	1072
3379	2071
7263	4296
7284	4126
8821	4793
16067	8352
20471	10444
38644	19606
25902	14096
20955	12585
3155	1745

Observed vital statistics (2013)

Age group	Mid-year population (2012)	Deaths	Stroke deaths	Death rate	Stroke death rate
	Male				
0	3842		0	0.00	0.00
5	2809		0	0.00	0.00
10	3741		0	0.00	0.00
15	4613	11	0	1.19	0.00
20	4648	22	0	2.37	0.00
25	4183	10	1	1.20	0.12
30	3499	34	0	4.86	0.00
35	3708	34	1	4.58	0.13
40	2984	46	4	7.71	0.67
45	3054	48	4	7.86	0.65
50	2246	60	9	13.36	2.00
55	2084	64	11	15.36	2.64
60	1324	47	8	17.75	3.02
65	1708	89	24	26.05	7.03
70	1000	96	17	48.00	8.50
75	444	107	20	120.50	22.52
80	187	56	12	149.73	32.09
85+	127	43	7	169.29	27.56
Total	46201	767	118	8.30	1.28

	Female			
Age group	Mid-year population (2012)	Deaths	Stroke deaths	Death rate
0	3726		0	0.00
5	2693		0	0.00
10	3526		0	0.00
15	4598	13	0	1.41
20	4259	13	0	1.53
25	3823	13	0	1.70
30	3412	21	2	3.08
35	3505	15	1	2.14
40	3031	19	0	3.13
45	2936	33	5	5.62
50	2181	26	7	5.96
55	1808	27	5	7.47
60	1815	48	10	13.22
65	1986	87	22	21.90
70	962	96	21	49.90
75	543	108	26	99.45
80	254	51	6	100.39
85+	158	80	6	253.16
Total	45216	650	111	7.19

Stroke death rate	Age group	Total		
		Mid-year population (2012)	Deaths	Stroke deaths
0.00	0	7568	0	0
0.00	5	5502	0	0
0.00	10	7267	0	0
0.00	15	9211	24	0
0.00	20	8907	35	0
0.00	25	8006	23	1
0.29	30	6911	55	2
0.14	35	7213	49	2
0.00	40	6015	65	4
0.85	45	5990	81	9
1.60	50	4427	86	16
1.38	55	3892	91	16
2.75	60	3139	95	18
5.54	65	3694	176	46
10.91	70	1962	192	38
23.94	75	987	215	46
11.81	80	441	107	18
18.99	85+	285	123	13
1.23	Total	91417	1417	229

Death rate	Stroke death rate
0.00	0.00
0.00	0.00
0.00	0.00
1.30	0.00
1.96	0.00
1.44	0.06
3.98	0.14
3.40	0.14
5.40	0.33
6.76	0.75
9.71	1.81
11.69	2.06
15.13	2.87
23.82	6.23
48.93	9.68
108.92	23.30
121.32	20.41
215.79	22.81
7.75	1.25

Observed stroke prevalence

Male					Fem	
Age group	Population	Cases	Prevalence		Age group	Population
0	1740	0	0.00		0	1636
5	1979	0	0.00		5	1968
10	2248	1	0.44		10	2107
15	2739	0	0.00		15	2711
20	2115	1	0.47		20	1875
25	1879	2	1.06		25	1761
30	1643	2	1.22		30	1728
35	1841	1	0.54		35	1939
40	1508	6	3.98		40	1565
45	1426	3	2.10		45	1306
50	970	7	7.22		50	880
55	854	13	15.22		55	788
60	581	19	32.70		60	693
65	561	27	48.13		65	655
70	350	14	40.00		70	387
75	169	11	65.09		75	202
80	65	7	107.69		80	84
85+	49	4	81.63		85+	55
Total	22717	118	5.19		Total	22340

ıale			Total			
Cases	Prevalence		Age group	Population	Cases	Prevalence
1	0.61		0	3376	1	0.29621
0	0.00		5	3947	0	0.00000
0	0.00		10	4355	1	0.22962
1	0.37		15	5450	1	0.18349
0	0.00		20	3990	1	0.25063
1	0.57		25	3640	3	0.82418
3	1.74		30	3371	5	1.48324
1	0.52		35	3780	2	0.52910
2	1.28		40	3073	8	2.60332
2	1.53		45	2732	5	1.83016
6	6.82		50	1850	13	7.02703
5	6.35		55	1642	18	10.96224
8	11.54		60	1274	27	21.19309
7	10.69		65	1216	34	27.96053
15	38.76		70	737	29	39.34871
3	14.85		75	371	14	37.73585
2	23.81		80	149	9	60.40268
0	0.00		85+	104	4	38.46154
57	2.55		Total	45057	175	3.88397

Standard Life Tables

Age group	GBD 2017	WHO 2012	India SRS 2006-2010
0	87.885872	89.51	63.50
5	83.035378	84.52	63.30
10	78.050774	79.53	58.70
15	73.069237	74.55	54.00
20	68.110138	69.57	49.30
25	63.157372	64.60	44.80
30	58.207291	59.63	40.40
35	53.27124	54.68	36.00
40	48.368408	49.73	31.70
45	43.49641	44.81	27.40
50	38.703121	39.92	23.50
55	33.98209	35.07	19.70
60	29.31563	30.25	16.20
65	24.73456	25.49	13.10
70	20.32095	20.86	10.50
75	16.09445	16.47	8.30
80	12.18093	12.49	6.70
85	8.7796783	9.07	5.40

ß

Text

Checklist of information that should be included in new reports of global health estimates

Item #	Checklist item	Reported on page #
Objectives and funding		
1	Define the indicator(s), populations (including age, sex, and geographic entities), and time period(s) for which estimates were made.	5
2	List the funding sources for the work.	17
Data Inputs		
For all data inputs from multiple sources that are synthesized as part of the study:		
3	Describe how the data were identified and how the data were accessed.	6
4	Specify the inclusion and exclusion criteria. Identify all ad-hoc exclusions.	9
5	Provide information on all included data sources and their main characteristics. For each data source used, report reference information or contact name/institution, population represented, data collection method, year(s) of data collection, sex and age range, diagnostic criteria or measurement method, and sample size, as relevant.	Webappendix
6	Identify and describe any categories of input data that have potentially important biases (e.g., based on characteristics listed in item 5).	15,16
For data inputs that contribute to the analysis but were not synthesized as part of the study:		
7	Describe and give sources for any other data inputs.	8,9
For all data inputs:		
8	Provide all data inputs in a file format from which data can be efficiently extracted (e.g., a spreadsheet rather than a PDF), including all relevant meta-data listed in item 5. For any data inputs that cannot be shared because of ethical or legal reasons, such as third-party ownership, provide a contact name or the name of the institution that retains the right to the data.	17
Data analysis		
9	Provide a conceptual overview of the data analysis method. A diagram may be helpful.	Webappendix
10	Provide a detailed description of all steps of the analysis, including mathematical formulae. This description should cover, as relevant, data cleaning, data pre-processing, data adjustments and weighting of data sources, and mathematical or statistical model(s).	Webappendix
11	Describe how candidate models were evaluated and how the final model(s) were selected.	n/a
12	Provide the results of an evaluation of model performance, if done, as well as the results of any relevant sensitivity analysis.	12
13	Describe methods for calculating uncertainty of the estimates. State which sources of uncertainty were, and were not, accounted for in the uncertainty analysis.	Webappendix
14	State how analytic or statistical source code used to generate estimates can be accessed.	Webappendix
Results and Discussion		
15	Provide published estimates in a file format from which data can be efficiently extracted.	Webappendix
16	Report a quantitative measure of the uncertainty of the estimates (e.g. uncertainty intervals).	n/a
17	Interpret results in light of existing evidence. If updating a previous set of estimates, describe the reasons for changes in estimates.	13-15
18	Discuss limitations of the estimates. Include a discussion of any modelling assumptions or data limitations that affect interpretation of the estimates.	15,16

This checklist should be used in conjunction with the GATHER statement and Explanation and Elaboration document, found on gather-statement.org