

Review title: Stroke in India: a systematic review of the burden (incidence, prevalence) outcome including case fatality

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Funder: NIHR

Conflicts of interest: Nil

Anticipated start date:

1 June 2020

Anticipated completion date:

30 May 2021

Review stage:

Preliminary searches

Started

19/06/2020

Completed

22/07/2020

Piloting of the study selection process

02/08/2020

24/08/2020

Formal screening of search results against eligibility criteria

10/08/2020

Ongoing

Data extraction

Risk of bias (quality) assessment

Data analysis

Background

Stroke occurs when there is a sudden loss of blood supply to a localised area of the brain which damages the surrounding brain cells, may result in death and can have lasting physical, psychological, social and financial effects for survivors, their family and their community^{1, 2}. Globally, there are over 80 million people living who have had a stroke and each year 15 million strokes occur³. Of these, approximately 5 million people die and another 5 million experience permanent disability making stroke the second largest cause of death and disability globally³.

The number of incident cases of stroke in India in 2016 was estimated as 1,175,778 (95% uncertainty interval 1,076,048 to 1,274,427) in the Global Burden of Disease project³. However, there are few high-quality stroke incidence studies using complete population-based case ascertainment methods including prospective recruitment and overlapping sources of notification to determine true incidence rates across urban, rural and tribal regions. We conducted a comprehensive systematic review to summarise the epidemiological profile of stroke across India.

Review question

What is the epidemiology of stroke in India?

Objectives

The primary objective is to determine the incidence of stroke across India

Secondary objectives are to determine, where data are available, the age-adjusted cumulative incidence per 100,000 people, crude prevalence per 100,000 people, age-adjusted prevalence per 100,000 people, sex-disaggregated incidence rate, and 28-day case fatality rate. Data will be further disaggregated by region, urban, rural and tribal.

Methods

The systematic review will be reported following MOOSE guidelines for meta-analysis of observational studies⁴ and the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines⁵.

Criteria for considering studies for this review

Condition being studied

Stroke is a sudden interruption in the blood supply of the brain. The interruption can be caused by a blockage (ischaemic stroke, 80% of all strokes) or a bleed (intracerebral haemorrhagic caused by the rupture of an artery within the brain; subarachnoid haemorrhage, a sudden rupture of an artery where blood enters the space surrounding the brain – the subarachnoid).

Types of included studies

- a. Studies published from and including 1997 (date the Stroke Unit Trialists' Collaboration systematic review⁶ was published) to the present
- b. Prospective recruitment (consecutive recruitment; prespecified sampling strategy etc)
- c. Complete community-based case ascertainment with multiple overlapping sources
- d. Non-community-based case ascertainment including case series and case-control studies, grouped by location of recruitment e.g. acute hospital-based registry, rehabilitation-based registry
- e. Population boundaries clearly defined by geography and time, within India

Types of excluded studies

Cross-sectional recruitment, convenience sampling, retrospective recruitment, qualitative assessment, participants of randomised controlled trials, and case studies.

Types of participants

- a. Confirmed history of stroke as defined by the World Health Organization (WHO)⁷
- b. Stroke defined according to clinical criteria (may or may not be confirmed by imaging)
- c. Cerebral infarction, intracerebral haemorrhage, subarachnoid haemorrhage, uncertain pathological subtypes
- d. No restrictions based on age, sex or other characteristics including degree of impairment post stroke or interventions received
- e. Excludes studies of mixed populations (e.g. stroke and head injury) unless separate results for people with stroke can be isolated
- f. Excludes studies with the following limits TIA, lesion location, carers of stroke survivors

Types of outcome measures

- a. Incidence of stroke in India (incidence rate or cumulative stroke incidence)
- b. Prevalence of stroke in India (prevalence rate or cumulative stroke prevalence)
- c. 28-day case fatality following stroke in India
- d. Morbidity

Primary outcome

The primary analyses will focus on cumulative incidence of stroke per 100,000 people.

Secondary outcomes

- a. Age-adjusted cumulative incidence per 100,000 people
- b. Crude prevalence per 100,000 people
- c. Age-adjusted prevalence per 100,000 people
- d. Sex-disaggregated incidence rate
- e. 28-day case fatality rate
- f. Where available, data will be further disaggregated by region, urban, rural and tribal

Search methods for identification of studies

We will search for relevant published studies in all languages and arrange for translation of reports where necessary. The search strategy will be modified from the Cochrane Stroke strategy⁸ with the addition of InterTASC Information Specialists' Sub-Group (ISSG) search filters to identify epidemiological studies⁹.

Electronic searches

We will search the following bibliographic databases: Medline (OVID), Embase (OVID), IMSEAR via Global Index Medicus, Science Citation Index Expanded (SCI-EXPANDED), Social Sciences Citation Index (SSCI), and Arts & Humanities Citation Index (A&HCI) within ISI Web of Science.

We will search the reference lists of relevant studies and systematic reviews and known review articles on community-based incidence and prevalence of stroke in India.

Data collection and analyses

Selection of studies

One review author will review all citations and discard those that are irrelevant, based on the title of the publication and its abstract. Two further independent review authors will review 10% of all the citations and inter-rater reliability will be calculated. In the presence of any suggestion that an article is possibly relevant, we will retrieve the full-length article for further assessment. Two review authors will independently select the new studies for inclusion in the review from the culled citation list. Disagreements will be resolved by discussion. If consensus is not reached MH will arbitrate. The selection process will be presented in a PRISMA flow diagram.

Data extraction, selection and coding

Information from each study will be extracted by one reviewer and checked by a second independent reviewer using specially designed forms. Any discrepancies will be resolved following discussion between the reviewers. If consensus is not reached MH will arbitrate.

We will collect data on:

- a. The report: author, year, and source of publication
- b. The study: sample characteristics, social demography, definition and criteria used for stroke
- c. The participants: stroke sequence (first ever versus recurrent), stroke type, nature of outcome, estimate
- d. The denominator/population: time, date, geographical boundaries and size
- e. The research design and features: source/location of recruitment where recruitment is non-community-based, sampling mechanism, non-response
- f. Incidence, prevalence and their respective age- and sex-specific incidence or prevalence rates and outcome of stroke including 28-day case fatality

Study reports with evidence of overlapping recruitment sites, study dates, grant funding numbers, and similar or identical reported patient characteristics will be considered to be from the same cohort if not explicitly stated in the publications. If several articles report outcomes from the same study population, data will be taken from the first publication that referred to each endpoint or outcome. If multiple measures were used to assess an endpoint at the same time-point in the same sample, data from the sample with the largest denominator will be included. If the denominator is the same, data from the assessment with the highest proportion of participants with the outcome of interest will be included.

Assessment of risk of bias in included studies

The methodological quality of the included studies will be assessed using the Newcastle Ottawa Scale¹⁰.

We will narratively describe:

- a. Number (proportion) not consented
- b. Number (proportion) with outcome (stroke) not assessed
- c. Number (proportion) lost to follow-up (for outcome studies)
- d. If the method ascertaining stroke was inappropriate
- e. If the method ascertaining stroke varied across recruitment centres
- f. If there were large gaps between first symptoms and presentation to a healthcare professional (> 3 days)

Strategy for data synthesis

A random effect meta-analysis will be conducted on crude stroke incidence, prevalence and 28-day case fatality rates with pooled effect of stroke presented per 100,000 person years or population, respectively.

A meta-regression will be conducted to examine the impact of any of the following if data are available: region of India, year of study, age of participants in 10-year age bands (e.g. 45-54 years, 55-64 years etc), sex. The size of the 'bubble' will correspond to the sample size.

We will also calculate the standardised male to female rate ratios for studies providing the number of strokes separately for men and women along with person-years at risk.

Disclaimer and funding statement

This research was commissioned by the National Institute for Health Research (NIHR) Global Health Research Group on Improving Stroke Care in India, University of Central Lancashire (16/137/16) using UK aid from the UK Government. The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

During the completion of this work, Maree L. Hackett was in receipt of a National Health and Medical Research Council (NHMRC) of Australia. Caroline L. Watkins was in receipt of funding from the National Institute for Health Research, UK; Arthritis Research, UK. Jeyaraj Pandian was in receipt of funding from the Indian Council of Medical Research, India; National Institute for Health Research, UK; NHMRC, Australia; Population Health Research Institute, Canada; Department of Biotechnology, India. Liz Lightbody was in receipt of funding from the National Institute for Health Research, UK. Pallab K. Maulik was funded by NIHR grant (GHR Group 16/137/16) - Developing a Global Health Research Group for Stroke, NHMRC grant (APP1143911) - Systematic Medical Appraisal, Referral and Treatment for Common Mental Disorders in India - SMART Mental Health, and MRC grant (MR/S023224/1) - Adolescents' Resilience and Treatment nEeds for Mental health in Indian Slums (ARTEMIS). Sylaja PN was in receipt of funding from the Indian Council of Medical Research Funding.

These funding bodies had no role in study design, data collection, data analysis, data interpretation, or writing of the review.

References

1. Mahmoud S, Nahla A, Elaziz A. Impact of stroke on life satisfaction and psychological adjustment among stroke patients during rehabilitation. *Life Sci J.* 2016; 13:7-17.
2. Wolfe CD. The impact of stroke. *British Medical Bulletin.* 2000; 56:275-86.
3. GBD 2016 Stroke Collaborators. Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurology* 2019; 48: 439-458.
4. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000; 283: 2008-2012.
5. Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *British Medical Journal* 2009; 339: DOI: 10.1371/journal.pmed.1000097.
6. Stroke Unit Trialists' Collaboration. Collaborative systematic review of the randomised trials of organised inpatient (stroke unit) care after stroke. *BMJ* 1997; 314: 1151-1159.
7. WHO MONICA Project Principal Investigators. The World Health Organisation MONICA project (Monitoring Trends and Determinants in Cardiovascular Disease): a major international collaboration. *Journal of Clinical Epidemiology* 1988; 41: 105-114.
8. Cheyne JD. Search strategy for retrieval of references on stroke healthcare in MEDLINE Ovid, [text]. University of Edinburgh. College of Medicine and Veterinary Medicine. Cochrane Stroke Group. <https://doi.org/10.7488/ds/2821>, 2020.
9. ISSG Search Filter Resource [Internet]. The InterTASC Information Specialists' Sub-Group, <https://sites.google.com/a/york.ac.uk/issg-search-filters-resource/home> (2008 [updated 2020 February 4; cited September 2020]).
10. Luchini C, Stubbs B, Solmi M, et al. Assessing the quality of studies in meta-analyses: Advantages and limitations of the Newcastle Ottawa Scale. *World Journal of Meta-Analysis* 2017; 5: 80-84.