Temporal Patterns in Stroke Recurrence at Younger Ages: A Systematic Review and Meta-Analysis

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Introduction

Stroke incidence at younger ages (<55 years) has increased in several high-income settings since the early 2000s[1,2]. Although recurrence is an important concern after stroke, it remains unknown whether recurrence rates have changed over time among young stroke survivors. In this systematic review and meta-analysis, we explored temporal patterns in recurrence after ischemic stroke (IS) or IS and transient ischemic attack (TIA) in young individuals.

Methods

We searched Ovid EMBASE and Ovid MEDLINE from January 1, 1970, to February 25, 2026 (eMethods). Eligible studies were prospective or retrospective cohort studies enrolling patients aged up to 55 years with IS or IS+TIA from high-income countries (as defined by the World Bank) and reporting the incidence rate of IS or any stroke (ischemic, hemorrhagic or undetermined) during at least one year of follow-up. Titles and abstracts were screened by one author (A.N.) and verified by a second author (L.L.). Additional studies were identified by searching the reference lists of included articles and prior systematic reviews of stroke recurrence[3-5].

We assessed the association between the study mid-period and the annualized incidence rate of recurrence using generalized linear mixed-effects models with a Poisson distribution. We included a random intercept for each study and adjusted for the duration of follow-up, the upper age limit of the study population, and the type of event included. Results were presented as incidence rate ratios (IRR) per 1 standard deviation increase in mid-period, overall and stratified by study design.

Results

The search identified 41 eligible studies reporting data for 45 separate populations or time periods between 1965 and 2021 (eFigure 1). Thirty-one studies reported recurrence after IS, and 10 reported recurrence after IS or TIA. Twenty-seven studies reported recurrent IS, and 14 reported any recurrent stroke.

In total, 45,419 patients were included, with 4,834 recurrent events reported during a mean follow-up of 4.7 years (range, 1–17 years). Four studies ascertained recurrences exclusively using administrative coding data (37,661 patients; 4,141 recurrences), whereas 37 studies relied on prospectively or routinely collected clinical follow-up data (7,758 patients; 693 recurrences).

One study reported data from the same population across multiple time periods[6]. In this administrative data-based study of 17,149 28-day survivors after IS, the rate of recurrent IS decreased between 1987–1991 and 2002–2006 (IRR, 0.42; 95% CI, 0.37–0.47). However, this trend was largely driven by earlier study periods, with a less pronounced decline from 1997–2001 to 2002–2006 (IRR, 0.86; 95% CI, 0.79–0.93).

Overall, annualized recurrence rates were lower in studies with later mid-periods (IRR, 0.53 per 11.9 years; 95% CI, 0.49–0.58) (Figure 1A). This result was attenuated after excluding the previously described administrative data-based study, which exclusively ascertained recurrences using coding data (IRR, 0.83 per 12.3 years; 95% CI, 0.65–1.07) (Figure 1B). In this analysis, compared with before 1990, recurrence rates were lower in 1990–1999 (IRR, 0.78; 95% CI, 0.46–1.32) and after 2000 (IRR, 0.77; 95% CI, 0.42–1.40), with similar rates after 2000 compared with 1990–1999 (IRR, 0.99; 95% CI, 0.59–1.66).

Recurrence rates in later mid-periods were also lower in the 37 studies that relied on clinical follow-up data (IRR, 0.75 per 12.3 years; 95% CI, 0.57–0.99) (Figure 1C). Recurrence rates were lower during 1990–1999 than before 1990 (IRR 0.70; 95% CI, 0.39–1.25), with a smaller difference after 2000 compared with 1990–1999 (IRR 0.87; 95% CI, 0.50–1.52). Results were consistent after excluding the 6 studies that had >10% loss to follow-up (IRR, 0.79 per 11.8 years; 95% CI, 0.60–1.03), the 9 studies that defined imaging-positive events lasting <24 hours as IS (IRR, 0.75 per 11.9 years; 95% CI, 0.55–1.02), and the 13 studies reporting any recurrent stroke (IRR, 0.70 per 13.1 years; 95% CI, 0.54–0.91).

Discussion

In this systematic review and meta-analysis, later study mid-periods were associated with lower annualized incidence rates of stroke recurrence after IS or IS+TIA in young individuals, after accounting for measured differences in study characteristics. However, this association was partly driven by differences before 2000, as recurrence rates were similar starting from the 1990s. Consistent with this finding, stagnating recurrence rates in young adults have been reported since the early 2000s in the Danish Stroke Registry (recurrent stroke)[7] and in the Helsinki Young Stroke Registry (composite vascular outcome)[8].

This study has limitations, including the lack of data allowing for within-study comparisons. The only study reporting within-study temporal trends found that the risk of recurrent stroke was halved between the 1980s and the early 2000s, with a less pronounced decline between the late 1990s and the early 2000s[6].

Given the potential for ecological bias, our results suggest a temporal association. Further studies are needed to determine whether stroke recurrence at younger ages declined over time, accounting for changes in patient characteristics, recurrence definitions, and methods of ascertainment.

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Author Contributions

Drs Nehme and Li had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of Interest Disclosure

None.

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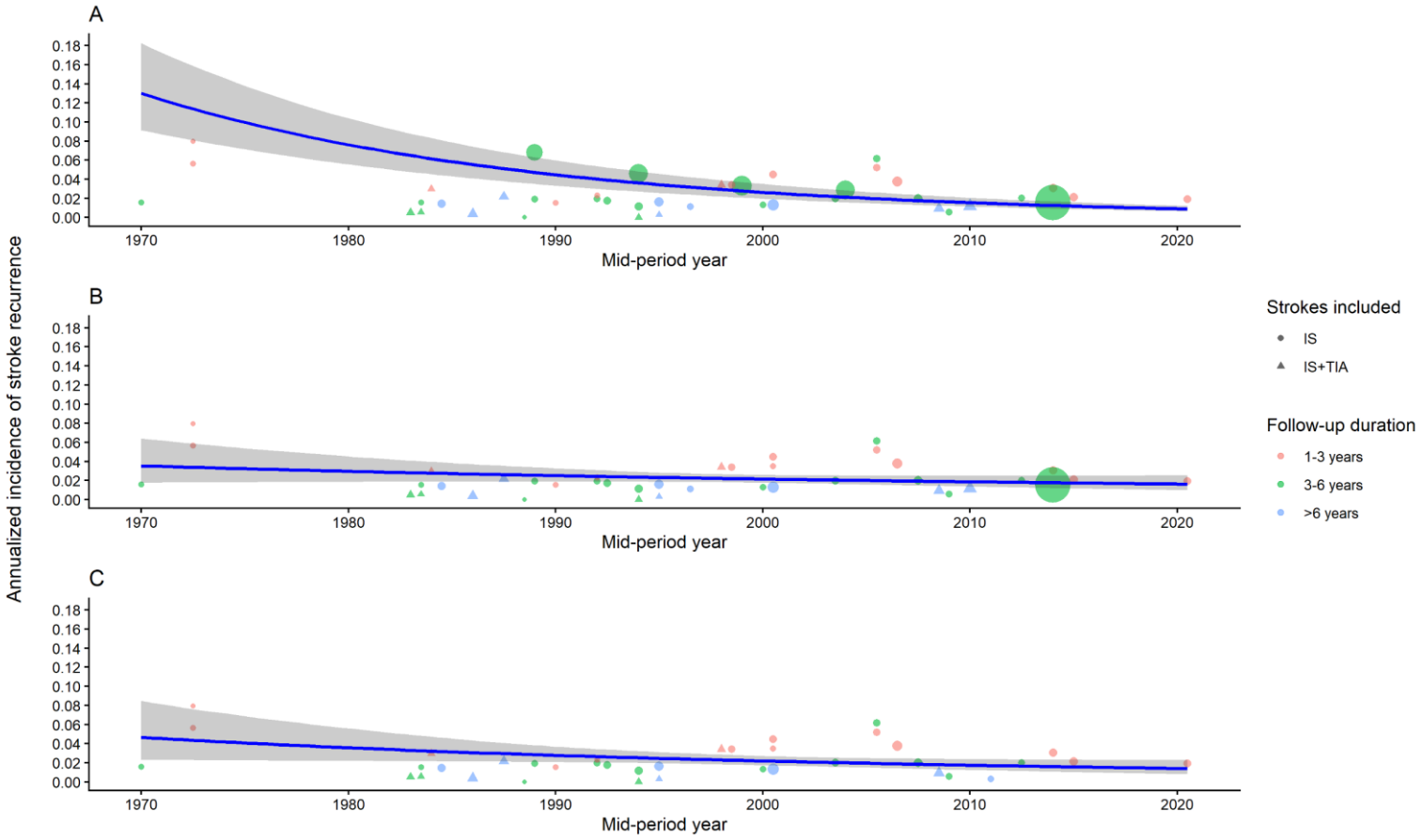
Figure 1. Temporal patterns in stroke recurrence at younger ages

Legend: Studies were plotted if they reported the annualized incidence of ischemic stroke or any stroke after ischemic stroke or ischemic stroke and transient ischemic attack, up to age 55 years. Model predictions were plotted separately for all studies (A), after excluding the only study that reported data for multiple time periods (reference 6) (B), and after excluding all studies that exclusively ascertained recurrence using administrative coding data (C). Larger points correspond to larger population sizes.



Supplemental Online Content

eMethods. Search Strategy and Study Selection

Registrations, Search and Study Selection

This systematic review was pre-registered (PROSPERO 1146314) and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. Ovid EMBASE and Ovid MEDLINE were searched from January 1, 1970, to February 25, 2026, without language restrictions, using the following strategy:

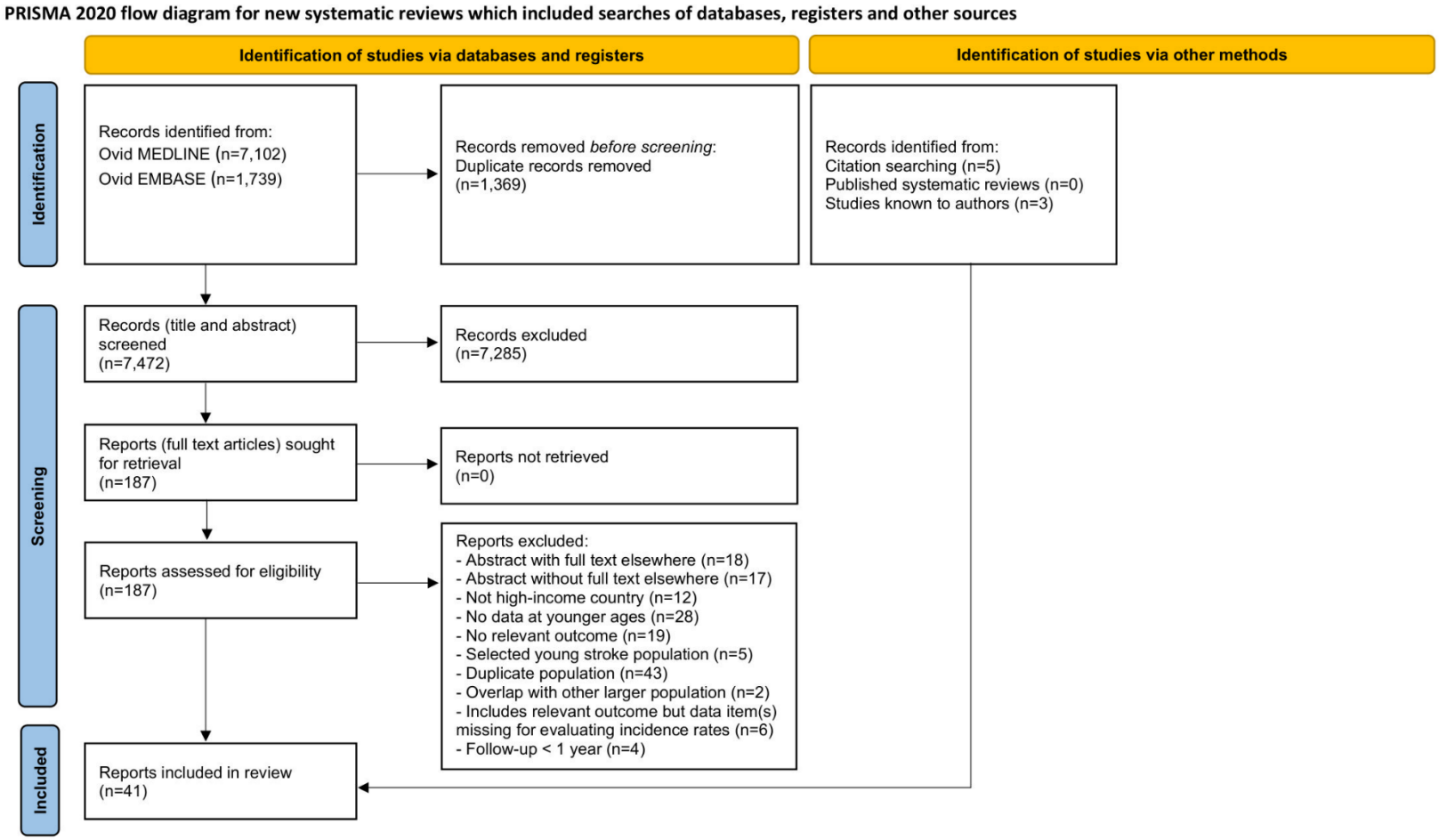
1. "Stroke[MeSH]" OR "Ischemic Stroke[MeSH]" OR "Hemorrhagic Stroke[MeSH]" OR "Brain Ischemia[MeSH]" OR "Cerebral Hemorrhage[MeSH]" OR "Intracranial Hemorrhages[MeSH]" OR "Intracranial Embolism and Thrombosis[MeSH]" OR "Brain Infarction[MeSH]" OR "Ischemic Attack, Transient[MeSH]" OR "stroke*[ti,ab]" OR "cerebrovascular accident*[ti,ab] OR "intracerebral h?emorrhage[ti,ab]" OR "intracranial h?emorrhage*[ti,ab]" OR "ICH[ti,ab]"
2. "Animal[MeSH]" NOT ("Human[MeSH]" OR "human*[ti,ab]"
3. "letter[pt]" OR "editorial[pt]" OR "case reports[pt]" OR "randomized controlled trial[pt]" OR "clinical trial[pt]" OR "clinical trial protocol[pt]" OR "comment[pt]" OR "controlled clinical trial[pt]" OR "meta-analysis[pt]" OR "textbook[pt]" OR "pragmatic clinical trial[pt]" OR "review[pt]" OR "trial[ti,ab]" OR "case report[ti,ab] OR "case study[ti,ab]"
4. "Recurrence[MeSH]" OR "recurren*[ti,ab]"
5. "Young Adult[MeSH]" OR "young[ti,ab]" OR "premature[ti,ab]" OR "early-onset[ti,ab]" OR "trend*[ti,ab]" OR "time-series[ti,ab]"
6. 1 NOT (2 OR 3)
7. 4 AND 5 AND 6

Eligible studies were prospective or retrospective cohort studies enrolling patients aged up to 55 years with ischemic stroke (IS) or IS and transient ischemic attack from high-income countries (as defined by the World Bank) and reporting the incidence rate of recurrent IS or any stroke during at least one year of follow-up. Pediatric studies or reports limited to a specific IS subtype were not eligible. Titles and abstracts were screened by one author (A.N.) and verified by a second author (L.L.). Additional studies were identified by searching the reference lists of included articles, prior systematic reviews of stroke recurrence[3-5], and other relevant publications known to the authors.

Statistical Analysis

To improve the stability of the generalized linear mixed-effects models, continuous variables (study mid-period and follow-up duration) were standardized by centering them at zero and scaling by their standard deviations. Model assumptions were assessed using residual and diagnostic plots (distributional assumptions of the random effects and overdispersion). Marginal prediction lines were obtained with Monte-Carlo simulations of fixed effects, with integration over the normal random intercept. Analyses were conducted using RStudio version 4.5.1.

eFigure 1. PRISMA Flowchart



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

The included reports are identified in the eReferences (reference 1 and 4–43)[3,9-48].

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