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ORIGINAL RESEARCH

Disparities in Stroke Incidence Over Time by Sex and Age in Latin America and the Caribbean Region 1997 to 2021: A Systematic Review and Meta-Analysis

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BACKGROUND: High-income country studies show unfavorable trends in stroke incidence (SI) in younger populations. We aimed to estimate temporal change in SI disaggregated by age and sex in Latin America and the Caribbean region.

METHODS AND RESULTS: A search strategy was used in MEDLINE, WOS, and LILACS databases from 1997 to 2021, including prospective population-based observational studies with first-ever stroke incidence in Latin America. Reports without data broken down by age and sex were excluded. Risk of bias was assessed with The Joanna Briggs Institute's guide. The main outcomes were incidence rate ratio and relative temporal trend ratio of SI, comparing time periods before 2010 with after 2010. Pooled relative temporal trend ratios considering only studies with 2 periods in the same population were calculated by random-effects meta-analysis. Meta-regression analysis was used to evaluate incidence rate determinants. From 9242 records identified, 6 studies were selected including 4483 first-ever stroke in 4 101 084 individuals. Crude incidence rate ratio in younger subjects (<55 years) comparing before 2010:after 2010 periods showed an increase in SI in the past decade (incidence rate ratio, 1.37 [95% CI, 1.23–1.50]), in contrast to a decrease in older people during the same period (incidence rate ratio, 0.83 [95% CI, 0.76–0.89]). Overall relative temporal trend ratio (<55:≥55 years) was 1.65 (95 CI%, 1.50–1.80), with higher increase in young women (pooled relative temporal trend ratio, 3.08 [95% CI, 1.18–4.97]; *P* for heterogeneity <0.001).

CONCLUSIONS: An unfavorable change in SI in young people, especially in women, was detected in population-based studies in the past decade in Latin America and the Caribbean. Further investigation of the explanatory variables is required to ameliorate stroke prevention and inform local decision-makers.

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Key Words: epidemiology ■ intracranial hemorrhage ■ ischemic stroke ■ women, sex, and gender

See Editorial by Oliveria-Filho.

Stroke is one of the most important causes of combined death and disability, worldwide.[1] Efforts to reduce the incidence of stroke and to guide health policies have been implemented in various countries. Stroke prevention has focused on reducing systolic arterial hypertension, high fasting plasma glucose and

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CLINICAL PERSPECTIVE

What Is New?

- An unfavorable stroke incidence change in young people, especially women, was detected during the past decade in Latin America and the Caribbean region, in contrast with a global stroke incidence decline during 2010 to 2019 compared with 2000 to 2009.

What Are the Clinical Implications?

- These results warrant further research to determine explanatory factors in order to guide future health policies and to prevent further increases in the stroke burden in these countries, and indicate the need for more research in underrepresented lower-income populations of the region.

Nonstandard Abbreviations and Acronyms

FES	first-ever stroke
IR	incidence rate
IRR	incidence rate ratio
LAC	Latin America and the Caribbean
pRTTR	pooled relative temporal trend ratio
RTTR	relative temporal trend ratio

cholesterol, high body index mass, smoking, and other factors.[1–3] However, these risk factors are becoming increasingly prevalent in young people.[3,4]

The Global Burden Disease has reported that from 1990 to 2019, there has been an increase in the burden of stroke in low- and upper-middle-income countries. Moreover, there has been an increase in the incidence of stroke in those <70 years of age, with a substantial increase in the past decade (2010–2019).[5]

Recently, studies in high-income countries reported divergent temporal trends in stroke incidence at age 55 years and older. Younger people (<55 years) had a less favorable incidence of stroke in the past decade compared with older people in the same period (≥55 years).[1] Unique features of the burden of stroke in Latin America and the Caribbean (LAC) region are that rates are high compared with averages worldwide[6] and there is no assessment of age and sex disparities that have been noted elsewhere. Because local data can guide future policies, we aimed to estimate temporal trends in stroke incidence disaggregated by age and sex in LAC.

METHODS

A systematic review is reported according to Meta-analysis of Observational Studies in Epidemiology and Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines[7] (Figures S1–S3). The protocol was registered in the International Prospective Register of Systematic Reviews (CRD42022332563).

Selection Criteria and Search Strategy

Prospective observational studies in LAC region from 1997 to 2021 reporting first-ever stroke (FES) incidence were included. FES reporting had to be supported by clinical or imaging diagnosis. If there was a breakdown by subtype, it was included regardless of definition. Only studies published in English, Portuguese, and Spanish were considered. Retrospective studies, reviews, commentaries, and editorials were excluded.

The search strategy followed the same parameters of our previous publication.[8] A modified search strategy of the Cochrane Stroke Group filtered by terms for Latin American and the Caribbean was used to identify studies that met the selection criteria. The search strategy was conducted between January 1, 1997 and December 31, 2021, considering this start date as a landmark in global standardization of poststroke care.[9] Data were extracted from MEDLINE (Ovid), LILACS, and Science Citation Index Expanded, Social Sciences Citation Index and Arts, and Humanities Citation Index within Web of Science (from inception to May 27, 2022) (Figures S2 through S4). This study was based on the review of previously published data, therefore institutional review board approval was waived and informed consent was not required. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Selection Process and Data Extraction

Two independent reviewers (C.D. and M.N.), before the duplicate elimination process in EndNote 20, analyzed and selected all relevant abstracts or titles through the Joanna Briggs Institute software (http://www.jbisumari.org/).[10] In case of disagreement a third reviewer was necessary to reach a decision.

For the full-text assessment, a standardized form was made with the data of the article to be extracted: authors, periods, city, country of study, and annual incidence rate of FES. Only reports with annual incidence rate of FES disaggregated for age and sex for the LAC region between January 1, 1997 and December 31, 2021 were considered, as this was the main result extracted. Reports without disaggregation by age and sex were excluded in this step, when applicable. Annual incidence rate of FES was presented per 100 000 people.

Studies Quality and Risk of Bias Assessment

Two independent reviewers assessed data quality and study design. A third reviewer was consulted in case of disagreement (Tables S1–S3). Risk of bias assessment was performed using the Joanna Briggs Institute's checklist for a cohort studies.[10]

Statistical Analysis

Disaggregated data of incidence rate (IR) were extracted from each article by sex and age (men: women, and age groups of <55 versus ≥55 years and <45 versus ≥45 years). The cutoff age of 55 was selected because it is the youngest age criterion used in previous epidemiological studies.[1] When enough data were available, a cutoff age of 45 years was used, given current concerns regarding stroke in the young. Incidence rate ratio (IRR) comparing 2 time periods (IR ≥2010:IR <2010), different sexes (IRmen:IRwomen), and different age groups (IR<55:≥55 years and <45:≥45 years) were calculated. A cutoff in year 2010 was considered because several initiatives have been implemented to improve stroke care in LAC countries after this time point.[11] Random effects meta-regression with Poisson model was performed to assess IR by the following potential effect modifiers: age, sex, and time period. The overall relative temporal trend ratio (RTTR) comparing age groups in the overall population and by sex groups were determined (IRR<55:IRR≥55 and IRR<45:IRR≥45 years).[1] Pooled RTTRs (pRTTR) including only studies with 2 time periods with the same population were calculated by random-effects meta-analysis. When 2 periods in the same population were compared in the pRTTR, the time difference between the earliest and the latest period was 10.6 years (SD 1.8).[1] A subgroup analysis by sex was performed. The heterogeneities of the pRTTRs were calculated using Cochrane's Q test. All of outcomes were processed with a 95% CI. STATA version 17.1 was used for statistical analysis.

RESULTS

Of 9242 identified records, after the duplicate elimination process (n=1941), 7301 titles and abstracts were screened by 2 authors independently. A total of 7185 were excluded because they did not relate to the study aims. A total of 116 full-text articles were reviewed, and only 6 prospective observational studies (9 periods) in LAC fr1997 and 2021 fulfilled the eligibility criteria.[2,12–16] A total of 4483 FES in 4 101 084 individuals were considered. The Preferred Reporting Items for Systematic reviews and Meta-Analyses flow diagram is available in Figure S5.

Incidence Rate

FES incidence rates per study are described in Table 1, evidencing large variations between countries. The meta-analyses results of the FES IR for each group (sex, age, and period) are shown in Table S2.

Incidence Rate Ratio

The IR in men was higher than in women, with an IRR 1.12 (95% CI, 1.04–1.21 [tau^2=0.00, *P*=0.15]). (Figure 1A).

Crude IRR for stroke by age was compared between 2 periods of time (≥2010 and <2010). Those aged <55 years were found to have a higher IR in the latest period (≥2010) compared with the previous period (IRR, 1.37 [95% CI, 1.23–1.50]). In contrast, the IR of the older group (≥55 years) decreased in the same periods (IRR, 0.83 [95% CI, 0.76–0.89]) (Figure S6). Crude IRR for stroke by age was analyzed using a cutoff point of <45 years old and also showed a worse trend in the past decade for those <45 years (≥2010:<2010; IRR, 1.59 [95% CI, 1.36–1.82]). Crude IRR for stroke in ≥45 years age group showed a reduction in stroke incidence in the past decade (≥2010:<2010; IRR, 0.89 [95% CI, 0.83–0.95]) that was similar to the ≥55 years age group. (Figure S7).

Relative Temporal Trend Ratio

When comparing incidence period ≥2010 to <2010 between age groups, the overall RTTR for stroke incidence was less favorable in those <55 years old (IRR <55 versus IRR ≥55 years; RTTR, 1.65 [95% CI, 1.50–1.80]) (Figure 1B). Overall, women experienced a higher increase in stroke incidence (<55 versus ≥55 years; RTTR, 1.98 [95% CI, 1.75–2.21]) compared with men (<55 versus ≥55 years; RTTR, 1.42 [95% CI, 1.22–1.63]).

Metaregression analysis of IRs showed that all considered variables were independently related to FES incidence (age, sex, and time period) (Table S2), and subgroup analyses are also presented in Table S3.

The overall RTTR analysis using a cutoff point of <45 years old is described in Figure 1C and Figure S7.

Pooled Relative Temporal Trend Ratio

Studies reporting 2 periods in the same population with the <55 years age cutoff point were considered to calculate pRTTR. The pRTTR comparing <55 versus ≥55 years was 1.77 (95% CI, 1.59–1.95; *P* for heterogeneity=0.59). When disaggregated by sex with cutoff point at 55 years, women had a pRTTR equal to 2.23 (95% CI, 1.41–3.04; *P* for heterogeneity=0.004) and men had a pRTTR equal to 1.48 (95% CI, 1.23–73; *P* for heterogeneity=0.72) (Figure 2A).

Using <45 years as the cutoff point, the pRTTR <45 versus ≥45 years was pRTTR 2.15 (95% CI, 1.81–2.48; *P* for heterogeneity=0.30; Figure 2B).

Table 1. Summary of Data From Studies in Latin America and the Caribbean

Study and publication year	Country (location)	Study period	Duration of surveillance (mo)	Approach tool	Cases of stroke	Population	Mean age in years (SD)	Women cases N (%)	Incidence rate in men/10^5 N (95% CI)	Incidence rate in women/10^5 N (95% CI)	Income level
Bahit MC, 2016[12]	Argentina (Tandil)	5 January 2013 to 30 April 2015	28	Sudlow and Warlow criteria. WHO STEPS	334	261 182	72.2 (14.4)	175 (52)	125.9 (107.1–147.0)	129.8 (11.2–150.5)	Upper middle
Cabral NL, 2013*[13]	Brazil (Joinville)	2005–2006	12	WHO STEPS	759	987619	NS	367 (48)	80.2 (72.5–88.5)	73.5 (66.2–81.4)	Upper middle
		2012–2013	12		922	1073318	63.7 (15.5)	450 (48)	88.6 (80.8–97.0)	83.3 (75.8–91.4)	
Minelli C, 2020*[15]	Brazil (Matao)	1 November 2003 to 31 October 2004	12	WHO definition	81	76786	65.2 (11.8)	30 (37)	37.5 (101.2–178.7)	37.5 (53.9–114.1)	Upper middle
		1 August 2015 to 31 July 2016	12		81	78890	71 (13.1)	40 (50)	38.9 (73.4–139.8)	39.9 (73.7–139.3)	
Lavados PM, 2005[14]	Chile (Iquique)	1 July 2000 to 31 June 2001	24	Sudlow and Warlow criteria	292	396712	64.8 (5.1) [♂: 68.5 (14.6); ♀ 61.2 (16.6)]	128 (44)	81.8 (69.3–94.3)	65.3 (53.9–76.6)	Upper middle
Lavados PM, 2021[2]	Chile (Ñuble)	1 April 2015 to 30 March 2016	12	WHO STEPS Stroke	890	493464	70.3 (14.1) [♂: 71.8 (14.6); ♀:68.8 (13.4)]	443 (49)	185.8 (168.9–203.8)	175.2 (159.3–192.3)	High income
Olindo S, 2014*[16]	Martinique	1 June 1998 to 31 May 1999	12	WHO	580	362259	71.2 (14)	295 (50)	165.8 (146–186)	154.9 (138–182)	High income
		1 November 2011 to 31 Oct 2012	12		544	370854	72 (15)	252 (46)	171.2 (152–190)	125.7 (110–141)	

NS indicates not stated; STEPS, STEPwise approach to noncommunicable disease risk factor surveillance; and WHO, World Health Organization. *studies with 2 time periods in the same population.

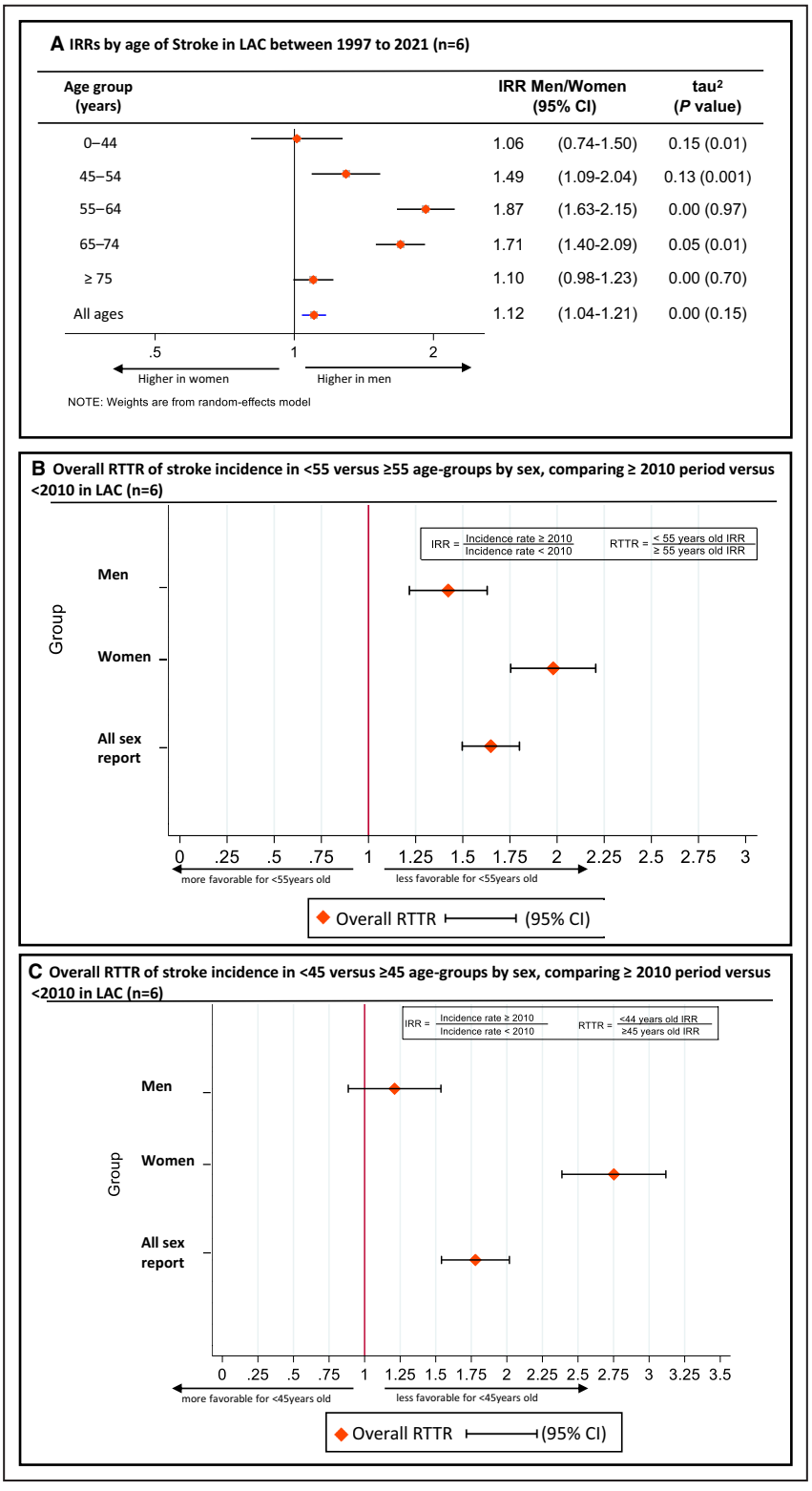

Figure 1. Incidence rate ratio by age and overall relative temporal trend ratios of stroke in Latin America and the Caribbean.

A, IRRs by age of stroke in LAC between 1997 to 2021 (n=6). **B**, Overall RTTR of stroke incidence in <55 vs ≥55 years age groups by sex, comparing ≥2010 time period vs<2010 in LAC (n=6). **C**, Overall RTTR of stroke incidence in <45 vs ≥45 years age groups by sex, comparing ≥2010 time period vs <2010 in LAC (n=6). IRR indicates incidence rate ratio; LAC, Latin America and the Caribbean; and RTTR, relative time trend ratio.

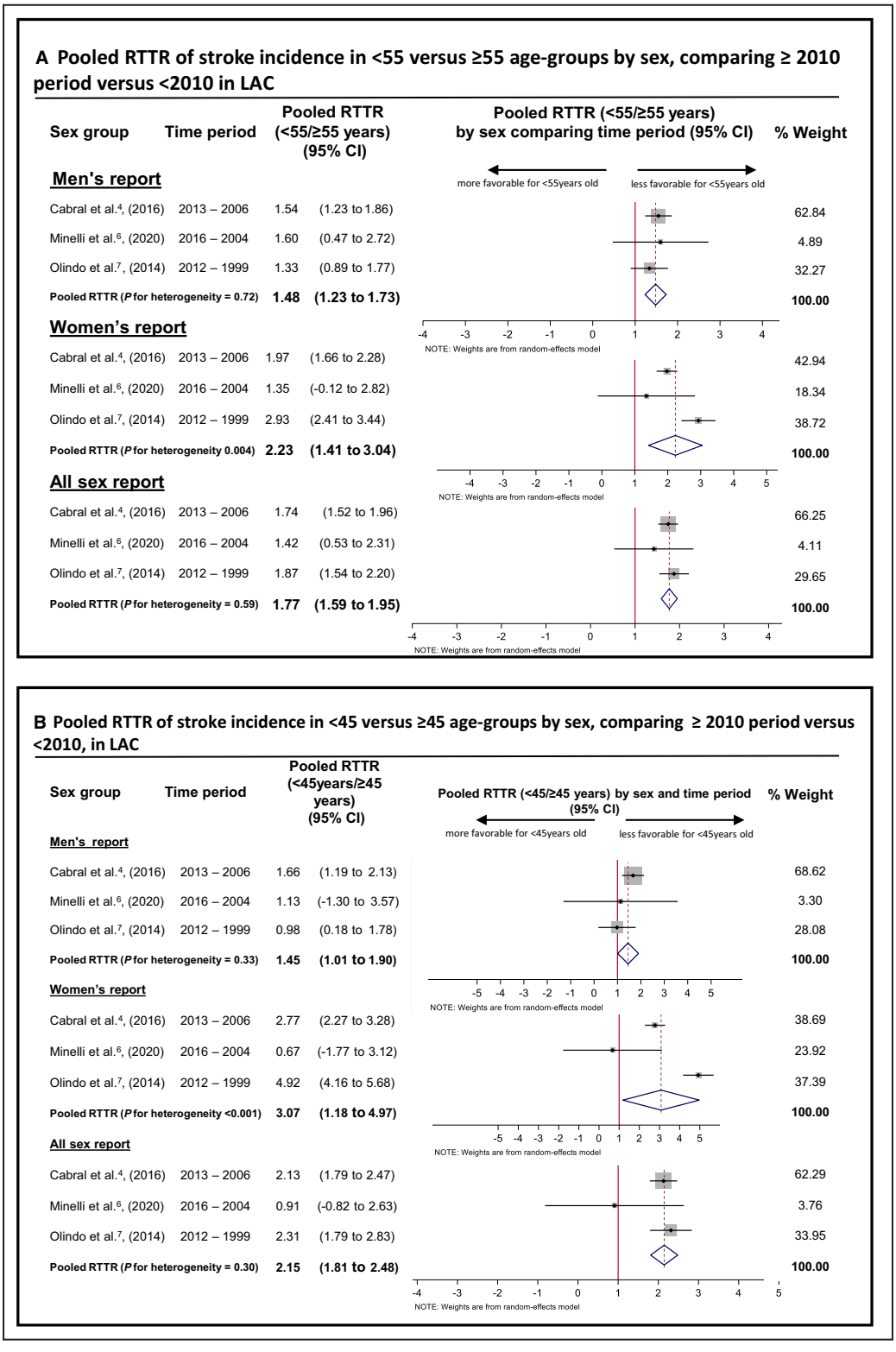

Figure 2. Pooled RTTR of stroke incidence by age groups.
A, Pooled RTTR of stroke incidence in <55 vs ≥55 years age groups by sex, comparing ≥2010 time period vs <2010 in LAC. **B**, Pooled RTTR of stroke incidence in <45 vs ≥45 years age groups by sex, comparing ≥2010 time period vs <2010, in LAC. LAC indicates Latin America and the Caribbean; and RTTR, relative time trend ratio.

Funnel plots were applied for each subgroup to assess the risk of bias. All funnel plots showed symmetrical representation (Figure S8).

DISCUSSION

Our systematic review and meta-analysis show an unfavorable temporal trend in stroke incidence in LAC for younger people, particularly in young women. This contrasts with a global decline in stroke incidence during 2010 to 2019 compared with 2000 to 2009, which has been driven by older populations.[1,5]

The divergence of temporal trends in stroke incidence, with an increase in those <55 years and a decrease in people ≥55 years in the most recent decade (≥2010) compared with the earlier period (<2010), is consistent with the results of a recent prospective population-based incidence study in England,[17] and other similar data from high-income countries in the 21st century.[1] In younger people, unfavorable outcomes may be associated with increases in conventional vascular risk factors, such as hypertension, obesity, sedentary lifestyle, unhealthy diets, dyslipidemia, diabetes, and smoking.[2,14,16] Also, the emergence of new risk factors such as air pollution, long working hours, and stress, but also better patient awareness and access to acute stroke diagnosis, may also have a role in these changes.[1,18] Hormonal factors could be specifically relevant to younger women.[13,15,19]

The strengths of this systematic review include the 24-year coverage period and the availability of population-based studies, most of which met the suggested "standard or advanced criteria for ideal stroke incidence studies" and covered a long period,[1,20] with age- and sex-disaggregated data available. However, there are only a limited number of published reports from few countries, so our results should be interpreted with caution due to possible selection bias, the potential for unmeasured confounders, the impossibility of separating the birth cohort from the appearance of the effect in one period or another, the lack of information on stroke severity/type and prevention strategies; and heterogeneity from the use of different methodology between older studies compared with more recent ones. In addition, even though our data were derived from varied populations (likely causing clinical heterogeneity), they may differ from those in other LAC countries where stroke incidence data were not available, particularly those in lower-income areas.

CONCLUSIONS

The unfavorable temporal trend in stroke incidence in LAC for younger populations, particularly in young women, highlighted in our study warrants further research to understand explanatory factors in order to guide future health policies and to prevent further increases in the disease burden.

ARTICLE INFORMATION

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Supplemental Material

Tables S1–S3
Figures S1–S8

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