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ORIGINAL RESEARCH

Stroke Outcomes in a Population-Focused Urban Hypertension Program in Brazil and Senegal

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BACKGROUND: Stroke is one of the major causes of death worldwide, mainly in low- and middle-income countries. The implementation of multifaceted strategies aiming at blood pressure control may change the global burden of stroke.

METHODS AND RESULTS: We evaluated the impact of a multisector urban cardiovascular health initiative (CARDIO4Cities) on stroke outcomes in Dakar, Senegal, and São Paulo, Brazil. Data covered preintervention, intervention, and follow-up periods with ongoing intervention from 2016 to 2021. An interrupted time series analysis and a segmented regression approach were used to evaluate temporal trends. The relative risk of stroke hospitalization was analyzed with a generalized linear model. In São Paulo, data could also be compared between intervention and control districts. A total of 3445 stroke hospitalizations were analyzed in Dakar and 4491 in São Paulo. In both cities, age-standardized stroke hospitalization rates (Dakar: −26%; São Paulo: −54% on average across 2 districts) and the risk of death from stroke declined over the intervention period. In São Paulo, the baseline risk of stroke hospitalization was comparable across the city. In the follow-up period, the risk was 24.5% lower in the intervention districts compared with the rest of the city (*P*<0.05). The COVID-19 situation did not change this dynamic.

CONCLUSION: The implementation of the multisectoral CARDIO4Cities initiative correlated with positive trends in stroke outcomes. Interventions to reduce cardiovascular risk and improve hypertension management at population level appear to rapidly translate into reduced stroke-related hospitalizations and mortality.

Key Words: cardiovascular disease ■ cardiovascular risk ■ hypertension ■ population health ■ stroke ■ urban

Around the world, stroke is the second most important cause of death, responsible for the loss of 6.55 million lives, and the third leading cause of death and disability with over 101 million survivors of stroke.[1] In 2019, 86% of all stroke deaths occurred in low- and middle-income countries.[1] The highest stroke incidence, prevalence, and mortality rates are observed in Southeast Asia, East Asia and Oceania, North Africa and Middle East, and sub-Saharan Africa. Age-standardized stroke mortality is 3.6 times higher in low-income countries compared with high-income countries and temporal trends in risk factor related disability reveal an increasing burden only in low- and upper-middle income nations.[1]

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CLINICAL PERSPECTIVE

What Is New?

- Population-based initiatives to improve hypertension management along the cascade of care result in reduced stroke hospitalization rates and risk of death from stroke in middle-income urban centers.

What Are the Clinical Implications?

- A focus on cardiovascular risk and hypertension management at population level can rapidly translate into health benefits irrespective of changes to clinical services and care.

Nonstandard Abbreviations and Acronyms

CARDIO Quality of Care, Early Access, Policy Reform, Data and Digital Technology, Intersectoral Collaboration, Local Ownership

However, the contemporary literature on systematic efforts to document stroke burden or the potential impact of population-focused stroke prevention and management efforts in these high-risk regions remains scarce.[2–6] These disparities in stroke burden and the lack of reliable evidence are in part also related to nonexistent or suboptimal surveillance systems and data infrastructure.[7]

Most stroke events can be attributed to cardiovascular risk factors like high systolic blood pressure, high body mass index, hyperglycemia, air pollution, and smoking.[1] Of these, high systolic blood pressure remains the leading risk factor, responsible for an estimated 55.5% of total stroke-related disability-adjusted life years.[1] In systematic reviews and meta-analyses of cohort and randomized trials, lowering of mean blood pressure is associated with appreciable reductions in the risk of stroke across blood pressure categories.[8,9] Indeed, a reduction in the mean systolic blood pressure by 10 mm Hg (or in the diastolic blood pressure by 5–6 mm Hg) is associated with a stroke risk reduction of 20% to 40%.[8,10,11]

Starting in 2018, in collaboration with city governments and local implementation partners, a global multisector urban health initiative, CARDIO4Cities, was designed and implemented to improve cardiovascular health in several major cities.[12–14] This initiative followed the CARDIO approach, a strategy based on the 6 pillars of quality of care, early access, policy reform, data and digital technology, intersectoral collaboration, and local ownership.[14] Within 2 years of implementation, blood pressure control rates increased by 50% in Dakar, Senegal, nearly tripled in São Paulo, Brazil and increased 6-fold in Ulaanbaatar, Mongolia.[12] A modeling study demonstrated that these results translate into a predicted reduction of up to 13% in stroke incidence and 12% in acute coronary events.[15] When modeling the impact over 10 years after implementation, it was found that up to 8% of deaths might be averted. Indeed, the primary goal of the CARDIO4Cities initiative was to apply a holistic urban health approach for cardiovascular risk factors such as hypertension along the cascade of care (diagnosed, treated, controlled) at primary health level. Motivated by the initial successes of the CARDIO4Cities initiative, we initiated an extended surveillance period to focus on the status of stroke in Dakar and São Paulo. In this study, we report on findings from our efforts to systematically document the burden of stroke and assess the impact of the CARDIO4Cities initiative on stroke incidence and fatality rates. Based on the previous modeling results, we hypothesized that the initiative's impact on hypertension control would translate into a reduced risk of fatal and nonfatal strokes.

METHODS

Implementation of the CARDIO4Cities Approach

The CARDIO4Cities initiative was implemented in Dakar (Senegal) and São Paulo (Brazil). Key characteristics of the cities including relevant cardiovascular health indicators have been described previously along with the implementation timeline and activities.[12] For the current study, we consider 3 phases: preintervention period (needs assessment, planning, and establishing necessary agreements), intervention period (implementation and scaling up of activities) and follow-up period (maintaining interventions) (Table S1). For Dakar, we determined the preintervention period from January 2017 to March 2018. Implementation was from April 2018 through December 2019. January 2020 to October 2021 is defined as follow-up period while interventions were maintained. In São Paulo, the preintervention and codevelopment phase was informed by the Design Thinking methodology,[16] followed by the gradual implementation of the initiative. Due to this paced scaling up, we defined a first preintervention period from July 2016 to June 2018 for the Itaquera district where the initiative was implemented in 6 health centers from July 2018 to September 2019. After a second preintervention phase from August 2019 to April 2020, the activities were replicated in another 18 health centers across Itaquera and Penha districts from May to December 2020. The population health approach was subsequently scaled to the entire city.[17] More details on the initiative's implementation can be found in the paper by Boch and coauthors[12] (Table S1). All supporting data are available within the article and its online supplementary files.

Data Collection

In Dakar, starting on December 1, 2021 we reviewed existing anonymized clinical stroke documentation and data collection tools in hospitals and health centers. Stroke care and surveillance guidance updates and related trainings were previously offered with an aim to improve routine stroke diagnosis and management practices. Capacity strengthening of health providers was performed by the Senegalese professional association of neurologists, the implementation partner IntraHealth and the American Heart Association. Although clinical definitions of stroke followed local guidelines, we found that data collection was not standardized. Hence, we developed data collection forms to assist data clerks in the extraction of stroke-related data from paper-based files identified by a clinical supervisor working in the facilities. Data sources included clinical observation sheets and files, referral sheets, and discharge summaries. The hospital and health center mortality records were also reviewed. Primary retrospective data were collected from 6 public hospitals and 16 health centers spread across the city for 2017, 2018, and 2019. Data were collected on electronic tablets using the Open Data Kit Collect software and exported to Excel and SPSS for analysis. Unique identifiers were assigned to all patients while ensuring anonymization. Population data were extracted from the 2013 Dakar census.

In Brazil, the Ministry of Health runs the DATASUS information system, a public data repository integrating 14 databases, including the Hospital Information System, containing anonymized information on acute health events from the public health system (Sistema Único de Saúde). Using DATASUS, we extracted claims data of patients aged ≥20 years with at least 1 *International Classification of Diseases, Tenth Edition* (*ICD-10*) coded stroke record between January 2016 and September 2021 for inclusion in the study. Data extraction started on December 6, 2021. The residential zip code was used to assign patients to the CARDIO4Cities intervention districts, namely Itaquera and Penha, or any of the other districts of São Paulo City. Census data were extracted from Fundação SEADE to provide region-level population estimates for the State of São Paulo.

Ethical and administrative approvals for the CARDIO4Cities activities were obtained in both cities, as appropriate. Data collection in Dakar was covered by ethical approval whereas in São Paulo, only publicly available data were used for the current study.

Statistical Analysis

Stroke-related outcomes (Table S2) were aligned with the definitions of the World Health Organization STEPwise approach to stroke surveillance manual.[18] Clinical risk-factor definitions were based on the World Health Organization Technical Packages[19,20] and Stroke manual[18] as appropriate. Data were analyzed using Microsoft Excel (Microsoft 365, Microsoft, Redmond, WA, USA) and R-4·1·0. Descriptive statistics, including the demographic characteristics of patients with stroke and clinical risk-factors, were summarized as counts and percentages across time periods and geographic locations as appropriate. Crude annual rates of key stroke-related outcomes were calculated by dividing the number of observations in each time period within a district by the population in that district. Case-fatality rates were calculated as the proportion of in-hospital stroke deaths divided by the total number of stroke hospitalization events in each period within a region. All annual rates were age-standardized to the World Health Organization reference population.

The CARDIO4Cities intervention population was defined as the population living in the implementation area during the time of intervention (Table S1). In São Paulo, this allowed for an outcomes comparison over time and between intervention districts and other city areas, whereas in Dakar comparison was possible only between time periods. An interrupted time series analysis was used to describe temporal trends in stroke-related outcomes. In the absence of a randomized controlled trial, the interrupted time series approach helps account for secular trends when evaluating the impact of population programs or quality improvement interventions.[21] Linearity and autocorrelation of data points was assessed before conducting the interrupted time series analysis. A similar number of months (time points) were included in the preintervention and follow-up periods.

The change in outcomes over time and, in São Paulo also between districts, was assessed using a segmented regression approach that allowed for the estimation of immediate changes in the rate of outcomes as well as changes in the trend (ie, a model with different intercept and slope coefficients for the preintervention and follow-up periods). Specifically in São Paulo, an attempt was made to identify the effect of the COVID-19 pandemic on stroke rates, with periods defined by major milestones in the local evolution of the pandemic.

For the count data on stroke hospitalizations, a generalized linear model of negative binomial regression with a logarithmic link function and an offset equal to

Table 1. Profile of Stroke Hospitalization Events in Dakar in the Period 2017 to 2021

	2017	2018	2019	2020	2021*
	Total N=682	Total N=767	Total N=830	Total N=672	Total N=494
Age, y					
20–29	12 (1.8%)	16 (2.1%)	19 (2.3%)	6 (0.9%)	12 (2.4%)
30–44	59 (8.7%)	88 (11.5%)	75 (9.0%)	84 (12.5%)	63 (12.8%)
45–59	159 (23.3%)	174 (22.7%)	172 (20.7%)	142 (21.1%)	124 (25.1%)
60–69	181 (26.5%)	181 (23.6%)	243 (29.3%)	185 (27.5%)	122 (24.7%)
≥70–79	242 (35.5%)	279 (36.4%)	295 (35.5%)	203 (30.2%)	172 (34.8%)
Missing	29 (4.3%)	29 (3.8%)	26 (3.1%)	52 (7.7%)	1 (0.2%)
Sex					
Women	375 (55.0%)	412 (53.7%)	414 (50.1%)	351 (52.2%)	242 (49.0%)
Missing	0	0	0	0	0
Stroke type[†]					
Ischemic	472 (69.2%)	514 (67.0%)	574 (69.2%)	472 (70.2%)	123 (24.9%)
Hemorrhagic	144 (21.1%)	165 (21.5%)	130 (15.7%)	117 (17.4%)	5 (1.0%)
Ischemic/hemorrhagic	30 (4.4%)	47 (6.1%)	90 (10.8%)	0 (0.0%)	1 (0.2%)
Undetermined	36 (5.3%)	41 (5.3%)	36 (4.3%)	83 (12.4%)	364 (73.7%)
Hypertension					
Diagnosis	430 (63.0%)	475 (61.9%)	510 (61.4%)	326 (48.5%)	287 (58.1%)
Missing	100 (14.7%)	136 (17.7%)	104 (12.5%)	104 (15.5%)	97 (19.6%)
Other risk factors					
Obese/overweight	15 (2.2%)	16 (2.1%)	11 (1.3%)	16 (2.4%)	6 (1.2%)
Obese/overweight missing	644 (94.4%)	723 (94.3%)	795 (95.8%)	547 (81.4%)	481 (97.4%)
Cigarette smoking	45 (6.6%)	55 (7.2%)	65 (7.8%)	36 (5.4%)	45 (9.1%)
Cigarette smoking missing	475 (70.0%)	438 (57.1%)	487 (58.7%)	396 (58.9%)	320 (64.8%)
Alcohol intake	29 (4.3%)	15 (2.0%)	29 (3.5%)	21 (3.1%)	18 (3.6%)
Alcohol intake missing	484 (71.0%)	459 (59.8%)	506 (61.0%)	406 (60.4%)	324 (65.6%)
Sedentary lifestyle	41 (6.0%)	35 (4.6%)	34 (4.1%)	38 (5.7%)	20 (4.0%)
Sedentary lifestyle missing	620 (90.9%)	714 (93.1%)	762 (91.8%)	520 (77.4%)	451 (91.3%)
Diabetes	108 (15.8%)	145 (18.9%)	143 (17.2%)	145 (21.6%)	87 (17.6%)
Diabetes missing	334 (49.0%)	335 (43.7%)	416 (50.1%)	266 (39.6%)	259 (52.4%)
Recurrent stroke					
Previous stroke	159 (23.3%)	190 (24.8%)	215 (25.9%)	217 (32.3%)	100 (20.2%)
Missing	212 (31.1%)	268 (34.9%)	338 (40.7%)	150 (22.3%)	152 (30.8%)

*Through October 2021.
[†]Stroke type defined by *International Classification of Diseases, Tenth Edition* (*ICD-10*) categories: Ischemic (I63, I65-66), Hemorrhagic (I60-62), Other (I67-68), Undetermined (I64).

the log of the population divided by 100 000 was used to generate relative risks and 95% CI. In addition, possible confounding factors (sex and age group) were considered in the model; sine and cosine functions, as needed, were used to improve the estimation of peaks and valleys of the series.

RESULTS

Dakar

For the period January 2017 to October 2021, a total of 3445 stroke hospitalization records were identified in Dakar (Table 1). Overall, 39.0% of all hospitalizations occurred in patients aged 59 years and younger, and roughly half (52.1%) happened in female patients. Of all strokes, 62.6% were ischemic and 25.6% were recurrent strokes. Overall, 58.9% of the patients with a stroke had been previously diagnosed with hypertension and 18.2% with diabetes.

In Dakar, age-standardized stroke hospitalization rates increased from 2017 to 2019, then declined between 2020 and 2021 (Table 2). In total, they decreased by 26% from 164.2 per 100 000 people in 2017 to 120.8 per 100 000 in 2021. Overall stroke hospitalizations, nonfatal stroke hospitalizations, and in-hospital

Table 2. Stroke Hospitalization Outcomes in Dakar in the Period 2017 to 2021.

Crude rates	2017	2018	2019	2020	2021
Stroke hospitalizations (per 100000)	88.3	100.1	106.2	84.5	66.8
In-hospital stroke mortality (per 100000)	24.4	28.0	27.7	18.4	13.9
Nonfatal stroke hospitalizations (per 100000)	62.9	72.1	78.5	66.1	52.9
Case-fatality rate (per 100)	29.8	28.0	26.1	21.8	20.9
Age-standardized rates*					
Stroke hospitalizations (per 100000)	164.2	182.9	198.1	151.9	120.8
In-hospital stroke mortality (per 100000)	50.8	54.8	55.6	34.5	26.6
Nonfatal stroke hospitalizations (per 100000)	113.4	128.1	142.5	117.4	94.2
Case-fatality rate (per 100 hospitalizations)	23.1	19.8	19.2	13.9	12.8

*Rates were standardized to the World Health Organization reference population.

stroke-mortality rates all rose between 2017 and 2019 and then fell from 2020 to 2021. Age-standardized in-hospital stroke mortality declined by 48% (from 50.8 per 100000 in 2017 to 26.6 per 100000 in 2021). Age-standardized case-fatality rates declined by 45% throughout the study period, from 23.1 deaths per 100 hospitalizations in 2017 to 12.8 deaths per 100 hospitalizations in 2021.

In multivariable regression models, adjusting for age and sex, in Dakar, we observed no statistically significant difference in the risk for stroke hospitalizations between preintervention and follow-up period (relative risk [RR], 0.97 [95% CI, 0.89–1.03]; *P*>0.05), but the risk for in-hospital stroke mortality was 18% lower at follow-up versus preintervention (RR, 0.82 [95% CI, 0.68–0.96]; *P*=0.006). There was also a 15% reduction in stroke case fatality risk over the observation period (RR, 0.85 [95% CI, 0.74–0.96]; *P*=0.004).

São Paulo

Between 2016 and September of 2021, 2204 and 2287 stroke hospitalizations were recorded respectively in Itaquera and Penha (Tables 3 and 4). About 34% of these occurred in patients 59 years and younger, and about half occurred in women. Age-standardized stroke hospitalization rates steadily declined in Itaquera between 2016 and 2021, decreasing by 60% (from 129.1/100000 population to 51.5/100000) (Table 5). In Penha, rates decreased by 48% from 111.9/100000 in 2016 to 58.1/100000 in 2021. Nonfatal stroke hospitalizations also declined in both Itaquera and Penha from 2016 to 2021.

In Itaquera, in-hospital stroke mortality rates increased in 2016 and 2017, and then progressively decreased till 2021, with an overall decline of 40% from 2016 to 2021. In Penha, a 45% decrease was observed when comparing 2016 (18.5 per 100000) with 2021 (10.2 per 100000) rates. Age-standardized case-fatality rates increased in Itaquera by 29% from 9.2 deaths per 100 hospitalizations in 2016 to 11.9 deaths per 100 hospitalizations in 2021. In Penha, however, there was no difference between the case fatality rate in 2016 (13.0 deaths per 100 hospitalizations) and 2021 (12.8 deaths per 100 hospitalizations).

From the preintervention to the follow-up period, we observed a 33% reduction in stroke hospitalization risk in Itaquera (RR, 0.67 [95% CI, 0.60–0.75], *P*<0.001), compared with a 10% risk reduction in the rest of São Paulo (RR, 0.90 [95% CI, 0.87–0.94], *P*<0.001). Whereas in the preintervention period, there was no statistically significant difference in the risk of stroke hospitalization between Itaquera and the rest of the city (RR, 0.94 [95% CI, 0.86–1.02]), at follow-up, that risk was 31% lower (RR, 0.69 [95% CI, 0.59–0.79]; *P*<0.01). As compared with the rest of São Paulo city, there was no difference in the risk of stroke hospitalization in the preintervention period in Penha (RR, 0.97 [95% CI, 0.81–1.16]) but a significant 18% lower risk (RR, 0.82 [95% CI, 0.71–0.95], *P*=0.01) at follow up.

The risk of in-hospital stroke mortality decreased by 23% (RR, 0.77 [95% CI, 0.58–1.01], *P*=0.056) between preintervention and follow-up periods in Itaquera, whereas it slightly increased in the rest of São Paulo city (RR, 1.06 [95% CI, 1.0–1.11], *P*=0.055). Overall, Itaquera displayed a statistically nonsignificantly lower risk of in-hospital stroke mortality preintervention compared with the rest of the city (RR, 0.84 [95% CI, 0.69–1.02], *P*=0.08) whereas that risk was significantly lower in the postintervention period (RR, 0.61 [95% CI, 0.49–0.76], *P*<0.01). In Penha, no difference in the risk of in-hospital stroke mortality was noted preintervention versus follow-up (RR, 0.95 [95% CI, 0.58–1.55]). In the rest of São Paulo city, there was an 11% higher risk for in-hospital stroke mortality at follow-up (RR, 1.11 [95% CI, 1.01–1.23]) compared with preintervention (*P*=0.036). Similarly to Itaquera, in Penha there was no statistically significant difference in the risk of

Table 3. Profile of Stroke Hospitalization Events in Itaquera, São Paulo, in the Period 2016 to 2021

	2016	2017	2018	2019	2020	2021*
	Total N=457	Total N=441	Total N=411	Total N=387	Total N=291	Total N=217
Age, y						
20–29	4 (0.9%)	3 (0.7%)	4 (1.0%)	3 (0.8%)	2 (0.7%)	3 (1.4%)
30–44	35 (7.7%)	33 (7.5%)	27 (6.6%)	23 (5.9%)	21 (7.2%)	16 (7.4%)
45–59	103 (22.5%)	101 (22.9%)	99 (24.1%)	88 (22.7%)	67 (23.0%)	45 (20.7%)
60–69	121 (26.5%)	107 (24.3%)	119 (29.0%)	111 (28.7%)	74 (25.4%)	58 (26.7%)
≥70–79	194 (42.5%)	197 (44.7%)	162 (39.4%)	162 (41.9%)	127 (43.6%)	95 (43.8%)
Missing	0	0	0	0	0	0
Sex						
Women	225 (49.2%)	233 (52.8%)	213 (51.8%)	187 (48.3%)	127 (43.6%)	109 (50.2%)
Missing	0	0	0	0	0	0
Race						
White	163 (35.7%)	198 (44.9%)	170 (41.4%)	166 (42.9%)	115 (39.5%)	86 (39.6%)
Black	38 (8.3%)	37 (8.4%)	27 (6.6%)	19 (4.9%)	21 (7.2%)	11 (5.1%)
Brown	117 (25.6%)	97 (22.0%)	88 (21.4%)	99 (25.6%)	81 (27.8%)	69 (31.8%)
Asian	1 (0.2%)	2 (0.5%)	0 (0%)	2 (0.5%)	1 (0.3%)	1 (0.5%)
Indigenous	0	0	0	0	0	0
Missing	138 (30.2%)	107 (24.3%)	126 (30.7%)	101 (26.1%)	73 (25.1%)	50 (23.0%)
Stroke type†						
Ischemic	52 (11.4%)	44 (10.0%)	40 (9.7%)	60 (15.5%)	39 (13.4%)	31 (14.3%)
Hemorrhagic	51 (11.2%)	59 (13.4%)	60 (14.6%)	40 (10.3%)	46 (15.8%)	35 (16.1%)
Other	9 (2.0%)	10 (2.3%)	11 (2.7%)	10 (2.6%)	2 (0.7%)	0 (0%)
Undetermined	345 (75.5%)	328 (74.4%)	300 (73.0%)	277 (71.6%)	204 (70.1%)	151 (69.6%)

*Through September 2021.
†Stroke type defined by *International Classification of Diseases, Tenth Edition* (*ICD-10*) categories: Ischemic (I63, I65-66), Hemorrhagic (I60-62), Other (I67-68), Undetermined (I64).

in-hospital stroke mortality as compared with the rest of the city preintervention (RR, 0.97 [95% CI, 0.61–1.43]) but at follow-up, we observed a 20% lower risk (RR, 0.80 [95% CI, 0.57–1.10]; *P*<0.01).

In Itaquera (RR, 1.15 [95% CI, 0.88–1.51]) and Penha (RR, 1.18 [95% CI, 0.72–1.93]), no difference in stroke case fatality risk was seen preintervention versus follow-up, but that risk was observed to increase in the entire city of São Paulo (RR, 1.18 [95% CI, 1.12–1.24], *P*<0.01).

To explore the impact of the COVID-19 pandemic on hospitalization rates in São Paulo, we conducted a secondary analysis of stroke hospitalizations stratified by periods during onset and evolution of the pandemic.[22] Using negative binomial regression, we examined trends in the outcome across 4 time periods: pre-COVID/preprogram (July 2016–June 2018); pre-COVID/during program (July 2018–February 2019); COVID/postprogram (March 2019–December 2020); and post-COVID-19 vaccine availability/postprogram (January 2021–September 2021) (Figure S1). The CARDIO4Cities approach, as a binary variable, was included in the model as a covariate (Table S1). Although no statistically significant difference in the relative risk of stroke hospitalization was noted between nonintervention districts in São Paulo and Itaquera at baseline, such a difference was noted for all intervention periods irrespective of the COVID-19 situation (Figure S2).

DISCUSSION

CARDIO4Cities was designed as a comprehensive approach to improve cardiovascular population health through multisector urban partnerships. The primary impact of this initiative on the outcomes of the hypertension cascade of diagnosis, treatment, and control have been reported elsewhere[12,15] and confirm the feasibility of population-based hypertension control interventions established previously.[23,24] The current analysis focused on stroke-related outcomes, with the objective to explore how CARDIO4Cities might have contributed to population health in Dakar, Senegal, and São Paulo, Brazil.

Systolic blood pressure reduction translates into a reduced risk for cardiovascular events.[25,26] Thus, as markers of cardiovascular health, the examination of stroke-related metrics can help highlight the impact of

Table 4. Profile of Stroke Hospitalization Events in Penha, São Paulo, in the Period 2016 to 2021

	2016	2017	2018	2019	2020	2021*
	Total N=461	Total N=439	Total N=423	Total N=405	Total N=303	Total N=256
Age, y						
20–29	4 (0.9%)	6 (1.4%)	6 (1.4%)	5 (1.2%)	3 (1.0%)	7 (2.7%)
30–44	23 (5.0%)	33 (7.5%)	28 (6.6%)	29 (7.2%)	14 (4.6%)	23 (9.0%)
45–59	108 (23.4%)	108 (24.6%)	115 (27.2%)	75 (18.5%)	56 (18.5%)	48 (18.8%)
60–69	108 (23.4%)	127 (28.9%)	111 (26.2%)	101 (24.9%)	74 (24.4%)	74 (28.9%)
≥70–79	218 (47.3%)	165 (37.6%)	163 (38.5%)	195 (48.1%)	156 (51.5%)	104 (40.6%)
Missing	0	0	0	0	0	0
Sex						
Women	224 (48.6%)	213 (48.5%)	200 (47.3%)	200 (49.4%)	161 (53.1%)	143 (55.9%)
Missing	0	0	0	0	0	0
Race						
White	107 (23.2%)	125 (28.5%)	127 (30.0%)	137 (33.8%)	99 (32.7%)	68 (26.6%)
Black	17 (3.7%)	16 (3.6%)	14 (3.3%)	18 (4.4%)	11 (3.6%)	7 (2.7%)
Brown	59 (12.8%)	59 (13.4%)	74 (17.5%)	56 (13.8%)	44 (14.5%)	30 (11.7%)
Asian	0 (0%)	2 (0.5%)	1 (0.2%)	1 (0.2%)	5 (1.7%)	0 (0%)
Indigenous	0	0	0	0	0	0
Missing	278 (60.3%)	237 (54.0%)	207 (48.9%)	193 (47.7%)	144 (47.5%)	151 (59.0%)
Stroke type†						
Ischemic	80 (17.4%)	85 (19.4%)	64 (15.1%)	86 (21.2%)	52 (17.2%)	76 (29.7%)
Hemorrhagic	51 (11.1%)	52 (11.8%)	58 (13.7%)	57 (14.1%)	44 (14.5%)	39 (15.2%)
Other	4 (0.9%)	13 (3.0%)	15 (3.5%)	7 (1.7%)	9 (3.0%)	6 (2.3%)
Undetermined	326 (70.7%)	289 (65.8%)	286 (67.6%)	255 (63.0%)	198 (65.3%)	135 (52.7%)

*Through September 2021.
†Stroke type defined by *International Classification of Diseases, Tenth Edition* (*ICD-10*) categories: Ischemic (I63, I65-66), Hemorrhagic (I60-62), Other (I67-68), Undetermined (I64).

population-based blood-pressure-focused interventions.[18] In hypertension control, every mm Hg counts, and among all acute cardiovascular events, strokes are the most sensitive indicators for improved hypertension control.[10] As such, we believe that the observed reduction in stroke hospitalizations may result from the improved hypertension control following CARDIO4Cities in the intervention areas as the connection between hypertension and stroke is well established[27] although most intervention studies report on hypertension outcomes rather than stroke.[23]

As the prime risk factor for acute cardiovascular events, there is a growing recognition of the need for better hypertension control in low- and middle-income settings. Evidence for the feasibility and impact of interventions in Africa for example is only starting to emerge.[28] In Dakar, we documented a decrease in stroke hospitalization and case fatality rates after the introduction of CARDIO4Cities as compared with baseline. Indeed, post intervention, we observed a statistically significant reduction in case fatality and in-hospital mortality risk for stroke. Although CARDIO4Cities focused on hypertension management, in Dakar, the professional neurologists association also offered stroke diagnosis and management training to health providers as part of the initiative, which may also have contributed to the improved stroke outcomes, while CARDIO4Cities interventions focused on hypertension guideline updates,[29] accelerated detection, and improved management of hypertension at primary health level. We believe that a majority of the stroke risk reductions can be linked to the rapidly improved hypertension control in the city population through CARDIO4Cities.

In São Paulo, statistically significant reductions were observed in the risk for stroke hospitalizations, in-hospital stroke mortality, and nonfatal stroke hospitalizations in the intervention districts of Itaquera and Penha as compared with the entire city of São Paulo. Age-adjusted stroke hospitalization and in-hospital stroke mortality already showed a long-term decreasing trend in Brazil before the onset of this study.[30,31] The risk for stroke hospitalizations was comparable at baseline and significantly lower in the intervention districts during follow-up. Of note, these trends were not reversed by the COVID-19 pandemic and associated health system disruptions, which are known to have affected stroke-related hospital admissions and myocardial infarction rates in high-income countries.[32] We assume that

Table 5. Stroke Hospitalization Outcomes in Itaquera and Penha, São Paulo, in the Period 2016 to 2021

	Itaquera						Penha					
Crude rates	2016	2017	2018	2019	2020	2021*	2016	2017	2018	2019	2020	2021*
Stroke hospitalizations (per 100.000)	117.68	112.16	103.25	96.05	71.36	52.77	128.76	122.15	117.28	111.90	83.44	70.42
In-hospital stroke mortality (per 100.000)	14.16	15.77	14.57	14.64	10.30	9.48	21.51	17.25	19.41	16.58	17.90	12.93
Nonfatal stroke hospitalizations (per 100.000)	103.52	96.39	88.68	81.40	61.06	43.28	107.25	104.90	97.87	95.32	65.54	57.49
Case fatality rate (per 100 hospitalizations)	12.04	14.06	14.11	15.245	14.433	17.972	16.703	14.123	16.548	14.815	21.452	18.359
Age-standardized rates†												
Stroke hospitalizations (per 100.000)	129.1	120.7	107.2	97.7	71.2	51.5	111.9	105.9	100.4	93.3	68.1	58.1
In-hospital stroke mortality (per 100.000)	15.7	17.4	14.9	14.7	10.4	9.4	18.5	14.5	16.4	13.3	14.3	10.2
Nonfatal stroke hospitalizations (per 100.000)	113.4	103.4	92.3	83.1	60.8	42.1	93.4	91.4	83.9	80.0	53.7	47.9
Case fatality rate (per 100 hospitalizations)	9.2	9.0	12.0	10.8	9.3	11.9	13.0	7.1	17.0	7.6	17.0	12.8

*Through September 2021.
†Rates were standardized to the World Health Organization reference population.

stroke hospitalizations are a good proxy to evaluate the population impact of CARDIO4Cities through improved cardiovascular risk management in primary care.[33]

Across cities, the observed age-standardized stroke hospitalization rate reductions of 26% in Dakar and 54% in São Paulo are even higher than those predicted in the long-term impact modeling of the CARDIO4Cities intervention.[15] The observed results are, however, in line with other studies showing how interventions aiming at population-wide blood pressure reduction can lead to improved stroke outcomes.[34–36]

Our study has some limitations that deserve comments. The observed trends have to be interpreted in the light of infrastructure and data differences between the 2 cities. Brazil, an upper-middle income country, has a federally mandated stroke data collection process whereas Senegal, a lower-middle income country, does not. In Dakar, the interest in stroke as a key outcome of cardiovascular disease led local health authorities to rethink the process and indicators important for stroke surveillance. This resulted in the development of a standardized algorithm for stroke diagnosis and management, combined with adequate training of hospital health providers. In Dakar, the lack of a proper tracking system for patient referral and follow-up after hospital discharge, can have contributed to inaccuracies and underestimations of the stroke metrics. Although primary health center data collection is susceptible to quality concerns,[37] Dakar also sees patients from outside the city boundaries. The fact that patients may not be part of the resident population implies that out-of-town patients may potentially have inflated the reported stroke rates. Vital statistics and cause of death determination may be incomplete, both in Senegal and Brazil, and stroke deaths in the community or after hospital discharge may go unreported.[38]

In São Paulo, official and arguably comprehensive public hospital data were available for analysis. It must be noted that a high proportion of strokes reported through this channel were of "undetermined" type. Although of concern in terms of accuracy of medical records, our analysis was not stratified by stroke type. Nevertheless, it is worth noting that temporal trends in the accuracy of stroke classification and documentation may affect analysis of stroke outcomes.[39] As stroke is a medical emergency, it is assumed that patients are most often managed in the closest facility rather than one of their choice, which might be private. The comparison of intervention districts to contemporary nonintervention districts and the detection of progressively differing trends between them increases the confidence in the association between observed trends and the CARDIO interventions. We are not aware of other overlapping quality improvement programs in either city that might have affected stroke management or reporting. Following the results presented here, we argue that the urban population health initiative CARDIO4Cities[12,15] not only improved blood pressure control but also directly affected stroke incidence and outcomes in the populations benefiting from the interventions.

CONCLUSIONS

Positive trends in stroke outcomes were observed in 2 urban centers in middle-income countries after implementing the multisectoral CARDIO4Cities initiative to improve hypertension control. This extends the evidence on the impact of improved blood pressure control on stroke incidence and mortality to middle-income settings. Operationally feasible and rapidly successful interventions to improve cardiovascular population health are now within reach for the populations that need them most.

ARTICLE INFORMATION

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Supplemental Material

Tables S1–S2
Figures S1–S2

REFERENCES

1. GBD Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease study 2019. *Lancet Neurol*. 2021;20:795–820. doi: 10.1016/S1474-4422(21)00252-0
2. Sagui E, M'Baye PS, Dubecq C, Ba Fall K, Niang A, Gning S, Bellefleur JP, Sane M, Debonne JM. Ischemic and hemorrhagic strokes in Dakar, Senegal: a hospital-based study. *Stroke*. 2005;36:1844–1847. doi: 10.1161/01.STR.0000177864.08516.47
3. Touré K, Thiam A, Sène Diouf F, Ndiaye M, Coumé M, Seck LB, Diagne NS, Diop MS, Dia AT, Diop AG, et al. Epidemiology of stroke at the Clinic of Neurology, Fann university teaching hospital, Dakar-Senegal. *Dakar Med*. 2008;53:105–110.
4. Basse AM, Diagne NS, Boubacar S, Sow AD, Gams DM, Coumé M, Matar N, Gaye MF, Cissé O, Bakhoum M, et al. Epidemiology of stroke: a Senegalese study. *Ann Clin Pathol*. 2017;5:1122.
5. Avezum A, Costa-Filho FF, Pieri A, Martins SO, Marin-Neto JA. Stroke in Latin America: burden of disease and opportunities for prevention. *Glob Heart*. 2015;10:323–331. doi: 10.1016/j.gheart.2014.01.006
6. de Santana NM, Dos Santos Figueiredo FW, de Melo Lucena DM, Soares FM, Adami F, de Carvalho Padua Cardoso L, Correa JA. The burden of stroke in Brazil in 2016: an analysis of the Global Burden of Disease study findings. *BMC Res Notes*. 2018;11:735. doi: 10.1186/s13104-018-3842-3
7. Akinyemi R, Sarfo F, Abd-Allah F, Ogun Y, Belo M, Francis P, Mateus MB, Bateman K, Naidoo P, Charway-Felli A, et al. Conceptual framework for establishing the African Stroke Organization. *Int J Stroke*. 2021;16:93–99. doi: 10.1177/1747493019897871
8. Brunström M, Carlberg B. Association of blood pressure lowering with mortality and cardiovascular disease across blood pressure levels: a systematic review and meta-analysis. *JAMA Intern Med*. 2018;178:28–36. doi: 10.1001/jamainternmed.2017.6015
9. Lackland DT, Carey RM, Conforto AB, Rosendorff C, Whelton PK, Gorelick PB. Implications of recent clinical trials and hypertension guidelines on stroke and future cerebrovascular research. *Stroke*. 2018;49:772–779. doi: 10.1161/STROKEAHA.117.019379
10. Waller DG, Sampson AP. Cerebrovascular disease and dementia. in: *Medical Pharmacology and Therapeutics*. 2018:161–167. doi: 10.1016/B978-0-7020-7167-6.00009-9
11. Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, Chalmers J, Rodgers A, Rahimi K. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet*. 2016;387:957–967. doi: 10.1016/S0140-6736(15)01225-8
12. Boch J, Venkitachalam L, Santana A, Jones O, Reiker T, Rosiers SD, Shellaby JT, Saric J, Steinmann P, Ferrer JME, et al. Implementing a multisector public-private partnership to improve urban hypertension management in low-and middle- income countries. *BMC Public Health*. 2022;22:2379. doi: 10.1186/s12889-022-14833-y
13. Piot P, Aerts A, Wood DA, Lamptey P, Oti S, Connell K, Dorairaj P, Boufford JI, Caldwell A, Perel P. Innovating healthcare delivery to address noncommunicable diseases in low-income settings: the example of hypertension. *Futur Cardiol*. 2016;12:401–403. doi: 10.2217/fca-2016-0032
14. Aerts A, Boufford J. A new whole-of-city strategy for addressing cardiovascular population health. *Cities Health*. 2021;7:296–302. doi: 10.1080/23748834.2021.1979774
15. Reiker T, Des Rosiers S, Boch J, Partha G, Venkitachalam L, Santana A, Srivasatava A, Barboza J, Byambasuren E, Baxter YC, et al. Population health impact and economic evaluation of the CARDIO4Cities approach to improve urban hypertension management. *PLOS Glob Public Health*. 2023;3:e0001480. doi: 10.1371/journal.pgph.0001480
16. Jarrett C, Baxter YC, Boch J, Carrasco C, Cobos Munoz D, Mauro Dib K, Pessoa L, Saric J, Silveira M, Steinmann P. Deconstructing design thinking as a tool for the implementation of a population health initiative. *Health Res Policy Syst*. 2022;20:91. doi: 10.1186/s12961-022-00892-5
17. Avezum Á, Drager LF, Reiker T, Bigoni A, Leonel LP, Abreu A, Bortolotto L, Palmeirim MS, Silveira M, Aquino B, et al. An intersectoral approach to hypertension care: solutions for improving blood pressure control in São Paulo, Brazil. *Am J Hypertens*. 2024;37:366–378. doi: 10.1093/ajh/hpae005
18. WHO. *WHO STEPS Stroke Manual: The WHO STEPwise Approach to Stroke Surveillance*. World Health Organization; 2005.
19. *WHO HEARTS: Technical Package for Cardiovascular Disease Management in Primary Health Care: Risk-Based CVD Management*. World Health Organization; 2020.
20. *WHO HEARTS: Technical Package for Cardiovascular Disease Management in Primary Health Care. Healthy-Lifestyle Counselling*. World Health Organization; 2018.
21. Penfold RB, Zhang F. Use of interrupted time series analysis in evaluating health care quality improvements. *Acad Pediatr*. 2013;13(6 Suppl):S38–S44.
22. Xiao H, Dai X, Wagenaar BH, Liu F, Augusto O, Guo Y, Unger JM. The impact of the COVID-19 pandemic on health services utilization in China: time-series analyses for 2016–2020. *Lancet Reg Health West Pac*. 2021;9:100122. doi: 10.1016/j.lanwpc.2021.100122
23. Peters MA, Noonan CM, Rao KD, Edward A, Alonge OO. Evidence for an expanded hypertension care cascade in low- and middle-income

countries: a scoping review. *BMC Health Serv Res*. 2022;22:827. doi: 10.1186/s12913-022-08190-0
24. Adeoye O, Nyström KV, Yavagal DR, Luciano J, Nogueira RG, Zorowitz RD, Khalessi AA, Bushnell C, Barsan WG, Panagos P, et al. Recommendations for the establishment of stroke systems of care: a 2019 update. *Stroke*. 2019;50:e187–e210. doi: 10.1161/STR.0000000000000173
25. Blood Pressure Lowering Treatment Trialists C. Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: an individual participant-level data meta-analysis. *Lancet*. 2021;397:1625–1636.
26. Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Cheng S, Delling FN, et al. Heart disease and stroke statistics—2021 update: a report from the American Heart Association. *Circulation*. 2021;143:e254–e743. doi: 10.1161/CIR.0000000000000950
27. Moran AE, Gupta R; Global Hearts Initiative C. Implementation of global Hearts Hypertension control programs in 32 low- and middle-income countries: JACC international. *J Am Coll Cardiol*. 2023;82:1868–1884.
28. Dzudie A, Rayner B, Ojji D, Schutte AE, Twagirumukiza M, Damasceno A, Ba SA, Kane A, Kramoh E, Anzouan Kacou JB, et al. Roadmap to achieve 25% hypertension control in Africa by 2025. *Glob Heart*. 2018;13:45–59. doi: 10.1016/j.gheart.2017.06.001
29. Cohn J, Bygrave H, Roberts T, Khan T, Ojji D, Ordunez P. Addressing failures in achieving Hypertension control in low- and middle-income settings through simplified treatment algorithms. *Glob Heart*. 2022;17:28. doi: 10.5334/gh.1082
30. Dantas LF, Marchesi JF, Peres IT, Hamacher S, Bozza FA, Quintano Neira RA. Public hospitalizations for stroke in Brazil from 2009 to 2016. *PLoS One*. 2019;14:e0213837. doi: 10.1371/journal.pone.0213837
31. Sousa LVA, Paiva LDS, Figueiredo F, Almeida T, Oliveira FR, Adami F. Trends in stroke-related mortality in the ABC region, São Paulo, Brazil: an ecological study between 1997 and 2012. *Open Cardiovasc Med J*. 2017;11:111–119.
32. Schutte AE, Srinivasapura Venkateshmurthy N, Mohan S, Prabhakaran D. Hypertension in low- and middle-income countries. *Circ Res*. 2021;128:808–826. doi: 10.1161/CIRCRESAHA.120.318729
33. Sacco RL, Benjamin EJ, Broderick JP, Dyken M, Easton JD, Feinberg WM, Goldstein LB, Gorelick PB, Howard G, Kittner SJ, et al. American Heart Association Prevention Conference. IV. Prevention and rehabilitation of stroke. Risk factors. *Stroke*. 1997;28:1507–1517. doi: 10.1161/01.str.28.7.1507
34. Lackland DT, Roccella EJ, Deutsch AF, Fornage M, George MG, Howard G, Kissela BM, Kittner SJ, Lichtman JH, Lisabeth LD, et al. Factors influencing the decline in stroke mortality: a statement from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:315–353. doi: 10.1161/01.str.0000437068.30550.cf
35. NCD Risk Factor Collaboration. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *Lancet*. 2021;398:957–980.
36. Mozheyko M, Eregin S, Danilenko N, Vigdorchik A, Tobe SW, Campbell N, McLean D, Baskakova Z, Klimovskaia I, Ramanathan K, et al. Hypertension in Russia: changes observed after 4 years of a comprehensive health system improvement program in the Yaroslavl region. *J Clin Hypertens (Greenwich)*. 2017;19:198–204. doi: 10.1111/jch.12885
37. Owolabi M, Olowoyo P, Popoola F, Lackland D, Jenkins C, Arulogun O, Akinyemi R, Akinyemi O, Akpa O, Olaniyan O, et al. The epidemiology of stroke in Africa: a systematic review of existing methods and new approaches. *J Clin Hypertens (Greenwich)*. 2018;20:47–55. doi: 10.1111/jch.13152
38. Revenga Becedas R, Sant Fruchtman C, Dincu I, De Savigny D, Cobos Muñoz D. Addressing the evidence gap in the economic and social benefits of civil registration and vital statistics systems: a systematic review. *Public Health Rev*. 2022;43:1604560.
39. Li L, Binney LE, Luengo-Fernandez R, Silver LE, Rothwell PM; Oxford Vascular S. Temporal trends in the accuracy of hospital diagnostic coding for identifying acute stroke: a population-based study. *Eur Stroke J*. 2020;5:26–35.