

# Global voices on atrial fibrillation management: Brazil



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Atrial fibrillation (AF) and stroke are prevalent conditions worldwide, and the AF burden is expected to concentrate in low- and middle-income countries like Brazil. The National Institute for Health and Care Excellence-funded Global Health Research Group on Atrial Fibrillation Management (GHRG-AF) had a Brazilian arm that addressed AF epidemiology and care in Brazil. GHRG-AF analyzed data from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil), a long-term cohort of 15,105 middle-aged adults in Brazil, focused on cardiovascular disease and diabetes. Additionally, the GHRG-AF used data from the Brazilian Study of Stroke Mortality and Morbidity (EMMA) study to understand AF impact on this cohort of 1863 stroke survivors, all admitted to a community hospital. The GHRG-AF also surveyed healthcare practices and the pathways of individuals who live with AF, interviewing health professionals and patients treated in different healthcare units in São Paulo. Despite these multiple approaches, those data were restricted to individuals

living in large urban centers. Approximately 70% of the Brazilian territory comprises sparsely populated cities (<10 inhabitants/km<sup>2</sup>), which, as a group, are home to 15 million individuals. In a new step, the GHRG-AF collaborators aim to improve cardiovascular research capacity in distant locations of the Brazilian Amazon, develop patient-centered protocols, empower community health agents in the region, and intensify collaboration with other research groups in remote parts of the country.

**KEYWORDS** Atrial fibrillation; Brazil; Epidemiology; Patient care; ABC pathway; Cohort

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## Introduction

Atrial fibrillation (AF) and stroke are prevalent conditions worldwide, and Brazil is not an exception.<sup>1,2</sup> The Global Burden of Disease 2021 estimates an AF prevalence of 4.6% and 3.6% in Brazilian men and women older than 55 years of age, respectively. Each year, 170,000 incident AF cases and 240,000 incident stroke events are expected to occur in the country.<sup>3</sup>

Comparing AF prevalence across multiple samples is difficult because they vary in the study setting (community or health service based), participants' age and diagnostic

methods. Low- and middle-income countries (LMICs),<sup>4,5</sup> like the BRICS (Brazil, Russia, India, China, and South Africa), an expanding group of emerging countries aiming at economic and development cooperation, show lower AF prevalences compared with Western high-income countries. However, most results point out that the health and economic AF burden is expected to be concentrated in LMICs in the next few decades. These countries have a rapidly aging population, leading to an increasing AF prevalence. Although lack of stroke prevention medications may be a widespread concern,<sup>6</sup> LMICs may face especially harsh financial constraints in providing adequate access to oral anticoagulants (OACs), a perception supported by low OAC use rates described in various reports from these settings.<sup>7–10</sup>

Nationwide studies address OAC use for AF-related stroke prevention in Brazil. Studies focusing on specific scenarios show that OAC use rates may be as low as 10%, which

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## KEY FINDINGS

- Atrial fibrillation burden is expected to concentrate in low- or middle-income countries, like Brazil.
- The Global Health Research Group on Atrial Fibrillation Management collaboration in Brazil addressed atrial fibrillation epidemiology, barriers, and facilitators for healthcare.
- We intend to expand the collaboration to remote areas of the Brazilian Amazon in the near future.

is lower in primary care facilities than in specialized centers.<sup>11</sup> Moreover, warfarin is by far the most used OAC in Brazil. Silva and colleagues<sup>5</sup> analyzed data from a large private health insurance dataset in Brazil and found that only 31% of patients with AF taking warfarin were in the therapeutic range for > 65% of the time.

Brazil is a large country, with an approximate national population of 203 million individuals and a population density of 23.9 population/km<sup>2</sup>. However, a significant heterogeneity in population distribution occurs in the country. Although 18 (0.3%) of 5570 Brazilian municipalities have a population density  $\geq 5000$  population/km<sup>2</sup>, cities with <10 population/km<sup>2</sup> correspond to 70% of the Brazilian territory and are home to more than 15 million Brazilians (Figure 1).<sup>12</sup> Brazilian population distribution also influences AF prevalence, mainly due to different demographics among regions. More distant, sparsely populated regions tend to have lower median population age and, consequently, lower AF prevalence. Global Burden of Disease state-level data show that crude AF prevalence in Brazil varies from 440

per 100,000 population (Amapá State) to 1175 per 100,000 population (Rio Grande do Sul State). After age standardization, these rates are much closer, ranging from 730 per 100,000 prevalence (Maranhão State) to 828 per 100,000 population (São Paulo State).<sup>3</sup>

In Brazil, universal healthcare is a constitutional right. Public and private services coexist in primary, secondary and tertiary care and are funded by governmental, company, and private expenditures. Besides the complexity of the Brazilian Health System, the heterogeneity found across the country in population density, socioeconomic development, and culture increases the challenge of understanding AF dynamics in our population. For a broader contribution to AF research in the country, the Brazilian arm of the National Institute for Health and Care Excellence Global Health Research Group on Atrial Fibrillation Management (GHRG-AF) embraced multiple branches of investigation. This strategy included the enrollment of patients with AF and their healthcare providers, as well as analyzing data from 2 long-term cohort studies in the country (Table 1).<sup>13–15</sup>

This overview summarizes the main insights and continued research promoted by this collaboration in Brazil, including innovative frontiers the GHRG-AF intends to explore during the next few years.

## Lessons from the Brazilian Longitudinal Study of Adult Health

One of the first steps toward a better understanding of the dynamics of AF burden and AF care in Brazil was diving into data from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil), one of the largest epidemiological studies in the country. ELSA-Brasil is a multicenter cohort study including 15,105 civil servants from 6 Brazilian state

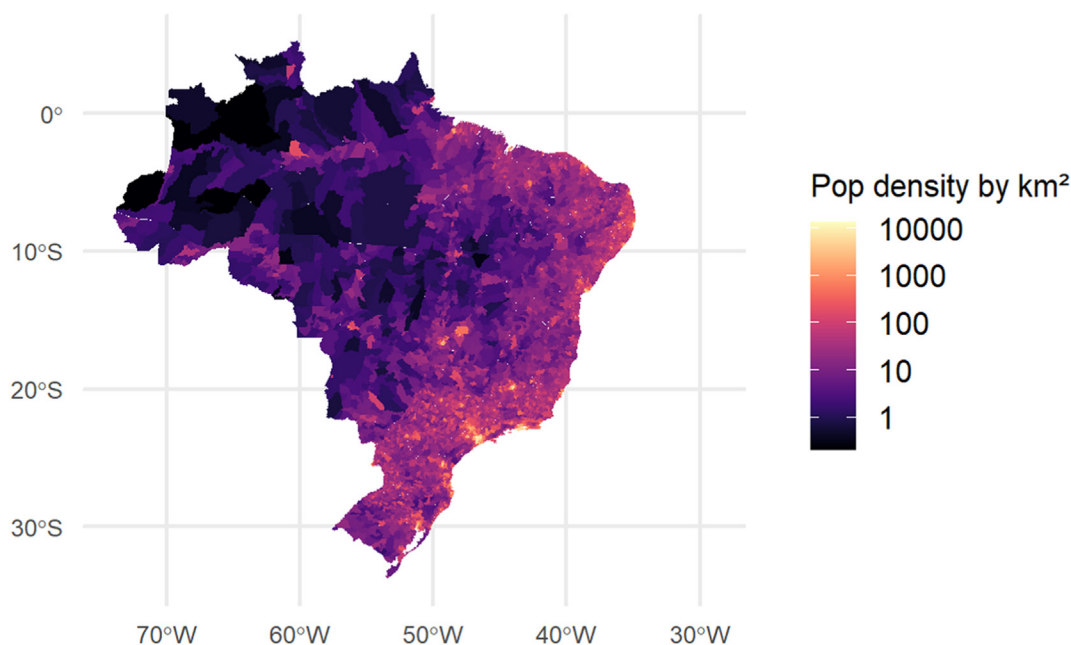


Figure 1 Brazilian population density heatmap.

**Table 1** ELSA-Brasil, EMMA, and GHRG-AF study and sample descriptions

Study	Study design	Eligible subjects	Participants	Goals/endpoints
ELSA-Brasil	Multicenter cohort	Civil servants age 35–74 y at baseline	15,105	Cardiovascular disease and diabetes incidence and their determinants in the Brazilian population
EMMA*	Cohort study based on WHO STEPS stroke surveillance approach	Patients age 35 y or older admitted to a community hospital due to stroke	1863	Poststroke mortality and functionality and their associated factors
GHRG-AF <sup>†</sup>	Patient and healthcare provider surveys; health data review and follow-up	Patients with AF and their healthcare providers	804 <sup>‡</sup>	Understand AF care pathways, barriers, and facilitators

AF = atrial fibrillation; ELSA-Brasil = Brazilian Longitudinal Study of Adult Health; EMMA = Brazilian Study of Stroke Mortality and Morbidity; GHRG-AF = Global Health Research Group on Atrial Fibrillation Management; WHO = World Health Organization.

\*The data refer to the EMMA long-term cohort (WHO STEPS 1).

<sup>†</sup>Data refers to recruited participants in the Brazilian arm of the study. A similar approach was adopted in Sri Lanka and China.

<sup>‡</sup>A total of 697 patients with AF and 107 healthcare providers.

capitals: São Paulo, Belo Horizonte, Rio de Janeiro, Salvador, Rio Grande do Sul, and Vitória.<sup>13,16</sup> Baseline assessments occurred in person from 2008 to 2010 in all investigation sites. It included validated questionnaires, medication use reviews, anthropometric measurements, and laboratory and imaging evaluations, all applied by trained staff following standardized protocols and strict quality control procedures.<sup>17–20</sup> Since then, participants have been followed (1) annually by telephone contact and (2) in person every 4 to 5 years, with electrocardiographic, laboratory, and imaging exams. As of 2024, in-person ELSA-Brasil assessments have occurred 4 times. ELSA-Brasil is an observational study, so medication use and laboratory testing related to healthcare during follow-up are not determined by the study protocol and occur at healthcare providers' discretion.

The GHRG-AF analyzed data from 13,260 ELSA-Brasil participants at baseline to describe AF prevalence, associated factors, and the use of stroke prevention medication in the cohort. AF prevalence at the ELSA-Brasil baseline was 2.5%, with similar rates for men (2.6%) and women (2.4%). According to age strata, the frequency of AF diagnosis was 1.2%, 2.2%, 2.9%, and 5.4% for ages <45, 45 to 54, 55 to 64, and >64 years, respectively. Individuals with prevalent AF at baseline had a median age of 56.0 (interquartile range, 49.0–63.0) years and 55.6% had a high ( $\geq 2$ ) CHA<sub>2</sub>DS<sub>2</sub>-VASc (congestive heart failure, hypertension, age  $\geq 75$  years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65–74 years, sex category) score. Hypertension (49.8%), obesity (27.9%), and diabetes (24.3%) were frequent comorbidities among ELSA-Brasil participants with AF. Additionally, 30 (9.0%) ELSA-Brasil participants with AF at baseline self-reported previous rheumatic fever diagnosis. It was not possible to properly determine how many of these individuals had rheumatic AF. Suboptimal stroke prevention was expected, as only 10.8% of participants with a high CHA<sub>2</sub>DS<sub>2</sub>-VASc score received anticoagulants.<sup>21</sup> Women

and younger participants had a trend towards lower stroke prevention rates.

Low OAC use was an even more striking finding in Brazil given that access to evidence-based medical treatments for common chronic conditions included in the National Essential Medicines List should be available free of charge in the country.<sup>22</sup> The last version (2022) of this list includes warfarin, a fair selection of antihypertensives (amlodipine, atenolol, captopril, enalapril, hydrochlorothiazide, methyldopa, propranolol, verapamil), antiarrhythmics (amiodarone, propafenone), and other cardiovascular disease (CVD)–related medications (aspirin, carvedilol, digoxin, furosemide, simvastatin), all for delivery in primary healthcare units. Other medications may be provided in specialized centers as well.<sup>23</sup> Of note, non-vitamin K oral anticoagulant (NOAC) use in Brazil is restricted to patients who can afford and agree to buy the medication. To date, NOACs have yet to be included in available medications for outpatient use in the Brazilian public health sector.

There has been increasing attention to Geoffrey Rose's concepts<sup>24</sup> of primordial prevention in CVD and the impact that influences on populational behavior and risk factor control levels (usually referred to under the concept of cardiovascular health [CVH]) may have on CVD incidence and mortality. An important initiative to standardize measurements on individual and populational CVH components was proposed by the American Heart Association Life's Simple 7 (LS7) metrics,<sup>25</sup> updated in 2022 to the Life's Essential 8 (LE8) score.<sup>26</sup> However, CVH components in these assessments (diet, physical activity, body mass index, smoking, blood pressure, fasting plasma glucose, blood cholesterol, and sleep habits) were defined based on their influence on atherosclerotic CVD. It is not clear which of these features are associated with AF prevalence.

In a subsequent analysis of ELSA-Brasil data,<sup>27</sup> the GHRG-AF analyzed the association between AF diagnosis and LS7 metrics and scores. In this large Brazilian sample, LS7 scores were not significantly associated with AF; however, analyzing each LS7 metric in separate disclosed the

heterogeneity in this lack of association. While ideal blood pressure, as expected, was inversely associated with AF prevalence, low cholesterol levels were related to high odds of AF, a phenomenon not completely understood and described as the AF “cholesterol paradox,”<sup>28</sup> which was also seen in the ELSA-Brasil data leading to the lack of association between AF and total LS7 scores.

### Lessons from stroke survivors in Brazil: The Brazilian Study of Stroke Mortality and Morbidity

Stroke is the most critical AF-associated outcome, considering both its frequency and associated multimorbidity. The GHRG-AF also explored data from the Brazilian Study of Stroke Mortality and Morbidity (EMMA) study to understand better the impact of AF and other risk factors on survival after stroke.

The EMMA study was based on the World Health Organization (WHO) STEPS stroke surveillance approach<sup>29</sup> for LMICs. The EMMA study occurred in community and hospital settings. In the community study (WHO STEP 3), trained interviewers administered a screening tool for 4496 individuals, aiming to detect previous stroke diagnoses, including the presence of long-term disabilities. All participants who had been screened positive for events suggestive of stroke in the past were invited to answer an individual questionnaire that included more detailed information.<sup>30</sup> Additionally, the EMMA study includes a long-term cohort of 1863 individuals who had a stroke event and were admitted from 2006 to 2014 to a community hospital (Hospital Universitário da Universidade de São Paulo) in São Paulo, Brazil (WHO STEPS 1). EMMA study participants usually live on the city outskirts, near the hospital, or in nearby cities. Baseline assessment included sociodemographic data, date and time of onset of stroke symptoms, hospitalization, history of traditional risk factors, medical treatment, and functionality (modified Rankin scale). Participants were enrolled, followed during hospital stay, and contacted 1 month, 6 months, and annually after the index event to update medication, physical and cognitive functionality, and vital status data. Whenever contact could not be achieved, official mortality records were also regularly consulted by the study team.<sup>14</sup> Like ELSA-Brasil, the EMMA study is an observational

study and all healthcare decisions are made at the discretion of healthcare providers.

The GHRG-AF analyzed EMMA study data, advancing the knowledge about the epidemiology after a stroke event in this Brazilian setting.<sup>31–34</sup> Specifically, there was evidence that individuals who had an AF-related stroke have poorer prognosis compared with those who suffered non-AF stroke events.<sup>35</sup> To analyze the impact of AF diagnosis and lack of anticoagulant use on survival after stroke in the EMMA cohort during a 12-year follow-up, data from 1121 participants with ischemic stroke were reviewed,<sup>31</sup> and 200 (17.8%) had AF. More than half of the study participants (58.3%) died within 12 years. Lack of anticoagulation occurred in 83.5% (during the first 6 months) and 78.8% (after 6 months) of EMMA participants with AF-related stroke, and it was a strong marker of poor survival (hazard ratio 1.82; 95% confidence interval 1.43–2.31). Information on non-pharmacological therapy was not available.

In an analysis of the frequency of use for other cardiovascular medications in the EMMA cohort, only 40% of the EMMA cohort received adequate long-term medications before and after the index event, and 15% did not receive adequate long-term medications prior to or after stroke.<sup>34</sup> As most medications for common chronic conditions are free of charge in Brazil, this may reflect restricted access to healthcare despite universal health coverage pursued by the Brazilian Health System.

### Understanding healthcare practices and pathways of individuals who live with AF

Providing adequate care for patients with AF is a challenging task. As stated previously, diverse barriers may hinder achieving this goal. The care pathway of individuals with AF in the city of São Paulo, Brazil, and how the COVID-19 pandemic impacted it was investigated in a mixed-methods study.<sup>36</sup> There were some barriers to access to primary healthcare for this group, and one-third of the sample reported discontinuity or increased difficulty for AF care during the pandemic. A subsequent mixed-methods study<sup>37</sup> interviewed health professionals from 11 primary care units in São Paulo, Brazil, where the main barriers and facilitators in this scenario are described in [Table 2](#).

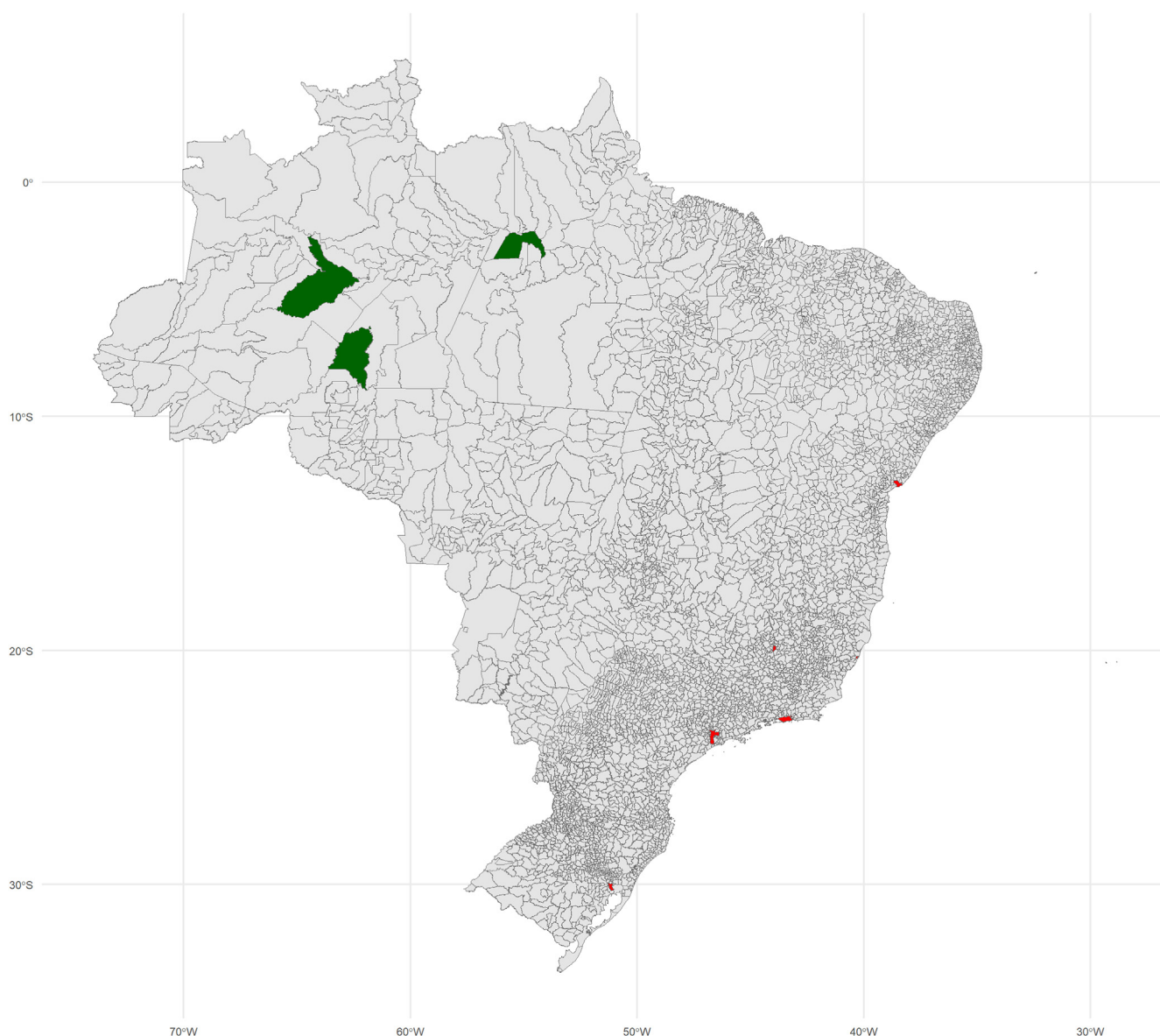
**Table 2** Main barriers and facilitators pointed by the healthcare professionals' views, when caring for patients with atrial fibrillation in São Paulo, Brazil<sup>24</sup>

	Barriers	Facilitators
Access to healthcare	Getting routine appointment	Home visits
Patient features	Multiple comorbidities	Patient adherence to treatment
	Impaired mobility (Lack of) patient adherence to treatment	Good doctor-patient-family relationship
	Financial impairments	
Local care	(Lack of) non-vitamin K oral anticoagulant availability	Warfarin availability
	(Lack of) prothrombin time availability	ECG availability
	Delayed prothrombin time results	
Health system, organization and external factors	Physical structure of the health units	Well-prepared health teams

Among the potential reasons for low warfarin use in this setting, participants highlighted the difficulty in obtaining international normalized ratio (INR) testing in a timely fashion and the lack of training and protocols for AF care. Additionally, there is a widespread use of aspirin for stroke prevention in patients with AF, especially in LMICs.<sup>11</sup> This fact supports the perception by healthcare providers that aspirin was a viable alternative for stroke prevention due to the lack of appropriate INR testing and perhaps due to an overestimation of anticoagulant treatment risks. Aspirin use results in a higher stroke and mortality risk for these patients compared with anticoagulation.<sup>38,39</sup> Increased INR testing availability and more widespread use of NOACs are potentially effective strategies to enhance AF-related stroke prevention in the country.

### A new step toward equality

Prior sections were restricted to individuals who lived in urban centers (Figure 2). However, this partially represents the Brazilian scenario, as expressed by the 2022 National Census Data.<sup>12</sup> A large proportion of the northern Brazilian territory is in the Amazon, a region characterized by a dense forest crossed by large rivers and high biodiversity, where many sparsely populated cities are located. Several communities are located inside riverbeds (*ribeirinha*) and on the riversides. Transport to and from these communities occurs mainly (in many cases, exclusively) by boats and depends on climate conditions. Additionally, inland rural communities are typically significantly far from one another (as well as from health units and teams), a setting that imposes great difficulties to access.<sup>40</sup>



**Figure 2** Brazilian cities included in the Brazilian Longitudinal Study of Adult Health, Brazilian Study of Stroke Mortality and Morbidity study, and Global Health Research Group on Atrial Fibrillation Management (red, urban centers) and those participating in the Enhancing the Quality of care in Amazonian remote Locations – targeting CardioVascular Health study (green, Amazon region).

These characteristics impair adequate access to healthcare in the region, a problem also aggravated by the lower socioeconomic level of northern Brazil compared with other Brazilian regions. Like other supplies, geographical barriers and long distances in Brazil impose additional difficulties in providing regular medication access, as Pereira and colleagues<sup>41</sup> pointed out. Not surprisingly, data from the Brazilian Medical Council also point to a low physician/population ratio in these areas.<sup>42</sup> In rural areas of the Amazonas and Para states, there are approximately 0.2 and 0.5 physicians per 1000 population, respectively. Although the adequate physician/population ratio for a region depends on the health system organization, these values are too low to ensure adequate access to healthcare, especially in a region where healthcare workforce efficiency is restricted due to long distances, difficult transportation, and impaired communication among communities and health units.

Some initiatives have taken place to reduce the vulnerability and inequality in healthcare affecting these regions. The Brazilian Family Health Strategy includes community health agents (CHAs), part of a multidisciplinary team supporting primary care.<sup>43</sup> In distant regions, these individuals usually live in the communities under their care and are a permanent link between the community and the other family health team members. However, despite available evidence of the potential of CHAs (or similar workers) training and engagement in healthcare,<sup>44–46</sup> this resource still needs to be explored in Brazil.

In the past decade, the More Doctors Program was created focusing on deprived areas to provide emergency provision of physicians, to improve primary healthcare infrastructure and to stimulate qualified medical training.<sup>47,48</sup> Since its

beginning, the heterogeneity in primary care physician distribution has reduced in the country, but significant inequality persists.<sup>48</sup> The Brazilian Ministry of Health has also stimulated governmental and nongovernmental organizations to provide boat-based access to healthcare, a program in the Family Health Strategy called “Fluvial Family Health” (Figure 3). Fluvial Family Health units include at least physician, dentist and nurse’s offices, a room for diagnostic procedures (including electrocardiograms), infrastructure for vaccination, staff accommodations, and other amenity facilities. Some of these units provide enhanced laboratory and pharmaceutical assistance, including medications available at Brazilian primary care centers, and some medications were distributed at specialized centers.<sup>38</sup> Unfortunately, the frequency of visits by these mobile units is insufficient to ensure adequate continuity of care.<sup>49</sup>

Although epidemiological data on CVH are limited in remote Amazonian locations, there is evidence that CVD-related conditions are a growing problem in the region,<sup>50,51</sup> prominently where deforestation and irregular occupation are important problems.<sup>52</sup> Two studies in the city of Coari suggest that stroke takes a high toll in the region (combining high mortality and high disability), especially in *ribeirinha* populations.<sup>53,54</sup> Despite this increasing concern, studies with adequate scientific rigor addressing which strategies are effective and culturally adequate to mitigate this problem still need to be performed. Specifically, no randomized controlled trials targeting CVH improvement have been conducted in this region.

In collaboration with local researchers, communities, and city officers in 3 Brazilian Amazon cities, we intend to build, implement, and evaluate patient-centered, CHA-



**Figure 3** Fluvial Family Health Unit, adopted by the Brazilian Ministry of Health to increase access to medical consultations and laboratory and pharmaceutical procedures. Image provided by the Santarém City Health Department.

delivered protocols to improve CVH in adults living in *ri-beirinha* and rural communities. These protocols will be based on the Brazilian Ministry of Health guidelines, aligned with the American Heart Association LE8<sup>26</sup> and WHO HEARTS<sup>55</sup> procedures, for 9 healthcare lines: weight optimization, increasing physical activity, smoking cessation, alcohol consumption reduction, healthy sleeping habits, blood pressure, glucose and lipids control, and polypharmacy reduction. We plan a co-production phase for these protocols with local communities and healthcare professionals to ensure that proposed interventions will be tailored to local needs, integrated into standard healthcare, and sustainable after the study. CHAs participating in the study will be trained and receive continuous support from other health professionals via the Internet, using already available technology in the region. Additionally, we envisage assessing the implementation of wearable/portable technology into CHA routine care in these regions, improving information delivery to healthcare teams. We aim to analyze the impact of these CHA-delivered interventions on Amazon residents' CVH (based on their LE8 scores) 12 months after their implementation. The protocols for CHA-delivered CVH interventions, as well as the wearable/portable technology to be incorporated in the trial are currently under discussion. It is not possible to state definitively at this point if portable electrocardiograms will be included in the protocol. Although focused on the Brazilian Amazon, this strategy may be reproduced in other settings where geographical barriers are important limitations to healthcare.

## Limitations

Our article needs to be interpreted within its context and the limitations of the studies conducted by the Brazilian arm of the GHRG-AF. Both ELSA-Brasil and the EMMA study are observational studies. Medication use and the frequency of exams were not determined by protocol, and the associations and risks described may be influenced by uncontrolled variables. Some of the ELSA-Brasil and EMMA analyses were cross-sectional. In those cases, information on mortality, stroke rates, number of emergency room consultations, or other relevant outcomes could not be addressed. Echocardiographic data were not available for most participants, precluding the assessment of structural heart diseases or left ventricular function. Finally, it is not possible to define all procedures for the proposed trial set in Brazilian Amazon as study protocol is currently under discussion.

## Conclusion

The knowledge of AF epidemiology and care in Brazil has expanded in recent years due to GHRG-AF actions. Aiming for a broader social impact, the GHRG-AF intends to intensify its collaboration with other groups in the country, expanding research to different and understudied scenarios.

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