

# CADASIL Argentine Registry: Study Design and Preliminary Data

Carolina Agata Ardochain Cristalli, MD1, Julieta Rosales, MD2, Fabio Gonzalez, MD3, Valentin Selvaggi, MD4, Julián Martín Alonso, MD5, Juan Ignacio López, MD6, Martín Aguilar, MD1, Marcelo Kauffman, PhD4, Danit G Saks, PhD7, Ricardo Allegri, PhD1, Gustavo Sevlever, PhD1, Hernan Chaves, MD1, Diana Olga Cristalli, PhD8 and Ismael Luis Calandri, MD1 (1)Fleni, Buenos Aires, Argentina, (2)La Sagrada Familia, Buenos Aires, Argentina, (3)Hospital Británico, Buenos Aires, Argentina, (4)Hospital Ramos Mejía, Buenos Aires, Argentina, (5)Hospital Posadas, Buenos Aires, Argentina, (6)Sanatorio Los Arcos, Buenos Aires, Argentina, (7)Centre for Healthy Brain Ageing (CHeBA), Sydney, Australia, (8)Centro Jesi, La Plata, Argentina



## INTRODUCTION

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), the most common hereditary small vessel disease, leads to early-onset stroke and vascular cognitive impairment (VCI). Despite its importance, data from Latin America remain scarce.

The CADASIL Argentine registry (CADASILAr) was created to harmonize clinical data, promote international collaboration, and provide a reproducible, longitudinal framework to study disease progression and expand to neighboring countries. **This study aims to present the cohort design and preliminary results from the cross-sectional phase.**

## METHODS

CADASILAr is a multicenter Argentinian cohort designed to document demographic, clinical, imaging, and genetic features of adults ( $\geq 18$  years) with confirmed or suspected CADASIL, and to explore factors related to disease progression and cognitive decline. It includes a cross-sectional phase (CADASILAr-C) and a 5-year longitudinal phase (CADASILAr-Long) (Figure 1).

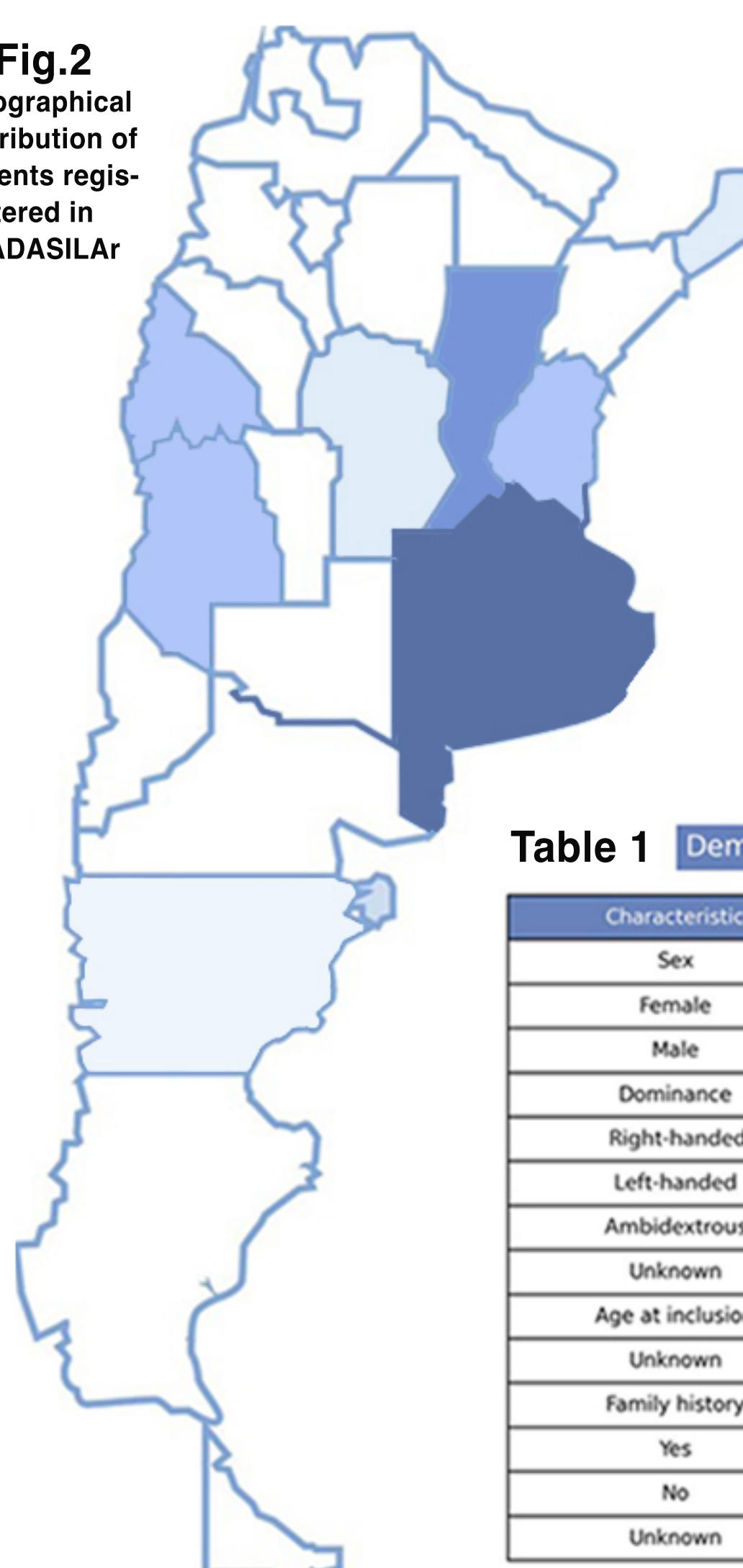
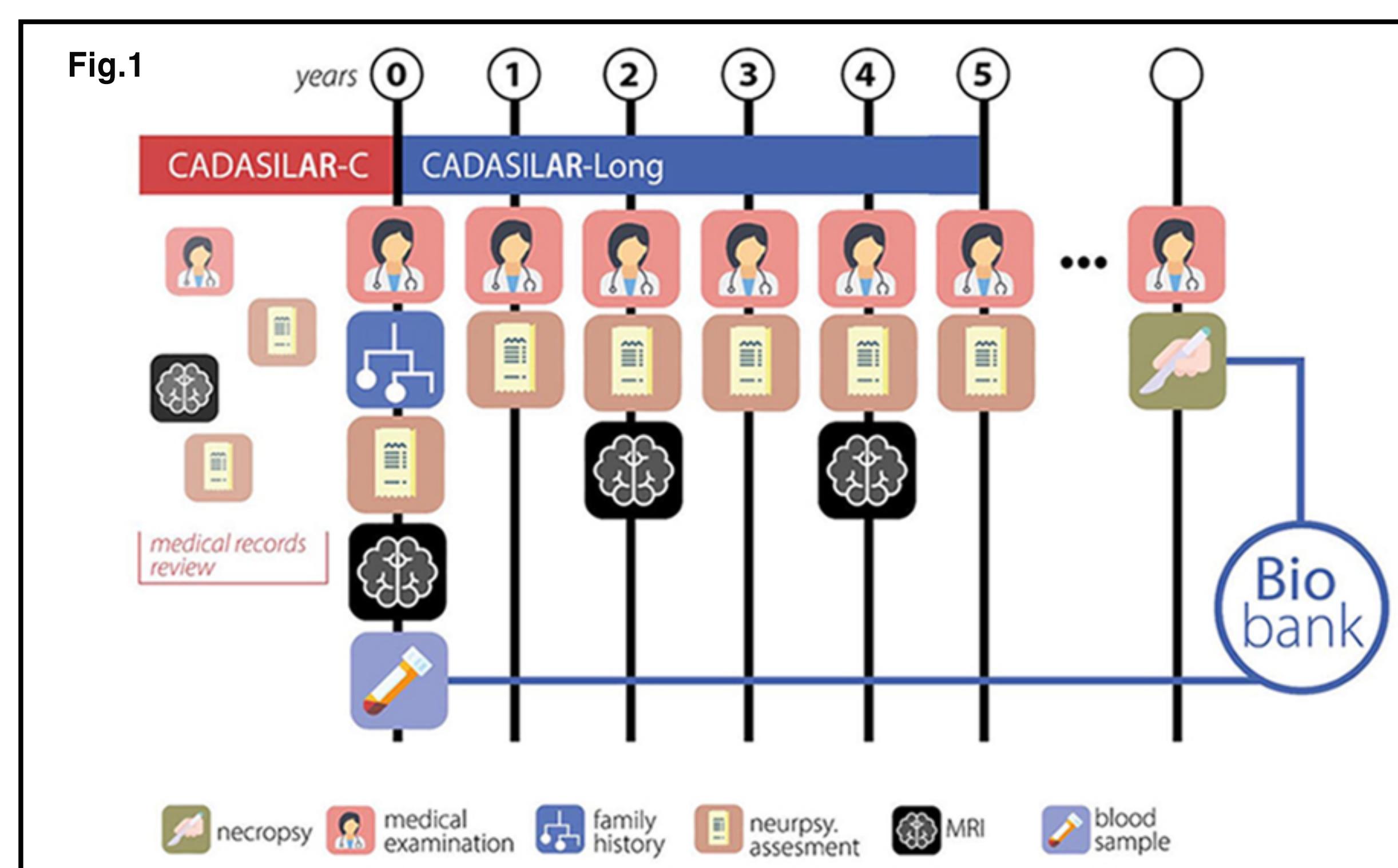


Fig.2  
Geographical distribution of patients registered in CADASILAr

Characteristic	N = 90
Sex	
Female	45 / 90 (50%)
Male	45 / 90 (50%)
Dominance	
Right-handed	56 / 63 (88.9%)
Left-handed	6 / 63 (9.5%)
Ambidextrous	1 / 63 (1.6%)
Unknown	27
Age at inclusion	43.8 (11.9)
Unknown	10
Family history	
Yes	76 / 83 (91.6%)
No	7 / 83 (8.4%)
Unknown	7

Collected data include symptom onset, vascular risk factors, cognitive assessments, and socio-economic variables. The study integrates biobanks, aligns with international registries, and includes a brain donation program to establish a national CADASIL brain bank

- Birth place:**  
-Buenos Aires: 72  
-Santa Fe: 5  
-San Juan: 3  
-Entre Ríos: 3  
-Mendoza: 3  
-Misiones: 2  
-Córdoba: 2  
-Chubut: 1

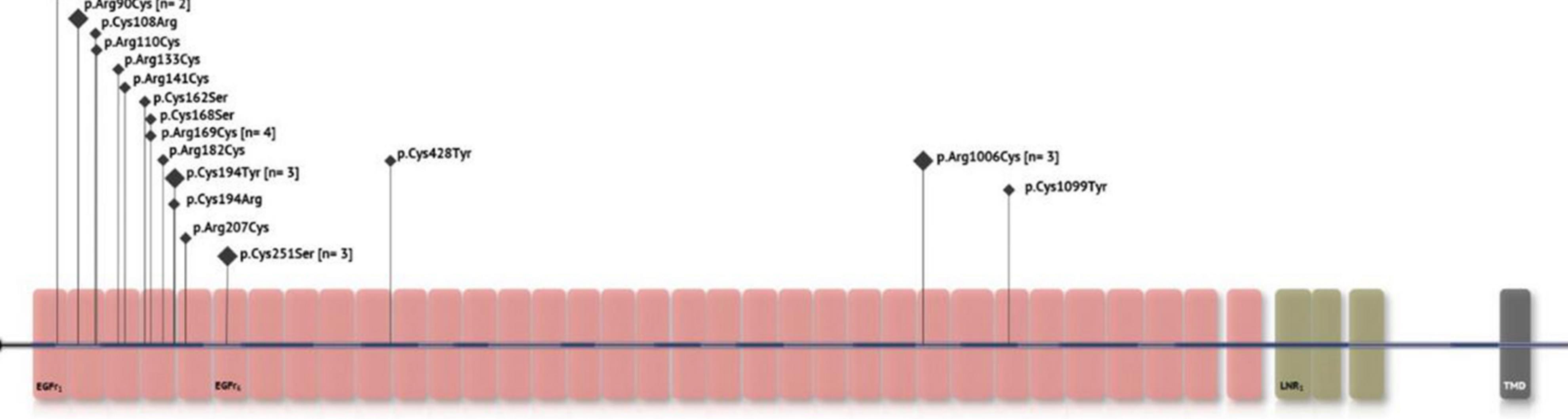


## RESULTS

Preliminary data from 90 patients, Figure 2, (50% female) show a mean age of  $43.8 \pm 11.9$  years, with 91.6% reporting a family history (Table 1). Main clinical presentations were cerebrovascular events (72.9%), migraine (69%), and cognitive impairment (56.7%). Common comorbidities included hypertension (64%) and dyslipidemia (55%).

Among 86 confirmed cases, 63 were diagnosed via genetic testing and 20 via skin biopsy. All showed cysteine-altering NOTCH3 mutations, mainly in epidermal growth factor-like repeats (Figure 3). In 33 patients assessed with MMSE, the median score was 28 (IQR: 22–29).

Fig.3



NOTCH3 variants found, using transcript NM\_000435.3 as a reference.  
EGFr<sub>1-34</sub>:epidermal growth factor-like repeat domains- LNR: lin12/notch repeat domains- TMD: transmembrane domain

## NOTCH3 variants

## CONCLUSION

CADASILAr is the first systematic effort to study this disease in Latin America and the twelfth global CADASIL registry. By integrating baseline and longitudinal data, it offers a robust platform to investigate genetic, neuroimaging, and cognitive outcomes while fostering international collaborations to advance research and understanding of CADASIL.

## TAKE-HOME MESSAGES

- CADASIL is underdiagnosed in Argentina.
- Geographic variability likely reflects a center effect rather than true prevalence.
- A harmonized national cohort with clinical, imaging, and genetic data was created.
- All confirmed cases showed cysteine-altering NOTCH3 mutations in EGF-like domains, reinforcing their pathogenic role.

## CONTACT

Carolina Agata  
Ardohain  
Cristalli MD

To learn more about this research or for further discussion, please contact me at caroardoahain@gmail.com

