

Investigating Lack Of Adherence To Medications Used For Primary Or Secondary Stroke Prevention In Rural Ecuador: Rationale And Protocol Of A Population-Based Study

Investigación de la Falta de Adherencia a Medicamentos Utilizados para la Prevención Primaria y Secundaria de Ictus en Zonas Rurales del Ecuador: Fundamentación y Protocolo de un Estudio Poblacional

Oscar H. Del Brutto, MD,^{1,2} Emilio E. Arias, MD,² Denisse A. Rumbela, MHA,² and Robertino M. Mera, MD, PhD³

Abstract

Background: Stroke is an emerging public health crisis in Latin America, particularly in rural areas of low- and middle-income countries (LMIC), where limited healthcare access exacerbates disease burden. Medication adherence plays a fundamental role in stroke prevention, yet information on this topic remains insufficiently known due to issues related to socioeconomic, educational, and infrastructural barriers.

Aims: This study introduces a protocol designed to assess adherence to primary and secondary stroke prevention medications in rural Ecuador. By identifying behavioral patterns and underlying barriers, this research aims to provide evidence-based recommendations for improving adherence and informing public health interventions.

Methods: The study will be conducted in Atahualpa, Ecuador, using a population-based design with an initial cross-sectional assessment followed by a 10-year longitudinal follow-up. Medication adherence will be evaluated through validated questionnaires, clinical examinations, and annual updates on vascular risk factors and social determinants of health. Statistical analyses will assess the relationship between adherence levels, demographic variables, and cerebrovascular outcomes.

Comment: This research provides essential insights into adherence behaviors in underserved populations, offering a foundation for targeted interventions. Findings will support healthcare accessibility, strengthen patient education, and improve adherence strategies to reduce stroke incidence and improve health outcomes in rural LMIC settings.

Keywords: Medication adherence, stroke, prevention, population study, rural settings, Ecuador.

Resumen

Antecedentes: El ictus representa una creciente crisis de salud pública en América Latina, especialmente en las zonas rurales de los países de ingresos bajos y medianos, donde el acceso limitado a la atención médica agrava la carga de la enfermedad. La adherencia a la medicación desempeña un papel fundamental en la prevención de ictus, pero la información sobre este tema sigue siendo insuficiente debido a barreras socioeconómicas, educativas y de infraestructura.

Objetivos: Este estudio presenta un protocolo diseñado para evaluar la adherencia a medicamentos de prevención primaria y secundaria de ictus en zonas rurales de Ecuador. Al identificar patrones de comportamiento y barreras subyacentes, esta investigación busca proporcionar recomendaciones basadas en evidencia para mejorar la adherencia e informar intervenciones en salud pública.

Métodos: El estudio se llevará a cabo en Atahualpa, Ecuador, utilizando un diseño poblacional con una evaluación transversal inicial seguida de un seguimiento longitudinal de 10 años. La adherencia a la medicación se evaluará mediante cuestionarios validados, exámenes clínicos y actualizaciones anuales sobre factores de riesgo vascular y determinantes sociales de salud. Se utilizarán análisis estadísticos para evaluar la relación entre los niveles de adherencia, variables demográficas y los resultados cerebrovasculares.

Comentario: Esta investigación ofrece conocimientos esenciales sobre los comportamientos de adherencia en poblaciones desatendidas, brindando una base para intervenciones específicas. Los hallazgos apoyarán la accesibilidad a la atención médica, reforzarán la educación del paciente y mejorarán las estrategias de adherencia para reducir la incidencia de ictus y mejorar los resultados de salud en entornos rurales de países en desarrollo.

Palabras clave: Adherencia a medicación, enfermedad cerebrovascular, prevención, estudio poblacional, ambientes rurales, Ecuador.

Rev. Ecuat. Neurol. Vol. 34, N° 1, 2025

¹School of Medicine and

²Research Center, Universidad Espíritu Santo – Ecuador, Samborondón, Ecuador;

³BioStatistics/Epidemiology, Freenome, Inc., South San Francisco, CA, USA.

Correspondence:

Oscar H. Del Brutto, MD.

Urbanización Toscana, Apt 3H, Km 4.5 vía Puntilla-Samborondón, 092301, Samborondón – Ecuador.

E-mail: oscardelbrutto@hotmail.com

Introduction

According to the Pan American Health Organization, non-communicable diseases – including stroke – will be the next epidemics affecting several Latin American countries.¹ This situation is complicated by the phenomenon called “epidemiologic transition”, in which the population slowly shifts from an age dominated by infections and famine to a more developed stage characterized by increased life expectancy and a rise in man-made diseases, such as stroke.²

Over the past two decades there has been an increased burden of stroke in rural areas of low- and middle-income countries (LMIC).³⁻⁵ Additionally, limited resources hinder the early recognition of key markers of cerebrovascular diseases in apparently healthy individuals at risk, allowing these conditions to progress undetected until irreversible brain damage has already occurred.⁶ Even in individuals who receive an early diagnosis, intervention options are complicated by limited access to healthcare facilities, financial constraints, and cultural beliefs that influence their perceptions of long-term medication usage.

Medication adherence is a critical component of effective disease prevention, management, and overall public health.⁷ However, in rural and underserved communities, adherence rates tend to be alarmingly low due to a combination of socioeconomic, educational, and infrastructural challenges.⁸⁻¹⁰ In Ecuador, as well as in many other LMIC, rural populations often face the aforementioned barriers. Understanding these obstacles is essential for developing strategies that improve medication adherence and, ultimately, reduce adverse outcomes among persons at risk or to those already diagnosed with cerebrovascular disease.

Here, we aim to present a protocol designed to assess and to better understand the factors contributing to poor adherence to medications used for primary or secondary prevention of cerebrovascular diseases in rural Ecuadorian villages, providing valuable information that can guide public health authorities in addressing this issue. By investigating the underlying causes and identifying patterns in adherence behavior, this research will offer evidence-based insights to support intervention programs tailored to the needs of underserved populations.

Methods

Study Population

The present study will be conducted in Atahualpa, a rural village of about 3,500 inhabitants located in Coastal Ecuador (2°18'S, 80°46'W). The climate is hot and dry, with 12 daily hours of sunlight year-round. The population is ethnically homogeneous, they have a short stature (mean height in the adult population: 150.3±8.7 cm), brown eyes and hair, an olive-moderate skin color (Type IV in the Fitzpatrick skin type scale), and a predominantly elliptical hard palate. These phenotypic characteristics strongly sug-

gest an Amerindian ancestry, with little evidence of cross-breeding.¹¹ In addition, a recent study confirmed the genetic ancestry of these people, which are 94.1% Amerindians.¹²

Inhabitants are homogeneous regarding lifestyles (almost all men work as artisan carpenters and most women are homemakers). The diet of villagers is traditionally rich in oily fish and carbohydrates but poor in other types of meat and dairy products as well as in highly processed foods. The villages have electricity but several houses do not have pipe water, and most streets are not paved. Inhabitants mobilize within the villages mainly by walking or bicycle riding, as only a few own a motor vehicle. Atahualpa has only one health center administered by the Ministry of Health, and there is a small hospital from the Ecuadorian Institute of Social Security located about 10 miles away in a small city (Ancón). There are no other medical centers – either public or private – in the village. In general, socio-economic levels are low but the population is not indigent, as nearly 90% of men earn at least the minimum wage. The low migration rate of residents together with the high adherence shown in previous studies conducted by our group, provide optimal grounds for carrying out prospective cohort studies.¹³

Background data

The Atahualpa Project was established in 2012 as an observational, population-based, prospective cohort study, designed to identify the prevalence and incidence of several non-communicable neurological and cardiovascular diseases, and to reduce their increasing burden in rural Ecuador.¹⁴ As per protocol, all Atahualpa residents aged ≥40 years were identified through annual door-to-door surveys, and were then invited to participate after they signed a comprehensive informed consent. During the study years, several conditions of interest have been investigated in these people through both cross-sectional and longitudinal studies.¹⁵ These included – but were not limited to – cardiovascular health, stroke, myocardial infarction, sleep disorders, cognitive function, neuroimaging markers of cerebral small vessel disease and systemic atherosclerosis.

Study Design

This population-based study will include an initial cross-sectional phase, followed by a prospective longitudinal follow-up. In the first phase, the primary aim will be to determine adherence to medications prescribed for primary or secondary stroke prevention. In addition, medical records of the Atahualpa Project will be reviewed to determine participants who have a history of an overt stroke or any vascular event at the time of enrollment. For this, we will not only use data from clinical interviews, but from complementary exams such as a brain MRI, head CT, MRA of intracranial and cervical arteries, transthoracic echocardiograms, carotid Doppler, 12-lead electrocardiogram,

ankle-brachial index determination, and other pertinent exams previously described by our group.¹⁶ Additionally, reasons for both poor and good adherence to medications, as well as their correlation with previous vascular events, will be recorded.

During the second phase, which is expected to last for 10 years, participants who remain in the study will be surveyed annually with the same questionnaire to update medication adherence and to investigate factors related to worse or better adherence over time. Our field personnel will be in frequent contact with the study population to determine whether they develop any new vascular event. Suspected individuals will be evaluated by a certified neurologist and those who have any condition of interest will undergo neuroimaging exams and other tests to confirm the diagnosis.

Participants who declined consent or emigrated will be censored at the date of the last survey where they were interviewed, and those who died will be censored at the date of death. All these individuals will count for the total years of follow-up. Incident strokes or the presence of any other vascular events will be recorded, and the association of these events with changes in medication adherence will be analyzed. These events will not constitute a reason to be censored before the end of the study.

Ethics considerations

The study is supported by an unrestricted academic grant from Universidad Espiritu Santo – Ecuador. The Sponsor has no role in the design of the study, nor in the collection, analysis, and interpretation of data. Informed consent forms, filled questionnaires, and complementary exams will be securely stored at the Community Center of the Atahualpa Project and safeguarded in accordance with the Health Insurance Portability and Accountability Act (HIPPA) (<https://www.hhs.gov/sites/default/files/privacysummary.pdf>). Research will be conducted following the ethical principles of the Declaration of Helsinki. The Independent Review Board of Hospital Clínica Kennedy, Guayaquil, Ecuador (FWA: 00030727), approved the study design and the informed consent form that must be signed by all individuals or proxies (in case of disability) before enrollment. The Atahualpa Project has been registered at ClinicalTrials.gov, and the unique identifier number is NCT01627600.

Field instrument to assess medication adherence: Before the start of this study, members of the Steering Committee of the Atahualpa Project met to discuss the best possible field instrument to be used for assessing medication adherence in the study population. Essentially, we took into account questionnaires previously constructed in the Spanish language, departing from the systematic review of this topic published by Intilangelo and co-workers,¹⁷ as well as others that take into account questions about medi-

Table 1. Open questions included in the field instrument to assess medication adherence used in this study (Spanish version with English translation).

1. ¿Vive solo? (Do you live alone?)
2. ¿Dónde recibe su atención médica regular? (Where do you receive your regular medical care?)
3. ¿Necesita estar acompañado en sus citas médicas? (Do you need to be accompanied to your medical appointments?)
4. ¿Dónde obtiene sus medicamentos? (Where do you get your medications?)
5. ¿Cuánto le cuestan a usted los medicamentos prescritos? (How much do prescribed medications cost you?)
6. ¿Dónde obtiene sus medicamentos si no están disponibles en su proveedor regular? (Where do you get your medications if they are not available from your regular provider?)
7. ¿Cuántos medicamentos toma de forma regular? (How many medications do you take regularly?)
8. ¿Qué medicamentos toma de forma regular? (What medications do you take regularly?)
9. ¿Qué enfermedades le ha diagnosticado su médico? (What illnesses have been diagnosed by your doctor?)
10. ¿Cuántas veces ha cambiado o aumentado su medicación o tratamiento? (How many times has your medication or treatment changed or increased?)
11. ¿Cuántas tomas realiza en el día? (How many doses do you take per day?)
12. ¿Debe cumplir alguna condición o restricción mientras toma medicamentos? (Do your medications need any specific storage conditions?)
13. ¿Sus medicamentos deben cumplir algún requisito para almacenarlos? (Do you know the side effects of your medications?)
14. ¿Conoce los efectos secundarios de sus medicamentos? (Do you know the side effects of your medications?)
15. ¿Algún médico le han dicho que tuvo un infarto del corazón, ataque al corazón o insuficiencia cardiaca? (Has any doctor told you that you had a heart attack or heart failure?)
16. ¿Toma algún medicamento que su médico indicara para prevenir infarto de corazón? (Do you take any medication that your doctor prescribed to prevent a heart attack?)
17. ¿Inició este tratamiento antes o después del diagnóstico de infarto del corazón? (Did you start this treatment before or after the heart attack diagnosis?)
18. ¿Algún médico le ha dicho que tuvo un ictus? (Has any doctor told you that you had a stroke?)
19. ¿Recibe tratamiento con aspirina, anticoagulantes o algún medicamento que su médico indicara para prevenir un stroke? (Do you receive treatment with aspirin, anticoagulants, or any medication your doctor prescribed to prevent a stroke?)
20. ¿Inició el tratamiento antes o después del diagnóstico de ictus? (Did you start the treatment before or after the stroke diagnosis?)

cation adherence that can be of practical use in developing or underserved regions.^{18,19} Then, questions were adapted to colloquial terms understandable for the study population. This comprehensive wording came from the investigators' experiences after 13 years of continuously working with these people. The final instrument resulted from thoughtful discussion and consensus of the Steering Committee members and included two sections, one consisting

of 20 open questions, and the other of 17 structured questions on a Likert scale categorized from 1 to 4 points.

The selected questionnaire will be used to collect data on medication adherence behaviors, barriers to consistent medication use, and perceptions surrounding health-care accessibility. Overall, the questionnaire includes self-reported adherence levels (frequency of missed doses, reasons for non-adherence), economic and logistical barriers (cost-related challenges, availability of pharmacies), health literacy and awareness (understanding of prescribed treatments, trust in medical recommendations), and social and cultural influences (family expectations, traditional medicine beliefs).

Tables 1 and 2 display these open and structured questions in their Spanish version together with their English versions, which were translated and back-translated by bilingual members of our group. Data will be collected through face-to-face interviews, ensuring responses are accurately recorded and allowing for clarifications where necessary. Disabled participants will be interviewed throughout their proxies or guardians. Trained local researchers or health workers will facilitate the administration of the questionnaire to enhance participants' comfort and comprehension. Before its use, the questionnaire was validated in 50 randomly selected eligible candidates who will be part of this study.

Table 2. Likert questionnaire to assess medication adherence (Spanish version with English translation).

Pregunta	Question	Completamente de acuerdo (Totally agree)	De acuerdo (Agree)	En desacuerdo (Disagree)	Completamente en desacuerdo (Totally disagree)
1	Entiendo lo que mi médico me explicó sobre mi medicamento y tratamiento				
2	Puedo mencionar los nombres de mis medicamentos y su propósito con facilidad				
3	Confío en mi médico y acepté los tratamientos que me recetó				
4	Mis medicamentos solo me ayudan si cumplo completamente las indicaciones de mi médico				
5	Los medicamentos son tóxicos y debo evitar tomarlos				
6	Me siento sano y dudo si debo realmente tomar los medicamentos que me fueron indicados				
7	Tomo mis medicamentos en horas fijas o junto a actividades fijas durante el día				
8	Pagar por mis medicamentos impide que los tome				
9	Me incomoda que las personas que conozco perciban que recibo medicamentos				
10	Para mí, los olvidos son un problema frecuente todos los días				
11	Me siento mal o deprimido con frecuencia				
12	Tengo problemas para cumplir la toma de mis medicamentos o con las condiciones que debo cumplir				
13	Tengo que atravesar dificultades para recibir atención médica				
14	Necesito ayuda para realizar mis actividades diarias y en la toma de mis medicamentos y no la recibo				
15	Me asustan los efectos adversos de mis medicamentos				
16	Si noto efectos adversos de mis medicamentos, los discuto con mi médico lo más pronto posible				
17	Si usted nota efectos adversos de mis medicamentos, disminuiría su toma o la detendría por completo				

Punctuation: Questions 1,2,3,4,7,16: scores from 1 to 4; Questions 5,6,8,9,10,11,12,13,14,15,17: scores from 4 a 1
The higher the score, the greatest the risk of non-adherence

This process used the Cronbach's alpha formula, and questions with a score ≥ 0.7 were selected. Then, a different sample of 50 potential participants was used to determine the consistency of the questions.

Clinical covariates

Demographic variables such as age and gender, as well as levels of education, presence of symptoms of depression, social risk, and traditional cardiovascular risk factors will be recorded at baseline and updated during each annual survey to analyze potential correlations with medication adherence rates over time. Demographic data and levels of education will be assessed by self-report, symptoms of depression through the depression axis of the Depression-Anxiety Scale-21 (DASS-21), and social risk using the social determinants of health included in the Gijon's Social Familial Evaluation Scale (SFES). The latter is a validated field instrument, originally constructed in the Spanish language, that evaluates five components of risk situations and social challenges, including family situation, economic status, housing, social relationships and support networks.²⁰ The Gijon SFES was selected due to its applicability to the living conditions of the study population and because it has been officially endorsed by the Ecuadorian Ministry of Health.²¹ Each of the five components of the Gijon Scale consists of five questions weighted on a 1 to 5 scale, with a maximum possible score of 25, with higher scores indicating higher social risk. Finally, cardiovascular risk factors will be investigated by the use of the Life's Simple 7 construct of the American Health Association.²² This construct is well-balanced, and considers both health behaviors and health factors, and the designated cut-offs for each metric (smoking status, central obesity, diet, physical activity, blood pressure, diabetes, and hyperlipidemia) were established after experts' consensus. We decided not to use the most recent construct of the AHA – the Life's Essential 8 – to assess cardiovascular risk factors,²³ because comparative studies have demonstrated that its efficacy is similar to that of the Life's Simple 7, with a higher degree of complexity that may complicate assessment of cardiovascular risk factors in remote settings.²⁴

Statistical analysis

Data analysis will be carried out using STATA version 18 (College Station, TX, USA). Continuous variables will be reported as means and standard deviations (or medians and interquartile ranges, depending on distribution), while categorical variables will be presented as absolute frequencies and percentages. Medication adherence will be used as the dependent variable, and the diverse factors potentially modifying this adherence (alone or in combination) will be treated as exposures, after adjustment for covariables of interest.

In unadjusted analyses, continuous variables will be compared using linear models and categorical variables

by using the chi-square or Fisher exact test, as appropriate. Unadjusted and multivariate logistic or generalized linear models, and parametric regressions will be fitted for cross-sectional analysis, and Poisson regressions or mixed-effects regression models will be used for longitudinal assessments on how adherence evolve over time and its association with incident vascular events. Longitudinal changes in adherence will be analyzed using generalized estimating equations to account for repeated measurements. By integrating these statistical approaches, the study will provide a comprehensive understanding of the barriers to medication adherence and offer targeted insights for public health intervention.

Comment

Poor adherence to stroke prevention medications significantly increases the risk of primary and recurrent strokes, leading to higher rates of disability, cognitive decline, and mortality.^{25,26} Inadequate medication use may also reduce the effectiveness of other primary prevention strategies, exacerbating the overall burden of cerebrovascular diseases in these communities. Addressing adherence issues is essential not only for reducing individual health risks but also for alleviating the broader socioeconomic impact of stroke-related complications on families and healthcare systems.²⁷

This study aims to present a protocol designed to assess the factors contributing to poor adherence to medications used for primary or secondary prevention of cerebrovascular diseases in rural Ecuadorian villages. The findings will provide valuable data that can guide public health authorities in addressing this issue. By investigating the underlying causes and identifying patterns in adherence behavior, this research will offer evidence-based insights to support intervention programs tailored to the needs of underserved populations.

The findings of this study will shed light on the challenges faced by rural Ecuadorian communities regarding medication adherence. This research can be instrumental in informing public health policies and developing targeted interventions that bridge healthcare gaps. By making public health authorities aware of this pressing issue, they will have the necessary data to improve healthcare accessibility, enhance patient education, and implement support systems that encourage sustained medication adherence. Ultimately, the goal is to strengthen healthcare outcomes for underserved populations and reduce the preventable consequences of non-adherence.

References

1. Legetic B, Campbell N. Reducing salt intake in the Americas: Pan American Health Organization actions. *J Health Commun* 2011;16(Suppl 2):37-48. Aug. <https://doi.org/10.1080/10810730.2011.601227>

2. Omran AR. The epidemiologic transition: a theory of the epidemiology of population change. *The Milbank Memorial Fund Quarterly* 1971;49(4):509-38. Oct. <http://www.doi.org/10.1111/j.1468-0009.2005.00398.x>
3. Rangamani S, Huliyaappa D, Kulothungan V, Saravanan S, Nurugan PK, Mahadevan R, et al. Stroke incidence, mortality, subtypes in rural and urban populations in five geographic areas of India (2018-2019): results from the National Stroke Registry Programme. *Lancet Reg Health Southeast Asia* 2023;23:100308. Oct 28. <https://doi.org/10.1016/j.lansea.2023.100308>
4. Tian X, Liu J, Yu C, Hou Y, Zhan C, Lin Q, et al. Long-term trends in Stroke management and burden among low-income women in a rural areas from China (1992-2019): a prospective population-based study. *Front Neurol* 2021;12:720962. Oct 22. <https://doi.org/10.3389/fneur.2021.720962>
5. Lavados PM, Hennis AJM, Fernandes JG, Medina MT, Legetic B, Hoppe A, et al. Stroke epidemiology, prevention, and management strategies at a regional level: Latin America and the Caribbean. *Lancet Neurol* 2007;6(4):362-72. Apr. [https://doi.org/10.1016/s1474-4422\(07\)70003-0](https://doi.org/10.1016/s1474-4422(07)70003-0)
6. Del Brutto OH, Mera RM, Costa AF, Zambrano M, Viteri EM, Nader JA, et al. Búsqueda de sustitutos de neuroimagen con propósitos de investigación: experiencia del Proyecto Atahualpa. *Rev Ecuat Neurol* 2017;26(2):128-34.
7. Njohjam MN, Falone NT, Ngoule MO. Barriers to medication adherence for secondary stroke prevention in rural communities in Cameroon: a qualitative study. *BMC Prim Care*. 2025;26(1):125. Apr 24. <https://doi.org/10.1186/s12875-025-02842-w>
8. Joseph P, Avezum A, Ramasundrathettige C, Mony PK, Yusuf R, Kazmi K, et al. Secondary prevention medications in 17 countries grouped by income level (PURE): a prospective cohort study. *J Am Coll Cardiol* 2025;85(5):436-47. Feb 11. <https://doi.org/10.1016/j.jacc.2024.10.121>
9. Archila Criollo DH, Aguilera JD, Cano Vaca LY, Galindo Fonseca NL, Martínez YV. Factores que influyen en la baja adherencia a los tratamientos médicos en pacientes con patologías crónicas y comorbilidades en Boyacá, según evidencia proporcionada en estudios investigativos y artículos médicos publicados entre 2015 y 2024. Universidad Nacional Abierta y a Distancia (UNAD). 2024. <https://repository.unad.edu.co/bitstream/handle/10596/63059/nlgalindof.pdf?sequence=1> (downloaded May 29, 2025).
10. García-Valle S. Factores de riesgo de no adherencia al tratamiento en pacientes mayores de un núcleo rural. *OFIL-ILAPHAR* 2020;30(2):115-20.
11. Castillo PR, Mera RM, Zambrano M, Del Brutto OH. Population-based study of facial morphology and excessive daytime somnolence. *Pathophysiology* 2014;21(4):289-92. Nov. <https://doi.org/10.1016/j.pathophys.2014.06.001>
12. Brandt CYC, Del Brutto OH, Nielsen R. Signatures of natural selection may indicate a genetic basis for the beneficial effects of oily fish intake in indigenous people from coastal Ecuador. *G3 (Bethesda)* 2025;15(4):jkaf014. Apr 17. <https://doi.org/10.1093/g3journal/jkaf014>
13. Del Brutto OH, Castillo PR, Sedler MJ, Del Brutto OH, Zambrano M, Mera RM, et al. Reasons for declining consent in a population-based cohort Study conducted in a rural South American community. *J Environ Public Health* 2018;2018:8267948. Nov 26. <https://doi.org/10.1155/2018/8267948>
14. Del Brutto OH, Peñaherrera E, Ochoa E, Santamaría M, Zambrano M, Del Brutto VJ. Door-to-door survey of cardiovascular health, stroke, and ischemic heart disease in rural coastal Ecuador—The Atahualpa Project: methodology and operational definitions. *Int J Stroke* 2014;9(3):367-71. Apr. <https://doi.org/10.1111/ijvs.12030>
15. Del Brutto OH, Mera RM, Castillo PR, Del Brutto VJ. Key findings from the Atahualpa Project: what should we learn? *Expert Rev Neurother* 2018;18(1):5-8. Jan. <https://doi.org/10.1080/14737175.2018.1400382>
16. Del Brutto OH, Del Brutto VJ, Zambrano M, Lam J. Enfermedad cerebrovascular en Atahualpa: prevalencia e incidencia. *Rev Ecuat Neurol* 2017;26(2):158-63.
17. Intilangelo A, Majic S, Palchik V, Traverso ML. Cuestionarios validados de adherencia a la medicación y factores asociados en pacientes crónicos: revisión sistemática. *Farmacia Hospitalaria* 2024;48(6):185-92. <http://www.doi.org/10.1016/j.farma.2024.01.001>
18. Chan AHY, Cooper V, Lycett H, Horne R. Practical barriers to medication adherence: what do current self- or observed-reported instruments assess? *Front Pharmacol* 2020;11:572. May 13. <https://doi.org/10.3389/fphar.2020.00572>
19. Muller S, Kohlmann T, Wilke T. Validation of the adherence barriers questionnaire – an instrument for identified potential risk factors associated with medication-related non-adherence. *MBC Health Serv Res* 2015;15:153. Apr 10. <https://doi.org/10.1186/s12913-015-0809-0>
20. García González JV, Díaz Palacios E, Salamea García A, Cabrera González D, Menéndez Caicoya A, Fernández Sánchez A, et al. Evaluación de la fiabilidad y validez de una escala de valoración social en el adulto. *Aten Primaria* 1999;23(7):434-40. Apr 20.
21. Ministerio de Salud Pública del Ecuador. Guías clínicas geronto-geriátricas de atención primaria de salud para el adulto mayor. Ministerio de Salud Pública del Ecuador (MSP). Quito, Ecuador, septiembre 2008. <https://vicenteayalabermeo.files.wordpress.com/2011/04/guc3adas-adulto-mayor.pdf> (downloaded May 29, 2025).

22. Lloyd-Jones D, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, et al. Defining and setting national goals for cardiovascular health promotion. The American Heart Association's strategic impact goal through 2020 and beyond. *Circulation* 2010;121(4):586-613. Feb 2. <https://doi.org/10.1161/CIRCULATIONAHA.109.192703>
23. Lloyd-Jones DM, Allen NB, Anderson CAM, Black T, Brewer LC, Foraker RE, et al. Life's Essential 8: Updating and enhancing the American Heart Association's construct of cardiovascular health: a presidential advisory from the American Heart Association. *Circulation* 2022;146(5):e18-e43. Aug 2. <https://doi.org/10.1161/CIR.0000000000001078>
24. Howard G, Cushman M, Blair J, Wilson NR, Yuan Y, Safford MS, et al. Comparative discrimination of Life's Simple 7 and Life's Essential 8 to stratify cardiovascular risk; is the added complexity worth it? *Circulation* 2024;149(12):905-13. Mar 19. <https://doi.org/10.1161/circulationaha.123.065472>
25. Bbau V, Sylaja PN, Soman B, Varma RP, Ms M, GI G, et al. A randomized controlled trial of medication adherence and management of risk factors for secondary prevention of stroke (MaMoRS) using a smart-phone-based population. *Int J Stroke* 2024;19(6):654-64. Jul. <https://doi.org/10.1177/17474930241245612>
26. Kohlhase K, Schafer JH, Tako LM, Willems LM, Hat-tigen E, Bohmann FO, et al. Large-vessel-occlusion in patients with previous ischemic stroke: an analysis of adherence to secondary preventive medication for different etiologies. *Neurol Res Pract* 2013;5(1):22. May 25. <https://doi.org/10.1186/s42466-023-00247-7>
27. Dalli LL, Olaiya MT, Kim J, Andrew NE, Cadillac D, Lindley R, et al. Antihypertensive medication adherence and risk of vascular events and falls after stroke: a real-world effectiveness study using linked registry data. *Hypertension* 2023;80(1):182-91. <https://doi.org/10.1161/hypertensionaha.122.19883>

Funding: Universidad Espíritu Santo – Ecuador.