

Cost-effectiveness of improving access to treatments for acute ischemic stroke in Peru

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Abstract

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Objective: In Peru, access to timely, high-quality acute ischemic stroke (AIS) care is severely limited. This study estimated the cost-effectiveness of strategies to improve uptake of treatments for AIS.

Methods: We developed a state-transition model of AIS and its sequelae and parameterized the baseline model using insurance system data, GBD estimates, and studies of stroke epidemiology and costs. Interventions were analyzed through their effects on the AIS “cascade of care”: 1) overall access to emergency departments, 2) access to hospitals capable of treating acute stroke, 3) presentation within 3 hours of symptom onset, 4) and appropriate use of thrombolytics.

Scenario 1 looked at certifying hospitals to become basic stroke care centers that could provide thrombolytics to persons currently seeking care. Scenario 2 built on scenario 1 by adding an evidence-based mass media campaign to increase care-seeking for acute stroke. Both scenarios incorporated the impact of expanded access to post-stroke care (e.g., rehabilitation and secondary

prevention) following on expanded access to treatment. We took a 20-year time horizon and used a 3% discount rate.

Results: Scenario 1 would improve timely access to thrombolytics from 2.3% of AIS to 5.7%; it would reduce stroke mortality by 0.47% and disability by 1.5%, averting 5 deaths among the current cohort of 55-year-old Peruvians (approximately 290,000 individuals). The scenario would cost an additional \$1270 per disability-adjusted life-year (DALY) averted. Scenario 2 would improve timely access to thrombolytics from 2.3% to 11.8%; would reduce stroke mortality by 4.2% and disability by 3.8%, averting 46 deaths in the same cohort. The scenario would cost an additional \$2,672 per DALY averted. Cost-effectiveness ratios for both scenarios are below Peru's 2023 GDP per capita (\$7900), so they are likely to be cost-effective.

Conclusion: Enhanced investment in acute ischemic stroke care is cost-effective and can reduce stroke-related mortality in Peru.

Introduction

Background

Stroke is one of the main causes of mortality and disability worldwide, and its burden continues to increase each year (1). In low and middle income countries, younger populations are being increasingly affected by stroke, which may be related to insufficient access to medical care (2).

The situation in Peru reflects a similar context, where, in addition to having an age-standardized incidence of 98.8 per 100,000 person-years, there is still great disparity in services throughout the country, especially between rural and urban areas (3,4). This number becomes much more problematic in the group over 65 years, where at-risk patients have an incidence of 372 per 100,000 person-years (3).

The Peruvian health system is classified into the Public sector, which includes the Ministry of Health, Essalud, and the Armed Forces; and the Private sector (5). The public sector has the comprehensive health insurance (SIS), which allows health insurance for all Peruvians within the Framework of Universal Health Insurance, through a subsidized and semi-contributory system (6).

Despite having interventions that have already demonstrated a reduction in the burden of stroke worldwide (7,8), most are inaccessible through the Peruvian national health system in all regions equally (9). For example, inadequate access or lack of access to intravenous alteplase (IV-tpa); poor quality of transport from the stroke site to the hospital system; insufficient infrastructure or medication supply are the main barriers to better service coverage (9). At the same time, for mechanical thrombectomy, the cost is 3.1 times higher than medical treatment and is not offered under national insurance, unlike the rest of Latin America (10).

Both the Peruvian state and the Ministry of Health need approval from the Ministry of Economy and Finance for budget allocation to strengthen or create any intervention supported by public investment (11). It is for this reason that the focus of this study will prioritize costs from the health system perspective, which will be identified in the literature of previously locally worked interventions, or failing that, information will be reconstructed (12). The local data from national sources will be used to allow us to have a more accurate measurement of the number of people insured by SIS and the absolute number of those treated in different centers for specific causes during a one-year period (13).

Finally, this study will allow policymakers to understand and demonstrate more clearly the impact of strengthening strategies in the treatment of acute stroke to reduce the disease burden and its repercussions in Peru.

Objectives

The main objective of this study was to determine the necessary economical resources to amplify the coverage in interventions related to the management of acute ischemic stroke in Peru.

The specific objectives of this study are:

- Identify the existing gaps between healthcare services and healthcare access on the treatment of acute ischemic cerebrovascular disease in Peru.
- To estimate the costs needed to achieve an increment of the coverage in the treatment of acute ischemic cerebrovascular disease.

- To estimate the reduction in disability and mortality rates through the increase in coverage of the treatment of acute ischemic cerebrovascular disease.

Methods

Health economics plan

A comprehensive health economics plan was developed for this study and was framed in the thesis protocol. It described the planification of the state transition model, the outcomes that were going to be measured (DALYs) and Deaths by cause averted, and the sensitivity analysis. It is available in the university's Canvas repository as part of the thesis documentation. For the final analysis the time horizon was expanded from 10 years to 20 years to better capture the long-term benefits and costs from the interventions.

Study Population

The study population includes the people insured under the Peruvian national insurance system (Seguro Integral de Salud- SIS). And the simulation cohort of people starts at 55 years old and is followed for 20 years. The age threshold was selected from the epidemiological risk in the Peruvian population of developing a stroke event compared to the rest of the population as mentioned in Lazo et al (3). Even though socioeconomic information from this population wasn't directly included in the model, the SIS predominantly supports low and middle-income Peruvian residents across the country.

Setting and location

The study was set in the Peruvian healthcare system under the program of the national health insurance financed by the ministry of health (SIS). This study does not include either the workers' insurance of ESSALUD, the Army/Air force/Police insurance and the Private sector. Also, to understand the impact on the Peruvian population, the results were calibrated with the Peruvian demographic distribution.

Comparators

The main comparators were three different scenarios of healthcare access after an acute ischemic stroke event in Peru.

Baseline Scenario

The baseline scenario described the current healthcare access context in Peru (Figure 2). Including not only access to healthcare as the main bottleneck but also, accessing the healthcare center with the appropriate resources for the management of an acute ischemic stroke event. The following node included the probability of arriving on time to those hospitals, where accessing the treatment with alteplase was the last step in the cascade.

Scenario 1

For scenario 1, the intervention used to improve access to treatment was implementing the stroke protocol following the example of Target: Stroke from the American Heart Association (14). This nationwide intervention included a series of internal education

sessions required for their accreditation as a stroke center and assured proper treatment and rehabilitation of patients during their hospitalization time. This intervention had a specific impact in the last node of receiving treatment with alteplase (Figure 3).

Scenario 2

For scenario 2, a mass media campaign of stroke awareness was added to the previous scenario (15). The changes in coverage were modified in two nodes, overall access to healthcare services and arriving on time for treatment. These interventions were chosen, since they target different bottlenecks in the whole pathway, allowing not only current patients to have a quality treatment but also allowing more people to benefit from it, in the adequate time-window (Figure 4).

Perspective

This study's perspective was from the healthcare system, in a setting where it is supported mostly by governmental funding. This perspective was appropriate considering the interventions that were included were a mass media stroke awareness campaign and a stroke certification of centers across the country. Both interventions affect different stages in the acute stroke care access continuum and include costs from not only the treatment in the emergency department and hospital stay but also secondary prevention after the event, and post-stroke rehabilitation. All these services encompass the overall pathway handled by the healthcare system.

Time horizon

The time horizon used started at 55 years and followed the same cohort for 20 years. As mentioned above, it incorporates the incremental epidemiological risk of developing a stroke event within the Peruvian population as reported in the population-based standardized incidence of stroke study by Lazo et al (3).

Being able to follow the same cohort for a period of time of 20 years allowed us to evidence not only the short term outcomes but also the impact of the long term ones.

Discount rate

An annual discount rate of 0.03 was applied to both costs and health benefits through the 20-year horizon of the model following international guidelines. Same as a half-cycle correction.

Selection of outcomes

The primary outcome measure was disability- adjusted life years (DALYs), which combine both years of life lost due to premature mortality (YLLs) and years lived with disability (YLDs) from both Acute ischemic stroke state and Post-Stroke State as described in the model. The report of DALYs was chosen to allow us to identify the beneficial effects of incrementing the coverage of thrombolysis, secondary prevention and rehabilitation between the Peruvian population through the increment in coverage of healthcare access. This increment in coverage of healthcare access

across the different scenarios was visualized after the impact of both a mass media stroke awareness campaign and the certification of basic stroke centers.

Measurement of outcomes

The disability weights derived from an acute ischemic stroke event in the acute and chronic phase were used from the Global Burden of Disease (GBD - 2021) (16). The YLLs were calculated by using the life-expectancy tables from Peru reported by the World Health Organization (17). And for the YLDs, their calculation was done by multiplying the incident cases per cycle to the weighted average disability weight of each state (Acute ischemic stroke state and Post-Stroke state).

Valuation of outcomes

For the calculation of the DALYs, the disability weights needed to pass through a calibration process. Those disability weights for each disability level within acute and chronic phases were weighed following the severity distribution of the study of De Havenon et al (18) and calibrated for the Peruvian population with the study of Abanto et al (19). On the other hand, no age-weight was given to the DALYs. Also, a sensitivity analysis was performed to evaluate uncertainty within these parameters.

Measurement of valuation and resources and costs

The costs were estimated by using a combination of national open source data, published literature and expert opinion. The costs for the acute ischemic stroke state came from the study of Dittrich et al (10), where a time-driven microcosting took place in a Peruvian hospital for all patients hospitalized after an acute ischemic stroke event. A weighted average unit cost was used for the specific acute state, which included infrastructure costs, labor costs, pharmacological agents received during the hospitalization period and imaging studies performed.

For the costs of the Post-stroke state, an average cost per year was calculated by using a combination of literature and expert opinion to estimate the annual cost of the coverage of pharmacological agents, consultations and rehabilitation sessions.

In the case of the intervention of the mass media campaign, costs were approximated by using the local prices of the both TV and radio national stations (20). For the certification of basic stroke centers, the costs were estimated following local expert opinion of the labor force and resources involved in each certification process.

Currency, price, date, and conversion

All costs are expressed in 2025 International Dollars (I\$). All the costs collected in the local currency (Peruvian Nuevos Soles S/.), passed a conversion process to I\$ to assure consistency on how costs were reported.

For a comparison with international scenarios, the conversion rates could be expressed as S/. 1 Nuevo Sol Peruano equals 0.27\$ US dollars in 2024.

Rationale and description of model

A model of states transitions (Figure 1) was developed including 5 transition states, where people could move from the well state to developing an acute ischemic stroke and moving forward to either a post-stroke state or dying from it; dying from other causes was also included. Once in the post-stroke state, patients could remain there, die from the disease or die from another cause.

The model was calibrated using coverage estimates from a cascade of treatment, which was elaborated to fit under the Peruvian context. This cascade of treatment included 4 stages or nodes throughout the whole pathway.

Three different cascades were developed according to the simulated scenario that was presented.

The first node described healthcare access in the context of whether people suffering an acute ischemic stroke event will arrive at an emergency department with the presumptive or definitive diagnosis of ischemic stroke in a year. The second node identifies whether patients are arriving at the right healthcare center (hospital) with the minimum resource requirements for accessing treatment. This node divides patients arriving at a hospital from patients arriving at a healthcare center.

In the third node, probabilities are divided over arriving on time or not arriving on time to a hospital with the resources for treating an ischemic acute stroke. The timeframe required for accessing treatment is within 4.5 hours after the stroke event; However, we are measuring it as arriving before 3 hours to give time for completing the protocol inside the hospital. And in the fourth node,

it is being divided over the probability of receiving acute treatment with alteplase from those patients arriving on time.

Analytics and assumptions

The estimates from the population are based on standardized incidence of ischemic stroke in Peru from GBD. These incidence values are calibrated by using the number of people insured in the public Peruvian insurance called “SIS” which account for an overall of 26,347,147 people insured until Dec 2024.

The first stage in this scenario was measured by using the Peruvian national ICD-10 national record of the discharge data of the emergency departments. In this registry, the codes utilized were both I63.9 (Unspecified Ischemic Stroke) and I64 (Unspecified either ischemic or hemorrhagic stroke), where the second code was triangulated with the prevalence of ischemic stroke vs hemorrhagic in Peru following the study of Abanto et al (19). In this study, 76.5% of strokes were ischemic and 23.5% hemorrhagic. Probability of obtaining access to medical attention was 0.488.

The second stage considered the probability of arriving at a hospital with the minimum resources for treating an acute ischemic stroke and arriving at a healthcare center. For this estimation, we used values from both codes I63 and I64, where the second one was triangulated with the distribution of both ischemic and hemorrhagic stroke (19). We assumed that hospitals over levels II-2 had resources needed to evaluate and treat patients with stroke. We triangulated data of the patients arriving to the emergency care department by category, obtaining a probability of 0.847 of arriving at a hospital instead of a healthcare center.

For the third stage, we divided arriving on time vs not arriving on time using the study of Kawano-Castillo et al, where they reported that 29.8% of patients within 3 hours of the stroke event (21).

Finally, for the fourth stage, probabilities were calculated for accessing treatment with alteplase for acute treatment of ischemic stroke vs not receiving the treatment. The probabilities come from the study of Málaga et al, where they reported that 4.8% of patients with ischemic stroke arriving at the hospital received alteplase treatment (22). In this case, the probability was recalculated to fit the new denominator of patients arriving on time and not from all patients with the diagnosis of ischemic stroke, obtaining 0.1902.

Scenario 1

For the first scenario, transition probabilities were updated by recalculating effectiveness estimates after the cascade treatment probabilities were changed by the intervention we were measuring. Calibrations were done by using the equation mentioned in Watkins et al from the NCD 2030 Countdown (23) to estimate the modification in effectiveness estimates after applying the intervention of the certification of centers as stroke care centers following the Target Stroke Intervention in the US (14). The change in probability will affect the last box of the cascade, being the patients that receive alteplase treatment once they arrive during the required time frame to a hospital with appropriate resources. The changes in coverages were driven by the study of man et al, where they described that there was an increment from 10% to 15% in 2003 to 43% to 46% in

2021 of the percentage of patients receiving thrombolytics from all of the patients arriving during the desired timeframe (24).

Scenario 2

For scenario 2 the effect of a mass media campaign was added. The study of Advani et al (15) reported that after a mass media intervention (MMI) there was an increment of 95.7% in the number of suspected acute ischemic stroke events admitted to the emergency department. However, the annual effect increment was 41.02%. That is why probabilities were recalculated going from 0.20514 to 0.28929. At the same time, the effect will be visualized in the node of “Arriving on time”, where a study with a similar mass media intervention described that patients had an OR 2.18 for arrival within 3 hours (25). After its conversion into probabilities the overall incremental effect was set in 0.48.

Characterizing heterogeneity

For this current study, heterogeneity of subpopulations was not addressed. Future versions of this study will evaluate stratification by geographic variations and patients’ characteristics.

Characterizing distributional effects

Our study did not incorporate an evaluation of distributional effects. Both health outcomes and costs were not adjusted to consider a differential effect on priority populations.

Characterizing uncertainty

For evaluating uncertainty of parameters, both a one-way sensitivity analysis and a probabilistic sensitivity analysis were performed.

The one-way sensitivity analysis was performed by varying every parameter following the upper and lower limits, evaluating changes in the ICER estimates. The results were presented in two tornado diagrams, a tornado diagram for scenario 1 (Figure 5) and a tornado diagram for scenario 2 (Figure 6).

The probabilistic sensitivity analysis was done by using Monte Carlo simulations with 2000 iterations. Distributions were assigned to each parameter based on their characteristics.

Approach to engagement with patients and others affected by the study

All parameters were selected from published literature and expert clinical opinion. The study didn't include a formal patient engagement.

Results

Table 1. Study Parameters

Model Parameters for Cost-Effectiveness Analysis			
Parameters	Value	Ranges	Sources
Transition Probabilities			

Probability of Acute Ischemic Stroke	0.000396	0.0003452-0.0004533	GBD (16)
Background Mortality	0.0104662245	0.008896290846-0.01224548269	GBD (16) (Adjusted by age)
Case Fatality Ratio from Acute Ischemic Stroke	0.3172	0.3054-0.333	GBD (16)
Effectiveness Parameters			
Mortality reduction from Thrombolysis in Acute Ischemic Stroke State	0.685	0.55485-0.85625	Heo et al (26)
Mortality reduction from Thrombolysis in Post-Stroke State	0.9858	0.798498-1.28154	Heo et al (26)
Mortality reduction from Antiplatelets in Post-Stroke State	0.45	0.28-0.74	Heo et al (26)
Mortality reduction from Anticoagulants in Post-Stroke State	0.46	0.28-0.75	Heo et al (26)
Mortality reduction from Antihypertensives in Post-Stroke State	0.86	0.75-0.97	Wang et al (27)
Disability reduction from Thrombolysis in Acute Ischemic Stroke State	0.78125	0.9453125-0.0777264	Wardlaw et al (28)
Disability reduction from Thrombolysis in Post-Stroke State	0.524024527	0.817478262-0.13234293	Marler et al (29)
Disability reduction from Rehabilitation in Acute Ischemic Stroke State	0.187	0.0935-0.2805	Manchi et al (30)
Disability reduction from Rehabilitation in Post-Stroke State	0.1	0.05-0.15	Dajpratham et al (31)

Healthcare Cost			
Acute Ischemic Stroke State (Baseline)	5,805.55	4,180.00-8,243.88	Dittrich et al (10)
Acute Ischemic Stroke State (Scenario 1)	6,002.43	4,321.75-8,523.46	Dittrich et al (10)
Acute Ischemic Stroke State (Scenario 2)	6,207.30	4,469.25-8,814.36	Dittrich et al (10)
Post-Stroke Care	310.56	155.28-440.99	Calculated
Intervention Costs			
Mass Media Campaign (per capita cost)	0.0079566	0.0039783-0.0112984	Calculated
Certification (per capita cost)	0.0012849	0.0006425-0.0018246	Calculated
Recertification (per capita cost)	0.00049420	0.00024710-0.00070177	Calculated
Other Parameters			
Discount rate	0.03	0-0.06	Haacker et al (32)
Disability weight, Acute Ischemic Stroke State	0.236801250	0.1539208126-0.3315217503	GBD (16) (Weighed average)
Disability weight, Post-Stroke State	0.225602897	0.146641883-0.3158440558	GBD (16) (Weighed average)

Table 2. Incremental coverage

Access to Thrombolytics by Scenario	
Comparison of treatment access rates	
	Access to thrombolytics
Baseline Scenario	2.3%
Scenario 1	5.7%
Scenario 2	11.8%

Table 2, lists the changes in access to thrombolytics for each scenario. In the baseline scenario, overall access to thrombolytics was 2.3%. After certifying basic stroke centers in level II-2 hospitals and above, access to thrombolytic treatment increased towards 5.7%. Furthermore, in scenario 2, once the intervention of a mass media campaign was added, coverage of thrombolytic treatment increased to 11.8%.

Table 3. Deterministic results

Deterministic Results						
Base case analysis with incremental comparisons						
Strategy	Total Results			Incremental Analysis		
	Total Costs	Deaths	Total DALYs	Incremental Costs	Incremental DALYs	ICER (\$/DALY averted)
Baseline	\$17.01372	0.202228	2.860451746	-	-	-
Scenario 1	\$17.50380	0.202214	2.860065937	\$0.490089	-0.000385809	\$1,270.3
Scenario 2	\$23.32769	0.202102	2.858089377	\$6.313979	-0.002362369	\$2,672.7

Deterministic results in table 3, showed both interventions lie under Peru's 2023 GDP per capita (\$7900), making them cost-effective. Scenario 1 reported an ICER of \$1,270 dollars per DALY averted, compared to Scenario 2 where the ICER was \$2,672 dollars per DALY averted, making Scenario 1 more cost effective.

Probabilistic results

For the probabilistic results, it was plotted a Cost-Effectiveness Scatter plot (Figure 8), by using a Monte Carlo simulation of 2000 iterations. Every point of the plot represents one simulation by using the ranges from the distributions displayed in the parameters table. The x-axis represents the incremental DALYs, and the y-axis represents the incremental costs per Scenario. The dots falling below the willingness to pay threshold (WTP), represent every iteration where the intervention was cost-effective. Showing both scenarios are cost-effective under the WTP threshold, however scenario 2 has higher health benefits than scenario 1.

At the same time, the cost-effectiveness acceptability curve plotted in Figure 7, shows how the three different scenarios behave under different WTP thresholds. It is evident that under smaller WTP thresholds, the baseline scenario dominates, but as WTP increases, scenario 1 will turn most cost-effective. However, in the long run, with a higher willingness to pay threshold, scenario 2 becomes more cost-effective than both baseline scenario and scenario 1.

Table 4. Health Outcomes and Cost Comparison by Scenario - Population results

Health Outcomes and Cost Comparison by Scenario		
Relative improvements compared to baseline		
	Scenario 1	Scenario 2
Relative reduction in stroke mortality compared to baseline	0.47%	4.2%
Relative reduction in stroke disability compared to baseline	1.5%	3.8%
Potential stroke deaths averted among the current cohort of 55-year-old Peruvians compared to baseline	5	46
Incremental cost per capita compared to baseline	\$0.49	\$6.3

The relative improvements compared to baseline are listed in table 4, where it is shown that Scenario 2 had a greater relative reduction in stroke mortality compared to baseline than Scenario 1 (4.2% vs 0.47%). In the case of disability caused by stroke compared to baseline, Scenario 2 produced a greater reduction than Scenario 1 (3.6% vs 1.5%). Regarding the potential deaths caused by stroke that could be averted per scenario, Scenario 1 averted 5 deaths among the current cohort of 55-year-old Peruvians compared to baseline (290, 000 cohort members). However, Scenario 2 produced a greater reduction in deaths caused by stroke, averting 46 deaths compared to Scenario 1. The incremental costs varied across Scenarios, where in Scenario 1 the incremental cost per capita was \$0.49 dollars, whereas in Scenario 2 it was \$6.3 dollars per capita.

Effect of uncertainty

Some parameters were constant in the sensitivity analysis of the model. However, some could create uncertainty considering how the disease behaves. One of those parameters was sex, since incidences were calculated with an average of both females and males across different ages. Also, geographic differences weren't included due to lack of reliable regional data, which potentially could affect the access rates across different populations. At the same time, treatment adherence rates were held constant regarding secondary prevention, which could potentially overestimate effectiveness in our model.

Effect of engagement with patients and others affected by the study

As mentioned in the methods section, no formal patient, policymaker or public stakeholder was involved while doing this study. This study used clinical experts to approach a better sense of the feasibility and applicability of the model we developed.

Discussion

This study demonstrates that both intervention scenarios are highly cost-effective under the Peruvian willingness-to-pay threshold. Stroke center certification in centers at level II-2 and over offers excellent value at \$1,270 per DALY averted. And adding mass media campaigns increases the cost per DALY averted to \$2,672 but produces substantially greater health benefits.

Regarding treatment gaps in Peru, at baseline there is severe undercoverage, with only 2.3% of the population receiving treatment with thrombolytics. Implementing certification of basic stroke centers could improve this percentage to 5.7%. On the other hand, adding mass media campaigns would result in a higher number of people accessing the care treatment pathway and increasing coverage to 11.8%.

The certification of basic stroke centers provides an opportunity to improve stroke care during the hospitalization process as well as emphasize a multidisciplinary treatment approach to stroke management and rehabilitation (14). Adding mass media campaigns of stroke awareness creates the opportunity for people to pursue access to care (15) and with appropriate urgency to receive thrombolytic therapy (25).

In our study, both interventions, set in different scenarios, showed an impact not only on access to treatment but on mortality and disability as well. The scenario including only certification of stroke centers showed a relative reduction of 0.47% in mortality, and 1.5% in disability compared to the baseline. However, when adding in mass media campaigns, mortality was projected to be reduced to 4.2% and disability to 3.8%.

In Latin America, the World Stroke Organization in collaboration with the Iberoamerican Stroke Society (SIECV), started the certification process of essential stroke centers and advanced stroke centers in October 2020 (33). This certification process resembled the Target Stroke intervention carried out in the US (14). In August 2022, the first hospital certified in Peru as an essential stroke center under the national health insurance was the National Institute of Neurological Sciences (34). After that, several other hospitals and private clinics around the country started the process of

certification for both essential and advanced stroke centers. With this study, we can envision what could be improved once the scaling-up process is completed.

Furthermore, including a mass media campaign could have an incremental positive effect, as shown in scenario 2. Our analysis demonstrated that the best long-term strategy for acute stroke care improvement is the scenario where both interventions are included, despite its higher costs. However, the final choice depends on the availability of the country's resources to invest for obtaining a higher health benefit.

One of the main limitations of this study is our assumption of a uniform effect across populations. In addition, we did not examine the differential impact that both interventions could have across various geographical areas or socioeconomic sectors in Peru. Evaluating these contexts could highlight specific populations that may require a more tailored approach to determine which intervention would result in greater benefit in reducing the morbidity and mortality of stroke.

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Conflicts of interest

None of the authors had a conflict of interest for the elaboration of this study.

References

1. Feigin VL, Abate MD, Abate YH, Abd ElHafeez S, Abd-Allah F, Abdelalim A, et al. Global, regional, and national burden of stroke and its risk factors, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *The Lancet Neurology*. 2024 Oct;23(10):973–1003.
2. Rahbar MH, Medrano M, Diaz-Garelli F, Gonzalez Villaman C, Saroukhani S, Kim S, et al. Younger age of stroke in low-middle income countries is related to healthcare access and quality. *Ann Clin Transl Neurol*. 2022 Mar;9(3):415–27.
3. Lazo-Porras M, Bernabe-Ortiz A, Gilman RH, Checkley W, Smeeth L, Miranda JJ. Population-based stroke incidence estimates in Peru: Exploratory results from the CRONICAS cohort study. *The Lancet Regional Health - Americas*. 2022 Jan;5:100083.
4. Miranda J, Moscoso M, Yan L, Diez-Canseco F, Málaga G, Garcia H, et al. Addressing post-stroke care in rural areas with Peru as a case study. Placing emphasis on evidence-based pragmatism. *JOURNAL OF THE NEUROLOGICAL SCIENCES*. 2017 Apr 15;375:309–15.
5. Lazo-Gonzales O, Alcalde-Rabanal J, Espinosa-Henao O. El sistema de salud en Perú: situación y desafíos. 2016.
6. Ministerio de Salud, Peru. Seguro Integral de Salud: 10 años financiando la salud de los peruanos [Internet]. 2012. Available from: https://www.sis.gob.pe/portal/mercadeo/Material_consulta/BrochureSIS_10aniosfinansaludperuanos.pdf
7. Mistry EA, Mistry AM, Nakawah MO, Chitale RV, James RF, Volpi JJ, et al. Mechanical Thrombectomy Outcomes With and Without Intravenous Thrombolysis in Stroke Patients: A Meta-Analysis. *Stroke*. 2017 Sep;48(9):2450–6.
8. Lees KR, Emberson J, Blackwell L, Bluhmki E, Davis SM, Donnan GA, et al. Effects of Alteplase for Acute Stroke on the Distribution of Functional Outcomes: A Pooled Analysis of 9 Trials. *Stroke*. 2016 Sep;47(9):2373–9.
9. Almubaslat F, Sanchez-Boluarte SS, Diaz MM. A review of neurological health disparities in Peru. *Front Public Health*. 2023 Sep 7;11:1210238.
10. Dittrich LB, Beck Da Silva Etges AP, Siqueira De Souza J, Zago Marcolino MA, Rocha E, Amaya P, et al. Cost evaluation of acute ischemic stroke in Latin America: a multicentric study. *The Lancet Regional Health - Americas*. 2025 Jan;41:100959.

11. Dirección de Presupuesto Público. El Sistema Nacional de Presupuesto: Guía Básica [Internet]. Lima, Peru; 2011. Available from: https://www.mef.gob.pe/contenidos/presu_publ/capacita/guia_sistema_nacional_presupuesto.pdf
12. Instituto de Evaluación Tecnológica en Salud. Manual para la elaboración de evaluaciones económicas en salud. Bogotá; 2014.
13. Secretaria de Gobierno Digital, Peru. Plataforma Nacional de Datos Abiertos [Internet]. Available from: <https://www.datosabiertos.gob.pe/>
14. Fonarow GC, Smith EE, Saver JL, Reeves MJ, Hernandez AF, Peterson ED, et al. Improving Door-to-Needle Times in Acute Ischemic Stroke: The Design and Rationale for the American Heart Association/American Stroke Association's Target: Stroke Initiative. *Stroke*. 2011 Oct;42(10):2983–9.
15. Advani R, Naess H, Kurz M. Mass Media Intervention in Western Norway Aimed at Improving Public Recognition of Stroke, Emergency Response, and Acute Treatment. *Journal of Stroke and Cerebrovascular Diseases*. 2016 Jun;25(6):1467–72.
16. Institute for Health Metrics and Evaluation (IHME). GBD Results [Internet]. University of Washington; Available from: <https://vizhub.healthdata.org/gbd-results/>
17. World Health Organization. Life tables: Life tables by country Peru [Internet]. 2019. Available from: <https://apps.who.int/gho/data/view.searo.61280?lang=en>
18. De Havenon A, Tirschwell DL, Heitsch L, Cramer SC, Braun R, Cole J, et al. Variability of the Modified Rankin Scale Score Between Day 90 and 1 Year After Ischemic Stroke. *Neur Clin Pract* [Internet]. 2021 Jun [cited 2025 May 20];11(3). Available from: <https://www.neurology.org/doi/10.1212/CPJ.0000000000000954>
19. Abanto C, Ton TGN, Tirschwell DL, Montano S, Quispe Y, Gonzales I, et al. Predictors of Functional Outcome among Stroke Patients in Lima, Peru. *Journal of Stroke and Cerebrovascular Diseases*. 2013 Oct;22(7):1156–62.
20. Instituto Nacional de Radio y Televisión del Peru. APROBACIÓN DE LAS POLITICAS COMERCIALES DEL IRTP - 2022 [Internet]. 2022. (MEMORANDO N° D000047-2022-IRTP-GG). Report No.: MEMORANDO N° D000047-2022-IRTP-GG. Available from: <https://cdn.www.gob.pe/uploads/document/file/7551622/6416418-aprobacion-de-las-politicas-comerciales-del-irtp-2022.pdf?v=1738098243>
21. Kawano Castillo J, Chuquilín Arista M, Tipismana Barbarán M, Vizcarra Escobar D. Factores asociados a la demora del tratamiento hospitalario de los pacientes con enfermedad cerebrovascular aguda. *RevNeurol*. 2007;44(05):264.
22. Málaga G, De La Cruz-Saldaña T, Busta-Flores P, Carbajal A, Santiago-Mariaca K. La enfermedad cerebrovascular en el Perú: estado actual y perspectiva de investigación clínica. *Acta Med Peru*. 2018.

23. Watkins DA, Msemburi WT, Pickersgill SJ, Kawakatsu Y, Gheorghe A, Dain K, et al. NCD Countdown 2030: efficient pathways and strategic investments to accelerate progress towards the Sustainable Development Goal target 3.4 in low-income and middle-income countries. *The Lancet*. 2022 Mar;399(10331):1266–78.
24. Man S, Solomon N, Mac Grory B, Alhanti B, Saver JL, Smith EE, et al. Trends in Stroke Thrombolysis Care Metrics and Outcomes by Race and Ethnicity, 2003-2021. *JAMA Netw Open*. 2024 Feb 7;7(2):e2352927.
25. Wolters FJ, Paul NLM, Li L, Rothwell PM. Sustained Impact of UK Fast-Test Public Education on Response to Stroke: A Population-Based Time-Series Study. *International Journal of Stroke*. 2015 Oct;10(7):1108–14.
26. Heo NH, Lee MR, Yang KH, Hong OR, Shin JH, Lee BY, et al. Short- and long-term mortality after intravenous thrombolysis for acute ischemic stroke: A propensity score-matched cohort with 5-year follow-up. *Medicine*. 2021 Nov 5;100(44):e27652.
27. Wang H, Sandel ME, Terdiman J, Armstrong MA, Klatsky A, Camicia M, et al. Postacute care and ischemic stroke mortality: findings from an integrated health care system in northern California. *Pm r*. 2011 Aug;3(8):686–94.
28. Wardlaw JM, Murray V, Berge E, Del Zoppo G, Sandercock P, Lindley RL, et al. Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated systematic review and meta-analysis. *The Lancet*. 2012 Jun;379(9834):2364–72.
29. Marler JR, Tilley BC, Lu M, Brott TG, Lyden PC, Grotta JC, et al. Early stroke treatment associated with better outcome The NINDS rt-PA Stroke Study. 2000.
30. Manchi MR, Venkatachalam AM, Atem FD, Stone S, Mathews AA, Abraham AM, et al. Effect of inpatient rehabilitation facility care on ninety day modified Rankin score in ischemic stroke patients. *Journal of Stroke and Cerebrovascular Diseases*. 2023 Jun;32(6):107109.
31. Dajpratham P, Kuptniratsaikul V, Putthakumnerd W, Limumpai P. Walking Function at 1-Year after Stroke Rehabilitation: A Multicenter Study. 2014;97(1):107–12.
32. Haacker M, Hallett TB, Atun R. On discount rates for economic evaluations in global health. *Health Policy and Planning*. 2019 Oct 18;czz127.
33. World Stroke Organization. Stroke Center Certification on Latin America WSO/SIECV [Internet]. 2021. Available from: <https://www.world-stroke.org/news-and-blog/news/stroke-center-certification-on-latin-america-wso-siecv>
34. Ministerio de Salud, Peru. INCN recibe certificación de calidad en la atención del ataque cerebrovascular [Internet]. Available from: <https://www.incn.gob.pe/2022/08/17/incn-recibe-certificacion-de-calidad-en-la-atencion-para-ataque-cerebrovascular/>

Appendices.

Figure 1. Markov States

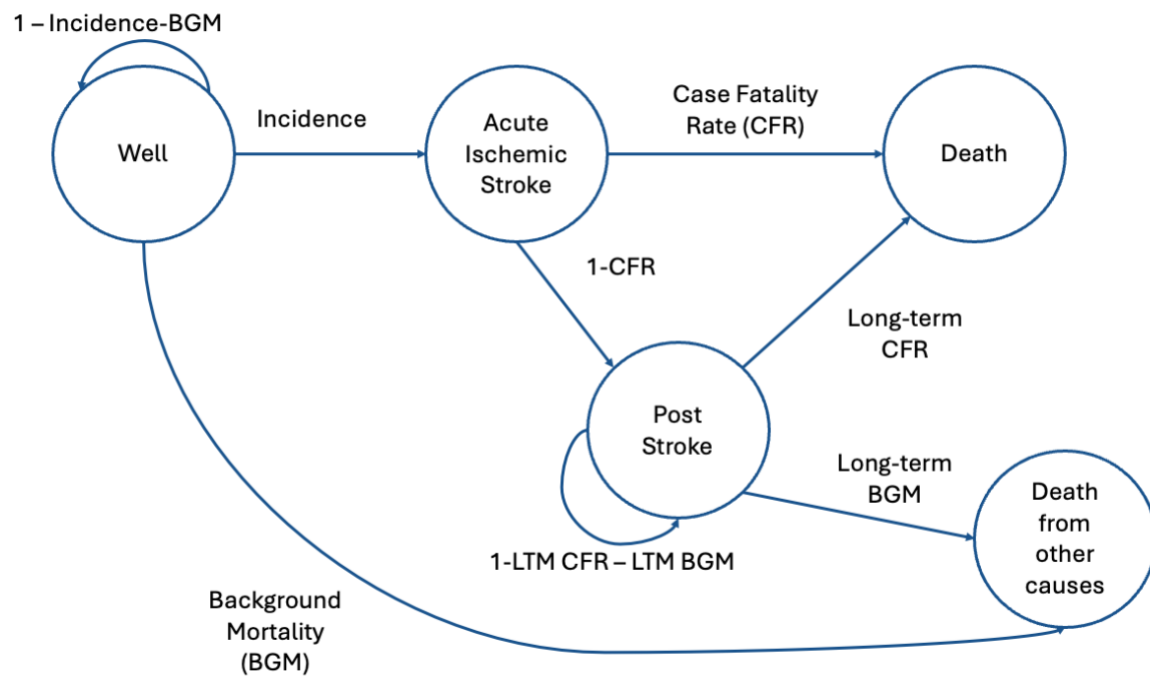


Figure 2. Cascade Treatment - Baseline Scenario

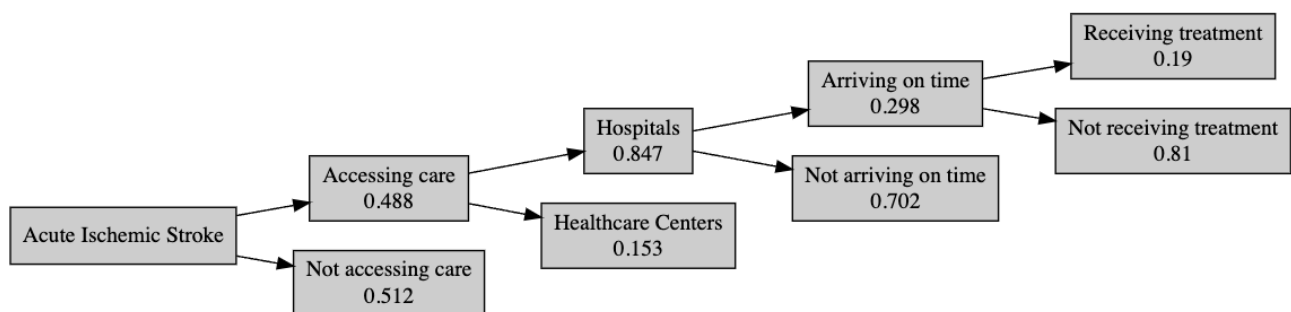


Figure 3. Cascade Treatment - Scenario 1

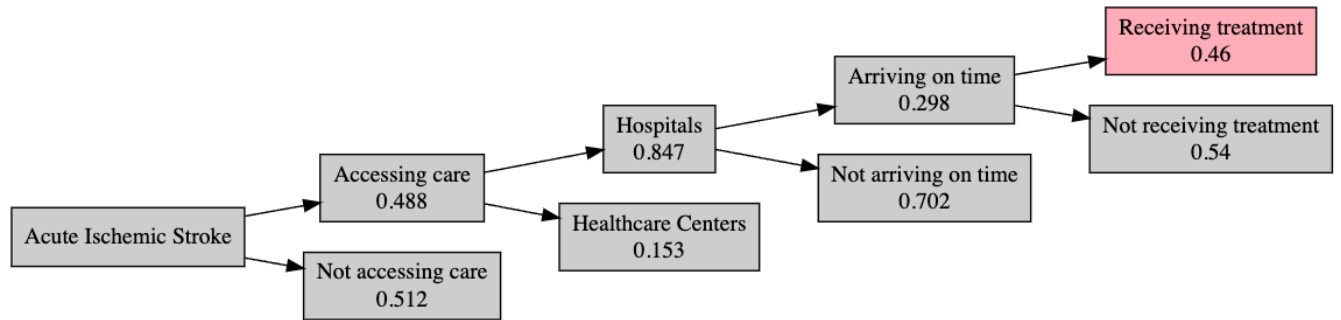


Figure 4. Cascade Treatment - Scenario 2

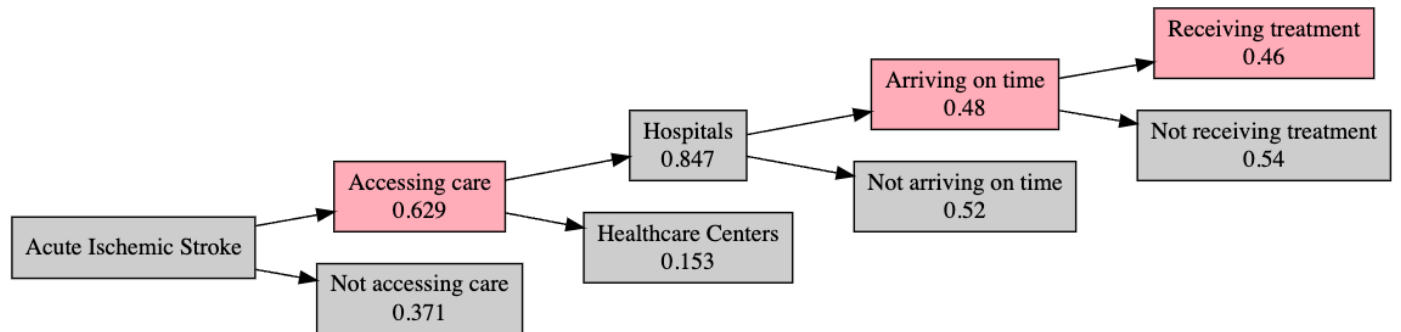


Figure 5. One-Way Sensitivity Analysis - Scenario 1

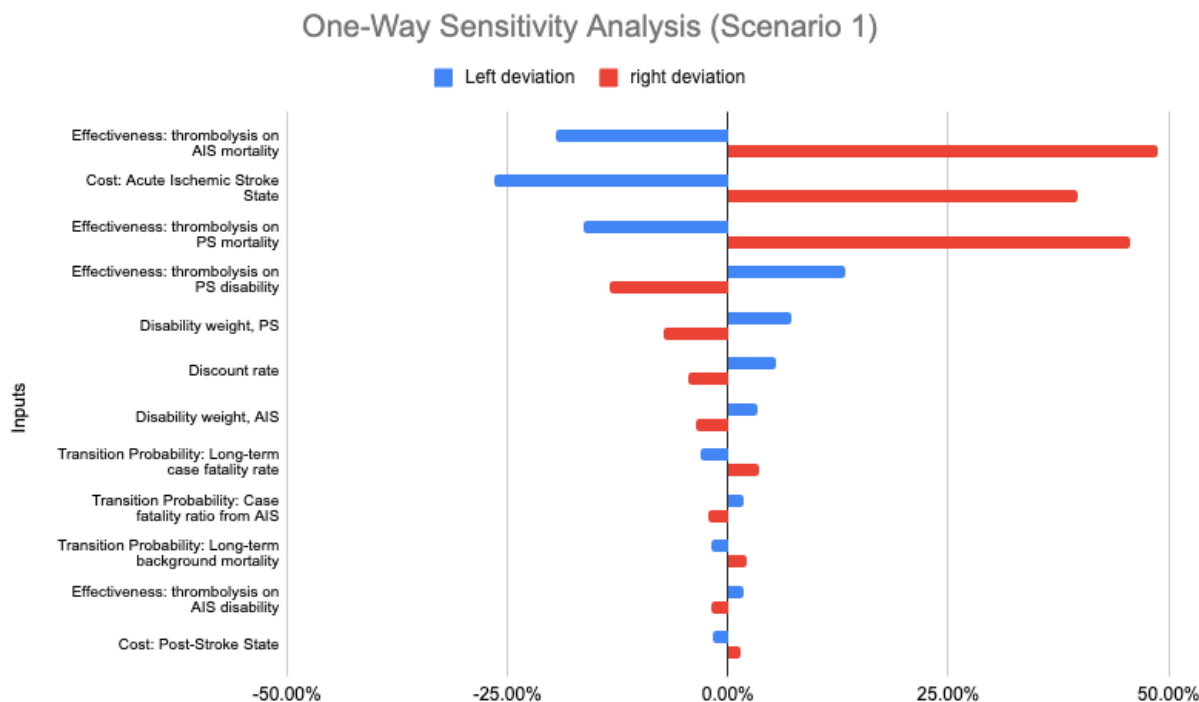


Figure 6. One-Way Sensitivity Analysis - Scenario 2

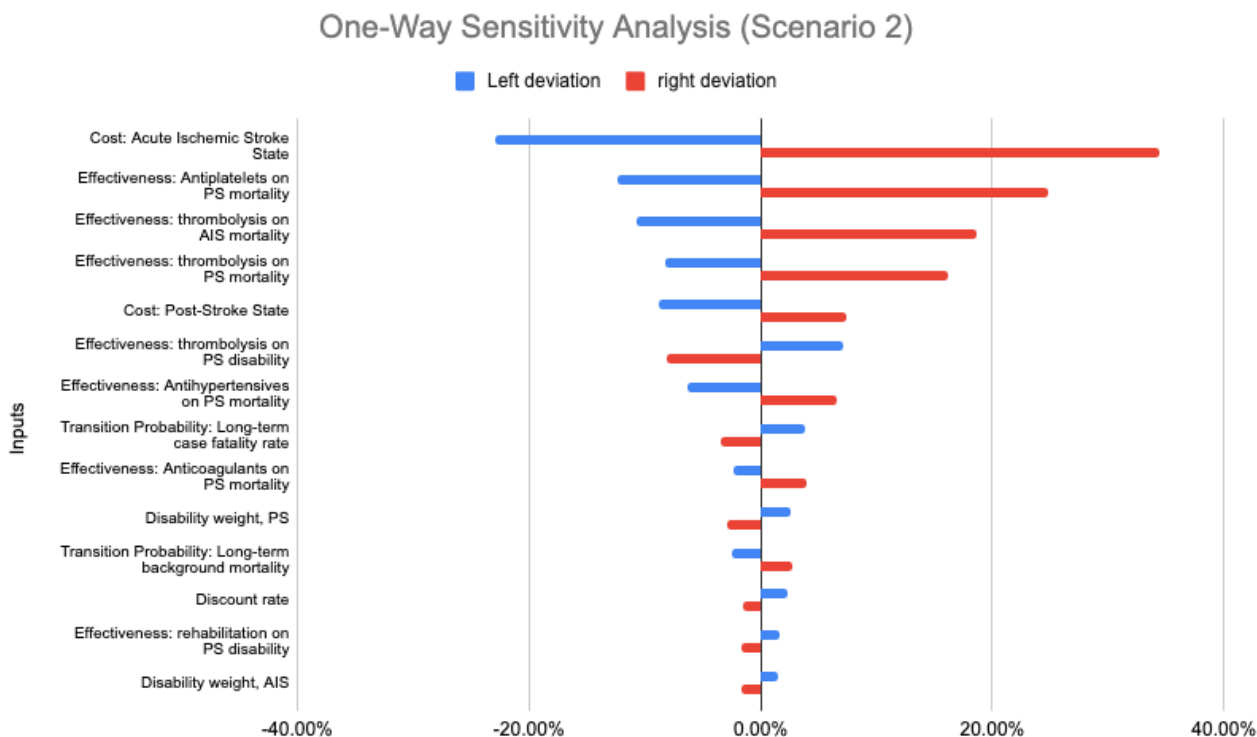


Figure 7. Cost-effectiveness Acceptability Curve

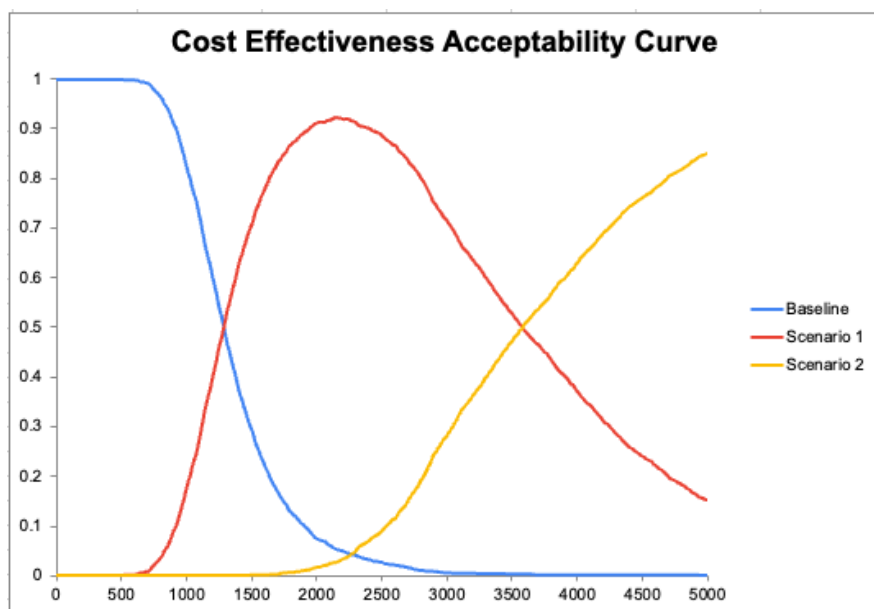


Figure 8. Cost-effectiveness Scatter plot

