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Brain Health Clinical Exchange

Decision Analysis to Address Clinical Dilemmas in Resource-Limited Settings:
Aspirin for Stroke of Undetermined Etiology as a Case Study

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Case

A 69-year-old woman with a history of hypertension presents to a health center in rural Haiti two days after sudden development of right sided paralysis and difficulty speaking.

A diagnosis of stroke is made. No CT scan is available to determine if the stroke is ischemic or hemorrhagic.

In addition to acute stabilization, evaluation for etiology, risk factor modification, and rehabilitation, would you initiate aspirin for long-term secondary stroke prevention?

Survey

For this patient with stroke and no CT available to determine if the stroke is ischemic or hemorrhagic, would you administer aspirin for long-term secondary stroke prevention?

A. Yes, I would treat the patient with aspirin
B. No, I would not treat the patient with aspirin

Use of secondary prevention drugs for cardiovascular disease in the community in high-income, middle-income, and low-income countries (the PURE Study): a prospective epidemiological survey

Salim Yusuf, Shofiqul Islam, Clara K Chow, Sumathy Rangarajan, Gilles Dagenais, Rafael Diaz, Rajeev Gupta, Roya Kelishadi, Romaina Iqbal, Alvaro Avezum, Annamarie Kruger, Raman Kutty, Fernando Lanas, Liu Lisheng, Li Wei, Patricio Lopez-Jaramillo, Aytekin Oguz, Omar Rahman, Hany Swidan, Khalid Yusoff, Witold Zatonski, Annika Rosengren, Koon K Teo, on behalf of the Prospective Urban Rural Epidemiology (PURE) Study Investigators

	Overall	High-income countries	Upper middle-income countries	Lower middle-income countries	Low-income countries	P_{trend}
Stroke	2292	213	691	1042	346	<0·0001
Antiplatelet drugs	557 (24·3%)	113 (53·1%)	137 (19·8%)	294 (28·2%)	13 (3·8%)	<0·0001
β blockers	215 (9·4%)	44 (20·7%)	87 (12·6%)	62 (6·0%)	22 (6·4%)	<0·0001
ACE inhibitors or ARBs	426 (18·6%)	89 (41·8%)	195 (28·2%)	135 (13·0%)	7 (2·0%)	<0·0001
Diuretics*	348 (15·2%)	48 (22·5%)	109 (15·8%)	180 (17·3%)	11 (3·2%)	<0·0001
Calcium-channel blockers†	331 (14·4%)	37 (17·4%)	80 (11·6%)	202 (19·4%)	12 (3·5%)	0·0307
Blood-pressure-lowering drugs‡	916 (40·0%)	129 (60·6%)	293 (42·4%)	449 (43·1%)	45 (13·0%)	<0·0001
Statins	206 (9·0%)	110 (51·6%)	72 (10·4%)	22 (2·1%)	2 (0·6%)	<0·0001

Lancet 2011; 378: 1231–43

Global Access to CT

World Health Organization

Global atlas of medical devices

WHO medical devices technical series

Global Access to CT

World Health Organization

Global atlas of medical devices

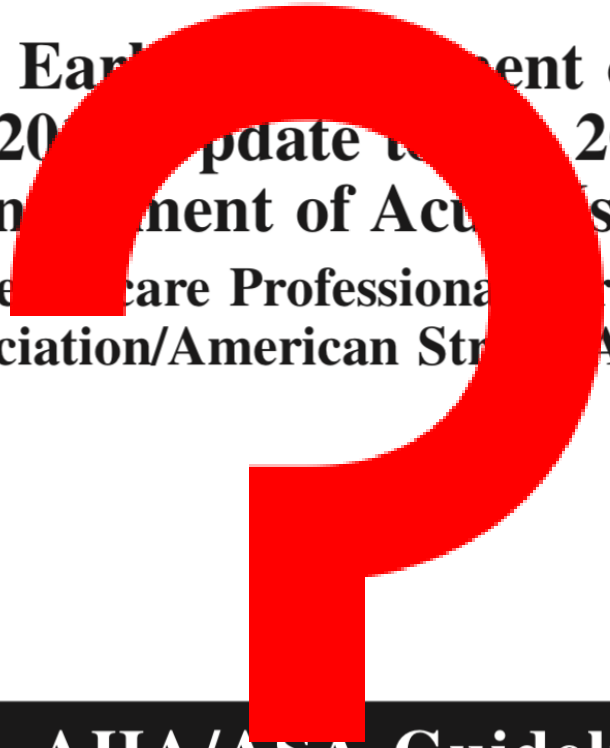
- High-income countries: **42** CT scanners per 1 million population

- Low-income countries: **0.32** CT scanners per 1 million population

AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association



AHA/ASA Guideline

Guidelines for the Management of Spontaneous Intracerebral Hemorrhage

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Aspirin for secondary prevention after stroke of unknown etiology in resource-limited settings

A decision analysis

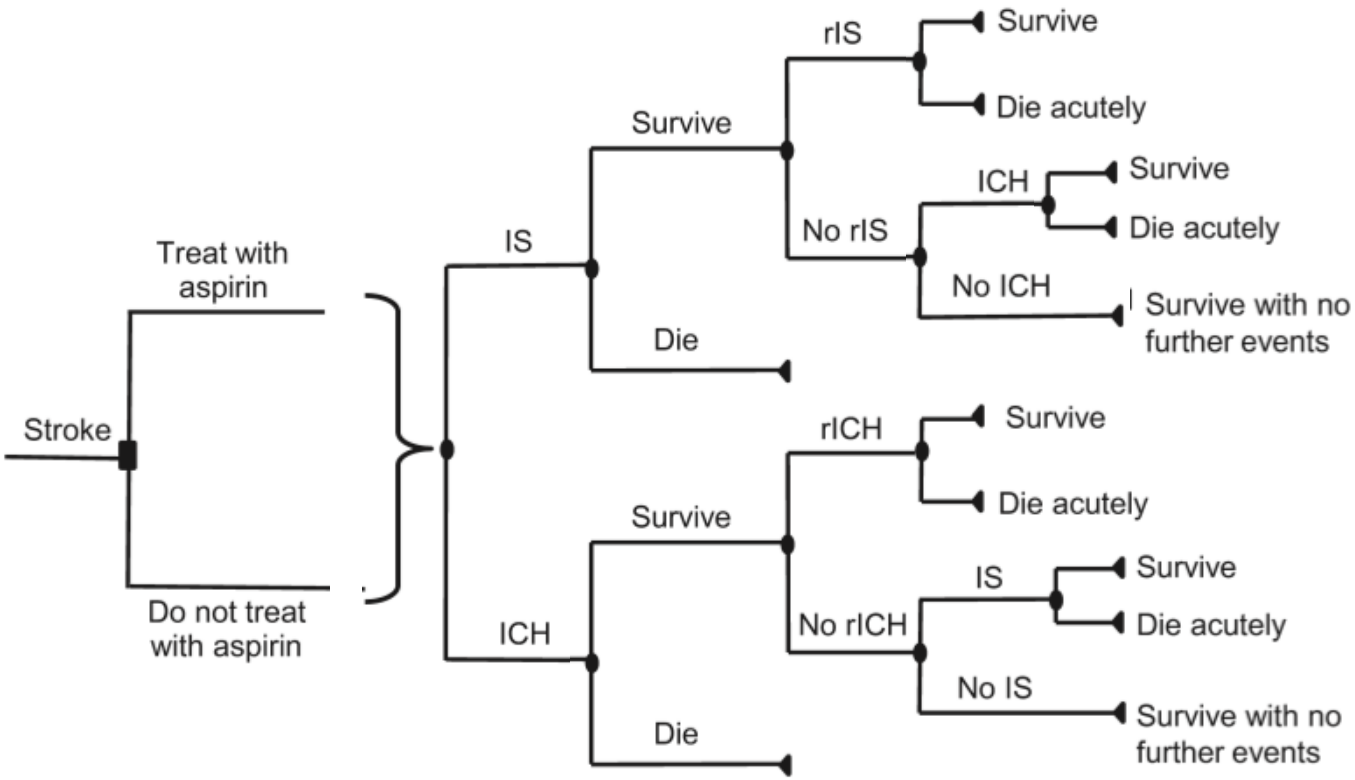
Aaron L. Berkowitz, M. Brandon Westover, Matt T. Bianchi, Sherry H-Y. Chou

Neurology® 2014;83:1-8

Decision analysis

- **Decision Tree**
- Inputs
- Base case
- Sensitivity analysis

Aspirin for secondary prevention after stroke of unknown etiology in resource-limited settings



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Decision analysis

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Aspirin for secondary prevention after stroke of unknown etiology in resource-limited settings

	Without aspirin, %	With aspirin, %	RR with aspirin	95% CI
Yearly rate of IS after IS[15]	4.53	3.58	0.78	0.68–0.91
Yearly rate of ICH after IS[15]	0.14	0.32	1.90	1.06–3.44
Yearly rate of IS after ICH[13]	2.31	0.51	0.23	0.03–1.68
Yearly rate of ICH after ICH[14]	1.34	2.54	1.74	1.00–3.04
Acute mortality rate after IS[16]	9.44	4.90	0.53	0.30–0.95
Acute mortality rate after ICH[17]	26.71	37.67	1.41	1.21–1.64

	Mild	Moderate	Severe
Outcomes after IS,[18] %	44	28	28
Outcomes after ICH,[19] %	31	40	29
Quality of life[22]	0.76	0.39	0.11

Abbreviations: CI = confidence interval; ICH = intracerebral hemorrhage; IS = ischemic stroke; RR = relative risk.

Neurology® 2014;83:1–8

Decision analysis

- Decision Tree
- Inputs
- **Base case analysis**
- Sensitivity analysis

Decision analysis

- Decision Tree
- Markov state transition model
- Inputs
- **Base case analysis**
  - **69-year-old (average age at stroke onset in LMIC)**
  - **34% of acute strokes due to ICH**
- Sensitivity analysis

Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study

	All (n=3000)	High-income countries* (n=422)	South America† (n=151)	Southeast Asia‡ (n=1146)	India (n=958)	Africa§ (n=323)
Age (years)	61·1 (12·7)	66·0 (13·3)	65·6 (13·4)	58·5 (11·6)	58·9 (12·0)	57·7 (15·3)
Age ≤45 years	415 (14%)	32 (8%)	13 (9%)	146 (13%)	147 (15%)	77 (24%)
Women	1106 (37%)	169 (40%)	71 (47%)	412 (36%)	313 (33%)	141(44%)
Intracerebral haemorrhagic stroke	663 (22%)	40 (9%)	39 (26%)	257 (22%)	218 (23%)	109 (34%)
Ischaemic stroke	2337 (78%)	382 (91%)	112 (74%)	889 (78%)	740 (77%)	214 (66%)

Data are mean (SD) or number (%). OCSP=Oxfordshire Community Stroke Project. ECG=electrocardiogram. *Australia, Canada, Croatia, Denmark, Germany, Iran, and Poland. †Argentina, Brazil, Chile, Colombia, Ecuador, and Peru. ‡China, Malaysia, and Philippines. §Mozambique, Nigeria, South Africa, Sudan, and Uganda. ¶Percentages are proportions of the number of cases with ischaemic stroke.

Table 1: **Demographic and clinical characteristics of cases**

Lancet 2010: 376; 112–23

Aspirin for secondary prevention after stroke of unknown etiology in resource-limited settings

Table 2 Predicted 1-year outcomes per 1,000 patients for base case analysis

	No treatment with aspirin	Treatment with aspirin
Mortality (per 1,000 patients per year)	103.32	102.97
Ischemic strokes (per 1,000 patients per year)	33.32	22.26
Intracerebral hemorrhages (per 1,000 patients per year)	4.78	8.55

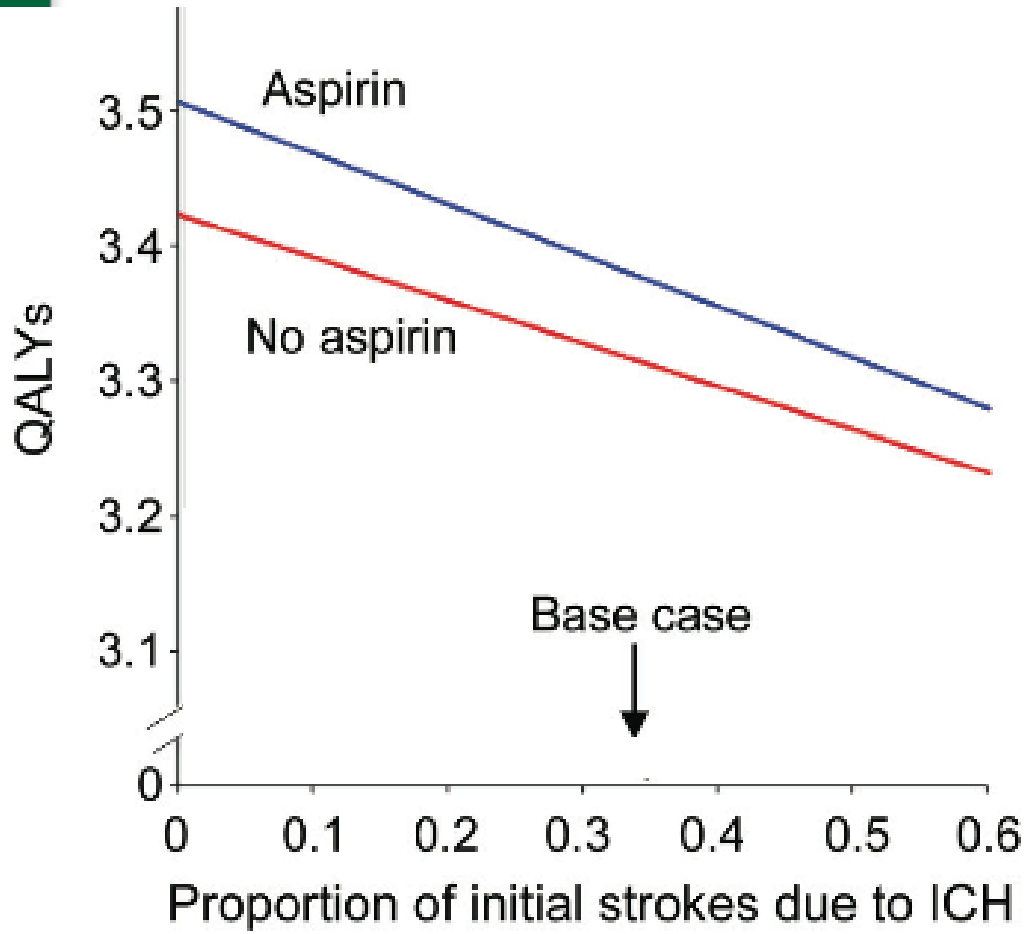
- Based on estimated ~12 million strokes in LMIC per year, aspirin administration to **all** patients with stroke would be predicted to lead to:
  - *estimated yearly decrease of ~**85,000** recurrent strokes*
  - *estimated yearly decrease of ~**4,000** stroke-related mortalities*

Neurology® 2014;83:1-8

Decision analysis

- Decision Tree
- Inputs
- Base case analysis
- **Sensitivity analysis**

Aspirin for secondary prevention after stroke of unknown etiology in resource-limited settings



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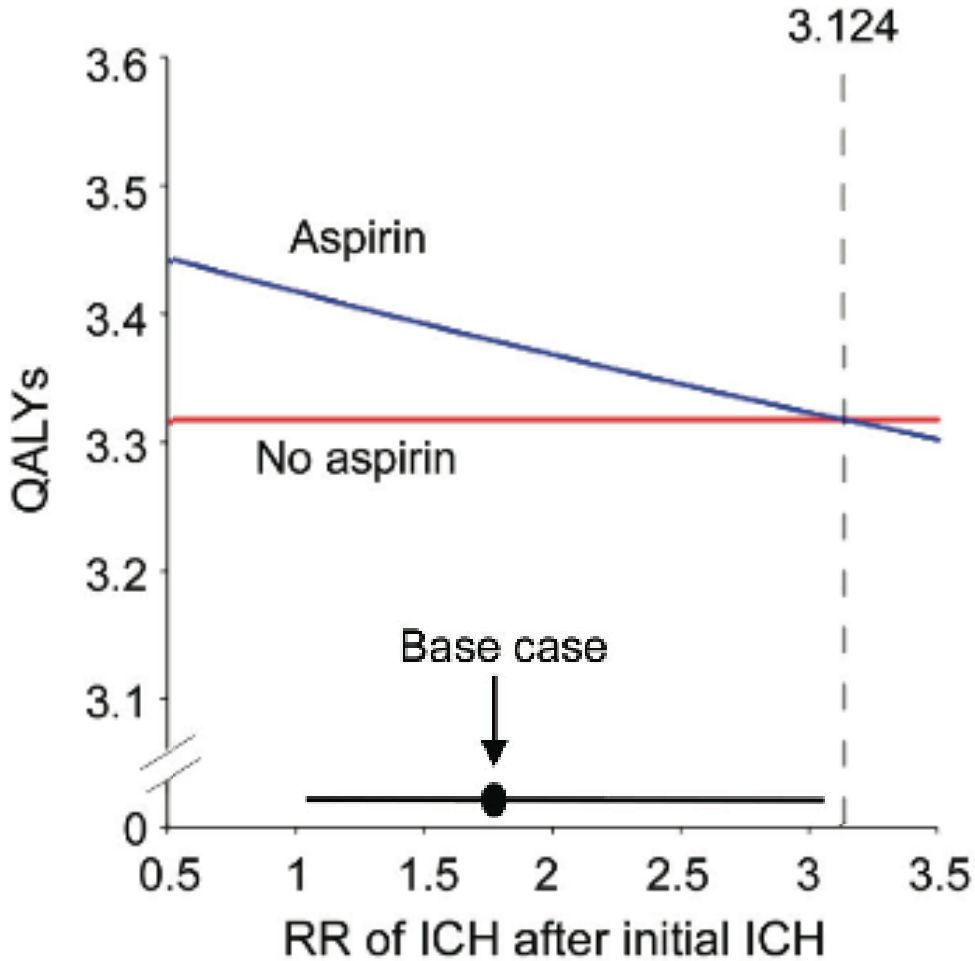
Aspirin for secondary prevention after stroke of unknown etiology in resource-limited settings



Neurology® 2014;83:1-8

Effects of antiplatelet therapy after stroke due to intracerebral haemorrhage (RESTART): a randomised, open-label trial

*RESTART Collaboration**

Interpretation These results exclude all but a very modest increase in the risk of recurrent intracerebral haemorrhage with antiplatelet therapy for patients on antithrombotic therapy for the prevention of occlusive vascular disease when they developed intracerebral haemorrhage. The risk of recurrent intracerebral haemorrhage is probably too small to exceed the established benefits of antiplatelet therapy for secondary prevention.

Lancet 2019; 393: 2613–23

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See Comment page 2567

*Members listed at end of the

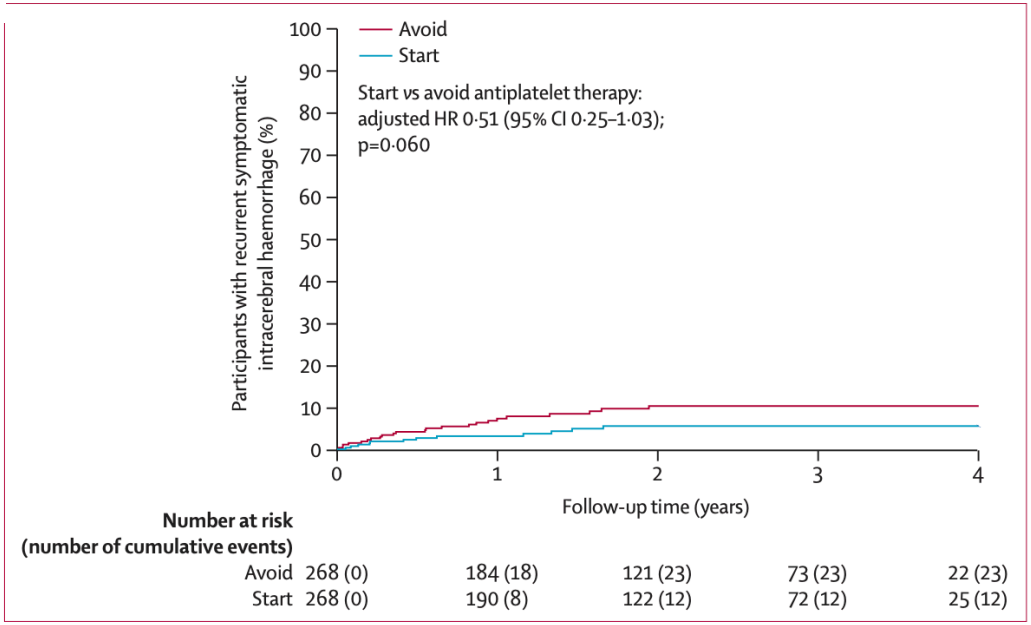

Figure 2: **Kaplan-Meier plot of the first occurrence of recurrent symptomatic intracerebral haemorrhage**
Numbers at risk refer to survivors under follow-up at the start of each year according to treatment allocation. Cumulative events indicate the participants in follow-up with a first event. HR=hazard ratio.

Stroke

COMMENTS AND OPINIONS

Inpatient Management of Acute Stroke of Unknown Type in Resource-Limited Settings

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Fred Stephen Sarfo, MD, PhD; Gentle S. Shrestha, MD; Aaron Berkowitz, MD, PhD*; Nirali Vora MD*

ABSTRACT: Stroke is the second leading cause of death and disability worldwide, with a disproportionate burden on low- and middle-income countries. Critical elements of guideline-based stroke care developed in high-income countries are not applicable to resource-limited settings, where lack of access to neuroimaging prevents clinicians from distinguishing between ischemic stroke and intracranial hemorrhage, requiring challenging clinical decision-making, particularly in the acute setting. We discuss strategies for acute inpatient management of stroke of unknown type with a focus on blood pressure management and antiplatelet therapy when neuroimaging is unavailable, and review some of the challenges and strategies for successfully implementing stroke unit care in resource-limited health care settings.

Key Words: blood pressure ■ cause of death ■ clinical decision-making ■ inpatient ■ neuroimaging

American Stroke Association.
A division of the American Heart Association.

Discussion

What clinical dilemma(s) have you encountered for which a decision analysis model may be useful?

Consider:

- Clinical trials unlikely to ever be performed
- Clinical questions for which there is available data on which to base the model