Cost-effectiveness analysis of atrial fibrillation screening for Japanese hypertensive patients using microsimulation

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Background

- ✓Non-valvular atrial fibrillation (AF) increases with age and is associated with the risk of cardiovascular events, including stroke, myocardial infarction, heart failure, and death.
- ✓The Japan Stroke Society conducts public awareness campaigns regarding the necessity of stroke prevention through medical management.
- ✓Regarding the usefulness of systematic atrial fibrillation screening, cost-effectiveness evaluations have been conducted in some foreign countries, but not in Japan.

About Microsimulation

PROS

- ✓Unlike conventional cost-effectiveness methods using expected values for the entire cohort, this enables modeling of each individual subject.
- ✓Unlike conventional Markov models, where transition probabilities depend solely on the current state, transition probabilities can vary based on frequency of state occupancy or patients' background.

CONS

- ✓Because each subject performs a random walk, the uncertainty of the estimation results increases.
- ✓High computational load / Heavy computational burden

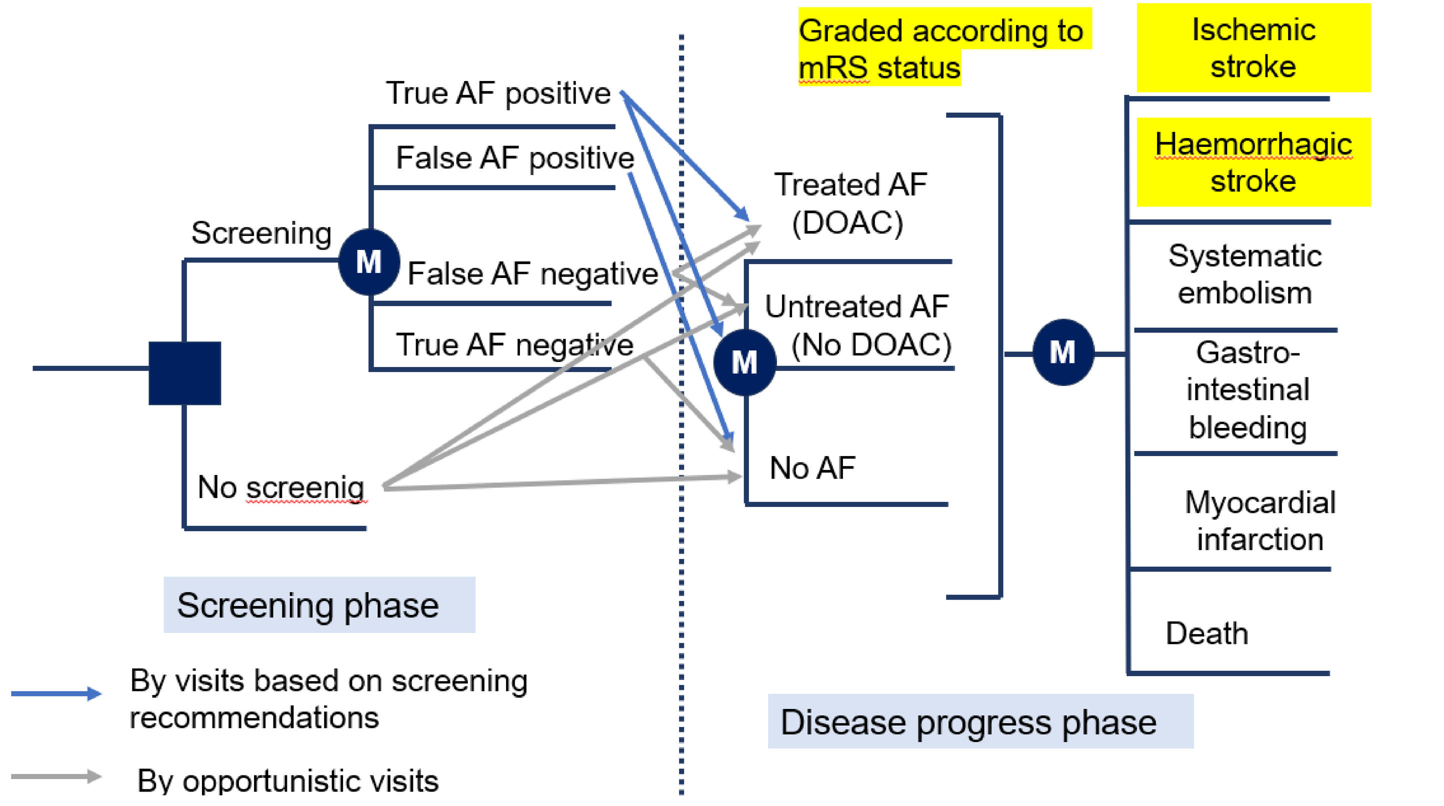
Data Used and Corresponding Parameter Estimates

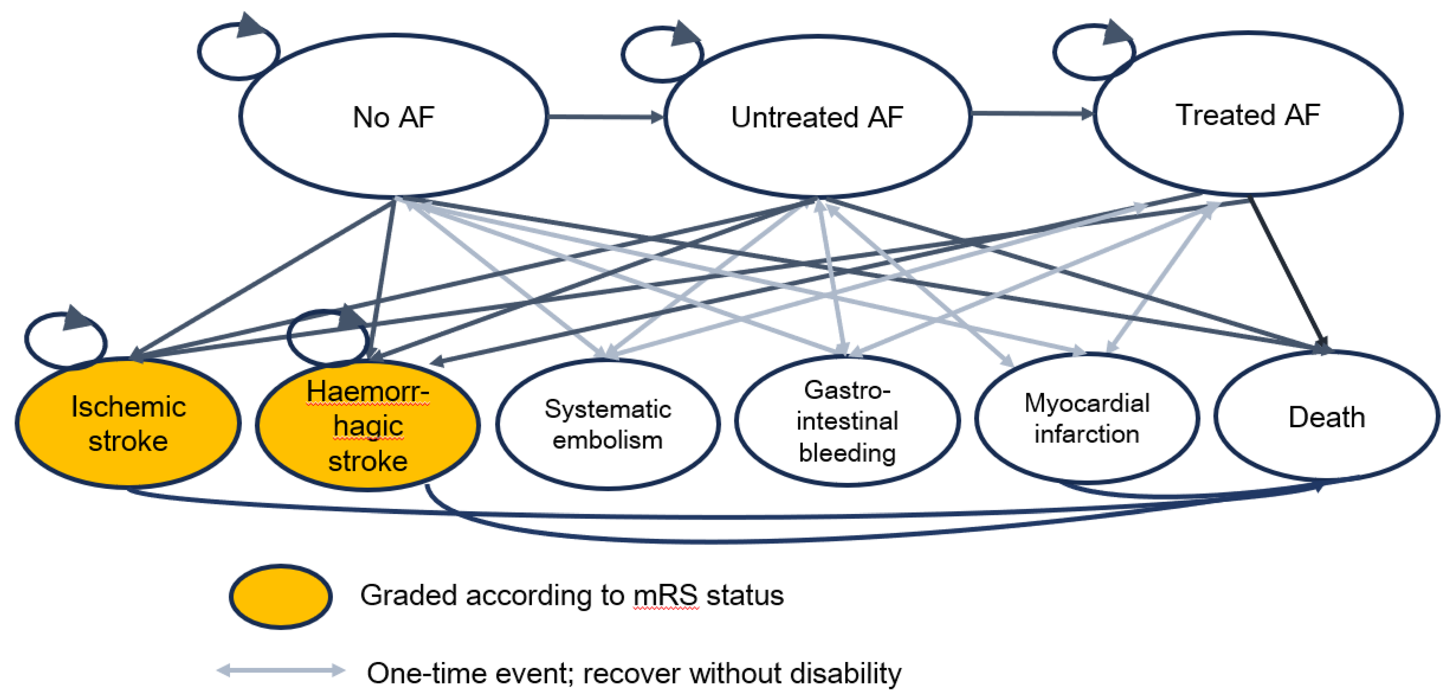
Data	Parameter
Vital Statistics of Japan	Baseline mortality rate
Observational studies targeting Japanese AF patients (**ANAFIE, SHINKEN, J-RHYTHM, Fushimi-AF**)	State transition probabilities
An observational study monitoring Japanese hypertensive patients with ECG-monitored blood pressure monitors (**Omron Heart Study**)	Detection rate of undiagnosed/silent AF by screening
Japan Stroke Patient Registry (**Japan Stroke Data Bank**)	Post-stroke QOL (estimated from mRS)

Object

To estimate, using a **microsimulation** approach, the cost-effectiveness of **screening with an ECG-monitored blood pressure monitor** to detect asymptomatic atrial fibrillation (AF) and **treating with direct oral anticoagulants (DOACs)**, compared with **opportunistic diagnosis and treatment of AF,** in a population of **elderly individuals with hypertension**.

Model Used





Results

Table1. Results of N=10,000 Microsimulation

Sex	Age	Strategy	Cost	Incremental Cost	QALY	Incremental QALY	ICER
Male	60	non-screening	¥2,691,895		17.269		
		screening	¥2,784,997	¥93,102	17.439	0.170	¥547,603
	65	non-screening	¥2,401,449		14.715		
		screening	¥2,516,862	¥115,413	14.847	0.132	¥876,843
	70	non-screening	¥2,148,409		12.200		
		screening	¥2,265,820	¥117,412	12.342	0.142	¥828,289
Female	60	non-screening	¥2,783,930		20.669		
		screening	¥2,892,052	¥108,122	20.813	0.144	¥750,090
	65	non-screening	¥2,593,693		18.063		
		screening	¥2,712,541	¥118,848	18.180	0.117	¥1,013,510
	70	non-screening	¥2,298,908		15.389		
		screening	¥2,320,371	¥21,463	15.523	0.135	¥159,541

Across all age and sex groups,

- ✓ ICERs were well below the threshold of 5 million JPY.
- ✓ Probabilistic sensitivity analysis demonstrated
  - ✓ the screening strategy was cost-effective in over 78% at threshold of 5 million yen per QALY
  - ✓ the screening strategy more acceptable at a willingness-to-pay of 2 million yen or higher

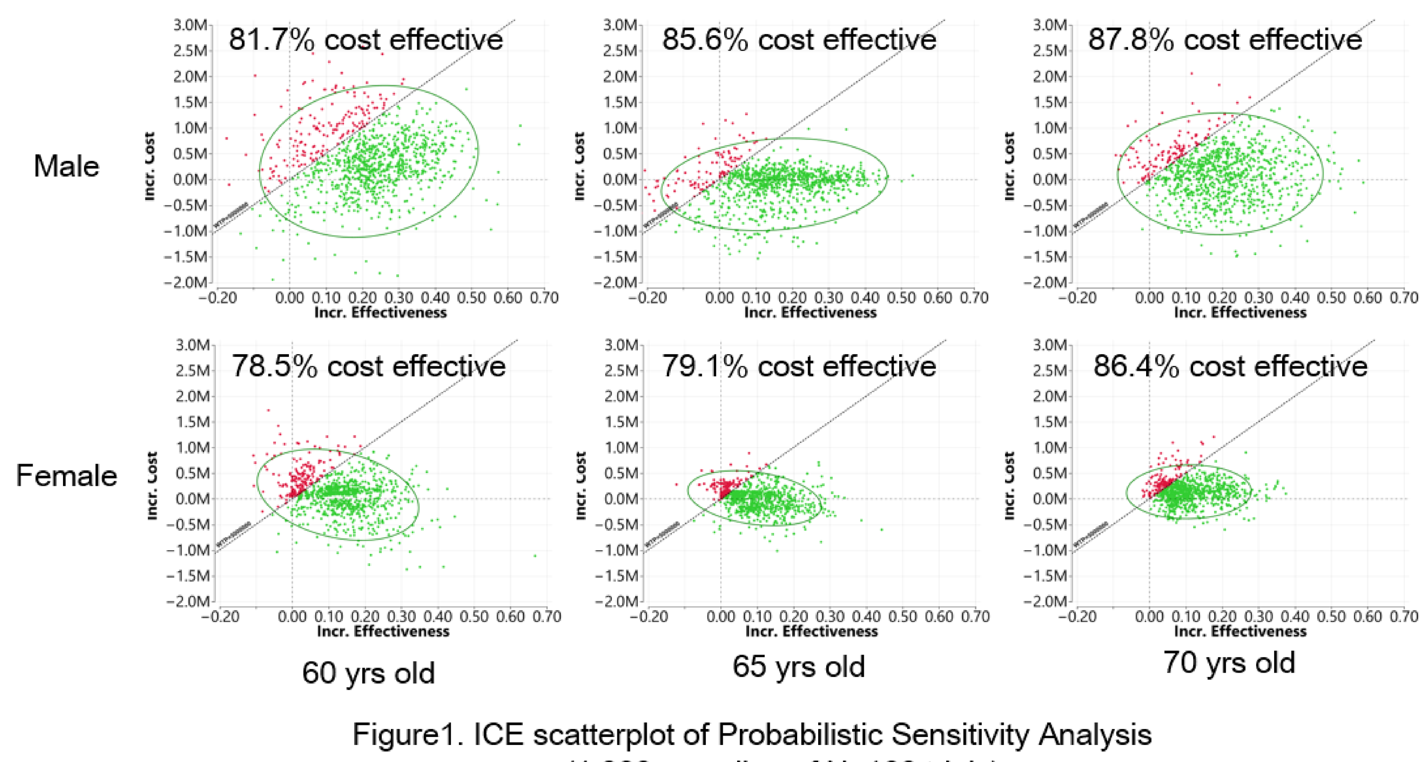


Figure1. ICE scatterplot of Probabilistic Sensitivity Analysis (1,000 sampling of N=100 trials)

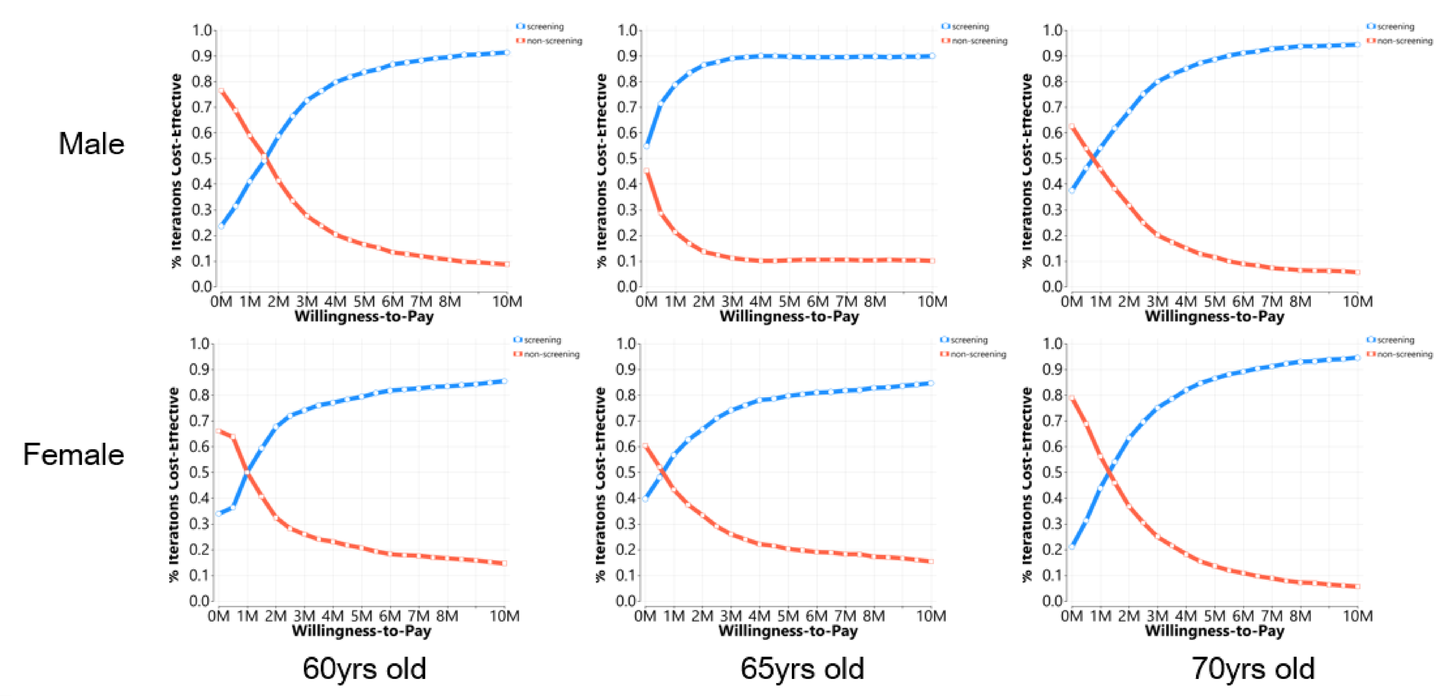


Figure2. Acceptability curve of Probabilistic Sensitivity Analysis (1,000 sampling of N=100 trials)

Conclusion

This microsimulation study demonstrated that systematic AF screening is highly cost- effective with the Japanese primary care setting.

Note: The parameter values used for estimation are available in the Supplemental Material.

Reference

1. Yoshimoto T et al. Impact of Previous Stroke on Clinical Outcome in Elderly Patients With Nonvalvular Atrial Fibrillation: ANAFIE Registry. Stroke. 2022;53(8):2549-2558.
2. Editorial Committee for the Japan National Cerebral and Cardiovascular Center Stroke Data Bank 2021. Stroke Data Bank 2021. Nakayama Shoten.
3. Takashima, N et al. Incidence, Management and Short-Term Outcome of Stroke in a General Population of 1.4 Million Japanese- Shiga Stroke Registry. Circulation Journal, 2017;81(11):1636-1646
4. Suzuki S et al.. Recent mortality of Japanese patients with atrial fibrillation in an urban city of Tokyo. J Cardiol. 2011;58(2):116-23.
5. Suzuki S et al. Incidence of ischemic stroke in Japanese patients with atrial fibrillation not receiving anticoagulation therapy--pooled analysis of the Shinken Database, J-RHYTHM Registry, and Fushimi AF Registry. Circ J. 2015;79(2):432-8.
6. Senoo K et al. Relationship Between Screening-Detected Atrial Fibrillation and Blood Pressure Levels in Elderly Hypertensive Patients: The OMRON Heart Study. Thromb Haemost. 2025;125(6):545-552.

Annual transition probability

	Age	No AF -> Ischemic Stroke	No AF -> Haemorrhagic Stroke	No AF -> Death	Treated AF -> Ischemic Stroke	Treated AF -> Haemorrhagic Stroke	Treated AF -> Systematic Embolism	Treated AF -> Gastro-intestinal bleeding	Treated AF -> Myocardial infarction	Treated AF -> Death	Untreated AF -> Ischemic Stroke	Untreated AF -> Haemorrhagic Stroke
Male	62	0.14%	0.08%	0.78%	0.44%	0.13%	0.01%	0.80%	0.37%	0.88%	0.70%	0.09%
	67	0.33%	0.08%	1.30%	0.49%	0.14%	0.01%	0.90%	0.37%	1.47%	0.78%	0.10%
	72	0.33%	0.08%	2.24%	0.49%	0.14%	0.01%	0.90%	0.37%	2.54%	0.78%	0.10%
	77	0.52%	0.16%	3.46%	1.01%	0.30%	0.03%	1.85%	0.37%	3.94%	1.61%	0.20%
	82	0.52%	0.16%	6.11%	1.01%	0.30%	0.03%	1.85%	0.37%	7.02%	1.61%	0.20%
	87	0.82%	0.22%	11.20%	1.29%	0.38%	0.04%	2.35%	0.37%	13.07%	2.07%	0.26%
	92	0.82%	0.22%	19.42%	1.29%	0.38%	0.04%	2.35%	0.37%	23.35%	2.07%	0.26%
	97	0.82%	0.22%	31.81%	1.29%	0.38%	0.04%	2.35%	0.37%	40.40%	2.07%	0.26%
	100	0.00%	0.00%	100.00%	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%	0.00%	0.00%
Female	62	0.05%	0.04%	0.35%	0.44%	0.13%	0.01%	0.74%	0.37%	0.39%	0.71%	0.09%
	67	0.14%	0.06%	0.54%	0.50%	0.15%	0.01%	0.82%	0.37%	0.61%	0.79%	0.10%
	72	0.14%	0.06%	0.92%	0.50%	0.15%	0.01%	0.82%	0.37%	1.04%	0.79%	0.10%
	77	0.34%	0.15%	1.51%	1.02%	0.30%	0.03%	1.70%	0.37%	1.71%	1.63%	0.21%
	82	0.34%	0.15%	3.04%	1.02%	0.30%	0.03%	1.70%	0.37%	3.46%	1.63%	0.21%
	87	0.76%	0.23%	6.41%	1.31%	0.38%	0.04%	2.16%	0.37%	7.36%	2.09%	0.26%
	92	0.76%	0.23%	12.82%	1.31%	0.38%	0.04%	2.16%	0.37%	15.05%	2.09%	0.26%
	97	0.76%	0.23%	24.57%	1.31%	0.38%	0.04%	2.16%	0.37%	30.17%	2.09%	0.26%
	100	0.00%	0.00%	100.00%	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%	0.00%	0.00%

Linear interpolation for ages
other than those shown

Annual transition probability

	Age	Untreated AF -> Systematic Embolism	Untreated AF -> Gastro-intestinal bleeding	Untreated AF -> Myocardial infarction	Untreated AF -> Death	Screening -> Treated AF (1st year)	Non-screening -> Treated AF (1st year)	Screening -> Untreated AF (1st year)	Non-Screening -> Untreated AF (1st year)	Screening : Untreated AF -> Treated AF	Non-screening : Untreated AF -> Treated AF	No AF -> Untreated AF
Male	62	0.02%	0.56%	0.45%	1.33%	1.60%	0.14%	4.08%	5.54%	28.13%	2.48%	0.75%
	67	0.02%	0.63%	0.45%	2.23%	1.60%	0.14%	4.08%	5.54%	28.13%	2.48%	0.75%
	72	0.02%	0.63%	0.45%	3.83%	1.95%	0.25%	7.97%	9.67%	19.64%	2.48%	0.75%
	77	0.04%	1.30%	0.45%	5.91%	1.95%	0.25%	7.97%	9.67%	19.64%	2.48%	0.75%
	82	0.04%	1.30%	0.45%	10.45%	1.92%	0.20%	6.28%	8.00%	23.40%	2.48%	0.75%
	87	0.05%	1.65%	0.45%	19.15%	1.92%	0.20%	6.28%	8.00%	23.40%	2.48%	0.75%
	92	0.05%	1.65%	0.45%	33.21%	1.92%	0.20%	6.28%	8.00%	23.40%	2.48%	0.75%
	97	0.05%	1.65%	0.45%	54.40%	1.92%	0.20%	6.28%	8.00%	23.40%	2.48%	0.75%
	100	0.00%	0.00%	0.00%	100.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.75%
Female	62	0.02%	0.52%	0.45%	0.59%	1.08%	0.07%	1.61%	2.62%	40.20%	2.48%	0.75%
	67	0.02%	0.58%	0.45%	0.92%	1.08%	0.07%	1.61%	2.62%	40.20%	2.48%	0.75%
	72	0.02%	0.58%	0.45%	1.57%	1.34%	0.12%	3.45%	4.67%	27.97%	2.48%	0.75%
	77	0.04%	1.19%	0.45%	2.59%	1.34%	0.12%	3.45%	4.67%	27.97%	2.48%	0.75%
	82	0.04%	1.19%	0.45%	5.20%	1.48%	0.16%	4.77%	6.09%	23.65%	2.48%	0.75%
	87	0.05%	1.51%	0.45%	10.95%	1.48%	0.16%	4.77%	6.09%	23.65%	2.48%	0.75%
	92	0.05%	1.51%	0.45%	21.92%	1.48%	0.16%	4.77%	6.09%	23.65%	2.48%	0.75%
	97	0.05%	1.51%	0.45%	42.02%	1.48%	0.16%	4.77%	6.09%	23.65%	2.48%	0.75%
	100	0.00%	0.00%	0.00%	100.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.75%

Linear interpolation for ages other than those shown

Proportion of modified Rankin Scale at discharge

Disease	Age	0	1	2	3	4	5	6
Ischemic Stroke	60-64	24.1%	35.5%	16.9%	8.1%	10.0%	3.4%	2.0%
	65-74	19.4%	28.8%	17.2%	10.4%	14.5%	6.8%	2.9%
	75-	10.2%	17.9%	13.4%	13.2%	22.1%	16.3%	6.9%
Haemorrhagic Stroke	60-64	8.9%	19.1%	14.4%	10.2%	25.6%	11.2%	10.6%
	65-74	6.8%	14.7%	11.8%	11.4%	26.8%	15.9%	12.6%
	75-	3.2%	7.2%	7.3%	9.8%	26.6%	25.9%	20.0%

Upon recurrence, the proportion is calculated under the condition that the mRS remains unchanged or worsens from the current baseline.

Cost by modified Rankin Scale

		0	1	2	3	4	5	6
QOL	point estimate	0.9	0.85	0.74	0.62	0.41	0.28	0
	SD	0.11	0.14	0.18	0.21	0.21	0.19	0
Acute phase costs (3 months)	Ischemic Stroke	¥1,013,427	¥1,013,427	¥1,013,427	¥1,681,015	¥1,681,015	¥1,798,141	¥899,071
	Haemorrhagic Stroke	¥1,433,231	¥1,433,231	¥1,433,231	¥2,109,022	¥2,109,022	¥2,063,411	¥1,031,706
Annual long-term care costs (yen)	point estimate	¥783,082	¥1,678,390	¥3,325,272	¥4,051,661	¥4,382,666	¥4,879,549	NA
	SD	¥115,730	¥120,586	¥1,240,701	¥702,166	¥906,413	¥947,524	NA

During the acute phase, QOL decreases by 0.14 (95% CI: 0.12, 0.16).
Acute phase costs were calculated as the point estimate multiplied by 1.2 to construct the 95% confidence interval.

Other Costs

Screening Cost		¥29,800
Annual cost of DOACs		¥97,129
One-time event	Systematic embolism	¥1,111,411
	Gastro-intestinal bleeding	¥613,693
	Myocardial infarction	¥2,133,181

Following a hemorrhagic stroke, DOACs were discontinued.
Following SE or MI, DOAC therapy was continued.
Following GI bleeding, 71% of patients resumed DOACs after a 3-month temporary discontinuation, while 29% permanently discontinued DOACs.

Discount rate **2%**

Parameters for Probabilistic Sensitivity Analysis

Parameters	Distribution	mean	sd	alpha	beta
Relative risk of death for untreated AF to non-AF	LogNormal	0.536	0.179		
Hazard ratio of death for treated AF to Warfarin	LogNormal	-0.163	0.046		
Hazard ratio of death for Warfarin to untreated AF	LogNormal	0.255	0.080		
Hazard ratio of death for ischemic stroke to treated AF	LogNormal	0.131	0.051		
Hazard ratio of death for haemorrhagic stroke to treated AF	LogNormal	0.000	0.214		
incidence rate of ischemic stroke for nonAF male 60-64	Gamma			140	98,522
incidence rate of ischemic stroke for nonAF male 65-74	Gamma			236	71,429
incidence rate of ischemic stroke for nonAF male 75-84	Gamma			231	44,638
incidence rate of ischemic stroke for nonAF male 85-	Gamma			92	11,209
incidence rate of ischemic stroke for nonAF female 60-64	Gamma			53	100,000
incidence rate of ischemic stroke for nonAF female 65-74	Gamma			108	75,683
incidence rate of ischemic stroke for nonAF female 75-84	Gamma			202	59,133
incidence rate of ischemic stroke for nonAF female 85-	Gamma			227	30,019
incidence rate of haemorrhagic stroke for nonAF male 60-64	Gamma			82	98,558
incidence rate of haemorrhagic stroke for nonAF male 65-74	Gamma			60	71,429
incidence rate of haemorrhagic stroke for nonAF male 75-84	Gamma			72	44,637
incidence rate of haemorrhagic stroke for nonAF male 85-	Gamma			25	11,206
incidence rate of haemorrhagic stroke for nonAF female 60-64	Gamma			37	100,000
incidence rate of haemorrhagic stroke for nonAF female 65-74	Gamma			43	75,704
incidence rate of haemorrhagic stroke for nonAF female 75-84	Gamma			88	59,140
incidence rate of haemorrhagic stroke for nonAF female 85-	Gamma			70	30,017
incidence rate of ischemic stroke for tAF	Gamma			439	40,275
incidence rate of ischemic stroke for utAF	Gamma			77	4,425
incidence rate of haemorrhagic stroke for tAF	Gamma			131	40,938
incidence rate of haemorrhagic stroke for utAF	Gamma			10	4,545
incidence rate of systematic embolism for tAF	Gamma			13	43,333
incidence rate of systematic embolism for utAF	Gamma			2	5,000
incidence rate of gastrointestinal bleeding for tAF	Gamma			763	39,948
incidence rate of gastrointestinal bleeding for utAF	Gamma			59	4,403
hazard ratio of stroke/see for women to men	LogNormal	0.010	0.071		
hazard ratio of major bleeding for women to men	LogNormal	-0.083	0.087		
hazard ratio of stroke/see for 85+ to -84	LogNormal	0.247	0.074		
hazard ratio of major bleeding for 85+ to -84	LogNormal	0.239	0.092		
utility of acute stroke (minus)	Beta			134	836
utility of chronic stroke mRS=0	Beta			6	1
utility of chronic stroke mRS=1	Beta			5	1
utility of chronic stroke mRS=2	Beta			4	1
utility of chronic stroke mRS=3	Beta			3	2
utility of chronic stroke mRS=4	Beta			2	3
utility of chronic stroke mRS=5	Beta			1	3
cost of acute ischemic stroke mRS 0-2	Gamma			96	10,552
cost of acute ischemic stroke mRS 3-4	Gamma			96	17,503
cost of acute ischemic stroke mRS 5	Gamma			96	18,723
cost of acute ischemic stroke mRS 6	Gamma			96	9,361
cost of acute haemorrhagic stroke mRS 0-2	Gamma			96	14,923
cost of acute haemorrhagic stroke mRS 3-4	Gamma			96	21,960
cost of acute haemorrhagic stroke mRS 5	Gamma			96	21,485
cost of acute haemorrhagic stroke mRS 6	Gamma			96	10,742
cost of chronic stroke mRS=0	Gamma			46	17,103
cost of chronic stroke mRS=1	Gamma			194	8,664
cost of chronic stroke mRS=2	Gamma			7	462,921
cost of chronic stroke mRS=3	Gamma			33	121,688
cost of chronic stroke mRS=4	Gamma			23	187,462
cost of chronic stroke mRS=5	Gamma			27	183,993
cost of systematic embolism	Gamma			96	11,572
cost of GI bleeding	Gamma			96	6,390
cost of myocardial infarction	Gamma			96	22,211
prevalence of undetected AF for male 60-69 1st year	Beta			114	1892
prevalence of undetected AF for male 70-79 1st year	Beta			59	536
prevalence of undetected AF for male 80- 1st year	Beta			5	56
prevalence of undetected AF for female 60-69 1st year	Beta			13	470
prevalence of undetected AF for female 70-79 1st year	Beta			7	139
prevalence of undetected AF for female 80- 1st year	Beta			1	15
prevalence of possible AF for male 60-69	Beta			849	1157
prevalence of possible AF for male 70-79	Beta			307	288
prevalence of possible AF for male 80-	Beta			31	30
prevalence of possible AF for female 60-69	Beta			243	240
prevalence of possible AF for female 70-79	Beta			91	55
prevalence of possible AF for female 80-	Beta			11	5
prevalence of possible AF to diagnosed AF for male 1st year	Beta			25	249
prevalence of possible AF to diagnosed AF for female 1st year	Beta			4	73
prevalence of CHAD2>=2	Beta			12	17
prevalence of undetected AF to diagnosed AF in nonscreening	Gamma			115	1,917
incidence of undetected AF from non-AF(unknown)	Uniform			0.005	0.010
probability of DOAC discontinuation after GI bleeding	Beta			2	4
hazard ratio of stroke for 65-74 to -64	LogNormal	0.1133	0.3824		
hazard ratio of stroke for 75+ to -64	LogNormal	0.8372	0.3425		
hazard ratio of mi for treatedAF to untreatedAF	LogNormal	-0.1863	0.5200		
hazard ratio of ischemic stroke recurrence	LogNormal	0.8713	0.0771		
hazard ratio of haemorrhagic stroke recurrence	LogNormal	0.3365	0.1080		
cost of treated AF	Gamma			96	1,011