



Watchman In Asia Pacific (WASP) Registry 2 Year Outcomes

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Epidemiological Studies Have Demonstrated Significant Differences In **Ischemic Stroke Risk & Risk Of Bleeding** In **Asian Populations With NVAF** vs. Other Ethnicities¹⁻³

Increased stroke risk commencing from a **younger age** (from age 50 years) in Asians compared to non-Asians^{1,3}. This creates potential **increased duration of exposure to (N)OAC & long term compliance**

Rates of **under-treatment** with OAC remain stubbornly high in Asian countries despite the global penetration of NOAC into clinical practice⁴

Compared to non-Asians, Asians are at significantly **higher risk of warfarin-related intracranial bleeding** (HR = 4.06)²

Possible link between **macro- and micro-angiopathy** which are more prevalent in Asian populations (may be associated with an **increased risk of intracranial bleeding**)⁵

AF Poses A Considerable Threat To Health Care In Asia:

Under-treatment & High Stroke Rate Despite Treatment

AF in China

The **stroke rate** in Chinese *AF patients ranged from 6% to 13%*^{3,4}

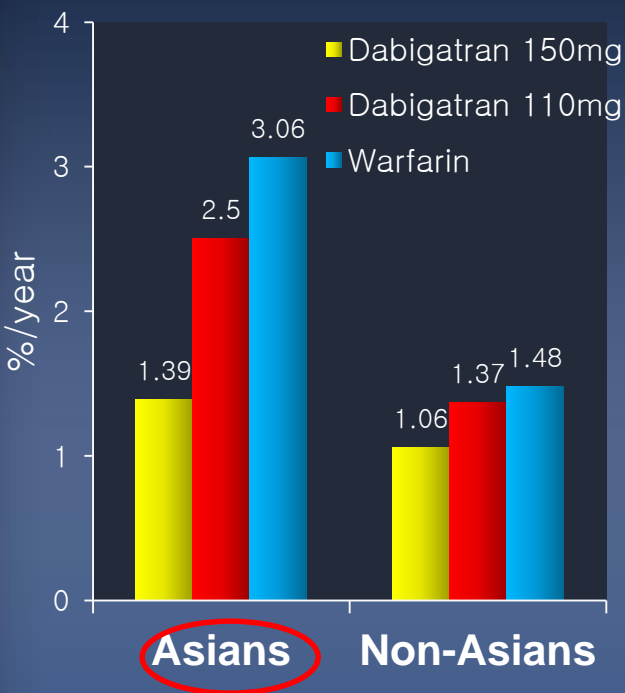
Large-cohort study also reported a **increasing trend in the incidence of AF and AF-related stroke** over the past decade³

Despite the high stroke incidence, **only 4.1% of Chinese pts with AF are currently under warfarin** therapy¹⁻³

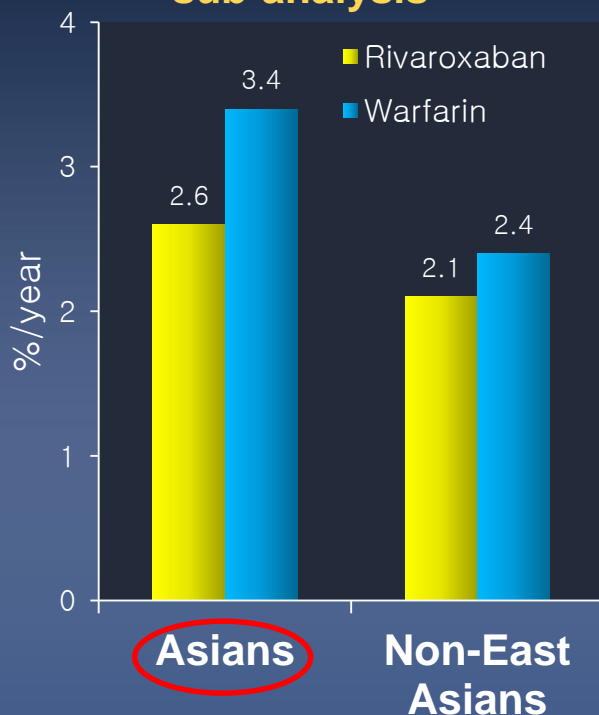
AF patients taking warfarin did not have lower stroke rate compared to patients taking Aspirin, probably due to a poor INR control⁵

Annual Risk of Stroke & Systemic Embolization for Asians & Non-Asians in 3 Clinical Trials of NOAC

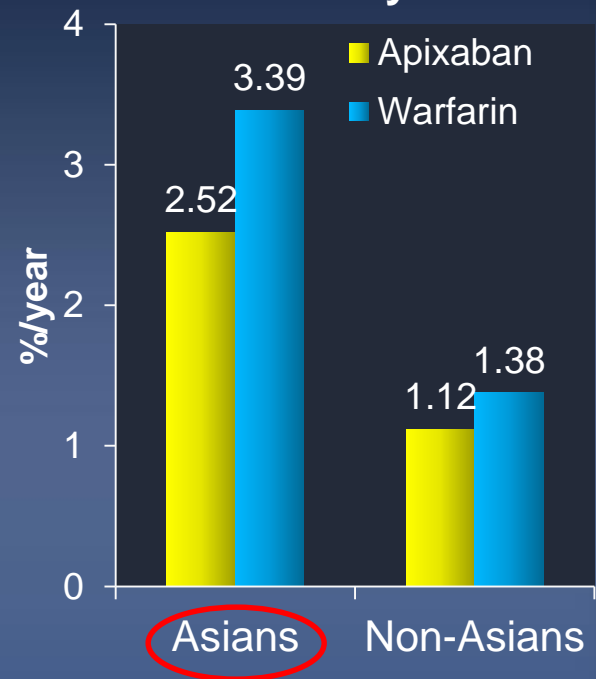
RE-LY trial & RE-LY Asia sub-analysis



ROCKET AF trial & ROCKET AF East Asia sub-analysis



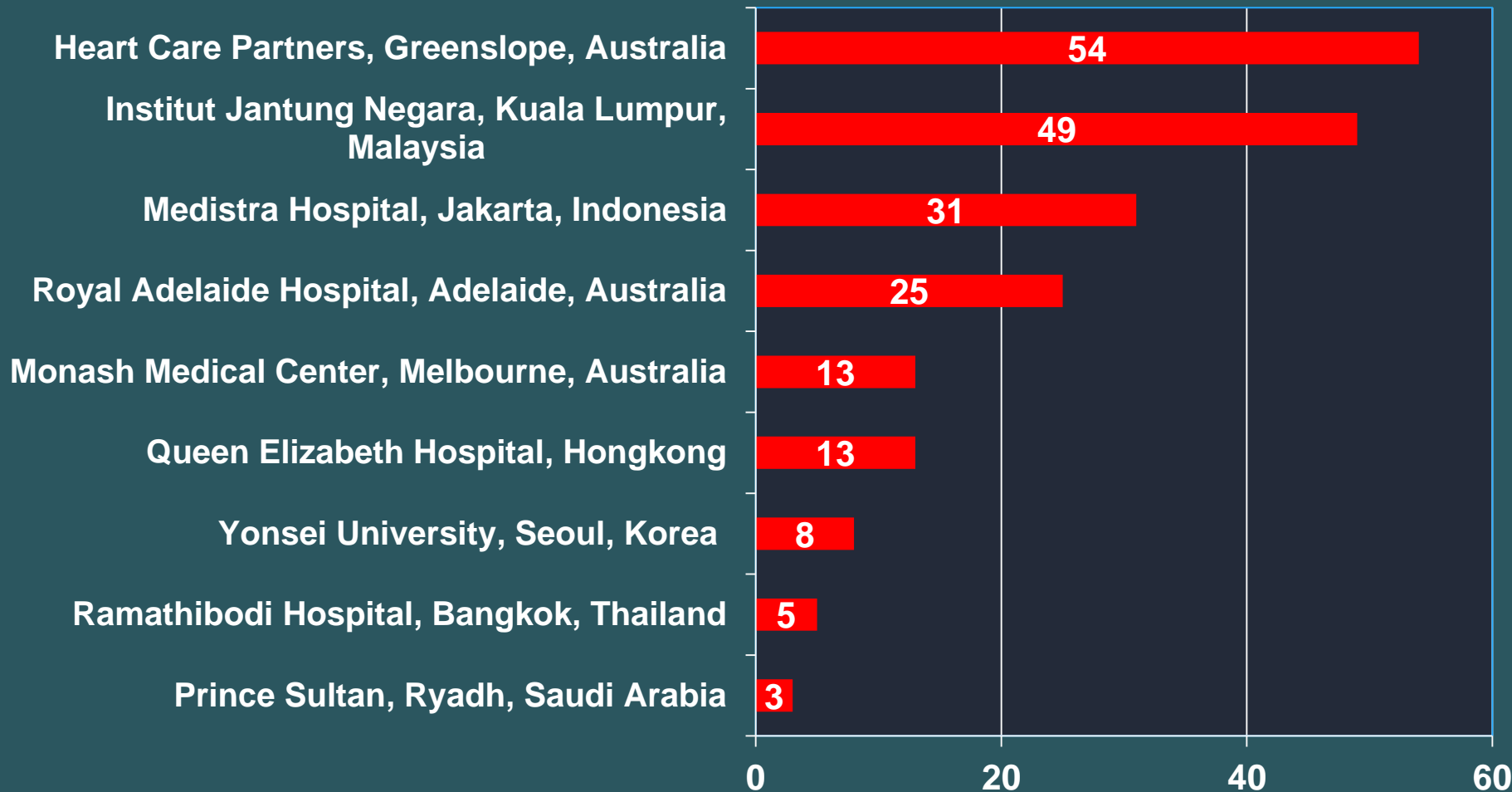
ARISTOTLE trial & ARISTOTLE Asia sub-analysis



Big issue: higher risk of stroke & systemic embolization in Asian patients on (N)OAC

WATCHMAN™ Asia Pacific Study (WASP)

Asia Pacific Prospective Multicentre Non-randomized Cohort Study*
201 pts enrolled between January 2014 and October 2015 across 7 countries

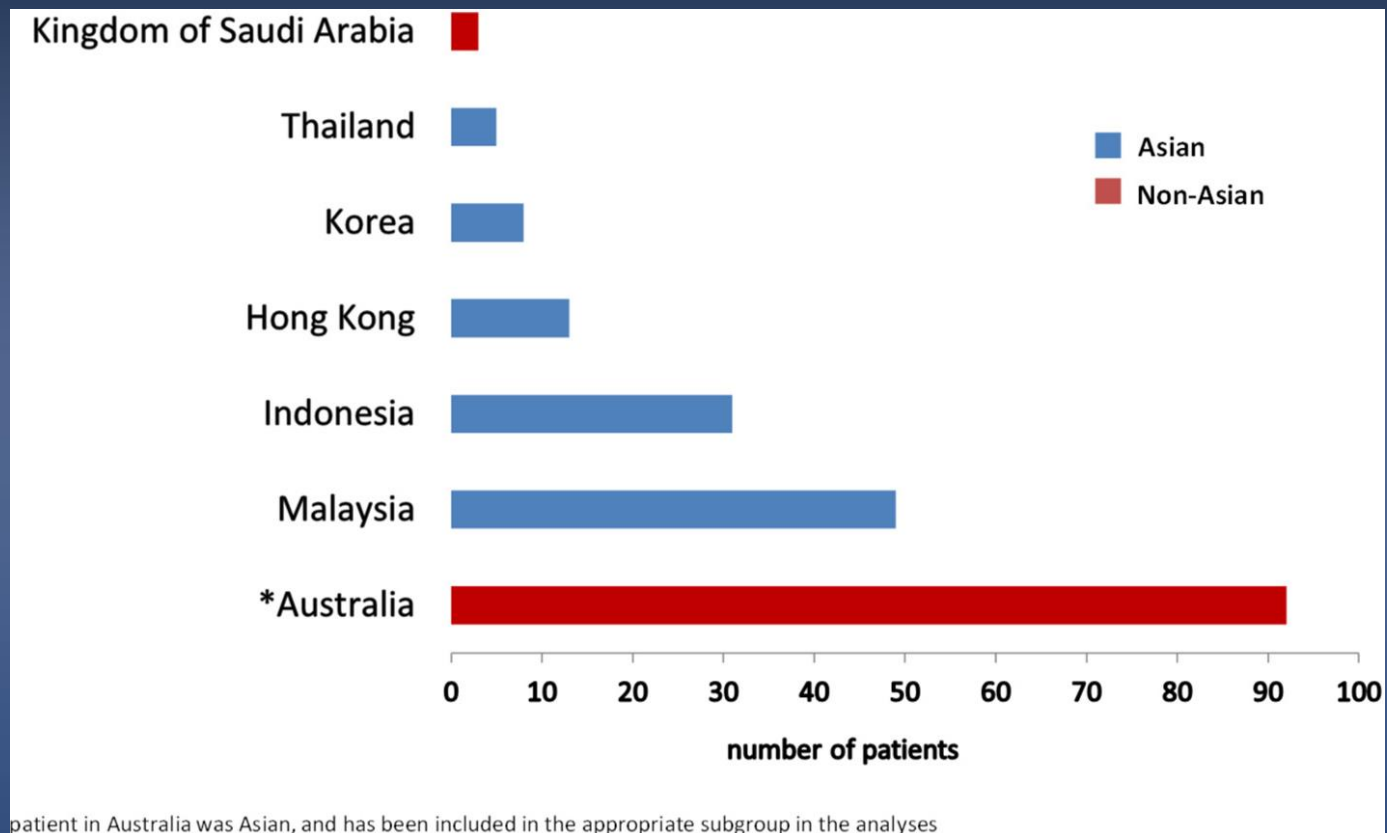


WATCHMAN™ Asia Pacific Study (WASP)

Asia Pacific Prospective Multicentre Non-randomized Cohort Study*
201 pts enrolled between January 2014 and October 2015 across 7 countries

Breakdown of study cohort by enrolling country

with **Asian patients** in **blue** and **Non-Asian patients** in **red**



Note: *One Australian patient was Asian.

WATCHMAN™ Asia Pacific Study (WASP)

	Asian N=107	Non Asian N=94	P value
Age	70.7 ± 9.4	70.8 ± 9.4	0.95
Age >80 yrs old	14.0%	17.0%	0.56
Male	62.6%	72.3%	0.18
CHADS ₂ Score	2.5 ± 1.3	2.4 ± 1.4	0.49
CHA₂DS₂- score	4.1 ± 1.7	3.7 ± 1.6	0.08
CHA ₂ DS ₂ - score (%)			0.25
≤ 1 (%)	8.4	7.4	
2-3 (%)	29.9	41.5	
≥ 4 (%)	61.7	51.1	
HAS-BLED score	2.2 ± 1.3	2.1 ± 0.9	0.66
HAS-BLED score (%)			0.28
< 3 (%)	65.4	73.4	
> 3 (%)	34.6	26.6	
Paroxysmal AF pattern	54.2%	47.3%	0.40

WATCHMAN™ Asia Pacific Study (WASP)

	Asian N=107	Non Asian N=94	P value
CHF (%)	20.6	10.6	0.08
Hypertension (%)	84.1	83.0	0.85
Age ≥ 75 (%)	38.3	34.0	0.56
Age 65-74 (%)	43.0	44.7	0.89
Diabetes (%)	46.7	19.1	< 0.0001
History of TIA/stroke (%)	30.8	45.7	0.04
Vascular disease	39.3	23.4	0.02
Abnormal renal function (%)	14.0	7.4	0.18
Abnormal liver function (%)	2.8	1.1	0.62
Hx ischemic /hemorrhagic stroke (%)	28.0	35.1	0.29
Prior major / predisposition to bleeding (%)	19.6	18.1	0.86
Labile INR (%)	20.6	4.3	0.0006
Concomitant use of drug (%)	33.6	50.0	0.02
Alcohol abuse (%)	2.8	13.8	0.007
LV dysfunction (LVEF ≤ 40%)(%)	7.5	5.4	0.58

WATCHMAN™ Asia Pacific Study (WASP): Procedural Results

	Asian N=107	Non Asian N=94	P value
Successful implant	99.1%	97.9%	0.60
LAA seal			
- Complete seal or jet < 5 mm	100%	100%	NS
LAA diameter			
- Mean \pm SD	23.4 \pm 4.1	21.2 \pm 1.3.2	<0.0001
- Median	23.00	21.50	
Last device size used (mm)			
- Mean \pm SD	27.4 \pm 3.4	25.3 \pm 3.2	<0.0001
- Median	27	24	
Compression of last device size used			
- Mean \pm SD	17 7%	17 6%	0.93
- Median	16%	17%	

WATCHMAN™ Asia Pacific Study (WASP)

Implant Procedure Safety

Device/procedure related post implant SAEs	Asian No of events	Non Asian No of events
Pericardial effusion requiring intervention	2	0
Hypotension	0	1
Vascular access major bleeding	0	1
Pulmonary edema	0	1
Oesophageal tear due to implant TEE causing death day 32	1	0
Femoral AV fistula	1	0
Device embolization	0	0
Stroke	0	0

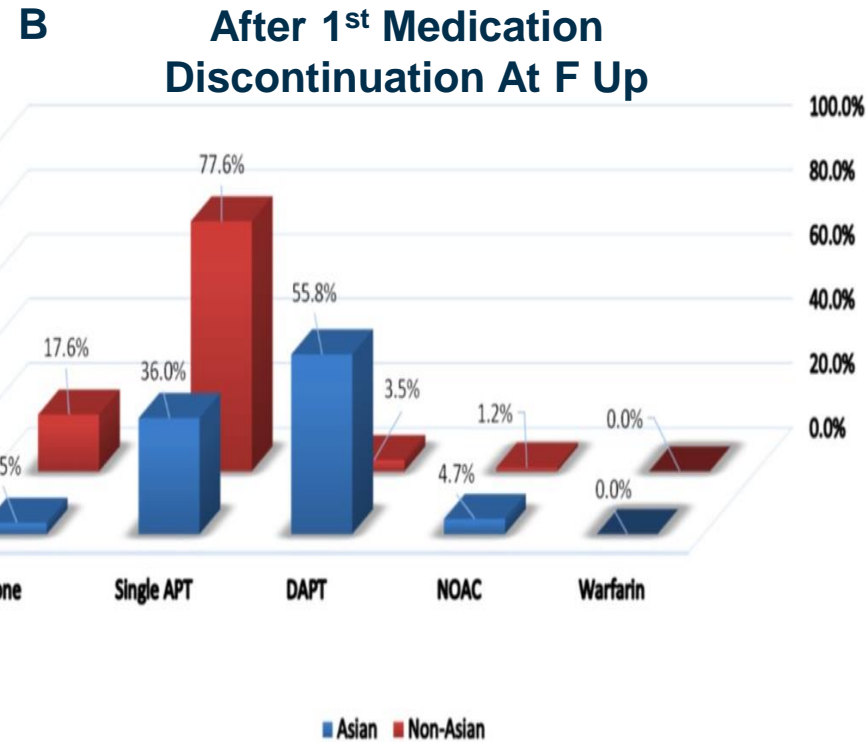
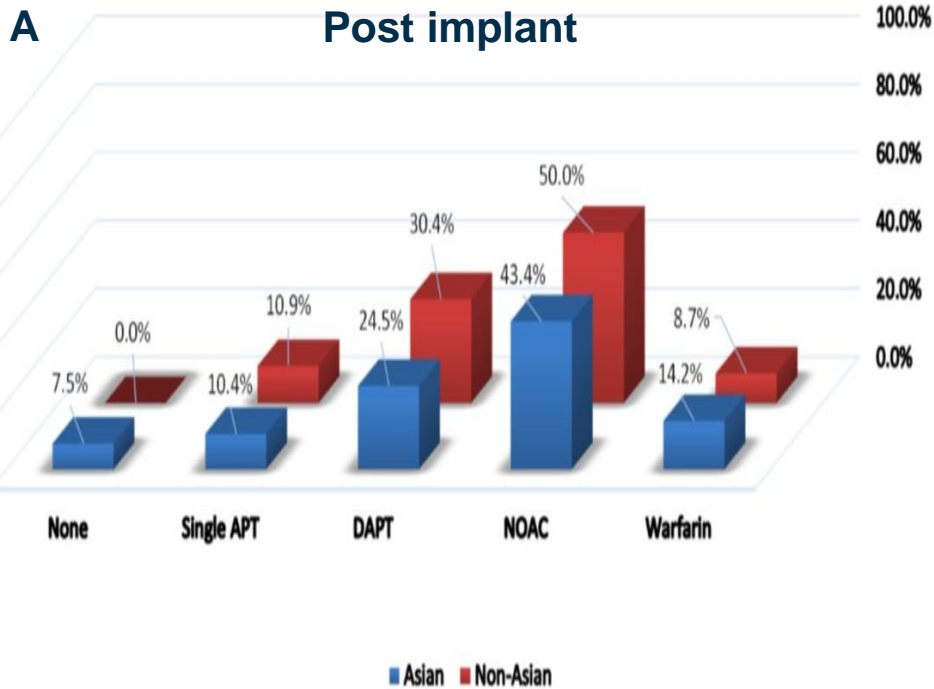
Device/procedure related post implant SAEs	Asians KM event rate	Non Asian KM event rate	All pts KM event rate
Kaplan-Meier event rate 7 days	2.9% (0.8, 7.5%)	3.2% (0.9, 8.3%)	3.0% (1.2, 6.1%)
Kaplan-Meier event rate 30 days	3.8% (1.3, 8.8%)	3.2% (0.9, 8.3%)	3.5% (1.6, 6.8%)

WATCHMAN™ Asia Pacific Study (WASP): Imaging On Follow Up

	Asian N=107	Non Asian N=94
Follow up imaging	84.9%	88%
- TEE	90.7%	100%
- CT scan	9.3%	0%
Device embolization	0%	0%
Successful LAA closure with residual leak < 5 mm	100%	100%
Device associated thrombus	2	3
- Neurological sequelae	0	0

WASP : Medications

Post Implant & At First Medication Discontinuation During Follow-up Visit



Medications used by subjects (A) post-implant, & (B) at first medication discontinuation follow-up visit.

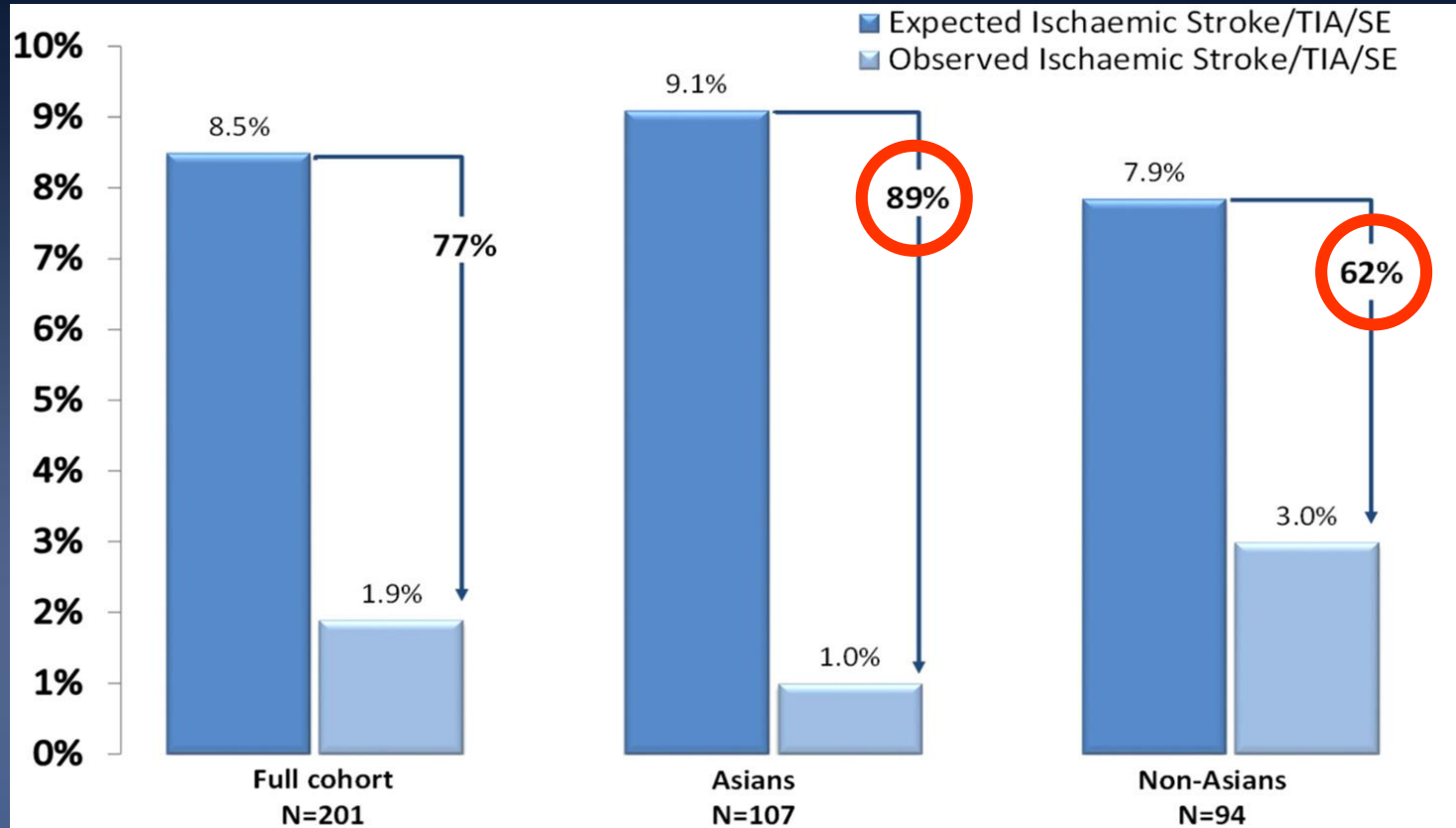
Single APT = single-antiplatelet therapy, DAPT = dual-antiplatelet therapy, NOAC = novel oral anticoagulant

WASP: Event Rates Per Patient Years

	Asian n=107		Non-Asian n=94		
Event	Rate Per 100 Pt-Yrs	95% CI	Rate Per 100 Pt-Yrs	95% CI	P-value (Asian vs Non-Asian)
Death	5.04	(2.71-9.36)	1.16	(0.29-4.63)	0.06
Ischaemic Stroke SAE	1.02	(0.25-4.06)	2.39	(0.90-6.36)	0.32
Ischaemic Stroke/TIA/SE SAE	1.02	(0.25-4.06)	3.02	(1.26-7.25)	0.19
Major Bleeding SAE	1.03	(0.26-4.11)	3.68	(1.65-8.20)	0.12
Non-Procedure or Device- Related Major Bleeding SAE	0.51	(0.07-3.65)	3.03	(1.26-7.28)	0.11

Ischemic Stroke In WASP

Expected vs Observed Event Rates per 100 Patient Years

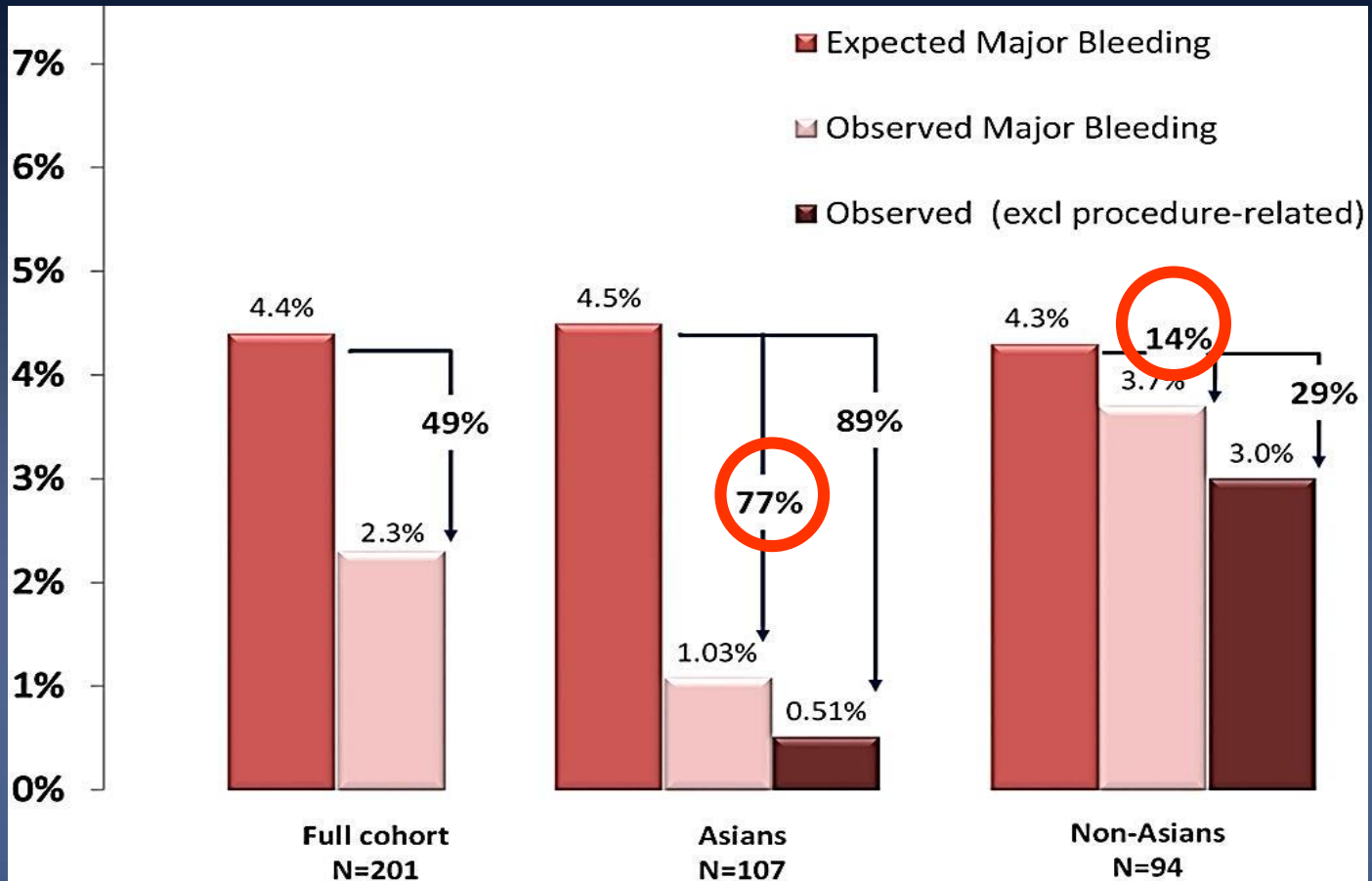


Effectiveness in stroke reduction vs. estimated in the absence of therapy for comparable CHA₂DS₂-VASc scores based on Friberg et al. EHJ 2012

**77% relative risk reduction for the overall population,
89% reduction for Asian patients & 62% reduction for non-Asians**

Bleeding Events In WASP

Expected vs Observed Event Rates per 100 Patient Years



49% relative risk reduction for bleeding events but a **more pronounced relative risk reduction in Asian subjects** as compared with non-Asians (77% versus 14%)

WASP: Serious Major Bleeding Events

	Days (Post-Implant)	Medication at time of event
Asian (n=107)		
Pericardial tamponade	0	aspirin
Gastrointestinal	74	DAPT
Non-Asian (n=94)		
Vascular Access	0	DAPT
Gastrointestinal†	1	NOAC
Gastrointestinal†	38	NOAC
Gastrointestinal	23	Warfarin
Gastrointestinal	72	NOAC
Varicose vein‡	102	aspirin
Gastrointestinal	555	aspirin
Gastrointestinal‡	561	aspirin

†, ‡ same patient experienced 2 major bleeding events

Guidelines & Recommendations On LAA Closure With The Watchman Device™

Guideline	Recommendation to consider LAAC	Class	Level of evidence
ESC AF Guideline 2016 ¹	Pts with high stroke risk & contraindication for long term OAC	IIb	B
EHRA/EAPCI 2014 ² LAAC Expert Consensus	Pts with high bleeding risk (HASBLED > 3), contraindications for (D)OACs or based on informed pts preference	NA	NA
ESC/EACTS Guidelines on Myocardial Revascularization 2014 ³	Pts with high stroke risk who are contraindicated for long term antiplatelet & OAC therapy	IIb	B
AHA/ASA 2014 Stroke Guidelines ⁴	Pts with high stroke risk who are unsuitable for anticoagulation	IIb	B
FDA label (March 2015)	Non-valvular AF pts eligible for OAC who have an appropriate reason to seek a non-pharmacological alternative to warfarin		

(D)OACs: (direct) oral anticoagulants; OAC: oral anticoagulation; NA: not applicable

1. Kirchhof P, et al. European Heart Journal (2016) 37, 2893–2962;
2. Meier B, et al. EuroIntervention 2014;10: 1109-1125;
3. Windecker S, et al. Eur Heart J 2014;35:2541-2619;
4. Meschia JF, et al. Stroke 2014;45:3754-3852;
5. Maisel WH. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf13/P130013a.pdf.

Summary

1. Epidemiological studies have demonstrated **significant differences in ischemic stroke risk & risk of bleeding (including hemorrhagic stroke) in Asian populations** with non-valvular AF compared with other ethnicity
2. **Real world experience with Watchman LAAC in Asia-Pacific** region has shown high successful implant rate, low peri-procedural risk, & efficacious stroke prevention with low bleeding risk on **long term follow up**
3. Another notable finding was a **larger mean LAA ostial diameter & median device size used in Asian patients** compared to non-Asians. This is important as LAA size was recognized as **an independent risk factor for stroke** in the SPAF study
4. Current Clinical Guidelines support the use of LAA device closure for patients with high stroke risk & contraindications to long term (N)OAC. The **current WASP study provides additional evidence that the Guidelines are also directly applicable to patients of Asian ethnicity**
5. As **LAA closure** provides life-long stroke prophylaxis without the need for daily OAC, it is even **more attractive to use in Asian patients.**