Low-Burden Atrial Fibrillation: Known Unknowns and Clinical Challenges for Stroke Prevention

Session:
ATRIAL FIBRILLATION BURDEN:
AN APPROVABLE INDICATION?
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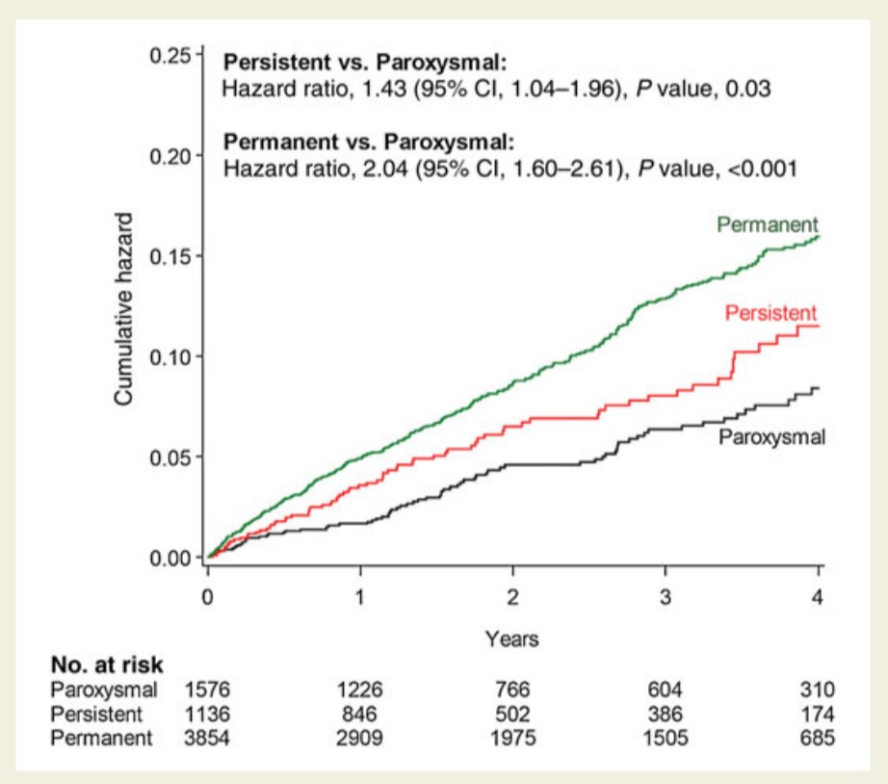
Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

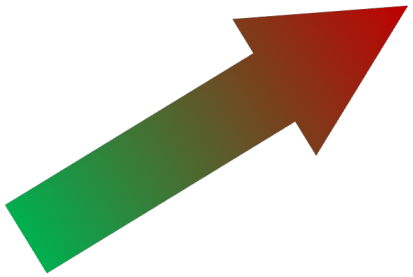
McMaster University

Stroke Risk is Proportional to AF Burden

Clinical, ECG-detected AF



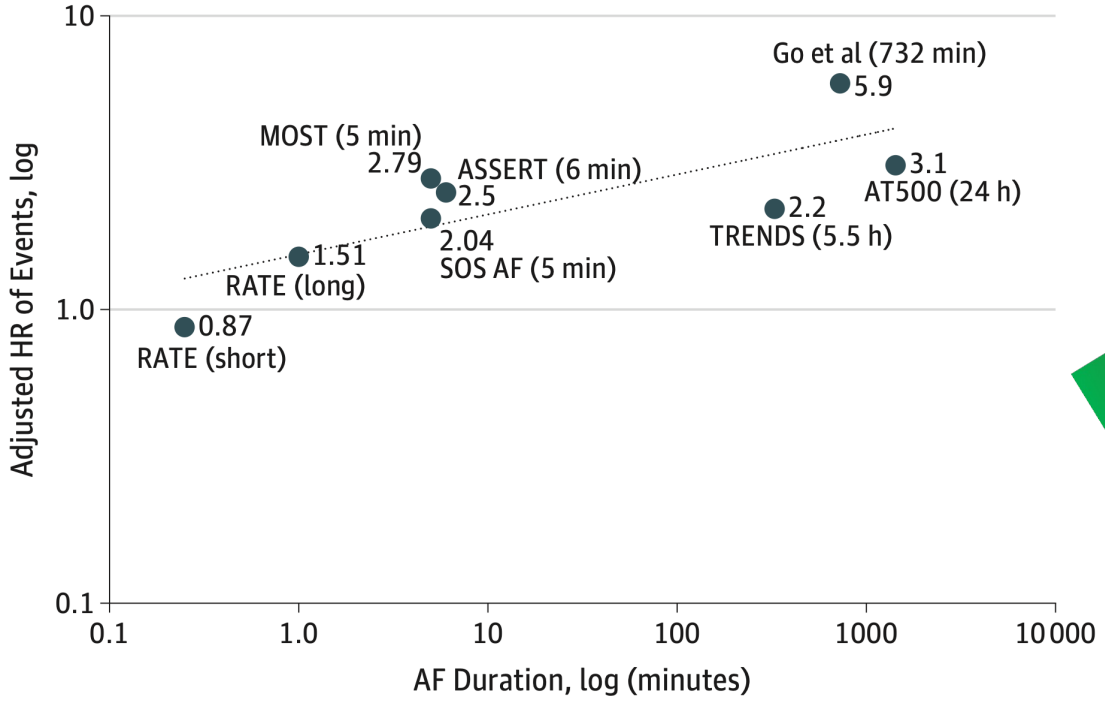
Gradient of Risk



Vanassche T *Eur Heart J.* 2015;281

Stroke Risk is Proportional to AF Burden

Figure. Estimates of Increased Stroke Risk According to the Burden of Paroxysmal Atrial Fibrillation Have Varied Significantly



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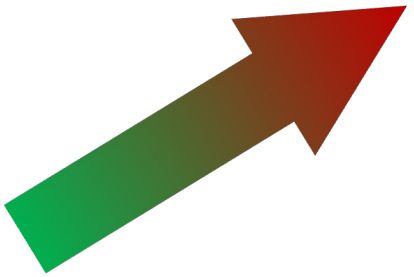
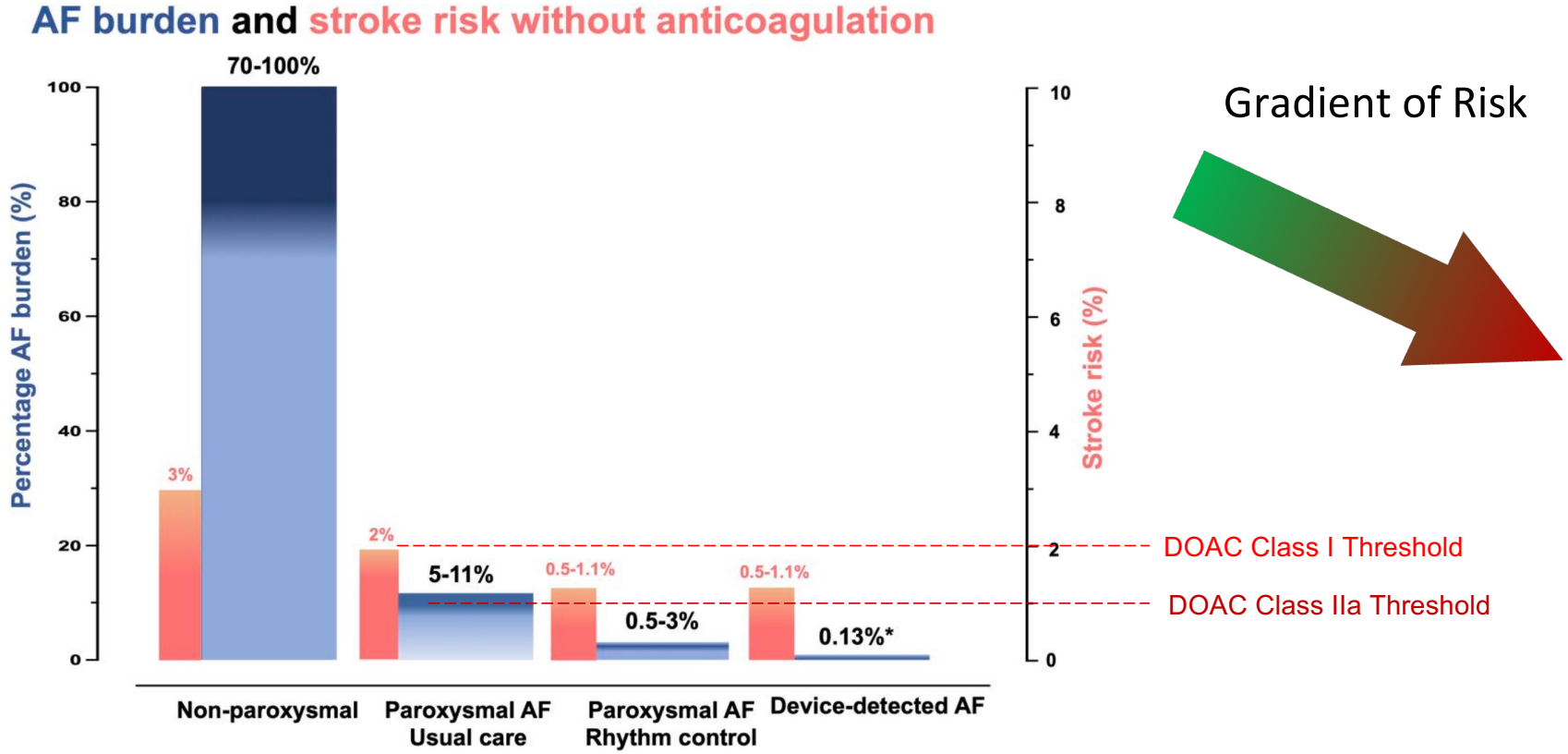


22nd Global Cardio Vascular Clinical Trialists Forum CVCT

Steinberg & Piccini JAMA Cardiology 2018

Stroke Risk is Proportional to AF Burden

Multi-dimensional-View



Becher et al. Eur Heart J 2024

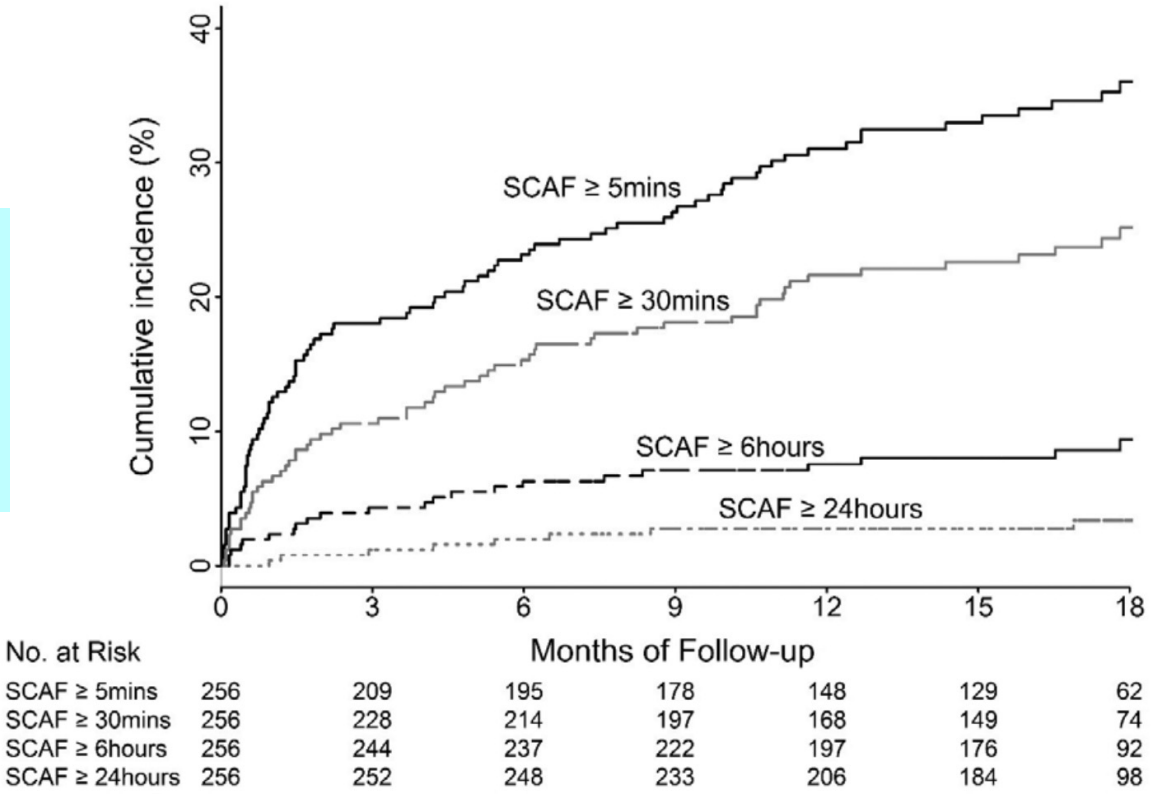
Clinical Challenges with Low Burden Atrial Fibrillation

- What are the burden cut-offs for clinical decision making?
- How do burden cut-offs translate across modalities?
- What's the interplay of AF burden with other risk factors?
- How do we account for the dynamic nature of AF burden?
- With safer therapies, could our risk thresholds change?

Yield of AF Detection Increases with Monitoring Intensity

ASSERT-II

CHA_2DS_2-VASc ≥2
Implantable Loop Recorder



No. at Risk							
SCAF ≥ 5mins	256	209	195	178	148	129	62
SCAF ≥ 30mins	256	228	214	197	168	149	74
SCAF ≥ 6hours	256	244	237	222	197	176	92
SCAF ≥ 24hours	256	252	248	233	206	184	98

Healey et al Circulation 2017

Clinical Challenges of Low Burden AF:

What are the burden cut-offs for clinical decision making?

The AF Burden Paradox

The longer you monitor, the more likely you are to find AF

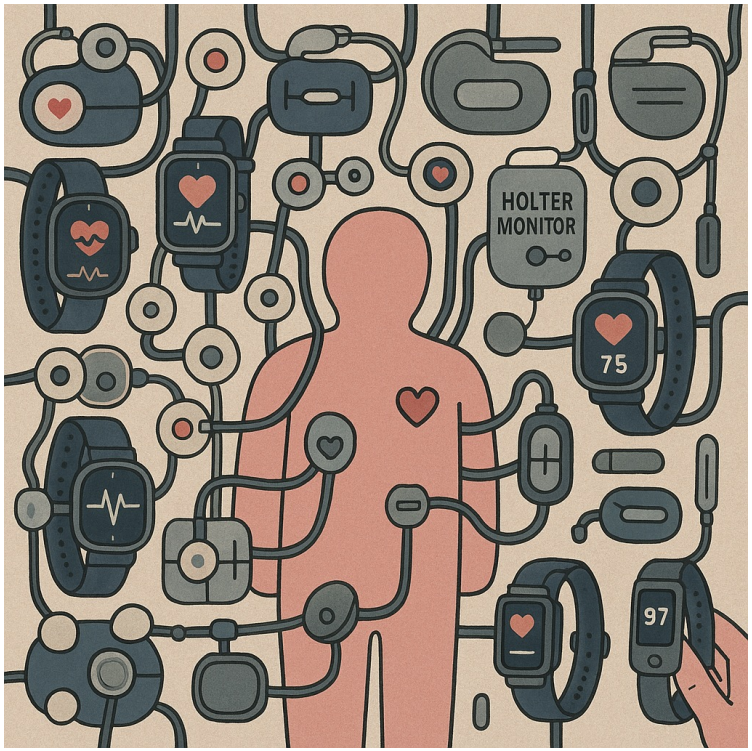
Stroke Risk is Proportional to AF Burden

The stroke risk
associated with AF
is inversely proportional to
the effort it took to capture it

Is there a "sweet spot"?

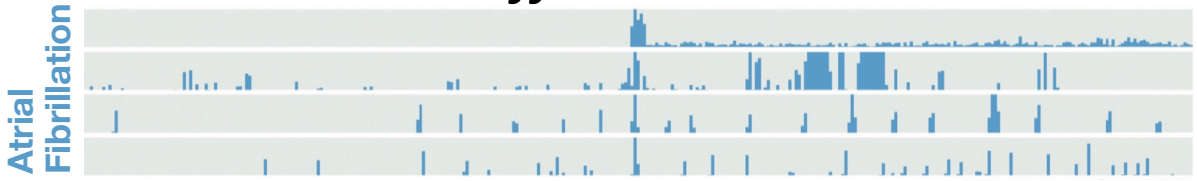
Clinical Challenges of Low Burden AF

How do we translate burden cut-offs across modalities?



Clinical Challenges of Low Burden AF

How do we translate burden cut-offs across modalities?



2470 Patients, mean CHA_2DS_2-VASc 4.0±1.3
Mean 2.5 Years of Follow-Up

1000 Randomly simulated 14 day Holters Per Patient

Estimated AF Prevalence and Stroke Risk With A 14-Day Holter

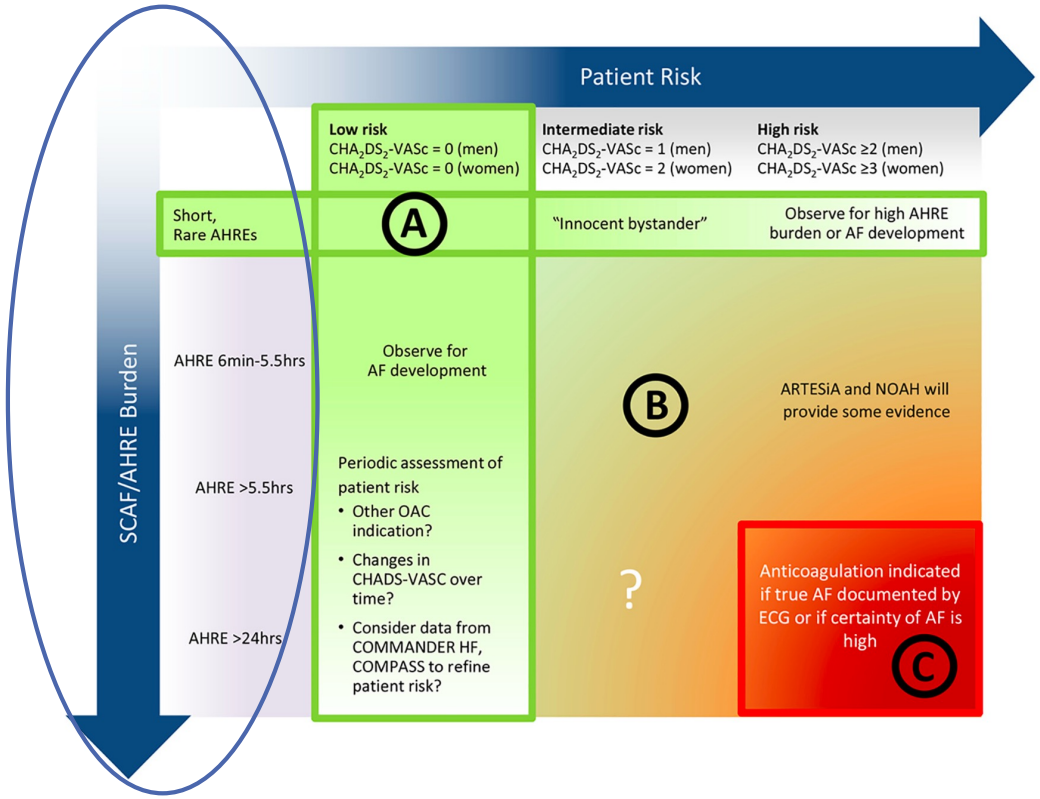
ASSERT

AF Duration on 14-Day Holter	Prevalence	Stroke Risk
< 6 min		0.70%/year Reference
> 6 min	3.1%	2.2%/year HR 3.0; 95%CI 1.3-5.7
> 15 min	2.9%	2.4%/year HR 3.3; 95%CI 1.4-6.4
> 30 min	2.6%	2.6%/year HR 3.5; 95%CI 1.5-6.7

McIntyre et al EP Europace 2022

Clinical Challenges of Low Burden AF

What's the interplay of AF Burden with other stroke risk factors?

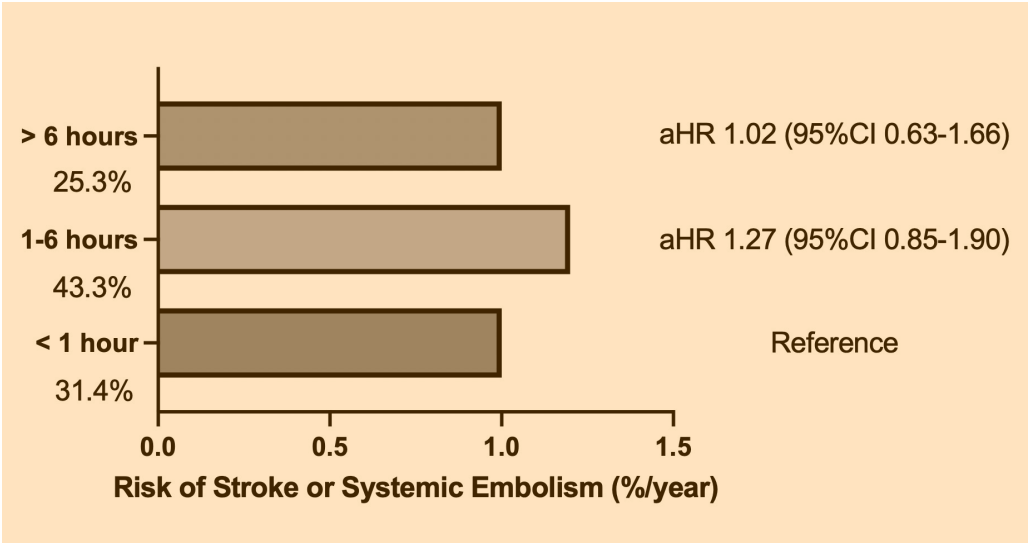


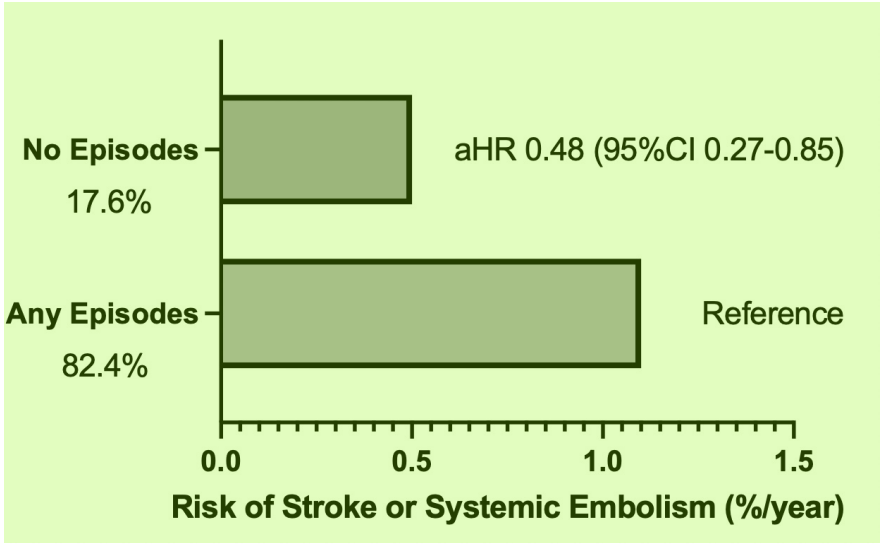
2024 ACC/AHA/HRS AF Guidelines

Clinical Challenges of Low Burden AF

What's the interplay of AF Burden with other stroke risk factors?

ARTESiA : Duration of Longest Device-Detected Subclinical AF Episode was Not Associated with Stroke Risk



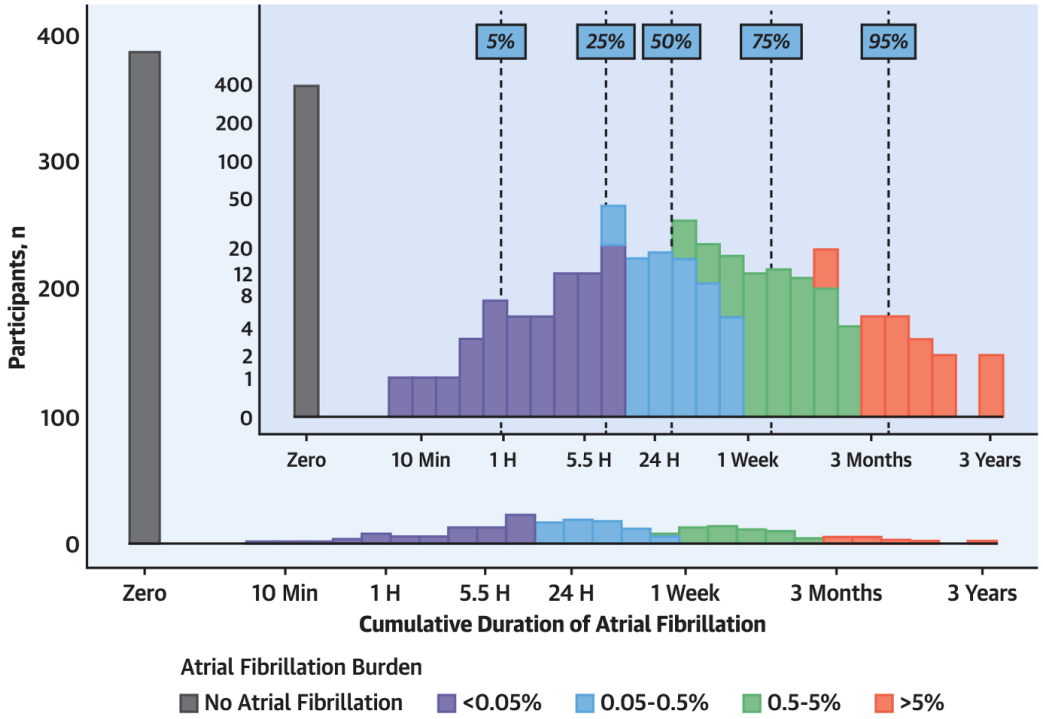


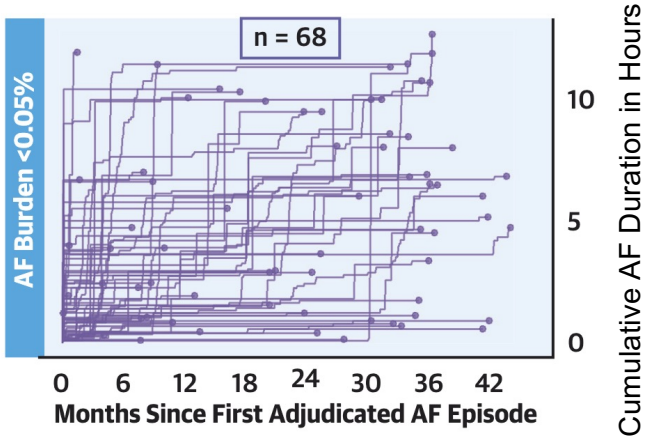
Adjusted for treatment allocation and CHA_2DS_2-VaSC score

McIntyre et al. Circulation. 2024

Clinical Challenges of Low Burden AF

How do we account for the dynamic nature of AF burden





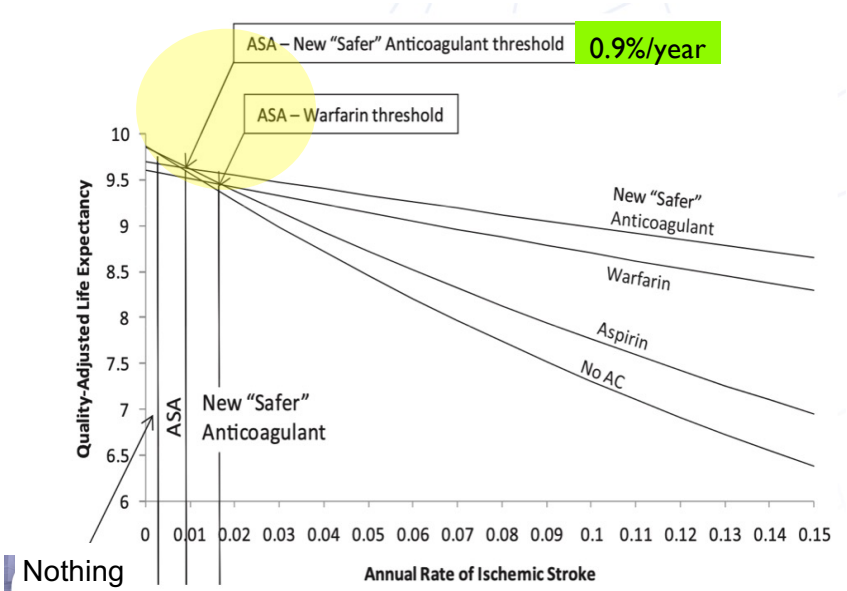
Regression
Remission
Dormancy

Diederichsen et al JACC 2019

Clinical Challenges of Low Burden AF

With safer therapies, could our risk thresholds change?

The annualized rate of stroke that justifies OAC is anchored in the safety profile



DOAC Alternatives that *could* be safer
if shown to be equally effective

- Factor XI inhibitors
- LAA Occlusion

Eckman MH et al. Circulation Cardiovasc Qual Outcomes 2011

Clinical Challenges of Low Burden AF

With safer therapies, could our risk thresholds change?

Annualized Rates of Stroke and Major Bleeding in the Device-Detected AF Trials

Outcome	Edoxaban (N=1270)	Placebo (N=1266)	Adjusted Hazard Ratio (95% CI)
	no. of patients with event/patient-yr (% per patient-yr)		
Ischemic stroke	22/2573 (0.9)	27/2519 (1.1)	0.79 (0.45 to 1.39)
Major bleeding	53/2534 (2.1)	25/2508 (1.0)	2.10 (1.30 to 3.38)

Outcome	Apixaban (N=2015)		Aspirin (N=1997)		Hazard Ratio (95% CI)	P Value
	no. of patients with event	*%/patient-yr*	*no. of patients with event*	*%/patient-yr*		
Stroke or systemic embolism	55	0.78	86	1.24	0.63 (0.45–0.88)	0.007
Major bleeding¶	106	1.53	78	1.12	1.36 (1.01–1.82)	0.04

Kirchhof et al NEJM 2023
Healey et al NEJM 2024

Conclusions

- AF Burden and stroke risk have a dose-response relationship
- Before AF Burden can be used for clinical decision making, we need:
  - Burden-based cut-offs for clinical guidance
  - A way to translate burden data between AF monitoring modalities
  - An understanding of how burden interacts with classic risk factors
  - An approach to assessing and reacting to changes in AF burden over time
  - Therapies with favourable risk-benefit profiles for patients with lower absolute risk

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