Scientific Sessions

Northwestern Medicine

RETHINKING ATRIAL FIBRILLATION (AF) BURDEN: AF DENSITY FURTHER STRATIFIES HEART FAILURE RISK IN A NATIONWIDE COHORT OF PATIENTS WITH CARDIAC DEVICES

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American Heart Association.

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FUNDING AND DISCLOSURES

Study Funding:
No external funding was provided for this research.

Research Funding:
NIH/NHLBI
Industry: Medtronic (research grants); Pfizer (consultant); Biotronik (ICM and digital health advisory board; consultant); Boston Scientific (research grants)
UNC Division of Cardiology

Disclosures:
Inventor, U.S. Patent 63/684,842, “Methods, Systems, And Computer Readable Media for Machine-Learning-Based Prediction Of Adverse Outcomes Using Data From Implantable Or Wearable Cardiac Devices.”

Inventor, U.S. Patent 63/962,514, "Methods, Systems, and Computer Readable Media for an Artificial Intelligence Platform for Continuous Stroke Risk Assessment and Personalized Prevention Strategies with Implantable or Wearable Cardiac Devices.”

BACKGROUND

- Atrial fibrillation (AF) affects >59 million adults worldwide and increases the risk of heart failure (HF).
- Among patients with both, risk of HF hospitalization and death is substantially higher.
- Current metrics (type, longest episode, burden) inadequately stratify HF risk, and there are no clinically relevant burden thresholds.

AF Density = Temporal distribution of AF episodes during a monitoring period Charitos et al 2012

Values range from 0 to 1: 0 = Dispersed, disconnected AF episodes; 1= Consolidated, uninterrupted AF

The Rainfall Analogy

Same 30-day rainfall, different impact

10"
over 30 days

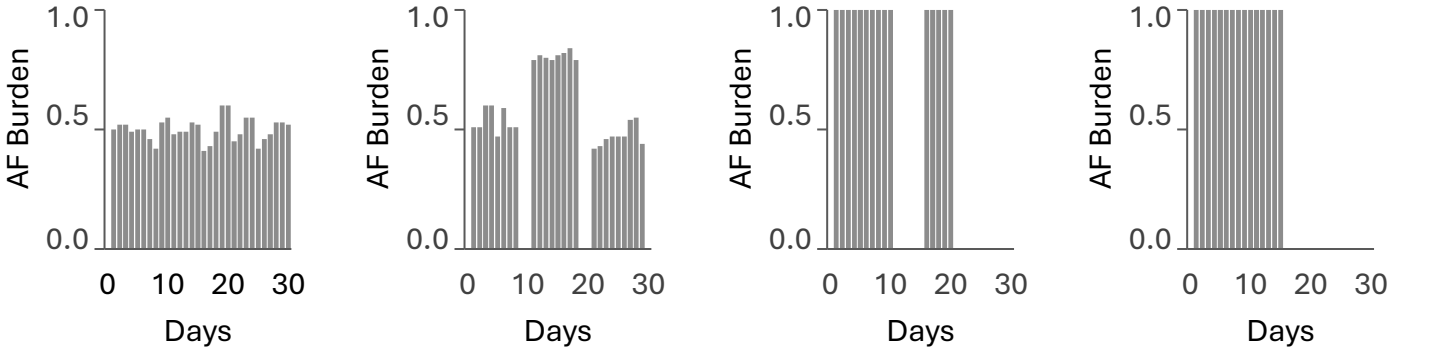
Manageable

vs

10"
in 1 day

Flooding

Patients with identical AF burden (50%) but disparate densities



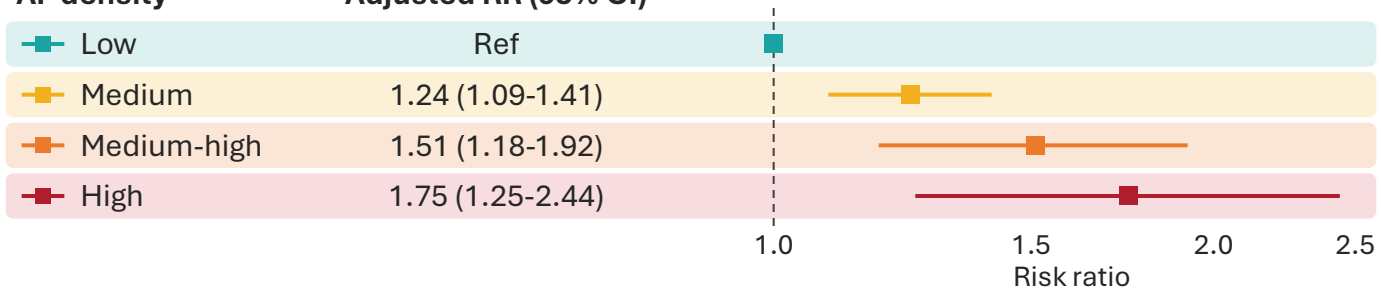
PRIOR STUDIES: AF DENSITY AND STROKE RISK

Rosman et al. AF Density as a Novel Biomarker for Ischemic Stroke Risk Prediction. *Eur Heart J*, Sept 2026

41,780 patients with CIEDs from 133 U.S. clinics, 2010–2025

Monthly AF burden and density categorized as: low (>0 to 0.3), medium (>0.3 to 0.6), medium-high (>0.6 to 0.9), and high (>0.9 to <1.0)

1-year risk of ischaemic stroke by AF density category



Independent effects of AF density and burden on stroke risk

AF burden	AF density: Low	Medium	Medium-high	High
Low	1 (Ref)	1.24 (1.09-1.41)	1.51 (1.18-1.92)	1.75 (1.25-2.44)
Medium	1.14 (1.03-1.27)	1.38 (1.22-1.56)	1.61 (1.33-1.94)	1.82 (1.40-2.36)
Medium-high	1.30 (1.00-1.67)	1.51 (1.21-1.89)	1.72 (1.39-2.15)	1.94 (1.51-2.49)
High	1.40 (0.95-2.05)	1.62 (1.14-2.30)	1.83 (1.36-2.46)	2.02 (1.51-2.71)

AF, atrial fibrillation; **CI**, confidence interval; **CIED**, cardiac implantable electronic device; **RR**, risk ratio

Key Findings

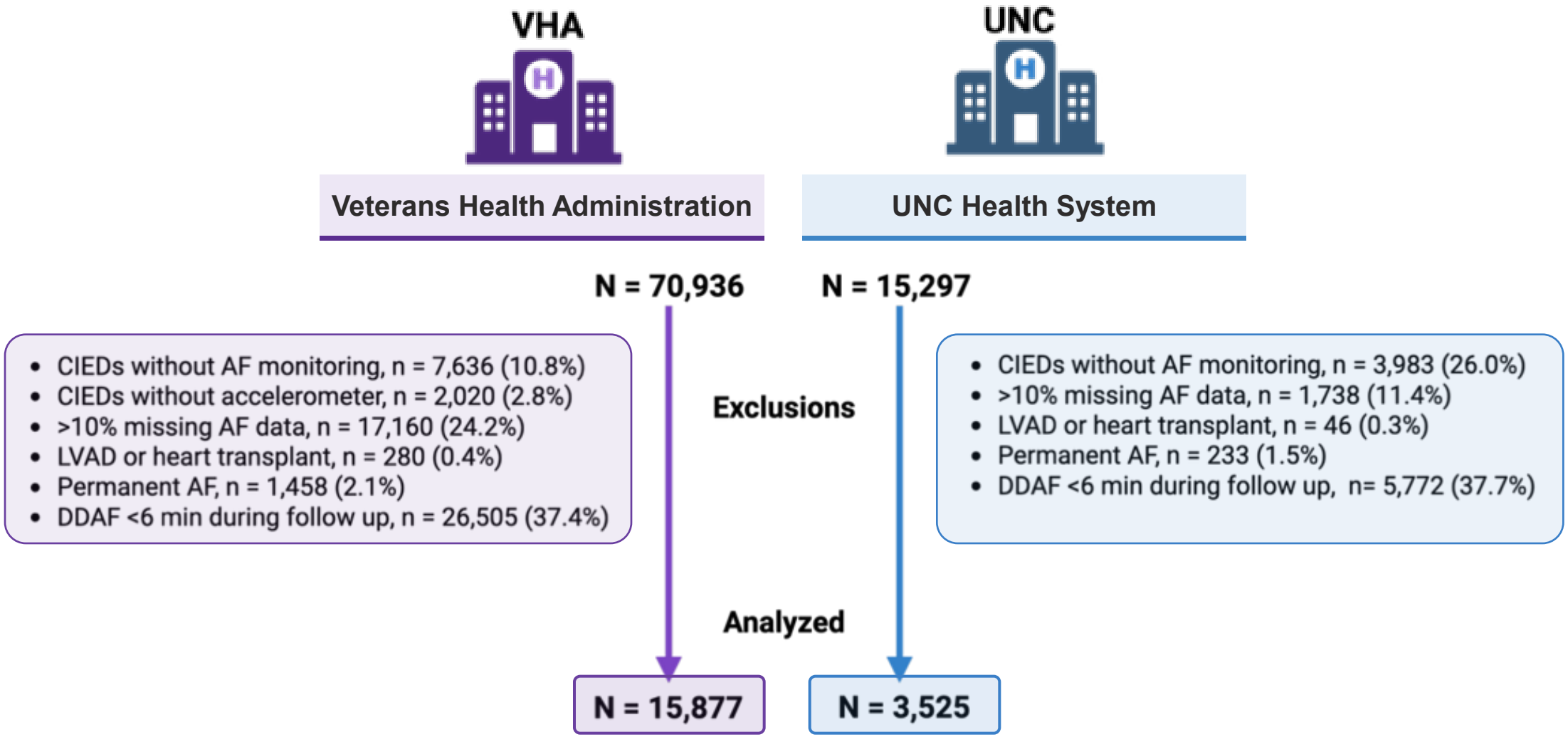
- Dose-response relationship: ↑ density → ↑ stroke risk, independent of burden and established risk factors.
- Consistent across ages, device types, comorbidities, and anticoagulation status.

Patients with low burden but high-density AF had higher stroke risk than those with high burden but low-density AF.

STUDY DESIGN AND METHODS

Study Aims	(1) Evaluate associations between AF density and risk of new-onset HF and HF hospitalization. (2) Compare AF density vs. AF burden for HF risk stratification.
Design	Multicenter, prospective, observational study.
Study Period	June 2010 to August 2024.
Study Cohorts	Patients with cardiac implantable electronic devices [CIEDs: pacemakers (PMs), implantable cardioverter defibrillators (ICDs) and implanted cardiac monitors (ICMs)] remotely monitored by the Veterans Health Administration (VHA; 122 clinics nationwide) and the University of North Carolina Health System (UNC; 11 hospitals).
Data and Sources	EHR: clinical data; HF ascertainment from inpatient hospital discharge codes & outpatient codes. CIED data: Daily AF burden, AF density, physical activity.
Analysis	Only individuals with device detected AF (DDAF) >6 min during follow up were included. G methods: Relative risks (RRs) and meta-analysis methods to generate pooled estimation. Models adjusted for >40 baseline covariates (e.g., daily activity) and time-varying confounders.
Exposure	Monthly AF burden and density were categorized as low (>0 to 0.3), medium (>0.3 to 0.6), medium-high (>0.6 to 0.9), and high (>0.9 to <1.0).
Outcomes	(1) New-onset HF among patients without HF at baseline CIED implant. (2) HF hospitalization among patients with HF at baseline CIED implant.

CURRENT STUDY - FLOW DIAGRAM



Device manufacturers: Medtronic, Boston Scientific and Biotronik

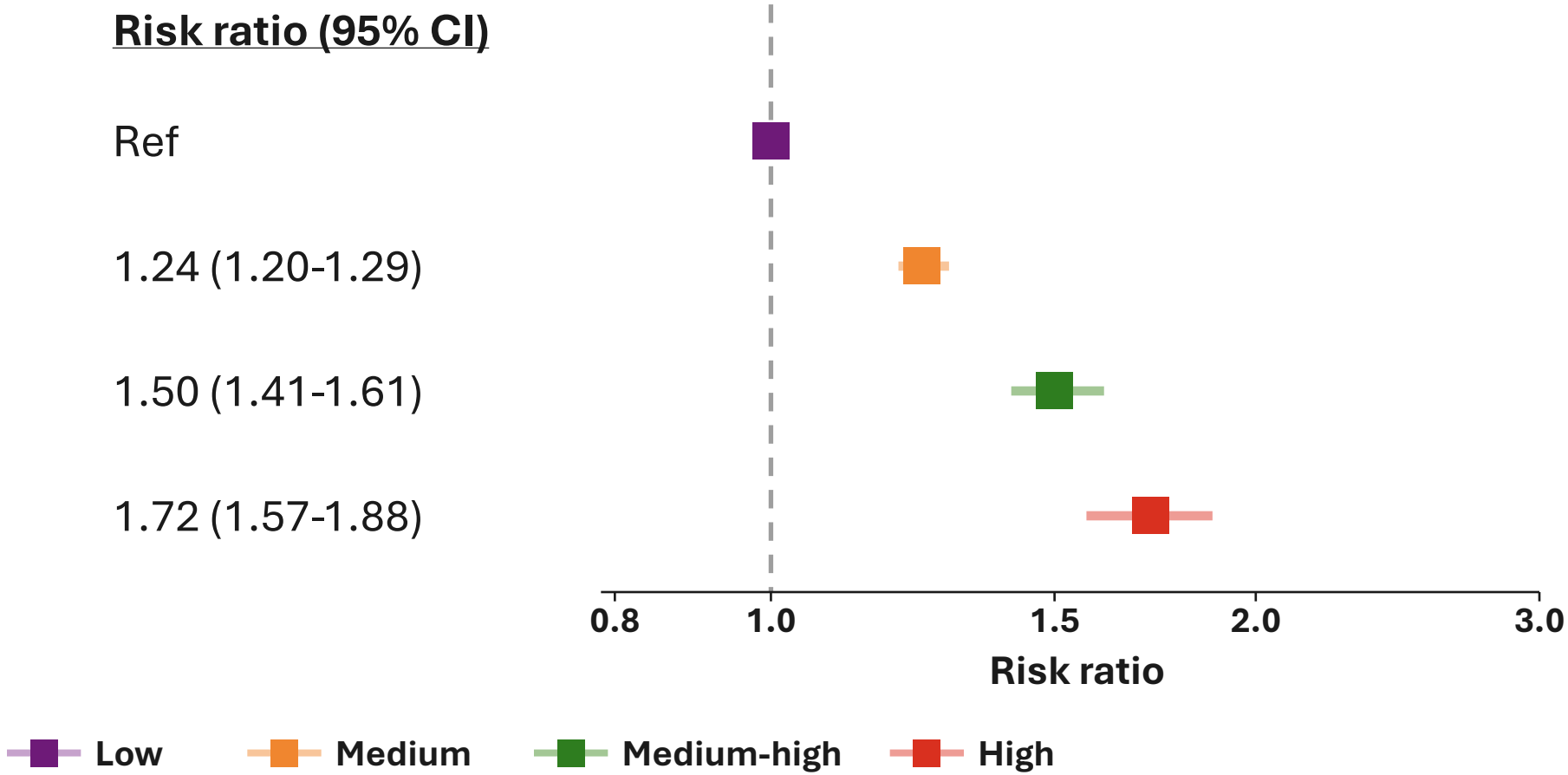
BASELINE CLINICAL CHARACTERISTICS OF THE STUDY COHORTS

	VHA			UNC		
	All Patients	HF at Baseline		All Patients	HF at Baseline	
	(n=15,877)	Yes (n=7,151)	No (n=8,726)	(n=3,525)	Yes (n=1,628)	No (n=1,897)
Age (years)	73.1 (9.5)	72.8 (8.9)	73.4 (9.9)	73.5 (11.3)	72.5 (11.3)	74.3 (11.2)
Female	423 (2.7)	165 (2.3)	258 (3.0)	1,608 (45.6)	691 (42.4)	917 (48.3)
White	12,732 (80.2)	5,607 (78.4)	7,125 (81.7)	2,858 (81.1)	1,246 (76.5)	1,612 (85.0)
BMI	30.2 (6.0)	30.6 (6.3)	29.8 (5.6)	28.5 (6.6)	29.0 (7.0)	28.0 (6.2)
AF/flutter	8,963 (56.5)	4,934 (69.0)	4,029 (46.2)	2,033 (57.7)	1,058 (65.0)	975 (51.4)
Ischemic heart disease	10,183 (64.1)	6,063 (84.8)	4,120 (47.2)	1,688 (47.9)	1,061 (65.2)	627 (33.1)
Hypertension	13,871 (87.4)	6,839 (95.6)	7,032 (80.6)	2,671 (75.8)	1,383 (85.0)	1,288 (67.9)
Diabetes	7,428 (46.8)	4,027 (56.3)	3,401 (39.0)	942 (26.7)	558 (34.3)	384 (20.2)
Beta blocker	7,340 (46.2)	4,470 (62.5)	2,870 (32.9)	2,283 (64.8)	1,345 (82.6)	938 (49.4)
ARNI/ACE-I/ARB	7,516 (47.3)	4,126 (57.7)	3,390 (38.8)	1,495 (42.4)	913 (56.1)	582 (30.7)
LVEF at implant, % median [IQR]	52.0 [35.0 - 60.0]	40.0 [27.0, 55.0]	55.0 [50.0, 60.0]	55.0 [45.0 - 60.0]	45.0 [30.0, 55.0]	55.0 [55.0, 60.0]
HFrEF	—	3,806 (53.2)	—	—	585 (35.9)	—
HFmrEF	—	563 (7.9)	—	—	80 (4.9)	—
HFpEF	—	2,493 (34.9)	—	—	632 (38.8)	—
Missing	2,671 (16.8)	289 (4.0)	2,382 (27.3)	1,023 (29.0)	331 (20.3)	692 (36.5)
Device Type						
ICM	943 (5.9)	289 (4.0)	654 (7.5)	333 (9.4)	88 (5.4)	245 (12.9)
Pacemaker/CRT-P	9,614 (60.6)	2,878 (40.2)	6,736 (77.2)	2,298 (65.2)	744 (45.7)	1,554 (81.9)
ICD/CRT-D	5,320 (33.5)	3,984 (55.7)	1,336 (15.3)	894 (25.4)	796 (48.9)	98 (5.2)
Events, n (%)	6,595 (41.5)	3,746 (52.4)	2,849 (32.6)	1,430 (40.6)	831 (51.0)	599 (31.6)
Event rate per 100 person-years	14.58	22.59	9.94	13.64	19.16	9.74

NEW-ONSET HF

Adjusted 1-year risk of new-onset HF by AF density (no HF at baseline)

AF density	Risk ratio (95% CI)
Low	Ref
Medium	1.24 (1.20-1.29)
Medium-high	1.50 (1.41-1.61)
High	1.72 (1.57-1.88)



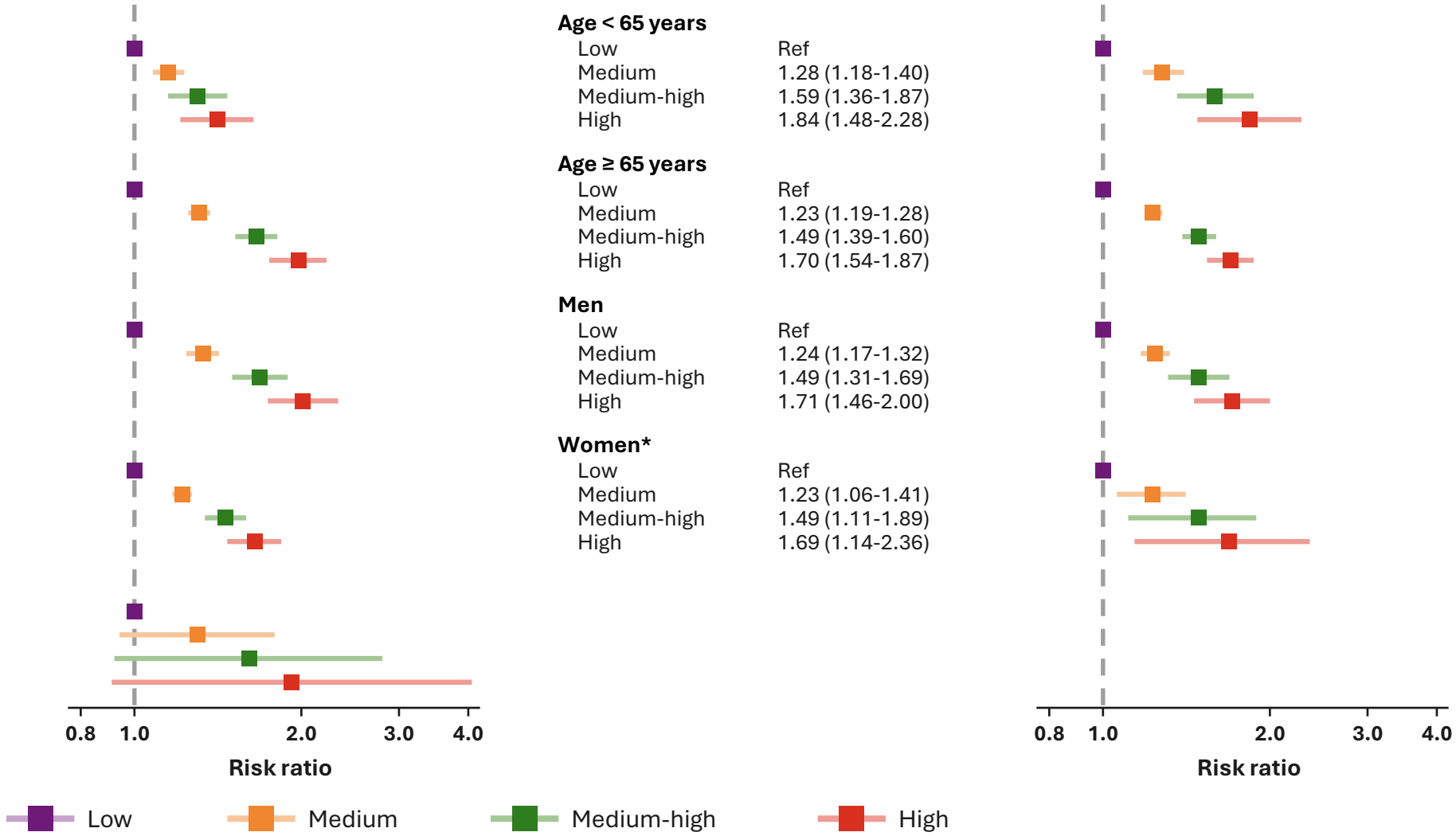
Pooled VHA and UNC estimates (random-effects meta-analysis). Parametric g-formula adjusted for baseline and time-varying covariates, including AF burden; 95% CIs from 500 bootstrap samples.

NEW-ONSET HF: SUBGROUPS

Adjusted 1-year risk of new-onset HF by AF density (no baseline HF)

AF density	Risk ratio (95% CI)
AF at Baseline	
Low	Ref
Medium	1.15 (1.08-1.23)
Medium-high	1.30 (1.15-1.47)
High	1.41 (1.21-1.64)
No AF at Baseline	
Low	Ref
Medium	1.31 (1.25-1.37)
Medium-high	1.66 (1.52-1.81)
High	1.98 (1.75-2.22)
ICD	
Low	Ref
Medium	1.33 (1.24-1.42)
Medium-high	1.68 (1.50-1.89)
High	2.01 (1.74-2.33)
Pacemaker	
Low	Ref
Medium	1.22 (1.17-1.27)
Medium-high	1.46 (1.34-1.59)
High	1.65 (1.47-1.84)
ICM	
Low	Ref
Medium	1.30 (0.94-1.79)
Medium-high	1.61 (0.92-2.80)
High	1.92 (0.91-4.06)

AF density	Risk ratio (95% CI)
Age < 65 years	
Low	Ref
Medium	1.28 (1.18-1.40)
Medium-high	1.59 (1.36-1.87)
High	1.84 (1.48-2.28)
Age ≥ 65 years	
Low	Ref
Medium	1.23 (1.19-1.28)
Medium-high	1.49 (1.39-1.60)
High	1.70 (1.54-1.87)
Men	
Low	Ref
Medium	1.24 (1.17-1.32)
Medium-high	1.49 (1.31-1.69)
High	1.71 (1.46-2.00)
Women*	
Low	Ref
Medium	1.23 (1.06-1.41)
Medium-high	1.49 (1.11-1.89)
High	1.69 (1.14-2.36)

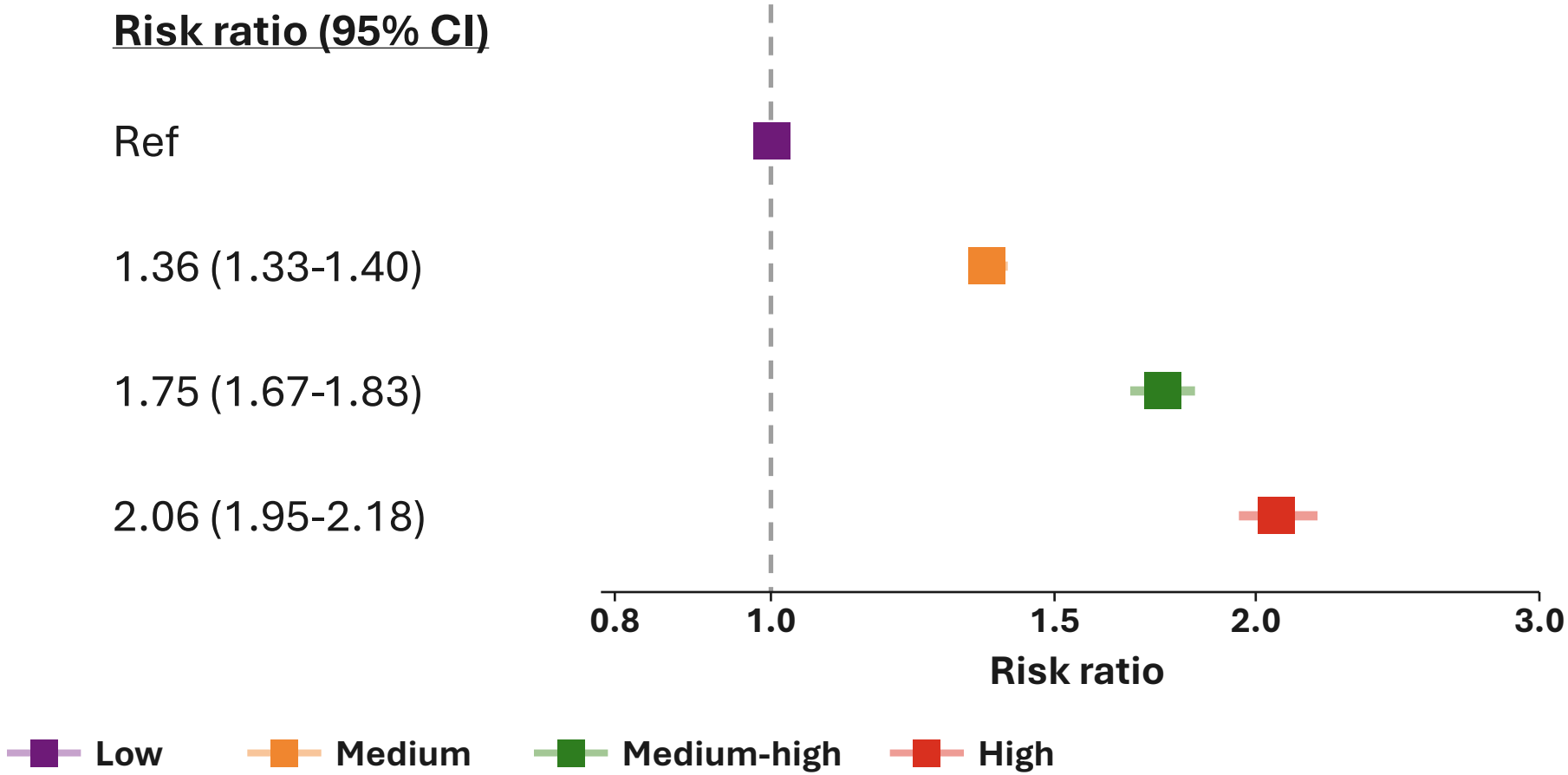


Pooled VHA and UNC estimates (random-effects meta-analysis); g-formula adjusted for baseline and time-varying covariates, including AF burden. *UNC only.

HF HOSPITALIZATION

Adjusted 1-year risk of HF hospitalization by AF density (baseline HF)

AF density	Risk ratio (95% CI)
Low	Ref
Medium	1.36 (1.33-1.40)
Medium-high	1.75 (1.67-1.83)
High	2.06 (1.95-2.18)



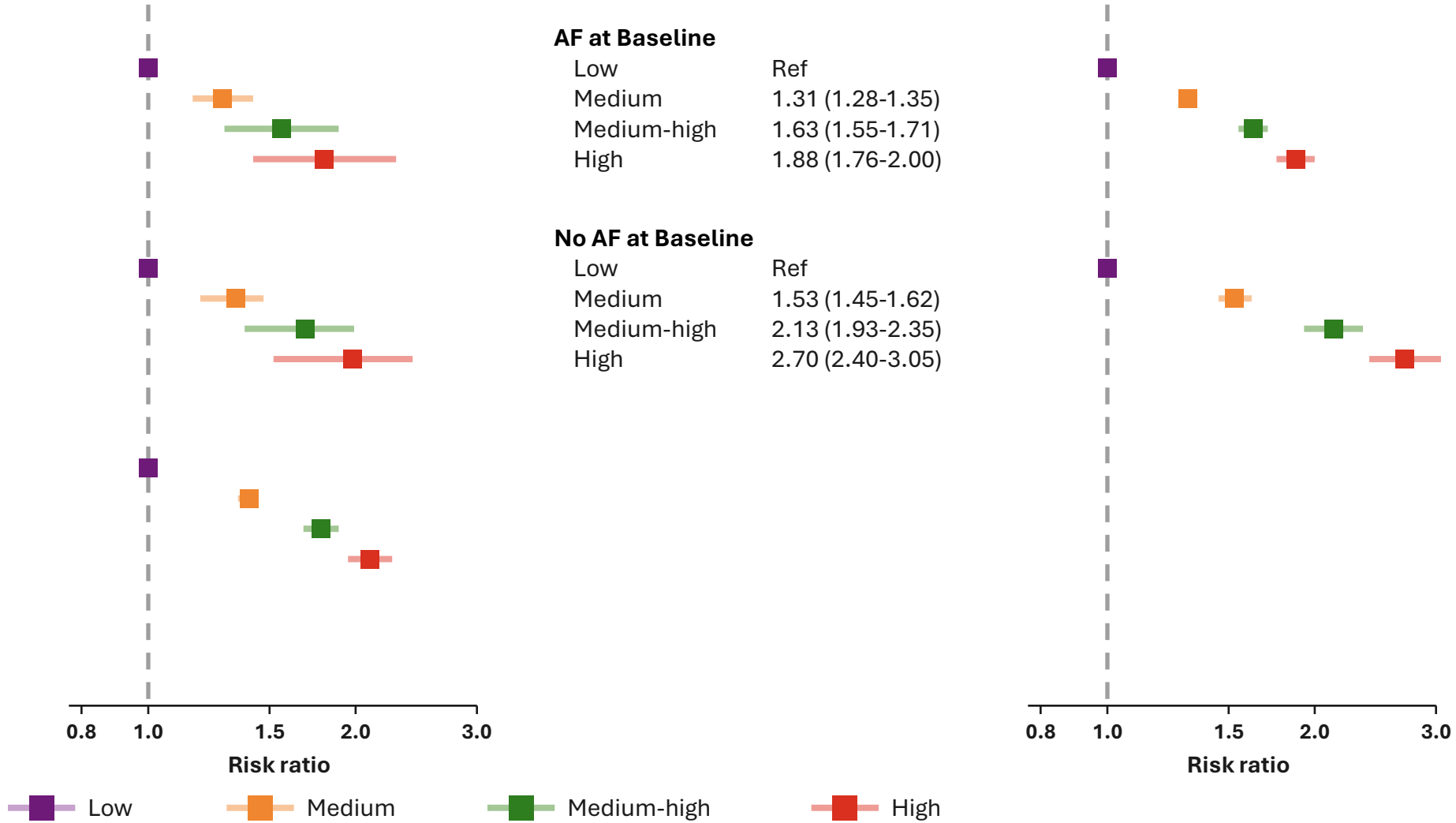
Pooled VHA and UNC estimates (random-effects meta-analysis). Parametric g-formula adjusted for baseline and time-varying covariates, including AF burden; 95% CIs from 500 bootstrap samples.

HF HOSPITALIZATION: SUBGROUPS

Adjusted 1-year risk of HF hospitalization by AF density (baseline HF)

AF density	Risk ratio (95% CI)
HFpEF	
Low	Ref
Medium	1.28 (1.16-1.42)
Medium-high	1.56 (1.29-1.89)
High	1.80 (1.42-2.29)
HFmrEF	
Low	Ref
Medium	1.34 (1.19-1.47)
Medium-high	1.69 (1.38-1.99)
High	1.98 (1.52-2.42)
HFrEF	
Low	Ref
Medium	1.40 (1.35-1.44)
Medium-high	1.78 (1.68-1.89)
High	2.10 (1.95-2.26)

AF density	Risk ratio (95% CI)
AF at Baseline	
Low	Ref
Medium	1.31 (1.28-1.35)
Medium-high	1.63 (1.55-1.71)
High	1.88 (1.76-2.00)
No AF at Baseline	
Low	Ref
Medium	1.53 (1.45-1.62)
Medium-high	2.13 (1.93-2.35)
High	2.70 (2.40-3.05)



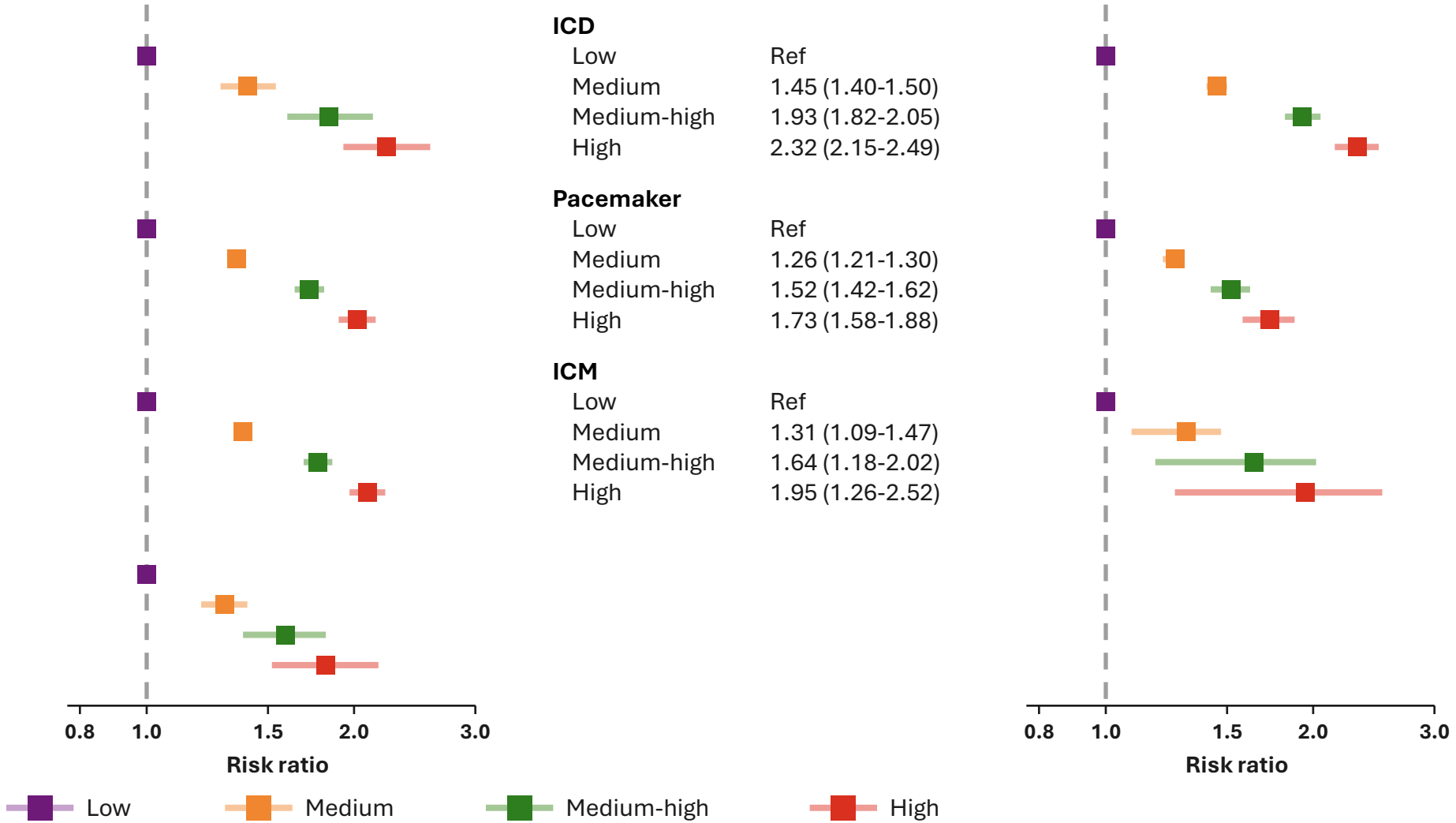
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HF HOSPITALIZATION: SUBGROUPS

Adjusted 1-year risk of HF hospitalization by AF density (baseline HF)

AF density	Risk ratio (95% CI)
Age < 65 years	
Low	Ref
Medium	1.40 (1.28-1.54)
Medium-high	1.84 (1.60-2.13)
High	2.23 (1.93-2.58)
Age ≥ 65 years	
Low	Ref
Medium	1.35 (1.31-1.39)
Medium-high	1.72 (1.64-1.81)
High	2.02 (1.90-2.15)
Men	
Low	Ref
Medium	1.38 (1.34-1.42)
Medium-high	1.77 (1.69-1.86)
High	2.09 (1.97-2.22)
Women	
Low	Ref
Medium	1.30 (1.20-1.40)
Medium-high	1.59 (1.38-1.82)
High	1.82 (1.52-2.17)

AF density	Risk ratio (95% CI)
ICD	
Low	Ref
Medium	1.45 (1.40-1.50)
Medium-high	1.93 (1.82-2.05)
High	2.32 (2.15-2.49)
Pacemaker	
Low	Ref
Medium	1.26 (1.21-1.30)
Medium-high	1.52 (1.42-1.62)
High	1.73 (1.58-1.88)
ICM	
Low	Ref
Medium	1.31 (1.09-1.47)
Medium-high	1.64 (1.18-2.02)
High	1.95 (1.26-2.52)



Pooled VHA and UNC estimates (random-effects meta-analysis); g-formula adjusted for baseline and time-varying covariates, including AF burden.

JOINT EFFECTS OF AF BURDEN AND DENSITY ON HF OUTCOMES

1-year risk of new-onset HF by AF burden and density (no HF at baseline)

	AF Density			
AF Burden	**Low**	**Medium**	**Medium-high**	**High**
Low	1 (Ref)	1.23 (1.19-1.28)	1.49 (1.39-1.59)	1.71 (1.56-1.88)
Medium	1.45 (1.41-1.50)	1.70 (1.64-1.76)	1.94 (1.84-2.06)	2.17 (2.01-2.33)
Medium-high	2.04 (1.91-2.18)	2.32 (2.19-2.46)	2.61 (2.46-2.77)	2.88 (2.69-3.08)
High	2.51 (2.30-2.74)	2.83 (2.62-3.06)	3.17 (2.94-3.42)	3.47 (3.21-3.75)

1-year risk of HF hospitalization by AF burden and density (baseline HF)

	AF Density			
AF Burden	**Low**	**Medium**	**Medium-high**	**High**
Low	1 (Ref)	1.38 (1.35-1.42)	1.79 (1.71-1.87)	2.12 (2.00-2.24)
Medium	1.20 (1.17-1.24)	1.59 (1.55-1.64)	1.95 (1.87-2.03)	2.25 (2.15-2.36)
Medium-high	1.43 (1.36-1.51)	1.79 (1.71-1.88)	2.15 (2.05-2.25)	2.45 (2.34-2.57)
High	1.59 (1.49-1.70)	1.96 (1.85-2.08)	2.34 (2.21-2.47)	2.65 (2.51-2.79)

***Adjusted 1-year RR (95% CI) vs. low burden/low density (Ref); pooled VHA and UNC cohorts. CI, confidence interval; RR, risk ratio.**

CONCLUSIONS

1. We show a clinically relevant dose–response relationship between increasing AF density and both new-onset HF and HF hospitalization at 1 year, after adjustment for known HF risk factors and AF burden.

2. Associations were consistent across HFrEF, HFmrEF, and HFpEF and across key subgroups.

3. Density further stratified HF risk within every level of AF burden; risk was highest with both high burden and high density (RR 3.47).

Strengths: continuous device-detected AF data from multiple manufacturers; two large U.S. health systems; g-methods for time-varying confounding and competing risks.

Limitations: possible EHR misclassification; no NYHA class or symptom data; AF detection varies by device.

Clinical Implications and Next Steps

- Combined with prior findings, AF density may serve as a device-derived marker of risk across CVD outcomes.
- AF density refines HF risk assessment beyond AF burden.
- Prospective studies should test whether density-guided monitoring and rhythm management reduce HF events.

ACKNOWLEDGEMENTS

Co-Investigators

Rod Passman, MD, MSCE

Kaicheng Wang, MD, MPH

Shantanu Sarkar, PhD

Paul Ziegler, MS

Tony Mazzella, MD

Sanjiv Shah, MD

Acknowledgements

- **VHA National Cardiac Device Surveillance Program**
  Merritt Raitt, MD, and Sanket Dhruva, MD
- **UNC Cardiovascular Device Surveillance Registry**
- **Patients enrolled in the VHA and UNC registries**
- **Industry partners who provided CIED data**

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Thank you

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