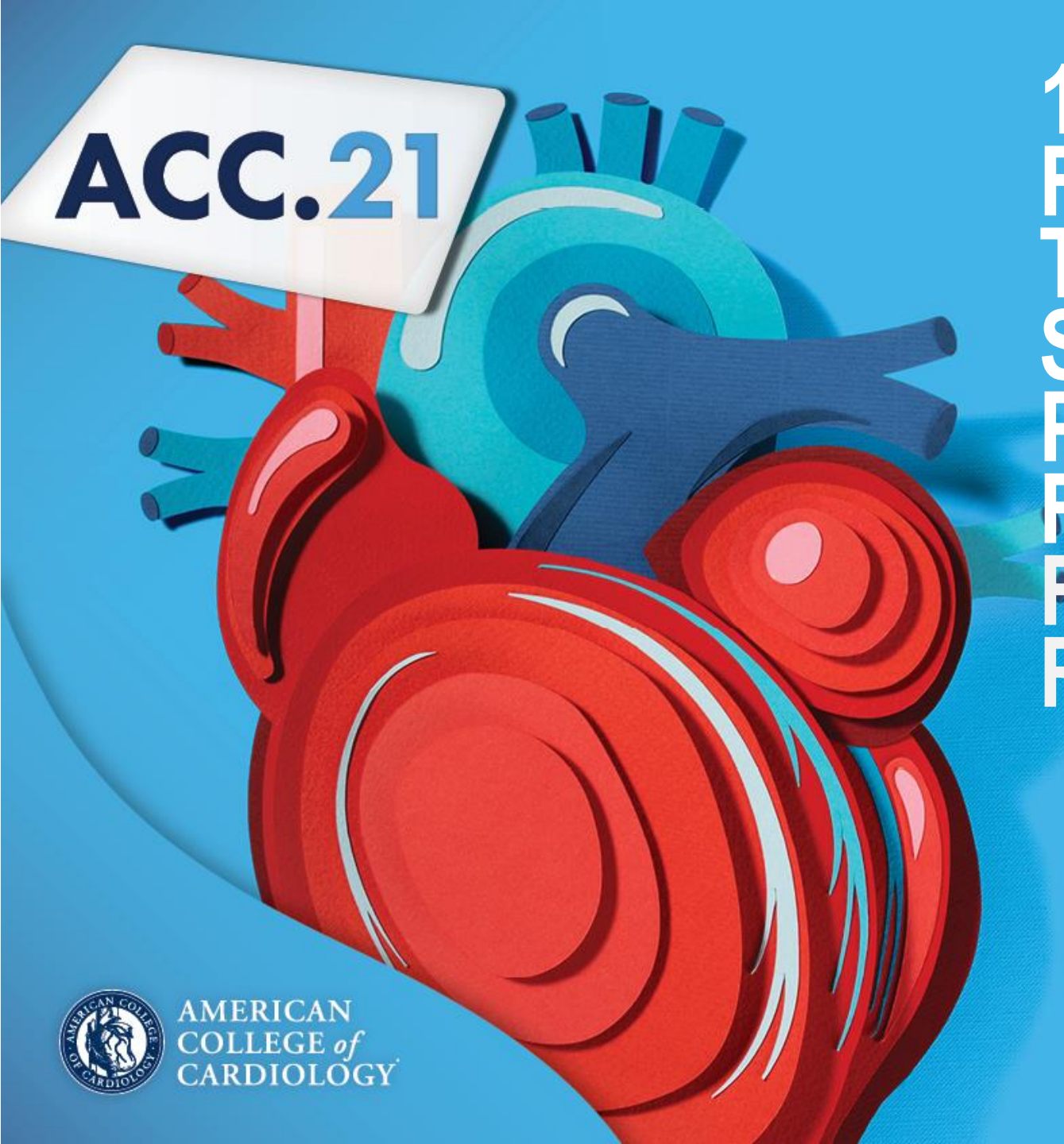

1-Year Clinical Outcomes Following Watchman Transcatheter LAAO For Stroke Prevention In Patients With Atrial Fibrillation: A Report From The NCDR LAAO Registry

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on behalf of the NCDR LAAO Steering Committee

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Background

- WATCHMAN transcatheter left atrial appendage occlusion (LAAO) is an alternative approach to OAC for stroke prevention in AF
- Population enrolled in RCTs differs substantially from that indicated in the CMS coverage decision for LAAO
- The NCDR LAAO registry, which is required for all Watchman procedures to qualify for Medicare reimbursement, allows for assessment of clinical outcomes

Differences Between the Inclusion Criteria of Pivotal Trials and Criteria for CMS Coverage Decision for WATCHMAN LAAC

PROTECT-AF and PREVAIL Trials

Thromboembolic risk:

$CHADS_2 \geq 1$ [PROTECT AF]

$CHADS_2 \geq 2$ or $CHADS_2 \geq 1$ with conditions [PREVAIL]

***Bleeding risk*:**

Eligible for long-term warfarin

CMS Coverage Decision

Thromboembolic risk:

$CHADS_2 \geq 2$ or CHA_2DS_2-VASc ≥ 3

Bleeding Risk:

Suitable for short-term warfarin but deemed unable to take long-term OAC

Baseline Clinical Characteristics of Patients Enrolled in The Pivotal Trials Compared With Patients in the NCDR LAAO Registry

Characteristic	PROTECT AF trial (N=463 implants)	PREVAIL trial (N=269 implants)	LAAO Registry (N=38,158)
Age, mean (SD), year	71.7 (8.8)	74.0 (7.4)	76.0 (8.1)
Female Sex, N (%)	137 (29.6)	87 (32.3)	15,672 (41.1)
Prior ischemic stroke/TIA, N (%)	82 (17.7)	74 (27.5)	10,425 (29.8)
Prior CHF, N (%)	124 (26.8)	63 (23.4)	14,266 (37.4)
Prior diabetes mellitus, N (%)	113 (24.4)	91 (33.8)	14,396 (37.7)
Prior hypertension, N (%)	413 (89.2)	238 (88.5)	35,148 (92.1)
Prior intracranial bleeding, N (%)	NA	NA	4550 (11.9)
Prior clinically relevant bleeding, N (%)	NA*	NA*	26,466 (69.4)
CHA_2DS_2-VASc score	3.4 ±1.5	3.8 ±1.2	4.6 ±1.5
HAS-BLED score	NA**	NA**	3.0 ±1.1

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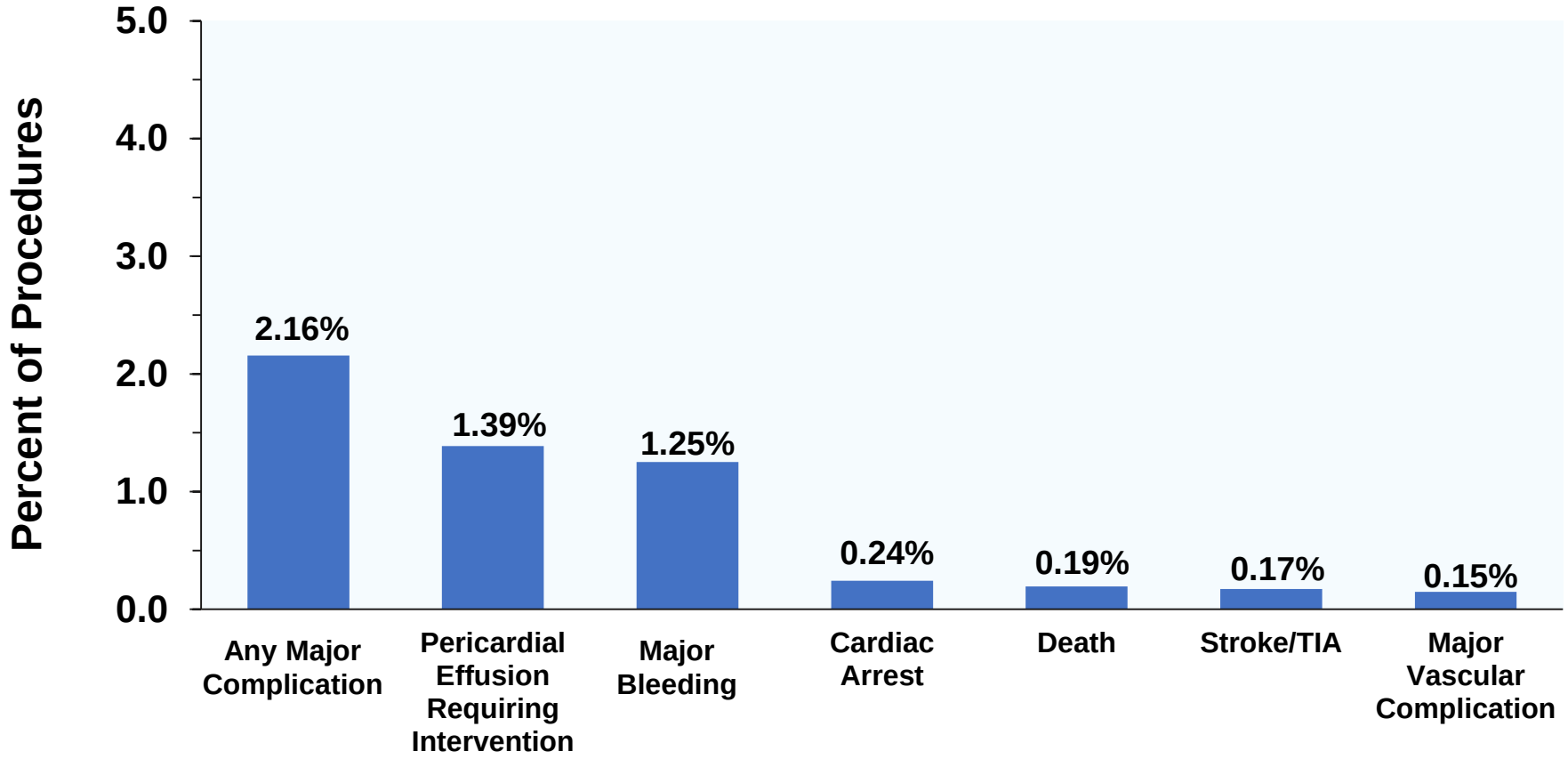
*"Prior major bleeding" reported to be 13.1% in the pooled PROTECT/PREVAIL cohort[2]
**Liver dz and labile INR not collected in PROTECT/PREVAIL; a modified HAS-BLED not including these variables = 1.9 ± 0.9 for the pooled cohort[2]

[1]Freeman JV et al. J Am Coll Cardiol. 2020;75:1503-1518
[2]Price MJ, et al. *JACC Cardiovasc Interv*. 2015;8:1925-32

NCDR LAAO: Major In-hospital AEs



[1]Freeman JV, Varosy P, Price MJ et al, J Am Coll Cardiol. 2020

Study Aims

- A substantial gap in knowledge exists regarding the longer-term safety and effectiveness of transcatheter LAAO in contemporary U.S. practice
- We sought to assess the rates of thromboembolic and bleeding events after transcatheter LAAO with the Watchman device over the 1st year of follow-up in the NCDR LAAO Registry.

Methods

- **Design**: Observational, cohort study
- **Study population**: Patients who underwent attempted or successful Watchman implantation in the NCDR LAAO and who were eligible for 1-year FU
- **Endpoints**:

  Primary endpoint: ischemic stroke

  Other endpoints: death, SE, major bleeding*
- **Endpoint adjudication:** central adjudication using a computer-based algorithm; manual adjudication when registry data elements are incomplete or conflicting by the algorithmic approach alone

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*any bleed requiring hospitalization, and/or causing a decrease in Hgb> 2g/dL, and/or requiring blood transfusion that was not hemorrhagic stroke.

Methods: Statistical Analysis

- **Kaplan-Meier method** was used to estimate 1-year survival estimates
  - Since the FU window extended to 60 days beyond 12 months, we report the KM-estimated 1-year event rates through 425 days in order to capture all potential events
- **Mean CHA_2DS_2-VASc score** calculated to estimate the ischemic stroke rate compared to the expected rate without OAC
- **Data audits** at 136 sites: 92.1% agreement rate between registry-reported data and source documents over course of study

Study Population

66450 patients

28165 not eligible for 1-year FU (discharge date not between January 1, 2016 and December 31, 2018)

38,285 patients

1250 with no information entered about which device used

37,035 patients

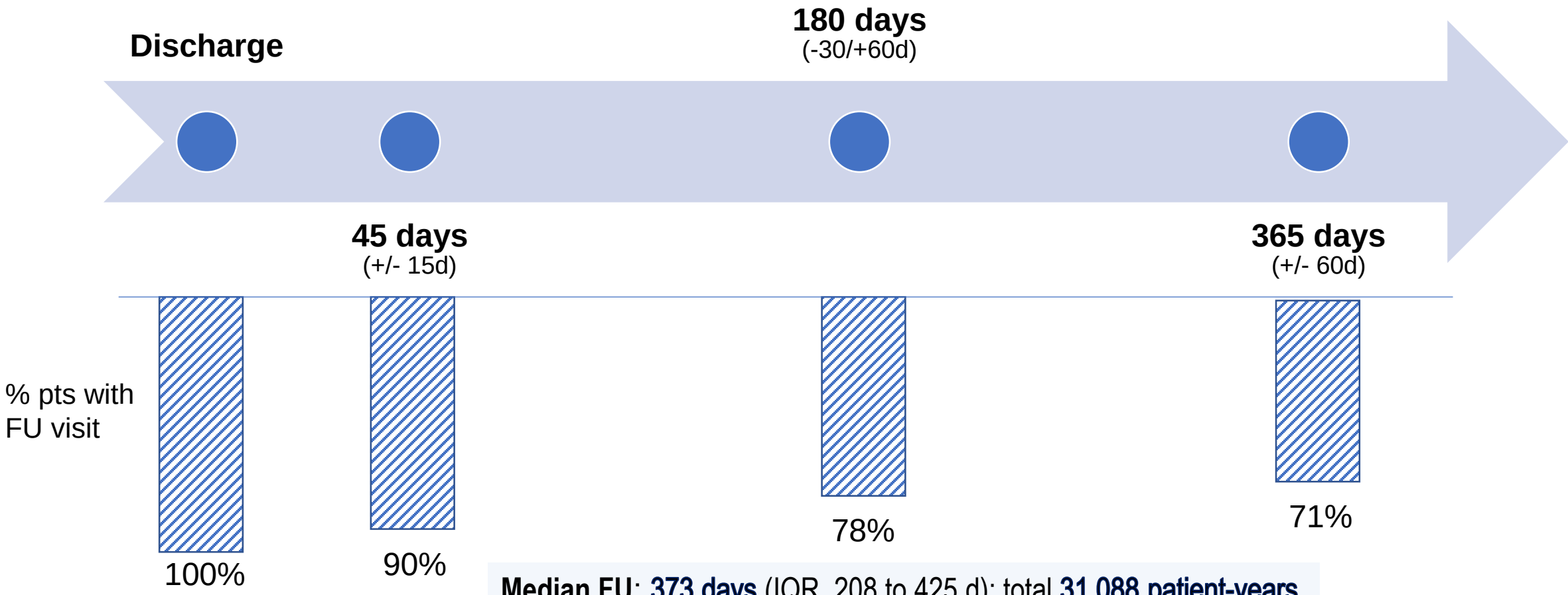
354 device was not a WATCHMAN

36,681 patients

Results: Clinical Characteristics of the Study Population

Characteristic	N = 36681
Age, yrs	76.0±8.1
Male sex, No. (%)	21,595 (58.9)
CHA_2DS_2VASc score	**4.8±1.5**
Risk factors for stroke, No. (%)	
Congestive heart failure	13642 (37.3)
History of hypertension	33808 (92.2)
Diabetes	13879 (37.9)
Prior stroke	9338 (25.5)
Prior TIA	5293 (14.5)
Prior thromboembolic event	6706 (18.3)
HAS-BLED score	**3.0±1.1**
Clinically relevant prior major bleeding, No.(%)	**25424 (69.5)**
Prior intracranial hemorrhage, No. (%)	4355 (11.9)
Prior gastrointestinal bleeding, No. (%)	15323 (41.8)

NCDR LAAO Follow-up Visits



Median FU: **373 days** (IQR, 208 to 425 d); total **31,088 patient-years**
At least one post-discharge FU in 93.6% of patients

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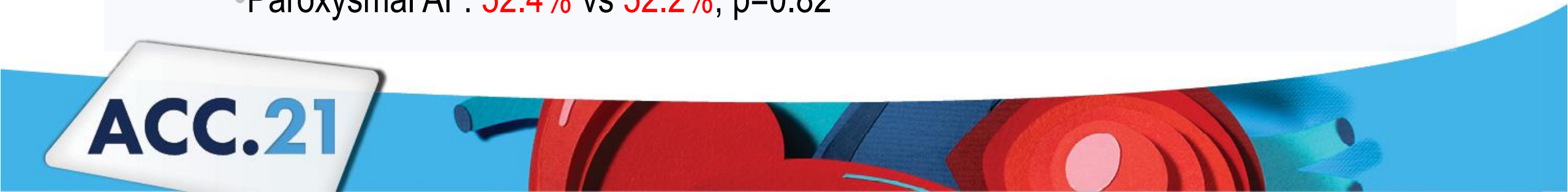
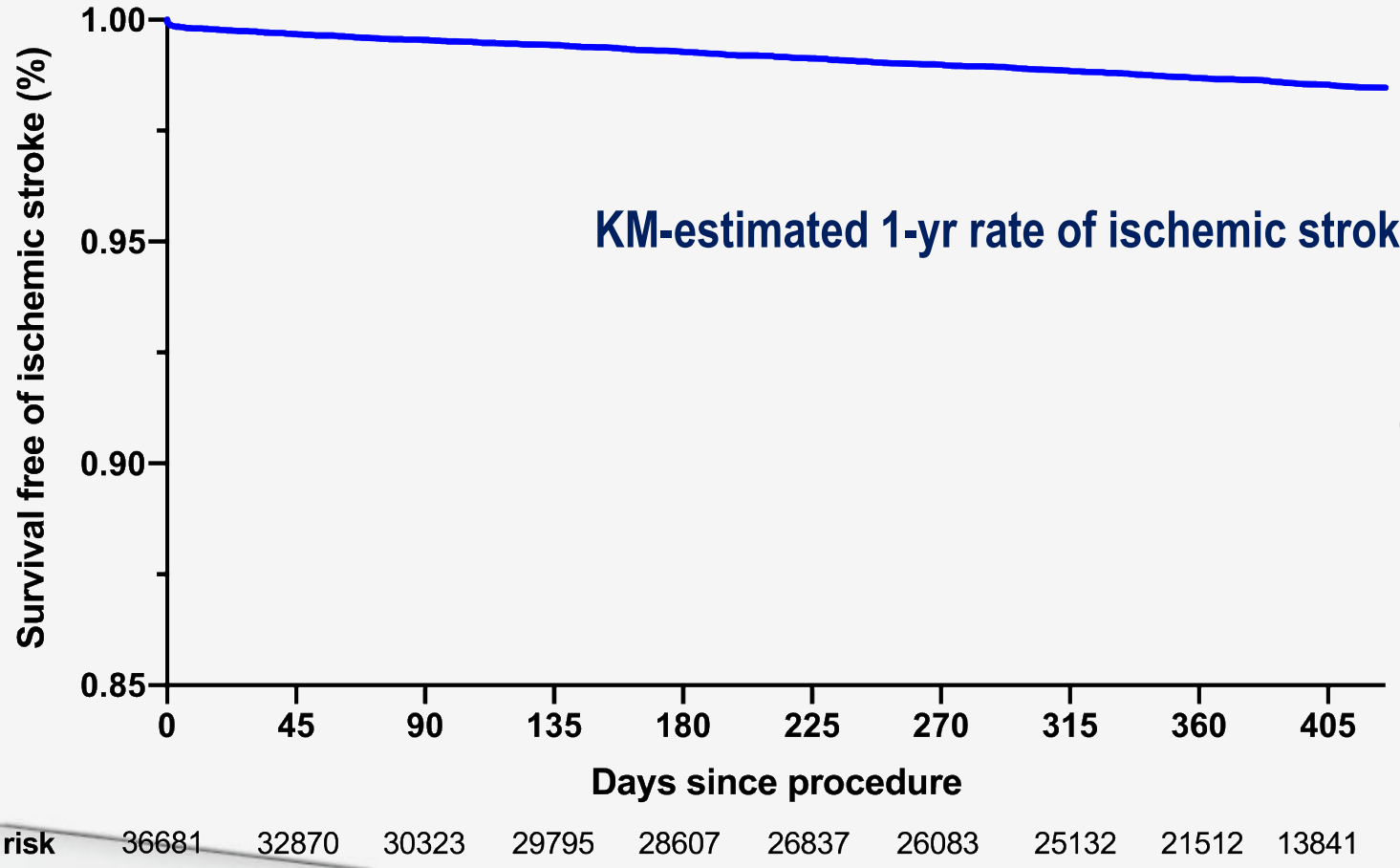
*additional 30% of patients also had a FU outside of a window

Characteristics of Patients With and Without Post-Discharge Follow-up

- **Similar thromboembolic risk**
  - CHA_2DS_2-VASc: 4.8±1.5 vs 4.8±1.5, p=0.28
- **Similar bleeding risk**
  - HAS-BLED: 3.0±1.1 vs 3.0±1.2, p=0.91
  - Clinically relevant prior bleeding in 69.4% vs. 70.2%, p=0.39
- **Similar AF classification**
  - Paroxysmal AF: 52.4% vs 52.2%, p=0.82



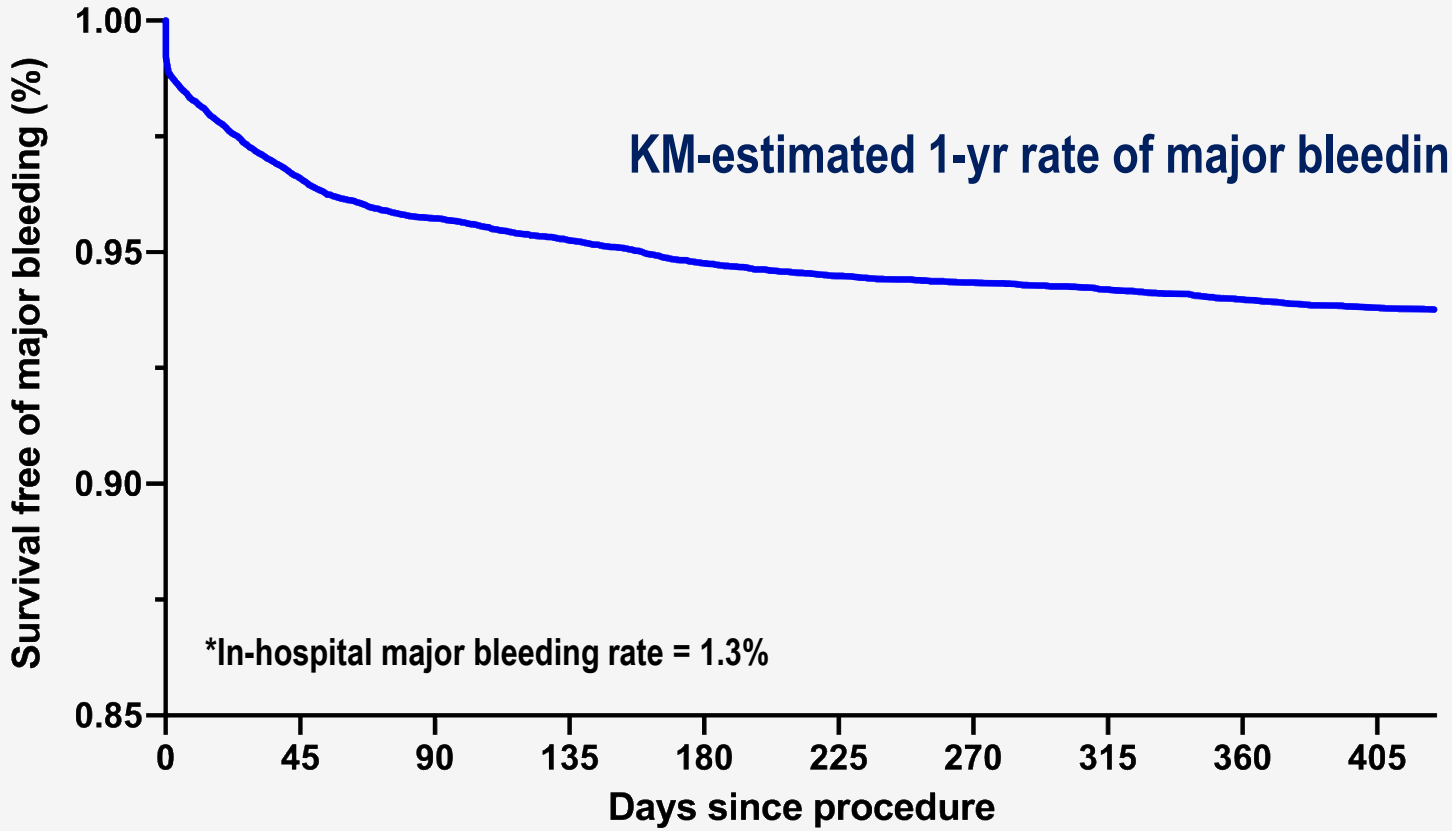
Primary Endpoint: Freedom from Ischemic Stroke



KM-estimated 1-yr rate of ischemic stroke: 1.53% [95% CI, 1.40% to 1.66%]

Cumulative rate: 1.40 per 100 PY [95% CI, 1.27-1.53]

Results: Freedom from Major Bleeding

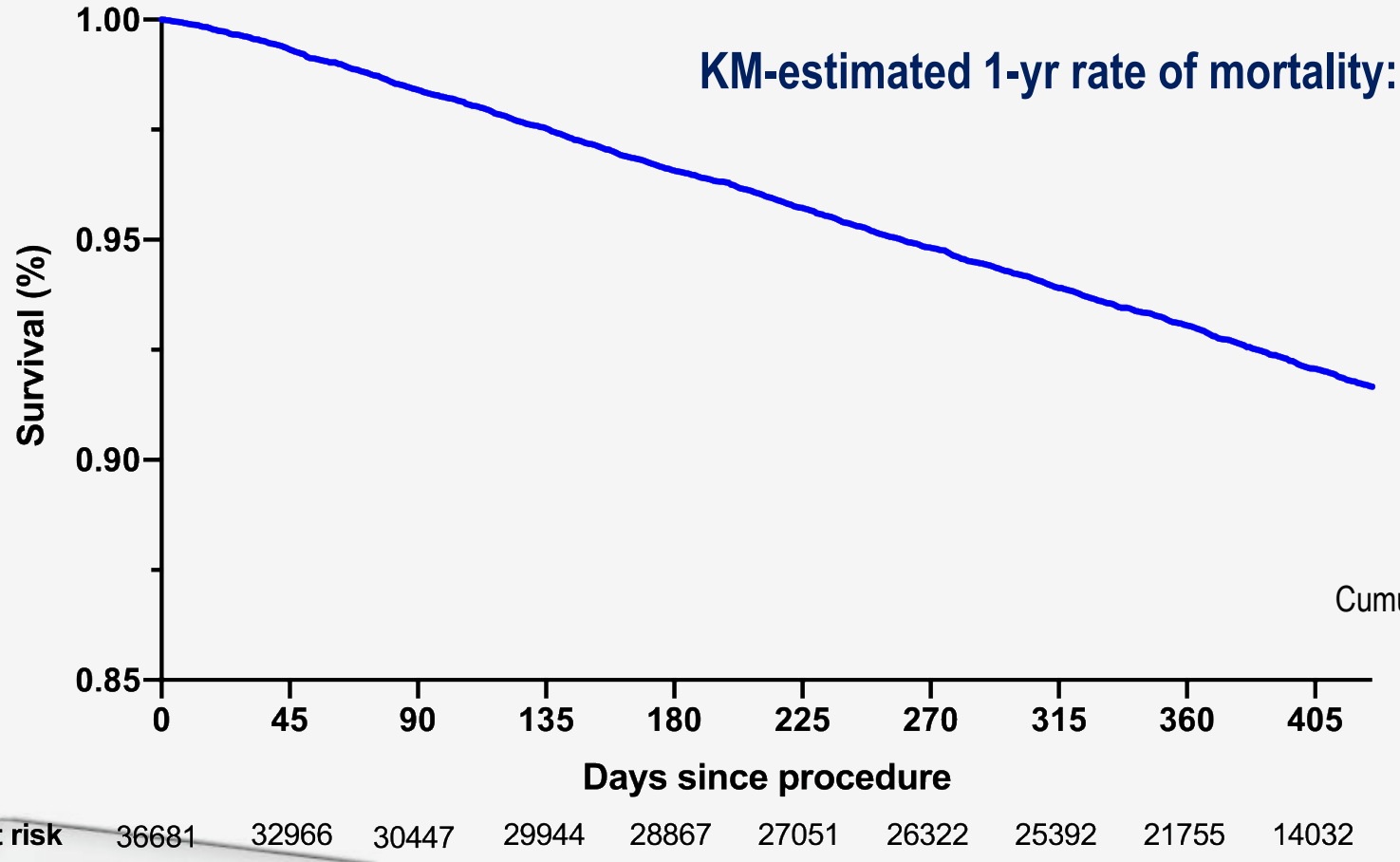


KM-estimated 1-yr rate of major bleeding: 6.2% (95% CI, 6.0% to 6.5%)

Cumulative rate: 7.08 per 100 PY [95% CI, 6.80-7.37]

No. at risk	36681	31907	29238	28631	27472	25662	24957	24050	20596	13152

Results: All-Cause Mortality

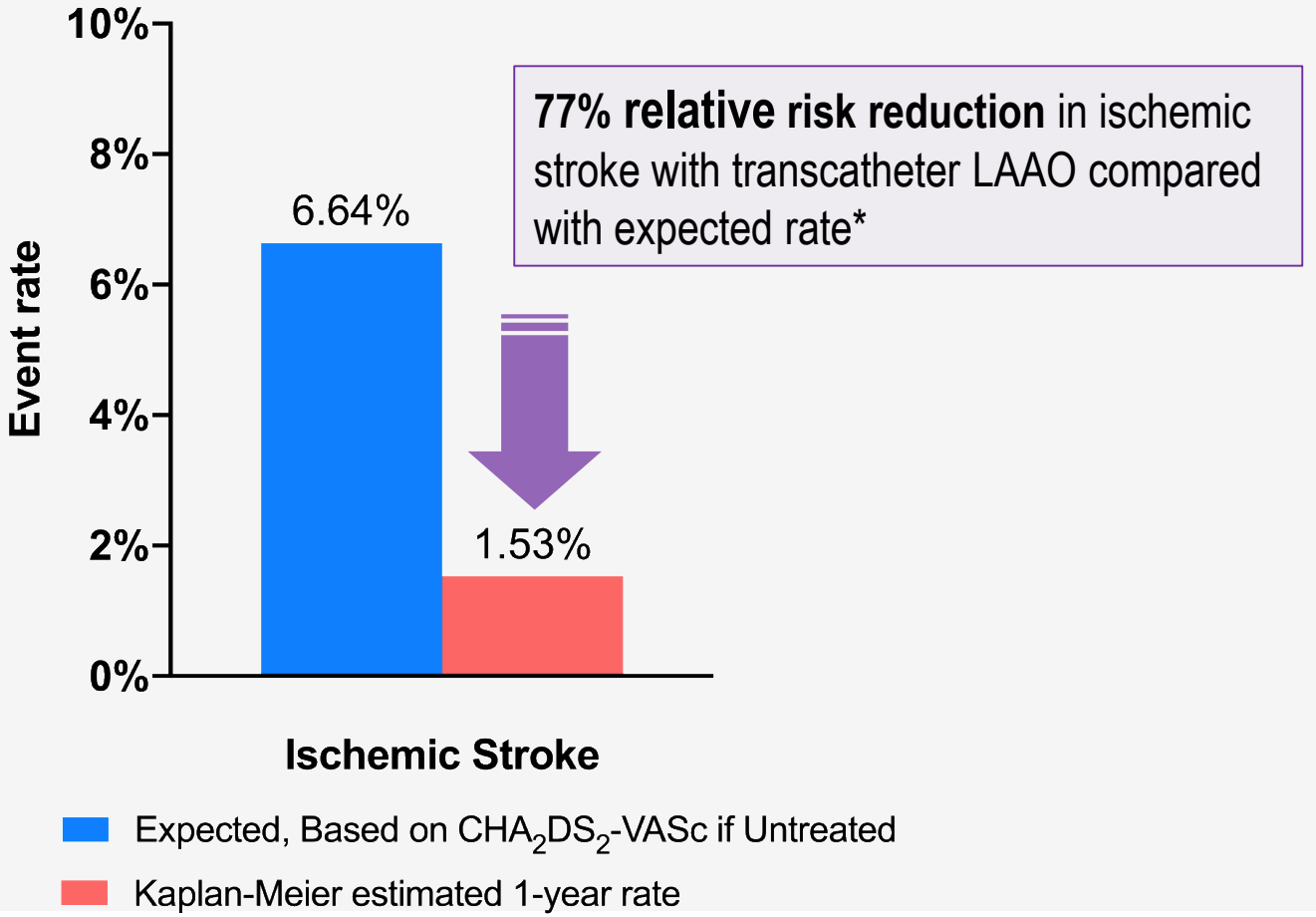


KM-estimated 1-yr rate of mortality: 8.52% (95% CI, 8.23% to 8.81%)

CV mortality: 32.6% of cases
Non-CV mortality: 60.3%
Not specified by site: 7.1%

Cumulative rate: 7.58 per 100 PY (95% CI, 7.31 to 7.85)

Rate of 1-Year Ischemic Stroke in NCDR LAAO Compared With Expected Rate



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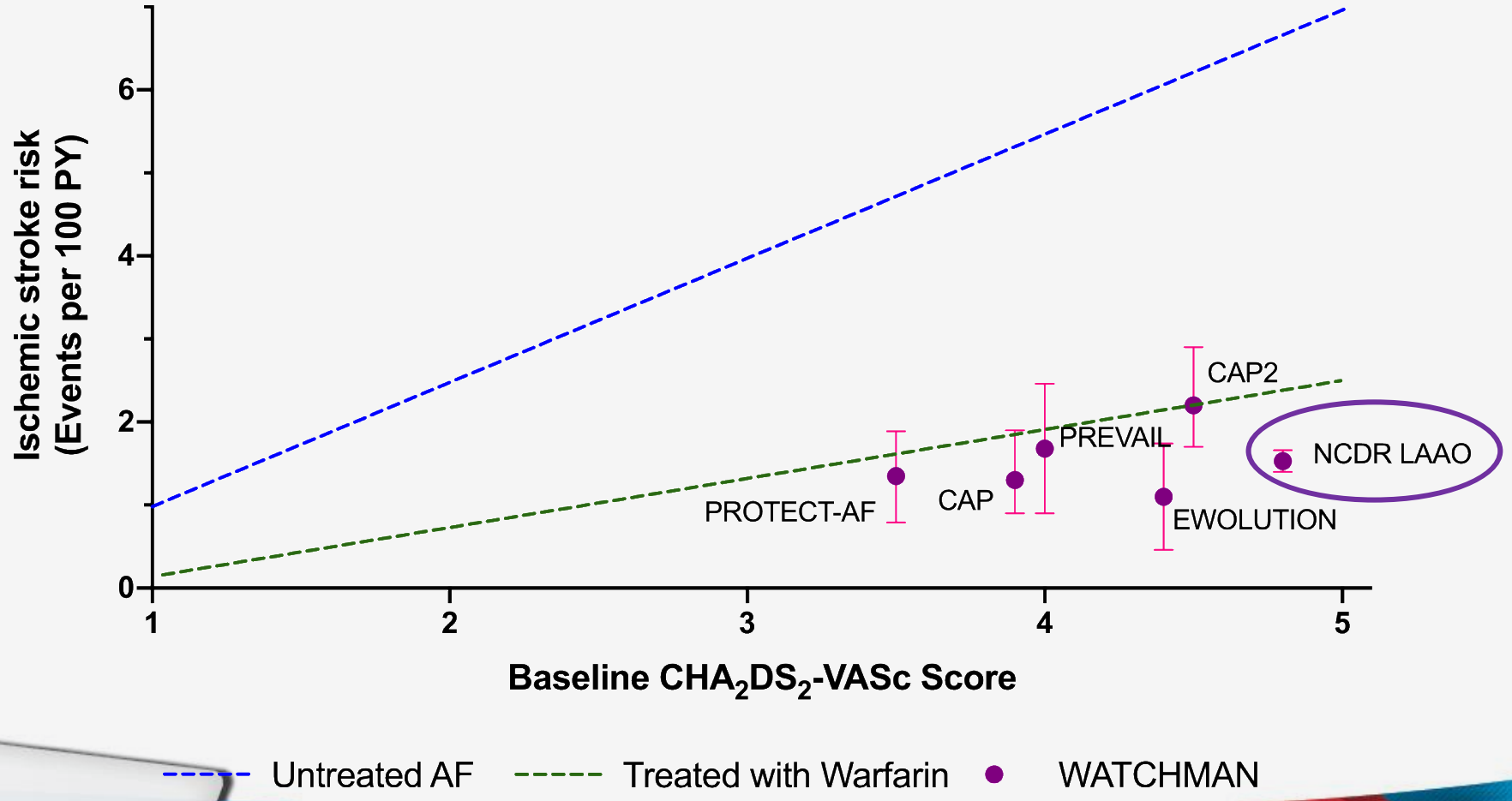
* Derived from Friberg L et al. *Eur Heart J*. 2012;33:1500-10.

Ischemic Stroke Rates in RCTs and Observational Registries of Watchman LAAO As a Function of Baseline CHA_2DS_2VASc



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Reddy VY et al, J Am Coll Cardiol. 2017;70:2964-2975. Boersma LV et al, Heart Rhythm, 017;14:1302-1308.
Holmes DR et al, J Am Coll Cardiol. 2019;74:2878-2889.

Limitations

- Incomplete follow-up may result in underestimate of event rates
  - No differences in thromboembolic and bleeding risk between patients with and without FU
  - KM estimates used to account for variable follow-up
- Routine post-procedural pharmacotherapy likely contributes in part to stroke risk reduction observed at 1-year
  - Details of length and type of OAC/antiplatelet therapy not available
- No control group
  - Method to determine expected event rate derived from baseline thromboembolic risk is commonly used in the literature

Conclusions

- Thromboembolic events at 1-year are infrequent among patients undergoing commercial Watchman implantation
    - Supports the early-to-mid term clinical effectiveness of transcatheter LAAO as it is currently being utilized in the United States.
- Risks of bleeding in the early post-discharge period and of death unrelated to thromboembolism should be incorporated into patient-centered decision-making when selecting a stroke prevention strategy for AF patients unable to take long-term OAC