

AntiCoagulation Therapy for atrial fibrillatION in the ICU setting (ACTION-ICU)

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Introduction

Atrial Fibrillation (AF) in the Critically Ill

- AF is a common condition in the ICU (prevalence in medical ICUs: 6-26%¹)
- There is limited information describing stroke risk in critically ill patients with AF, but some data to suggest it may be higher than in the ambulatory population (e.g. patients with severe sepsis and new-onset AF have 2.6% in-hospital stroke risk²)
- Despite the adoption of scoring tools for assessing risk of stroke and bleeding (e.g. CHADS₂, HAS-BLED) in national and international guidelines^{3,4}, no such scoring tools have been validated in the critically ill

Stroke Prophylaxis in the Critically Ill

- Pharmacologic stroke prophylaxis is often complicated by the associated clotting and bleeding risk associated with critical illness, as well as the tentative and/or unpredictable need for procedures^{1, 5}
- Stroke prophylaxis benefit has never been studied and no clear recommendations exist for initiation or continuation of therapy¹
- There is no local standard of practice for initiation or continuation of stroke prophylaxis in the critically ill AF patients

Study Objectives

- Assess intensivists' approach to stroke prophylaxis in critically ill AF patients through case-based clinical scenarios in a survey
- Quantify and characterize the use of stroke prophylaxis in critically ill AF patients in a local ICU population
- Determine rates of major bleeding and stroke events stratified by stroke prophylaxis status in a local ICU population

Methods

Survey

- Web based, 11-15 questions, estimated 5-10 minutes to complete
- Distributed to members of the BC Critical Care Society, Jan 2014
- Six weeks allotted for survey completion, one reminder email sent at 3 weeks
- Included a single septic shock case with two AF scenarios (CHADS₂*=2, HAS-BLED*=0)

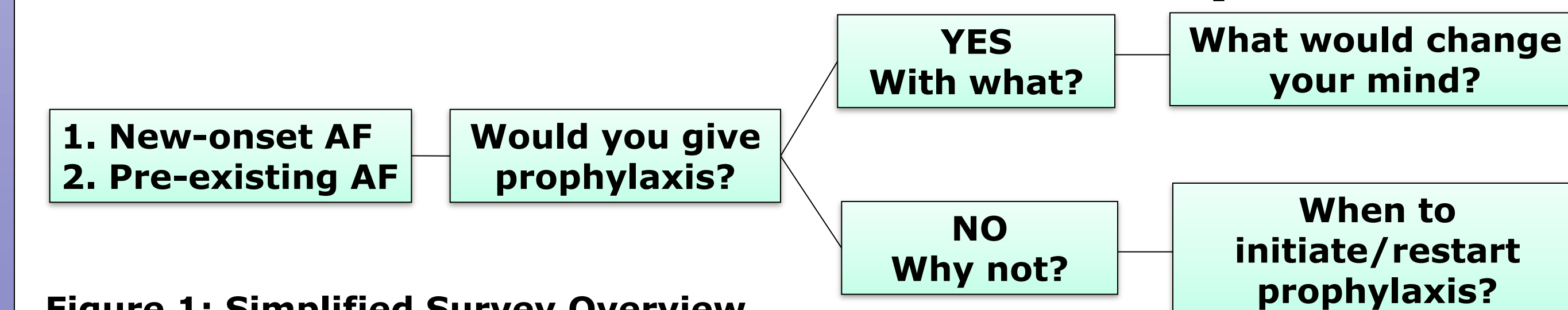


Figure 1: Simplified Survey Overview

- Specific outcome measures for each scenario:
 - “YES prophylaxis” – number of respondents, prophylaxis agent selected, specific factors that would dissuade use of prophylaxis
 - “NO prophylaxis” – rationale, anticipated timing of initiation/continuation

Prospective Observational Study

- Patients recruited Nov 2013-Apr 2014, at the Royal Jubilee Hospital (RJH) ICU
- Inclusion – critically ill patients > 18 years, new-onset or pre-existing AF
- Exclusion – pregnancy, mechanical or new bioprosthetic heart valve, severe head trauma, hypercoagulable disease, contraindications to receiving stroke prophylaxis during entire ICU stay
- Definitions:
 - AF encompassed paroxysmal, persistent and permanent types
 - New-onset AF: one episode>48 hours or 2 or more episodes greater than one hour in duration within 96 hours
 - Contraindications to stroke prophylaxis therapy included active bleeding, immediately post-operative and epidural spinal analgesia
 - Eligible ICU days for stroke prophylaxis: calculated (per patient) as total days in ICU minus days of contraindications to stroke prophylaxis
- Specific outcome measures:
 - Proportion of days of prescribed stroke prophylaxis (on eligible ICU days)
 - Bleeding and stroke events

Survey VS Prospective Observational

- Comparison of the survey findings to the practice in the RJH ICU

Statistical Methods

- Convenience sampling was used for the prospective observational study and survey
- Descriptive analyses were used to compare data
- Fisher's exact test was used to compare survey and prospective observational results

* CHADS₂ Score: 1 point for Congestive Heart Failure, Hypertension (HTN), Age≥75, Diabetes, and 2 points for Stroke

HAS-BLED Score: 1 point each, HTN>160, Renal Impairment, Liver Impairment, Stroke, Bleed History, Labile INRs, Age ≥65, Drugs, Alcohol

Results: Survey

Response Rate

- 15/49 (30.6%) intensivists responded, 13/15 (87%) completed the survey in its entirety

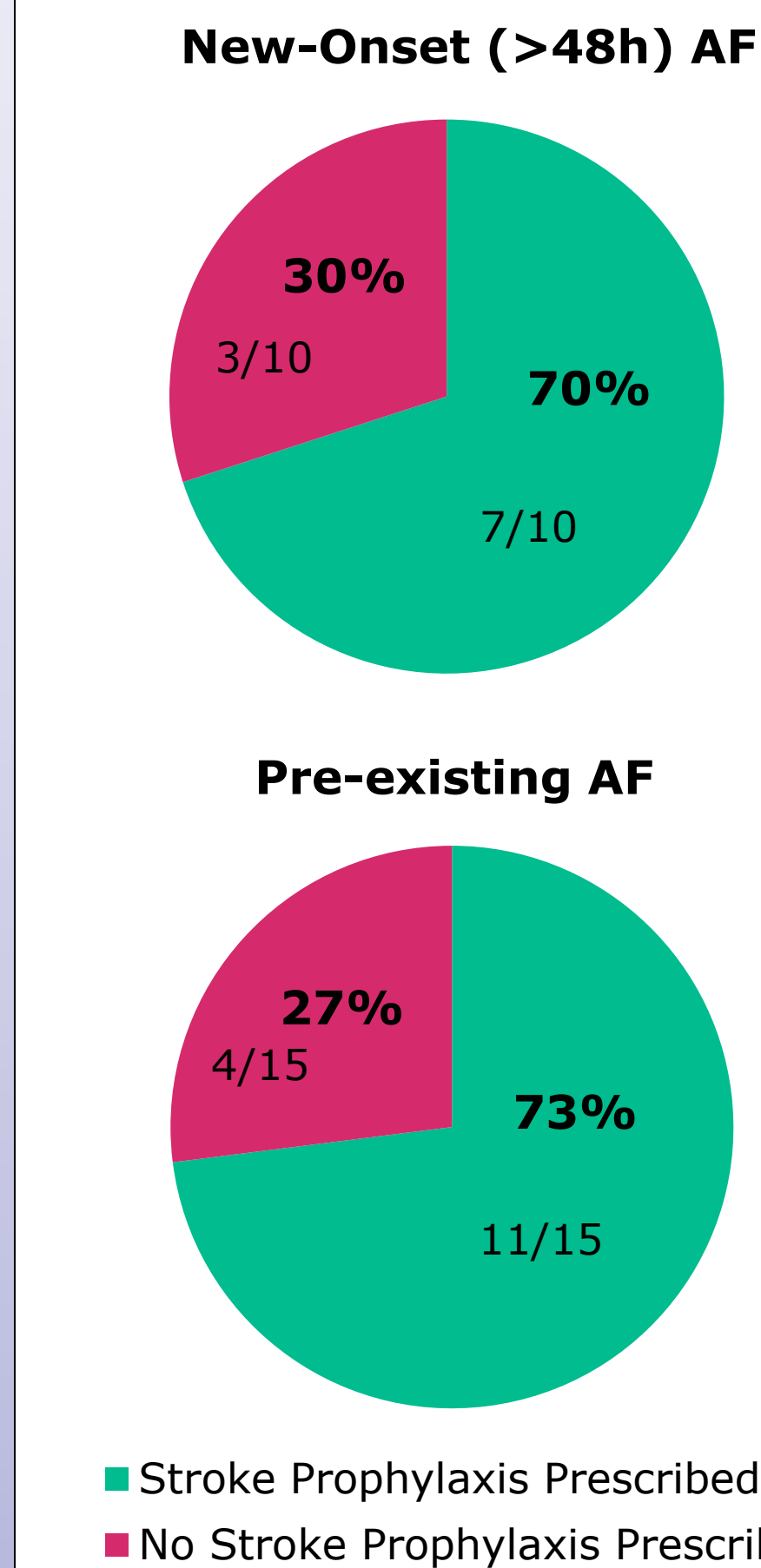


Figure 2: Intensivists Who Would Prescribe Stroke Prophylaxis in Case Scenarios

Table 1: Bleeding Risk Assessment (number of HAS-BLED criteria required to dissuade initiation of stroke prophylaxis)		
	0-2 HAS-BLED criteria	3 or more HAS-BLED criteria
New-Onset AF	2/7 (29%)	5/7 (71%)
Pre-existing AF	3/11 (27%)	8/11 (73%)

Medication Chosen for Stroke Prophylaxis

- New-Onset AF
 - UFH* continuous infusion or therapeutic dose LMWH*: 7/7 (100%)
- Pre-existing AF
 - UFH* continuous infusion or therapeutic dose LMWH*: 10/11 (91%)
 - Warfarin: 1/11 (9%)

Individual Risk Factors that Would Probably/Definitely Dissuade Intensivists from Initiating/Continuing Stroke Prophylaxis

- HTN >160mmHg: 1/18 (6%)
- Liver impairment: 2/18 (11%)
- Major bleeding history: 13/18 (72%)
- Labile INRs: 2/18 (11%)
- Drugs or alcohol: 4/18 (22%)
- Alcohol: 2/18 (11%)
- Renal impairment, stroke, age ≥65 not selected

Anticipated Timing of Initiating/Restarting Stroke Prophylaxis

- New-Onset AF
 - Once the patient is hemodynamically stable, off vasopressors and inotropes and no further invasive procedures: 1/3 (33%)
 - Not in ICU: 2/3 (66%)
- Pre-existing AF
 - Once the patient is hemodynamically stable, off vasopressors and inotropes and no further invasive procedures required: 2/4 (50%)
 - Not in ICU: 2/4 (50%)

* UFH=Unfractionated Heparin, LMWH=Low Molecular Weight Heparin

Results: Prospective Observational

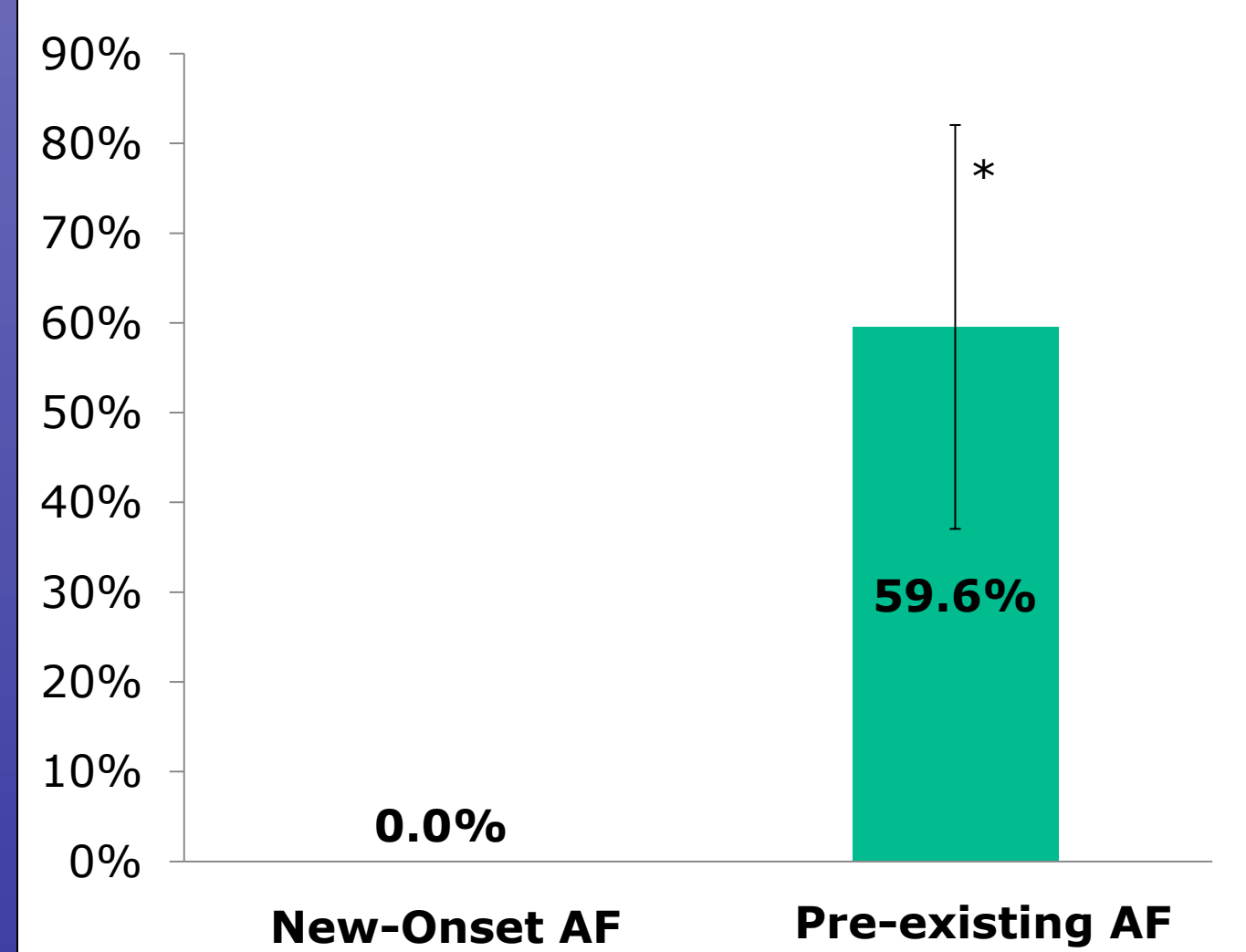
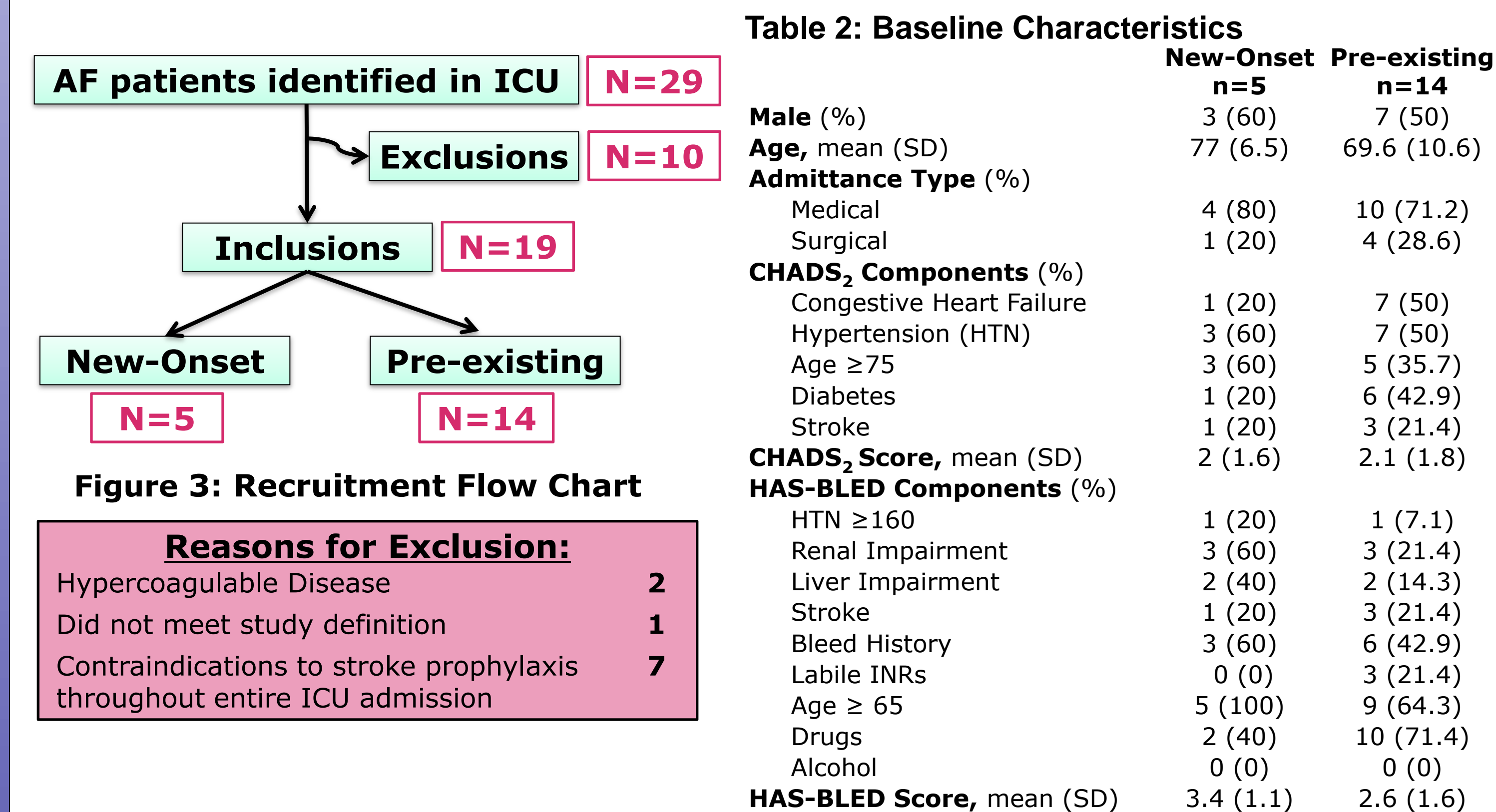


Figure 4: Mean Proportion of Days Receiving Stroke Prophylaxis for Eligible Days in ICU, Comparison by AF Type

Table 2: Baseline Characteristics		
	New-Onset n=5	Pre-existing n=14
Male (%)	3 (60)	7 (50)
Age, mean (SD)	77 (6.5)	69.6 (10.6)
Admittance Type (%)		
Medical	4 (80)	10 (71.2)
Surgical	1 (20)	4 (28.6)
CHADS ₂ Components (%)		
Congestive Heart Failure	1 (20)	7 (50)
Hypertension (HTN)	3 (60)	7 (50)
Age ≥75	3 (60)	5 (35.7)
Diabetes	1 (20)	6 (42.9)
Stroke	1 (20)	3 (21.4)
CHADS ₂ Score, mean (SD)	2 (1.6)	2.1 (1.8)
HAS-BLED Components (%)		
HTN ≥160	1 (20)	1 (7.1)
Renal Impairment	3 (60)	3 (21.4)
Liver Impairment	2 (40)	2 (14.3)
Stroke	1 (20)	3 (21.4)
Bleed History	3 (60)	6 (42.9)
Labile INRs	0 (0)	3 (21.4)
Age ≥ 65	5 (100)	9 (64.3)
Drugs	2 (40)	10 (71.4)
Alcohol	0 (0)	0 (0)
HAS-BLED Score, mean (SD)	3.4 (1.1)	2.6 (1.6)

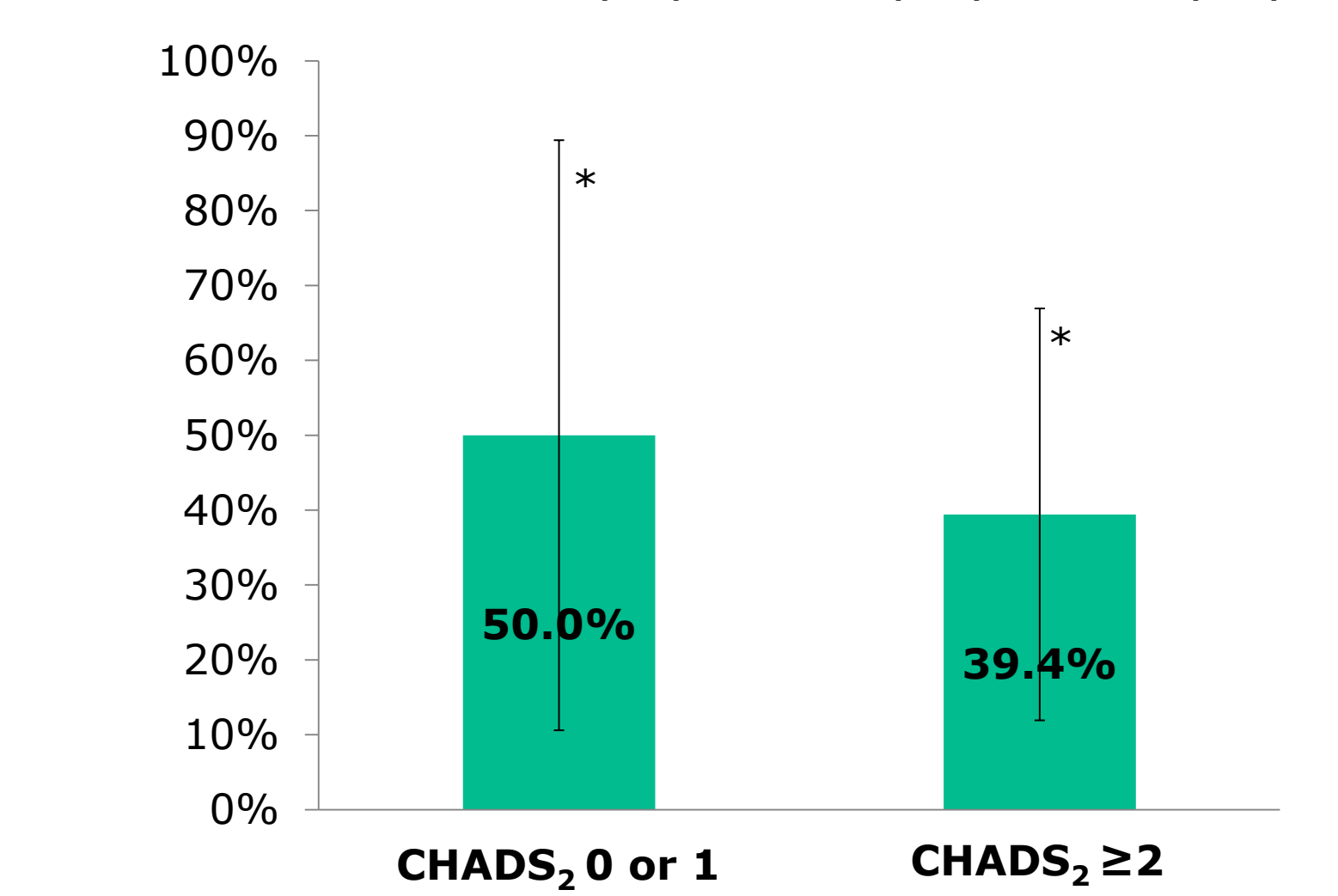


Figure 5: Mean Proportion of Days Receiving Stroke Prophylaxis for Eligible Days in ICU, Comparison by CHADS₂ Score

Results: Prospective Observational

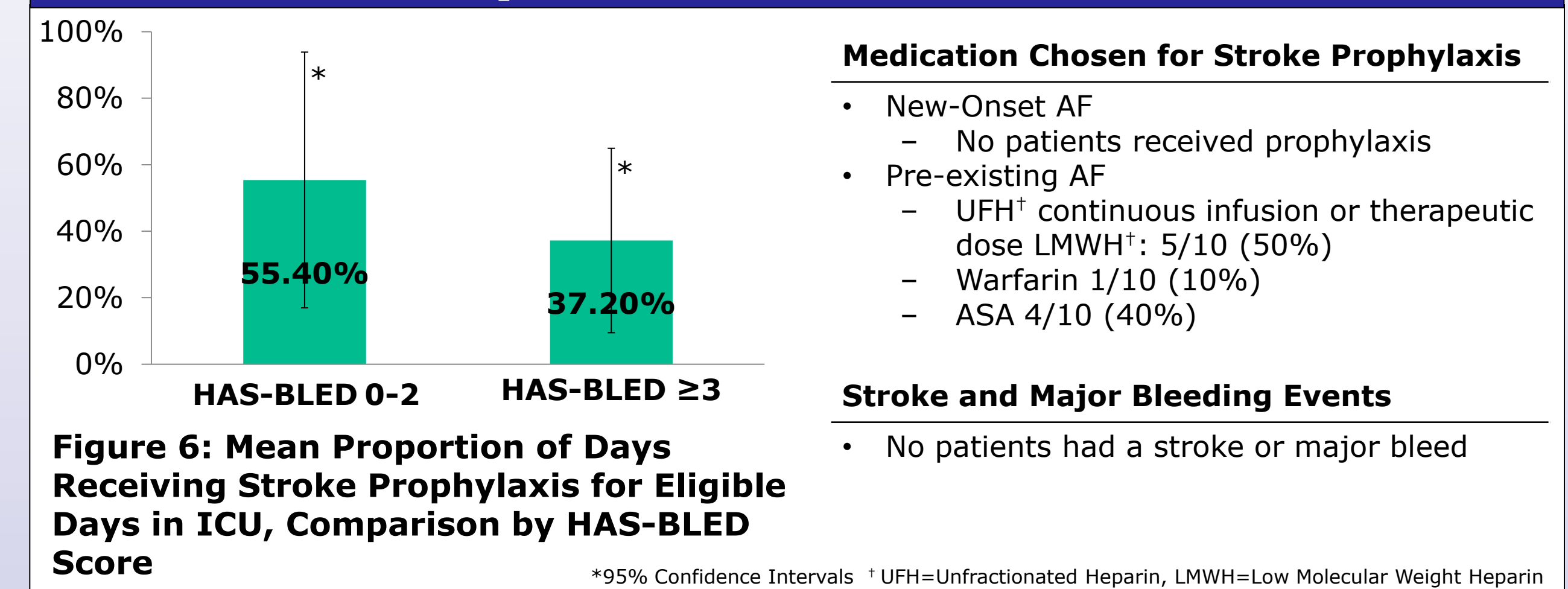


Figure 6: Mean Proportion of Days Receiving Stroke Prophylaxis for Eligible Days in ICU, Comparison by HAS-BLED Score

Medication Chosen for Stroke Prophylaxis

- New-Onset AF
 - No patients received prophylaxis
- Pre-existing AF
 - UFH* continuous infusion or therapeutic dose LMWH*: 5/10 (50%)
 - Warfarin 1/10 (10%)
 - ASA 4/10 (40%)

Stroke and Major Bleeding Events

- No patients had a stroke or major bleed

Results: Survey vs. Prospective

	Survey	Prospective Observational	P value
New-Onset	7/10 (70%)	0/5 (0%)	0.0256
Pre-existing	11/15 (73%)	11/14 (79%)	1
All Patients	18/25 (72%)	11/19 (58%)	0.357

Table 3: Stroke Prophylaxis in ICU Patients, Survey vs. Actual Practice

Discussion

Survey

- Intensivists reported they would prescribe stroke prophylaxis the majority of the time regardless of whether the AF is new-onset or pre-existing
- Intensivists tolerated bleeding risk in favour of providing stroke prophylaxis. Less than one third of intensivists reported that they would be dissuaded in their decision to give stroke prophylaxis in patients with up to 2 HAS-BLED bleeding risk factors
- Bleeding history was the most important variable in dissuading intensivists from using stroke prophylaxis, despite it being assigned equal weight relative to the other variables in the HAS-BLED scoring tool
- Reversibility was a priority as reflected by choice of stroke prophylaxis agent

Prospective Observational

- Baseline Characteristics: Stroke risk was relatively balanced between new-onset and pre-existing groups, but bleeding risk was higher in the former
- Intensivists seemed to prioritize stroke prophylaxis in patients with pre-existing AF higher than in those patients with new-onset AF
- Best estimation of stroke risk (by using the CHADS₂ score) did not seem to correlate with the use of stroke prophylaxis
- When stroke prophylaxis was used, intensivists did not appear to be dissuaded by significant bleeding risk over one-third of the time
- Intensivists were not likely to use warfarin for stroke prophylaxis, possibly due to slow reversibility

Survey Compared to Prospective Observational

- Intensivists' decision-making with respect to stroke prophylaxis was similar between reported and observed practice for patients with pre-existing AF but was contrary for patients with new-onset AF

Limitations

- Small sample size and survey response rate → hypothesis generating
- High exclusion in observational study → necessary to capture target population
- CHADS₂ and HAS-BLED have not been validated in the critically ill

Conclusion

- When asked, a majority of intensivists placed a high priority on the stroke risk associated with both new-onset and pre-existing AF in the ICU and accepted even a moderate bleeding risk to provide prophylaxis
- In practice, critically ill patients with pre-existing AF were more likely to receive expected stroke prophylaxis versus patients with new-onset AF
- There is a need for validated risk scores assessing stroke and bleed risk in critically ill AF patients

Application to practice

- This is the first study to specifically evaluate decision-making around stroke prophylaxis for AF in the ICU, and sets the stage for further study
- Our prospective, observational methodology could be applied to a broader patient sample to elaborate on and confirm our findings