#AHA22

PRECISE

Comparison of a Precision Care Strategy With Usual Testing To Guide Management Of Stable Patients With Suspected Coronary Artery Disease

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Funded by HeartFlow, Inc

American Heart Association.

Background

- New onset stable chest pain is a common problem and requires performance of approximately 4 million tests annually in the US alone
- All clinical practice guidelines (AHA/ACC, ESC, NICE) agree on evaluation goals for such patients, and propose similar strategies to accomplish them. These goals are to:
  - Reduce unnecessary testing by risk stratification and deferred testing
  - Improve diagnostic yield of testing and catheterization
  - Reduce complications and costs by serving as an efficient gatekeeper to invasive testing
  - Optimize preventive medical treatment

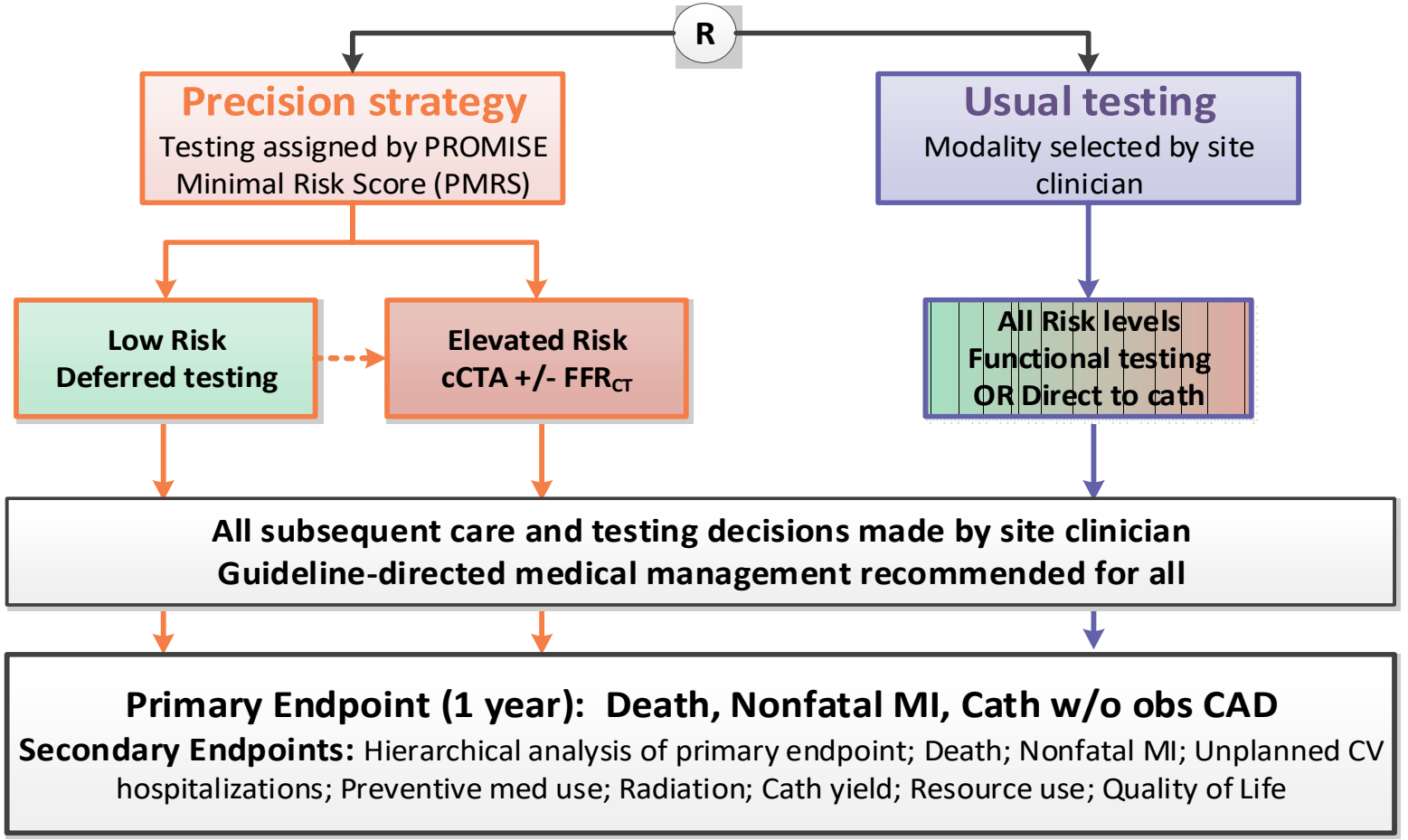
Need for Evidence and Hypothesis

- Randomized trial-level evidence is needed to determine the best care pathway to accomplish these consensus goals
  - Prospective validation of a pre-test probability assessment to guide decision making regarding deferral vs immediate testing
  - Prospective evaluation of the safety of deferred testing in symptomatic patients
  - Once a patient is determined to need testing, randomized trial evidence comparing cCTA with selective FFR_{CT} versus other modalities as first test
- **PRECISE Hypothesis**
  - In stable, symptomatic patients with suspected CAD, a **Precision Strategy** care pathway incorporating a set of actions based on Guideline recommendations will improve outcomes compared to **Usual Testing**

PRECISE Trial

Non-acute chest pain or equivalent patients requiring testing for suspected CAD
No history of obstructive CAD or CAD testing <1 year: N=2103

Randomization stratified by PROMISE Minimal Risk Score and preferred first test if usual care

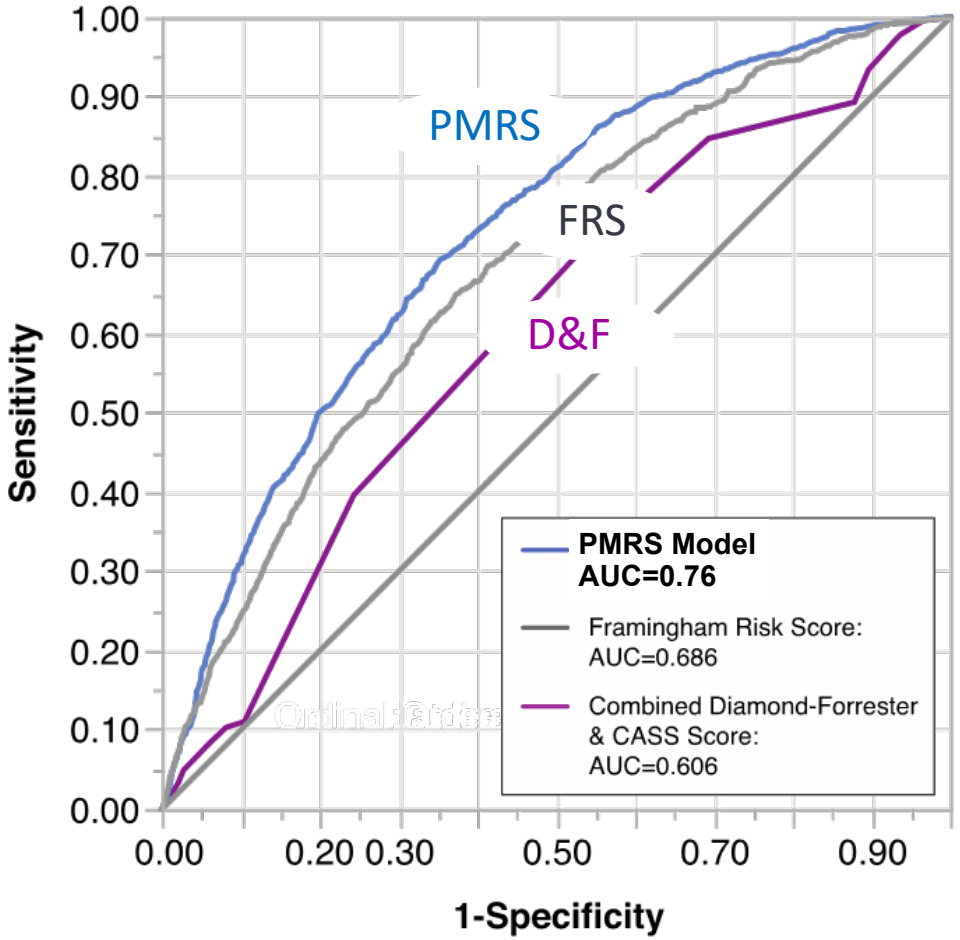


JAMA Cardiology | Original Investigation

Identification of Patients With Stable Chest Pain Deriving Minimal Value From Noninvasive Testing

The PROMISE Minimal-Risk Tool, A Secondary Analysis of a Randomized Clinical Trial

- Using 4,631 PROMISE cCTA pts, we modeled Minimal Risk: 27% w/o CAC, plaque or events
- Result: 10 clinical variables predicted Minimal Risk
- Validated in SCOT-Heart, Dan-NICAD (n=3,439)
- Combined in all 3 cohorts: C stat 0.76

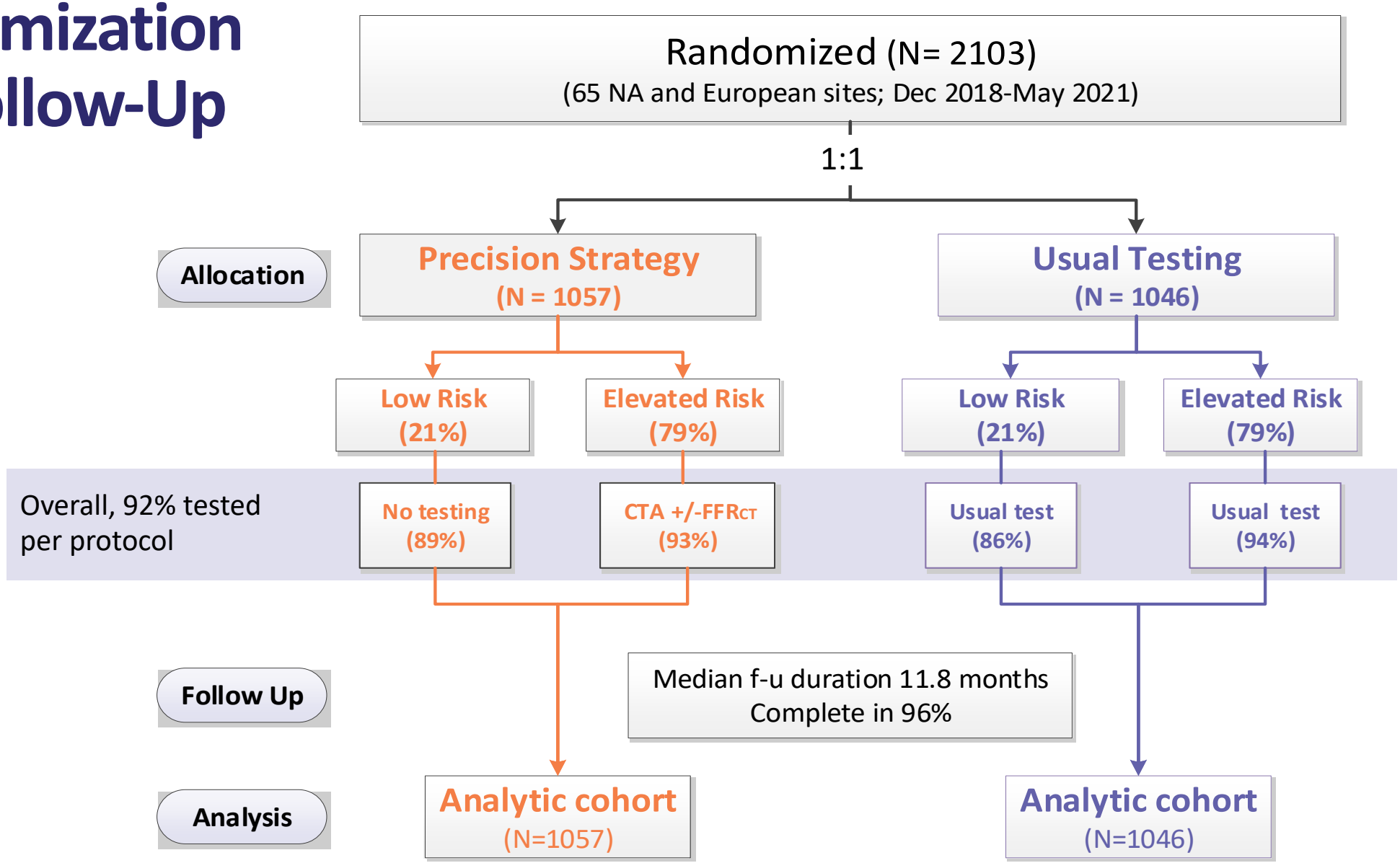


JAMA Cardiology 2017 2:400-408
Intl J Cardiology 2018 252:31-34
Intl J CV Imaging 2021 37:699–706

Trial Endpoints and Statistical Analysis

- **Composite primary endpoint: All-cause death, nonfatal MI, or cath w/o obstructive CAD**
  - Composite defines *net clinical effectiveness* (efficacy and safety) for this low-risk population
  - Catheterization without obstructive CAD was defined as the absence of any positive invasive FFR/iFR or any QCA-measured stenosis ≥50% in epicardial vessel ≥2mm diameter
  - Lower rates of cath w/o obs CAD associated w better QOL, fewer complications, lower costs
- All primary endpoint events were adjudicated by blinded Clinical Events Committee
- Statistical analysis
  - Sample size of 2100 provided ≥90% power to detect a 35% reduction in primary endpoint
  - All comparisons performed as Intention To Treat with time-to-event analysis, using log rank testing. Cox proportional hazards adjusted for age, sex, CAD risk equivalent, and intended test type at randomization
- The statistical team had full access to the complete data base and performed all analyses independently of the trial sponsor

Randomization and Follow-Up



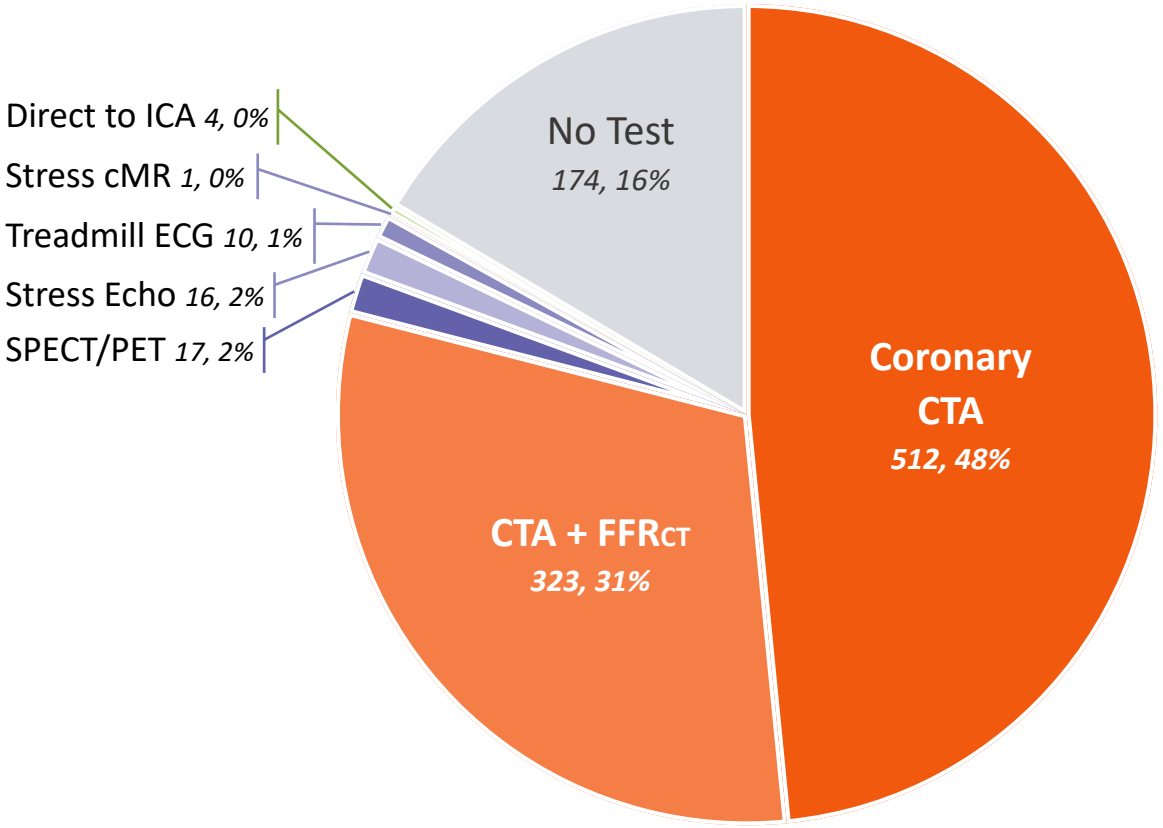
Baseline Characteristics

		Precision Strategy (N=1057)	Usual Testing (N=1046)
Demographics	Age — yr	58.0 ± 11.5	58.9 ± 11.6
	Women	508 (48%)	539 (52%)
	Racial or ethnic minority group	165 (16%)	171 (16%)
Risk factors	≥1 major CV risk factor	990 (94%)	985 (94%)
	Hypertension	642 (61%)	606 (58%)
	Diabetes mellitus	176 (17%)	197 (19%)
	Dyslipidemia	668 (63%)	681 (65%)
	Family history of premature CAD	404 (38%)	395 (38%)
	Current or past tobacco use	544 (52%)	554 (53%)
Risk scores	Updated D-F pretest probability	16.0 (10.0, 26.0)	16.0 (10.0, 26.0)
	ASCVD 10-year	7.92 (3.4, 15.7)	8.22 (3.3, 17.2)
Primary symptom	Chest pain	870 (82%)	876 (84%)
Anginal type	Typical angina (cardiac)	249 (24%)	257 (25%)

Initial Diagnostic Test Performed

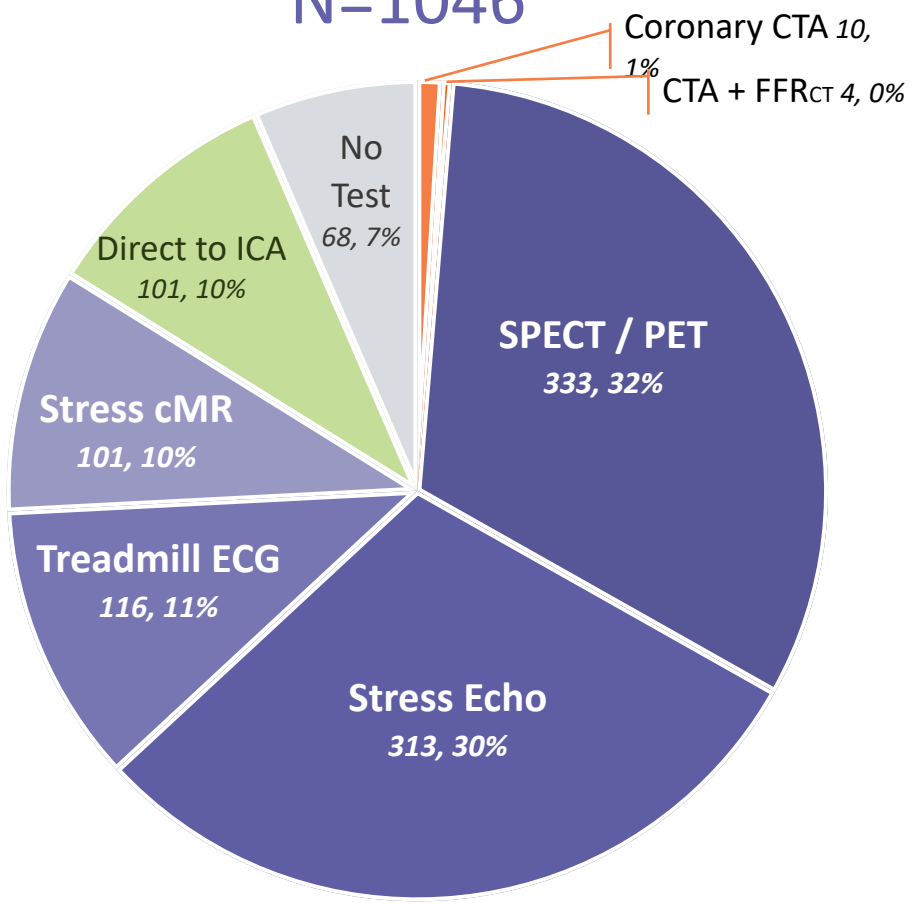
Precision Strategy

N=1057

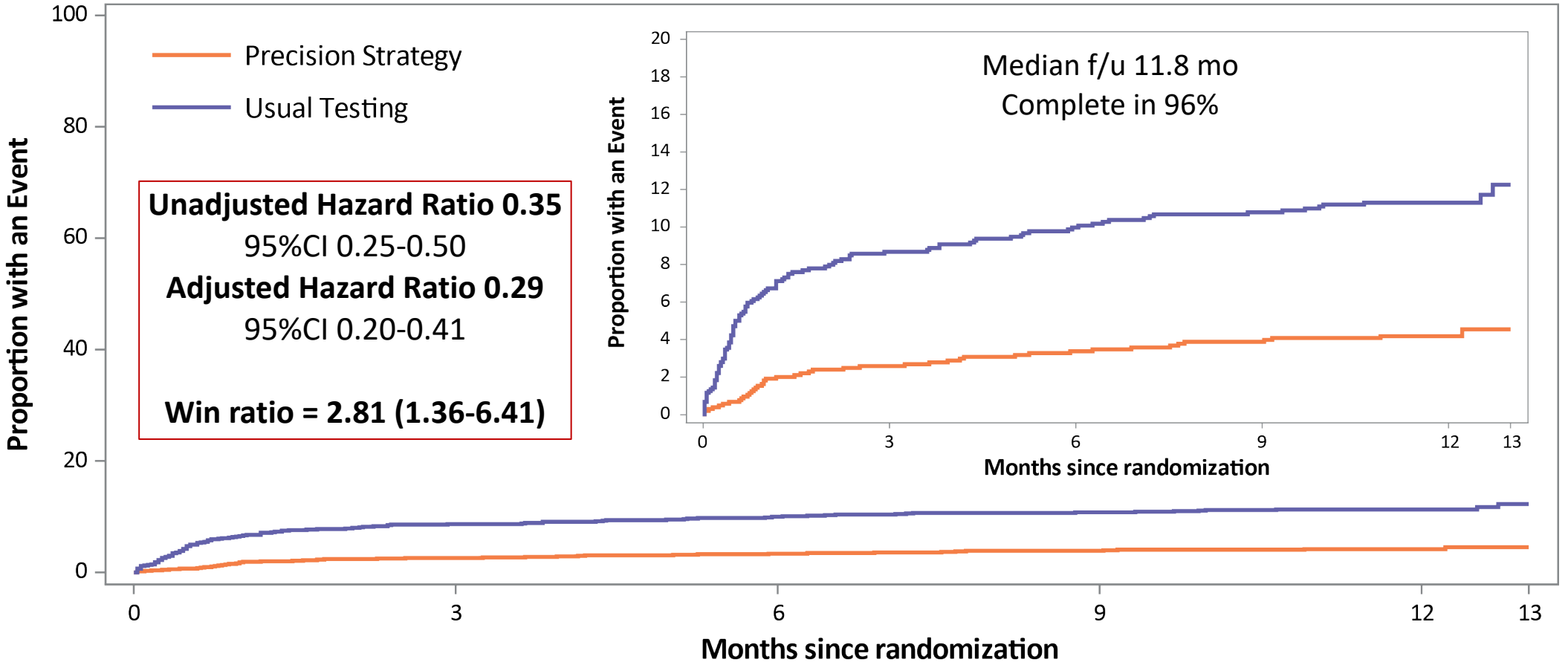


Usual Testing

N=1046



Primary Endpoint: Death, MI, or Cath w/o Obstructive CAD



Number at Risk					
PS	1057	997	971	945	431
UT	1046	922	898	869	421

Primary Endpoint Events

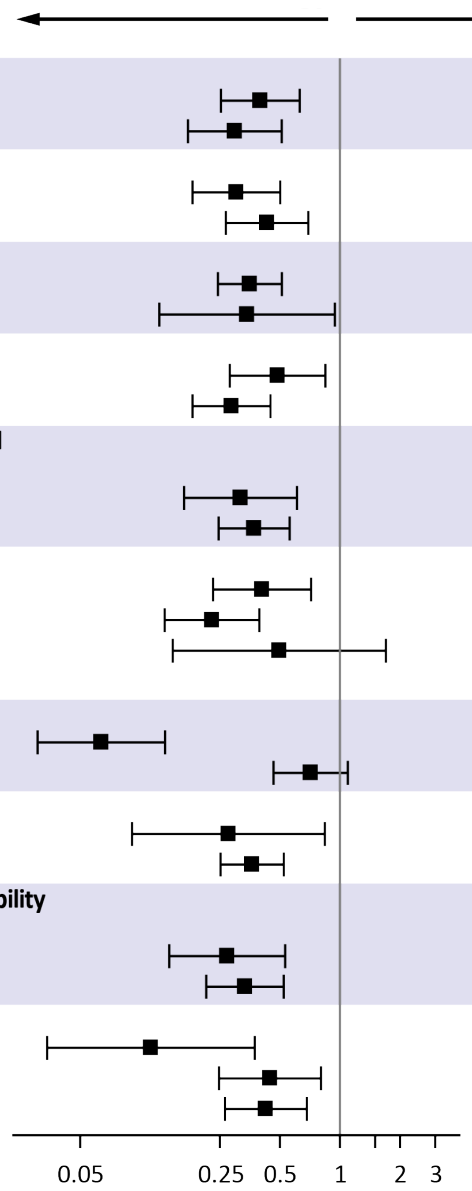
	Precision Strategy (N=1057)	Usual Testing (N=1046)	Adjusted Hazard Ratio (95% CI)	P-Value
Primary endpoint composite	44 (4.2%)	118 (11.3%)	0.29 (0.20-0.41)	<0.001
Death or MI	18 (1.7%)	12 (1.1%)	1.57 (0.76-3.27)	
All cause death	5 (0.5%)	7 (0.7%)	0.74 (0.24-2.35)	
Nonfatal MI	13 (1.2%)	5 (0.5%)	2.67 (0.94-7.52)	
ICA w/o obstructive CAD	27 (2.6%)	107 (10.2%)	0.18 (0.12-0.30)	

There were no death or MI events in the Precision Strategy participants assigned to deferred testing.

Notes: Deaths include one participant with a fatal MI.

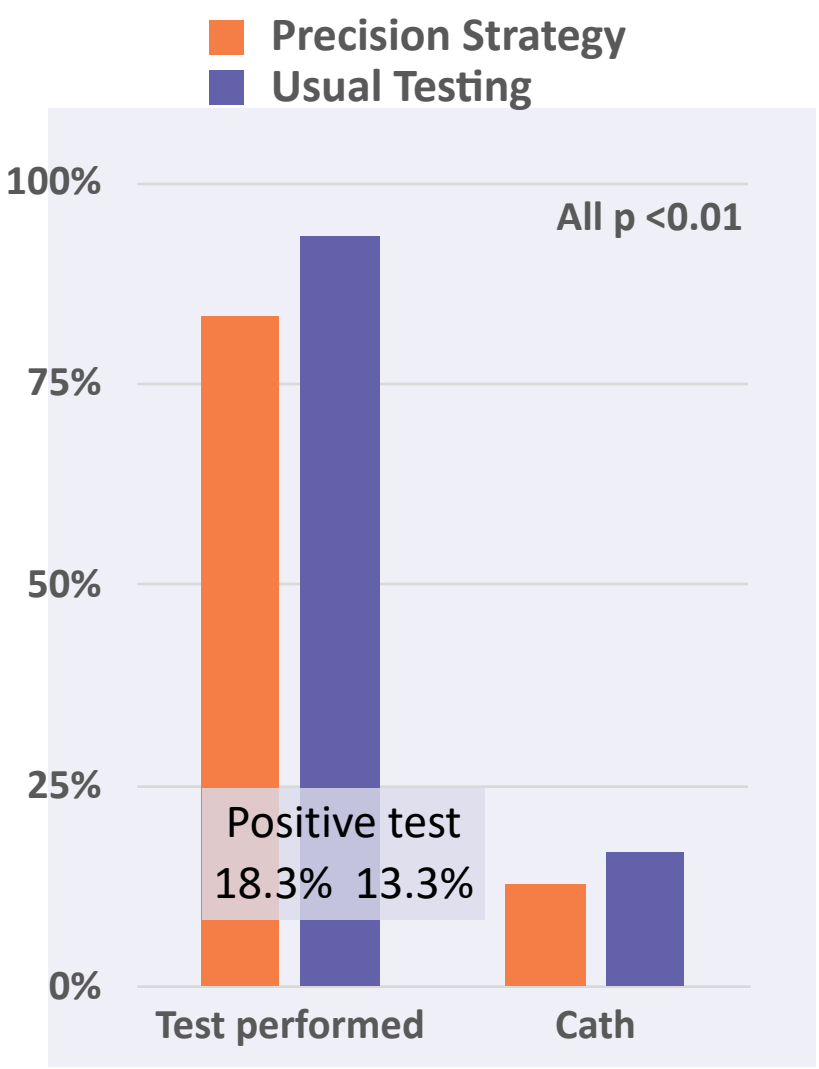
One MI on the day of randomization was determined by CEC to have preceded study entry and was excluded.

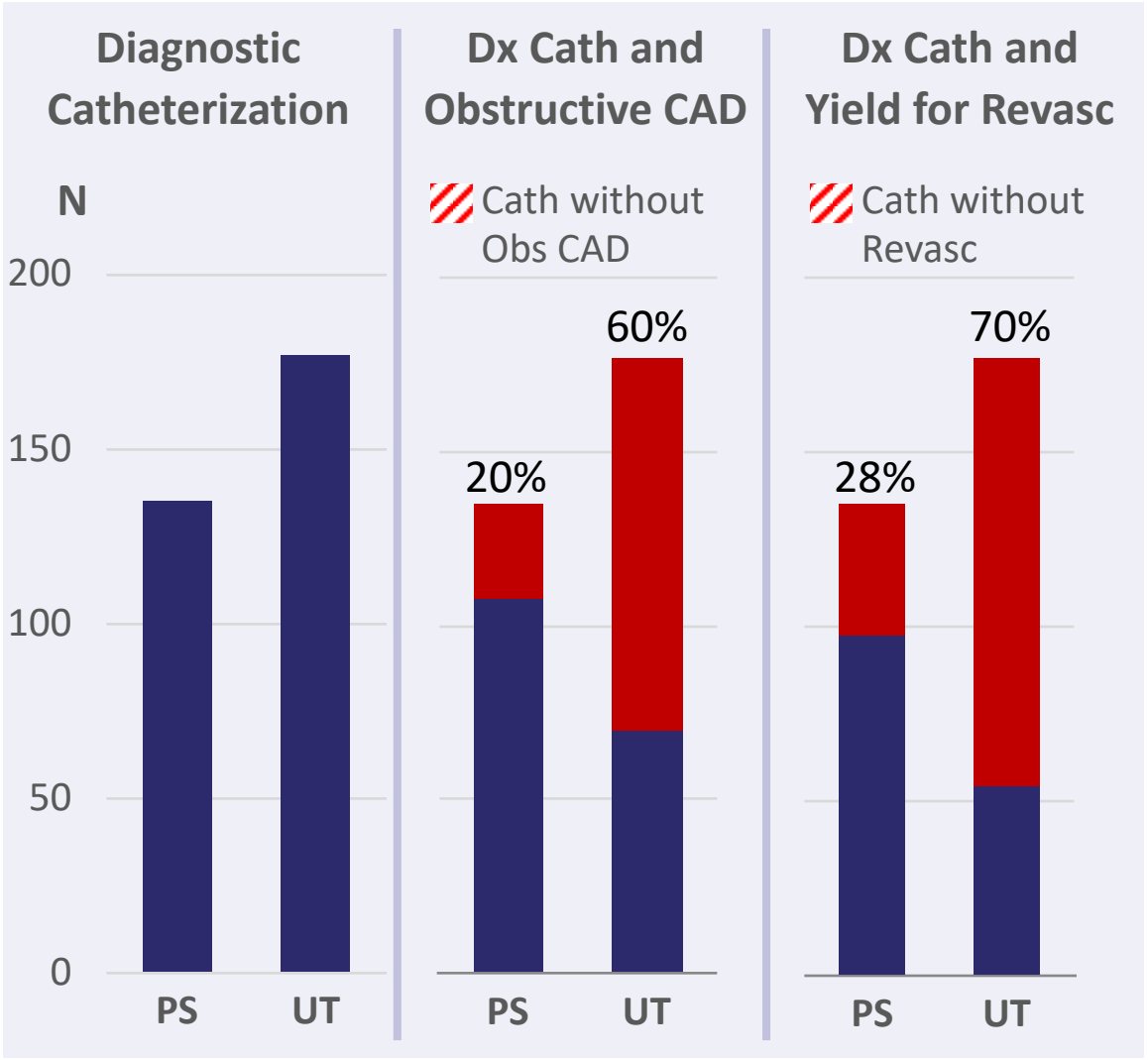
Primary Endpoint: Subgroup Analysis

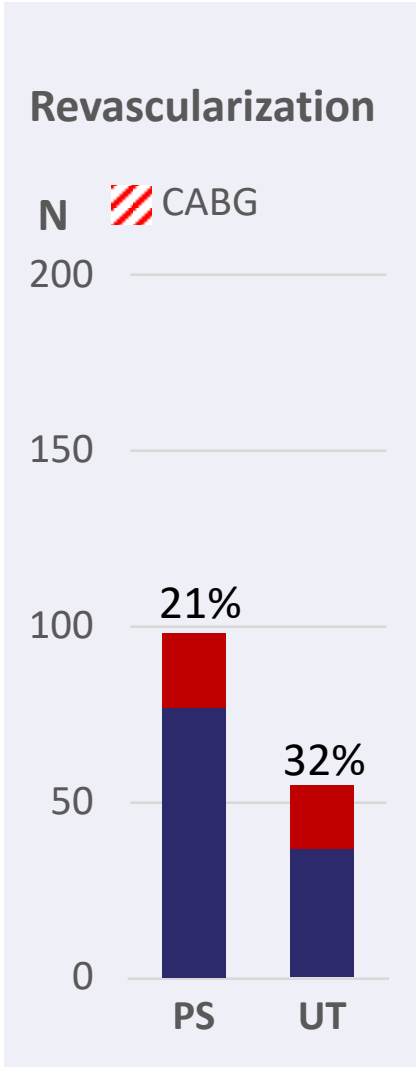


	PS	UT	Interaction P-value
Sex			0.417
Male	27/549 (5.6%)	60/507 (12.7%)	
Female	17/508 (3.4%)	58/539 (11.8%)	
Age			0.318
<65	20/737 (2.8%)	60/693 (9.4%)	
≥65	24/320 (8.8%)	58/353 (18.0%)	
Race/Ethnicity			0.954
White/non-Hispanic	39/892 (4.8%)	103/875 (12.6%)	
Other	5/165 (3.2%)	15/171 (10.3%)	
Geographic region			0.143
North America	19/609 (3.8%)	38/596 (7.7%)	
Europe	25/448 (5.6%)	80/450 (18.0%)	
CAD equivalent (diabetes or peripheral arterial or cerebrovascular disease)			0.690
Yes	12/226 (5.5%)	37/237 (15.8%)	
No	32/831 (4.3%)	81/809 (11.2%)	
Primary symptom presentation			0.451
Typical angina (cardiac)	17/249 (6.9%)	41/257 (16.3%)	
Atypical pain (possible cardiac)	16/600 (3.2%)	66/597 (11.8%)	
Dyspnea	4/86 (4.8%)	7/77 (15.5%)	
Non anginal (non-cardiac)/other	0/14 (0.0%)	0/7 (0.0%)	
Intended first test is			<0.001
Invasive	8/105 (7.7%)	68/105 (66.1%)	
Noninvasive	36/952 (4.2%)	50/941 (6.3%)	
PROMISE Minimal Risk Score			0.648
Low	4/224 (1.8%)	14/219 (8.0%)	
Elevated + atherosclerosis	40/833 (5.3%)	104/827 (13.2%)	
Diamond and Forrester pre test probability			0.882
<5% pretest probability	0/63 (0.0%)	1/44 (2.3%)	
5-15%	11/411 (2.8%)	39/411 (10.5%)	
>15%	26/475 (6.1%)	74/483 (16.4%)	
ASCVD 10-year event risk score			0.109
<7.5%	3/356 (0.9%)	25/345 (8.4%)	
7.5-15%	17/374 (4.6%)	32/327 (9.9%)	
>15%	24/327 (8.5%)	61/374 (17.7%)	

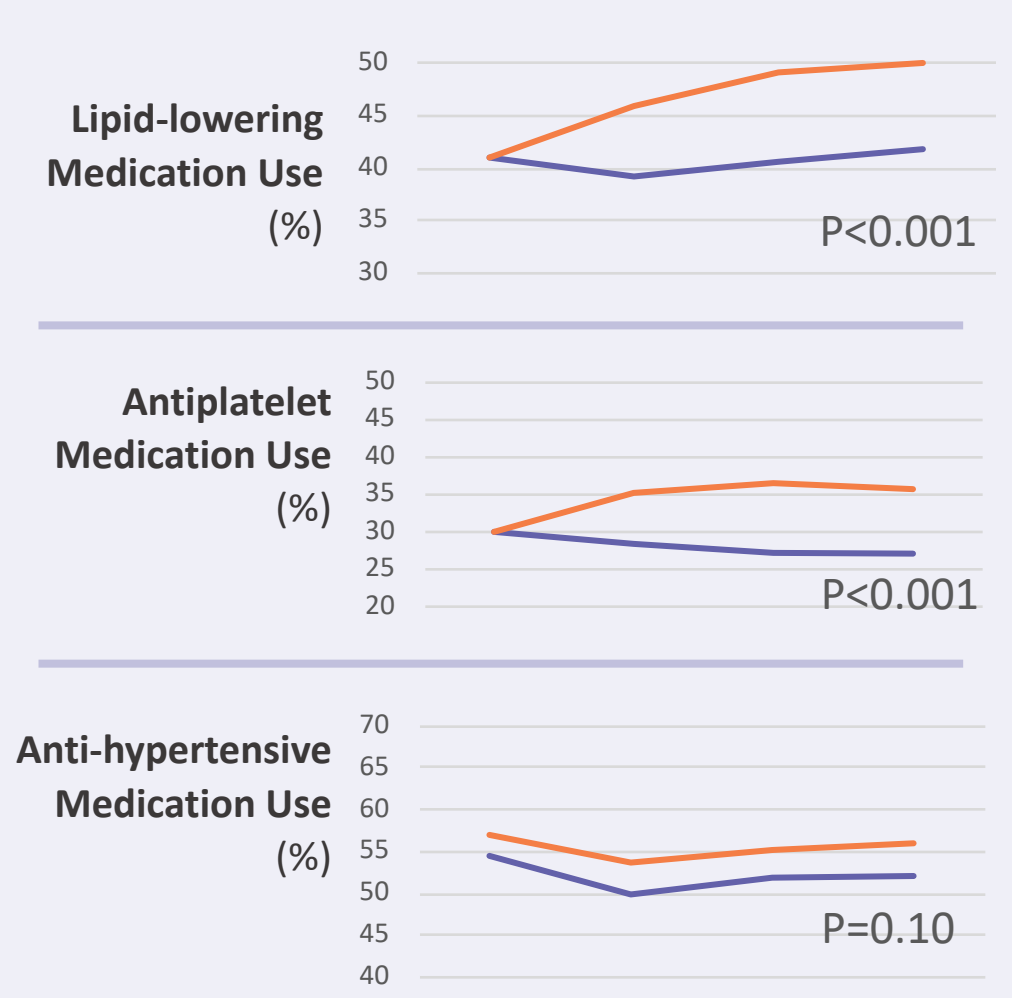
Secondary Effectiveness Endpoints

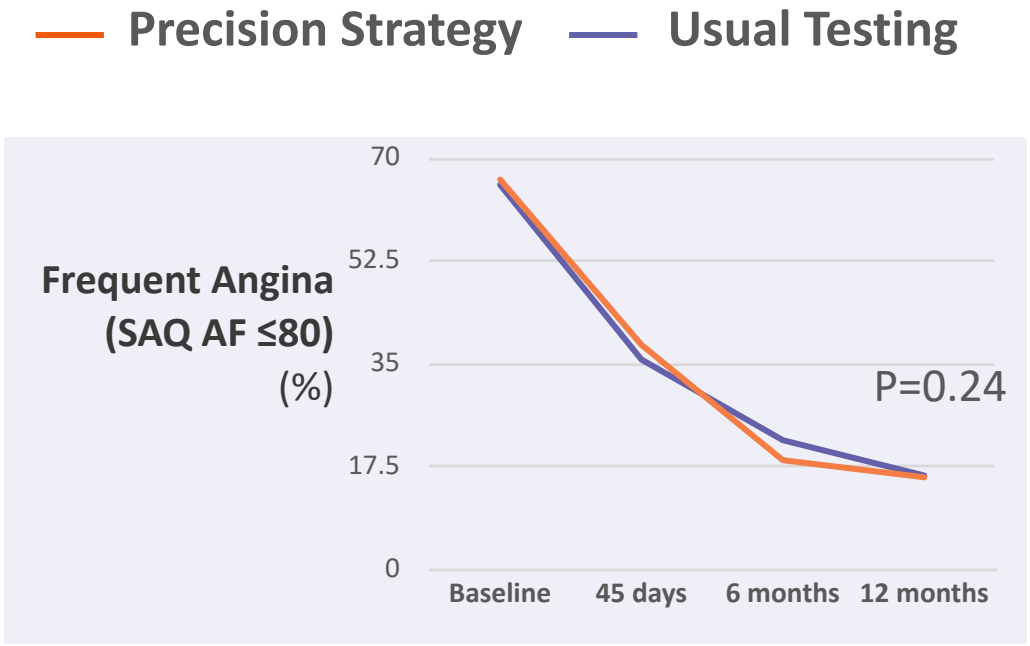






Secondary Effectiveness Endpoints, continued





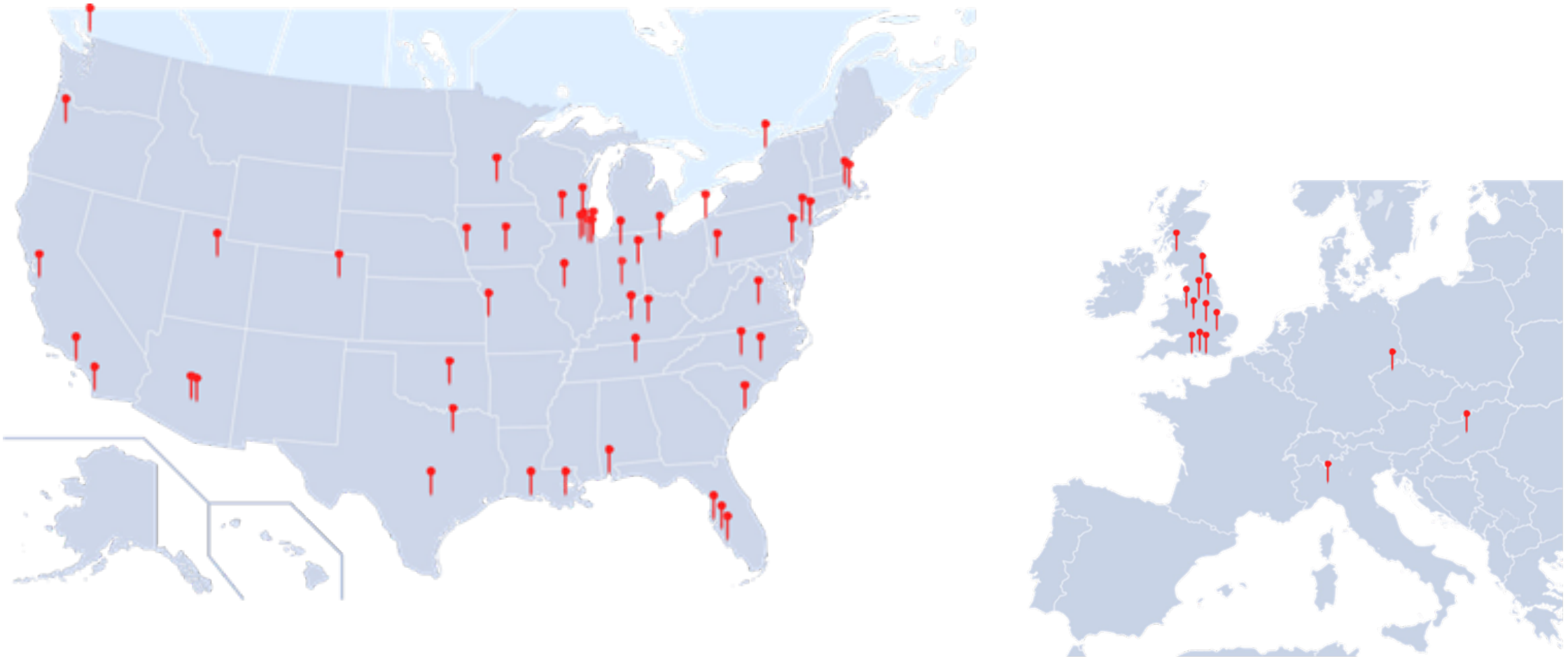
Limitations

- The Precision Strategy care pathway includes several actions reflective of real-world decision-making: risk stratification, deferred testing, and use of cCTA with selective FFR_{CT} as the initial test. The separate effects of each action cannot be determined
- PRECISE's pragmatic trial design precludes evaluation of different Usual Testing choices or close monitoring of the trial's recommendations to use Optimal Medical Treatment
- PRECISE does not address outcomes beyond the trial duration of 12 months
- Detailed results of outcomes in low risk participants and costs/resource use will be reported separately

PRECISE Summary and Conclusion

- **PRECISE demonstrates the net clinical effectiveness of the Precision Strategy with a 70% reduction of the composite of death, non-fatal MI or catheterization without obstructive CAD, compared to Usual Testing at 1 year**
- PRECISE addresses critical knowledge gaps in the evaluation of symptomatic, low-intermediate risk patients with suspected CAD, by defining and testing a specific care pathway concordant with Guideline recommendations
  - Outcomes were improved using deferred testing for quantitively-determined minimal-risk patients and cCTA with selective FFR_{CT} in all others
- The Precision Strategy is a preferred approach in evaluating patients with stable symptoms and suspected coronary artery disease

THANK YOU to PRECISE Participants, Investigators, Sites



THANK YOU to the PRECISE Team!!

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- Ozgu Melek Issever (non-voting)

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- Tina Harding
- Linda Davidson-Ray
- Thomas Redick
- PRO Interviewers

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THANK YOU

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Scientific Sessions

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