

New Oral Anticoagulants for Atrial Fibrillation

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Disclosure Statement of Financial Interest

I, **SORIN BRENER MD**, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Why not stick with warfarin?

- Prevents only 64% of embolic events in AF, compared with ASA or placebo
- Significant incidence of major bleeding – reduces overall efficacy
- INR monitoring
- Interaction with multiple medications and food items

PK/PD of 4 Novel Oral Anticoagulants

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Target	Ila	Xa	Xa	Xa
Hrs to Cmax	2	2-4	1-3	1-2
CYP Metabolism	None	32%	15%	NR
Half-Life	12-14h	9-13h	8-15h	8-10h
Renal Elimination	80%	33%	27%	50%

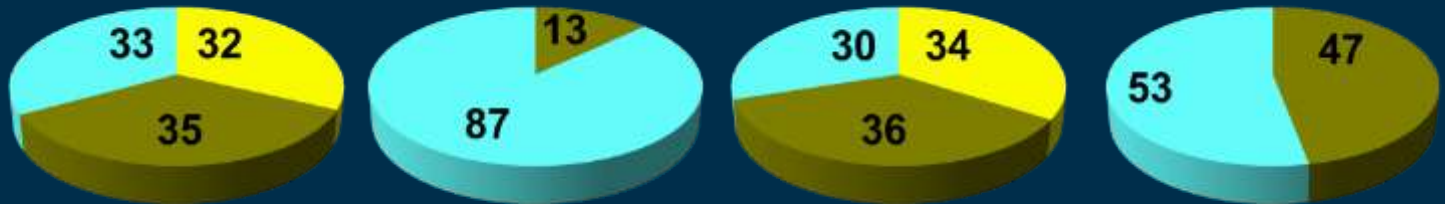
Phase III AF Trials

	Re-LY	ROCKET- AF	ARISTO TLE	ENGAGE AF-TIMI 48
Drug	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Dose (mg)	150, 110	20 (15*)	5 (2.5*)	60*, 30*
Freq	BID	QD	BID	QD
Dose Adjustment	No	20 → 15	5 → 2.5	60 → 30 30 → 15
N	18,113	14,266	18,206	21,105
Design	PROBE	2x blind	2x blind	2x blind
% VKA naive	50%	38%	43%	41%
Target INR	2.0-3.0	2.0-3.0	2.0-3.0	2.0-3.0

Baseline Characteristics

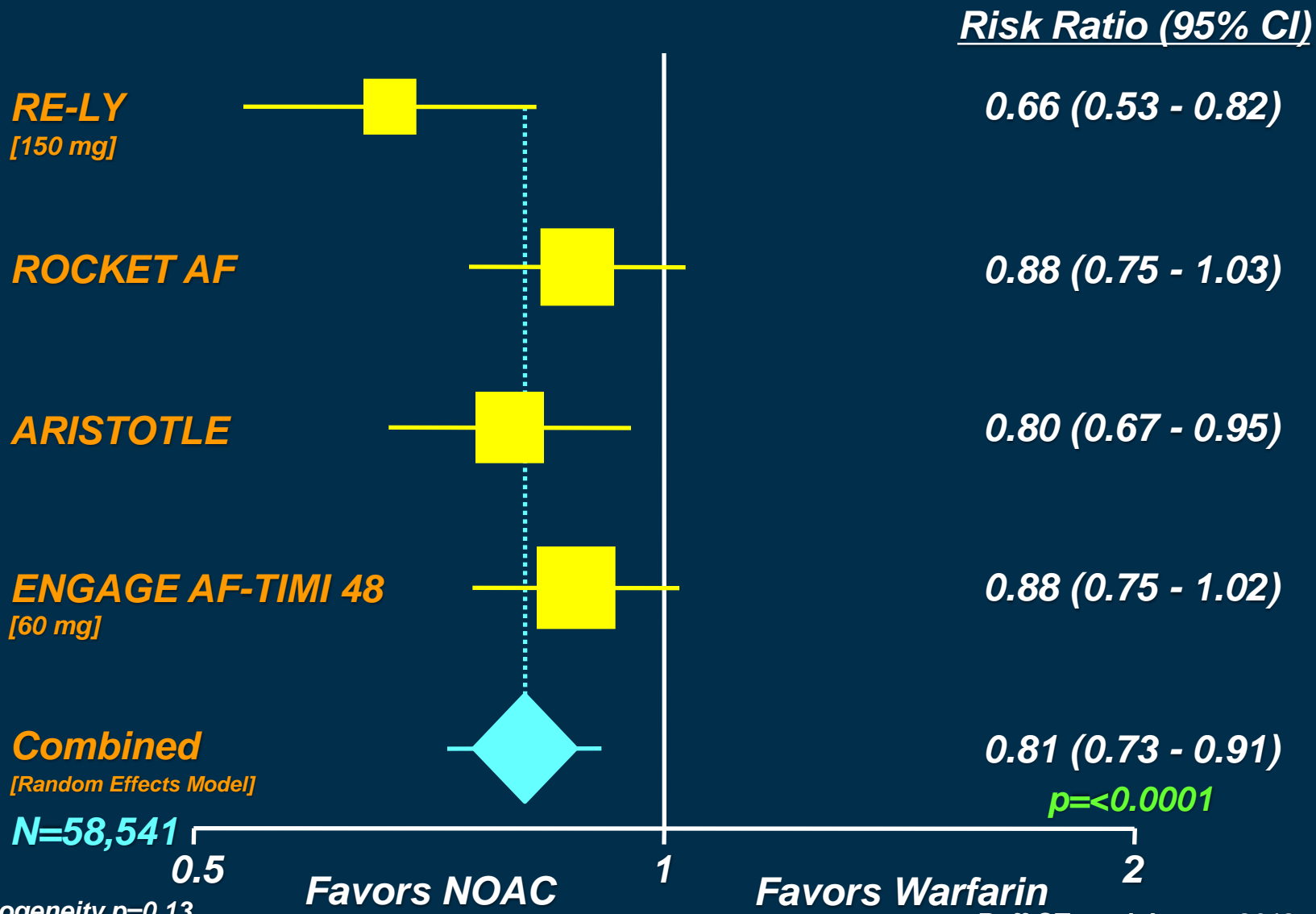
	RE-LY (Dabigatran)	ROCKET-AF (Rivaroxaban)	ARISTOTLE (Apixaban)	ENGAGE AF (Edoxaban)
Age, years	72 ± 9	73 [65-78]	70 [63-76]	72 [64-78]
Female, %	37	40	35	38
Paroxysmal AF	32	18	15	25
Aspirin Use	40	36	31	29
Median TTR	66%	58%	66%	68%
Median follow-up (years)	2.0	1.9	1.8	2.8

CHADS₂

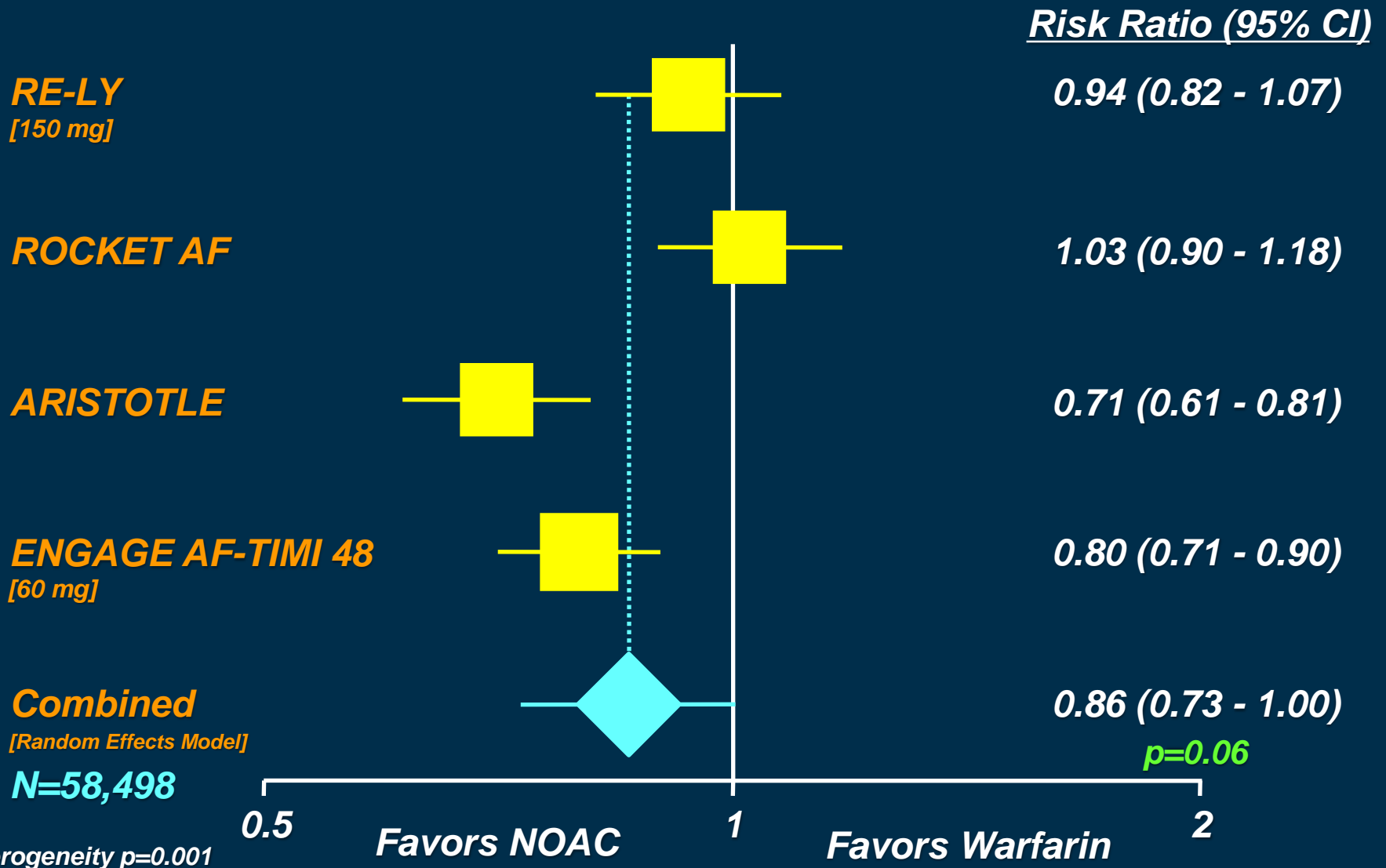


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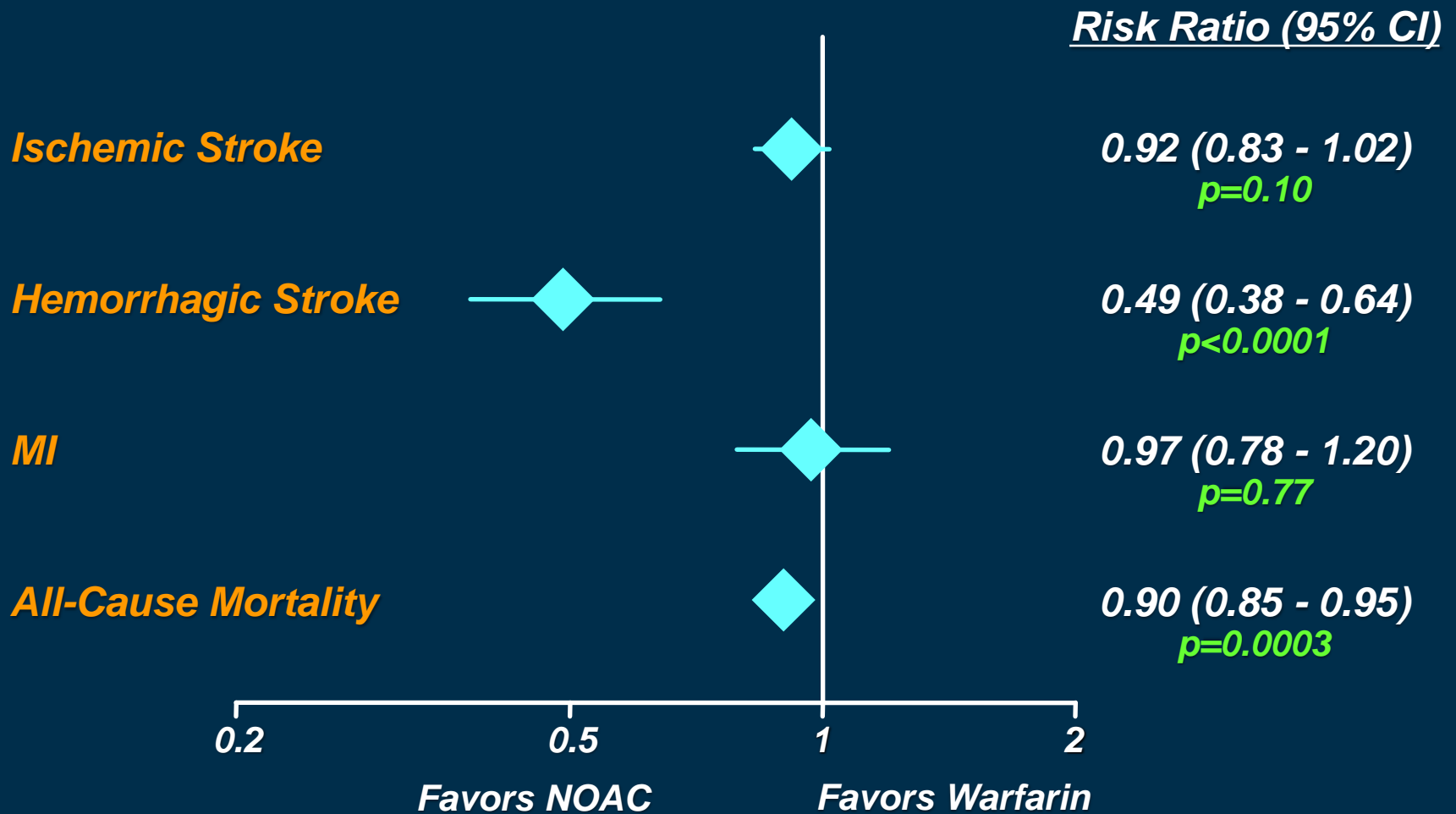
Stroke or SEE



Major Bleeding



Secondary Efficacy Outcomes



Heterogeneity $p=NS$ for all outcomes

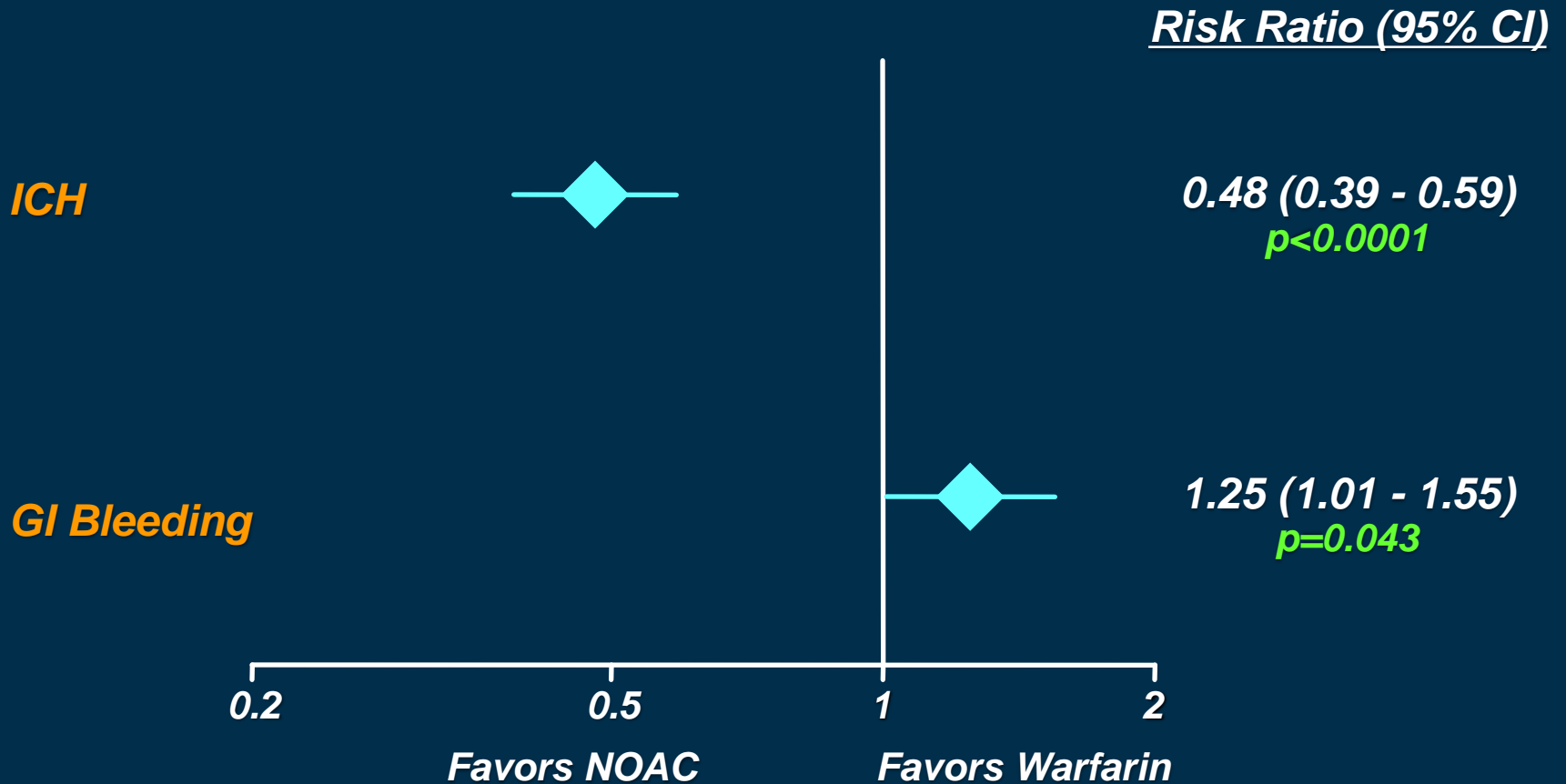
RE-LY

MI, Death and Net clinical Benefit

	D 110mg	D 150mg	warfarin	D 110mg vs. Warfarin		D 150mg vs. Warfarin	
	Annual rate	Annual rate	Annual rate	RR 95% CI	p	RR 95% CI	p
MI	0.7%	0.7 %	0.5 %	1.35 0.98-1.87	0.07	1.38 1.00-1.91	0.048
Death	3.8 %	3.6 %	4.1 %	0.91 0.80-1.03	0.13	0.88 0.77-1.00	0.05
Net Clinical Benefit	7.1 %	6.9 %	7.6 %	0.92 0.84-1.02	0.10	0.91 0.82-1.00	0.04

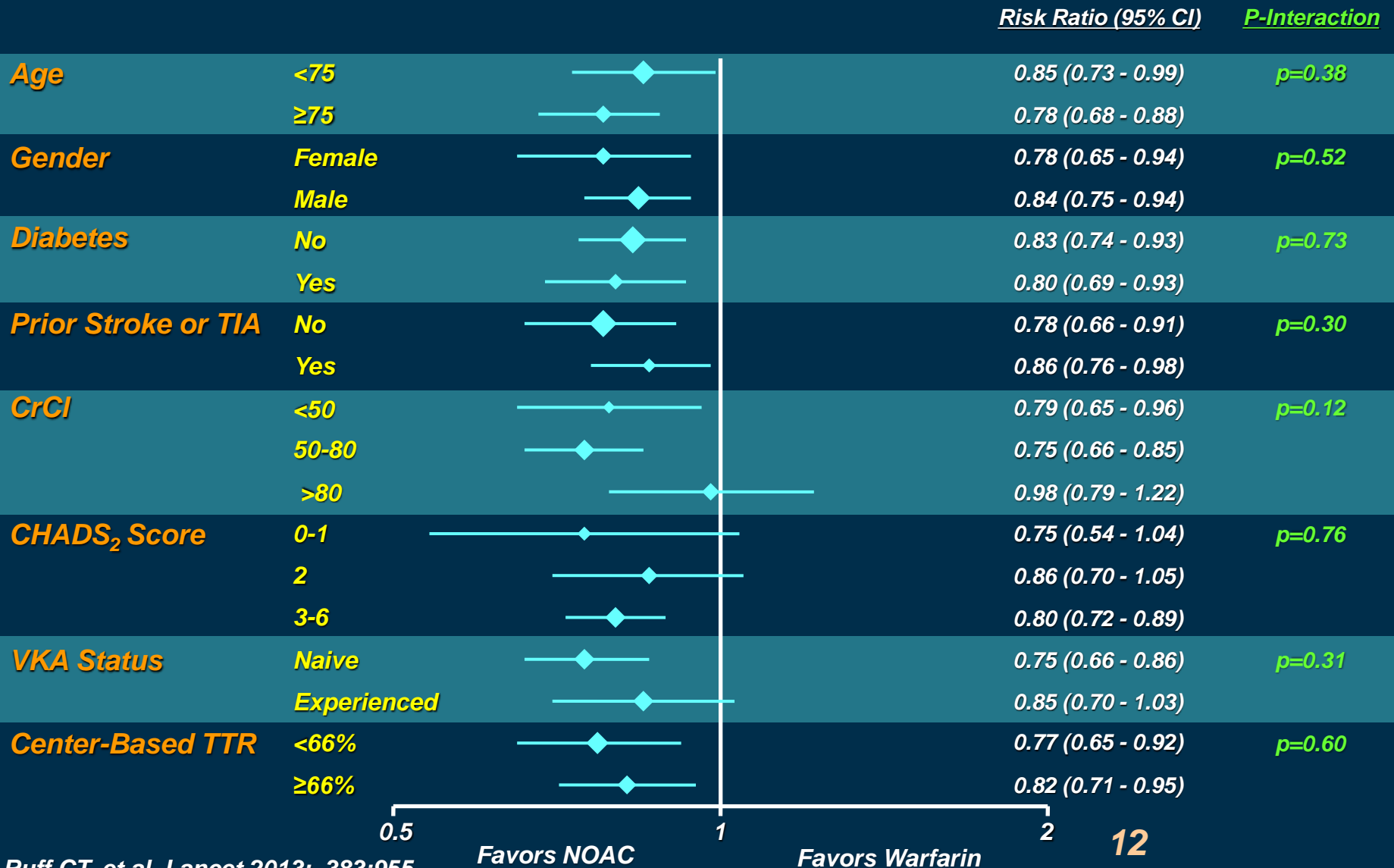
Net Clinical Benefit includes vascular events, death and major bleed

Secondary Safety Outcomes

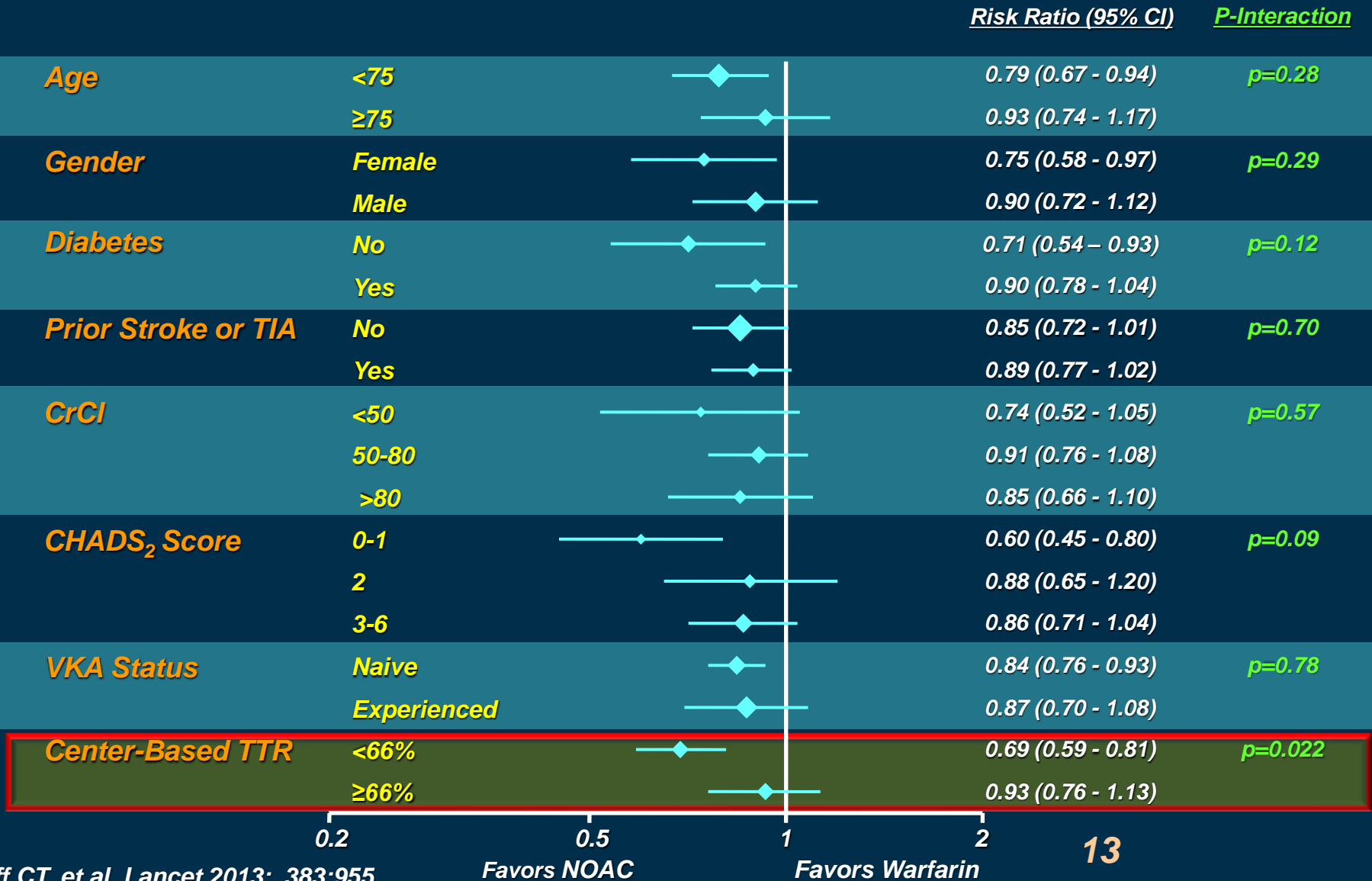


Heterogeneity
ICH, $p=0.22$
GI Bleeding, $p=0.009$

Subgroups: Stroke or SEE



Subgroups: Major Bleeding



Final thoughts

- ✓ NOACs significantly reduce stroke (↓19%)
 - ✓ Primarily driven by reduction in hemorrhagic stroke (↓51%)
- ✓ NOACs significantly reduce mortality (↓10%)
- ✓ Trend toward less major bleeding
 - ✓ Substantial reduction in ICH (↓52%)
 - ✓ Increased GI bleeding (↑25%)
- ✓ Dabigatran seems to increase MI – relevant in patients with CAD?