A Polygenic Risk Score to Identify Risk of Incident Stroke and Benefit from Primary Prevention Statin Therapy

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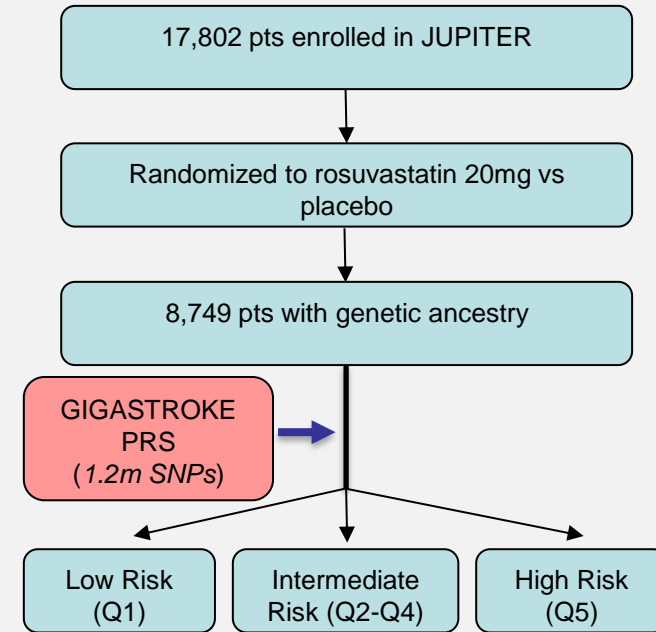**Presenter:** Daniel J McClintick
No Disclosures

- Primary prevention statin use can significantly reduce incidence of stroke

- Widely used clinical risk scores for statin eligibility do not specifically predict risk of stroke, particularly in primary prevention

- Polygenic risk scores (PRS) may identify individuals at high risk of stroke and select those more likely to benefit from statin therapy

We aimed to determine:
- *whether a novel PRS predict stroke in a primary prevention clinical trial population*
- *if those with higher PRS achieve greater benefit with primary prevention statin therapy*

METHODS

- JUPITER tested rosuvastatin in primary prevention and enrolled pts with LDL-C <130 mg/dL and hsCRP > 2 mg/L

- Primary outcome was occurrence of stroke

- Stroke rate was modeled per 1-SD increase in PRS, and hazard ratios calculated for intermediate & high-risk groups

- We also tested for a PRS by statin interaction, to determine if those at high PRS derive greater benefit
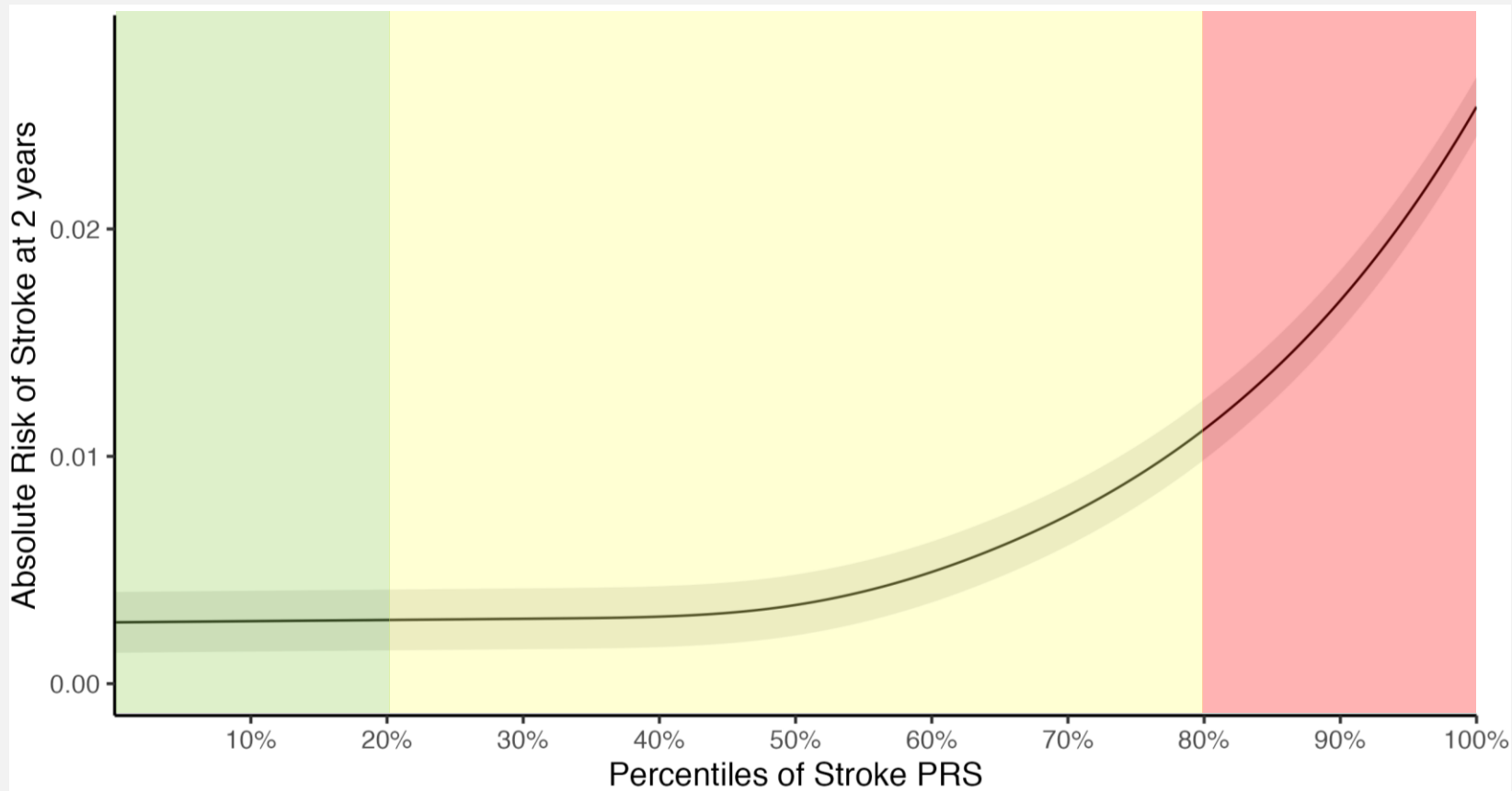
17,802 pts enrolled in JUPITER

↓

Randomized to rosuvastatin 20mg vs placebo

↓

8,749 pts with genetic ancestry

GIGASTROKE PRS (*1.2m SNPs*) →

Low Risk (Q1)   Intermediate Risk (Q2-Q4)   High Risk (Q5)

Baseline Demographics by PRS Subgroup

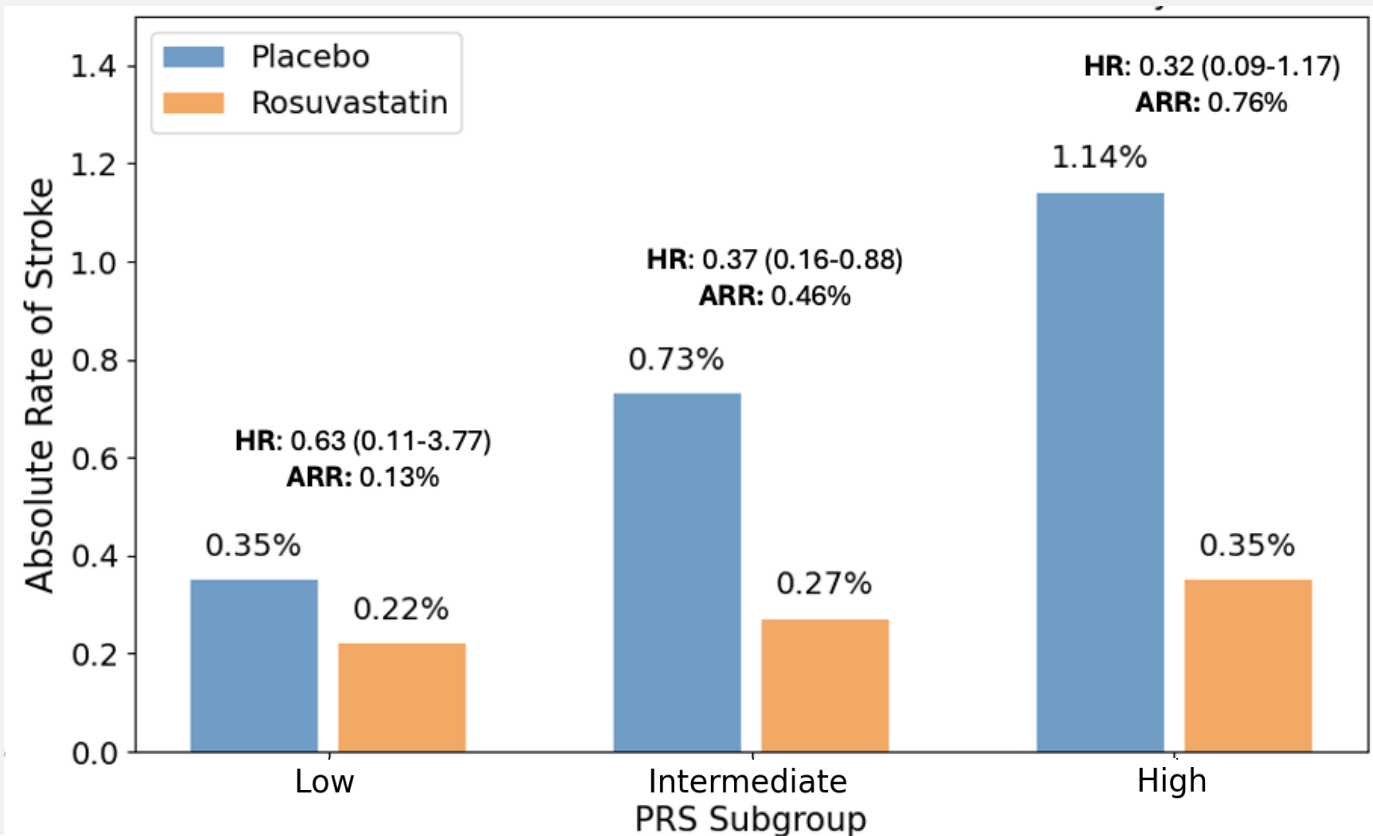|	Q1 n=1750	Q2-Q4 n=5250	Q5 n=1749	p-value
Age	67	66	65	<0.001
Male	31%	33%	32%	0.18
Hypertension	41%	65%	69%	<0.001
Atrial Fibrillation	2%	2.9%	3.3%	0.06
Smoking	11%	13%	15%	0.001
LDL-C, mean (mg/dL)	110	110	110	0.71
eGFR, mean (ml/min/1.73m^2)	72	73	73	0.12
hsCRP, mean (mg/L)	3.9	4.0	4.2	0.13

2-Yr Risk of Stroke as a Function of PRS Percentile in Placebo Arm

Treatment Effect of Rosuvastatin on Rate of Stroke by PRS Category

- The GIGASTROKE PRS can prospectively identify JUPITER patients with European ancestry with 2 to 4-fold increased risk of stroke

- Among those with high PRS, this risk may be offset by statin therapy, suggesting this tool may have clinical utility in primary prevention of stroke

Thank You

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