Lipoprotein(a) is a Prognostic Marker of Extracoronary Atherosclerotic Vascular Disease Progression

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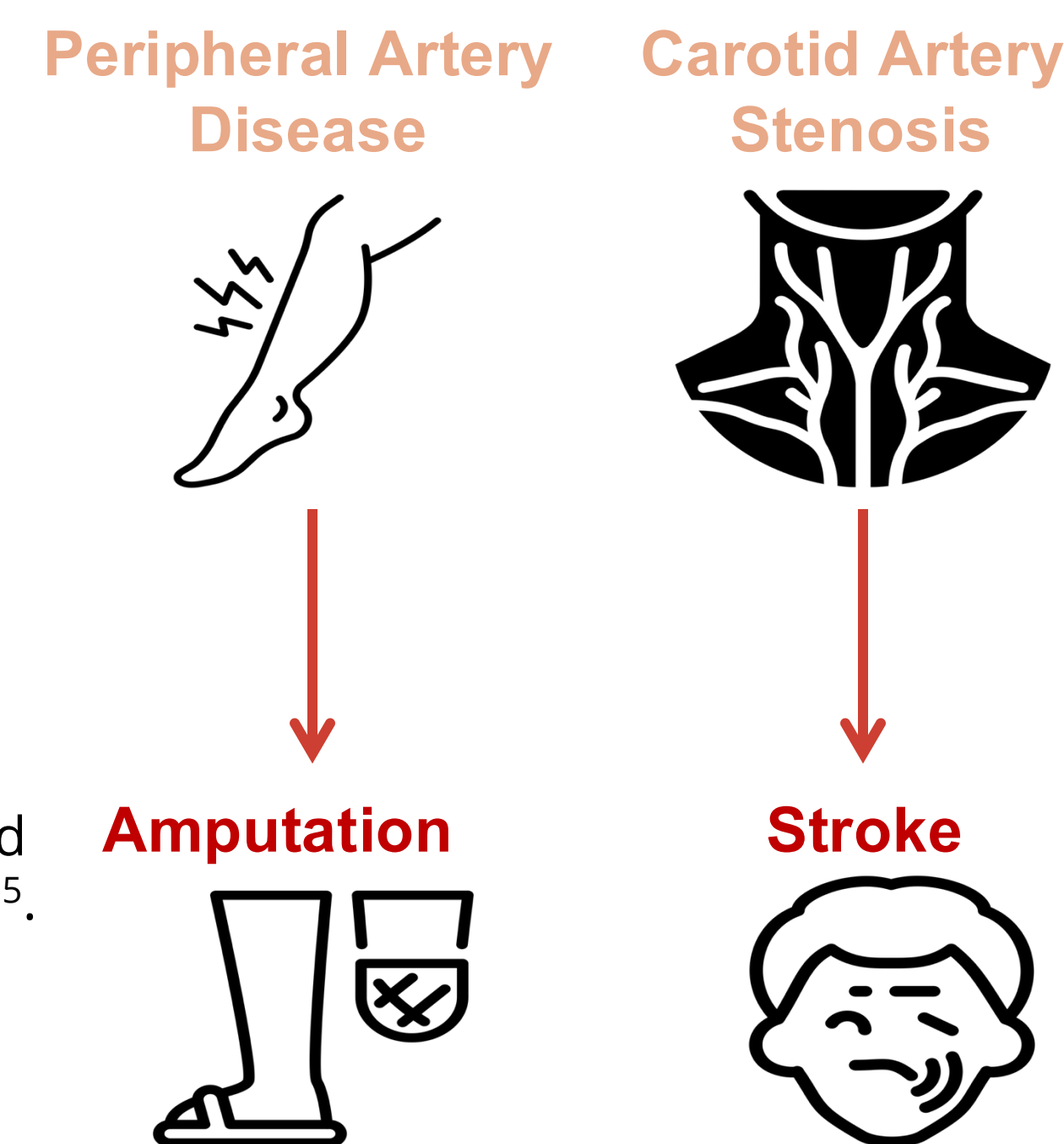
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OBJECTIVES

Vascular health beyond the coronary arteries affects over **200 million patients** worldwide[1].

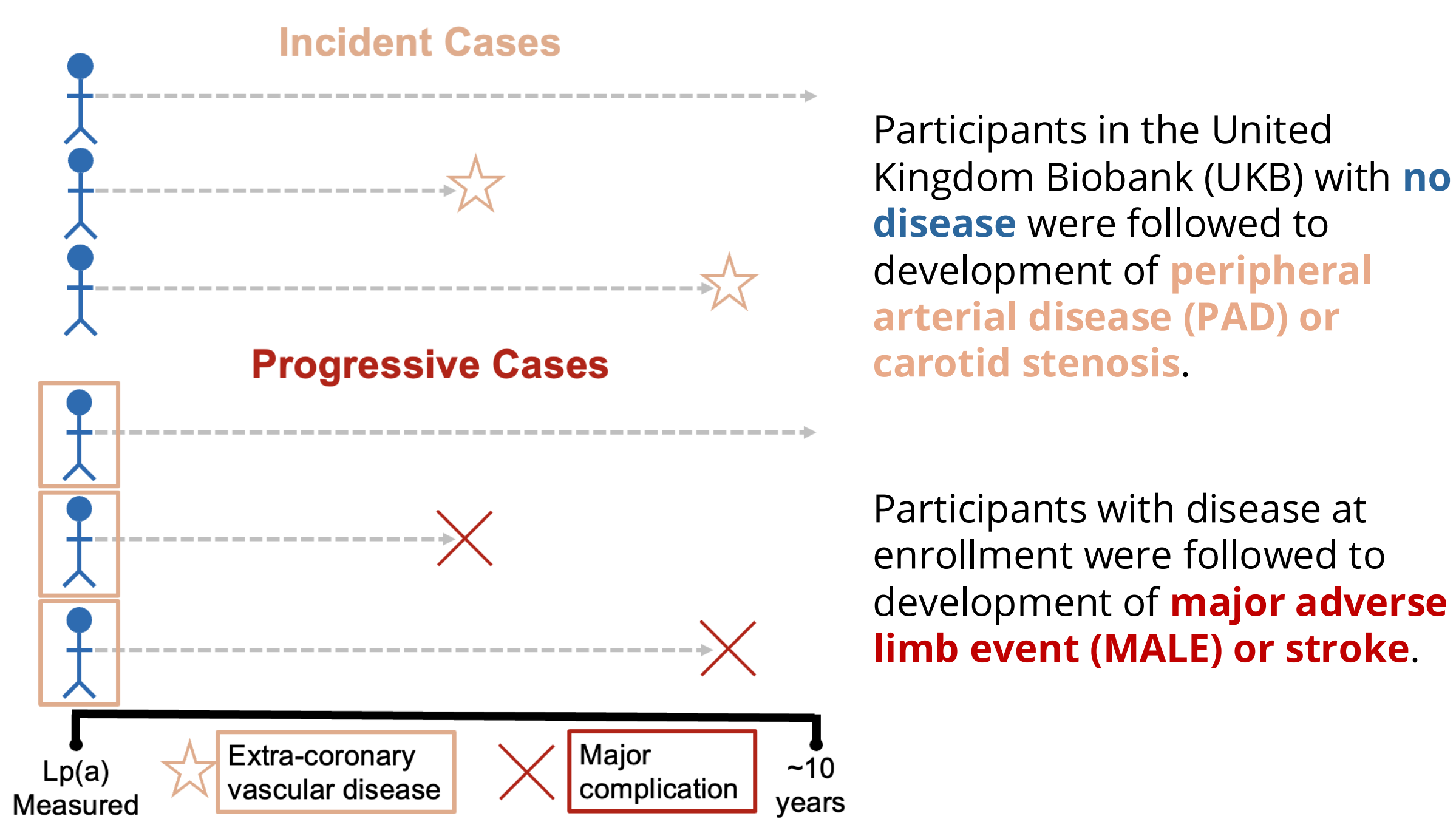**Peripheral Artery Disease**

Carotid Artery Stenosis

There are surgical treatment options available[2], but it is difficult to predict who will progress to a **morbid complication**[3].

Lipoprotein(a) [Lp(a)] is an independent causal risk factor for coronary artery disease[4] and medications are in clinical trials[5].

Amputation

Stroke

Can we quantify the risk of **incident** and **progressive extracoronary vascular disease** associated with Lp(a)?

METHODS

Incident Cases

Participants in the United Kingdom Biobank (UKB) with **no disease** were followed to development of **peripheral arterial disease (PAD)** or **carotid stenosis**.

Progressive Cases

Participants with disease at enrollment were followed to development of **major adverse limb event (MALE)** or **stroke**.

Lp(a) Measured — Extra-coronary vascular disease — Major complication — ~10 years

460,544 participants with measured Lp(a) concentrations (median 19.6, [IQR 7.6 - 73.8]) were included in this analysis.

Participants were on average 57 years old, 94.9% were European, and 54.2% were male followed over a median period of 13.6 [12.9 – 14.4] years.
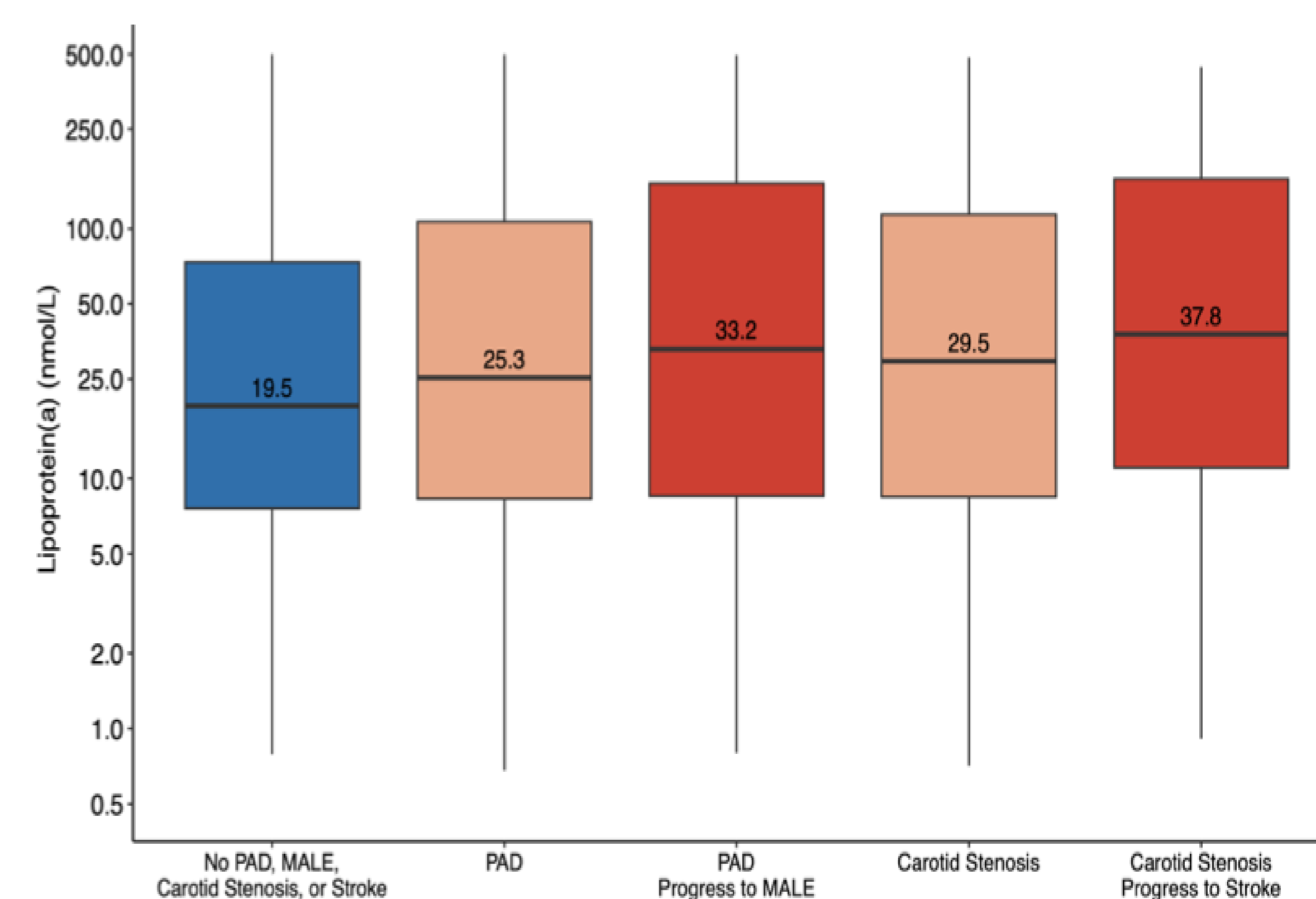
Incident Cases:

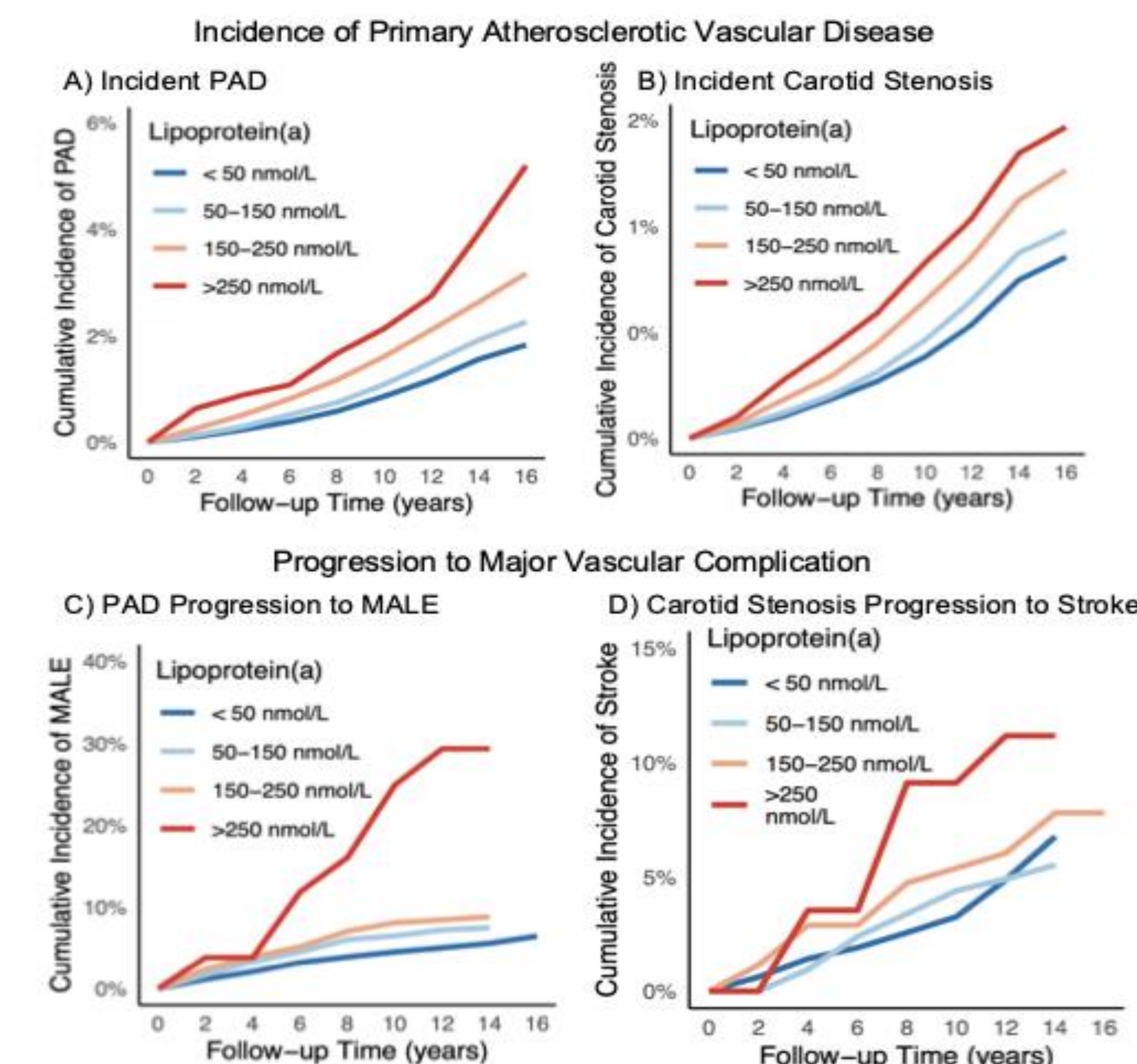PAD 7,144 (1.6%), Carotid stenosis 3,477 (0.8%)

Progressive Cases:

196 PAD → MALE (5.3%), 67 Carotid stenosis → Stroke (5.5%)

RESULTS

1. Lp(a) concentrations are highest in participants with progressive extracoronary vascular disease.

**2. There is a dose-response relationship between Lpa(a) and both incident disease and progressive disease.**

3. For each 50 nmol/L increment increase in lipoprotein(a), the risk of developing incident peripheral artery disease increases by 18%, and the risk of developing incident carotid stenosis increases by 17%.

Disease	Demographic	Affected/Total (%)	Incidence (1000 p-y)	p-value	HR (95% CI)	p-het
PAD	Total	7144 / 460554 (1.6 %)	1.18	<0.0001	1.18 (1.15 to 1.20)	
	Age<50	430 / 107811 (0.4 %)	0.29	<0.0001	1.26 (1.16 to 1.37)	0.07
	Age 50-60	1573 / 153203 (1 %)	0.77	<0.0001	1.21 (1.16 to 1.26)	
	Age >60	5141 / 199540 (2.6 %)	2.03	<0.0001	1.16 (1.13 to 1.19)	
	Women	2504 / 249460 (1 %)	0.76	<0.0001	1.17 (1.14 to 1.21)	0.712
	Men	4640 / 211094 (2.2 %)	1.71	<0.0001	1.18 (1.15 to 1.21)	
	African	93 / 8687 (1.1 %)	0.83	0.979	1.00 (0.83 to 1.20)	0.17
	European	6802 / 432928 (1.6 %)	1.20	<0.0001	1.18 (1.16 to 1.20)	
	South Asian	154 / 9902 (1.6 %)	1.21	0.183	1.12 (0.95 to 1.31)	
Carotid Stenosis	Total	3477 / 460554 (0.8 %)	0.57	<0.0001	1.17 (1.13 to 1.20)	
	Age<50	222 / 107811 (0.2 %)	0.15	0.216	1.09 (0.95 to 1.25)	0.183
	Age 50-60	704 / 153203 (0.5 %)	0.34	<0.0001	1.22 (1.15 to 1.30)	
	Age >60	2551 / 199540 (1.3 %)	0.99	<0.0001	1.16 (1.12 to 1.19)	
	Women	1270 / 249460 (0.5 %)	0.38	<0.0001	1.13 (1.08 to 1.18)	0.045
	Men	2207 / 211094 (1 %)	0.80	<0.0001	1.19 (1.15 to 1.24)	
	African	93 / 8687 (1.1 %)	0.83	0.979	1.00 (0.83 to 1.20)	0.17
	European	6802 / 432928 (1.6 %)	1.20	<0.0001	1.18 (1.16 to 1.20)	
	South Asian	154 / 9902 (1.6 %)	1.21	0.183	1.12 (0.95 to 1.31)	

RESULTS

4. The association with disease risk remained robust after adjustment for cardiovascular comorbidities and was consistent when modeled using splines.
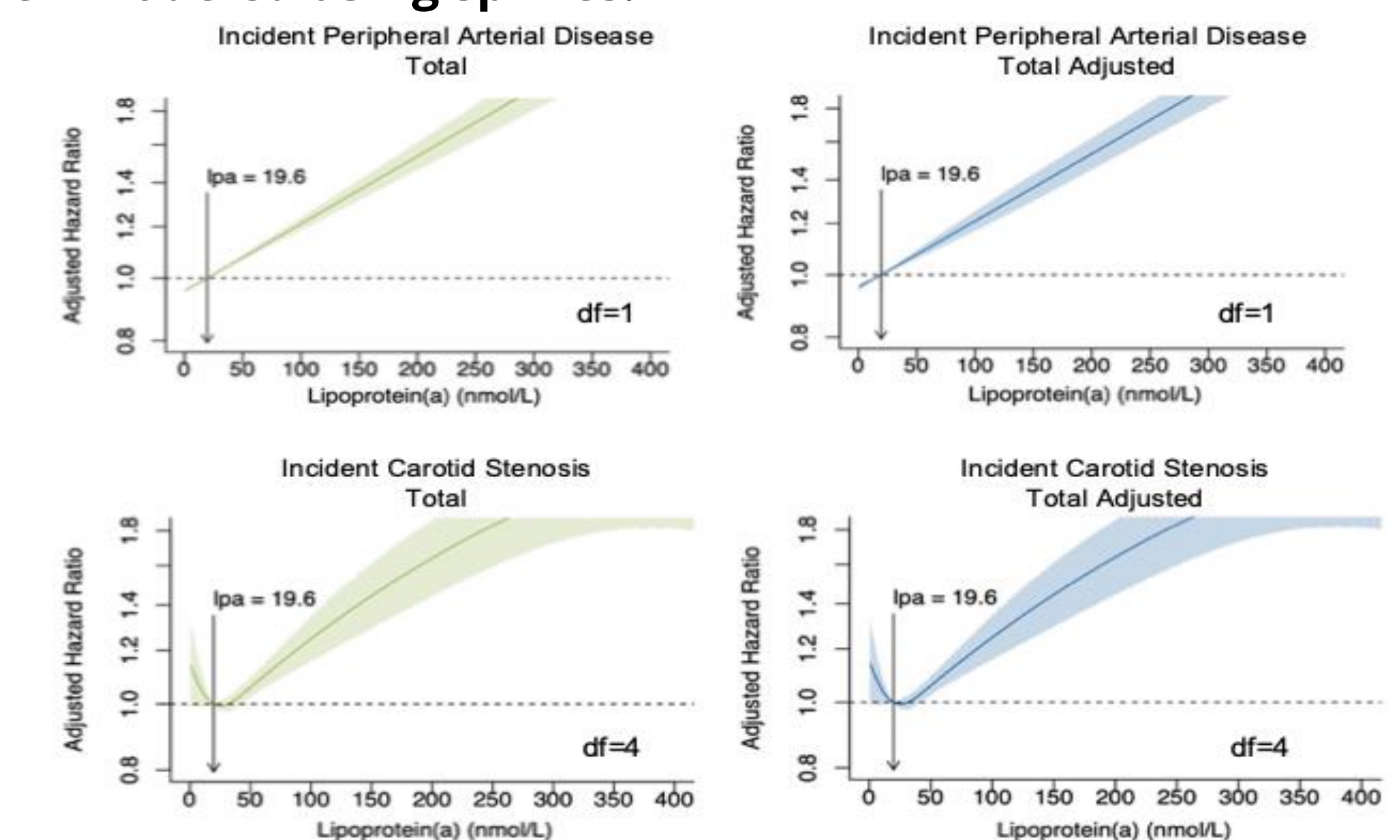
5. Those with high Lp(a) concentrations were at 1.57 times the risk of developing MALE (95% CI 1.14-2.16, p-value=0.006 and 1.40 times the risk of developing stroke (95% CI 0.81-2.40, p-value=0.228).

CONCLUSIONS

Lp(a) could serve as a potential biomarker for **incidence** and **progression** of extra-coronary atherosclerotic vascular disease.

Therapies aimed at **lowering Lp(a)** should be considered in individuals at high risk for **extracoronary atherosclerotic vascular disease.**

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