Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Polak JF, Pencina MJ, Pencina KM, O'Donnell CJ, Wolf PA, D'Agostino RB Sr. Carotid-wall intima–media thickness and cardiovascular events. N Engl J Med 2011;365:213-21.

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: JF Polak, MJ Pencina, KM Pencina, CJ O'Donnell, PA Wolf, RB D'Agostino Sr. Carotid wall intima-media thickness (IMT), plaque and cardiovascular events.

Supplementary Appendix for Polak et al: Carotid intima-media wall thickness (IMT), plaque and cardiovascular events.

I. Breakdown of cardiovascular events

II. Re-classification Tables for CCA IMT and ICA IMT

III. Ultrasound images showing the location of IMT measurements.

IV. Kaplan-Meir curves for common and internal carotid artery intima-media thickness (IMT) by quartiles

Supplemental Table 1:

Types of cardiovascular events and associated hazard ratios for internal carotid artery (ICA) intima-media thickness (IMT).

Type of event	Number	Percent	Hazards ratio and 95% Confidence Limits	p-value
Coronary Heart Disease	152	51.2	1.15 (0.98, 1.34)	0.08
Stroke	74	24.9	1.35 (1.19, 1.53)	< 0.0001
Peripheral Arterial Disease	26	8.8	1.42 (1.16, 1.73)	0.0006
Congestive Heart Failure	45	15.1	1.22 (0.99, 1.49)	0.056

Supplemental Table 2

Reclassification into new Framingham Risk Score categories as a function of original Framingham Risk Score categories for common carotid Artery Intima-Media Thickness.

Non-Events	New low risk	New moderate risk	New high risk
Low risk (< 6%)	1151	36	0
Moderate risk (6-20%)	45	1185	25
High risk (> 20%)	0	26	239

Events	New low risk	New moderate risk	New high risk
Low risk (< 6%)	33	3	0
Moderate risk (6-20%)	0	120	4
High risk (> 20%)	0	8	90

Reclassification for non-events: - 0.4% (10 cases / 2707)

Reclassification for events: - 0.4% (-1 / 258)

Net Reclassification Index: -0.4% - (-0.4%) = 0%

IMT (Intima-Media Thickness) is used as a continuous variable.

Supplemental Table 3

Reclassification into new Framingham Risk Score categories as a function of original Framingham Risk Score categories using Internal carotid Artery Intima-Media Thickness >1.5 mm as a cut-point for plaque.

Non-Events	New low risk	New moderate risk	New high risk
Low risk (< 6%)	1078	78	0
Moderate risk (6-20%)	199	948	109
High risk (> 20%)	0	72	202

Events	New low risk	New moderate risk	New high risk
Low risk (< 6%)	22	13	0
Moderate risk (6-20%)	6	101	19
High risk (> 20%)	0	15	84

Reclassification for non-events: - 3.1% (84 / 2686)

Reclassification for events: 4.2% (11 / 260)

Net Reclassification Index: 4.2% - (-3.1%) = 7.3%

Section III

Figure 1

Typical location of carotid artery intima-media thickness measurements is defined by the rectangle. This location is below the distal common carotid artery bifurcation where the wall thickness progressively and can readily reach IMT values consistent with plaques (arrows). Inclusion of measurements made near the bifurcation (arrows) biases the intima-media thickness measurement towards values representing early plaque formation in a subset of the population.

Figure 2

Typical location of internal carotid artery intima-media thickness measurement at the location of a plaque (arrow). The maximum intima-media thickness at this location corresponds to plaque thickness and this definition of plaque is consistent with measurements made on intravascular ultrasound images. Specifically, pathologically defined plaque included only the intima while ultrasound defined plaque includes both the intima and the media.

Figure 1

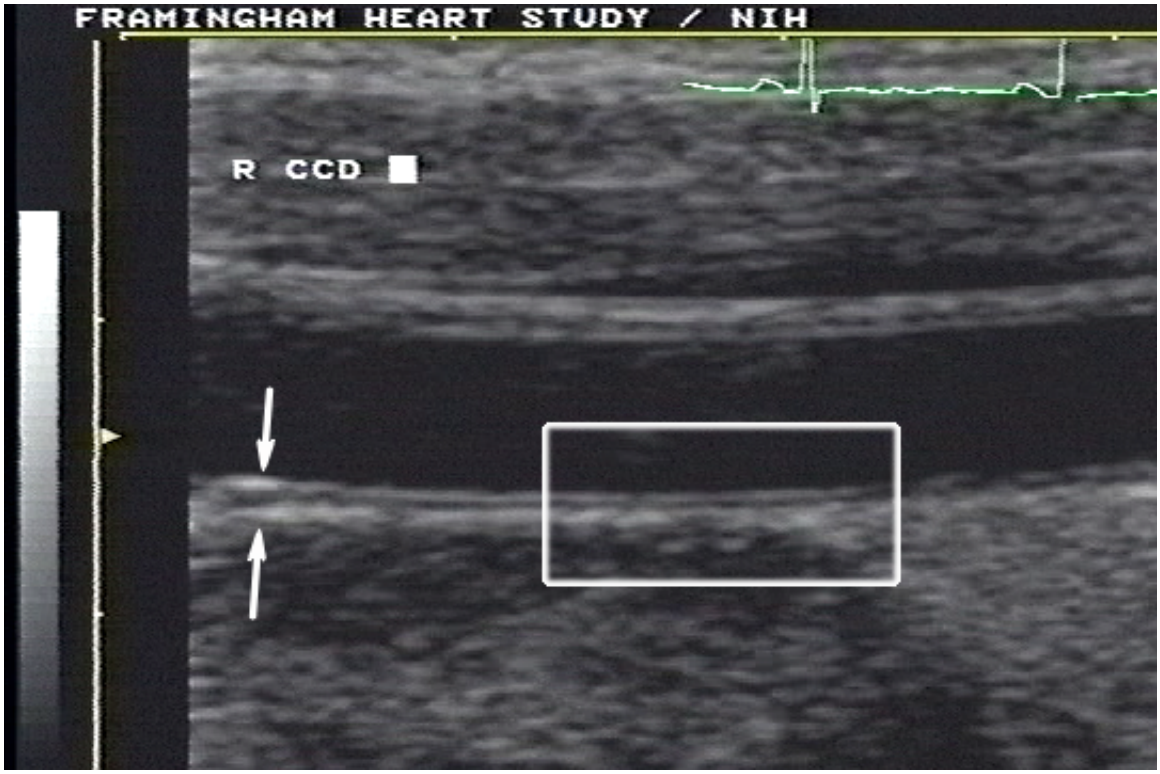
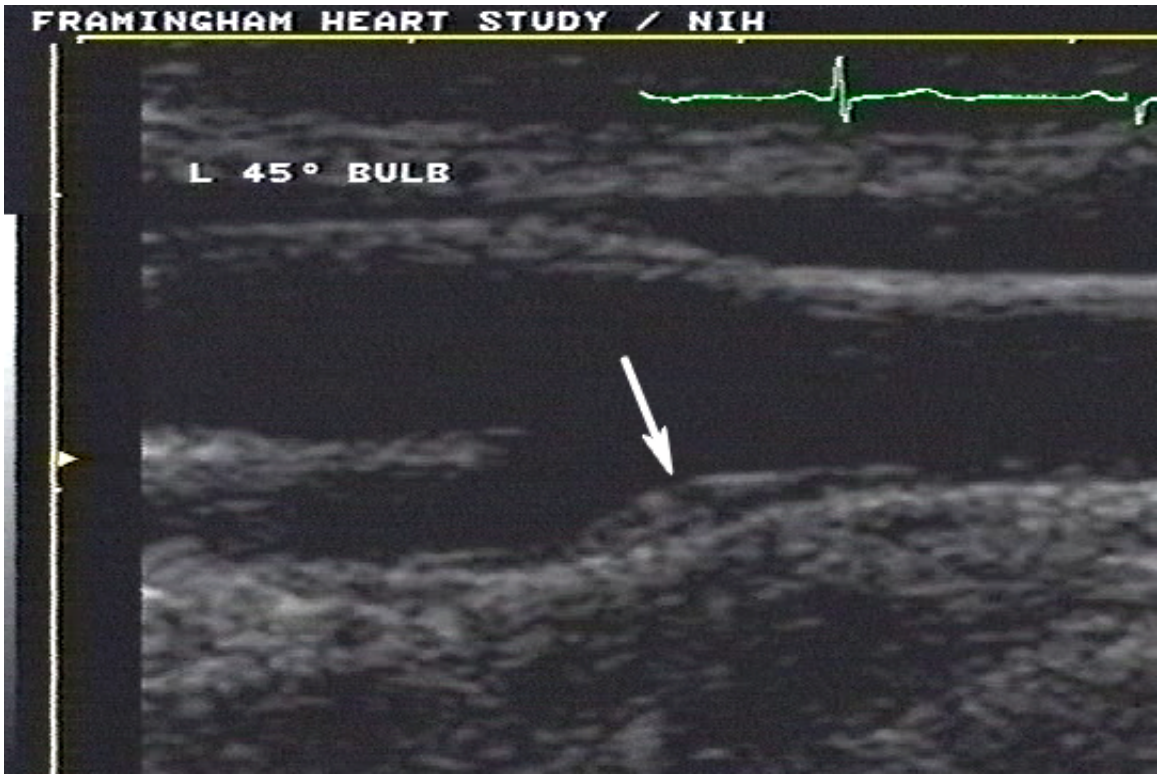


Figure 2



Section IV

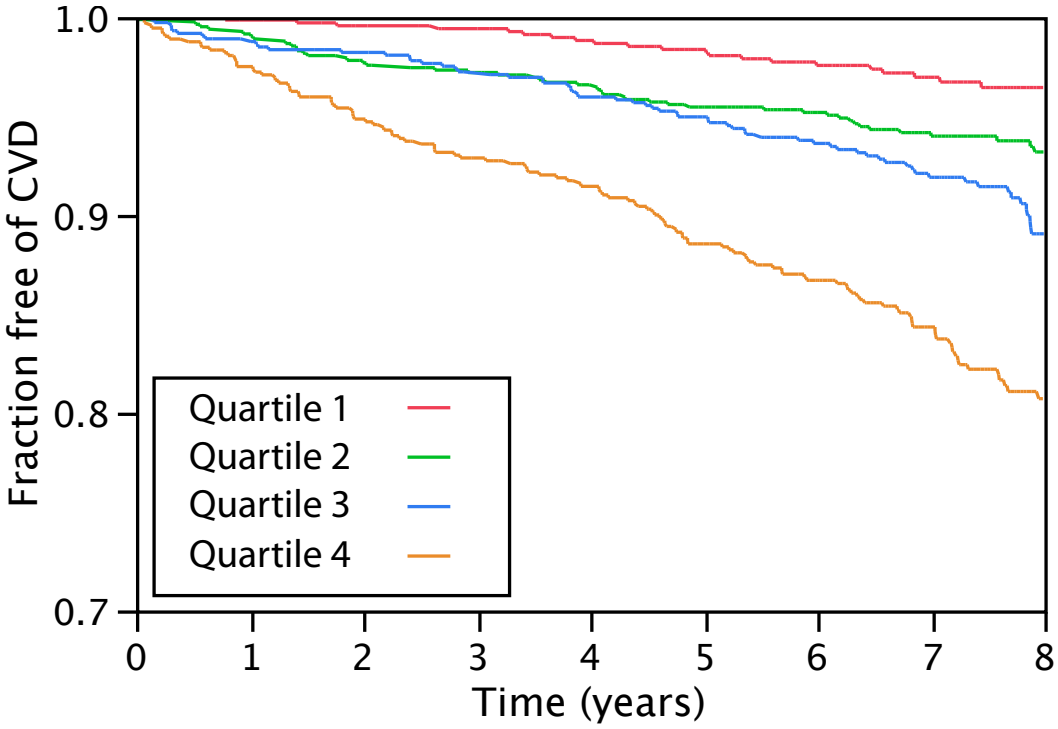
Figure 3:

Kaplan-Meier curves for mean common carotid artery intima-media thickness presented as quartiles and for time to incident cardiovascular event as outcome.

Figure 4:

Kaplan-Meier curves for maximum internal carotid artery intima-media thickness presented as quartiles and for time to incident cardiovascular event as outcome.

Figure 3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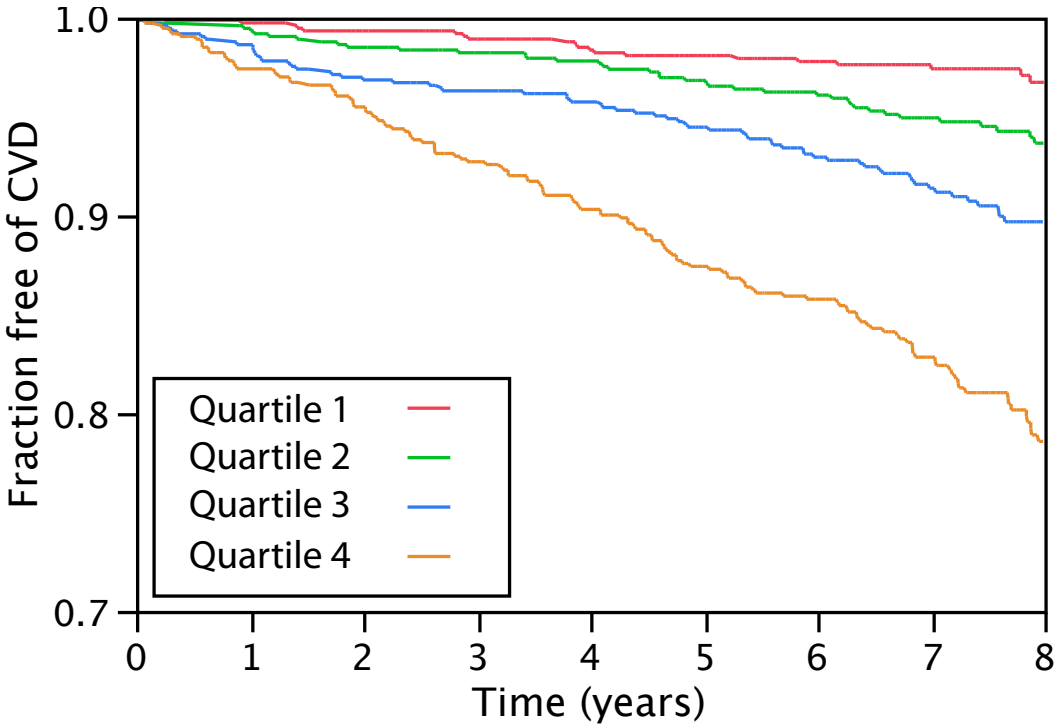
0.9
0.8
0.7
Fraction free of CVD
Quartile 1
Quartile 2
Quartile 3
Quartile 4
0
1
2
3
4
5
6
7
8
Time (years)

Figure 4


1.0
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Quartile 1
Quartile 2
Quartile 3
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8
Time (years)