

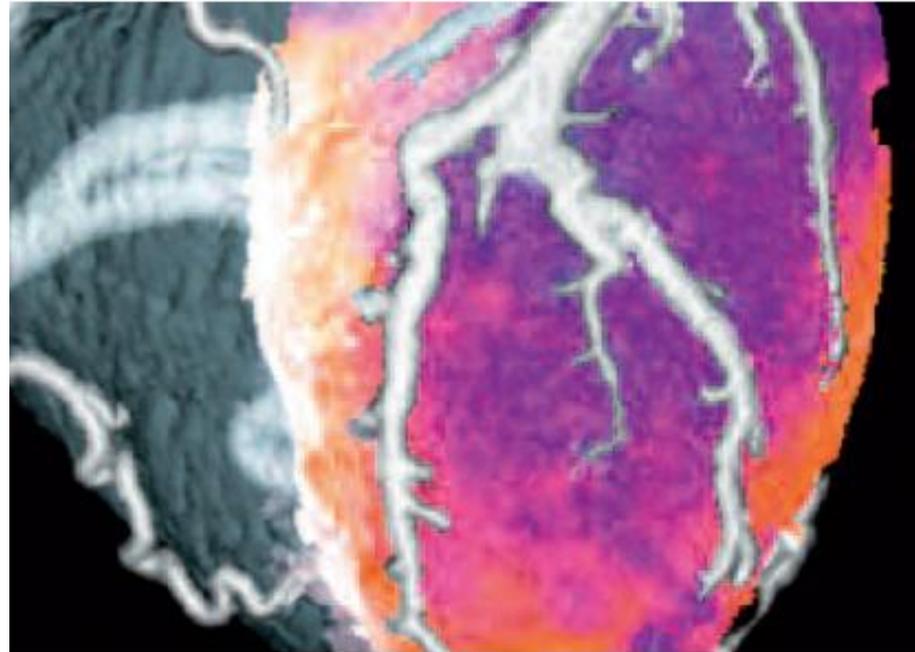
Cardiology Update® 2013



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Davos, Switzerland, 10–15 February 2013

20th International Postgraduate Course on Cardiovascular Disease

Prevention and Coronary Artery Disease



Progression of coronary artery calcification: risk and risk factors

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German Cardiac Society



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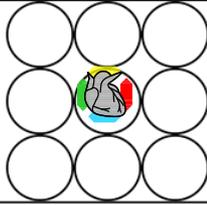
Ruth Amstein, Zurich, Switzerland



ZÜRICH
HEART HOUSE

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors

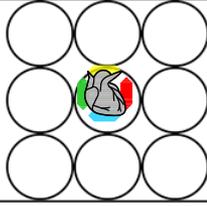


Content

- Basic considerations
- Natural history
- Risk factors
- Cardiovascular events
- Treatment options

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors

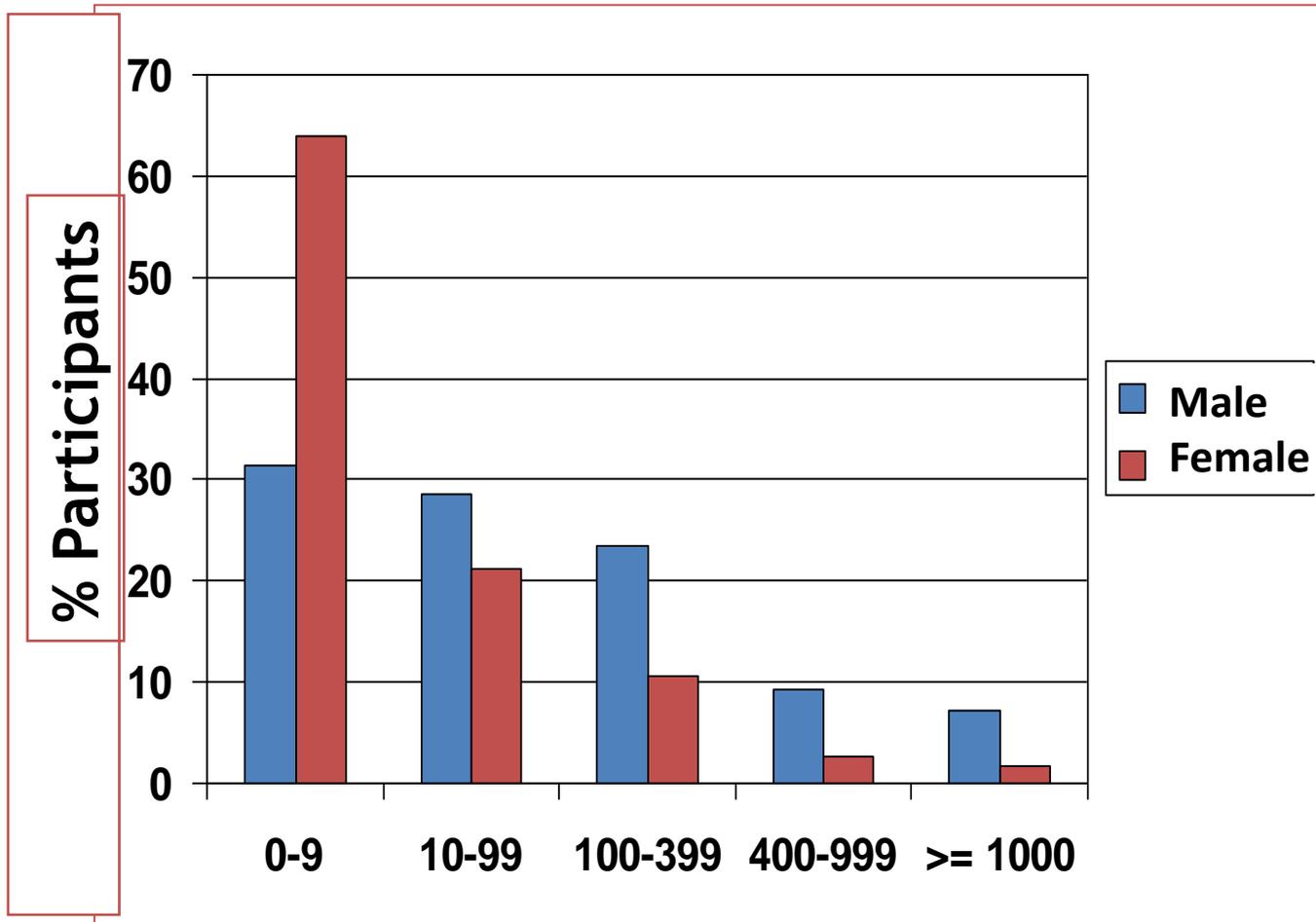


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Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



Prevalence of
CAC (45 – 75y)
in healthy
82 % Men
55 % Women

In CAD
Prevalence 6.8%
100% Men
84% Women

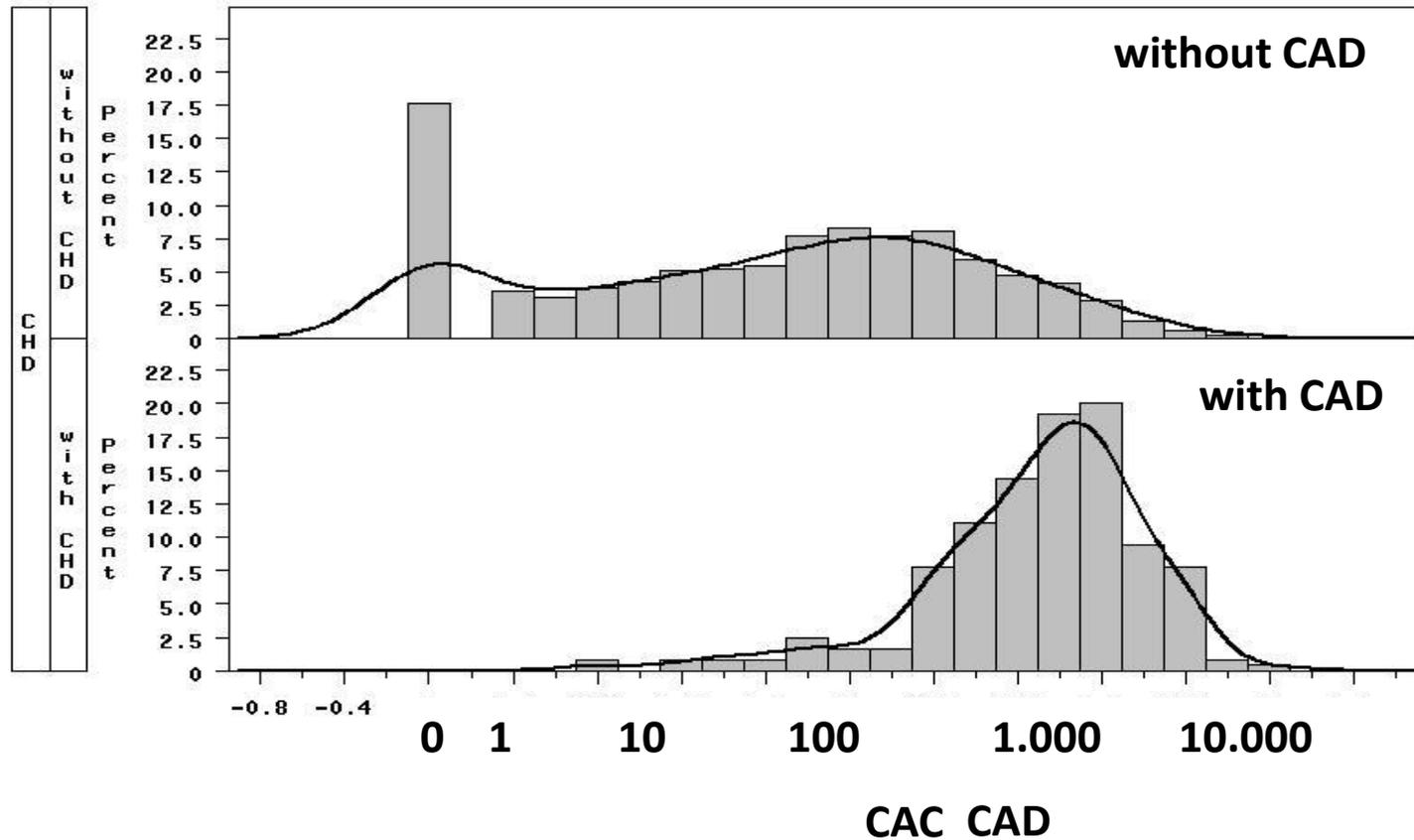
Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



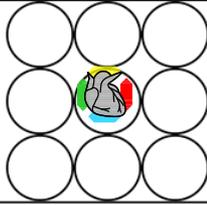
Comparative Analysis of Subjects with and without CHD

Sex=Male



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Progression of coronary artery calcification: risk and risk factors



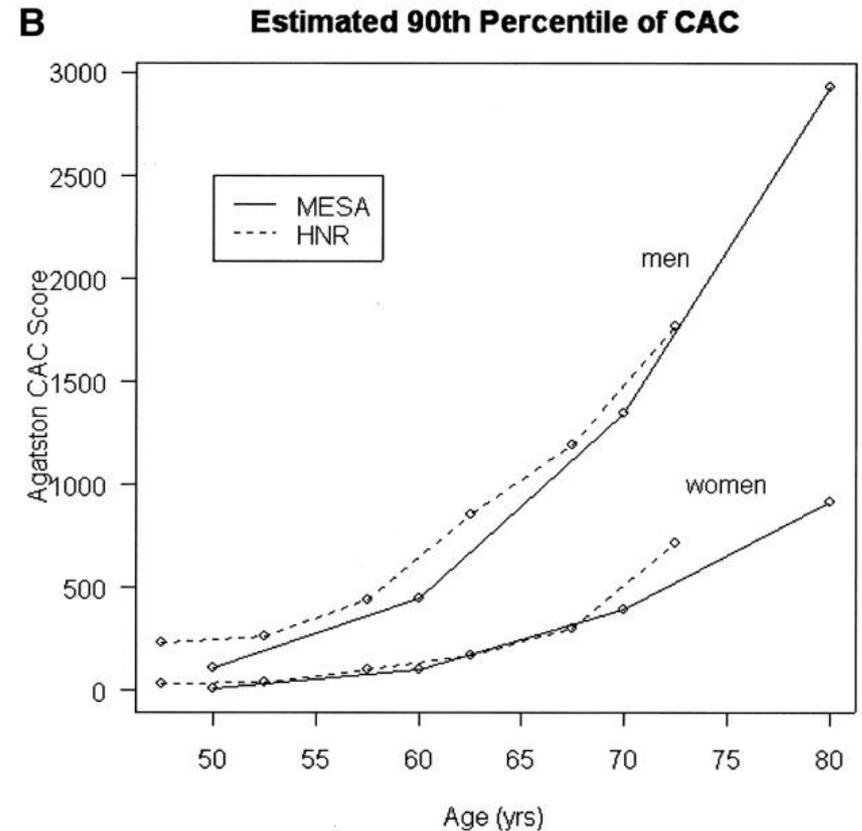
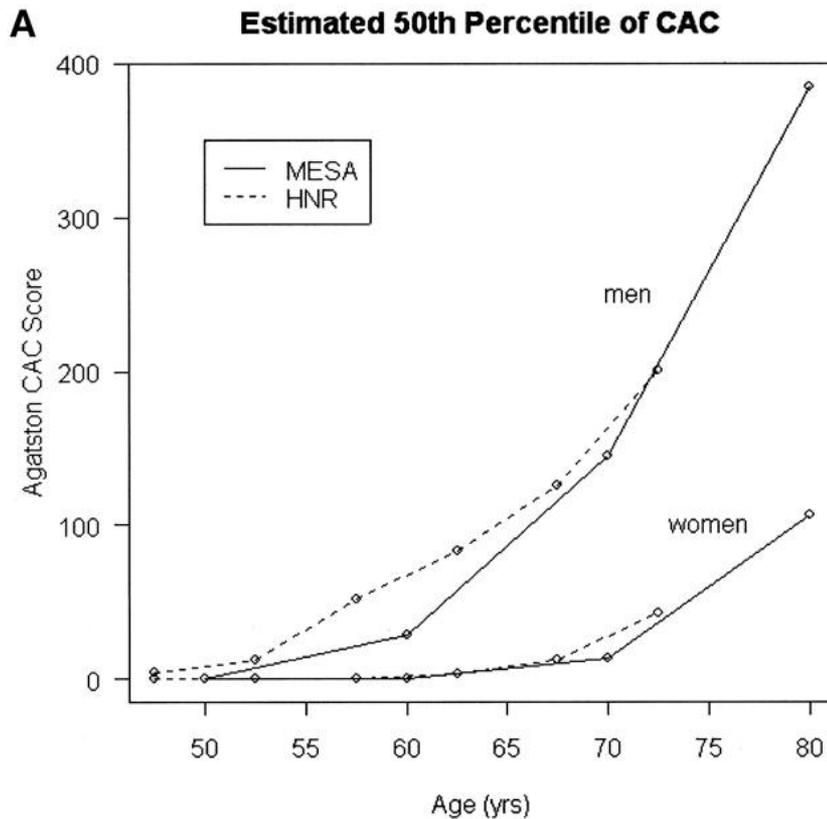
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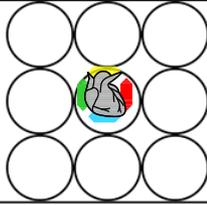
Progression of coronary artery calcification: risk and risk factors

Comparability of estimated percentiles from MESA with the Heinz Nixdorf Recall (HNR) Study (MESA estimates are for whites only).



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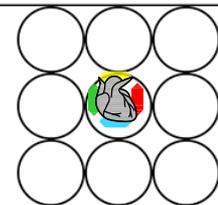
Progression of coronary artery calcification: risk and risk factors



What is the pathophysiology of CAC progression ?

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



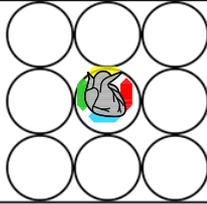
Potential mechanism of CAC progression

- Vascular dysfunction,
- Vasomotion abnormalities
- Inflammation
- Autoantibodies to oxidized LDL
- Increased apo B-100 immune complexes
- lipoprotein (a)

independent of age, gender, traditional risk factors

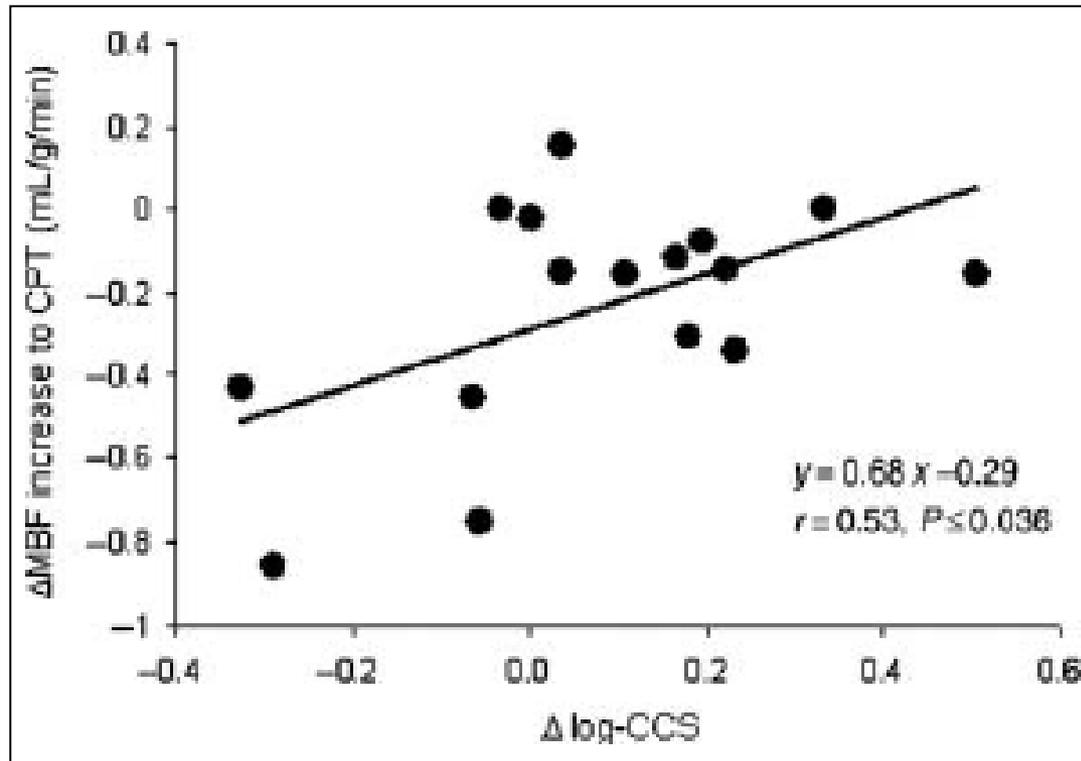
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Progression of coronary artery calcification: risk and risk factors



CPT =
cold pressure
Test

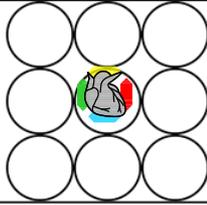
Δ MBF =
myocardial blood
flow by PET



increases in Δ MBF to CPT after glucose-lowering treatment remained a statistically significant independent predictor of the progression of CAC

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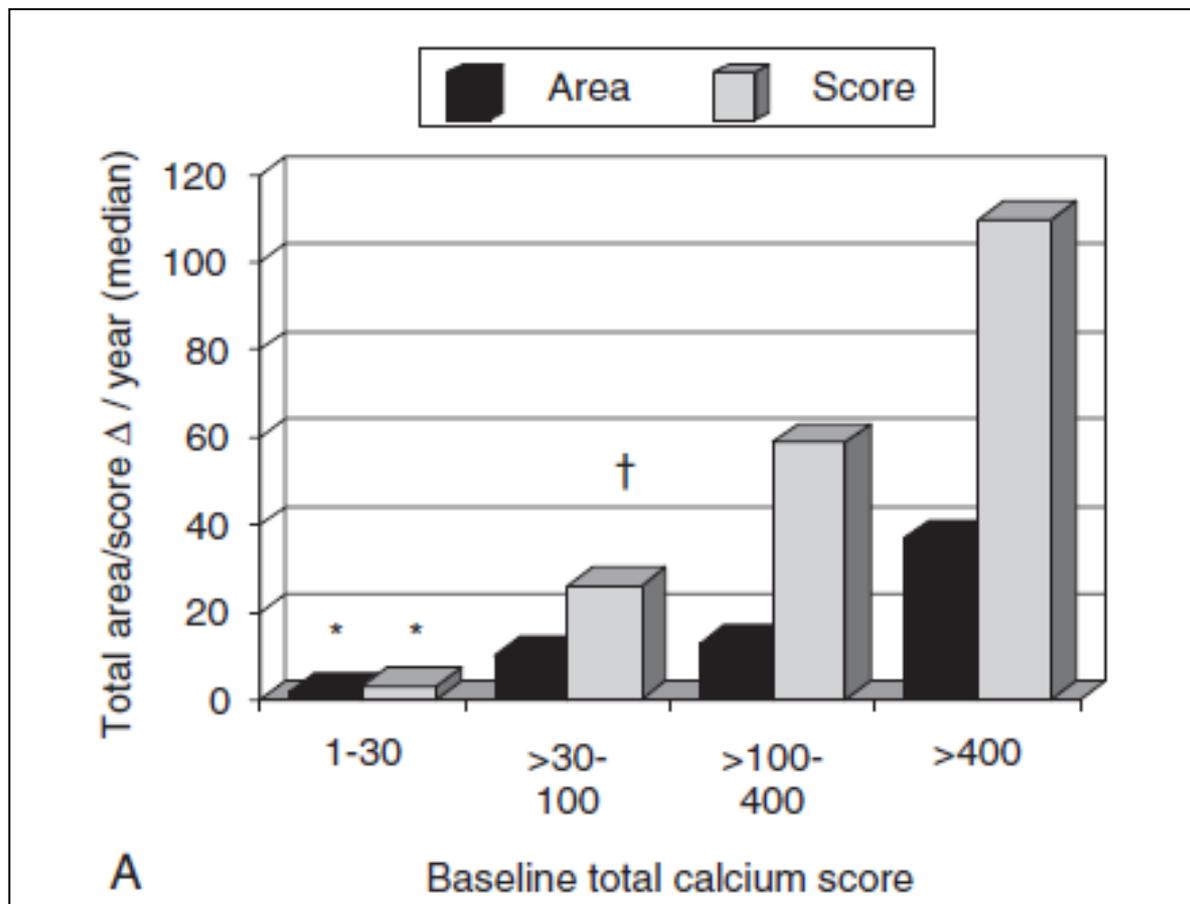
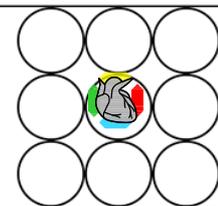
Progression of coronary artery calcification: risk and risk factors



What is the change of CAC per year?

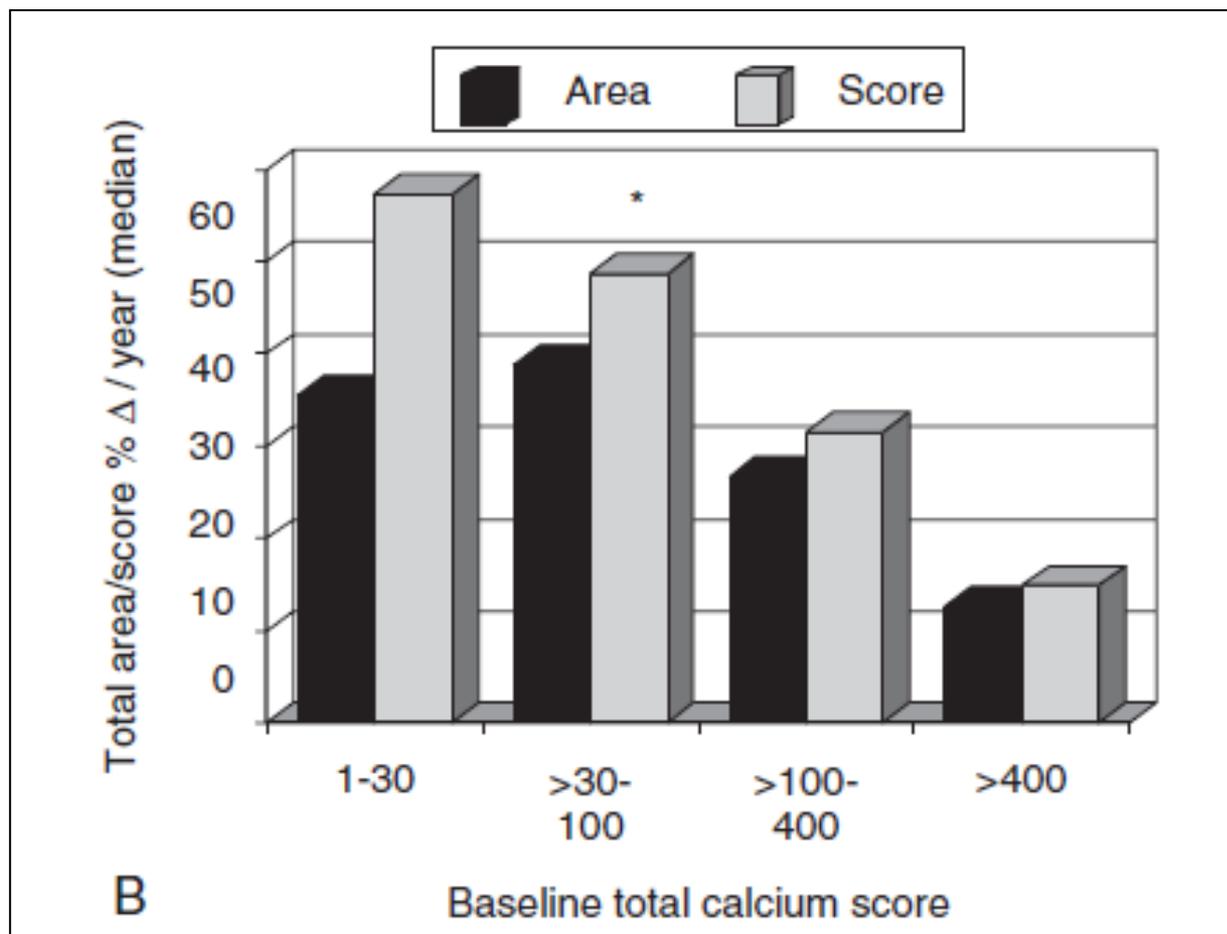
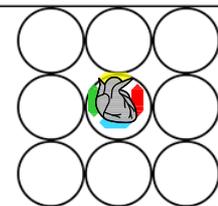
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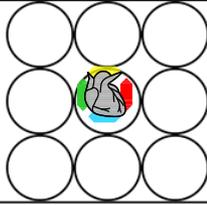
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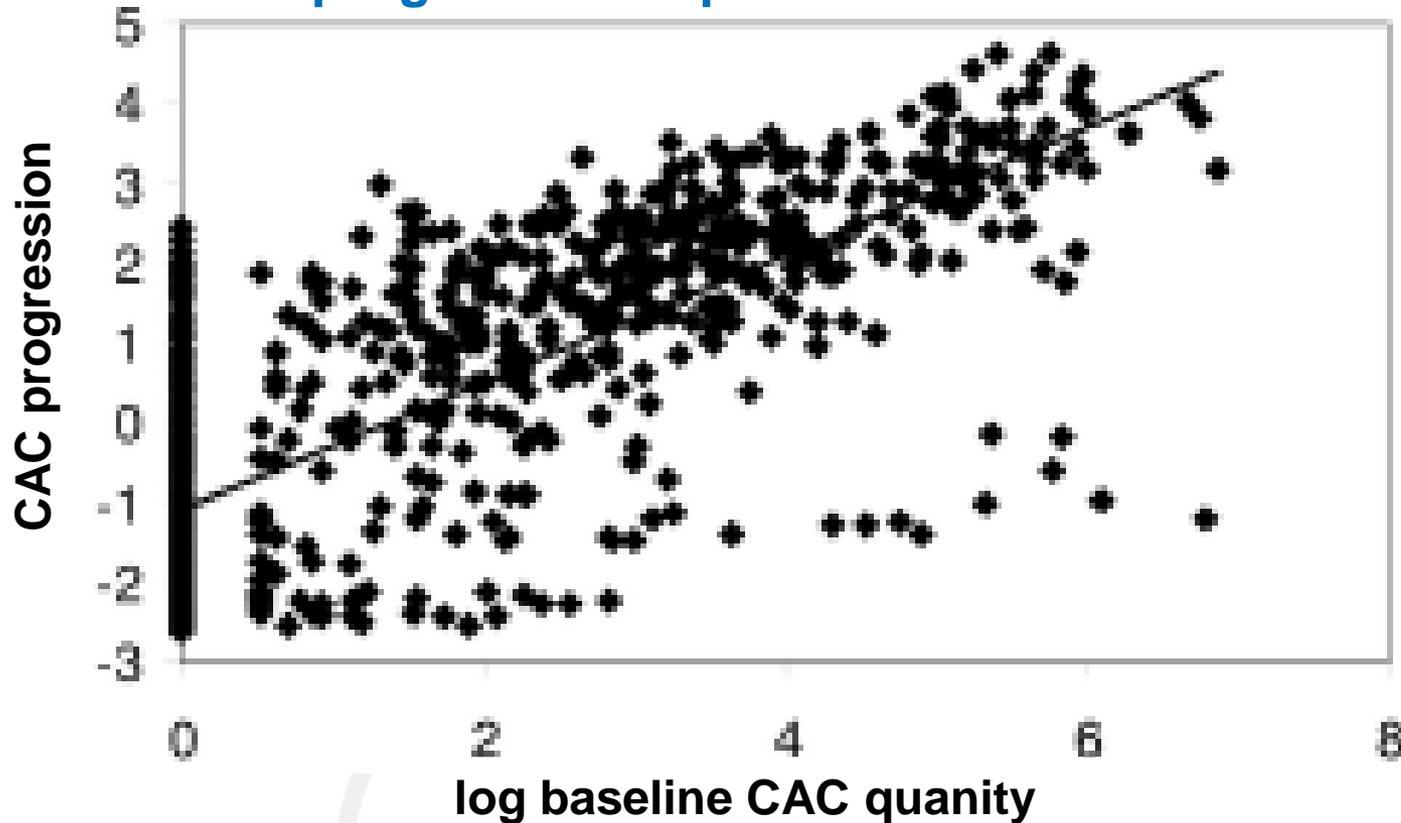


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Progression of coronary artery calcification: risk and risk factors



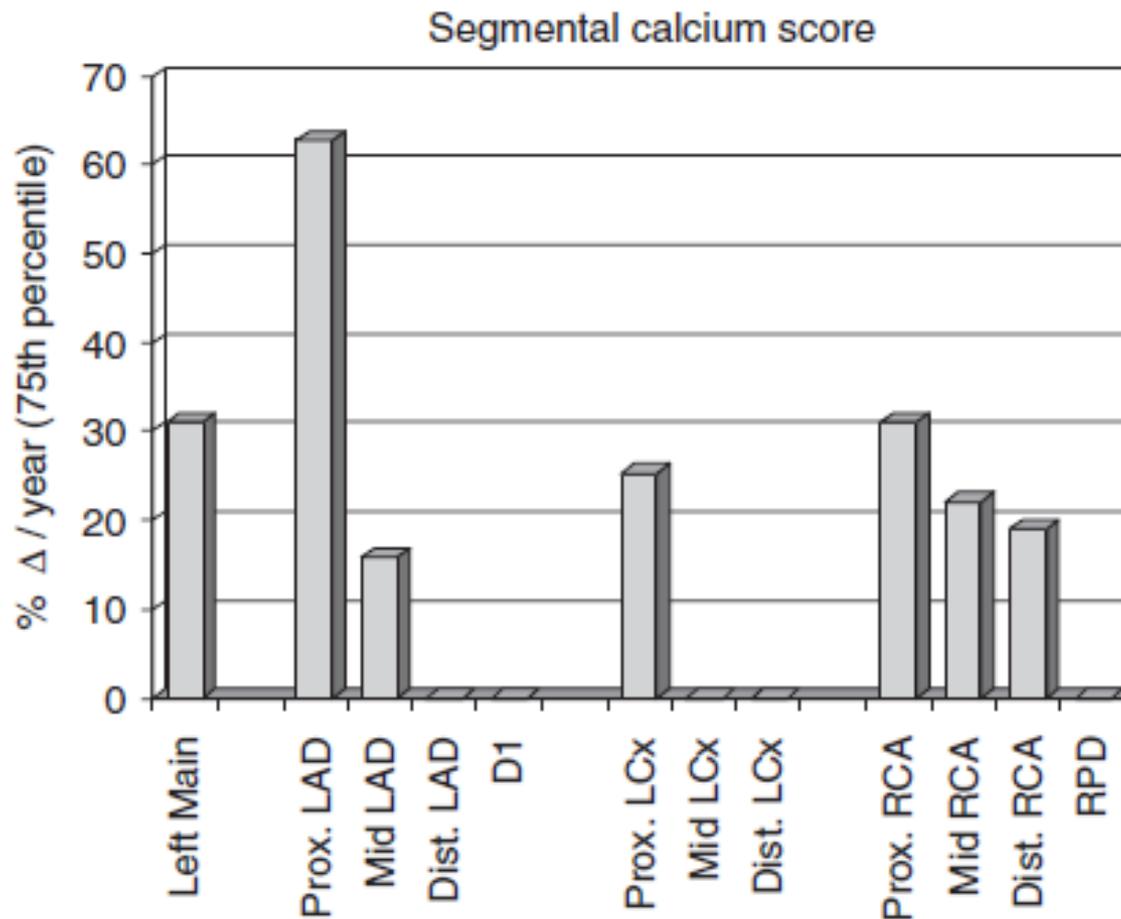
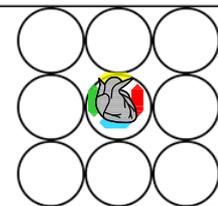
CAC progression dependent on baseline values



CAC progression = $-1.080 + 79 \times (\log \text{ baseline CAC quantity})$ $P < 0.0001$, $R^2 = 0.57$.

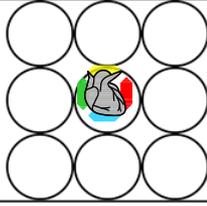
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Progression of coronary artery calcification: risk and risk factors



Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors

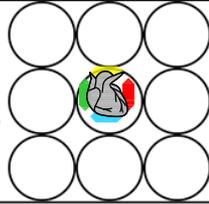


But what is the mean change of CAC per year?

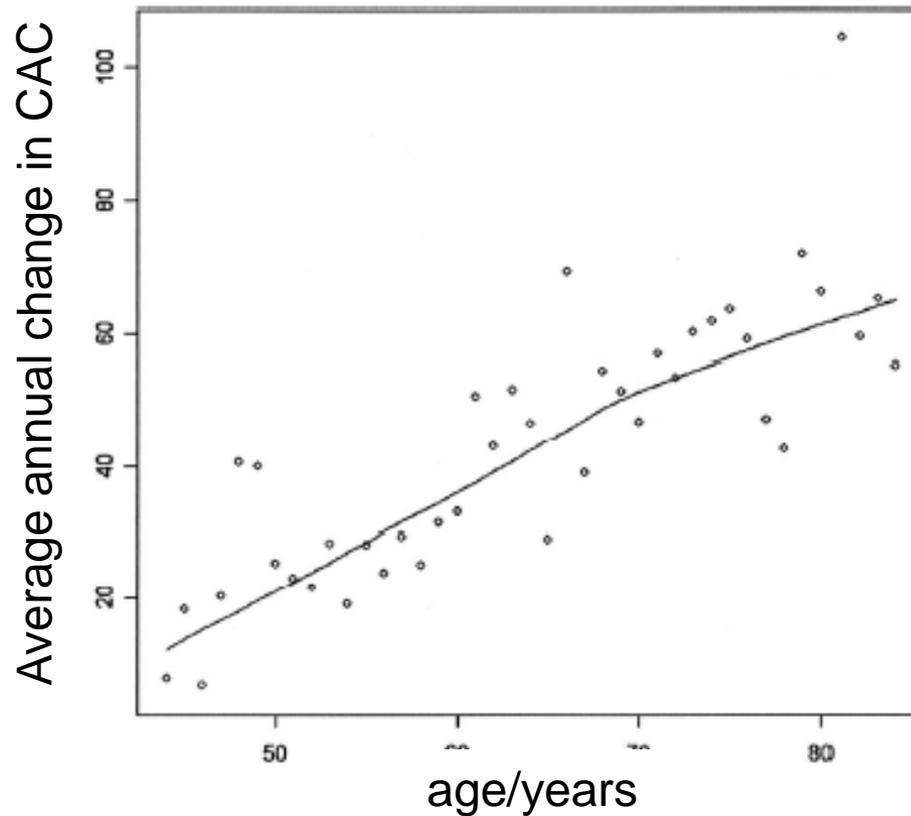
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Progression of coronary artery calcification: risk and risk factors

MESA Results



5756 participants average of 2.4 years



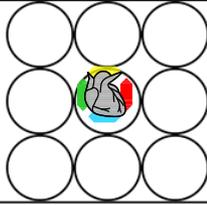
Median annual
CAC change

21 CAC score in M

14 CAC score in F

Prevention and Coronary Artery Disease

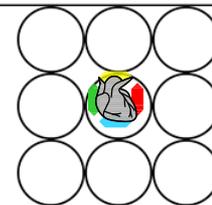
Progression of coronary artery calcification: risk and risk factors



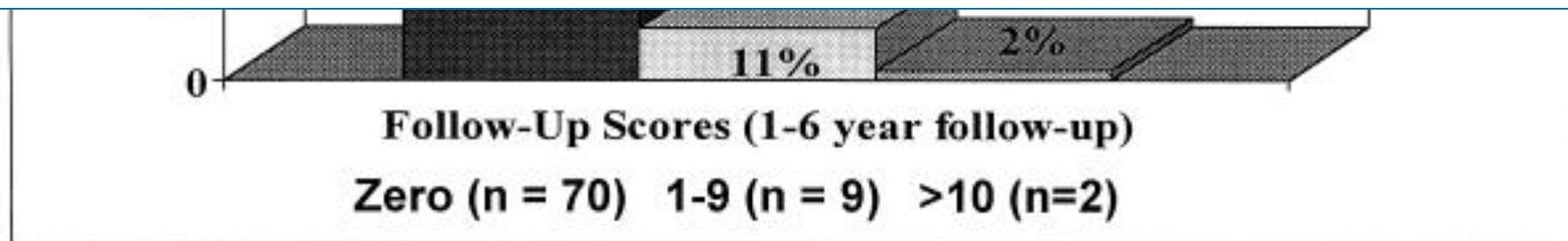
But what is the mean change for those
with zero calcification?

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Progression of coronary artery calcification: risk and risk factors



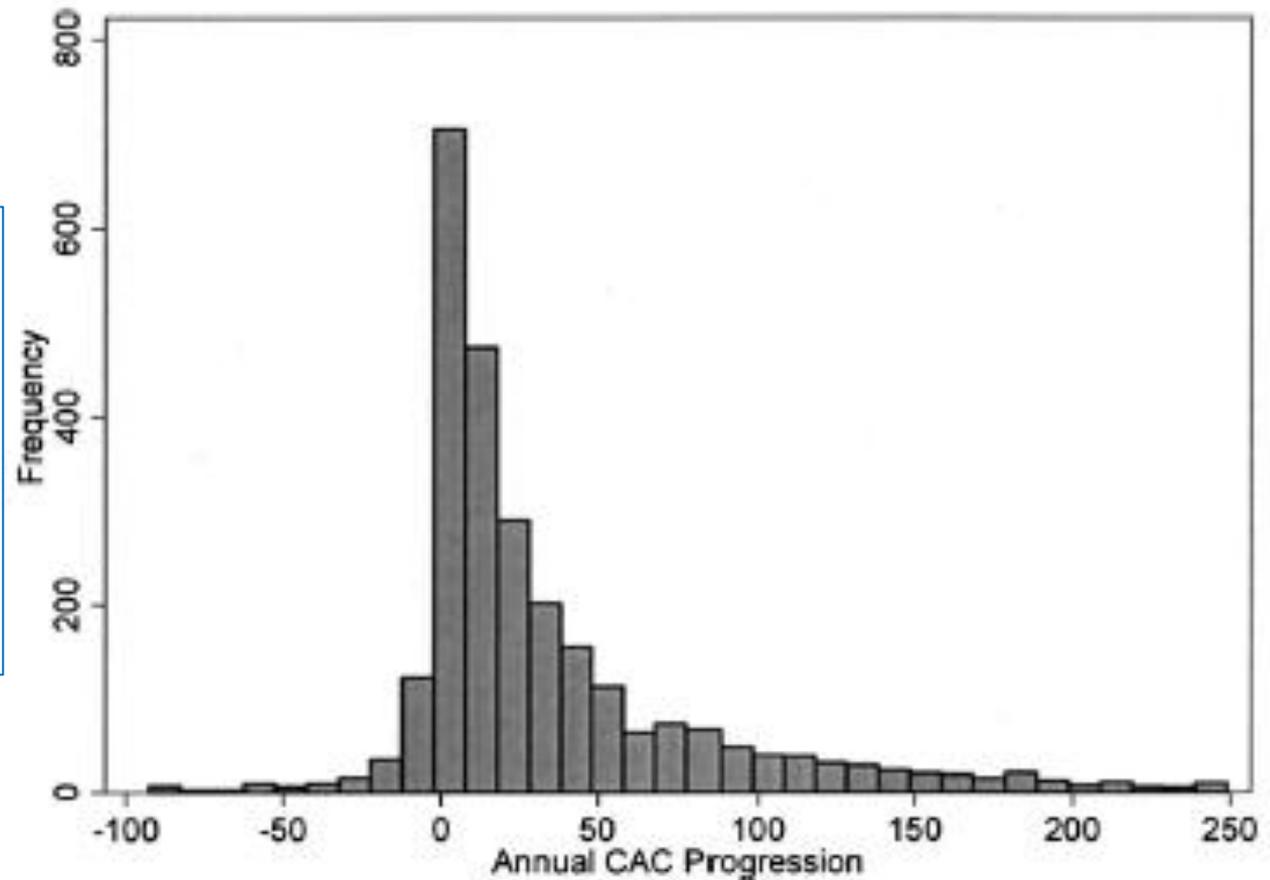
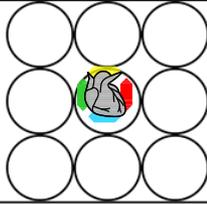
during FU no CAC > 100



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Progression of coronary artery calcification: risk and risk factors

- Effect of age on incidence of new CAC -

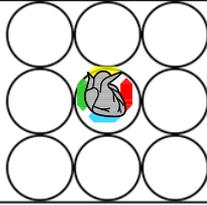


incidence
new CAC
averaged
6.6% per year.

<5% /year at 50 years,
12%/year 80 years

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors

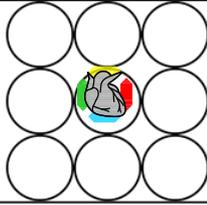


Zero CAC means very low risk, but zero CAC does not mean zero for ever!

- in 106 (25.1%) of 422 patients rate of conversion
13.4% in the first 4 years and 25.1% at 5 years
- progression non-linear, slow and flat in the first two and more rapid increase in the next 3 years,
reflecting the sex- and age-adjusted percentiles distribution of CAC

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Progression of coronary artery calcification: risk and risk factors

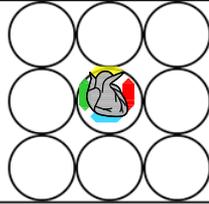


What about changes in CAC in relation to other organs?

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors

- Progression in association with disease at different organs -



Prospective Army Coronary Calcium (PACC) Project

n= 180

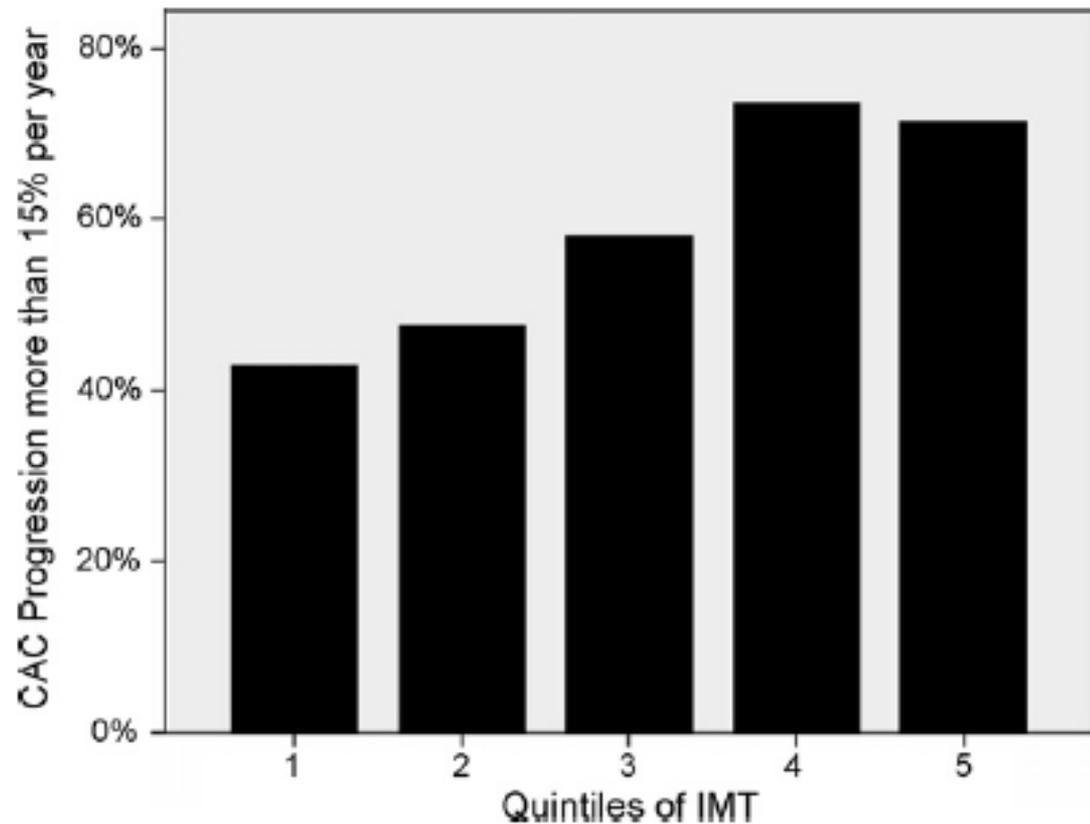
40 – 50 years M/F

1. CAC: 101 ± 259

2. CAC: 178 ± 417

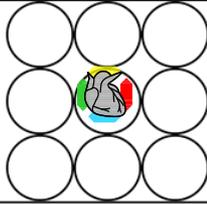
FU 4.2±1.3 years

Range 1.5–6.6 years



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Progression of coronary artery calcification: risk and risk factors

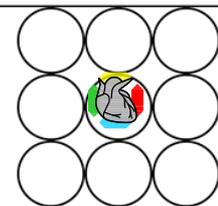


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Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



CARDIA Study

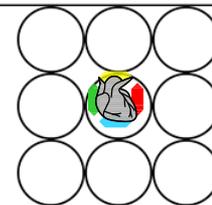
Coronary Artery Risk Development in Young Adults

2.831 subjects, 33-45 year old adults

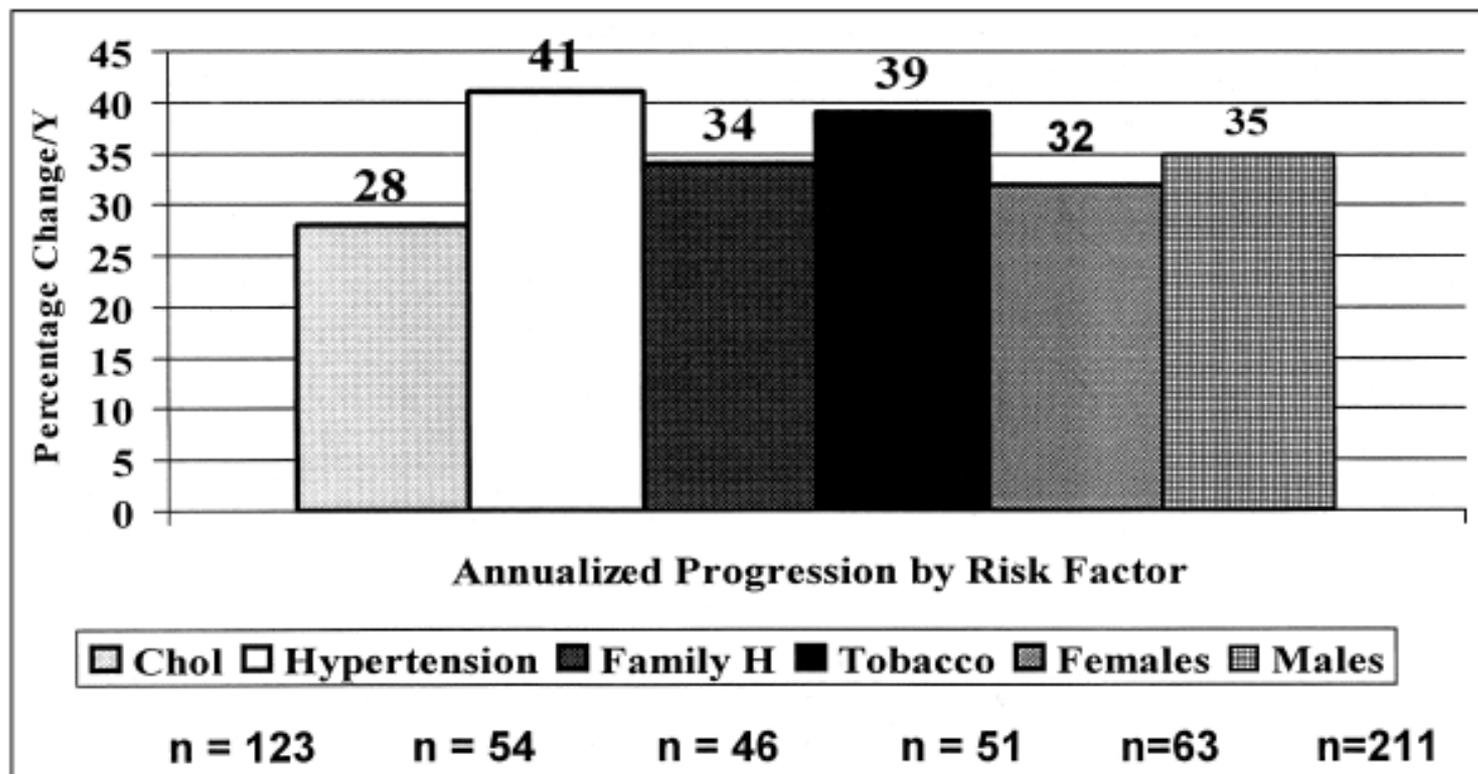
FRS	0 – 2.5%	2.6 – 5.0%	5.1 – 10%	> 10%
CAC> 0	7.3%	20.2%	19.1%	44.8%
CAC>100	1.3 %	2.4%	2.4%	17.2%

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



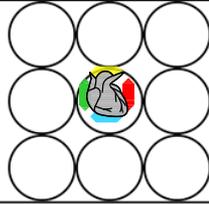
299 asymptomatic pts (227M/72F), 2 EBTs ≥ 1 year, range 1 – 6 years



Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors

MESA Study

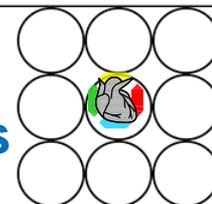


Risk factors for incidental and progression of CAC

Treated diabetes mellitus	26.8 (19.5 to 34.2)
Male gender	10.9 (6.3 to 15.5)
Lipid lowering medication	9.8 (4.2 to 15.4)
Family history of heart attack	9.0 (4.4 to 13.6)
Age (10 y)	8.8 (6.4 to 11.2)
Antihypertensive medication	8.0 (3.3 to 12.8)
Systolic BP	1.9 (0.8 to 3.1)
Smoking >10 pack years	1.4 (0.2 to 2.6)
Body mass index	0.9 (0.4 to 1.3)

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



**Risk Factor:
Diabetes mellitus**

FU time

56 ± 11 months

Baseline demographics at the time of the initial computed tomographic scan

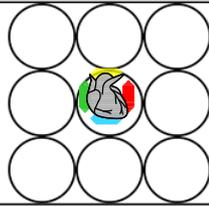
Variable	Matched Controls [†] (n = 300)	Patients With DM (n = 296)	p Value
Age (yrs)	59 ± 6	59 ± 6	—
Women	29% (87)	29% (86)	—
Baseline CAC score	276 ± 41	291 ± 49	0.9
Statin therapy	50% (150)	55% (163)	0.8
Hypertension	26% (78)	68% (201)	0.03
Family history of premature CAD [§]	50% (150)	40% (118)	0.7
Current tobacco smokers	16% (48)	19% (56)	0.6
Absolute annual CAC score change	34.3 ± 4.8	80.6 ± 10	0.0001
ΔCAC%*	10.2 ± 6.7	29.4 ± 8.7	0.0001
CAC progressors [†]	33.6% (101)	62.5% (185)	0.0001

* CAC Progression (ΔCAC%) = (Annual change in CAC/baseline CAC) × 100.

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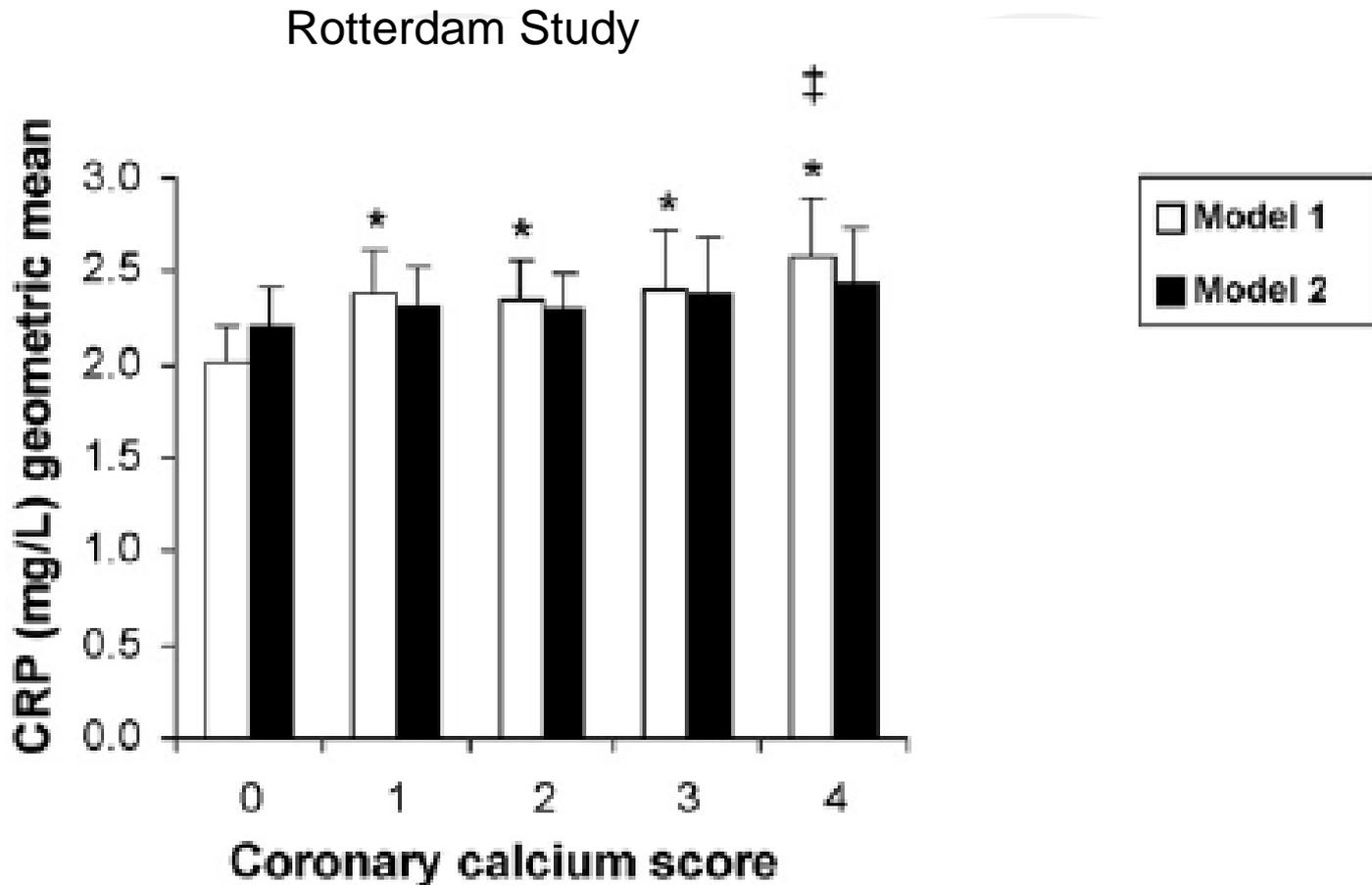
Progression of coronary artery calcification: risk and risk factors

Risk Factor: Inflammation



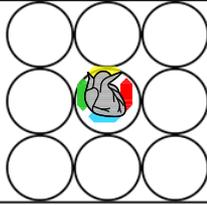
hs-CRP

n= 1962



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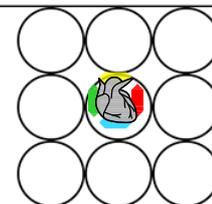
Progression of coronary artery calcification: risk and risk factors



Risk Factors of CAC Progression
from Zero to $CAC > 0$

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Progression of coronary artery calcification: risk and risk factors



Follow up time 27 years

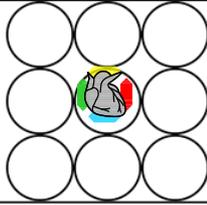
Table 2

**ORs and 95% CIs for CAC in Adulthood
in a Multivariable Logistic Regression Model
(N = 563) Adjusted for All of the Listed Variables**

	OR	95% CI	p Value
Age	1.09	0.99–1.20	0.09
Male	2.52	1.56–4.05	0.0001
Adolescence LDL-C	1.34	1.05–1.70	0.02
Adolescence systolic BP	1.38	1.08–1.77	0.01
Δ LDL-C	1.07	0.84–1.37	0.58
Δ Systolic BP	1.25	0.98–1.60	0.08

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Progression of coronary artery calcification: risk and risk factors

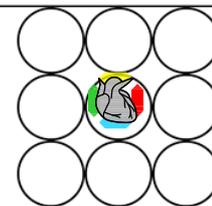


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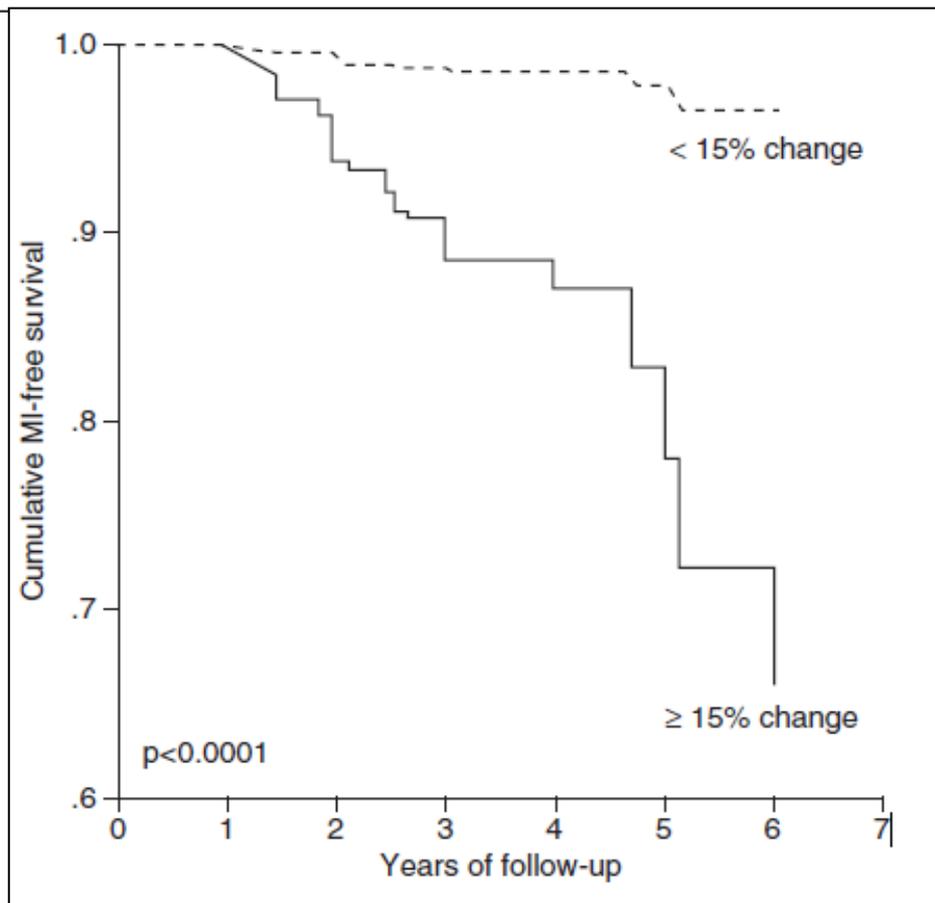
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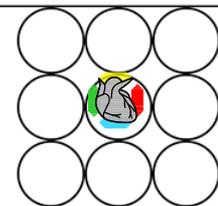


495 pts
2 scans within
 1.9 ± 1 year
all on
statin therapy



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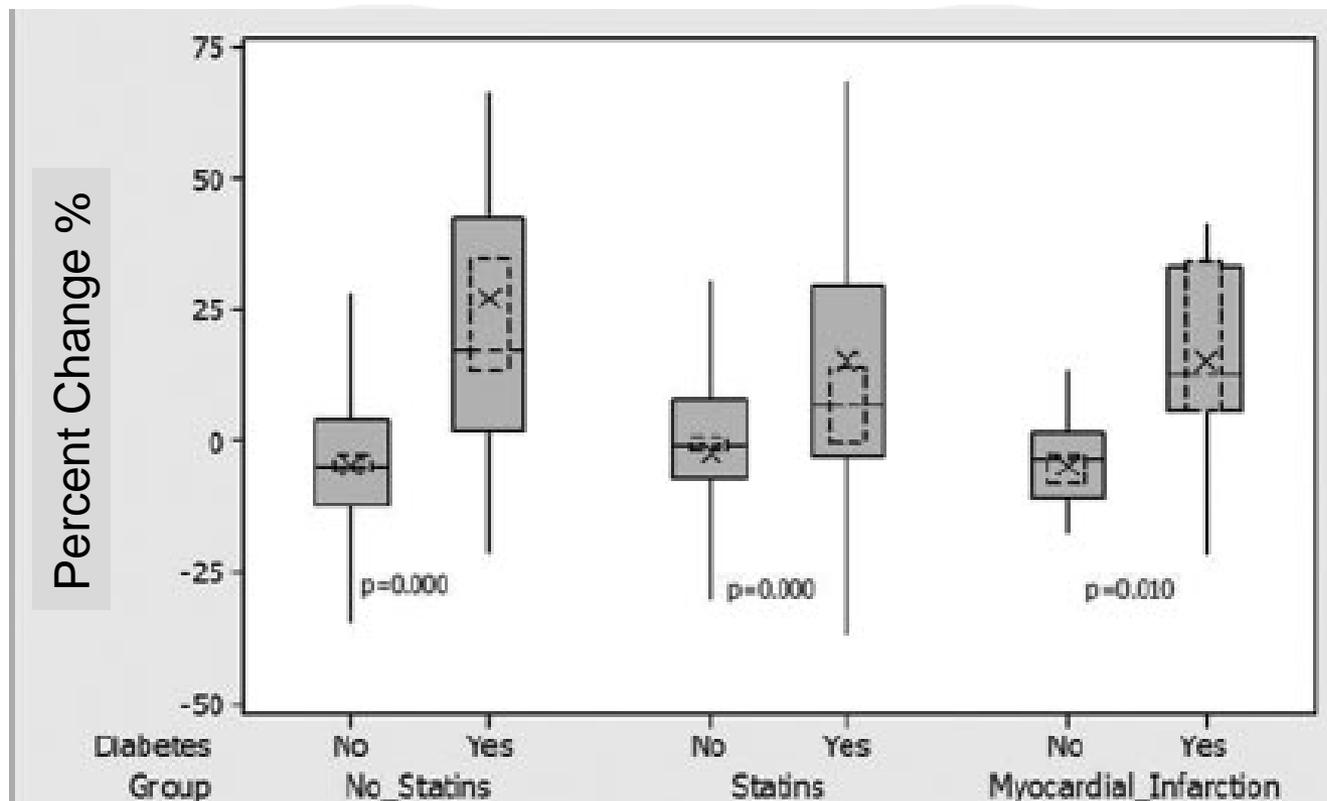
1153 pts

157 DM

2 scans >1 year

CAC >15 %/year

true progression

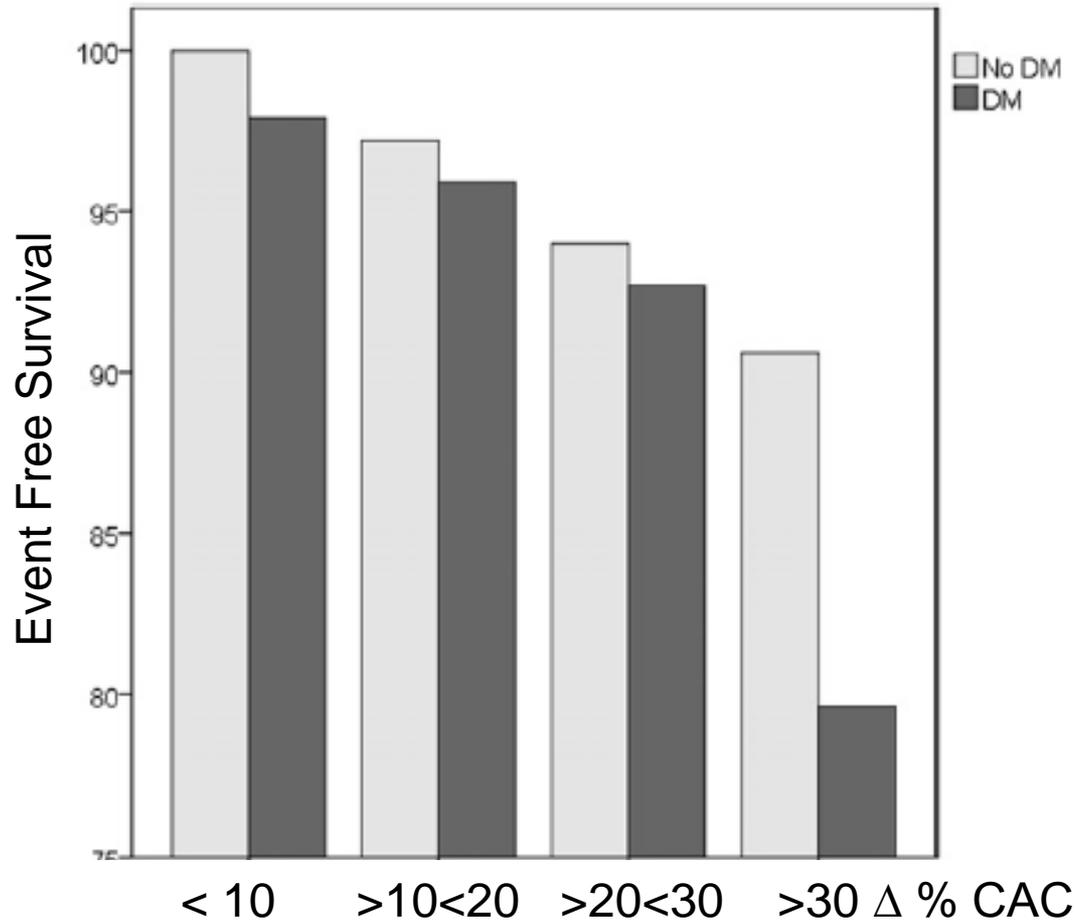
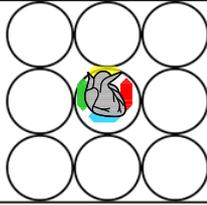


Raggi et al.

Hypertension 46:238-243, 2005

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors

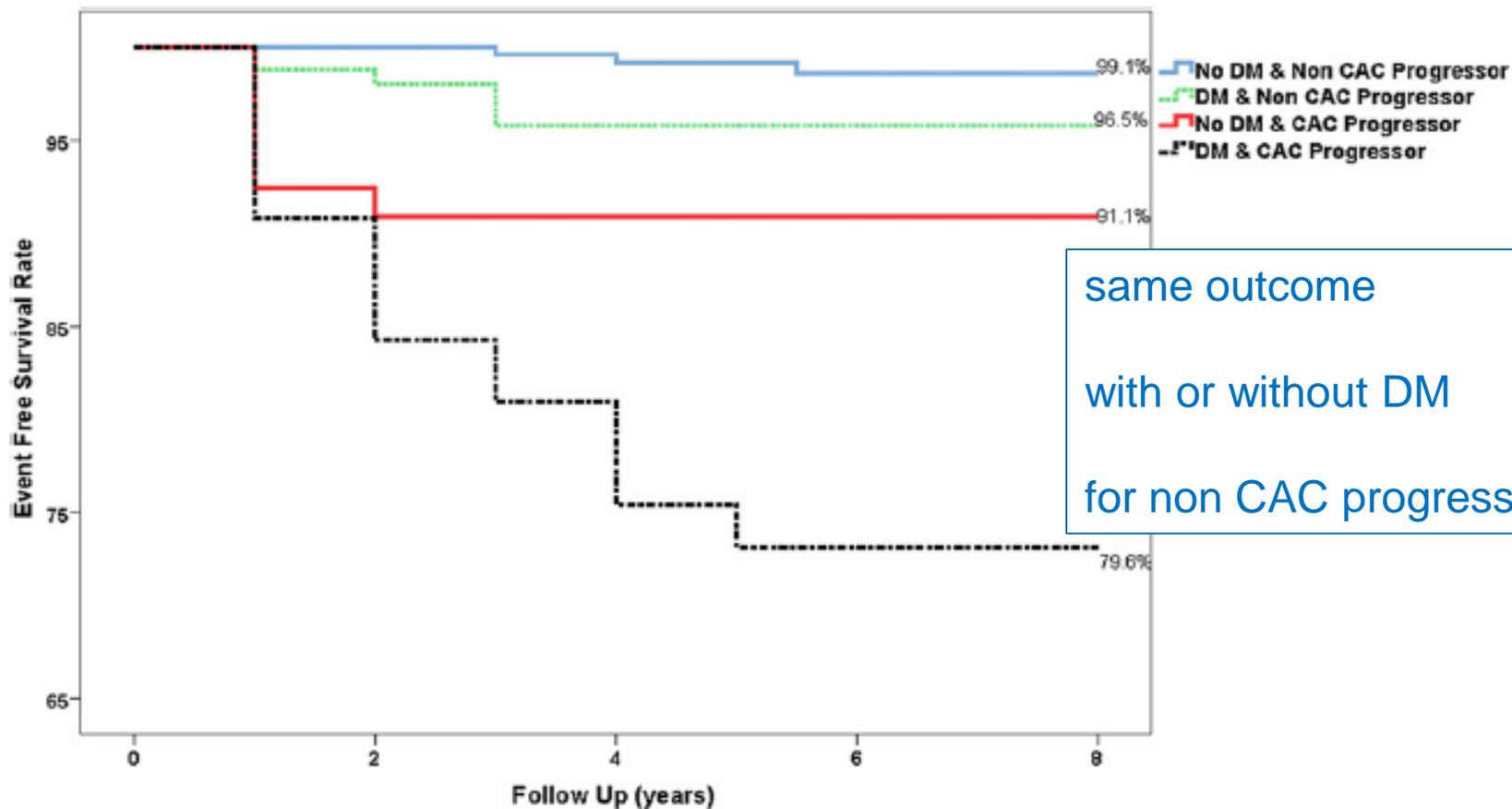
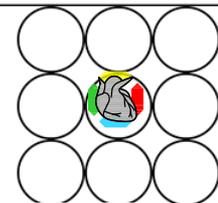


Kiramijyan S et al

AJC 2012, in press

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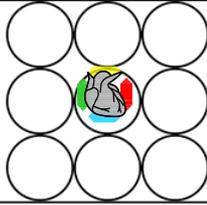
same outcome
with or without DM
for non CAC progression

Kiramijyan S et al

AJC 2012, in press

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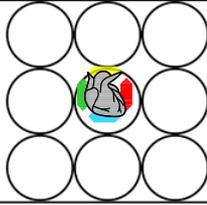
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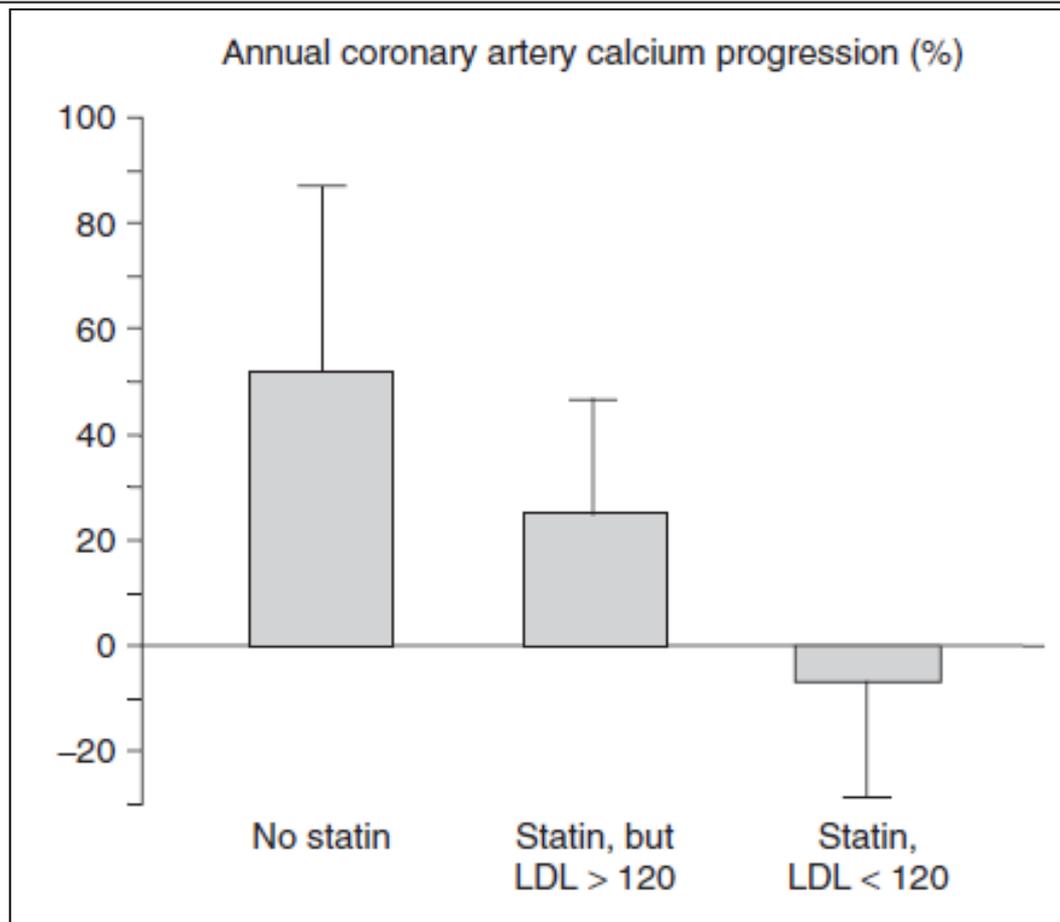
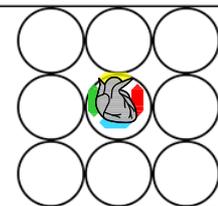
Pharmacological Interventions

for treatment of CAC

- statins -

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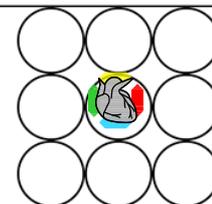


Callister TQ et al.

New Engl J Med 339: 1972–78, 1998

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



Verum:

atorvastatin 20 mg
 vitamin C 1 g,
 vitamin E 1,000 U
 aspirin 81 mg

	Treatment	Control	p Value
	490	515	
	528	563	—
	379	370	0.96
th percentiles	184, 636	183, 671	—

Placebo

aspirin 81 mg

	417	431	—
	647	723	—
	482	505	—
th percentiles	231, 820	251, 901	

FU 2 years

Absolute	137 ± 310	155 ± 358	0.86
Percent	38 ± 75	36 ± 58	0.86

Year four			
n	281	288	
Mean	846	922	—
Median	623	673	—
25th, 75th percentiles	335, 1,077	343, 1,138	—

FU 4 years

Change (year four minus baseline)			
Absolute	331 ± 421	323 ± 385	0.80
Percent	81 ± 89	73 ± 93	0.76

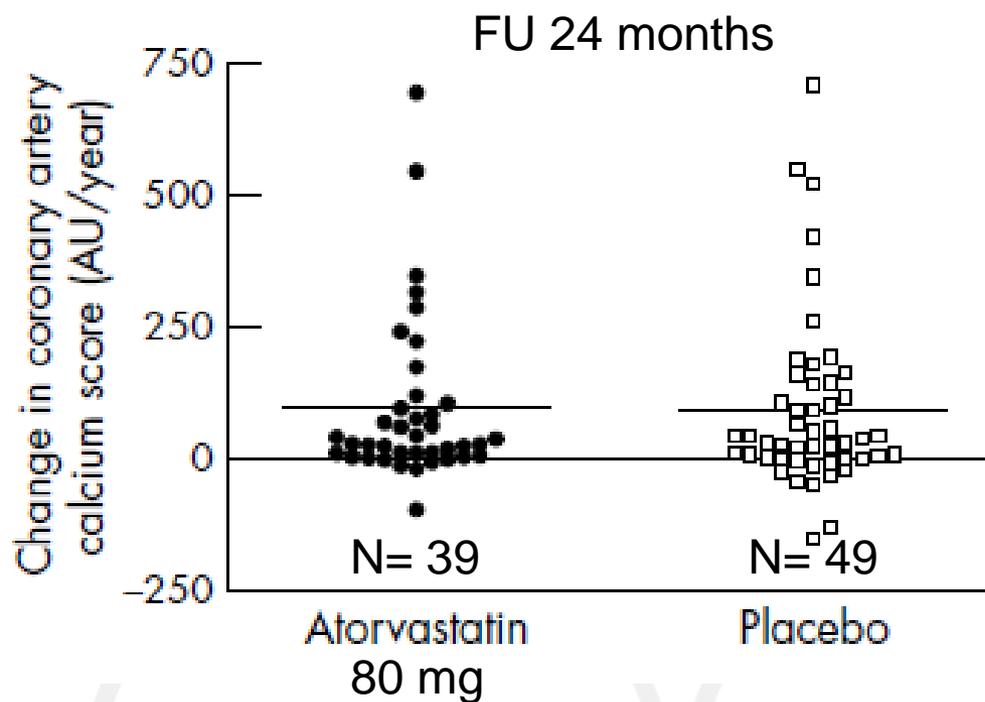
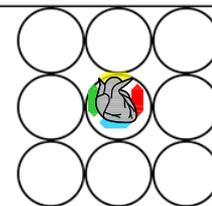
Because baseline calcium scores were not normally distributed, p values are based on the distribution of calcium scores (median, interquartile range [Wilcoxon rank sum test]), rather than mean values. Change in calcium scores was normally distributed and the p value is based on comparison of the mean values and their respective variances.

Arad Y et al

J Am Coll Cardiol 46:166–72, 2005

Prevention and Coronary Artery Disease

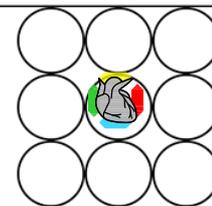
Progression of coronary artery calcification: risk and risk factors



Houslay ES et al

Heart 92:1207–1212, 2006.

Prevention and Coronary Artery Disease
Progression of coronary artery calcification: risk and risk factors



Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Aggressive Versus Moderate Lipid-Lowering Therapy in Hypercholesterolemic Postmenopausal Women: Beyond Endorsed Lipid Lowering With EBT Scanning (BELLES)

Paolo Raggi, Michael Davidson, Tracy Q. Callister, Francine K. Welty, Gloria A. Bachmann, Harvey Hecht and John A. Rumberger

Circulation 2005;112;563-571; originally published online Jul 11, 2005;

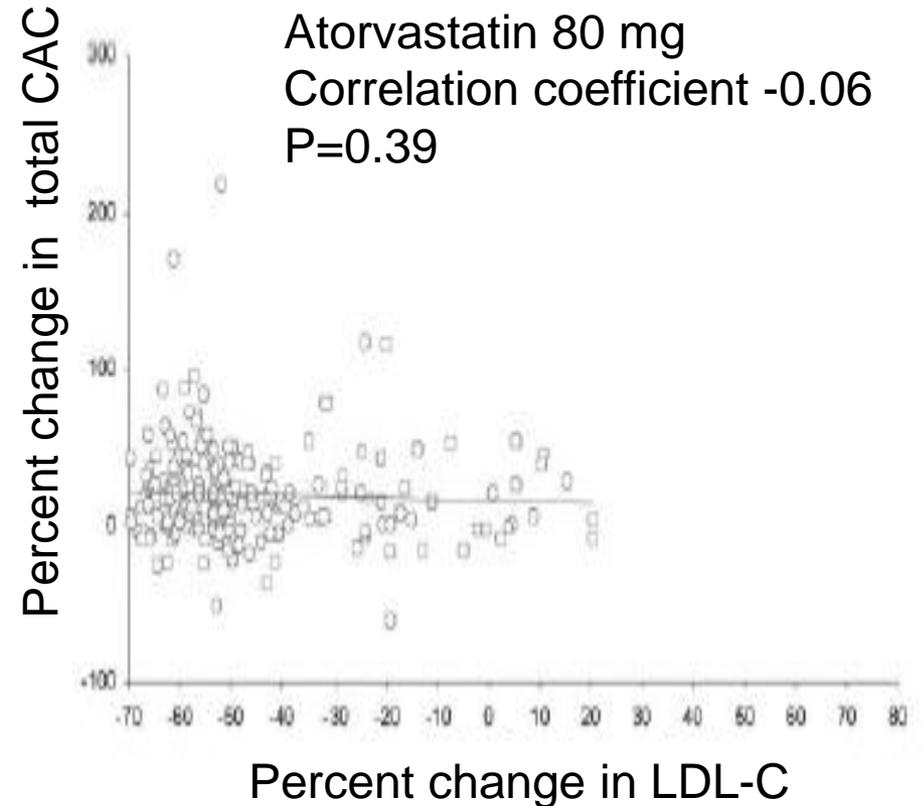
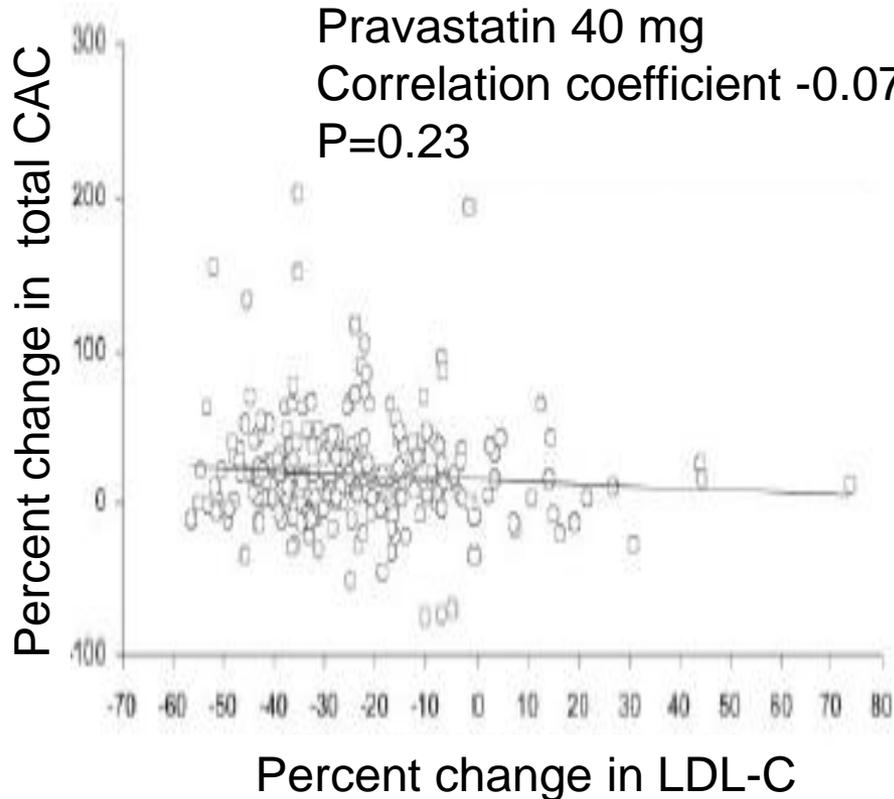
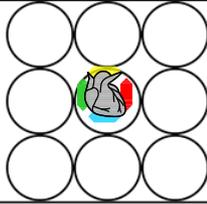
DOI: 10.1161/CIRCULATIONAHA.104.512681

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Progression of coronary artery calcification: risk and risk factors

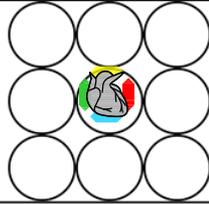


Raggi P et al

Circulation. 112:563-571, 2005

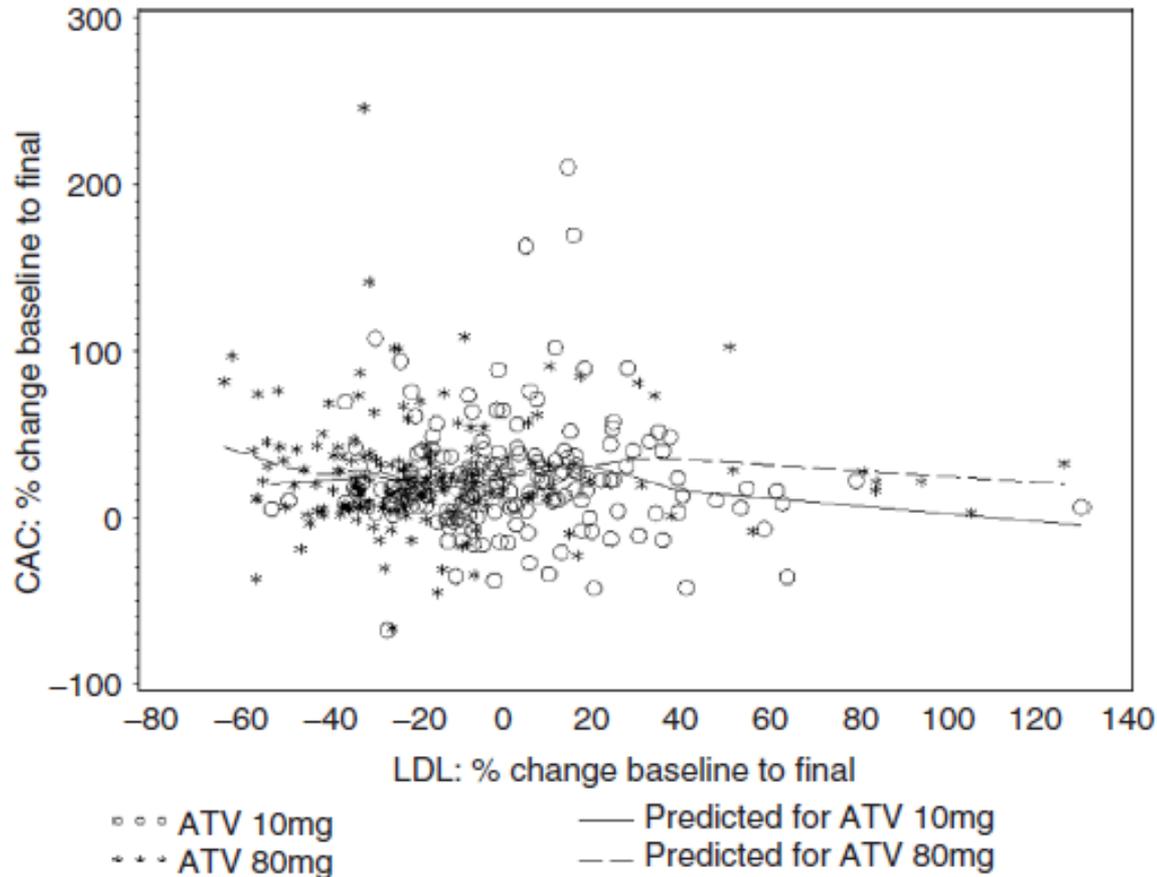
Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



Atorvastatin

**10 mg
versus
80 mg**

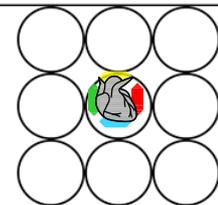


Schmermund A et al

Circulation 113:427–37, 2006

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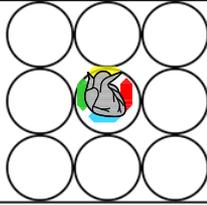


As follow-up studies demonstrate CAC progression in the range of 15 – 25 % per year, the question arises: can we check the efficacy of the risk factor modification by CT?

The answer is **No**, because

four randomized, placebo and verum controlled studies in different patient cohorts did not demonstrate any attenuation of CAC progression over time.

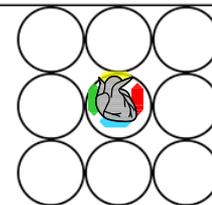
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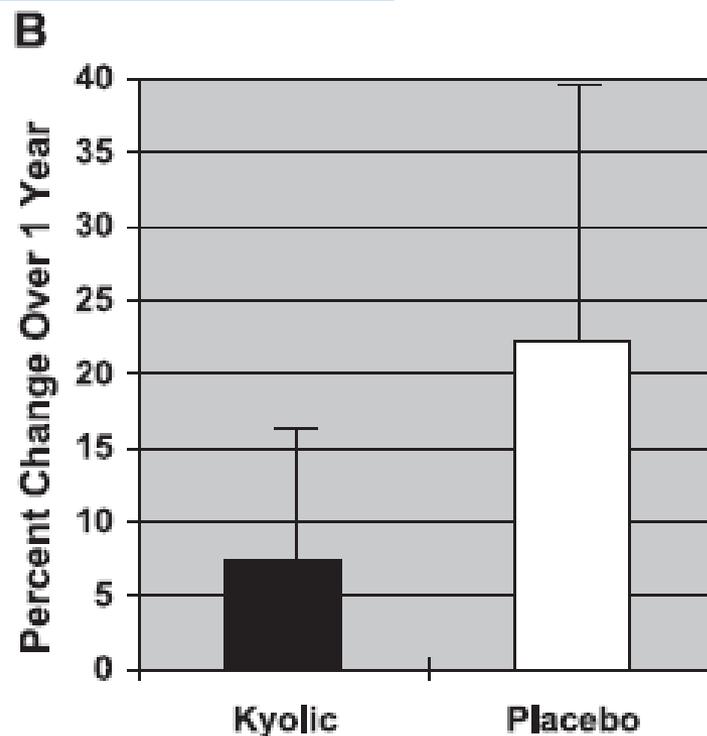
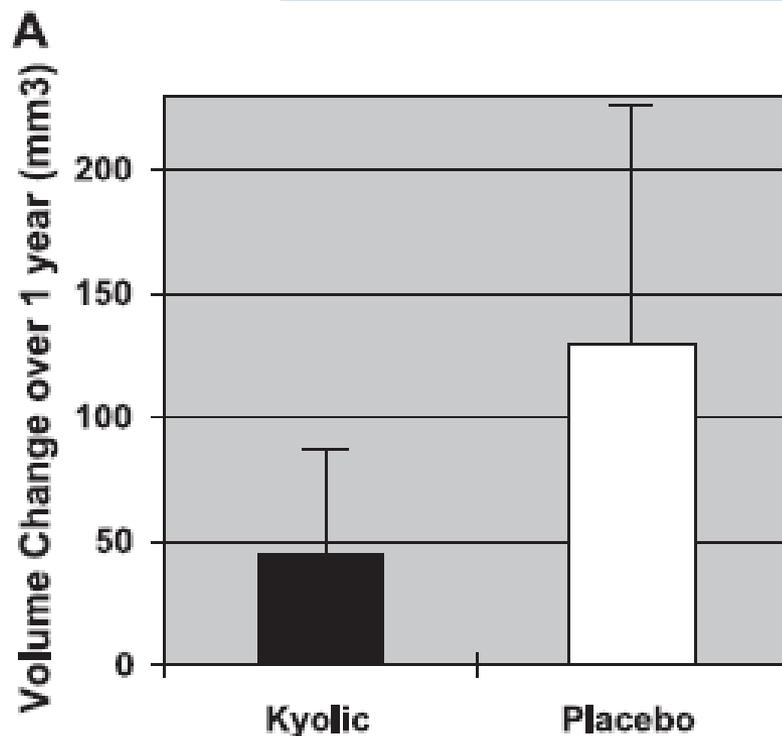
Pharmacological Interventions
for treatment of CAC
- other than statins -

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



N = 19, 4 ml Aged Garlic Extract for 1 year

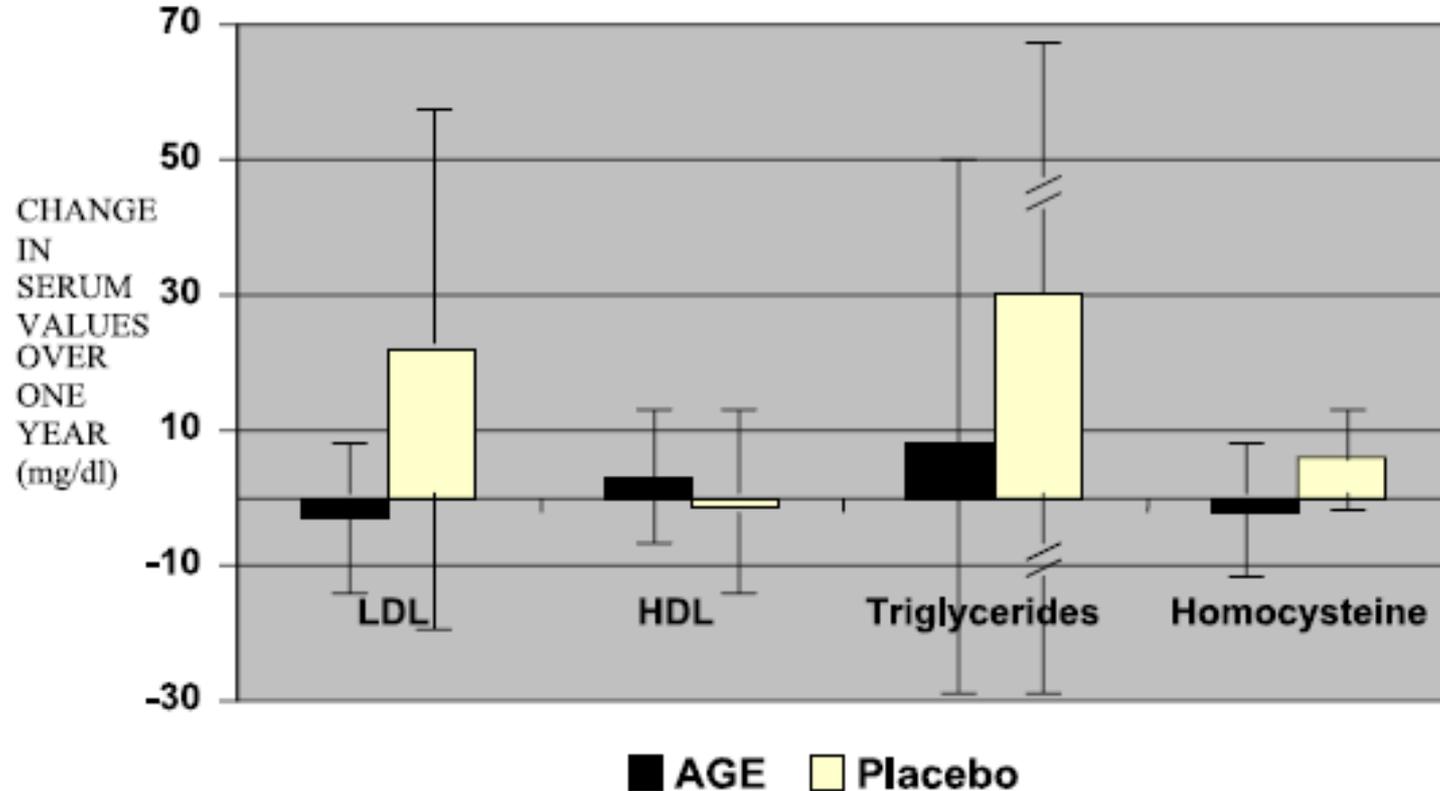
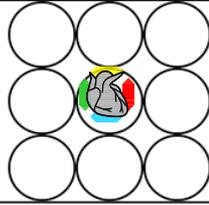


Budoff MJ et al

Preventive Medicine 39, 985–991, 2004

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors

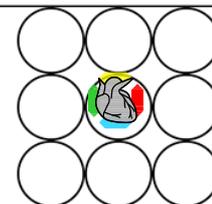


Budoff MJ et al

Preventive Medicine 39, 985–991, 2004

Prevention and Coronary Artery Disease

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RCT with 65 firefighters at intermediate risk (55±6years
1200 mg age garlic extract and 120 mg Q 10 for 1 year

**CAC progression
annual rate
32 ± 6
vs
58 ± 8**

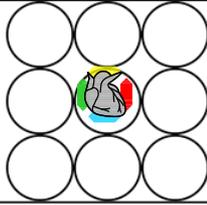
Variables	AGE +CoQ10	Placebo	P value
<i>Baseline</i>			
Age (years)	55 ± 6	54 ± 5	0.6
Gender (Male)	100%	100%	-
CAC	169 ± 29	211 ± 49	0.6
hsCRP	1.9 ± 2.1	1.9 ± 2.4	0.9
BMI	28 ± 3	29 ± 4	0.5
<i>Absolute change at 1-year follow-up</i>			
CAC	32 ± 6	58 ± 8	0.01
hsCRP	-0.12 ± 0.24	0.91 ± 0.56	0.01
BMI	-0.47 ± 0.82	0.28 ± 1.27	0.03

Zeb I et al

J Cardiovasc Dis Res 3: 185-190, 2012

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



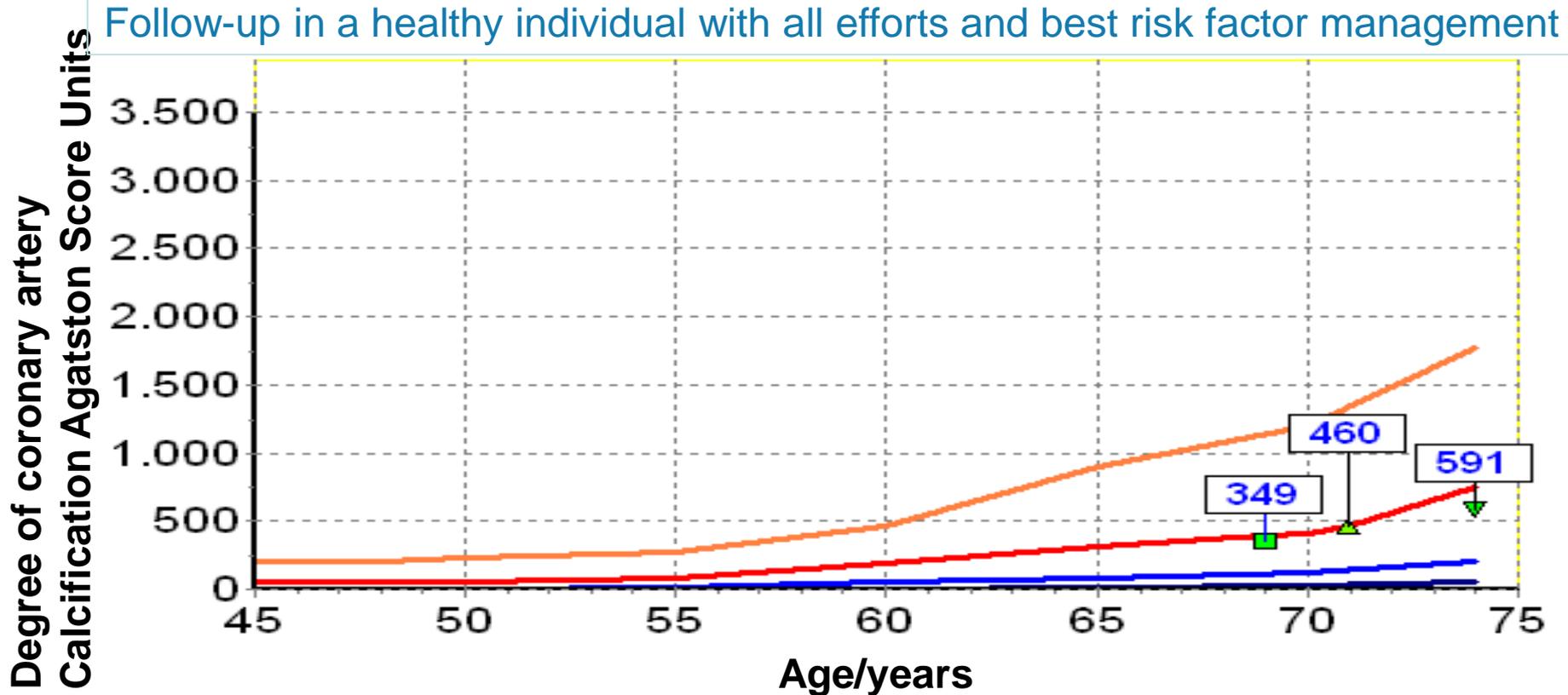
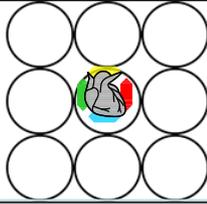
Pharmacological Interventions

for treatment of CAC

- optimized RF adjustment-

Prevention and Coronary Artery Disease

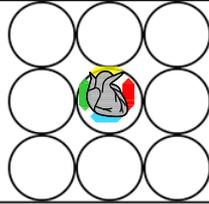
Progression of coronary artery calcification: risk and risk factors



- At the age of 74, the score of 591 is above the 70th percentile
- At the age of 71, the score of 460 is above the 67th percentile
- At the age of 69, the score of 349 is above the 72nd percentile

Prevention and Coronary Artery Disease

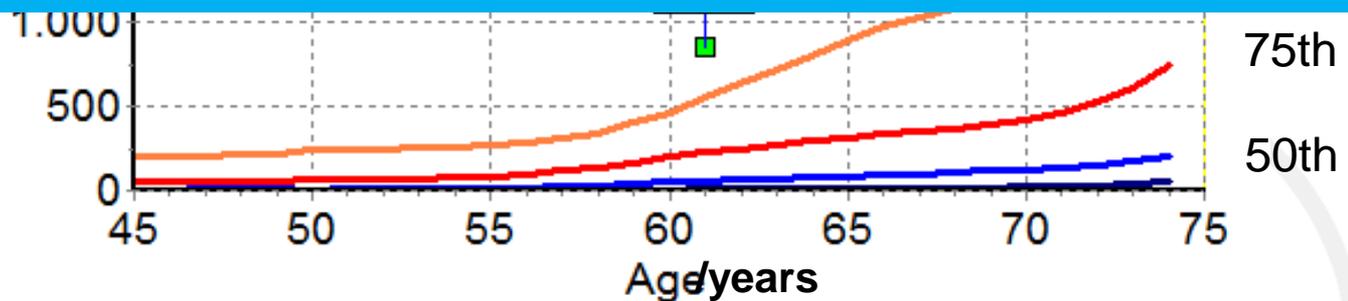
Progression of coronary artery calcification: risk and risk factors



10-year Follow-up EBCTs in a healthy check-up individual

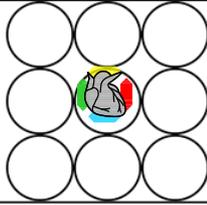
That means:

Once you are on a CAC percentile you will stay,
increase of CAC over time can be predicted and calculated.



Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



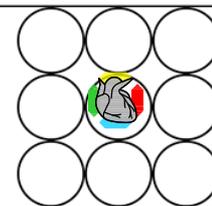
Conclusion

Progression of CAC

- Natural history
- RF: known FRS and hs-CRP
- Diabetes
- High rate of progression means high risk
- No convincing data on drug treatment
- Progression genetically determined?

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



Coronary Heart Disease

Coronary Artery Calcification Progression Is Heritable

Andrea E. Cassidy-Bushrow, PhD, MPH; Lawrence F. Bielak, DDS, MPH; Patrick F. Sheedy II, MD;

Gregory T. Taylor, MD, MPH; J. Kent M. Willerson, MD, PhD; Daniel R. Bandaru, PhD

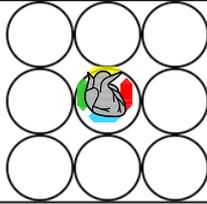
Conclusions—Evidence was found that many but not all genetic factors influencing baseline CAC quantity also influence CAC progression. The identification of common and unique genetic influences on these traits will provide important insights into the genetic architecture of coronary artery atherosclerosis. (*Circulation*. 2007;116:25-31.)

risk factors and CAC quantity, the estimated heritability of CAC progression was 0.40 ($P < 0.001$). Baseline risk factors and CAC quantity explained 64% of the variation in CAC progression. Thus, genetic factors explained 14% of the variation $[(100 - 64) \times (0.40)]$ in CAC progression. After adjustment for risk factors, the estimated genetic correlation (pleiotropy) between baseline CAC quantity and CAC progression was 0.80 and was significantly different than 0 ($P < 0.001$) and 1 ($P = 0.037$). The environmental correlation between baseline CAC quantity and CAC progression was 0.42 and was significantly different than 0 ($P = 0.006$).

Conclusions—Evidence was found that many but not all genetic factors influencing baseline CAC quantity also influence CAC progression. The identification of common and unique genetic influences on these traits will provide important insights into the genetic architecture of coronary artery atherosclerosis. (*Circulation*. 2007;116:25-31.)

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



...symptoms of atheroma are very rare.

There is neither a method

to detect an atheroma during life, nor,

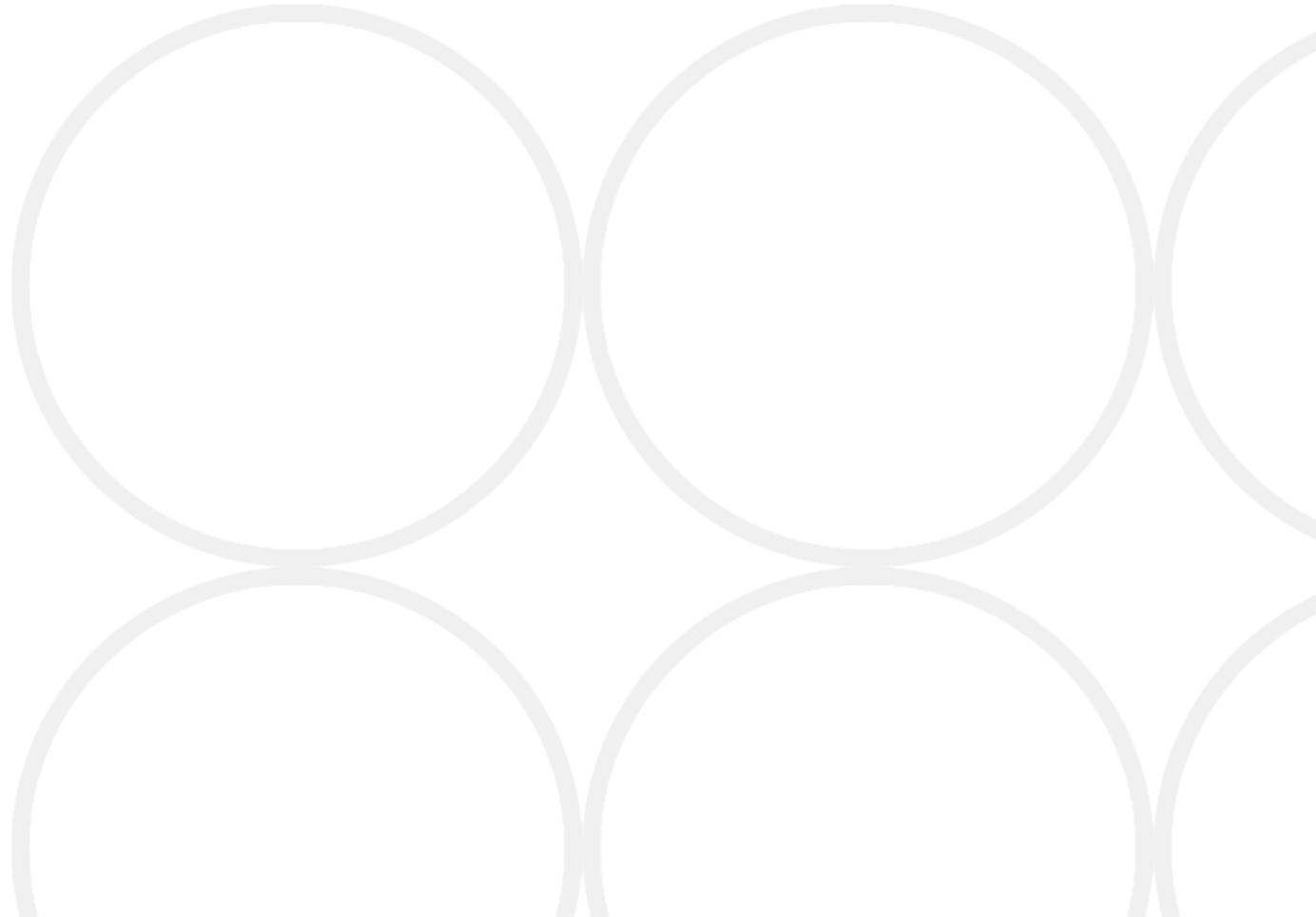
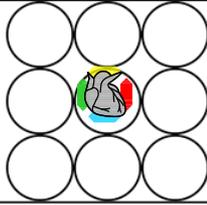
if it is detected, to induce regression.

**...die Symptomatologie des Atheroms ist sehr gering.
Es gibt weder ein Mittel das Atheroma der Arterien sicher
im Leben zu erkennen, noch, wenn es erkannt sein sollte,
dasselbe rückgängig zu machen“**

Lobstein. Stuttgart, 1835, Bd II 465 u folg.

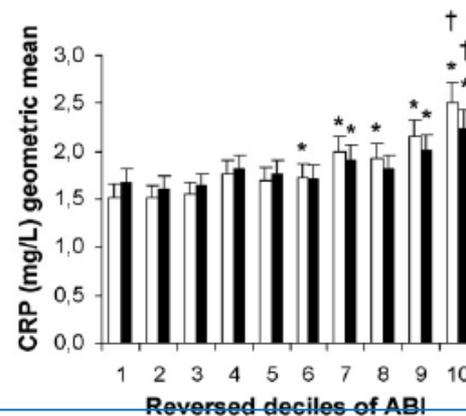
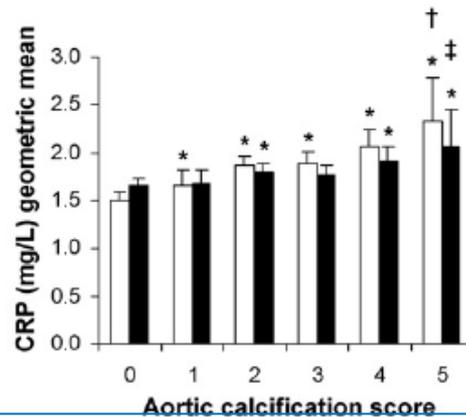
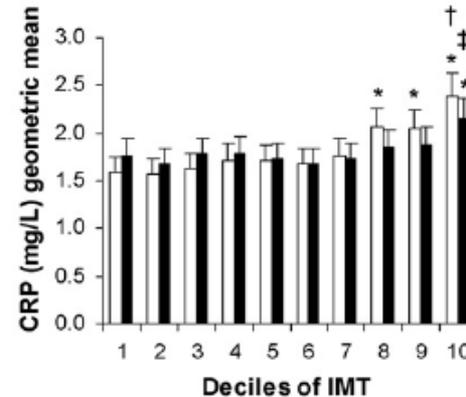
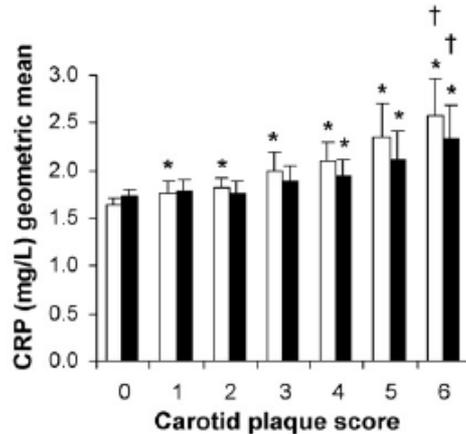
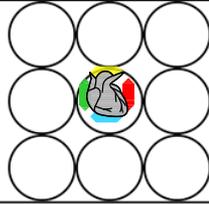
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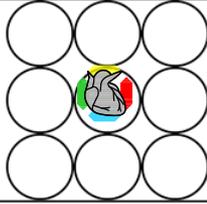


Elias-Smale SE et al. /

Atherosclerosis 195, e195–e202, 2007

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



Zero CAC means very low risk, but zero CAC does not mean zero for ever!

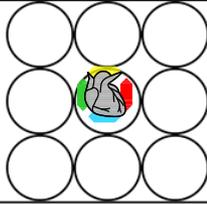
Editorial

Change of zero CAC to $CAC > 0$ does not mean primarily enhanced risk
as few go beyond CAC 100 or even higher in that time period.

Thus, cost savings in such a group of patients during a 3–5-year period
could be of great magnitude.

Prevention and Coronary Artery Disease

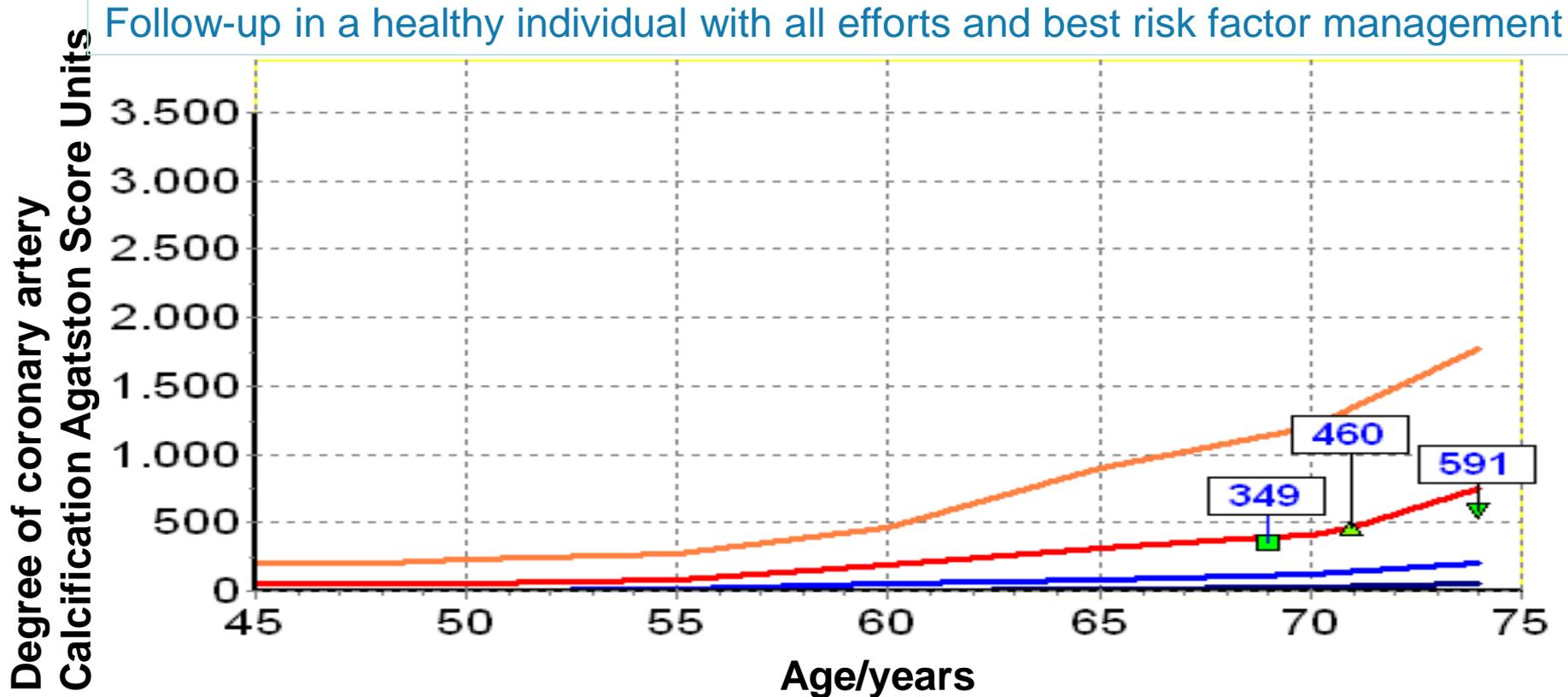
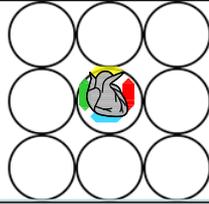
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As follow-up studies demonstrate CAC progression in the range of 15 – 25 % per year, the question arises: can the efficacy of the risk factor modification be assessed by CT?

Prevention and Coronary Artery Disease

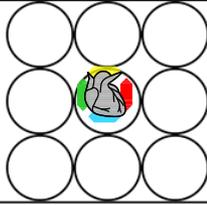
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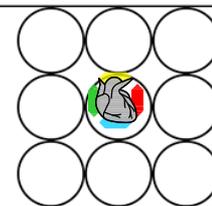
Progression of coronary artery calcification: risk and risk factors



Achenbach

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors

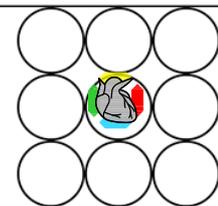


RCT for Evaluation of Statin Therapy on CAC

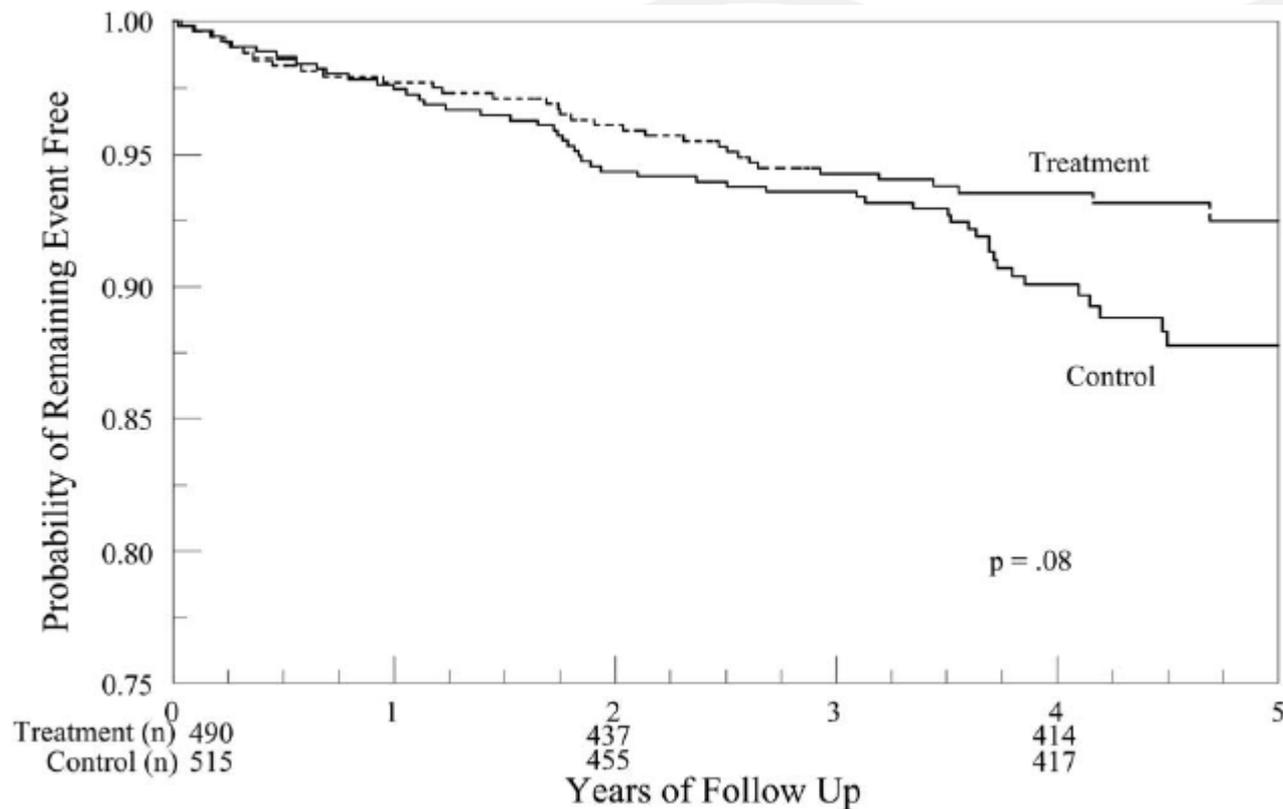
	Year	N	Years	Pts	Statin/mg	Effect/ %
Arad	2005		4.3		20A+ vs 0	81 vs 73
Raggi	2005		1.0		80A vs 40P	
Schmermund	2006		1.0	266	80A vs 10A	27 vs 25
Housley	2006		2.0	88	80A vs 0	26 vs 18

Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



FU 4.3 years, 1005 pts, 50 to 70 years \geq 80 percentile of CAC, age and gender related



Verum:
atorvastatin 20 mg
vitamin C 1 g,
vitamin E 1,000 U
aspirin 81 mg

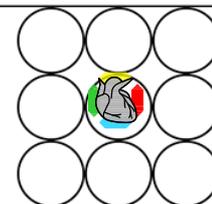
Placebo
aspirin 81 mg

Arad Y et al

J Am Coll Cardiol 46:166 –72, 2005

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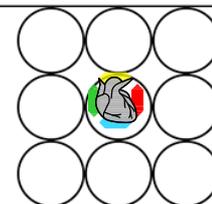
Lipid Parameter	Atorvastatin 80 mg (n=218)	Pravastatin 40 mg (n=257)	<i>P</i>
Total cholesterol, mg/dL			
Baseline	268.6 (35.3)	267.7 (40.4)	
Month 12	176.2 (41.6)	219.5 (35.4)	
Percent change to month 12	-33.8 (15.3)	-17.2 (13.1)	<0.0001
LDL-C, mg/dL			
Baseline	175.3 (32.3)	173.6 (35.6)	
Month 12	92.2 (36.1)	129.0 (31.0)	
Percent change to month 12	-46.6 (19.9)	-24.5 (18.5)	<0.0001
HDL-C, mg/dL			
Baseline	56.3 (14.0)	58.7 (14.2)	
Month 12	57.0 (13.6)	60.5 (14.7)	
Percent change to month 12	2.3 (13.8)	3.9 (13.0)	0.0606
Apo B, mg/dL			
Baseline	166.5 (27.3)	164.7 (29.9)	
Month 12	101.1 (31.2)	128.9 (26.5)	
Percent change to month 12	-39.0 (16.5)	-21.2 (14.9)	<0.0001
Peripheral arterial disease		21 (6.9)	21 (6.8)

Raggi P et al

Circulation. 112:563-571, 2005

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	Atorvastatin 80 mg (n=218)		Pravastatin 40 mg (n=257)		P*
	Mean (SD)	Median	Mean (SD)	Median	
Total CVS					

	Atorvastatin 80 mg (n=218)		Pravastatin 40 mg (n=257)		P*
	Mean (SD)	Median	Mean (SD)	Median	
Total CVS					
Baseline	204.7 (297.1)	107.1	267.0 (403.9)	132.9	0.04
12-Month follow-up	233.2 (350.1)	118.6	297.9 (408.3)	160.3	
Absolute change	28.5 (87.4)	14.2	30.9 (65.1)	18.5	0.21
Percentage change	20.1 (30.8)	15.1	19.8 (34.8)	14.3	0.64

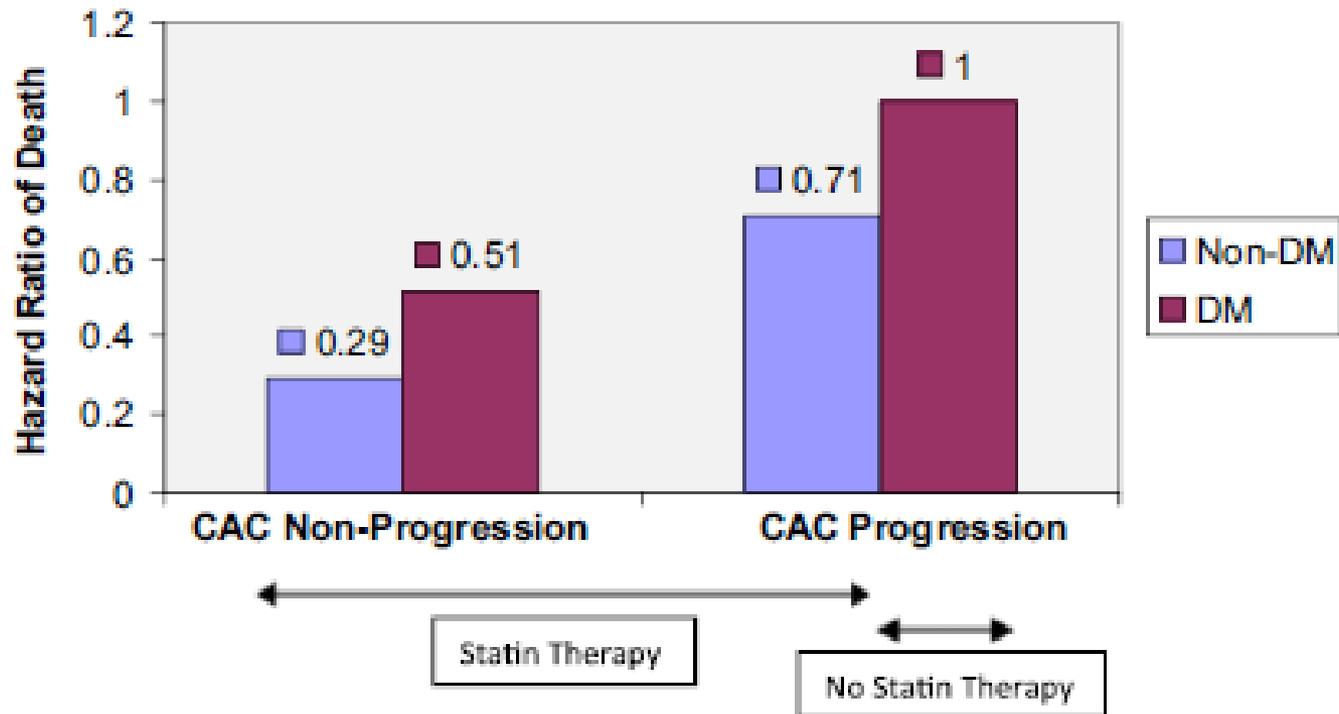
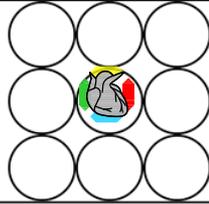
12-Month follow-up	23.7 (88.4)	0.0	41.8 (102.8)	3.4	
Absolute change	6.6 (59.5)	0.0	5.3 (25.9)	0.0	0.35
Right coronary artery†					
Baseline	65.2 (144.9)	7.2	94.0 (213.4)	13.7	0.14
12-Month follow-up	72.8 (154.5)	13.1	102.0 (205.4)	18.1	
Absolute change	7.7 (31.2)	0.0	8.0 (43.4)	0.0	0.95

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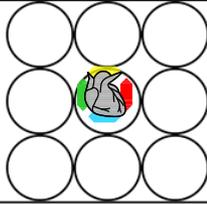


Kiramijyan S et al

AJC 2012, in press

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Conclusion of the study

- 2 year FU CAC for risk assessment
- risk modification
- medical optimization
- to control lipid levels on the basis of severity

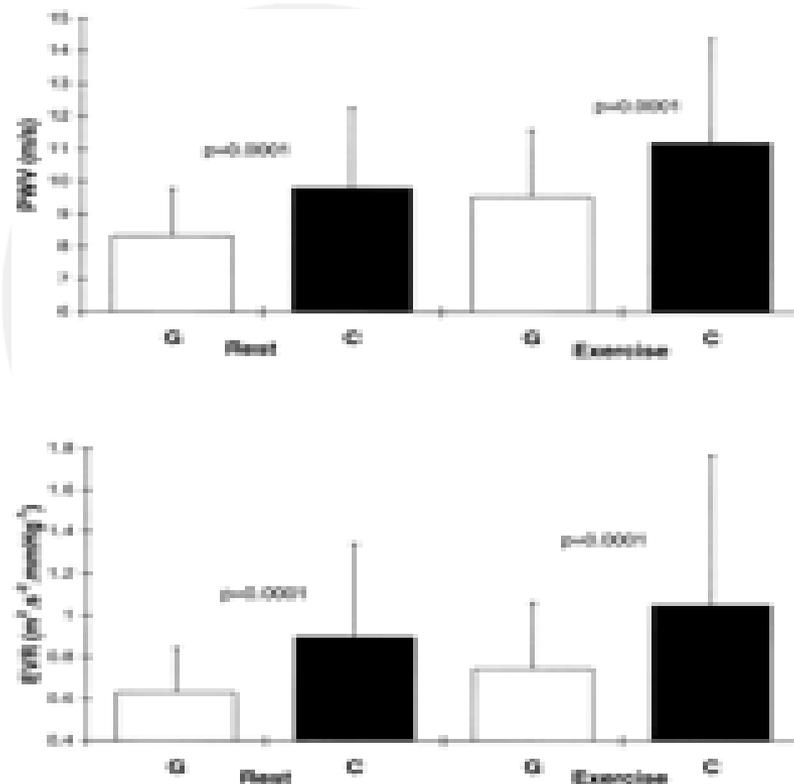
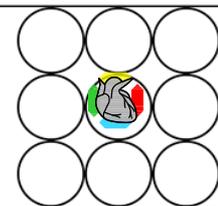
CAC progression in DM

Kiramijyan S et al

AJC 2012, in press

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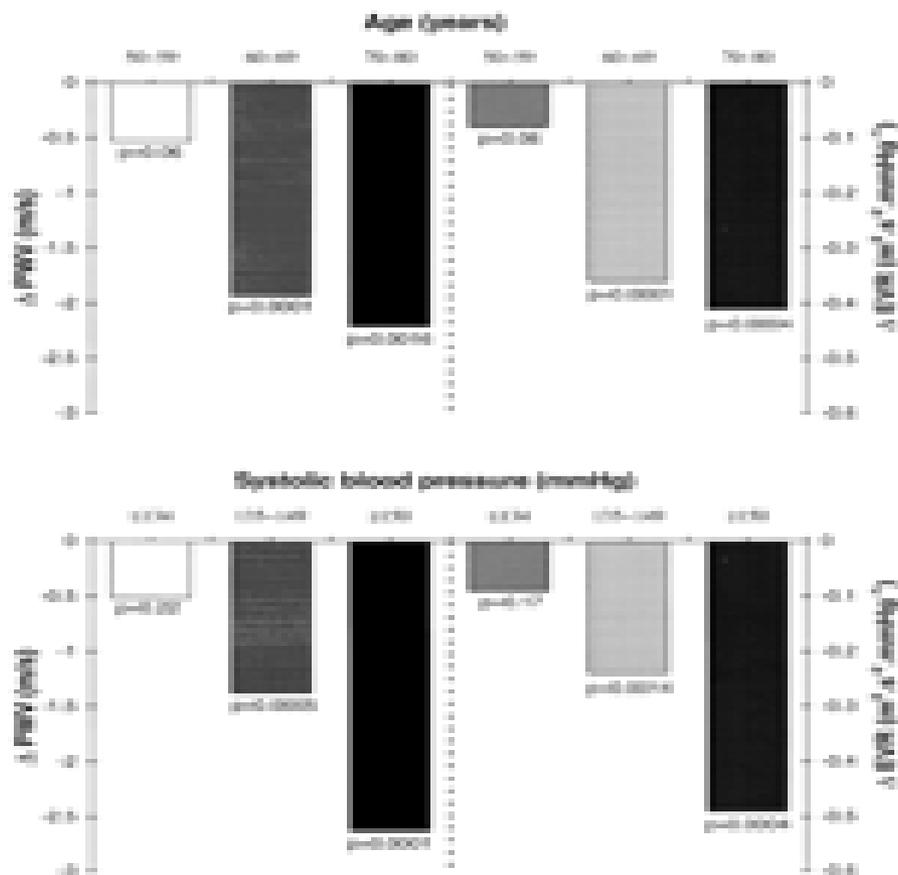
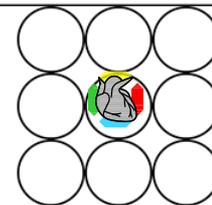


Breithaupt-Grögler K et al

Circulation 96: 2649-2655, 1997

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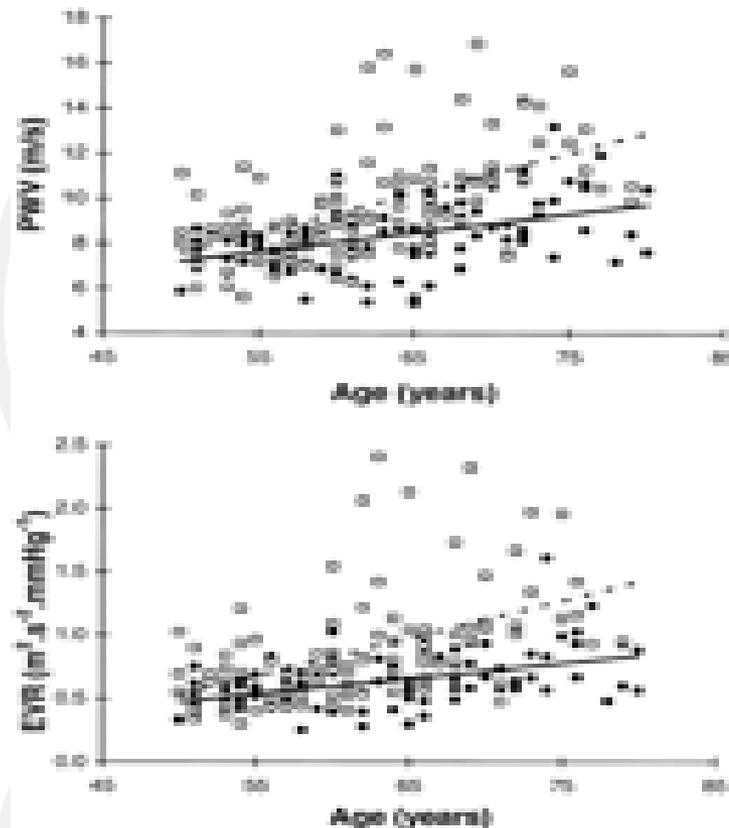
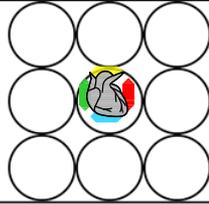


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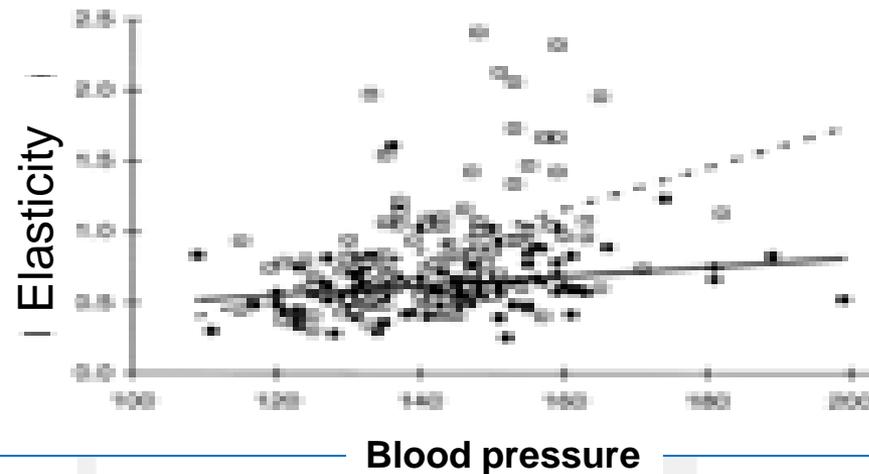
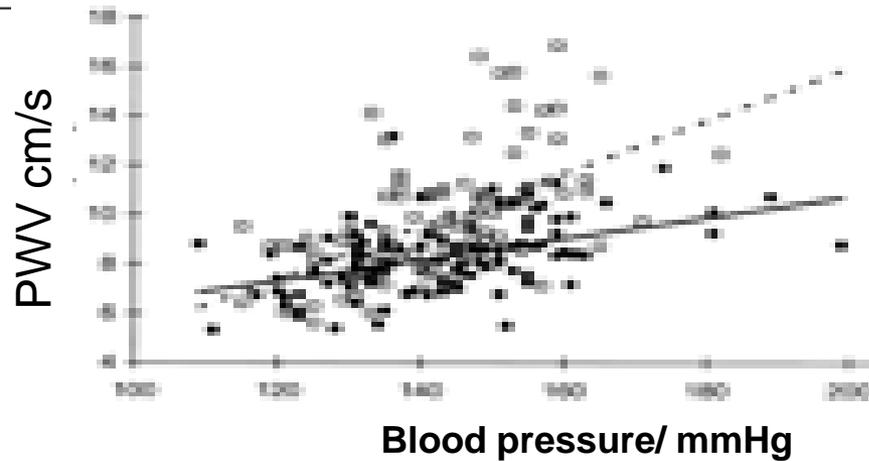
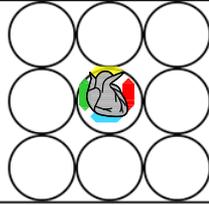


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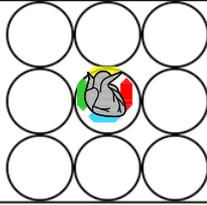


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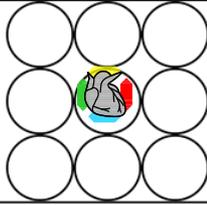
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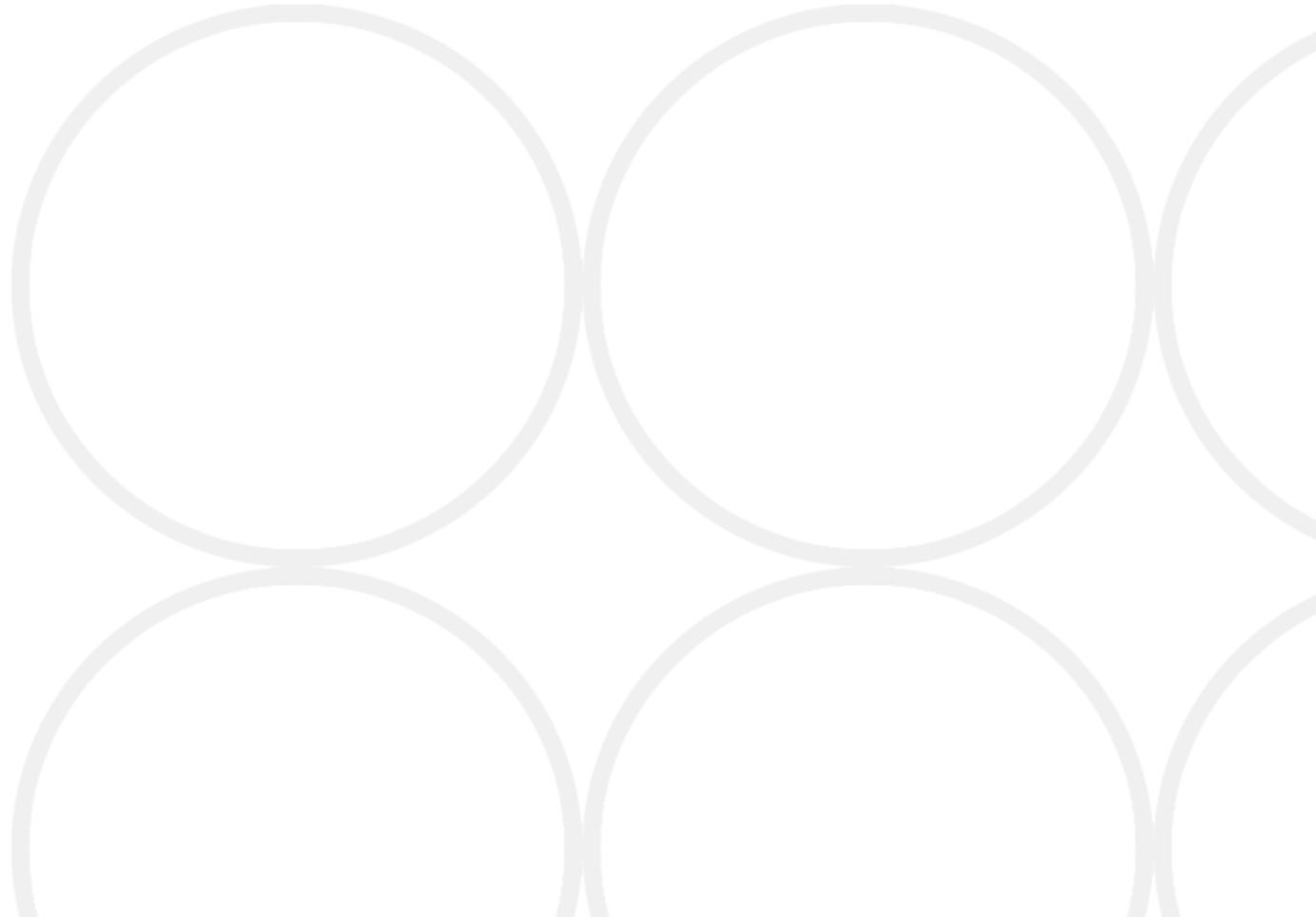
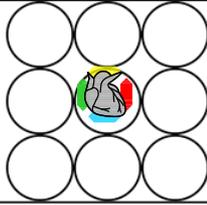
Prevention and Coronary Artery Disease

Progression of coronary artery calcification: risk and risk factors



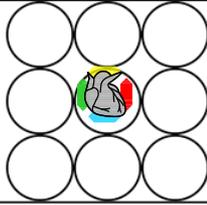
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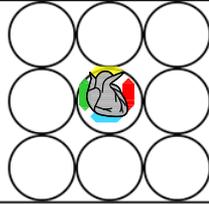
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CAC Progression as a sign of coronary atherosclerosis is
genetic determined and not influencable!?

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Heritability estimates for log baseline CAC quantity and CAC progression

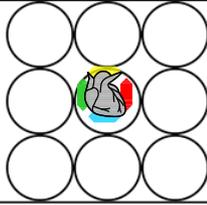
Trait	h^2 (SE)	Covariate Variance*	Covariates Adjusted for:	% of Variance Explained by Genetic Factors†
Log baseline CAC quantity	0.488 (0.104)	0.00	None	48.8
	0.391 (0.097)	0.35	Age, sex	25.4
	0.376 (0.096)	0.43	Age, sex, LDL-C, SBP, DBP, log (pack-years of smoking+1), diabetes, family history of CHD, sex×LDL-C	21.4
CAC progression	0.782 (0.101)	0.00	None	78.2
	0.671 (0.108)	0.35	Age, sex	43.6
	0.592 (0.109)	0.44	Age, sex, waist-to-hip ratio, LDL-C, log (pack-years of smoking+1), diabetes, hypertension, family history of CHD	33.2
	0.396 (0.133)	0.64	Age, sex, waist-to-hip ratio, LDL-C, log (pack-years of smoking+1), hypertension, baseline CAC quantity, age×baseline CAC quantity	14.3

Cassidy-Bushrow, AE et al

Circulation 116:25-31, 2007

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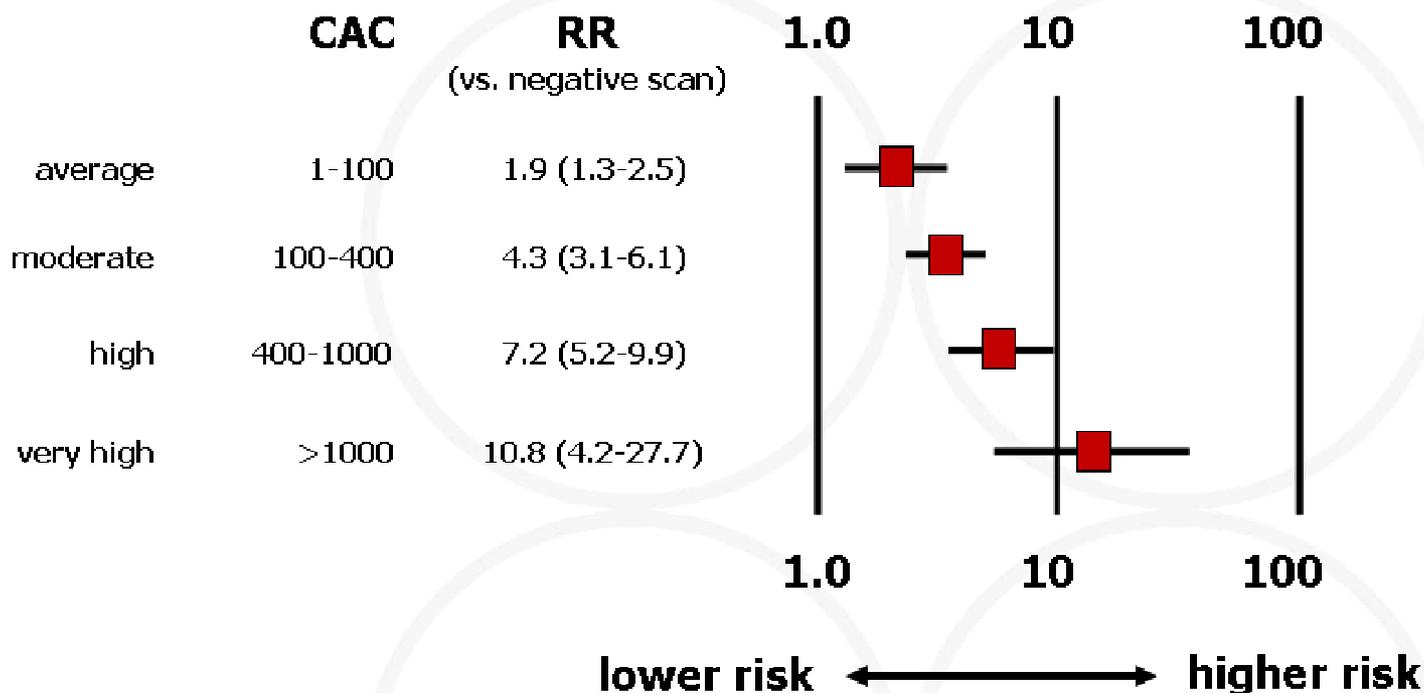
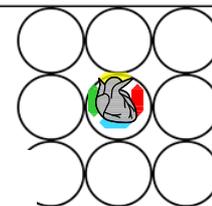


Figure 1: Increase in relative risk (RR) with increasing CAC scores in asymptomatic persons in comparison to asymptomatic persons without CAC (modified from (13)).

Annual Rate of Myocardial Infarction or Cardiac Death

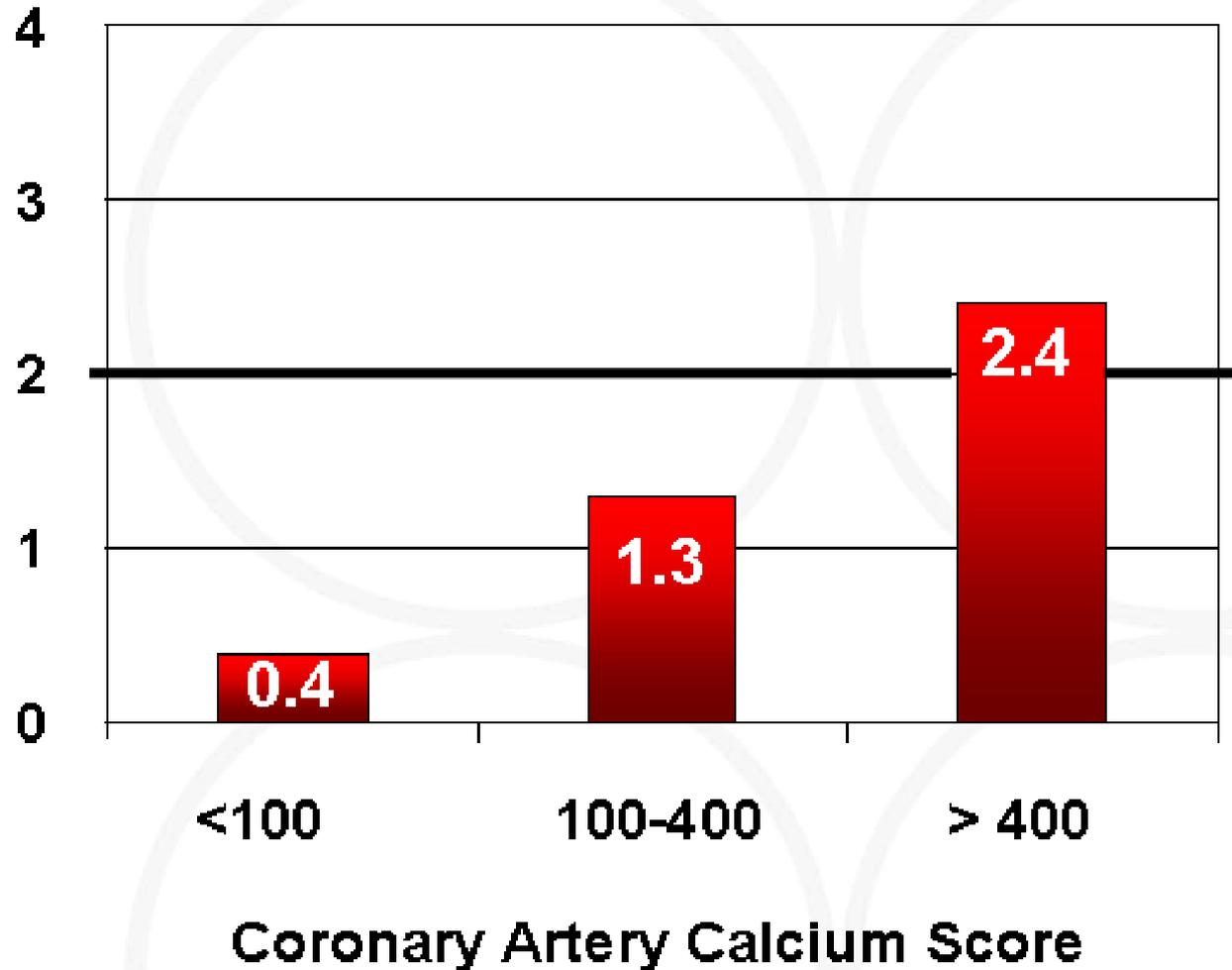


Figure 2 Annual rate of myocardial infarction or cardiac death in categories of CAC burden in persons at intermediate risk based on convention risk factor assessment. In persons with a high CAC score (>400), the annual event rate exceeds the threshold for intensive risk factor modification, i.e. >2% per year (black line). A CAC score > 400 in intermediate risk persons may therefore be considered as a risk equivalent (modified from (13))

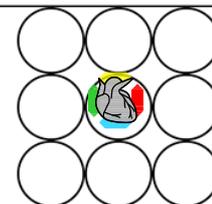


Figure 3. The Absolute and Percent Change in Baseline Agatston Score on Serial CT Imaging

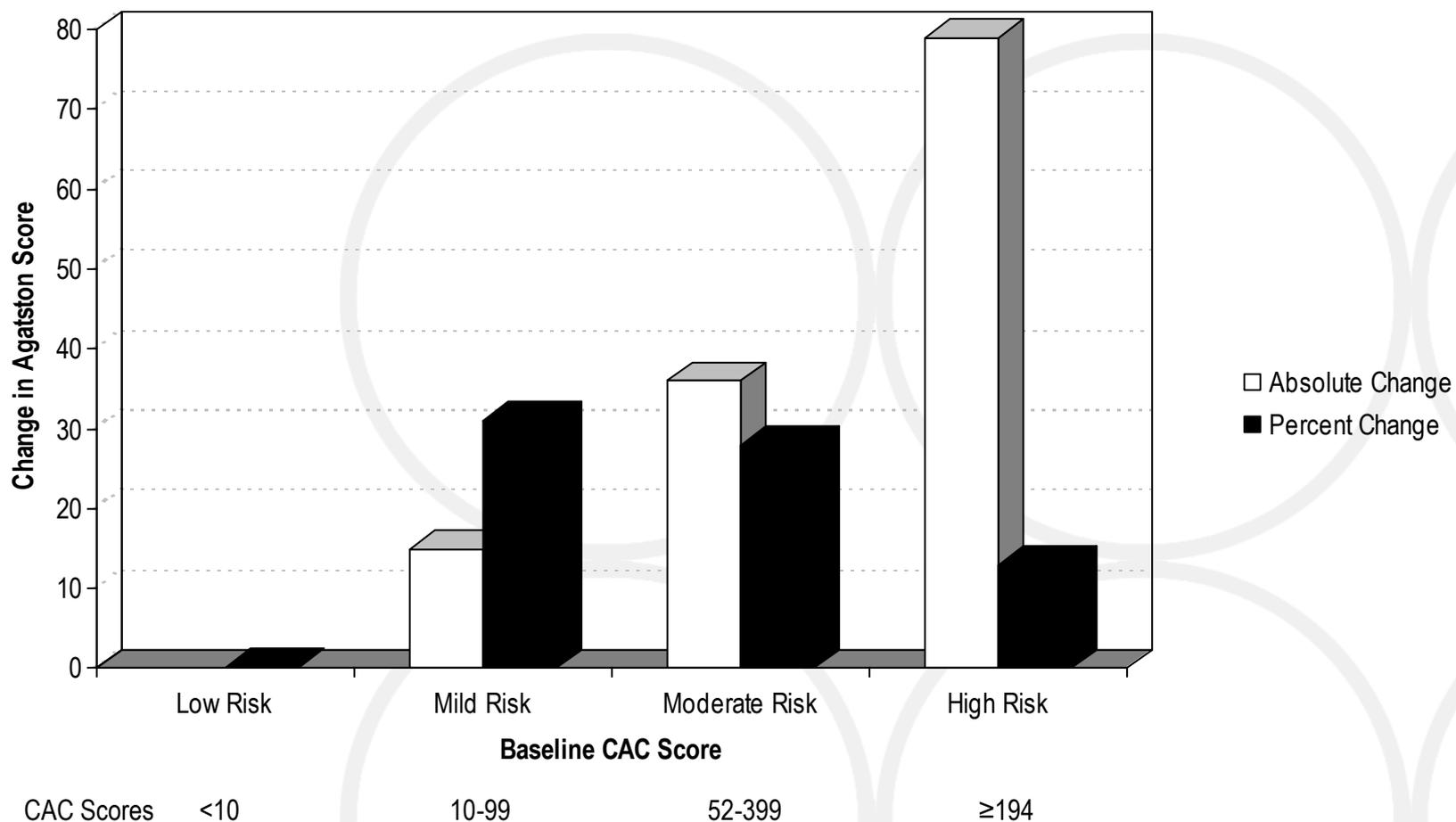
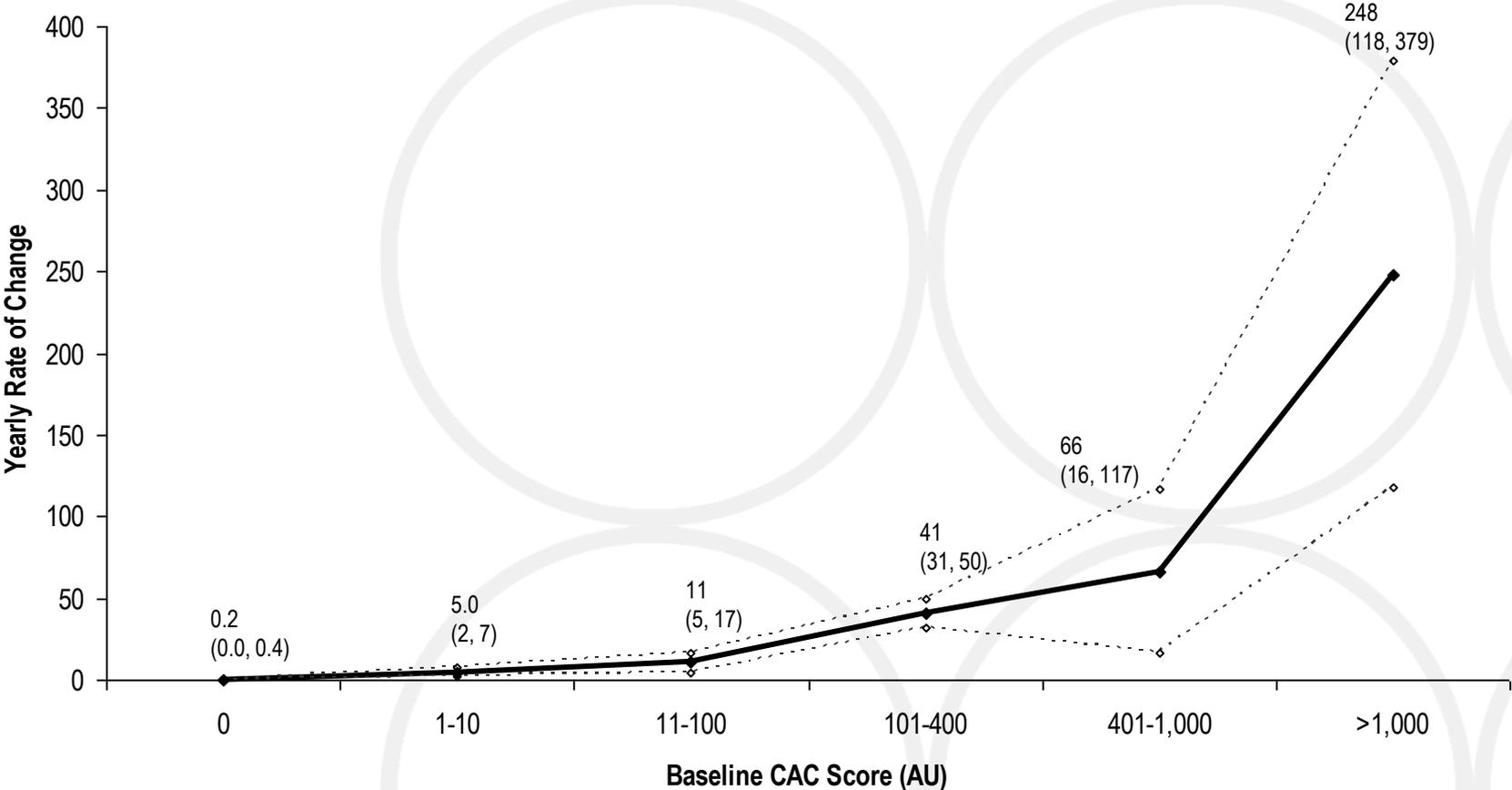
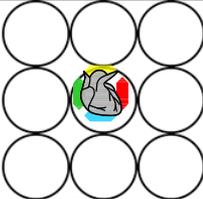


Figure 4. Expected Yearly Rate of Change (95% Confidence Intervals) from Baseline for Coronary Artery Calcium Scores Ranging from 0 to $\geq 1,000$ Agatston Units (AU)



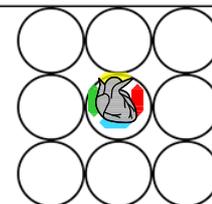


Figure 5. 95% Confidence Intervals for Repeatability of Coronary Artery Calcium Scores from 0 to $\geq 1,000$

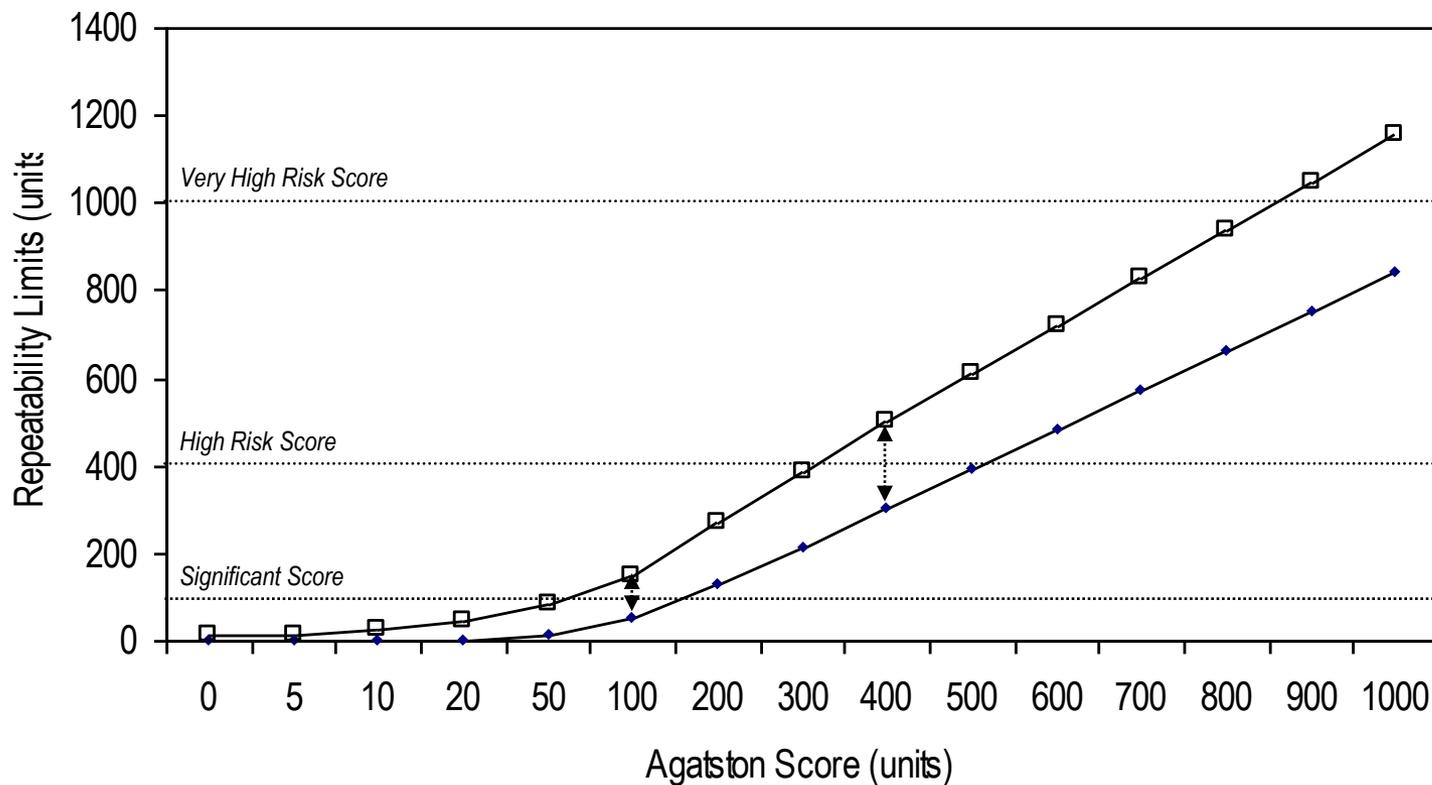
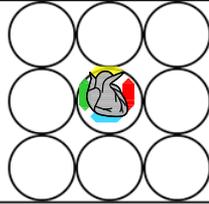
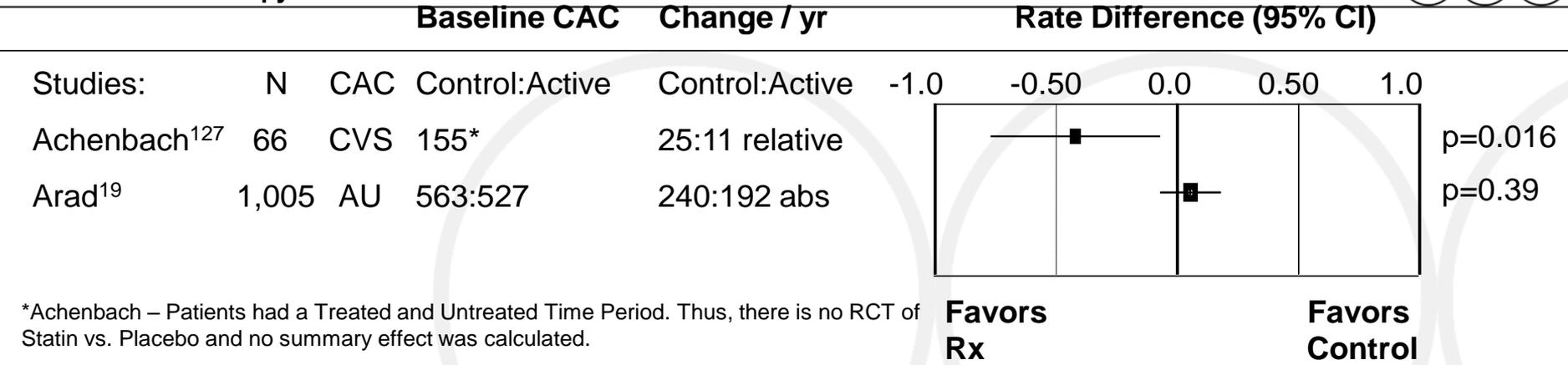


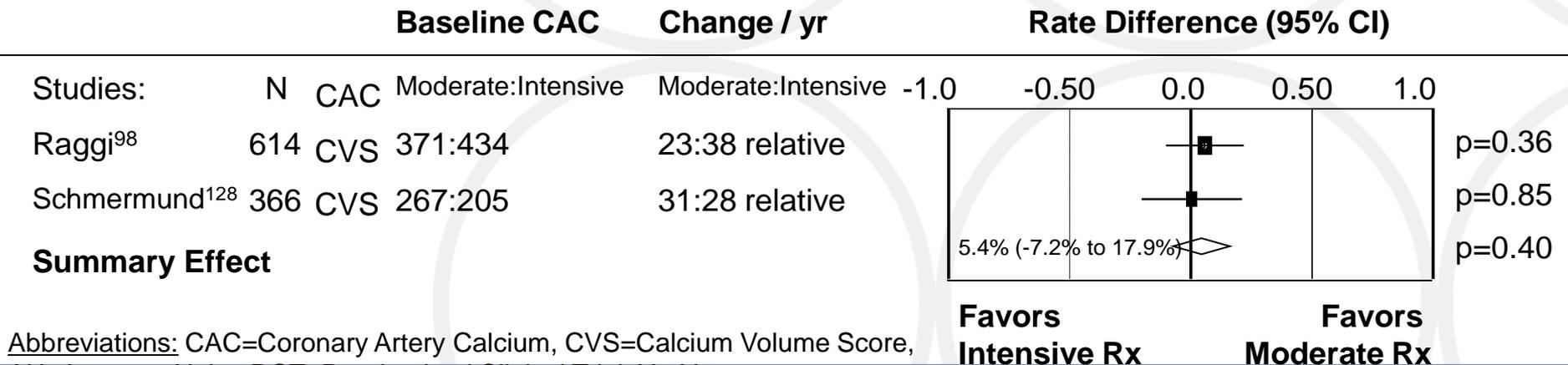
Figure 6. Summary Meta-Analysis of Randomized Control Trials (RCT) on the Effect of Statin Therapy (Rx) on CAC Progression



RCTs of Statin Therapy vs. Placebo



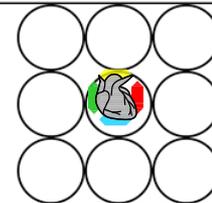
RCTs of Moderate vs. Intensive Statin Therapy



Abbreviations: CAC=Coronary Artery Calcium, CVS=Calcium Volume Score, AU=Agatston Units, RCT=Randomized Clinical Trial, Yr=Year,

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Cardiovascular Risk

Adolescence Risk Factors Are Predictive of Coronary Artery Calcification at Middle Age

The Cardiovascular Risk in Young Finns Study

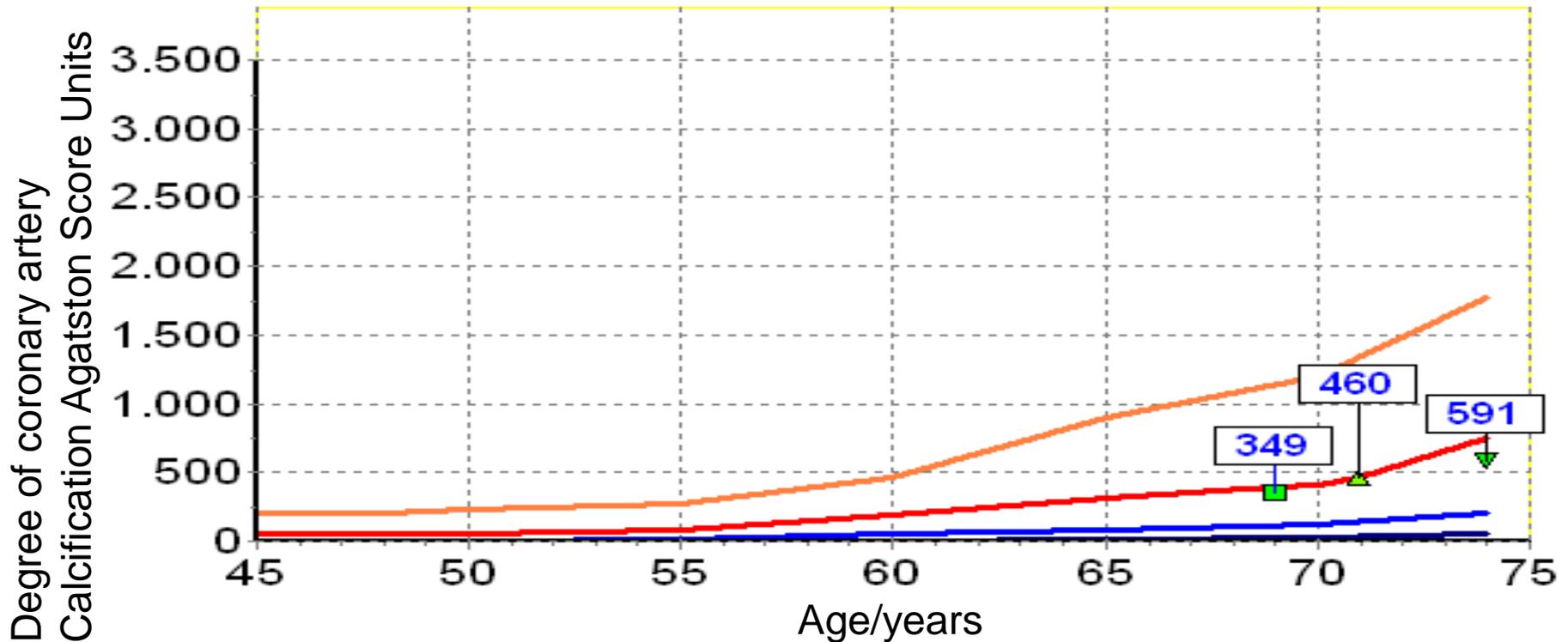
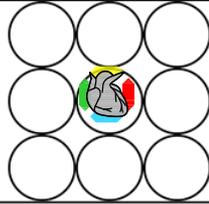
Olli Hartiala, BM,* Costan G. Magnussen, PhD,*†‡ Sami Kajander, MD, PhD,§
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J Am Coll Cardiol 2012;60:1364–70)

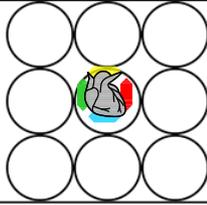
Non Invasive Assessment of Subclinical Coronary Sclerosis: EBCT



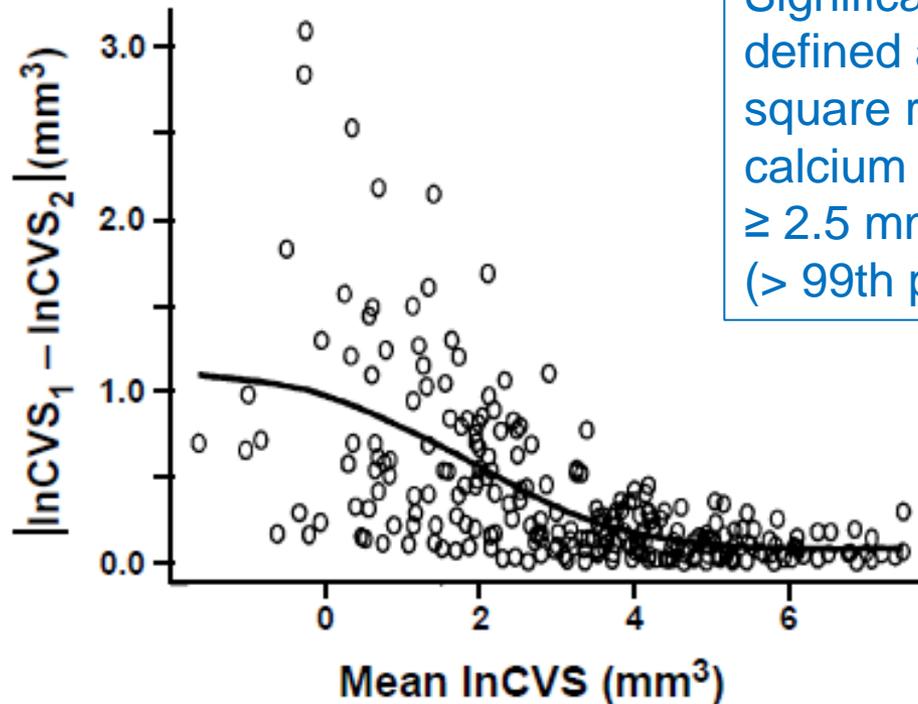
- ▼ Im Alter von 74 liegt der Verkalkungswert von 591 oberhalb der 70. Perzentile.
- ▲ Im Alter von 71 liegt der Verkalkungswert von 460 oberhalb der 67. Perzentile.
- Im Alter von 69 liegt der Verkalkungswert von 349 oberhalb der 72. Perzentile.
- 90. Perzentile
- 75. Perzentile - oberhalb hat der Wert eine größere klinische Bedeutung
- 50. Perzentile
- 25. Perzentile

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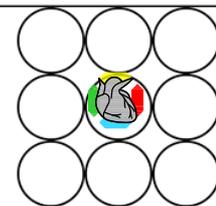
calcium volume scores taken a mean of 2.7 years apart in 109 diabetics



Significant change in CVS defined as a difference between square root-transformed to calcium volume scores $\geq 2.5 \text{ mm}^3$ (> 99 th percentile interscan variat..)

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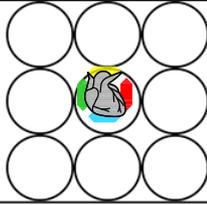
Potential mechanism of CAC progression

Inverse relationship to

- changes in vascular function
 - oxidized phospholipids/apolipoprotein B-100 complexes lipoprotein (a)
- lipoprotein (a)

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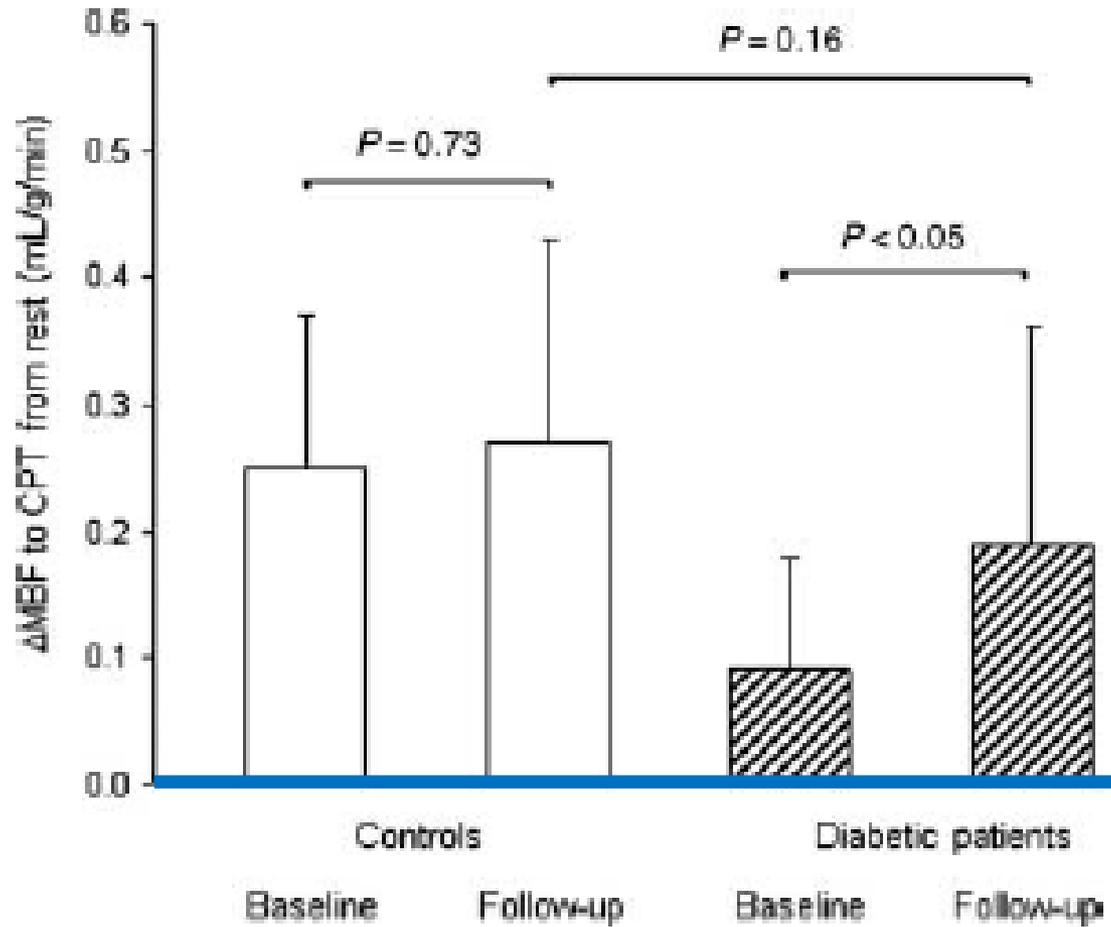
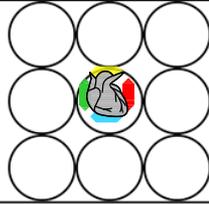


What is the Pathophysiology of CAC Progression in Relation
to Endothelium Function and Myocardial Blood Flow

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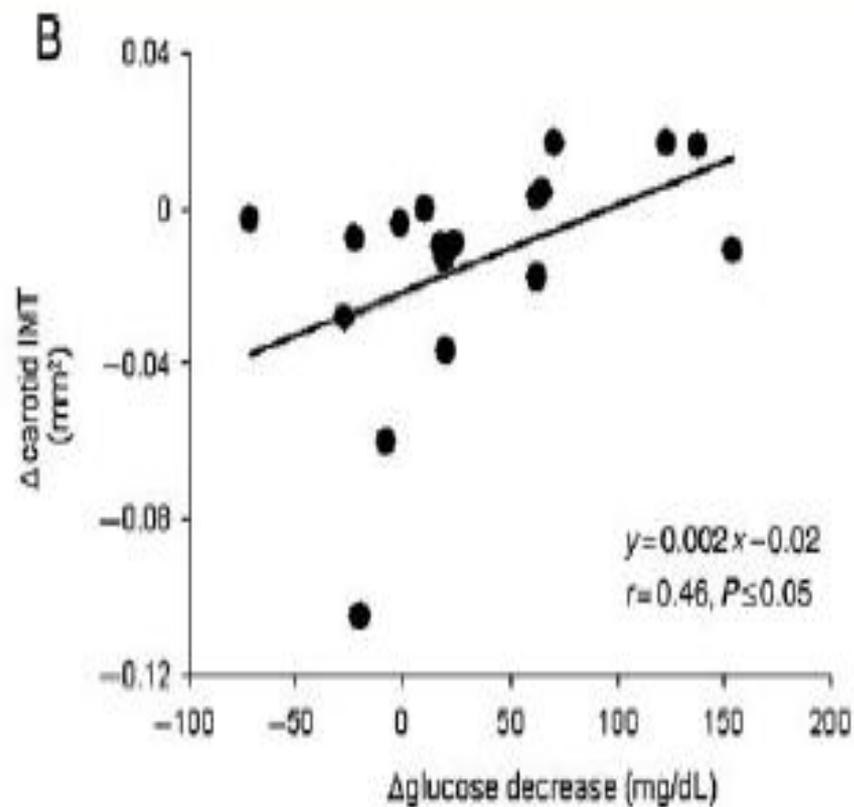
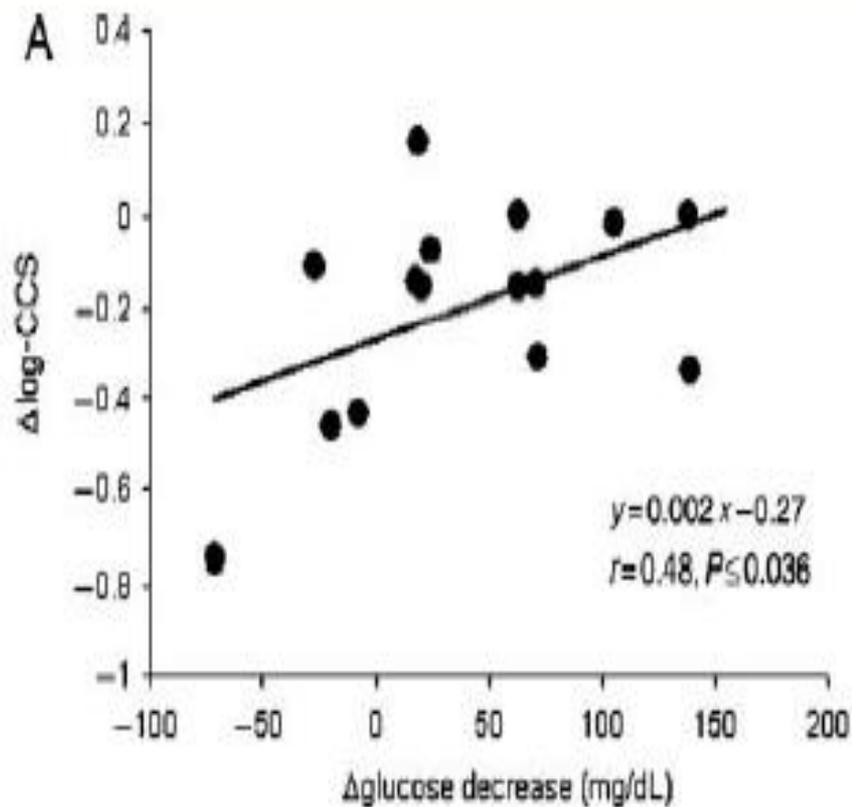
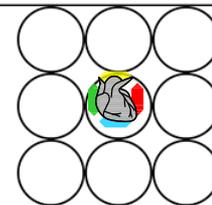
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Relation to Myocardial Blood flow



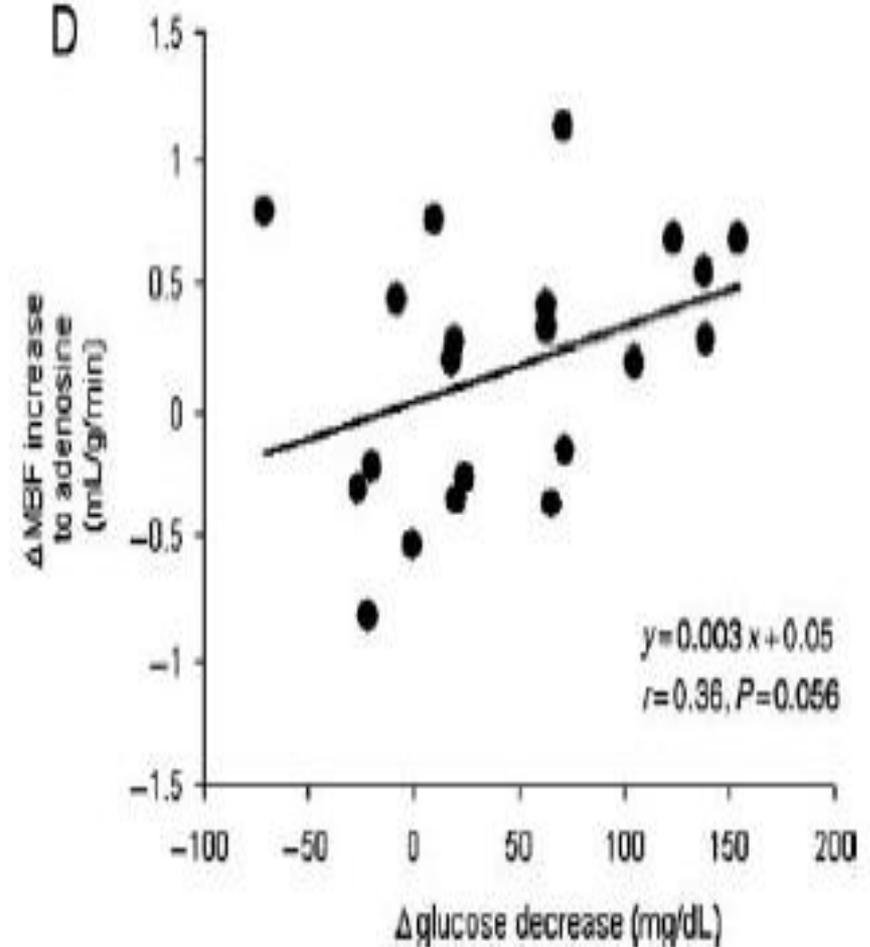
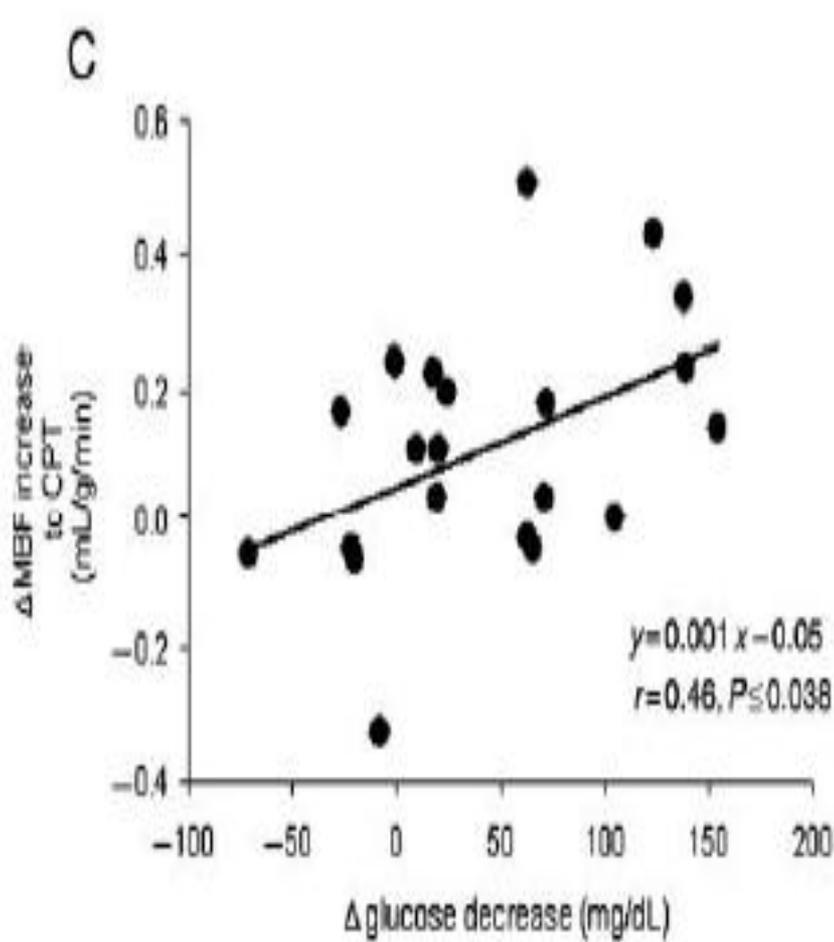
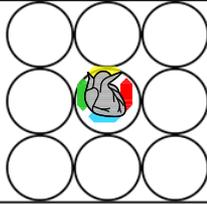
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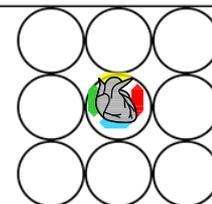
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Models of coronary artery calcium progression

Model	Δ CAC%	Matched Controls	Patients With DM	p Value
1	10%–20% vs <10%	1.0 (reference)	1.88 (1.51–2.36)	0.0001
2	21%–30% vs <10%	1.0 (reference)	2.29 (1.56–3.38)	0.0001
3	>30% vs <10%	1.0 (reference)	6.95 (2.23–11.53)	0.0001

Hazard ratios of risk for death and 95% CIs (in parentheses) across various categories of CAC progression in subjects with diabetes compared to subjects without DM as a reference using Cox proportional-hazard regression analysis (n = 596).

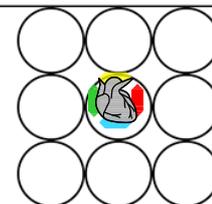
Adjusted for age, gender, hypertension, hyperlipidemia, family history of CHD, baseline CAC, and smoking.

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Risk factor—adjusted event-free survival (depicted in Figure 1)

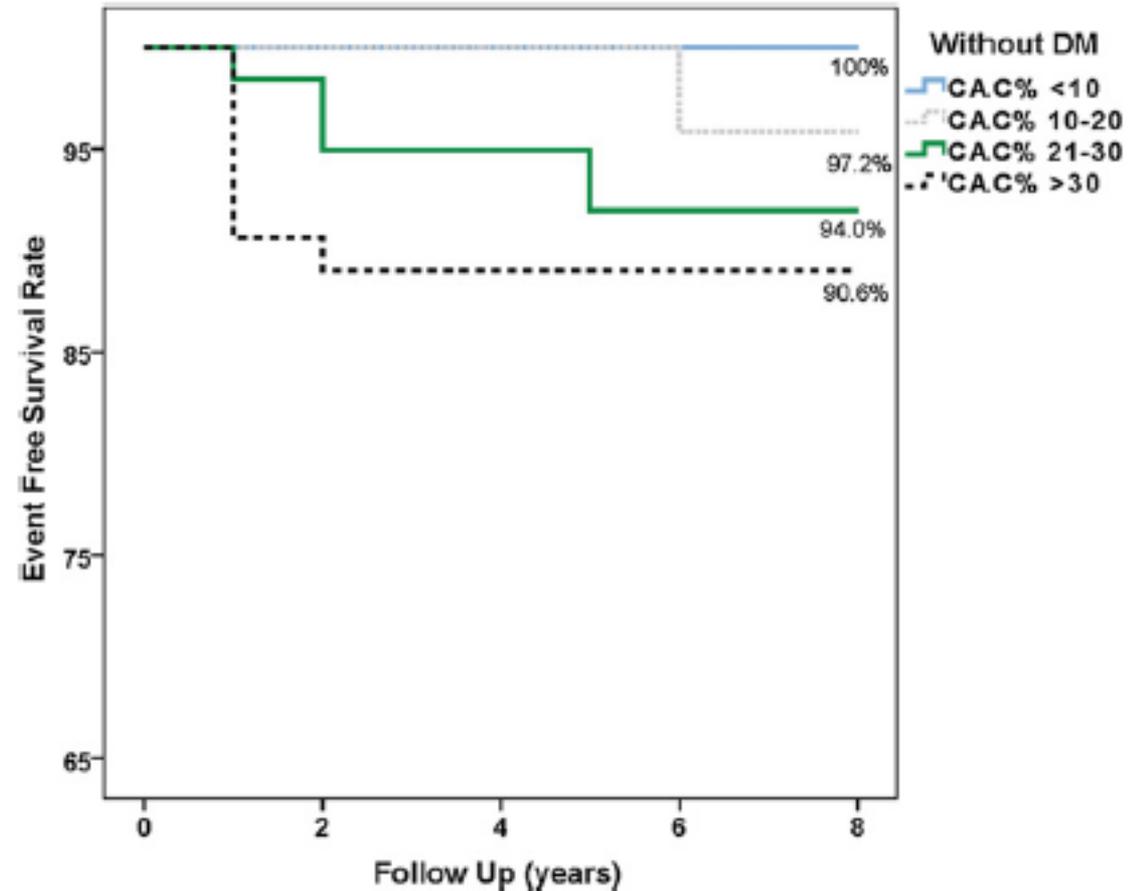
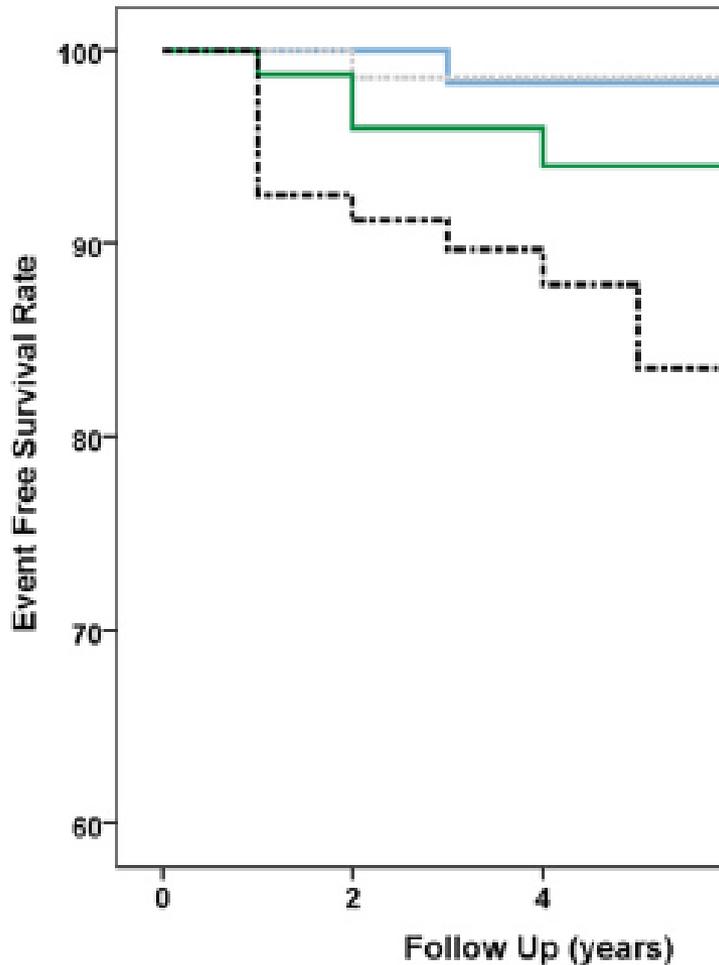
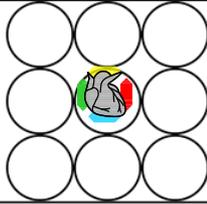
Variable (Δ CAC)	DM	No DM	p Value
<10%	97.9%	100%	0.50
10%–20%	95.9%	97.2%	0.01
21%–30%	92.7%	94%	0.01
>30%	79.6%	90.6%	0.0001

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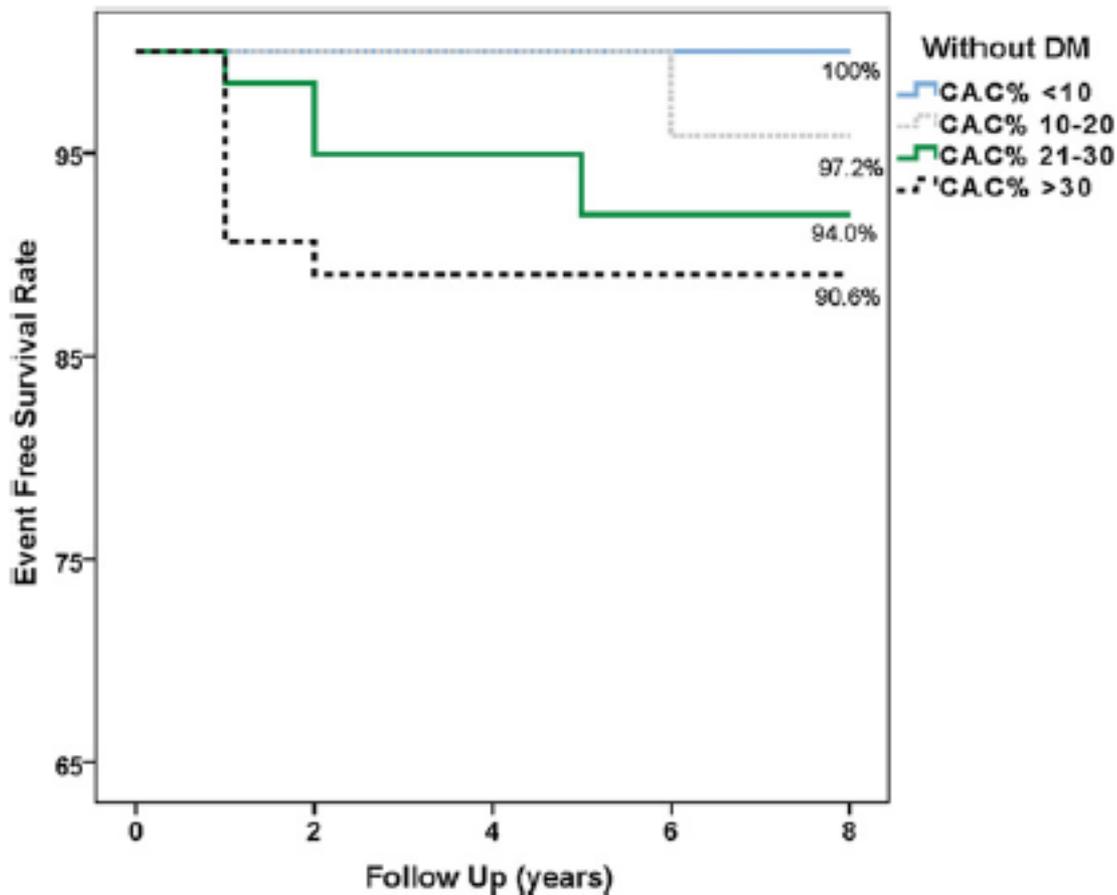
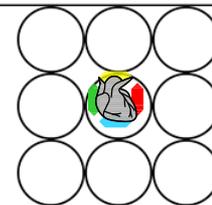
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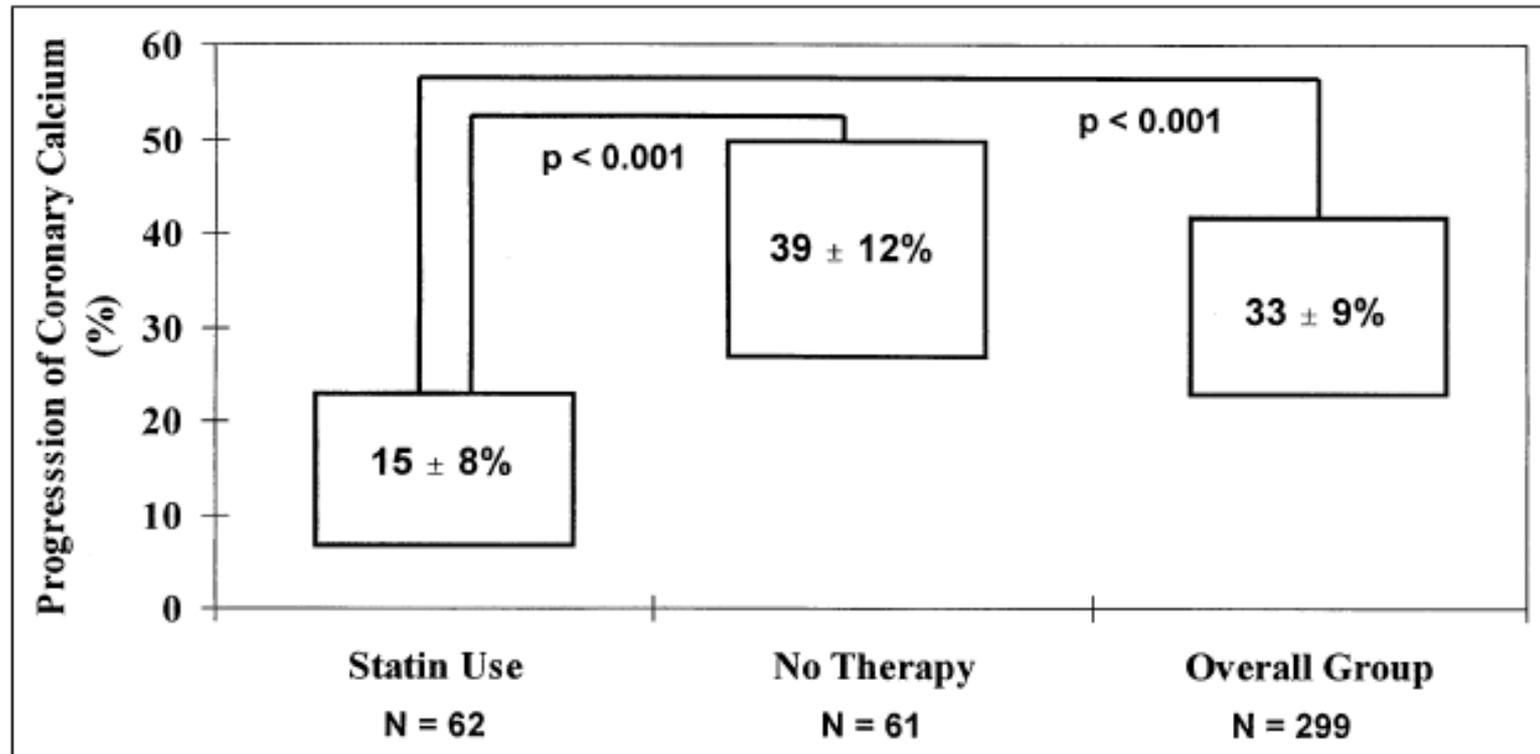
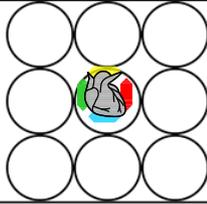


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Am J Cardiol 86:8–11, 2000