SUPPLEMENTAL MATERIAL TO

Exercise Volume versus Intensity and the Progression of Coronary Atherosclerosis in Middle-aged and Older Athletes: Findings from the MARC-2 Study

Running title: Exercise and Coronary Atherosclerosis

Vincent L. Aengevaeren, MD, PhD[a,b]
Arend Mosterd, MD, PhD[c]
Esmée A. Bakker, PhD[a]
Thijs L. Braber, MD, PhD[d]
Hendrik M. Nathoe, MD, PhD[e]
Sanjay Sharma, MD[f]
Paul D. Thompson, MD[g]
Birgitta K. Velthuis, MD, PhD[h*]
Thijs M.H. Eijsvogels, PhD[a*]

Radboud Institute for Health Sciences, Departments of Physiology[a] and Cardiology[b], Radboud University Medical Center, Nijmegen, The Netherlands
[c]Department of Cardiology, Meander Medical Center, Amersfoort, The Netherlands
[d]Department of Cardiology, Isala Ziekenhuis, Zwolle, The Netherlands
[e]Department of Cardiology, University Medical Center Utrecht, The Netherlands
[f]Cardiology Clinical and Academic Group, St George's University of London, United Kingdom
[g]Division of Cardiology, Hartford Hospital, Hartford, CT, USA
[h]Department of Radiology, University Medical Center Utrecht, The Netherlands
*Shared senior authorship

Addresses for correspondence:
Dr. Vincent Aengevaeren, Department of Physiology (392), Radboud University Medical Center, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands, Tel +31 24 36 13 650, Fax +31 24 36 16413,
E-mail: Vincent.Aengevaeren@radboudumc.nl

Supplemental Tables 1-10

Supplemental Figure 1

Supplemental Table 1. Frequency of sports participation during follow-up

Type of sport	Frequency (%)	MET-score*
Athletics	1 (0%)	6.7
Badminton	1 (0%)	5.5
Boxing	1 (0%)	8.7
Cycling	184 (64%)	6.8/7.5/8.5/10
Racebike	171 (59%)	7.5
Mountainbike	29 (10%)	8.5
Spinning	18 (6%)	10
City-/hybridbike	7 (2%)	6.8
Dancing	2 (1%)	5
Diving	1 (0%)	7
Fitness – cardio/bootcamp	64 (22%)	5.5/7.3/7.8
Fitness – Strength training	18 (7%)	3.5/4.5
Golf	23 (8%)	4.8
Hockey	9 (3%)	7.8
Horse riding	2 (1%)	5.5
Judo/Karate/Jujutsu	3 (1%)	5.3
Korfball	1 (0%)	6.5
Motor cross	1 (0%)	4
Mountain climbing	2 (1%)	6.6
Paragliding	1 (0%)	1.8
Rowing	18 (6%)	9.2
Running	146 (51%)	6/7/9.3/11.8
Sailing/windsurfing	3 (1%)	3/4.5/5
Shooting sport	2 (1%)	4.3
Soccer	12 (4%)	7
(Inline) Speed skating	34 (12%)	7.5/9
Squash	3 (1%)	9.7
Swimming	32 (11%)	8/10
Tennis	24 (8%)	5/7.3
Triathlon	3 (1%)	9.8
Walking	25 (9%)	4.3
Water polo	13 (5%)	10
Yoga	8 (3%)	2.5

MET: Metabolic Equivalent of Task; *MET-score can differ based on level of competition and specific type of sport (e.g. cycling can be racing/spinning/touring/etc.)

Supplemental Table 2. Study definitions of exercise and plaque characteristics.

Study definitions	Explanation
Exercise volume	Refers to the volume of exercise an individual performed during follow-up. Expressed as MET-hrs per week and was calculated per sport by multiplying the MET score for the specific sport with the reported weekly exercise hours (session duration * frequency/week), months of practice per year and total years of practice
Exercise intensity	Refers to the intensity at which exercise is performed. This is expressed in METs based on the "Compendium of Physical Activities" and categorized into light (<3 MET), moderate (3-6 MET), vigorous (6-9 MET) and very vigorous (≥ 9 MET) exercise. Since light intensity exercise was negligible in this cohort, we did not report it.
Moderate intensity	Refers to exercise at 3-6 MET. This includes for example golf, walking, horse riding and most types of fitness training.
Vigorous intensity	Refers to exercise at 6-9 MET in our study. Vigorous exercise includes for example most cycling activities, soccer and hockey.
Very vigorous intensity	Refers to exercise at ≥ 9 METs. This includes for example most running categories, water polo and rowing.
Tertiles of exercise volume	We categorized exercise volume (total MET-hrs/week) into 3 groups based on tertiles.
Tertiles of exercise intensity	We categorized exercise intensity (% of total MET-hrs/week) into 3 groups based on tertiles. We did this for both vigorous and very vigorous intensity exercise separately.
Coronary artery calcification progression	Coronary artery calcification was quantified using the Agatston CAC score and the change was measured using delta CAC score. This was subsequently transformed using the natural logarithm because it was not normally

	distributed, and 1 was added since delta CAC score could be 0 which is not possible with the natural logarithm.
Plaque morphology	Plaque morphology was determined based on the CCTA images and individual plaques were scored as being 1) calcified, i.e. with no non-calcified component; 2) non-calcified, when there was no calcium in the respective plaque or 3) partially calcified/mixed plaque including components of both calcified and non-calcified plaque.
Plaque progression	Plaque progression was defined quantitatively and subsequently dichotomized. We report analyses with the changes in number of plaques (delta plaques, Figure 3) and dichotomized plaque progression as yes/no (Figure 4).

MET, Metabolic Equivalent of Task; CAC, coronary artery calcification; CCTA, coronary computed tomography angiography.

Supplemental Table 3. Baseline characteristics of MARC-1 participants that did (n=291) and did not (n=27) participate in MARC-2.

	MARC-2 Participants (n=291)	**Non-participants (n=27)**	**P Value**
Age, years	53.6 (50.1-59.8)	56.1 (50.4-63.7)	0.08
Height, cm	183 (7)	181 (8)	0.13
Weight, kg	83.1 (10.7)	81.9 (9.4)	0.59
Body mass index, kg/m^2	24.4 (23.1-26.4)	24.5 (23.4-26.6)	0.63
Body surface area, m^2	2.05 (0.15)	2.02 (0.14)	0.33
Systolic BP, mmHg	128.7 (13.3)	132.8 (15.2)	0.13
Diastolic BP, mmHg	79.7 (8.5)	80.8 (8.5)	0.52
Antihypertensive use, n (%)	20 (7%)	1 (5%)	0.53
Total cholesterol, mmol/L	5.4 (0.9)	5.6 (1.0)	0.14
Statin use, n (%)	16 (6%)	2 (7%)	0.68
Diabetes mellitus, n (%)	4 (1%)	0 (0%)	0.54
CAC present, %	153 (53%)	15 56%)	0.77
CAC score, au	1 [0-32]	1 [0-124]	0.30

BP, Blood pressure; CAC, coronary artery calcification. Data is presented as mean (SD), n (%) or median (interquartile range).

Supplemental Table 4. Exercise characteristics of the MARC-2 cohort.

	Lifelong at baseline	**Lifelong at follow-up**	**P-Value**	**During follow-up**
Years of exercise, n	36 (27-42)	43 (34-49)	<0.001	6.3 ± 0.5
Sessions/week, n	1.9 (1.2-2.8)	2.2 (1.5-2.9)	<0.001	3.2 (2.4-4.5)
Duration/session, hrs	1.5 (1.2-1.8)	1.5 (1.2-1.8)	0.63	1.4 (1.1-1.9)
Exercise duration/week, hrs	2.8 (1.8-4.3)	3.1 (2.1-4.4)	<0.001	5.0 (3.1-7.2)
MET-minutes/week, au	1,342 (868-2,048)	1,540 (1,005-2,122)	<0.001	2,432 (1,529-3,399)
MET-hours/week, au	22.4 (14.5-34.1)	25.7 (16.7-35.4)	<0.001	40.5 (25.5-56.6)
Moderate intensity, (%)	3 (0-17)	5 (0-19)	.22	0 (0-19)
Vigorous intensity, (%)	47 (13-79)	47 (15-77)	.67	44 (0-84)
Very vigorous intensity, (%)	33 (0-72)	37 (4-67)	.32	34 (0-80)
Total MET-hours, au	49,290 (31,551-76,668)	63,428 (42,535-92,588)	<0.001	13,160 (8,341-18,427)

Hrs, hours; Au, arbitrary units; MET, Metabolic Equivalent of Task. Data is presented as median (interquartile range) or mean ± SD. Exercise characteristics since age 12.

Supplemental Table 5. Participant characteristics of tertiles of exercise volume during follow-up.

	EXERCISE VOLUME (MET-hours/week)			
	Tertile 1 (low) N=96	**Tertile 2 (medium) N=96**	**Tertile 3 (high) N=97**	**P Value**
Participant characteristics at follow-up				
Age, years	58.6 (55.5-65.5)	59.6 (56.0-63.9)	62.7 (57.5-68.1)	0.02
Body mass index, kg/m^2	25.1 (23.4-27.9)	24.3 (23.2-26.9)	23.8 (22.1-25.3)	<0.001
Systolic BP, mmHg	139.7 (17.0)	140.5 (17.5)	137.9 (18.6)	0.58
Antihypertensive use, n (%)	8 (8%)	13 (14%)	10 (10%)	0.50
Total cholesterol, mmol/L	5.4 (1.0)	5.4 (1.0)	5.4 (1.0)	0.90
Statin use, n (%)	15 (16%)	16 (17%)	13 (13%)	0.81
Diabetes mellitus, n (%)	2 (2%)	2 (2%)	2 (2%)	1.00
Smoking, pack-years	0.0 (0.0-5.2)	0.0 (0.0-7.5)	1.2 (0-9.5)	0.24
Exercise characteristics during follow-up				
Exercise duration/week, hrs	2.6 (1.9-3.3)	5.0 (4.0-5.8)	8.0 (6.9-10.4)	<0.001
MET-hours/week, au	21.1 (15.4-25.6)	40.5 (36.1-45.7)	64.0 (56.6-76.3)	<0.001
Moderate intensity, (%)	0 (0-24)	1 (0-18)	0 (0-16)	0.67
Vigorous intensity, (%)	41 (0-88)	41 (0-82)	50 (14-83)	0.29
Very vigorous intensity, (%)	26 (0-73)	39 (0-83)	35 (0-79)	0.38
Coronary atherosclerosis at follow-up				
CAC score, Agatston units	26 (0-155)	41 (0-186)	30 (0-105)	0.43
Delta CAC score, Agatston units	26 (0-124)	30 (0-123)	17 (0-89)	0.55
CAC score >0, n (%)	64 (67%)	71 (74%)	70 (72%)	0.51
Presence of plaque, n (%)	77 (81%)	81 (85%)	81 (84%)	0.74
Plaque progression, n (%)	70 (75%)	76 (80%)	70 (74%)	0.54

BP, Blood pressure; MET, metabolic equivalent of task; CAC, coronary artery calcification. Data is presented as mean (SD), n (%) or median (interquartile range).

Supplemental Table 6. Participant characteristics of the proportion of vigorous intensity exercise tertiles.

	VIGOROUS INTENSITY EXERCISE (% OF EXERCISE VOLUME)			
	Tertile 1 (low) N=96	**Tertile 2 (medium) N=97**	**Tertile 3 (high) N=96**	**P Value**
Participant characteristics at follow-up				
Age, years	60.2 (55.7-65.7)	60.0 (56.5-67.3)	59.9 (56.7-65.9)	0.55
Body mass index, kg/m^2	24.4 (22.8-26.6)	24.6 (23.5-26.7)	24.4 (22.7-26.6)	0.47
Systolic BP, mmHg	139.6 (17.2)	140.6 (19.4)	137.8 (16.5)	0.53
Antihypertensive use, n (%)	8 (8%)	12 (12%)	11 (12%)	0.64
Total cholesterol, mmol/L	5.4 (1.0)	5.3 (1.0)	5.4 (1.0)	0.72
Statin use, n (%)	11 (12%)	17 (18%)	16 (17%)	0.45
Diabetes mellitus, n (%)	3 (3%)	1 (1%)	2 (2%)	0.59
Smoking, pack-years	2 (0-8.6)	0 (0-6.5)	0.4 (0-9.6)	0.26
Exercise characteristics during follow-up				
Exercise duration/week, hrs	3.8 (2.9-6.0)	5.2 (3.4-7.6)	5.3 (3.2-7.9)	0.001
MET-hours/week, au	37.1 (24.5-54.3)	44.8 (27.1-56.8)	40.2 (23.5-57.1)	0.53
Moderate intensity, (%)	0 (0-20)	0 (4-33)	0 (0-9)	0.001
Vigorous intensity, (%)	0 (0-0)	44 (29-56)	95 (83-100)	<0.001
Very vigorous intensity, (%)	90 (76-100)	41 (18-56)	0 (0-5)	<0.001
Coronary atherosclerosis at follow-up				
CAC score, Agatston units	38 (0-145)	32 (0-121)	21 (0-177)	0.56
Delta CAC score, Agatston units	30 (0-114)	28 (0-94)	14 (0-109)	0.43
CAC score >0, n (%)	72 (75%)	73 (75%)	60 (63%)	0.08
Presence of plaque, n (%)	83 (87%)	82 (85%)	74 (78%)	0.20
Plaque progression, n (%)	76 (81%)	74 (78%)	66 (70%)	0.16

BP, Blood pressure; MET, metabolic equivalent of task; CAC, coronary artery calcification. Data is presented as mean (SD), n (%) or median (interquartile range).

Supplemental Table 7. Participant characteristics of the proportion of very vigorous intensity exercise tertiles.

	VERY VIGOROUS INTENSITY EXERCISE (% OF EXERCISE VOLUME)			
	Tertile 1 (low) N=96	**Tertile 2 (medium) N=96**	**Tertile 3 (high) N=97**	**P Value**
Participant characteristics at follow-up				
Age, years	60.1 (57.3-66.0)	60.8 (55.8-67.7)	59.2 (55.8-64.4)	0.24
Body mass index, kg/m^2	24.4 (23.1-26.7)	24.7 (22.8-26.7)	24.4 (22.8-26.4)	0.58
Systolic BP, mmHg	137.6 (15.3)	140.4 (18.4)	140.1 (19.2)	0.48
Antihypertensive use, n (%)	9 (9%)	12 (13%)	10 (10%)	0.77
Total cholesterol, mmol/L	5.2 (1.0)	5.5 (1.0)	5.5 (0.9)	0.03
Statin use, n (%)	20 (21%)	15 (16%)	9 (9%)	0.08
Diabetes mellitus, n (%)	3 (3%)	1 (1%)	2 (2%)	0.60
Smoking, pack-years	0 (0-8)	0.1 (0-8.4)	0.8 (0-7.5)	0.93
Exercise characteristics during follow-up				
Exercise duration/week, hrs	5.1 (2.9-7.9)	5.7 (3.7-8.1)	3.8 (3.0-5.8)	<0.001
MET-hours/week, au	36.3 (20.0-55.8)	45.0 (28.5-58.1)	42.6 (27.3-55.7)	0.02
Moderate intensity, (%)	7 (0-33)	1 (0-23)	0 (0-5)	<0.001
Vigorous intensity, (%)	92 (66-100)	52 (39-72)	0 (0-14)	<0.001
Very vigorous intensity, (%)	0 (0-0)	34 (18-47)	90 (80-100)	<0.001
Coronary atherosclerosis at follow-up				
CAC score, Agatston units	19 (0-208)	47 (0-165)	30 (0-105)	0.51
Delta CAC score, Agatston units	14 (0-111)	36 (0-116)	23 (0-91)	0.48
CAC score >0, n (%)	64 (67%)	71 (74%)	70 (72%)	0.51
Presence of plaque, n (%)	77 (81%)	78 (81%)	84 (88%)	0.40
Plaque progression, n (%)	68 (72%)	70 (75%)	78 (81%)	0.32

BP, Blood pressure; MET, metabolic equivalent of task; CAC, coronary artery calcification. Data is presented as mean (SD), n (%) or median (interquartile range).

Supplemental Table 8. Multivariable-adjusted linear regression analyses between exercise characteristics and progression of coronary artery calcification score and plaques.

	Progression of CAC (Ln delta CAC score +1)		***Progression of plaques (Delta number of plaques)***	
	B (95% CI)	***P-value***	***B (95% CI)***	***P-value***
Exercise volume				
MET-hrs/week, per 10	0.01 (-0.05 – 0.08)	0.65	0.00 (-0.15 – 0.14)	0.96
Exercise volume tertiles				
Low (<30.1 MET-hrs/wk)	Reference		Reference	
Medium (30.1 – 51.6 MET-hrs/wk)	0.09 (-0.29 – 0.47)	0.64	0.29 (-0.59 – 1.17)	0.52
High (>51.6 MET-hrs/wk)	0.11 (-0.28 – 0.49)	0.59	0.31 (-0.59 – 1.20)	0.50
*Exercise intensity, % MET-hrs/wk****				
Moderate intensity (per 10%)	-0.01 (-0.08 – 0.05)	0.69	0.06 (-0.10 – 0.22)	0.48
Vigorous intensity (per 10%)	-0.05 (-0.09 – -0.01)	0.02	-0.02 (-0.11 – 0.07)	0.68
Very vigorous intensity (per 10%)	0.05 (0.01 – 0.09)	0.01	0.01 (-0.08 – 0.11)	0.80
*Vigorous intensity tertiles****				
Low (<17%)	Reference		Reference	
Medium (17-70%)	-0.11 (-0.48 – 0.25)	0.54	0.07 (-0.80 – 0.94)	0.87
High (>70%)	-0.54 (-0.90 – -0.17)	0.004	-0.39 (-1.25 – 0.48)	0.38
*Very vigorous intensity tertiles****				
Low (<2%)	Reference		Reference	
Medium (2-62%)	0.24 (-0.14 – 0.62)	0.21	0.49 (-0.40 – 1.38)	0.28
High (>62%)	0.45 (0.07 – 0.82)	0.02	0.04 (-0.85 – 0.92)	0.94

MET, metabolic equivalent of task; CAC, coronary artery calcification. Adjusted for baseline confounders: age, body mass index, systolic blood pressure, use of antihypertensive, pack years smoked, total cholesterol, family history of coronary heart disease, use of statin and diabetes. Additionally adjusted for time between CT scans and baseline coronary artery calcification score or number of plaques. *additionally adjusted for MET-hrs/week between baseline and follow-up.

Supplemental Table 9. Multivariable-adjusted logistic regression analyses between exercise characteristics and progression of plaque and plaque types.

	Progression of plaque (yes/no)		***Increase in Calcified plaque (yes/no)***		***Increase in Mixed plaque (yes/no)***		***Increase in non-calcified plaque (yes/no)***	
	OR (95% CI)	***P-value***	***OR (95% CI)***	***P-value***	***OR (95% CI)***	***P-value***	***OR (95% CI)***	***P-value***
MET-hrs/week, per 10	0.96 (0.86 – 1.08)	0.52	0.98 (0.88 – 1.08)	0.66	1.04 (0.94 – 1.15)	0.49	0.94 (0.84 – 1.05)	0.24
Exercise volume tertiles								
Low (<30.1 MET-hrs/wk)	Reference		Reference		Reference		Reference	
Medium (30.1-51.6 MET-hrs/wk)	1.31 (0.63 – 2.75)	0.47	1.30 (0.69 – 2.45)	0.42	1.21 (0.66 – 2.25)	0.54	1.17 (0.63 – 2.18)	0.63
High (>51.6 MET-hrs/wk)	1.03 (0.50 – 2.11)	0.93	1.32 (0.69 – 2.51)	0.40	1.32 (0.71 – 2.45)	0.38	0.69 (0.36 – 1.34)	0.27
*Exercise intensity, % MET-hrs/week**								
Moderate intensity (per 10%)	0.99 (0.86 – 1.13)	0.83	0.94 (0.83 – 1.05)	0.27	1.09 (0.97 – 1.22)	0.15	1.02 (0.92 – 1.15)	0.69
Vigorous intensity (per 10%)	0.94 (0.87 – 1.02)	0.13	0.96 (0.90 – 1.03)	0.26	0.98 (0.92 – 1.04)	0.49	0.99 (0.92 – 1.06)	0.71
Very vigorous intensity (per 10%)	1.09 (1.01 – 1.18)	0.04	1.07 (1.00 – 1.15)	0.053	1.00 (0.94 – 1.07)	0.90	1.01 (0.95 – 1.08)	0.71
*Vigorous intensity tertiles**								
Low (<17%)	Reference		Reference		Reference		Reference	
Medium (17-70%)	0.83 (0.39 – 1.77)	0.63	0.88 (0.47 – 1.65)	0.70	2.06 (1.15 – 3.82)	0.02	0.99 (0.53 – 1.85)	0.97
High (>70%)	0.50 (0.24 – 1.04)	0.07	0.72 (0.39 – 1.35)	0.31	0.78 (0.42 – 1.44)	0.43	0.91 (0.48 – 1.70)	0.76
*Very vigorous intensity tertiles**								
Low (<2%)	Reference		Reference		Reference		Reference	
Medium (2-62%)	1.24 (0.61 – 2.56)	0.55	1.72 (0.90 – 3.28)	0.10	1.97 (1.05 – 3.70)	0.04	0.91 (0.47 – 1.73)	0.77
High (>62%)	2.04 (0.93 – 4.15)	0.06	2.09 (1.09 – 4.00)	0.03	0.98 (0.53 – 1.81)	0.94	0.98 (0.52 – 1.86)	0.96

MET, metabolic equivalent of task. Adjusted for baseline confounders: age, body mass index, systolic blood pressure, use of antihypertensive, pack years smoked, total cholesterol, family history of coronary heart disease, use of statin and diabetes. Additionally adjusted for baseline number of plaques and time between CT scans.
*additionally adjusted for MET-hrs/week between baseline and follow-up.

Supplemental Table 10. Sensitivity analyses of progression of coronary artery calcification using different methods.

Progression of CAC	*Ln delta CAC score +1*		*Annualized Ln delta CAC score + 1*		*Squared root Method*		*Annualized Squared root Method*		*Squared root Volume score*		*Annualized Squared root volume score*	
	B (95% CI)	*P-value*	*B (95% CI)*	*P-value*	*B (95% CI)*	*P-value*	*B (95% CI)*	*P-value*	*B (95% CI)*	*P-value*	*B (95% CI)*	*P-value*
Exercise volume												
MET-hrs/week, per 10	0.01 (-0.05 – 0.08)	0.65	0.002 (-0.008 – 0.012)	0.69	0.04 (-0.12-0.19)	0.63	0.004 (-0.02 – 0.03)	0.73	0.02 (-0.13 – 0.17)	0.79	0.002 (-0.02 – 0.03)	0.90
Exercise volume tertiles												
Low (<30.1 MET-hrs/wk)	Reference		Reference		Reference		Reference		Reference		Reference	
Medium (30.1 – 51.6 MET-hrs/wk)	0.09 (-0.29 – 0.47)	0.64	0.015 (-0.05 – 0.07)	0.63	0.71 (-0.24 – 1.66)	0.14	0.10 (-0.05 – 0.25)	0.18	0.78 (-0.15 – 1.70)	0.10	0.11 (-0.03 – 0.26)	0.12
High (>51.6 MET-hrs/wk)	0.11 (-0.28 – 0.49)	0.59	0.014 (-0.05 – 0.07)	0.65	0.26 (-0.70 – 1.22)	0.59	0.02 (-0.13 – 0.17)	0.75	0.26 (-0.67 – 1.20)	0.58	0.03 (-0.12-0.17)	0.74
*Exercise intensity, % MET-hrs/wk****												
Moderate intensity (per 10%)	-0.01 (-0.08 – 0.05)	0.69	-0.002 (-0.013 – 0.009)	0.72	-0.10 (-0.27 – 0.07)	0.25	-0.015 (-0.04 – 0.01)	0.27	-0.09 (-0.25 – 0.08)	0.31	-0.13 (-0.04 – 0.13)	0.34
Vigorous intensity (per 10%)	-0.05 (-0.09 – -0.01)	0.02	-0.008 (-0.014 – -0.001)	0.02	-0.10 (-0.20 – 0.005)	0.06	-0.016 (-0.03 – 0.00)	0.05	-0.09 (-0.19 – 0.10)	0.08	-0.14 (-0.03 – 0.001)	0.06
Very vigorous intensity (per 10%)	0.05 (0.01 – 0.09)	0.01	0.008 (0.002 – 0.014)	0.01	0.13 (0.03 – 0.23)	0.01	0.02 (0.005 – 0.04)	0.01	0.12 (0.03 – 0.22)	0.01	0.02 (0.01 -0.04)	0.01
*Vigorous intensity tertiles****												

Low (<17%)	Reference		Reference		Reference		Reference		Reference		Reference	
Medium (17-70%)	-0.11 (-0.48 – 0.25)	0.54	-0.02 (-0.07 – 0.04)	0.58	-0.48 (-1.41 – 0.45)	0.31	-0.07 (-0.21 – 0.07)	0.34	-0.31 (-1.21 – 0.59)	0.50	-0.04 (-0.18 – 0.10)	0.54
High (>70%)	-0.54 (-0.90 – -0.17)	0.004	-0.08 (-0.14 – -0.03)	0.01	-1.13 (-2.06 – -0.20)	0.02	-0.18 (-0.32 - -0.04)	0.02	-1.05 (-1.96 – -0.14)	0.02	-0.17 (-0.31 – -0.03)	0.02
*Very vigorous intensity tertiles**												
Low (<2%)	Reference		Reference		Reference		Reference		Reference		Reference	
Medium (2-62%)	0.24 (-0.14 – 0.62)	0.21	0.05 (-0.01 – 0.11)	0.12	0.51 (-0.44 – 1.46)	0.30	0.10 (-0.05 – 0.25)	0.18	0.51 (-0.42 – 1.43)	0.28	0.10 (-0.05 – 0.24)	0.18
High (>62%)	0.45 (0.07 – 0.82)	0.02	0.07 (0.01 – 0.13)	0.02	1.08 (0.13 – 2.03)	0.03	0.18 (0.03 – 0.32)	0.02	1.02 (0.09 – 1.94)	0.03	0.17 (0.02 – 0.31)	0.02

MET, metabolic equivalent of task; CAC, coronary artery calcification. Adjusted for baseline confounders: ln baseline coronary artery calcification score, age, body mass index, systolic blood pressure, use of antihypertensive, pack years smoked, total cholesterol, family history of coronary heart disease, use of statin and diabetes. Time between CT scans was included in the models for the non-annualized variables. *additionally adjusted for MET-hrs/week between baseline and follow-up.

Supplemental Figure 1. Flowchart of in- and exclusion of study population.