

Supplementary Online Content

DeFina LF, Radford NB, Barlow CE, et al. Association of all-cause and cardiovascular mortality with high levels of physical activity and concurrent coronary artery calcification. *JAMA Cardiol*. Published online January 30, 2019. doi:10.1001/jamacardio.2018.4628

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

eTable 1. Baseline Characteristics of 9501 Generally Healthy Women by Physical Activity Level and Coronary Artery Calcification Categories

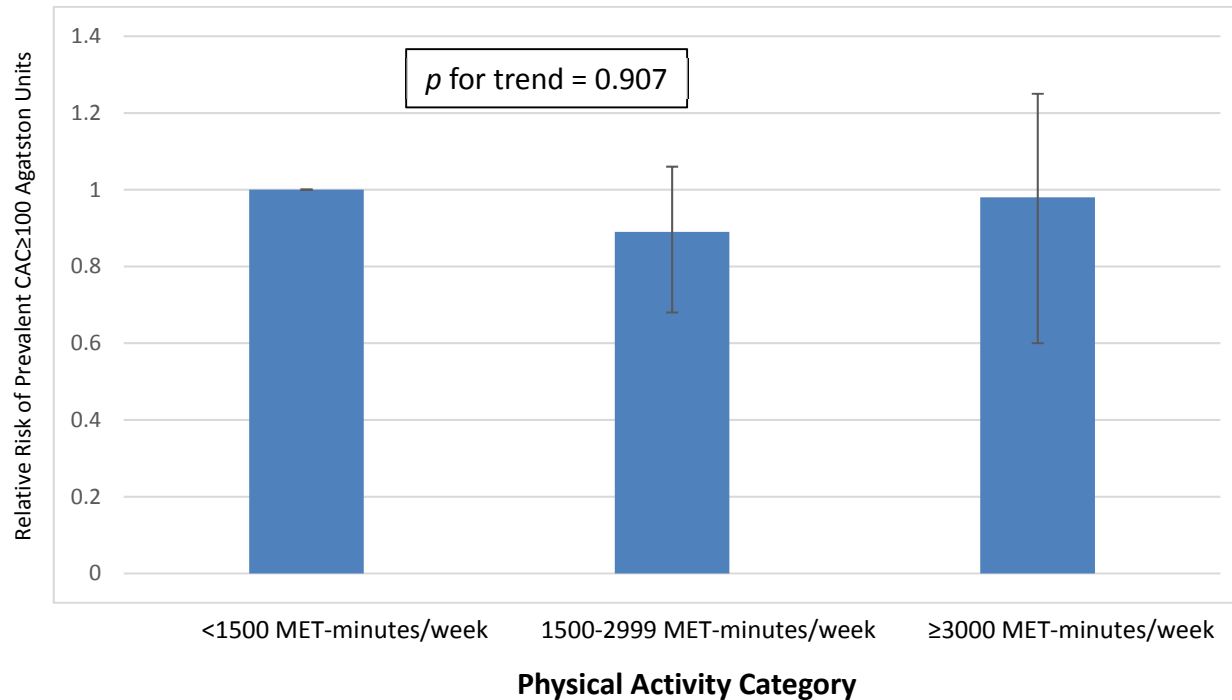
Coronary Artery Calcification Category	<100 AU*				≥100 AU				Total (n=9,501)
	Physical Activity Category	<1500 MET-minutes/week (n=6,727)	1500-2999 MET-minutes/week (n=1,513)	≥3000 MET-minutes/week (n=560)	p for trend	<1500 MET-minutes/week (n=588)	1500-2999 MET-minutes/week (n=80)	≥3000 MET-minutes/week (n=33)	
Age, mean (SD), y	52.3 (8.0)	50.6 (7.3)	50.6 (7.3)	<.001	62.5 (8.7)	62.3 (8.8)	60.5 (9.5)	0.416	52.7 (8.4)
White, No. (%)	6114 (90.9)	1405 (92.9)	517 (92.3)	0.203	536 (91.2)	76 (95.0)	32 (97.0)	0.620	8680 (91.4)
Current smoker, No. (%)	373 (5.5)	51 (3.4)	20 (3.6)	<.001	41 (7.0)	4 (5.0)	3 (9.1)	0.737	492 (5.2)
Statin use, No. (%)	513 (8.2)	82 (5.7)	30 (5.7)	<.001	152 (27.6)	18 (22.8)	8 (24.2)	0.345	803 (9.0)
Body mass index, mean (SD), kg/m ²	25.6 (5.2)	24.0 (4.0)	23.8 (3.8)	<.001	26.6 (5.5)	25.3 (4.5)	24.0 (3.8)	0.002	25.3 (5.0)
Systolic blood pressure, mean (SD), mmHg	118.0 (16.1)	115.4 (14.7)	116.4 (16.0)	<.001	130.2 (19.1)	126.6 (17.8)	125.4 (16.7)	0.045	118.3(16.4)
Glucose, mean (SD), mg/dL	94.1 (14.8)	92.3 (10.2)	92.6 (12.2)	<.001	101.0 (25.0)	96.1 (15.9)	93.0 (11.5)	0.006	94.2 (15.0)
Cholesterol, mean (SD), mg/dL	204.3 (35.8)	198.3 (33.8)	201.2 (36.1)	<.001	212.6 (39.5)	215.3 (38.7)	206.2 (22.7)	0.855	203.8 (35.9)
LDL cholesterol, mean (SD), mg/dL	116.5 (31.9)	110.1 (30.0)	110.8 (31.6)	<.001	122.6 (35.8)	125.5 (35.8)	112.7 (20.1)	0.512	115.6 (32.0)
HDL cholesterol, mean (SD), mg/dL	66.2 (17.3)	70.3 (17.2)	72.2 (17.9)	<.001	64.4 (19.4)	68.8 (17.7)	74.5 (12.4)	<.001	67.2 (17.6)
Triglycerides, mean (SD), mg/dL	108.1 (67.5)	89.7 (50.4)	94.2 (97.7)	<.001	129.0 (79.3)	104.5 (50.5)	94.8 (41.8)	<.001	105.6 (68.5)
Calcium, mean (SD), mg/dL	9.2 (0.4)	9.2 (0.4)	9.2 (0.4)	0.110	9.3 (0.4)	9.4 (0.4)	9.3 (0.4)	0.371	9.2 (0.4)
Framingham Risk Score, mean (SD), %	4.5 (3.1)	3.6 (2.6)	3.6 (2.8)	<.001	7.2 (4.2)	5.9 (2.9)	5.1 (2.4)	<.001	4.5 (3.2)
Physical activity, mean (SD), MET-minutes/week	461.5 (462.1)	2083.8 (420.3)	4504.8 (1946.8)	<.001	365.6 (444.5)	2044.3 (412.6)	4589.8 (1263.5)	<.001	979.9 (1271.3)
Physical activity, mean (SD), minutes/week	119.7 (126.6)	386.7 (131.1)	724.5 (330.8)	<.001	94.2 (114.0)	394.7 (123.5)	766.1 (234.6)	<.001	200.8 (223.8)
Physical activity lifetime, mean (SD), y	15.1 (12.6)	19.7 (12.4)	23.0 (13.0)	<.001	15.8 (14.6)	26.3 (16.7)	27.9 (16.6)	<.001	17.0 (13.1)
CAC score, mean (SD), AU	4.6 (14.9)	3.2 (11.8)	4.5 (15.2)	0.014	442.4 (518.2)	375.3 (335.2)	315.4 (374.0)	0.065	35.6 (174.9)
Calcification volume, mean (SD)	4.4 (12.1)	3.4 (10.1)	4.3 (12.6)	0.071	267.4 (306.3)	230.2 (205.2)	205.6 (269.6)	0.093	27.5 (115.9)

Coronary Artery Calcification Category	<100 AU*				≥100 AU				
Physical Activity Category	<1500 MET-minutes/week (n=6,727)	1500-2999 MET-minutes/week (n=1,513)	≥3000 MET-minutes/week (n=560)	p for trend	<1500 MET-minutes/week (n=588)	1500-2999 MET-minutes/week (n=80)	≥3000 MET-minutes/week (n=33)	p for trend	Total (n=9,501)
Number of calcification lesions, mean (SD)	0.4 (1.0)	0.3 (0.9)	0.3 (1.1)	0.077	7.7 (7.3)	6.4 (5.6)	6.1 (7.4)	0.022	1.0 (3.0)
Cardiorespiratory fitness, mean (SD), METs	9.0 (1.7)	10.3 (1.8)	10.7 (1.9)	<.001	8.1 (1.6)	9.0 (1.6)	9.7 (1.9)	<.001	9.3 (1.8)
VO ₂ max, mean (SD), ml/kg/min	31.4 (5.9)	36.2 (6.2)	37.5 (6.7)	<.001	28.2 (5.6)	31.7 (5.5)	34.1 (6.8)	<.001	32.4 (6.5)
≥50 ml/kg/min, No. (%)	7 (0.1)	11 (0.8)	18 (3.8)	<.001	0 (0.0)	0 (0.0)	1 (3.7)	0.020	37 (0.5)
Maximum heart rate, mean (SD), bpm	171.2 (13.4)	173.5 (12.1)	172.2 (12.2)	<.001	160.3 (14.4)	162.3 (12.3)	164.5 (17.9)	0.107	171.1 (13.4)
Heart rate recovery@1min, mean (SD), bpm	22.9 (8.1)	25.5 (8.2)	26.3 (8.4)	<.001	20.0 (8.1)	20.9 (8.3)	25.6 (9.7)	0.008	23.4 (8.3)

Abbreviations: AU, Agatston units; BMI, body mass index; LDL, low density lipoprotein; HDL, high density lipoprotein; MET, metabolic equivalent of task; BPM, beats per minutes
SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259; to convert triglycerides to millimoles per liter, multiply by 0.0113.
Sample sizes were reduced where a specific observation was missing with resulting minimum sample sizes for statin use (n=8,873), LDL cholesterol (n=9,477), calcium (n=6,691), physical activity lifetime (n=5,653), calcification volume (n=7,702), number of calcification lesions (n=7,733), and cardiorespiratory fitness (n=7,614)

eFigure 1. Relative Risk of Prevalent Coronary Artery Calcification (≥ 100 Agatston Units) by Physical Activity Category in 9501 Generally Healthy Women

Model was adjusted for age, BMI, glucose, cholesterol, systolic blood pressure, and smoking status. The error bars represent the 95% confidence intervals. Abbreviation: MET, metabolic equivalent of task



eTable 2. Total Number of All-Cause and Cardiovascular Disease Mortality in 9501 Generally Healthy Women by Physical Activity Category and Coronary Artery Calcification Category

Coronary Artery Calcification Category	<100 AU			≥100 AU			Total
	<1500	1500-2999	≥3000	<1500	1500-2999	≥3000	
Physical Activity Category (MET-minutes/week)							
Total participants	6,727	1,513	560	588	80	33	9,501
Average follow-up (years)	10.1	9.6	9.8	10.3	10.3	10.2	10.0
Total follow-up (years)	68,005.5	14,487.2	5,470.5	6,047.4	822.3	335.3	95,168.2
All-cause deaths	126	16	2	55	8	3	210
Incidence (per 1000 person-years)	1.9	1.1	0.4	9.1	9.7	8.9	2.2
Cardiovascular disease deaths	19	3	1	17	2	2	44
Incidence (per 1000 person-years)	0.3	0.2	0.2	2.8	2.4	6.0	0.5

Abbreviation: AU, Agatston units; MET, metabolic equivalent of task

eTable 3. Mean Physical Activity Reported by 9501 Generally Healthy Women by Physical Activity Category and Coronary Artery Calcification Category

		CAC AU			CAC AU		
		< 100			≥100		
		Physical activity category (MET-minutes/week)			Physical activity category (MET-minutes/week)		
All	<1500	1500-<3000	≥3000	<1500	1500-<3000	≥3000	
Running	118.6	40.3	298.0	633.3	20.2	170.5	742.7
Walking	281.2	200.9	527.0	604.2	179.7	689.2	716.7
Bicycling	114.5	42.7	265.0	608.8	42.3	212.1	513.6
Racquet Sports	108.1	13.3	197.8	1076.3	7.8	105.0	686.5
Elliptical/Stairs	39.8	20.8	99.3	133.5	10.6	45.5	87.3
Swimming	32.9	10.8	71.7	189.8	2.6	181.4	272.0
Aerobics/Dance	81.9	41.5	215.2	247.1	27.3	153.0	222.7
Cross-Country Skiing	3.3	2.0	3.8	16.1	0.3	10.1	65.5
Other Sports	27.1	4.8	54.4	237.5	1.6	58.1	120.9
Other	88.2	17.8	208.6	608.1	15.4	248.0	1026.6
All	979.9	461.5	2083.8	4504.8	365.6	2044.3	4589.8

eTable 4. Mean Physical Activity Reported by 21 758 Generally Healthy Men by Physical Activity Category and Coronary Artery Calcification Category

		CAC AU			CAC AU		
		< 100			≥100		
		Physical activity categories (MET·minutes/week)			Physical activity categories (MET·minutes/week)		
	All	<1500	1500- <3000	≥3000	<1500	1500- <3000	≥3000
Running	246.3	126.8	589.0	910.0	84.6	487.1	683.3
Walking	187.0	125.9	276.9	446.1	149.8	394.7	599.1
Bicycling	183.4	67.0	367.2	1037.1	67.8	319.5	876.2
Racquet Sports	107.5	27.2	225.6	727.9	17.2	204.2	656.2
Elliptical/Stairs	47.0	30.3	95.9	118.7	22.6	112.4	112.0
Swimming	35.6	12.6	74.6	189.4	11.0	79.3	177.7
Aerobics/Dance	9.4	5.0	19.9	27.0	4.7	20.9	40.6
Cross-Country Skiing	3.9	2.6	8.8	5.8	2.6	9.7	5.6
Other Sports	57.4	17.8	111.1	392.1	9.1	84.6	356.8
Other	112.9	19.0	251.6	705.6	6.0	275.4	1012.7
All	1040.6	473.8	2077.9	4618.2	430.7	2087.1	4646.9

eTable 5. Hazard Ratio for All-Cause and Cardiovascular Disease Mortality in 21 758 Generally Healthy Men by Coronary Artery Calcification (0 vs ≥ 1 AU) and Physical Activity Category^a

Physical Activity Category	Coronary Artery Calcification	
	0 AU	≥ 1 AU
All-Cause Mortality		
<1500 MET-minutes – Referent	1	1
1500-2999 MET-minutes	0.73 (0.45, 1.20)	0.85 (0.67, 1.08)
≥ 3000 MET-minutes	0.84 (0.44, 1.63)	0.63 (0.44, 0.92)
Cardiovascular Disease Mortality		
<1500 MET-minutes – Referent	1	1
1500-2999 MET-minutes	1.13 (0.41, 3.12)	0.57 (0.32, 1.01)
≥ 3000 MET-minutes	0.84 (0.17, 4.23)	0.65 (0.32, 1.33)

^aAdjusted for age, BMI, glucose, cholesterol, systolic blood pressure, smoker

Abbreviations: AU, Agatston units; MET, metabolic equivalent of task; MET-min, MET-minutes per week

eTable 6. Hazard Ratio for All-Cause and Cardiovascular Disease Mortality in 21 758 Generally Healthy Men by Coronary Artery Calcification (<400 vs ≥ 400 AU) and Physical Activity Category^a

Physical Activity Category	Coronary Artery Calcification	
	<400 AU	≥ 400 AU
All-Cause Mortality		
<1500 MET-minutes – Referent	1	1
1500-2999 MET-minutes	0.82 (0.62, 1.08)	0.83 (0.58, 1.19)
≥ 3000 MET-minutes	0.69 (0.46, 1.05)	0.65 (0.39, 1.08)
Cardiovascular Disease Mortality		
<1500 MET-minutes – Referent	1	1
1500-2999 MET-minutes	0.70 (0.36, 1.38)	0.61 (0.30, 1.26)
≥ 3000 MET-minutes	0.44 (0.13, 1.43)	0.88 (0.41, 1.90)

^aAdjusted for age, BMI, glucose, cholesterol, systolic blood pressure, smoker

Abbreviations: AU, Agatston units; MET, metabolic equivalent of task;

eTable 7. Hazard Ratio for All-Cause and Cardiovascular Disease Mortality in 20 239 Generally Healthy Men by Coronary Artery Calcification (<100 vs ≥100 AU) and Physical Activity Category With Reported Medication Use to Allow Adjustment for Statin Use (n=3770)

Physical Activity Category	Coronary Artery Calcification			
	<100 AU		≥100 AU	
	Age-adjusted	Fully adjusted*	Age-adjusted	Fully adjusted*
All-cause mortality				
<1500 MET-minutes – Referent	1	1	1	1
1500-2999 MET-minutes	0.75 (0.54, 1.04)	0.79 (0.57, 1.10)	0.80 (0.60, 1.09)	0.84 (0.62, 1.14)
≥3000 MET-minutes	0.49 (0.28, 0.88)	0.45 (0.24, 0.83)	0.77 (0.52, 1.16)	0.82 (0.56, 1.22)
Cardiovascular Disease Mortality				
<1500 MET-minutes – Referent	1	1	1	1
1500-2999 MET-minutes	0.73 (0.33, 1.61)	0.80 (0.36, 1.75)	0.63 (0.34, 1.17)	0.69 (0.37, 1.29)
≥3000 MET-minutes	0.47 (0.11, 1.92)	0.42 (0.09, 1.93)	0.83 (0.40, 1.71)	0.89 (0.43, 1.83)

^aAdjusted for age, BMI, glucose (+), cholesterol, systolic blood pressure (+), smoker (+), statin use (+)

Abbreviations: AU, Agatston units; MET, metabolic equivalent of task