

# Association of Fatal Myocardial Infarction with Past Level of Physical Activity

A pooled analysis of cohort studies

**Supplementary Material**

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## Appendix Tables

Appendix Table 1: Study characteristics of the 10 participating European cohorts

<b>Appendix Table 1 Study characteristics of the 10 participating European cohorts</b>						
<b>Cohort</b>	<b>Country</b>	<b>Brief description</b>	<b>Recruitment period</b>	<b>Follow-up, years</b>	<b>Total number of participants</b>	<b>Total number of MI during follow-up (fatal outcome at 28 days)</b>
ATTICA	Greece	Participants >18 years and residing in the Attica region within the greater Athens area.	2001-02	10	3042	177 (69)
BELSTRESS	Belgium	Participants aged 35-59 years, who were workers from 25 companies in Belgium.	1994-98	1	13 897	39 (17)
CCHS	Denmark	A random draw from the Danish Civil Registration System of participants aged 20-93 years and residing in Østerbro.	1976-78	34	14 223	1664 (647)
CGPS	Denmark	A random draw from the Danish Civil Registration System of participants aged 20-93 years and residing in Herlev and Østerbro.	2003-14	1-11	104 801	1401 (161)
CONOR	Norway	Consisting of 10 population surveys of adults: Tromsø IV, HUNT II, HUSK, Oslo II, HUBRO, OPPHED, Tromsø V, I-HUBRO, TROFINN, MoRo II.	1994-2003	Ongoing	173 236	9120 (1917)
CRPH	Denmark	Consisting of 5 combined cohorts: MONICA I, II and III, Inter99, and Health 2006. Random samples of the general population in up to 11 municipalities in the greater Copenhagen area.	1982-2008	Ongoing	17 571	778 (95)
MORGEN-project	The Netherlands	A random sample of participants aged 20-65 years in three towns in the Netherlands (Amsterdam, Doetinchem, Maastricht).	1993-97	13-17	17 888	337 (53)
Million Women Study	United Kingdom	Recruitment of one in every four UK women born in 1935-50 at 66 NHS breast screening centres.	1996-2001	Ongoing	632 177	10 451 (1509)
Rotterdam study	The Netherlands	Participants aged ≥40 years residing in the Ommord district of Rotterdam.	1990-	Ongoing	14 926	384 (87)
UK Biobank	United Kingdom	Participants 40-69 years of age from the general population.	2006-10	Ongoing	502 536	3789 (421)
BELSTRESS, Belgian Job Stress Study. CCHS, Copenhagen City Heart Study. CGPS, Copenhagen General Population Study. CONOR, Cohort of Norway. CRPH, Cohort of the Research for Prevention and Health. MORGEN-project, Monitoring Risicofactoren en Gezondheid in Nederland. UK Biobank, United Kingdom Biobank.						

Appendix Table 2: Pooled baseline characteristics for patients with MI, by level of PA

	Level of physical activity			
	Sedentary	Low	Moderate	High
<b>No. Patients</b>	5504	5654	5628	11 354
<b>Demographics:</b>				
Age, years	69.1 (11.6)	68.4 (10.5)	67.7 (10.1)	68.9 (7.5)
Males, %	59.3	59.4	54.0	22.0
<b>Risk factors:</b>				
Diabetes mellitus, %	27.6	18.2	13.6	8.5
Arterial hypertension, %	57.7	51.0	47.2	39.2
Family history of CVD, %	50.2	49.1	48.9	51.3
Active smoking, %	43.0	41.7	39.8	48.5
<b>Biometrics:</b>				
Body-mass index [kg/m <sup>2</sup> ]	27.6 (4.5)	26.9 (4.1)	26.9 (4.2)	26.7 (4.5)
Total cholesterol [mmol/L]	6.4 (1.3)	6.4 (1.3)	6.2 (1.1)	6.0 (1.2)
Systolic blood pressure [mmHg]	147.3 (22.7)	145.8 (21.2)	144.9 (20.6)	145.4 (19.6)
Diastolic blood pressure [mmHg]	83.8 (12.3)	84.6 (12.0)	84.1 (11.5)	83.6 (10.8)
<b>Time from baseline to MI:</b>				
>5 years, %	67.7	68.6	68.8	70.8
CVD, Cardiovascular disease. Numbers are mean (standard deviation) unless otherwise is specified. Each characteristic was weighted by [cohort sample size/total sample size].				

Appendix Table 3: Pooled ORs, 95% CIs, and I<sup>2</sup> statistics for fixed- and random-effects multivariate models

Appendix Table 3 Pooled odds ratios, 95% confidence intervals, and I <sup>2</sup> statistics for fixed- and random-effects multivariate models											
		Level of physical activity									
		Fixed-effects models				Random-effects models					
	Number of cohorts	Number of patients (events)	Sedentary	Low	Moderate	High	Sedentary	Low	Moderate	High	I <sup>2</sup> , %
<b>Instant fatal MI</b>											
<b>Unadjusted</b>	10	28 140 (3101)	1	0.86 (0.76-0.97)	0.72 (0.63-0.81)	0.63 (0.55-0.72)	1	0.83 (0.70-0.98)	0.69 (0.58-0.82)	0.61 (0.51-0.73)	18.3
<b>Adjustment</b>											
Age and sex	9	27 798 (3055)	1	0.82 (0.73-0.93)	0.73 (0.64-0.82)	0.62 (0.53-0.71)	1	0.74 (0.59-0.93)	0.65 (0.52-0.82)	0.56 (0.44-0.70)	44.5
Age, sex, and CVD risk factors	6	26 602 (2990)	1	0.85 (0.75-0.97)	0.76 (0.66-0.87)	0.65 (0.54-0.79)	1	0.76 (0.59-0.97)	0.67 (0.52-0.86)	0.58 (0.44-0.77)	49.0
Age, sex, CVD risk factors, alcohol consumption, smoking, and socioeconomic status	6	26 602 (2990)	1	0.90 (0.78-1.03)	0.77 (0.66-0.90)	0.63 (0.50-0.80)	1	0.79 (0.60-1.04)	0.67 (0.51-0.89)	0.55 (0.40-0.76)	47.3
<b>28-day fatal MI</b>											
<b>Unadjusted</b>	7	24 618 (1868)	1	0.82 (0.72-0.94)	0.61 (0.53-0.71)	0.66 (0.56-0.78)	1	0.86 (0.71-1.03)	0.64 (0.52-0.77)	0.67 (0.55-0.83)	24.9
<b>Adjustment</b>											
Age and sex	6	24 256 (1808)	1	0.78 (0.68-0.90)	0.63 (0.54-0.73)	0.66 (0.56-0.79)	1	0.78 (0.68-0.90)	0.63 (0.54-0.73)	0.66 (0.56-0.79)	<0.1
Age, sex, and CVD risk factors	6	24 256 (1808)	1	0.78 (0.67-0.90)	0.64 (0.54-0.75)	0.69 (0.56-0.84)	1	0.78 (0.67-0.90)	0.64 (0.54-0.75)	0.69 (0.56-0.84)	<0.1
Age, sex, CVD risk factors, alcohol consumption, smoking, and socioeconomic status	4	19 736 (1334)	1	0.85 (0.71-1.03)	0.64 (0.51-0.80)	0.72 (0.51-1.00)	1	0.85 (0.71-1.03)	0.64 (0.51-0.80)	0.72 (0.51-1.00)	<0.1

CI, confidence interval. CVD, cardiovascular disease. CVD risk factors include diabetes mellitus, arterial hypertension, family history of CVD, total cholesterol levels, and body-mass index.

Appendix Table 4: Pooled ORs, 95% CIs, and I<sup>2</sup> statistics for fixed- and random-effects network meta-analysis

Appendix Table 4 Pooled odds ratios, 95% confidence intervals, and I <sup>2</sup> statistics for fixed- and random-effects network meta-analysis										
	Number of cohorts	Number of patients (events)	Level of physical activity				Heterogeneity			
			Sedentary	Low	Moderate	High	Q	d.f.	p-value	I <sup>2</sup> , %
<b>Instant fatal MI</b>										
<b>FE model</b>	10	28 140 (3101)	1	0.86 (0.76-0.97)	0.72 (0.63-0.81)	0.63 (0.55-0.72)	-	-	-	-
<b>RE model</b>	10	28 140 (3101)	1	0.84 (0.76-1.01)	0.68 (0.56-0.83)	0.59 (0.47-0.72)	32.6	26	0.17	20.2
<b>28-day fatal MI</b>										
<b>FE model</b>	7	24 618 (1868)	1	0.82 (0.72-0.94)	0.61 (0.53-0.71)	0.66 (0.56-0.78)	-	-	-	-
<b>RE model</b>	7	24 618 (1868)	1	0.84 (0.68-1.03)	0.65 (0.53-0.81)	0.65 (0.52-0.83)	25.1	18	0.12	28.2

FE, fixed-effects. RE, random-effects.

Appendix Table 5: Assessment of PA, by individual cohort

Appendix Table 5 Assessment of physical activity, by individual cohort							
Cohort	Country	Recruitment period	Assessment of physical activity				
			Method	No. of items	Time frame		
					1 week	4 weeks	1 year
ATTICA	Greece	2001-02	SRQ	7	x		
Belstress	Belgium	1994-98	SRQ	1	x		
CCHS	Denmark	1976-78	SRQ	1			x
CGPS	Denmark	2003-14	SRQ	1			x
CONOR	Norway	1994-2003	SRQ	2			x
CRPH	Denmark	1982-2008	SRQ	5	x		
MWS	United Kingdom	1996-2001	SRQ	2	x		
MORGEN-Project	The Netherlands	1993-97	SRQ	3			x
Rotterdam study	The Netherlands	1990-	SRQ	28	x		
UK Biobank	United Kingdom	2006-10	SRQ	11		x	

SRQ, self-reported questionnaire

Appendix Table 6: No. of outcomes, by individual cohort and level of physical activity

<b>Appendix Table 6 No. outcomes, by individual cohort and level of physical activity</b>					
	<b>Level of physical activity</b>				<b>Total</b>
	<b>Sedentary</b>	<b>Low</b>	<b>Moderate</b>	<b>High</b>	
<b>No. Patients</b>	5504	5654	5628	11 354	28 140
<b>Instant fatal MI</b>					
ATTICA	47/109	9/21	4/16	9/31	<b>69/177</b>
BELSTRESS	4/11	10/19	3/9	0/0	<b>17/39</b>
CCHS	111/346	227/898	83/398	4/22	<b>425/1664</b>
CGPS	13/110	43/707	36/511	3/73	<b>95/1401</b>
CONOR	546/3896	299/2332	240/2129	75/763	<b>1160/9120</b>
CRPH	5/208	12/424	4/141	0/5	<b>21/778</b>
MWS	46/255	84/606	193/1585	897/8005	<b>1220/10 451</b>
MORGEN-Project	1/7	3/14	0/32	42/284	<b>46/337</b>
Rotterdam study	1/4	3/12	2/26	21/342	<b>27/384</b>
UK Biobank	3/558	11/621	1/781	6/1829	<b>21/3789</b>
<b>Total</b>	<b>777/5504</b>	<b>701/5654</b>	<b>566/5628</b>	<b>1057/11 354</b>	<b>3101/28 140</b>
<b>28-day fatal MI</b>					
ATTICA	NA	NA	NA	NA	<b>NA</b>
BELSTRESS	NA	NA	NA	NA	<b>NA</b>
CCHS	48/235	129/671	44/315	4/18	<b>225/1239</b>
CGPS	6/97	33/664	24/475	3/70	<b>66/1306</b>
CONOR	392/3350	200/2033	120/1889	46/688	<b>758/7960</b>
CRPH	25/203	32/412	17/137	0/5	<b>74/757</b>
MWS	9/209	25/522	36/1392	219/7108	<b>289/9231</b>
MORGEN-Project	0/6	0/11	1/32	6/242	<b>7/291</b>
Rotterdam study	2/3	3/9	5/24	50/321	<b>60/357</b>
UK Biobank	65/555	65/610	79/780	191/1823	<b>400/3768</b>
<b>Total</b>	<b>547/4658</b>	<b>487/4932</b>	<b>326/5044</b>	<b>519/10 275</b>	<b>1879/24 909</b>
<b>Out-of-hospital deaths*</b>					
ATTICA	NA	NA	NA	NA	<b>NA</b>
BELSTRESS	NA	NA	NA	NA	<b>NA</b>
CCHS	NA	NA	NA	NA	<b>NA</b>
CGPS	NA	NA	NA	NA	<b>NA</b>
CONOR	449/3896	237/2332	199/2129	58/763	<b>943/9120</b>
CRPH	14/208	27/424	11/141	0/5	<b>52/778</b>
MWS	55/255	106/606	242/1585	1159/8005	<b>1562/10 451</b>
MORGEN-Project	NA	NA	NA	NA	<b>NA</b>
Rotterdam study	0/4	8/12	11/26	112/342	<b>131/384</b>
UK Biobank	NA	NA	NA	NA	<b>NA</b>
<b>Total</b>	<b>518/4363</b>	<b>378/3374</b>	<b>463/3881</b>	<b>1329/9115</b>	<b>2688/20 733</b>
BELSTRESS, Belgian Job Stress Study. CCHS, Copenhagen City Heart Study. CGPS, Copenhagen General Population Study. CONOR, Cohort of Norway. CRPH, Cohort of the Research for Prevention and Health. MI, myocardial infarction. MORGEN-project, Monitoring Risicofactoren en Gezondheid in Nederland. UK Biobank, United Kingdom Biobank. * Included all out-of-hospital deaths in the study populations regardless of cause.					



Appendix Table 7: Post-hoc analysis of pooled ORs, 95% CIs, and I<sup>2</sup> statistics, by selected cohort characteristics

Appendix Table 7 Post-hoc analysis of pooled odds ratios (95% CIs) for instant fatal myocardial infarction, by selected cohort characteristics							
	Number of cohorts	Number of patients (events)	Level of physical activity				I <sup>2</sup> , %
			Sedentary	Low	Moderate	High	
<b>Region</b>							
Scandinavia	4	12 958 (1701)	1	0.71 (0.51-0.98)	0.66 (0.47-0.92)	0.56 (0.38-0.84)	64.4
Other European	5	14 840 (1354)	1	0.81 (0.58-1.15)	0.60 (0.43-0.82)	0.54 (0.40-0.72)	<0.1
<b>Recruitment period<sup>a</sup></b>							
<1990	3	2821 (473)	1	0.69 (0.53-0.90)	0.53 (0.38-0.74)	0.31 (0.15-0.64)	<0.1
1990-2000	2	9159 (1177)	1	0.87 (0.75-1.02)	0.84 (0.71-0.99)	0.71 (0.54-0.93)	<0.1
>2000	4	15 818 (1405)	1	0.66 (0.46-0.95)	0.55 (0.39-0.78)	0.49 (0.35-0.68)	14.2
<b>Information on prior heart failure</b>							
Yes	6	23 197 (2996)	1	0.68 (0.53-0.88)	0.61 (0.47-0.79)	0.53 (0.41-0.69)	60.1
No	3	4601 (59)	1	1.64 (0.77-3.46)	0.88 (0.32-2.45)	0.39 (0.13-1.23)	<0.1
<b>Proportion of cohort in high PA group</b>							
<40%	6	13 174 (1787)	1	0.71 (0.53-0.94)	0.65 (0.48-0.88)	0.55 (0.38-0.79)	50.4
≥40%	3	14 624 (1268)	1	0.83 (0.57-1.20)	0.61 (0.44-0.86)	0.55 (0.40-0.75)	<0.1
<b>Prevalence of instant fatal MI</b>							
<10%	4	6347 (164)	1	0.83 (0.37-1.89)	0.73 (0.31-1.72)	0.29 (0.12-0.74)	55.3
≥10%	5	21 451 (2891)	1	0.75 (0.60-0.95)	0.67 (0.53-0.84)	0.59 (0.46-0.75)	52.7

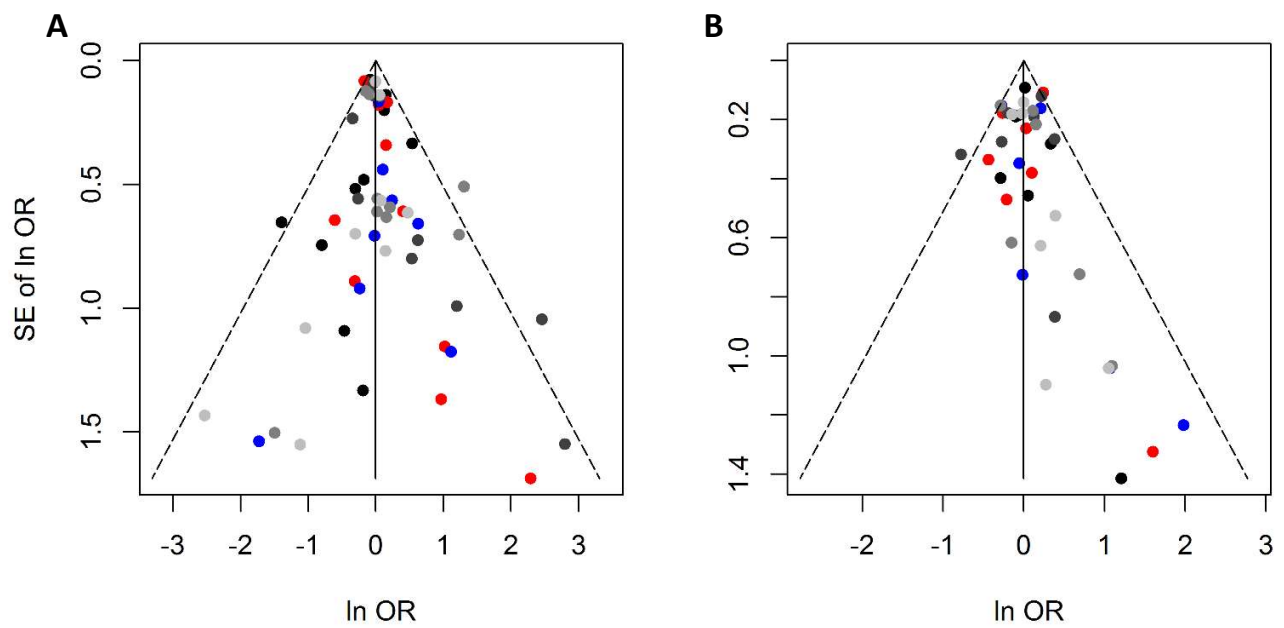
CI, confidence interval. MI, myocardial infarction. PA, physical activity All estimates have been adjusted for age and sex. <sup>a</sup> First year of recruitment.

## Appendix Figures

### Appendix Figure 1: Comparison-adjusted funnel plots

**Appendix Figure 1** Comparison-adjusted funnel plots displaying the natural logarithms of odds ratios against their SEs for (A) instant and (B) 28-day fatal MI, respectively.

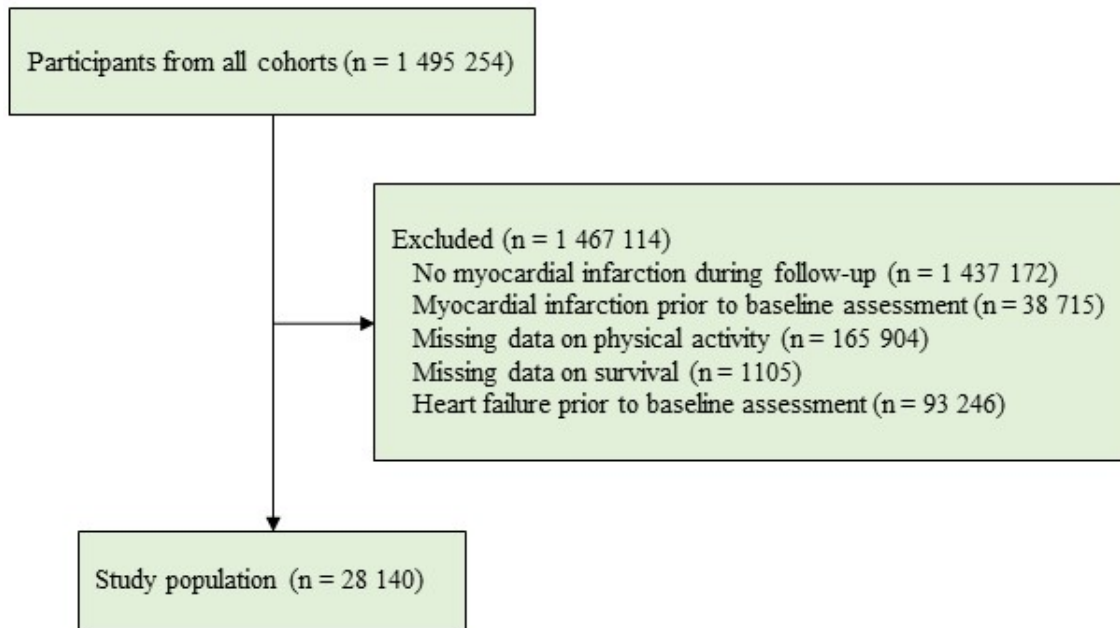
Dots represent study-specific comparisons: black = low vs. sedentary ; red = moderate vs. sedentary ; blue = high vs. sedentary ; dark grey = moderate vs. low ; grey = high vs. low ; light grey = high vs. moderate.



Appendix Figure 2: Flow diagram summarizing the derivation of the study population

**Appendix Figure 2** Flow diagram summarizing the derivation of the study population.

Please note that a participant may meet more than one exclusion criteria.



## Appendix Text

### Standardisation of physical activity level

Current guidelines recommend that healthy adults of all ages engage in at least 150 minutes of moderate intensity or 75 minutes a week of vigorous intensity PA or an equivalent combination thereof; for additional benefit these durations may be doubled (10). This confers with approximate minimum values of weekly net energy expenditure of 7.5 to 14.75 MET-hrs, or 15 to 29.5 MET-hrs, respectively.

Intensity of PA	IPAQ-based conversion rule
<b>Walking (MET-min/week)</b>	3.3 x minutes of walking x walking days
<b>Moderate (MET-min/week)</b>	4.0 x minutes of moderate intensity activity x moderate intensity activity days
<b>Vigorous (MET-min/week)</b>	8.0 x minutes of vigorous intensity activity x vigorous intensity activity days
<b>Cumulative PA (MET-hrs per week)</b>	(Walking MET-min/week + Moderate MET-min/week + Vigorous MET-min/week) / 60 min/hrs
IPAQ, International Physical Activity Questionnaire. MET, metabolic equivalents. PA, physical activity	

Applying the above conversion algorithm to the categorization of leisure-time PA used in the Copenhagen City Heart Study (21,23):

CCHS PA category	IPAQ-based calculation
<b>Inactive or light physical activity &lt;2 hours per week</b>	(3.3 x 120 minutes x 1 day) / 60 min/hrs ≈ 7 MET-hrs/week
<b>Light physical activity 2-4 hours per week</b>	(4.0 x (120 to 240 minutes x 1 day) / 60 min/hrs ≈ 7 to 16 MET-hrs/week
<b>Light activity &gt;4 hours per week or strenuous activity 2-4 hours per week</b>	(4.0 x (>240 minutes x 1 day) / 60 min/hrs ≈ > 16 MET-hrs/week (8.0 x (120 to 240 minutes x 1 day) / 60 min/hrs ≈ 16 to 32 MET-hrs/week
<b>Strenuous activity &gt;4 hours per week or hard training</b>	(8.0 x (>240 minutes x 1 day) / 60 min/hrs ≈ > 32 MET-hrs/week
IPAQ, International Physical Activity Questionnaire. MET, metabolic equivalents. PA, physical activity	

These cut-off values are in excellent agreement with those stated in the 2016 European Guidelines of Cardiovascular Prevention in Clinical Practice (10) as shown above.