

# Exercise-related out-of-hospital cardiac arrest in the general population: incidence and prognosis

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## Aims

Although regular physical activity has beneficial cardiovascular effects, exercise can trigger an acute cardiac event. We aimed to determine the incidence and prognosis of exercise-related out-of-hospital cardiac arrest (OHCA) in the general population.

## Methods and results

We prospectively collected all OHCA in persons aged 10–90 years from January 2006 to January 2009 in the Dutch province North Holland. The relation between exercise during or within 1 h before OHCA and outcome was analysed using multivariable logistic regression, adjusted for age, gender, location, bystander witness, bystander cardiopulmonary resuscitation (CPR), automated external defibrillator (AED) use, initial rhythm, and Emergency Medical System response time. Of 2524 OHCA, 143 (5.7%) were exercise related (7 ≤35 years, 93% men). Exercise-related OHCA incidence was 2.1 per 100 000 person-years overall and 0.3 per 100 000 person-years in those ≤35 years. Survival after exercise-related OHCA was distinctly better than after non-exercise related OHCA (46.2 vs. 17.2%) [unadjusted odds ratio (OR) 4.12; 95%CI 2.92–5.82;  $P < 0.001$ ], even after adjustment for abovementioned variables (OR 2.63; 95%CI, 1.23–5.54;  $P = 0.01$ ). In the 69 victims aged ≤35 years, exercise was not associated with better survival: 14.3 vs. 17.7% in non-exercise-related OHCA (OR 0.77; 95%CI 0.08–7.08;  $P = 0.82$ ).

## Conclusion

Exercise-related OHCA has a low incidence, particularly in the young. Cardiac arrests occurring during or shortly after exercise carry a markedly better prognosis than non-exercise-related arrests in persons >35 years. This study establishes the favourable outcome of exercise-related OHCA and should have direct implications for public health programs to prevent exercise-related sudden death.

## Keywords

Cardiac arrest • Exercise • Incidence • Prevention • Resuscitation • Survival

## Introduction

Although regular exercise reduces the risk of cardiovascular disease, the risk of an acute cardiac event is transiently increased during and immediately after acute, mainly vigorous exercise.<sup>1,2</sup> This is known as the paradox of exercise.<sup>3</sup> Despite this paradox and the worldwide discussion on the prevention of exercise-related events,<sup>4,5</sup> population-based information on the incidence and prognosis of exercise-related out-of-hospital cardiac arrests (OHCA) is scarce.<sup>6</sup>

We set out to assess the incidence of exercise-related OHCA in the general population and to determine whether exercise-related

OHCA are associated with higher survival rates than non-exercise-related OHCA. As pre-participation screening of athletes ≤35 years is encouraged,<sup>4</sup> we performed separate analyses for this age group. In the Netherlands, routine pre-participation screening is not mandatory.

## Methods

### Setting

The Amsterdam Resuscitation Studies (ARREST) research group maintains a prospective database of all resuscitation efforts in the Dutch

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province North Holland, covering  $\sim 2671 \text{ km}^2$  and a population of 2.4 million people (1.2 million persons are men; 1.0 million persons are aged 35 years or younger). In case of a medical emergency in The Netherlands, one dials the national emergency number (112), where an operator connects the call to a regional ambulance dispatch centre. If a cardiac arrest is suspected, the dispatcher sends out two ambulances of a single tier. The standard Emergency Medical System (EMS) consists of ambulances manned by a team equipped with a manual defibrillator (LIFEPAK 12, Physio Control, Redmond, WA, USA) and qualified to perform advanced cardiopulmonary life support according to the guidelines of the European Resuscitation Council. Also, the dispatcher sends out a first responder—fire fighters or police officers—equipped with an automated external defibrillator (AED; LIFEPAK 500/ LIFEPAK 1000, Physio Control, Redmond, WA, USA). Many public areas like supermarkets, sport centres, and office buildings have an AED onsite. Trained lay rescuers can attach this AED prior to arrival of the dispatched first responders or ambulance team.

## Data collection

Between 1 January 2006 and 1 January 2009, we prospectively collected data on all persons in whom resuscitation was attempted during an OHCA of suspected cardiac cause. Arrests were considered non-cardiac if the EMS rescuers or the physicians at the hospital could identify a non-cardiac origin such as trauma, drowning, drug overdose, asphyxia, exsanguination, or any other unequivocal non-cardiac condition. Patients ( $n = 79$ ) younger than 10 years or older than 90 years, in whom recreational exercise is unusual, were excluded, as were those ( $n = 52$ ) in whom the physical activity level could not be determined (Figure 1). An OHCA was considered exercise related if the victim was exercising during or shortly before the arrest. Exercise was defined as being physically active during or within 1 h before the arrest in a sport discipline, e.g. bicycling, swimming, tennis, running, and fitness workouts at the gym. Manual labour was not considered exercise. To obtain information on the activity of the victim, all ambulance case report forms and other available documents were independently reviewed by two investigators (J.B. and M.F.d.B.).

## Data sources

Information on OHCA cases (numerator) was obtained from five different sources: (i) the ambulance dispatch centres provided daily reports of OHCA (either suspected or confirmed onsite); (ii) ambulance personnel contacted the study centre after they were either dispatched for a possible OHCA and/or confirmed an OHCA onsite; (iii) first responders (police officers, fire fighters, general practitioners) contacted the study centre if an AED was used; (iv) the resuscitation coordinators (responsible for monitoring of resuscitation efforts, including victims of OHCA) of hospitals in the study region provided the study centre information on victims of OHCA presented to the respective hospitals; and (v) increasingly, through public awareness campaigns, lay persons involved in resuscitation efforts voluntarily informed the study centre about events.

Using this approach, we have never come across a case of OHCA in one of the hospitals in the study region that we had not already identified. Estimates of person-years at risk (denominator) were obtained from the database of Statistics Netherlands (The Hague, The Netherlands).

After each resuscitation attempt, ambulance paramedics routinely send the continuous ECG recording from their manual defibrillators to the study centre by modem, where clock times are synchronized. These data are stored and analysed with dedicated software (Code Stat Reviewer 7.0, Physio Control, Redmond, WA, USA). The paramedics report whether an AED had been connected prior to ambulance arrival.

Study personnel visit the site of the AED shortly after the cardiac arrest to collect the ECG recording of the AED. Rhythms were categorized as shockable (ventricular fibrillation or rapid ventricular tachycardia) or non-shockable (asystole or electromechanical dissociation). Emergency Medical System response time was defined as the time interval between emergency call and attachment of defibrillator. Data items concerning the resuscitation are collected according to the Utstein recommendations.<sup>7</sup> The Medical Ethics Review Board of the Academic Medical Centre, Amsterdam, approved the study and waived the obligation of (written) informed consent.

## Follow-up

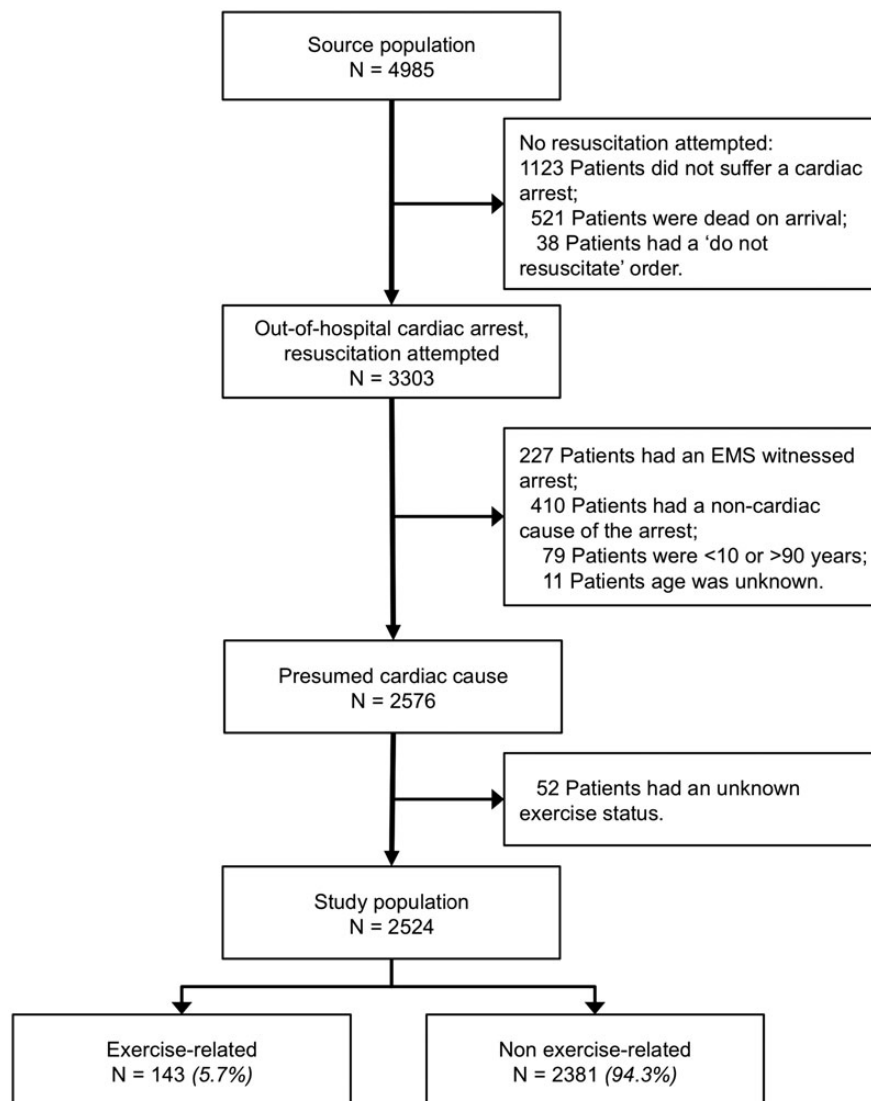
Survival was verified by contacting the hospital of admission and confirmed in the civic registry. Patients who survived to admission were surveyed after the resuscitation attempt by contacting the hospital department. We retrieved in-hospital treatment data and information on neurological outcome at discharge from the hospital charts to determine the cerebral performance category (CPC): good cerebral performance (1); moderate cerebral disability (2); severe cerebral disability (3); coma or vegetative state (4); death (5). A cerebral performance category score of 1 or 2 was classified as favourable neurological status.

## Data analyses

The incidence of OHCA was calculated as the number of events per 100 000 person-years with corresponding 95% confidence intervals. We examined the association between exercise during or within 1 h before the OHCA and both the primary outcome (survival to discharge) and the secondary outcome (neurologically-intact survival, defined as CPC 1 or 2). Survival in relation to exercise was analysed by logistic regression analysis according to the *a priori* identified prognostic factors age, gender, location of OHCA (public place or residential area), bystander witnessed arrest, bystander cardiopulmonary resuscitation (CPR), AED use, initial rhythm (shockable or non-shockable), and EMS response time. We then performed subgroup analyses in patients with a shockable initial rhythm, patients with a shockable initial rhythm at public places, patients aged  $\leq 35$  years, 36–50 years, 51–65 years, and those aged  $> 65$  years. We tested for interaction between age group and exercise. The small number of events in those aged 35 years or less (seven exercise-related OHCA) precluded multivariable analysis in this subgroup. We repeated all analyses for the secondary outcome neurologically intact survival to discharge. Comparisons of continuous variables were made with *t*-tests; the Mann–Whitney *U* test was used when discrete variables were compared; the  $\chi^2$  test was used when binary variables were compared. All statistical tests were two-tailed, and a value of  $P < 0.05$  was considered to be statistically significant. All statistics were performed with SPSS (version 20 for Mac, SPSS, Inc., Chicago, IL, USA).

## Results

During the 3-year study period, resuscitation was attempted in 3303 patients suffering an OHCA in the study area (Figure 1). After exclusion of 227 patients with an EMS witnessed arrest (per the Utstein recommendations),<sup>7</sup> 410 patients with a non-cardiac arrest, 79 patients aged younger than 10 or older than 90 years, 11 patients whose age was unknown, and 52 patients without information regarding physical activity, a study population of 2524 OHCA cases remained. Of these, 143 (5.7%) were exercise related. Patient and resuscitation characteristics are shown in Table 1. Patients suffering an exercise-related OHCA were younger and more likely to be male. Exercise-related OHCA occurred more frequently in public places,



**Figure 1** Flow chart, selection of study subjects.

were more frequently witnessed, had higher rates of bystander CPR and AED use, and were more likely to have a shockable initial rhythm than non-exercise-related OHCA. Ventricular fibrillation, rather than rapid ventricular tachycardia, was the predominant shockable initial rhythm (in 98% of exercise-related OHCA and 96% of non-exercise-related OHCA, respectively). Exercise-related OHCA occurred during or shortly after cycling ( $n = 49$ , 34.3%), tennis ( $n = 22$ , 15.4%), workouts at the gym ( $n = 16$ , 11.2%), swimming ( $n = 13$ , 9.1%), and miscellaneous other activities ( $n = 43$ , 30.1%).

The incidence of exercise-related OHCA was 2.1 per 100 000 person-years and was more than 10-fold higher in men (4.0) than in women (0.3) (Table 2). In persons aged 35 years or younger, seven exercise-related events (six men, one woman) occurred, resulting in an incidence of 0.3 per 100 000 person-years. In persons older than 35 years, the incidence of exercise-related arrest was 3.0 per 100 000 person-years. The incidence of non-exercise-related OHCA was 35.5

per 100 000 person-years and was almost three times higher in men (52.1) than in women (19.4) (Table 2). In persons aged 35 years or younger, the incidence was 2.8 per 100 000 person-years, again higher in men (3.9) than in women (1.7).

Almost half (46.2%) of the 143 persons suffering an exercise-related OHCA survived, compared with 17.2% in non-exercise-related OHCA (Table 3). Exercise-related OHCA survival was three times higher in persons >35 years compared with those aged ≤35 years (47.8 and 14.3%, respectively;  $P = 0.09$ ). Survival after non-exercise-related OHCA was similar for persons aged ≤35 years and those aged >35 years (17.7 and 17.2%, respectively;  $P = 0.97$ ). All survivors of exercise-related OHCA were neurologically intact, which was not the case for those surviving a non-exercise-related OHCA ( $P = 0.01$ ).

Overall, survival after OHCA was significantly higher in patients aged 36–50 years, men, when the arrest occurred in a public location,

**Table 1** Characteristics of the study subjects according to exercise

	Out-of-hospital cardiac arrest		P-value
	Exercise related (n = 143)	Non-exercise related (n = 2381)	
Age, years	58.8 ± 13.6	11–87	<0.001
Age range, years	65.8 ± 14.1	13–89	
Men	133 (93.0)	1719 (72.3)	<0.001
Public location	142 (99.3)	607 (25.5)	<0.001*
Location unknown	0 (0)	1 (0)	
Bystander witnessed arrest	128 (89.5)	1818 (77.3)	0.001*
Bystander witness unknown	0	35 (1.4)	
Bystander CPR	124 (86.7)	1540 (64.7)	<0.001*
Bystander CPR unknown	0 (0)	57 (2.4)	
AED use <sup>a</sup>	51 (35.7)	533 (22.4)	0.001*
AED use unknown	0 (0)	5 (0.2)	
Shockable initial rhythm	114 (79.7)	1104 (46.4)	<0.001*
Initial rhythm unknown	7 (4.9)	59 (2.5)	
EMS response time (min)	9.8 (6.4–12.5)	10.1 (8.0–13.0)	0.350*
Time unknown	5 (3.5)	82 (3.4)	

Values are mean ± SD, median (25–75th percentile) or n patients (%).

<sup>a</sup>Patients with a shockable rhythm in whom an AED was not used were defibrillated by EMS personnel.

\*Adjusted for age and gender.

CPR, cardiopulmonary resuscitation; AED, automated external defibrillator; EMS, Emergency Medical System.

was bystander witnessed, if an AED was used, if the patient had a shockable initial rhythm, and if EMS response time was shorter ( $P < 0.001$ ) (Table 4).

Exercise-related OHCA, when compared with non-exercise-related OHCA, had higher survival rate (OR, 4.12; 95%CI, 2.92–5.82;  $P < 0.001$ ). Given the interaction between age group and exercise (age 35 years or younger  $P = 0.43$ , age 36–50 years  $P = 0.045$ , age 51–65 years  $P = 0.156$ ), an interaction term was included in the final multivariable model (Tables 4 and 5). The association between exercise-related OHCA and survival to discharge remained statistically significant after adjustment for age, gender, location, bystander witness, initiation of bystander CPR, AED use, initial rhythm, and EMS response time (adjusted OR, 2.63; 95%CI

**Table 2** Incidence of exercise-related and non-exercise-related out-of-hospital cardiac arrest in persons aged 10–90 years

	Out-of-hospital cardiac arrest			
	Exercise related		Non-exercise related	
	n	Incidence (95%CI)	n	Incidence (95%CI)
All ages				
All	143	2.1 (1.8–2.5)	2381	35.5 (34.1–37.0)
Men	133	4.0 (3.3–4.7)	1719	52.1 (49.6–54.6)
Women	10	0.3 (0.1–0.5)	658	19.4 (17.9–20.9)
≤35 years				
All	7	0.3 (0.1–0.5)	62	2.8 (2.1–3.5)
Men	6	0.5 (0.1–1.0)	43	3.9 (2.7–5.1)
Women	1	0.1 (0.0–0.3)	19	1.7 (0.9–2.5)
>35 years				
All	136	3.0 (2.5–3.6)	2319	51.9 (49.8–54.0)
Men	127	5.8 (4.8–6.8)	1676	76.4 (72.7–80.0)
Women	9	0.4 (0.2–0.7)	639	28.1 (25.9–30.3)

Incidence rates are per 100 000 person-years (95% confidence interval).

In 2007, the population aged 10–90 years in the province North Holland was 2 231 145, of whom 1 099 724 were men. The population aged 10–35 years was 741 358, of whom 368 185 were men.

**Table 3** Survival rates of exercise-related and non-exercise-related out-of-hospital cardiac arrest

	Exercise related		Non-exercise related		P-value
	n	Survival (%)	n	Survival (%) <sup>a</sup>	
All ages					
All	143	46.2	2381	17.2 (15.8)	<0.001
Men	133	47.4	1719	18.6 (17.0)	<0.001
Women	10	30.0	658	13.5 (12.8)	0.148
≤35 years					
All	7	14.3	62	17.7 (14.5)	1.000
Men	6	16.7	43	20.9 (18.6)	1.000
Women	1	0	19	10.5 (5.3)	1.000
>35 years					
All	136	47.8	2319	17.2 (15.9)	<0.001
Men	127	48.8	1676	18.6 (16.9)	<0.001
Women	9	33.3	639	13.6 (13.0)	0.117

<sup>a</sup>All survivors of exercise-related out-of-hospital cardiac arrest were neurologically intact. The percentages between parentheses in the non-exercise-related group indicate those surviving neurologically intact.

Of four cases (all non-exercise related and >35 years old) sex was not known. P-value calculated with Pearson  $\chi^2$  or Fisher's Exact Test (two-sided) where appropriate.

**Table 4** Determinants of survival to hospital discharge for all out-of-hospital cardiac arrest cases (n = 2524)

	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Exercise	4.12 (2.92–5.82)	<0.001	2.63 (1.23–5.54) <sup>a</sup>	0.011
Age (years)				
≤35	1.24 (0.66–2.37)	<0.498	1.19 (0.54–2.62)	0.665
36–50	2.23 (1.68–2.97)	<0.001	2.24 (1.56–3.22)	<0.001
51–65	1.76 (1.40–2.20)	<0.001	1.42 (1.07–1.89)	0.015
>65 (reference)				
Men	1.63 (1.28–2.09)	<0.001	0.91 (0.68–1.23)	0.536
Public location	3.55 (2.89–4.36)	<0.001	1.78 (1.37–2.31)	<0.001
Bystander witnessed arrest	4.91 (3.37–7.16)	<0.001	2.60 (1.72–3.94)	<0.001
Bystander CPR	1.06 (0.99–1.14)	0.082	1.06 (0.96–1.19)	0.251
AED use	1.50 (1.23–1.82)	<0.001	1.12 (0.88–1.43)	0.355
Shockable initial rhythm	20.39 (14.16–29.38)	<0.001	13.97 (9.49–20.56)	<0.001
EMS response time (per minute)	0.87 (0.84–0.89)	<0.001	0.90 (0.87–0.93)	<0.001

OR, odds ratio; CI, confidence interval; CPR, cardiopulmonary resuscitation; AED, automated external defibrillator; EMS, Emergency Medical System.

Interaction between age group and exercise: age ≤35 years *P* = 0.403; age 36–50 years *P* = 0.045; age 51–65 years *P* = 0.156. An interaction term was included in the final multivariable model.

<sup>a</sup>Survival in relation to exercise was analysed by logistic regression analysis according to all variables mentioned in the table.

1.23–5.54; *P* = 0.01). Analyses using neurological intact survival as an endpoint yielded similar results (univariable analysis: OR 4.56, 95%CI 3.22–6.44; *P* < 0.001; multivariable analysis: OR 2.89, 95%CI 1.37–6.13; *P* = 0.005).

The results of stratified analyses for those with a shockable initial rhythm (to diminish confounding by time interval from collapse to emergency call) and according to age groups are presented in Table 5. The adjusted odds ratio for survival of those suffering an exercise-related OHCA was 3.13 (95%CI, 1.42–6.87; *P* < 0.01) among patients with a shockable initial rhythm (*n* = 1218 of whom 114 were exercise related) and 2.98 (95%CI, 1.29–6.91; *P* = 0.01) among patients with a shockable initial rhythm at public places (*n* = 507, of whom 113 were exercise related). There was no relation between exercise-related OHCA and non-shockable initial rhythm (*n* = 1240 of whom 22 were exercise related): 0 vs. 2.7% neurologically intact survival in exercise and non-exercise-related OHCA respectively.

There was no relation between exercise-related OHCA and survival in the small group of persons ≤35 years (*n* = 69 of whom seven were exercise related; crude OR 0.77, 95%CI 0.08–7.08; *P* = 0.82). Events in the seven exercise-related OHCA victims aged 35 years or younger occurred during: cycling, horse riding, martial arts, tennis, soccer, and swimming. A diagnosis was available (hypertrophic cardiomyopathy, HCM) in only one of those seven persons. Odds ratios for survival in exercise-related OHCA increased with higher age subgroups.

The majority of OHCA survivors underwent coronary revascularisation, with no difference in the rate of percutaneous coronary interventions (PCI) between those surviving an exercise-related OHCA and those whose OHCA was not exercise related (48.5 against 41.3%; *P* = 0.35). Coronary artery bypass grafting (CABG) was

performed more often in exercise-related events (19.7 against 9.7%; *P* = 0.01). Implantation rates of cardioverter defibrillators (ICD) did not differ between survivors of exercise-related and non-exercise-related events (34.8 against 28.3%; *P* = 0.34).

Discussion

In this well-defined prospective cohort of 2524 OHCA patients in the general population, we demonstrate that the incidence of exercise-related OHCA is low, particularly in the young. This study for the first time establishes the favourable outcome of exercise-related OHCA; 46% of victims survive the event compared with 17% of victims of non-exercise-related OHCA. This benefit remains after adjusting for age and the fact that exercise-related OHCA occurred more frequently in public places, were more frequently bystander witnessed, had higher rates of bystander CPR and AED use, and were more likely to have a shockable initial rhythm.

Exercise-related OHCA mainly occurred in men (93 compared with 72% in non-exercise-related OHCA). The male predominance in (exercise related) OHCA is consistent with previous reports.<sup>6,8</sup> It has been attributed to lower sports participation rates and a later onset of coronary artery disease in women (coronary artery disease being the major cause of death in older athletes),<sup>1</sup> but a greater risk of exercise-related OHCA *per se* in men cannot be excluded. The majority (~70%) of cases occurred during cycling, tennis, work-outs at the gym, and swimming, which contrasts with previous Dutch studies in which acute cardiac events (including, but not limited to, OHCA, e.g. myocardial infarction not leading to cardiac arrest) occurred mostly during soccer.<sup>9</sup> The high number of OHCA during cycling in the current study can be explained by the frequent use of the bicycle as a means of transport in The



**Table 5** The influence of exercise on survival to hospital discharge after an out-of-hospital cardiac arrest according to shockable initial rhythm, shockable initial rhythm in a public location, and age groups

	Number of patients		Odds ratio (95% CI)			
	Exercise related	Non-exercise related	Univariable analysis	P-value	Multivariable analysis	P-value
All cases	143	2381	4.12 (2.92–5.82)	<0.001	2.63 (1.25–5.54) <sup>a</sup>	0.011
Shockable rhythm	114	1104	2.62 (1.77–3.88)	<0.001	3.13 (1.42–6.87) <sup>b</sup>	0.005
Shockable rhythm and public location	113	394	1.65 (1.08–2.52)	0.020	2.98 (1.29–6.91) <sup>c</sup>	0.011
Age ≤35 years	7	62	0.77 (0.08–7.08)	0.820		
Age 36–50 years	25	304	2.68 (1.17–6.11)	0.020	0.92 (0.34–2.52) <sup>d</sup>	0.876
Age 51–65 years	69	727	3.56 (2.15–5.90)	<0.001	1.46 (0.75–2.81) <sup>d</sup>	0.263
Age >65 years	42	1288	5.90 (3.15–11.04)	<0.001	2.55 (1.16–5.58) <sup>d</sup>	0.019

<sup>a</sup>Adjusted for age group, gender, location, bystander witnessed arrest, bystander CPR, initial rhythm, AED use, EMS response time, and interaction between age group and exercise.

<sup>b</sup>Adjusted for age group, gender, location, bystander witnessed arrest, bystander CPR, AED use, EMS response time, and interaction between age group and exercise.

<sup>c</sup>Adjusted for age group, gender, bystander witnessed arrest, bystander CPR, AED use, EMS response time, and interaction between age group and exercise.

<sup>d</sup>Adjusted for gender, location, bystander witnessed arrest, bystander CPR, initial rhythm, AED use, and EMS response time.

Netherlands and by the strict definition of sports in the previous studies. Our study explicitly addressed exercise in general rather than focusing on organized sports only.

The incidence (2.1 per 100 000 person-years overall) of exercise-related OHCA in our study is in line with the estimates (0.5–1.7 per 100 000 person-years) obtained in a contemporary French study with a design similar to ours [a nationwide prospective study of sports-related OHCA and sudden death (SD) in the general population from 2005 to 2010, using information from the nationwide emergency medical service and 275 newspapers].<sup>6</sup> Subjects in the French study were also predominantly men (95 vs. 93% in our study), but younger than our OHCA victims ( $46 \pm 15$  vs.  $59 \pm 14$  years). The incidence (0.3 per 100 000 person-years) of exercise-related OHCA in those ≤35 years is low compared with the often quoted incidence of 0.6–1.2 SD per 100 000 competitive athletes per year,<sup>8,10</sup> but very similar to the incidence (0.2 per 100 000 person-years) found in young non-competitive sport participants in the French study. The French documented an incidence of 1 per 100 000 person-years in competitive athletes aged 35 years or younger. This suggests that competitive athletes (generally defined as those participating in an organized sports program requiring regular training and competition) have a higher risk of cardiac arrest than recreational athletes. With the exception of the recent French study, the reported incidence rates of acute cardiovascular events in previous studies<sup>8,10–14</sup> cannot directly be compared with our study due to differences in age, gender, and ethnic distributions across study populations, definition of the source populations (e.g. athletes or persons exercising), methods of identification (autopsy reports, civil mortality registries, newspapers), and the retrospective nature of most studies. Similar issues arise in studies of SCD in the general population.<sup>15</sup> Nevertheless, the overall picture emerging is that fatal exercise-related cardiovascular events in the young are rare.

The survival to hospital discharge after exercise-related OHCA was three times higher in our study group than observed in the aforementioned French study (46.2 vs. 15.7%). In The Netherlands, 80% of the exercise-related cases had a shockable rhythm, compared with

47% in France.<sup>6</sup> Univariate predictors of survival in exercise-related OHCA were similar: younger age, shorter delay to initiation of CPR/defibrillation, bystander witnessed arrest, bystander initiation of CPR, and shockable initial rhythm. As most exercise-related events were bystander witnessed (90 vs. 93% in France), the most likely explanation for the remarkably better survival in The Netherlands relates to the high rate of the initiation of bystander CPR (87%) compared with 31% in France. The highest survival rates ( $\approx 50\%$ ) in France were found in two regions where bystanders initiated CPR in 90% of cases (compared with 87% in our population). Bystander CPR in The Netherlands included AED use in 36% of cases. AED use in France was <1% (personal communication Dr Marijon). Intriguingly, neurological outcome was somewhat better in survivors of exercise-related OHCA. The reason for this observation remains speculative.

As current recommendations advise pre-participation screening of competitive athletes aged 35 years or younger,<sup>4</sup> in whom OHCA is most often caused by inherited cardiac disease (e.g. cardiomyopathies, electrical heart disease),<sup>10,13</sup> we analysed the outcome of exercise-related OHCA using 35 years as a cut-off. In this small group ( $n = 7$ ) of exercise-related OHCA arrest victims survival was low (14%) and outcome was similar to that of subjects whose OHCA was not exercise related (18% survival). It is conceivable that defibrillation is more difficult in persons with inherited cardiac diseases and that lifestyle (including exercise) has a greater impact in those with coronary artery disease. Coronary artery disease accounts for the majority of exercise-related events in older persons,<sup>6</sup> reflected by the high rate of coronary revascularization—almost 70%—in victims surviving exercise-related OHCA in our group. The observation that exercise-related OHCA had a better outcome in higher age groups seems to support this hypothesis.

The better survival rates in those suffering an OHCA while exercising can partly be explained by favourable circumstances (e.g. bystanders that use an AED). Adjusting for these factors, the odds ratio declines from 4.12 to 2.63, but remains significant, still implying a 163% higher chance of survival in those suffering an exercise-related

OHCA. The cardio-protective effects of regular exercise are larger than can be explained by changes in cardiovascular risk factors.<sup>1,16</sup> Exercise may also prevent cardiovascular events by improving (endothelial) vascular function and inducing coronary collateral circulation.<sup>16,17</sup> A recent study in long distance runners suggested that ischaemia due to an imbalance between oxygen supply and demand rather than plaque rupture and coronary thrombosis is responsible for acute exercise-related cardiac events.<sup>18</sup> These effects, perhaps in combination with the higher arousal status of the sympathetic nervous system, may play a role in the more favourable outcome of exercise-related OHCA.

Irrespective of age, sudden death during exercise is a devastating event—whether this occurs during competitive or recreational sports—that invariably leads to calls for prevention. Timely identification of asymptomatic athletes at increased risk of OHCA or prompt resuscitation efforts with the use of an AED if an event occurs are two complementary strategies. Although the focus has been on pre-participation screening of young competitive athletes,<sup>4</sup> the rapidly growing group of middle aged/senior athletes should not be ignored.<sup>5,6</sup> The high survival rate of exercise-related OHCA in our study (and in specific regions in France), combined with known benefits of rapid AED deployment and the encouraging observations from on-site AED programs at sport venues,<sup>19</sup> should lead to widespread implementation of programs to educate about CPR and promote AEDs at sports venues.

Limitations of our study need to be mentioned. In particular, the low number (7) of exercise-related OHCA cases in those aged 35 years or younger, in only one of whom a definite diagnosis (HCM) was available. Recent studies from Scandinavia also reported low absolute numbers of sports-related sudden death ( $n = 15$  in Denmark and  $n = 23$  in Norway) in the young.<sup>10,14</sup> The low numbers (desirable as they are) preclude multivariable modelling and drawing firm conclusions (e.g. regarding odds of survival). We provide an accurate incidence calculation of exercise-related OHCA (numerator) in the general population (denominator). Unfortunately, the exact number of individuals engaged in sports in the Netherlands is not available. According to the 2010 ‘Sports: a lifetime long’ report of the Netherlands Institute for Social Research (Sociaal Cultureel Planbureau, ‘Sport: een leven lang’, figure 3.3, page 54, [www.scp.nl/publicaties](http://www.scp.nl/publicaties)), more than 50% of the Dutch population aged 12–35 years is regularly engaged in competitive and leisure time sports activities. This would imply that the incidence estimate (0.2 per 100 000 years) should at the most be doubled when taking those regularly active as the denominator, to arrive at an incidence estimate of 0.4 per 100 000 person-years in those  $\leq 35$  years.

The observational, population-based nature of our study and the absence of mandatory post-mortem examinations in the Netherlands unfortunately precludes complete ascertainment of information on medical history (e.g. presence of underlying heart disease—electrical heart disease, cardiomyopathy, coronary thrombosis or mere coronary artery disease—, severity of disease (extent of scar tissue), electrocardiograms before and after OHCA), cardiovascular risk factors and physical fitness (intensity and duration of exposure to the exercise) of the OHCA victims. Insight into these factors would be useful to identify mechanisms that are related to better survival following OHCA. The results of this study may not directly be translated to other regions, as the relatively good survival

following OHCA might be partially attributed to public resuscitation campaigns and wide availability of public AEDs in our study region. Similarly, we do not have specific follow-up information on patients who received an ICD (e.g. ICD discharges).

The main strengths of this study are the ascertainment of OHCA patients using strict data collection procedures, the contemporary nature of the data and the incidence of exercise-related OHCA rather than SD only. To our knowledge, we are the first to report a positive relation between exercise-related OHCA and survival to discharge in a large prospective, population-based study. This finding warrants confirmation in other populations and further exploration. Although exercise may trigger an acute cardiac event such as OHCA, our results suggest that the favourable effects of exercise mitigate the paradox of exercise. Regular physical activity remains the cornerstone of every initiative to improve cardiovascular health, but specific symptoms or complaints (e.g. chest discomfort, fainting during exercise, undue fatigue, flu like symptoms) should not be ignored.<sup>1,9</sup>

In conclusion, the incidence of exercise-related OHCA in the general population is low, especially in the young. Cardiac arrests occurring during or shortly after exercise carry a markedly better prognosis (46% survival) than non-exercise-related cardiac arrests in persons  $> 35$  years. Prompt bystander initiation of CPR with the use of an AED is likely to be the key to improve outcome, an observation that should have direct implications for public health programs to prevent exercise-related sudden death.

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