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Sudden cardiac death in marathons: a systematic review

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Abstract

The aim of this systematic review is to summarise the results of cohort studies that examined the incidence of SCD in marathons and to assess the quality of the methods used. A search of the PROSPERO international database revealed no prospective or published systematic reviews investigating SCD in marathons. The review was conducted using studies that reported and characterised the incidence of SCD in people participating in marathons. Studies were identified via electronic database searches (Medline, CINAHL, SPORTDiscus and Google Scholar) from January 1, 1966 to October 1, 2014 and through manual literature searches. 7 studies met the inclusion criteria and were included in this review. 6 of the studies were conducted in the USA and 1 in the UK. These studies covered a 34-year period involving between 215,413 and 3,949,000 runners. The SCD of between 4 and 28 people are recorded in the papers and the reported estimates of the incidence of SCD in marathons ranged widely from 0.6 to 1.9 per 100,000 runners. The proportion of those suffering SCD who were male ranged from 57.1% to 100% and the mean age reported in the papers, ranged from 37 to 48. This review raises 4 methodological concerns over i) collating reports of SCD in marathons; ii) time of death in relation to the marathon; iii) the use of registrants rather than runners in the estimates of sample size and iv) limited detail on runners exercise history. These four concerns all threaten the reliability and interpretation of any estimate of SCD incidence rates in marathons. This review recommends that the methods used to collect data on SCD in marathons be improved and that a central reporting system be established.

Introduction

The aim of this systematic review is to summarise the results of cohort studies that examined the incidence of sudden cardiac death (SCD) in marathons and to assess the quality of the methods used. A search of the PROSPERO international database revealed no prospective or published systematic reviews investigating SCD in marathons.

The health benefits of physical activity are well documented. [1] It has been established that regular physical activity and exercise have powerful prophylactic effects in the primary and secondary prevention of a number of chronic diseases.[2]

Participation in long-distance running races, especially marathons, has increased since the inception of the London Marathon. The inaugural event in 1981 registered <7000 participants whereas the race in 2014 recorded 35,798 finishers.[3] The increase in participation has, in part, been attributed to a greater public awareness of the health benefits of regular exercise.[4] Marathons are big and important events for race organisers, charities, and sponsors alike. A study commissioned by the New York Road Runners Club found the 2010 New York City Marathon was worth $340 million.[5]

Medical and health-care professionals recommend exercise, including running, as a health - enhancing physical activity. Tragically, for a very small number of marathon runners the outcome is SCD. Some have argued that the publicity surrounding these rare events reduces the public's enthusiasm for aerobic exercise.[6,7] A death during a marathon is particularly tragic because "the risk is voluntary, the outcome is catastrophic and the individual may otherwise have lived a long life" [6, p. 1].

Methods

Carney and Geddes [8] define systematic reviews as a "syntheses of primary research studies that use (and describe) specific, explicit and therefore reproducible methodological strategies to identify, assemble, critically appraise and synthesise as relevant issues on a specific topic". Informed by the approach of the Cochrane Library, [9] this systematic review was conducted to identify, appraise, and synthesize all the empirical evidence to date on SCD in marathons, in accordance with prespecified eligibility criteria. By doing so this systematic review adds new insights into the quality of the methodologies used in the selected studies and combines the findings from the selected studies to present amalgamated results.

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Guidelines [10] and prepared to the standards established by the International Prospective Register of Systematic Reviews (PROSPERO).

Search strategy

A systematic, computerized search of the databases Medline, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and SPORTDiscus was performed to identify potentially relevant studies, from inception (1966) until 1October 2014. The database search used combinations of "thesaurus terms" and free text words. Synonym lists were created on the themes of marathon and death. The following combinations of keywords were used: (marathon OR run* OR long distance run*) AND (sudden cardiac death OR sudden death OR cardiac death OR cardiac mortality OR cardiac arrest). The searches in Medline, CINAHL, and SPORTDiscus were restricted to peer-reviewed articles published in English. Google Scholar was also searched in an attempt to identify additional, relevant research using the following search terms: allintitle "marathon" OR "run" AND "sudden cardiac death" OR

“sudden death” OR “cardiac mortality” OR “cardiac arrest”. The results of these searches were combined and duplicates were removed.

Study selection

All search results were first screened on title, abstract, and keywords. Articles were considered relevant, as decided independently by two reviewers if the study met the following selection criteria: (1) participants were marathon runners; (2) an association with cardiac death; and (3) if the study examined data from original research. Disagreements between the two authors regarding the study’s eligibility were resolved by discussion until consensus was reached, or when necessary, a third author had the casting vote. Articles whose abstracts were imprecise with regard to selection criteria were considered for full text analysis.

The reference lists of the articles included following fulltext analysis were screened. This was performed to ensure that no relevant studies were missed, which is of particular importance due to the paucity of published studies in this area.

Assessment of methodological quality

The methodological quality of the studies was independently appraised by two reviewers using the Critical Appraisal Skills Programme (CASP) Cohort Study checklist.[11] Of the 12 main criteria outlined in the CASP Cohort Study checklist, criteria 7, 8, and 12 were omitted due to the qualitative nature of the questions while criteria 6 was not applicable and therefore exempt due to the nature of the studies included in this review. As a result, these criteria were not included in AQ1 the scoring system outlined in Table 1. The other 8 criteria for the

assessment of methodological quality were scored as “yes”, “no”, or “can’t tell” in case of inadequate reporting.

Each criterion that was scored “yes” scored 1 point, a “no” scored 0 points and if an item was unclear then a “?” was used to indicate this, and was treated as a missing case. Due to the sub-questions within criteria 5, the maximum obtainable score was 9. Accordingly, a higher summary quality score (>5) indicates high methodological quality, whereas a summary score ≤5 denotes low methodological quality. The reviewers pilot tested the methodological quality assessment on a subset of two included articles [12,13] for agreement on a common interpretation of the items. The inter-rater reliability of the quality assessment was statistically evaluated during the pilot testing process, and 100% agreement was found between the two reviewers.

Data extraction

Data extraction from the selected studies was performed independently by two reviewers using a standardized extraction form, informed by The Cochrane Collaboration.[14] The data extracted included study design and methods, subject characteristics, and results data relating to SCD incidence. In an attempt to improve agreement in data extraction, the reviewers pilot tested the extraction form on a subset of two included articles.[12,13]

Data analysis

To assess the incidence of SCD in marathons, the incidence rate and 95% confidence intervals (CIs) were extracted from the identified reports, where the data were presented. The reported incidence rates were checked for consistency in calculation, to ensure the rates were consistently calculated and reported to ensure comparability. As differences were found in

some of the calculations, incidence rates and CI s were calculated for the purposes of comparison using The Analytic Tools for Public Health Tool for incidence rates. As it could not be guaranteed that the number of deaths reported in each paper were all unique deaths, the independence of effect sizes assumption required for a meta-analysis could not be assumed and therefore a meta-analysis was not conducted on the data.

Results

Study selection

A total of 52 records were identified through electronic database searches with an additional 22 studies identified through the manual reference list searches. Following the removal of duplicate records, the total number of records screened was 59. Of the 59 records screened, 48 were not relevant and were subsequently excluded, leaving 11 full-text articles to be assessed thoroughly for eligibility (Figure 1). Of the 11 potentially relevant studies, 4 were excluded; 2 of these studies did not evaluate SCD incidence and 2 were correspondence papers and did not therefore include primary data. Seven studies met the selection criteria and were included in this review.

Figure 1 here

Study quality

Table 1 shows details of the methodological quality assessment of the seven included studies. Out of a maximum score of 9, the range of quality scores was between 3 and 7 with a mean score of 5.66 ± 1.75. All studies except Webner et al.'s study [15] were recruited from the cohort in an acceptable way – the retrospective design adopted in Webner et al.'s study may have led to recall bias. Webner et al. [12] and Kim et al. [13] did not report exposure adequately. For example, it is difficult to be sure that all race registrants actually competed in the event. All seven studies failed to identify all important confounding factors and therefore did not take this into account in their design or analysis. For example, they did not consider lifestyle factors like diet. Four of the seven studies were found to report trustworthy results when considering the design and methods adopted.[11] This was unclear in one study due to inadequate reporting while the results of two of studies were found to be unreliable due to the

methodologies used. All studies results could be applied to the population of marathon runners, despite variation in incidence rates across the studies. Overall, five studies were found to be of high methodological quality (71%), whereas two were found to be of low methodological quality (29%).

Table 1 here

Demographic data

As shown in Table 1 the studies included spanned a 34-year period, ranging from 1976 to 2010. Of the seven papers included in this review, six of the studies were conducted in the USA and one in the UK. The number of marathons included in the analyses in the papers ranged from 2 to 6 341 and included between 215,413 and 3,949,000 race registrants/finishers. One of the included studies [13] included race registrants in their sample and not competitors which may lead to an overestimation in the number of "runners".

Incidence of SCDs and demographic information on the deceased

The number of deaths ranged from 4 to 28, which yielded incidence rates ranging between 0.6 and 1.9 per 100,000, see Table 2. Where presented in the papers, we also documented the demographic information on the deceased, also presented in Table 2. The proportion of those suffering SCD who were male ranged from 57.1% to 100% and the mean age reported in the papers ranged from 37 to 48. Two of the papers provided the age range of the deceased, the youngest age reported was 19 and the oldest 68.

Table 2 here

Discussion

This study demonstrates the usefulness of a systematic review to "identify, appraise and synthesize all the empirical evidence that meets pre-specified eligibility criteria to answer a given research question".[9] A systematic review is more rigorous than a standard literature review which Rousseau et al. [18] state are "often position papers, cherry-picking studies to advocate a point of view". Given the importance of understanding the phenomenon of SCD in marathons, it is recommended that a systematic review of the literature is conducted every 5 years.

While a systematic review has been conducted on troponin elevation in marathon runners [19] to the best of the authors' knowledge, this is the first systematic review to assess the incidence of SCD in marathons. A finding of this review is that a very small number of participants died suddenly during or immediately after running a marathon.

The wide-ranging estimates of SCD in marathons published in the studies highlight the uncertainty surrounding the actual incidence of SCD in marathons. Discrepancies between the estimates of SCD may reflect the inconsistencies in the methodological approaches adopted and the quality of the studies. These issues are addressed in more detail later in this discussion.

While the included studies reported more men than women dying from SCD in marathons, care should be taken not to ignore the risk to women. If the demographics of participants change over time with more women taking part in marathons then the profile of those at risk may change. The included studies looked back to a time when more men than women ran marathons and in the future this might change.

The age distribution of marathon runners is wide ranging. However, SCD in marathon runners is most prevalent in those between 30 and 50 years of age. Roberts, Roberts and Lunos [15] report that the marathon population is ageing. They found that in 1982 only 25% of male marathon runners and 15% of female marathon runners were over 40 years of age compared to 45% and 29% in 2009. These findings suggest two things. First, that there are greater numbers of people in the "higher risk" age group running marathons now than in the past. Second, that as over time the demographic profile of those participating in marathons has changed care must be taken when comparing data taken from marathons in the past with current events. The studies reported here did not control for age and gender. Future studies should do so.

While the systematic review used the best available evidence, the methods used in the included studies demonstrate there is no standardized methodology for collecting data on SCD in marathons. Specifically, this review raises four concerns over (1) collating reports of SCD in marathons; (2) time of death in relation to the marathon; (3) the use of registrants rather than runners in the estimates of sample size; and (4) limited detail on runners exercise history. These four concerns all threaten the reliability and interpretation of any estimate of SCD incidence rates in marathons.

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history. These four concerns all threaten the reliability and interpretation of any estimate of SCD incidence rates in marathons.

As we argue that systematic reviews are an important method to amalgamate the findings from different studies, researchers should adopt procedures that enable the accurate collating of reports on SCD in marathons. When systematically reviewing the papers it was impossible to identify whether the deaths reported were unique incidences of SCD or whether there was considerable overlap between studies. For example, the Maron et al. [17] paper drew upon data from both the Marine Corps and Twin Cities marathons from 1976 to 1994; in addition, Roberts, Roberts, and Lunos [15] also drew upon the same marathons but from 1982 to 2009. Therefore, we are assuming that there will be some repeated reporting of incidence rates across these two papers. For this reason, a mean incidence rate was not calculated, as this would lead to inflation in the incidence rate which would exaggerate the risk.

There is a fundamental methodological inconsistency within the literature on the definition of what constitutes a marathon -linked SCD . Matthews et al. [16] included deaths that occurred up to 24 hours post-race, whereas Kim et al. [13] included only those occurring within 1 hour of race completion. We do not feel qualified to determine what the time of death in relation to the marathon should be to be categorized as an SCD but encourage researchers in this area to reach on consensus on this point.

Kim and colleagues [13] included all race registrants in their sample rather than race finishers. It has been reported that there can be substantial differences in the number of people who register and those who finish or participate in a marathon. The 2003 Chicago Marathon recorded 40,000 race registrants yet only 33,000 finishers. [20] The use of race

registrants and retrospective design in Kim et al. [13] may provide an explanation for the lower incidence rate reported as many of the race registrants may not have participated on race-day.

A better understanding of SCD in marathons could be achieved if researchers included more detail on the athletic and medical history of the deceased. For example, were they elite athlete, performance runners, or recreational joggers?

The lack of a central register for the reporting and recording of SCD in marathons is limiting the quality of research in this area. For example, all studies except Maron et al. [17] did not publish complete clinical data on all cases of SCD. A recommendation following this review is that a reporting register be set up to ensure complete and thorough reporting of all SCDs and SCAs in long-distance running events. Consequently, future research in this area could be conducted through accessing and utilizing a valid and reliable data source. Following this, more dependable research investigating the incidence of SCD in marathons could be conducted.

It was not the aim of this research to explore the causes of SCD in marathons, or means of preventing SCD, as other research has begun to address these issues. Siegel [21, p. 3] has recently concluded that “a prudent strategy for susceptible runners would be to take prerace low-dose aspirin on approval by their physician”. The Journal Circulation has published articles and letters on the theme “Can Intensive Exercise Harm the Heart?” which are making a contribution to the issues raised in this review.[22]

Conclusions

The studies included in this systematic review reported that a very small number of participants died suddenly during or immediately after running a marathon. The actual estimates ranged widely across the studies. More men are reported to have died than women and SCD in marathon runners is most prevalent in those aged between 30 and 50.

Four methodological issues were identified which if addressed could improve research in this area. It is recommended that that a reporting register be set up to ensure complete and thorough reporting of all SCDs and SCAs in long-distance running events.

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Figure 1. PRISMA (2009) Flow Diagram [10]

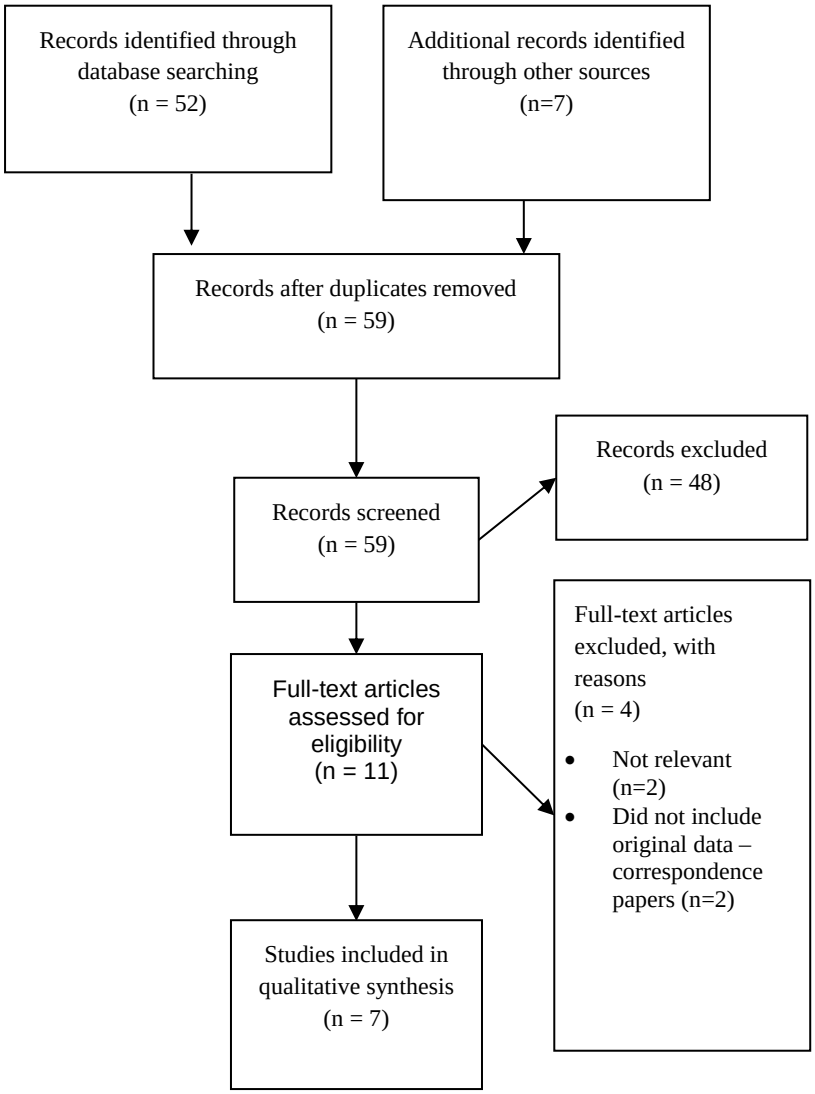

Table 1. Study Characteristics

Publication	Method of Estimation	Quality Rating[1]	Country	Years	Sample Size	Number of Marathons	Number of Deaths
Matthews et al (2012)	Racing and news databases, direct contact with race directors	7	USA	2000-2009	3,718,336	3,184 unique marathons (overall number of 6,341 races)	28
Redelmeier & Greenwald (2007)	Local newspapers, contact with race directors and local news media	7	USA	1975-2004	3,292,268	Screened 328 and selected a random sample of 26	26
Roberts, Roberts & Lunos (2015)	Race records, personal communication and newspaper accounts.	7	USA	1982-2009	548,092	2	7
Maron et al (1996)	Medical records, athletic history and interviews	7	USA	1976-1994	215,413	2	4
Pedoe (2007)	Data from St John Ambulance Brigade, hospitals receiving casualties and contact with coroner, autopsy attendance and postmortem	6	UK	1981-2006	650,000	26 London Marathons	8
Kim et al (2012)[2]	Interviews, medical records and postmortem data	4	USA	2000-2010	3,949,000	N/R	23
Webner et al (2012)	Web-based survey sent to marathon directors	3	USA	1976-2009	1,710,052	83[4]	10

[1] Maximal obtainable score = 9
[2] The sample size reported in Kim et al. [20] relates to race registrants and not finishers as reported in the other included studies.
[3] Kim et al. [20] did not report the precise number of SCDs in marathons, although incidence of cardiac arrest resulting in death in marathon runners was reported. Therefore, n=25 was calculated based on the sample size and incidence/100,000 reported.
[4] 83 marathon directors returned the survey, therefore we are assuming that the marathon directors were each reporting on a different marathon
Abbreviation: N/R = Not reported

Table 2: Sudden cardiac deaths, incidence rates and demographic information on deceased

Publication	Number of Deaths	Age of Deceased				Sex	Reported in the paper			Calculated for the purposes of this study		
		Range	Mean age of deceased	Median	%		Incidence	Lower CI 95%	Upper CI 95%	Incidence	Lower CI 95%	Upper CI 95%
Webner et al (2012)	10	N/R	N/R	N/R	N/R	N/R	0.58	N/R	N/R	0.6	0.4	0.9
Kim et al (2012)	25	N/R	33.9	N/R	N/R	19 (83%) male 6 (24%) female	0.63	0.41	0.93	0.6	0.4	0.9
Matthews et al (2012)	28	22-68	N/R	41.5	50% deaths (n=14) occurred in those under 45	22 (78.6) men 6 (21.4) women	0.75	0.38	1.13	0.8	0.5	1.1
Redelmeier & Greenwald (2007)	26	N/R	41	N/R	N/R	21 (81%) men 5 (19%) women	0.8	0.5	1.1	0.8	0.5	1.2
Pedoe (2007)	8	N/R	48	N/R	N/R	100% (n=8) male	1.25	N/R	N/R	1.2	0.5	2.4
Roberts, Roberts & Lunos (2013)	7	N/R	NR	N/R	N/R	4 (57.1) men & 3 (42.9) women	1.3	N/R	N/R	1.3	0.5	2.6
Maron et al (1996)	4	19-58	37	N/R	N/R	3 (75%) men & 1 (25%) woman	N/R	N/R	N/R	1.9	0.5	4.8

Abbreviation: N/R = Not reported