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Incidence of Sudden Cardiac Arrest and Death in Young Athletes and Military Members: A Systematic Review and Meta-Analysis

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Objective: To evaluate the quality of the evidence on the incidence of sudden cardiac arrest (SCA) and sudden cardiac death (SCD) in athletes and military members and estimate the annual incidence of SCA and SCD.

Data Sources: We searched MEDLINE, Embase, Cochrane CENTRAL, Web of Science, BIOSIS, Scopus, SPORTDiscus, PEDro, and ClinicalTrials.gov from inception to dates between February 21 and July 29, 2019.

Study Selection: Studies in which the incidence of SCA, SCD, or both in athletes or military members aged <40 years was reported were eligible for inclusion. We identified 40 studies for inclusion.

Data Extraction: Risk of bias (ROB) was assessed using a validated, customized tool for prevalence studies. Twelve had a low ROB, while the remaining 28 had a moderate or high ROB. Data were extracted for narrative review and meta-analysis.

Data Synthesis: Random-effects meta-analysis was performed in studies judged to have a low ROB in 2 categories: (1) 5 studies of regional- or national-level data, including athletes at all levels and both sexes, demonstrated 130 SCD events with a total of 11 272 560 athlete-years, showing a cumulative incidence rate of 0.98 (95% CI = 0.62, 1.53) per 100 000 athlete-years and high heterogeneity ($I^2 = 78\%$) and (2) 3 studies of competitive athletes aged 14 to 25 years were combined for a total of 183 events and 17 798 758 athlete-years, showing an incidence rate of 1.91 (95% CI = 0.71, 5.14) per 100 000 athlete-years and high heterogeneity ($I^2 = 97\%$). The remaining low-ROB studies involved military members and were not synthesized.

Conclusions: The worldwide incidence of SCD is rare. Low-ROB studies indicated the incidence was <2 per 100 000 athlete-years. Overall, the quality of the available evidence was low, but high-quality individual studies inform the question of incidence levels.

PROSPERO Registration: CRD42019125560

Key Words: sport, sudden death, cardiology, exercise

Key Points

- Authors of several published articles presented a clear picture of the estimate of sudden cardiac arrest and sudden death in athletes and military members, but the literature overall demonstrated a substantial risk of bias: only 12 of 40 included articles had a low risk of bias.
- Meta-analysis showed that sudden cardiac death was rare overall in athletes, with synthesis of high-quality, large population-level studies demonstrating a rate of 0.98 (95% CI = 0.62, 1.53) per 100 000 athlete-years and synthesis of more focused studies of competitive younger athletes demonstrating a rate of 1.91 (95% CI = 0.71, 5.14) per 100 000 athlete-years. Heterogeneity was high in both meta-analyses.

Sudden cardiac arrest (SCA) leading to death has been shown to be the leading medical cause of death in young competitive athletes.[1] Exercise and physical activity in athletes are thought to lead to episodes of arrhythmia and then to sudden death.[2] Screening athletes using an electrocardiogram (ECG) to prevent SCA and sudden cardiac death (SCD) has become a controversial topic in sports medicine[3,4] when balancing the effectiveness of screening for a low-incidence condition with the desire to prevent cardiac arrest in athletes. Authors have pointed out that the overall burden of SCD remains low, around 1 event per 100 000 athletes per year or less,[3] whereas others[5] believe the incidence of SCA and SCD to be chronically undercounted and have suggested that screening may decrease the incidence of SCA and SCD. A lack of consensus on methods used to attribute sudden deaths to cardiovascular causes further confuses the topic with calls for uniform reporting methods to address these concerns.[6] Surveys of high schools and universities,[7,8] searches of newspaper and web-based (all lc) reports,[9,10] use of national health and autopsy records,[11–13] catastrophic insurance records,[14,15] and reporting on nontraumatic deaths in the military[16–18] have been performed to determine incidence rates of SCA and SCD. The resulting estimates have varied widely, and although the validity of these different attempts has been questioned,[2–4] existing data and their quality have not been adequately or systematically assessed.

One systematic review[19] has been published on the incidence of "sports-related" SCD. The review was not preregistered, and the researchers did not report their methods according to existing reporting guidelines or assess the quality of evidence, resulting in more questions than answers. The United Kingdom National Screening Committee[20] reviewed data on incidence and screening in the young (age range, 12–39 years) and produced recommendations for practice. We are not aware of a comprehensive, preregistered, peer-reviewed systematic review of the evidence base for the incidence of SCA and SCD in young people (age ≤40 years) participating in regular exercise. Understanding the existing evidence on the epidemiology of SCA and SCD and its quality is important when considering professional body recommendations[2,21–25] for screening athletes using ECGs for conditions that may cause such events. Our objectives were to identify publications reporting on the incidence of SCA and SCD in athletes and military members aged ≤40 years, assess the quality of the evidence, and synthesize population-level incidences of SCA and SCD.

METHODS

This review is one portion of a systematic review with 2 objectives: (1) to identify the incidence of SCA and SCD in young athletes and military members and (2) to identify the effect of ECG screening in this population on SCA and SCD,[26] which is being published as a separate paper. The project was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses[27] guidelines and was registered with PROSPERO on March 18, 2019 (CRD42019125560). The full protocol and deviations from this protocol are available in Supplemental Materials 1 and 2, respectively, available online at http://dx.doi.org/10.4085/1062-6050-0748.20.S1.

Data Sources and Searches

The search strategy was designed with a medical librarian (M.S.) and combined the dual objectives of the project into a single search (Supplemental Material 3). Searches were performed using MEDLINE, Embase, Cochrane CENTRAL, Web of Science, BIOSIS, Scopus, SPORTDiscus, and PEDro between February 21 and March 1, 2019, and ClinicalTrials.gov on July 29, 2019, for available articles. Relevant review articles and position statements were hand searched for eligible articles,[2,5,19] and articles that were not identified in the online search but reported incidence rates were selected for screening. Language of publication and date were not limited. Conference abstracts, published abstracts, and full-text publications were included in the review.

Study Selection

Cohort studies, randomized controlled trials or other nonrandomized controlled studies, and survey studies that reported the incidence of SCA, combining both incidents of SCA and SCD or SCD alone, in athletes or military members aged ≤40 years were eligible for inclusion. Historical controlled trials included a control group in which researchers compared cohorts with data collected before (historical control group) and after (intervention group) the initiation of ECG screening in their country or organization. We selected an age cutoff of 40 years because of the increased incidence of coronary artery disease as a cause of SCA and SCD with increasing age and the desire to focus on causes other than coronary artery disease.[5,28] When multiple reports were published on 1 dataset, only the most recent or complete report was included.[11,29–34] For published articles in which the authors characterized their methods as prospective or retrospective, we used the authors' determination of the methods. When the methods were not explicitly stated, we decided whether the investigation was retrospective or prospective and, in some cases, added that a database was used for the study when the authors used a registry or database of information collected at least partially in a prospective fashion. Studies in which the authors did not report the incidence rate as an outcome were included if they provided a rate or data from which an incidence rate could be calculated.[11,33–40] When authors of the study reported events confirmed as SCA or SCD and suspected cases of SCA or SCD, only the confirmed cases were included in data syntheses.[10,16,33,41,42] In 1 case, the authors[32] used a multiplier to address concerns about the cases of SCA and SCD (numerator) identified in their study, and in many cases,[14,15,43,44] authors reporting on high school athletes in the United States used a calculation to transform individual sport participation numbers to total athlete-years eligible for inclusion (denominator). In all of these cases, we used the number presented by the authors. When age groups or athletes eligible for inclusion in our review were given as percentages of the total reported by the authors, the percentage was used to calculate the number eligible for this review.[37,38] We used the following formula to calculate either the numerator or denominator when the number of cases or person-years was not explicitly detailed: (total number of events/total number person years) $\times$ 100 000 $=$ incidence rate per 100 000 person-years.

Independent dual screening and selection of studies was performed by a team of 4 reviewers (A.L., N.P., C.M., and V.L.). The primary author (A.L.) screened all abstracts, titles, and full-text articles and was involved in resolutions of all disagreements at each stage of study selection. The other 3 reviewers dual screened all abstracts and titles and reviewed 90% ($n = 290$) of the full-text articles because of resources and timing. Disputes or questions arising from screening abstracts or full-text articles were settled by oral or electronic communication among screeners.

Data Extraction and Quality Assessment

Data extraction and evaluation of risk of bias (ROB) was performed for all eligible articles by the lead author (A.L.); 20 of the 40 eligible articles were independently assessed and extracted by a second person (N.P., V.L., or C.M.), and the remaining 20 individually assessed and extracted articles were checked by a senior author (D.N.). Disagreements were resolved by discussion of the 2 involved parties. Risk of bias was assessed using a validated tool developed to assess prevalence studies[45] and customized for the purposes of this review. We considered prospective studies to have the highest level of evidence. Retrospective projects using databases with largely prospectively collected data were also considered to have higher-quality evidence. Both the ROB tool and the data-extraction guide are included in Supplemental Materials 1 and 4.

Data Synthesis and Analysis

The primary outcome was the reported incidence rates of SCA and SCD in competitive athletes and active-duty military members aged ≤40 years. *Competitive athletes* were considered those participating in athletics of any form or level, including scholastic, recreational, club, collegiate or university, and professional in or out of season. Active-duty military members were included because of the high level of activity that is required of them, the similar age profile, and interest in preventing SCA and SCD. Prespecified subgroup analysis was planned by age, sex, race, and type of sport or military member, and level of sport (definitions provided in subgroup analysis in Supplemental Material 5). Analysis was performed using the meta[46] and metafor package[47] in R statistical software (The R Foundation).[48] A random-effects, generalized linear mixed model was used for meta-analysis. Summary findings are presented as events of SCA and SCD per 100 000 person-years with 95% CIs.

Heterogeneity was assessed using I^2 and χ^2; prespecified levels of heterogeneity for I^2 were as follows: <30%, *low*; 30% to 70%, *moderate*; and >70%, *high*. A P value of ≤.10 for the χ^2 statistic indicated statistical heterogeneity. Assessment of publication bias of the studies included was planned using funnel plots when ≥10 studies were pooled. Sensitivity analyses were planned, if necessary, to evaluate heterogeneity in the results.

RESULTS

Study Selection and Characteristics

After removing 10 780 duplicates, we identified 20 048 records through the search, and 11 further articles were added after the hand search. At the time of screening, we were aware of an important unpublished cohort, which we had elected to include in the final analysis after its publication in 2020.[44] A total of 20 060 abstracts were screened, and 323 full texts were assessed for inclusion, of which 40 studies met the criteria (Figure 1). The characteristics of the included studies are provided in Supplemental Material 6, and selected details are given in Table 1 (notable excluded studies are included in Supplemental Material 7).

A total of 34 studies included athletes, ranging from youth to professional levels. Articles included were on athletes from the United States (n = 16),* Europe (n = 13),† multiple countries (n = 1),[41] Canada (n = 1),[12] Argentina (n = 1),[37] Israel (n = 1),[9] and Australia (n = 1).[51] Five studies included military members: 4 in the United States[16–18,42] and 1 in Finland.[33] A study focusing on firefighters in the United States[49] was also included because of the participants' similarity to military members, and this research was grouped with military studies. Authors of 13 (33%) studies used a retrospective cohort design‡; 9 (23%) used a retrospective cohort design and databases or registries§; 6 (15%) used a prospective design[11,35,36,44,52,55]; 9 (23%) used a prospective design and databases or registries.|| Authors of 3 (8%) studies conducted surveys: 2 cross-sectional surveys[7,8] and 1 recurring annual survey.[37] Authors of 10 of the studies reported extractable data in men only.# In 5 studies, a large proportion of the included cohort was male.[16–18,42,50] Authors of 2 studies[37,41] did not include details about sex in their methods but were presumed to include either all males or a high proportion of males. Further details including ages and levels of sport are available in Table 1.

Risk-of-Bias Assessment and Quality Assessment

We determined that 13 (33%) studies presented a low overall ROB**; 10 (25%), a moderate ROB††; and 17 (43%), a high ROB.‡‡[8] Reviewers agreed on the overall ROB in 18 of the 20 studies that they dual reviewed. Of the studies considered to have a low ROB, 5 pertained to military members[16–18,42,49]; although all were retrospective, 4 were retrospective reviews of data collected in a prospective fashion.[16,17,49] Similarly, the 8 low-ROB articles on athletes included 5 prospective studies[1,11,30,44,50] and 3 retrospective studies on prospectively collected data.[12,13,29] Further details on ROB judgement of individual studies can be found in Table 2, with explanations for each study provided in Supplemental Material 6.

Study Findings and Data Synthesis

The studies included presented substantial clinical, statistical, and methodologic heterogeneity. Incidence levels of SCD ranged from 0.02 to 89.05 per 100 000 person-years (Figure 2). Studies in which the authors reported SCA had incidence levels ranged from 0.94 to 63.03 per 100 000 person-years (Figure 3).

Meta-analysis was performed only on studies considered to have a low ROB. Studies in which the authors included athletes' data collected at a population level[11–13,29,30] were combined separately from studies in which the authors focused on broad groups of competitive athletes aged <25 years.[1,44,50] The population-based studies had a point estimate of 0.98 (95% CI = 0.62, 1.53) SCDs per 100 000 athlete-years and high heterogeneity (Figure 4). After we removed the study by Corrado et al,[30] which was an outlier, sensitivity analysis revealed that heterogeneity in the estimate decreased from an I^2 of 78% to 0% and changed the point estimate to 0.90 (95% CI = 0.72, 1.13) SCDs per 100 000. Studies of competitive athletes only had a point estimate of 1.91 (95% CI = 0.71, 5.14) SCDs per 100 000 and high heterogeneity (Figure 4). It is notable in this meta-analysis that Peterson et al[44] only provided extractable detail from high school student-athletes on SCD events while offering detail only on a combination of university and high school athletes for SCA events. Sensitivity analysis involving removal of the study by Malhotra et al,[50] who included primarily male professional soccer players in the United Kingdom, and leaving 2 studies in which the authors included a broad sample of both male

*References 1, 7, 8, 10, 14, 15, 34, 36, 40, 43, 44, 52, 53, 56, 58, 59.
†References 1, 13, 29–32, 35, 38, 39, 50, 54, 55, 57.
‡References 9, 14, 15, 18, 31, 33, 38, 39, 41, 51, 53, 54, 59.
§References 12, 13, 16, 17, 29, 32, 42, 49, 57.
||References 1, 10, 30, 34, 40, 43, 50, 56, 58.
#References 31–33, 38–40, 49, 51, 57, 58.
**References 1, 11–13, 16–18, 29, 30, 42, 44, 49, 50.
††References 7, 10, 14, 32, 33, 39, 43, 51–53.
‡‡References 9, 15, 31, 34–38, 40, 41, 54–59.

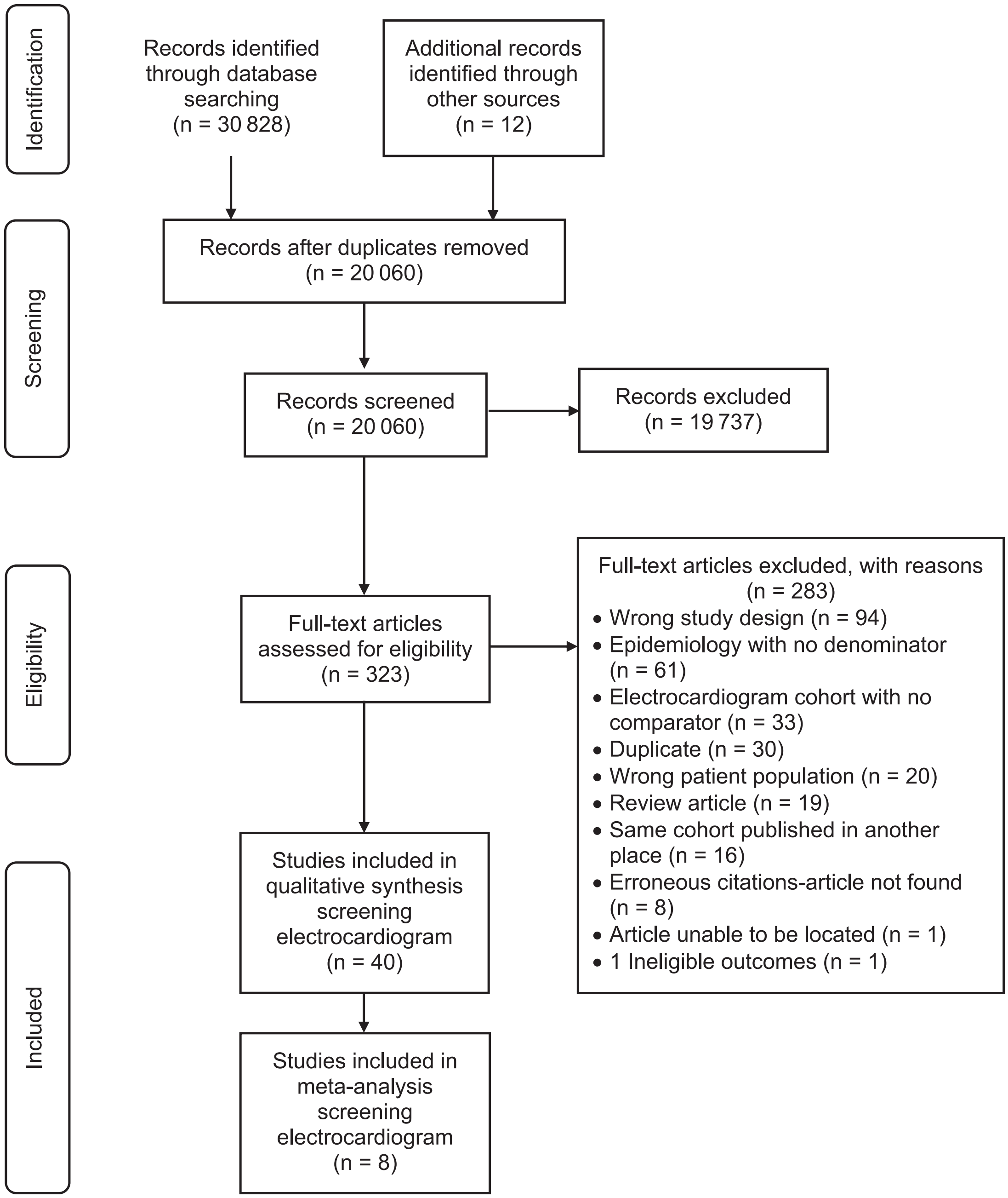


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.[27]

and female scholastic and university-level athletes, did not alter the heterogeneity present but decreased the point estimate to 1.14 (95% CI = 0.59, 2.22).

We elected not to perform synthesis of the low-ROB military studies. The populations of 2 studies[16,17] included substantial overlap of participants, with very different point estimates for SCD of 2.91[16] versus 0.98[17] per 100 000 military-years. The authors of the remaining 2 studies demonstrated substantial clinical heterogeneity in the population, with 1 study[18] dating back nearly 40 years before the other included studies, and the other included American firefighters.[49] Our reported rates for the papers from Koskenvuo[33] and Eckart et al[16,42] included only the deaths confirmed as SCD rather than deaths that were suspected to be SCD, which may have led to an underestimate of the true incidence in this population. The point estimates of the low-ROB studies in the military ranged from 0.98 in the most recent publication[17] to 11.36 SCDs per 100 000 person-years in the oldest.[18]

Inspection of studies in which the authors reported SCD in the moderate- and high-ROB categories were largely in line with the meta-analyses in the low-ROB studies. Of the 27 studies, 18§§ reported rates <2.00 per 100 000 athlete-years. The remaining 9 studies|||| had estimates that ranged up to 89.05 per 100 000 athlete-years. Three[36,38,39] of these were studies with no events, so the estimates should be taken with caution.

§§*References 7, 8, 10, 14, 15, 31, 34, 37, 40, 41, 43, 52, 53, 55–59.*
||||*References 9, 32, 33, 35, 36, 38, 39, 51, 54.*

Table 1. Characteristics of Included Studies Continued on Next Page

Study (Year)	Design	Population (Open) Versus Known (Closed) Cohort	Type of Cardiac Deaths	Method of Case Identification	SCA or SCD Reported	Category of Sport or Activity[a]	Level of Sport or Activity[a]	ECG Screened	Age, Range or Mean, y	Sex	Study Length, y	Risk of Bias
Phillips et al[18] (1986)	Retrospective cohort	Known	Exertion	Autopsy reports	SCD only	Military	Military	No	17–28	M and F	6	Low
Eckart et al[42] (2004)	Retrospective cohort with database	Known	All	Combined autopsy or other official records (eg, medical, military, athletic body)	SCD only	Military	Military	No	17–35	M and F	3.3	Low
Corrado et al[30] (2006)	Prospective cohort with database	Population	All	Combined media reports or autopsy and medical records	SCD only	Multiple	Competitive	Portion	12–35	M and F	24	Low
Holst et al[13] (2010)	Retrospective cohort with database	Population	Exertion	Death certificate	SCD only	Soccer	Competitive	ND	12–35	M and F	12	Low
Eckart et al[16] (2011)	Retrospective cohort with database	Known	All	Combined autopsy or other official records (eg, medical, military, athletic body)	SCD only	Military	Military	No	18–34	M and F	1	Low
Marijon et al[11] (2011)	Prospective cohort	Population	Exertion	Combined media reports or autopsy and medical records	SCD (SCA included in SCD count)	Multiple	Competitive	No	10–35	M and F	26	Low
Risgaard et al[29] (2014)	Retrospective cohort with database	Population	Exertion	Combined media reports or autopsy and medical records	SCD only	Multiple	Competitive	No	12–35	M and F	9	Low
Farioli et al[49] (2015)	Retrospective cohort with database	Population	All	Combined autopsy or other official records (eg, medical, military, athletic body)	SCD only	Military	Military	No	18–34	M	25	Low
Harmon et al[1] (2015)	Prospective cohort with database	Population	All	Combined media reports or autopsy and medical records	SCD only	Multiple	University	ND	17–24	M and F	26	Low
Smallman et al[17] (2016)	Retrospective cohort with database	Known	Exertion	Combined autopsy or other official records (eg, medical, military, athletic body)	SCD only	Military	Military	No	<35	M and F	10	Low
Landry et al[12] (2017)	Retrospective cohort with database	Population	Exertion	Combined autopsy or other official records (eg, medical, military, athletic body)	SCA and SCD	Multiple	Multiple	ND	12–35	M and F	32	Low
Malhotra et al[50] (2018)	Prospective cohort with database	Known	All	Combined autopsy or other official records (eg, medical, military, athletic body)	SCD only	Soccer	Elite	Yes	15–17 at time of screen	M and F	15	Low
Peterson et al[44] (2020)	Prospective cohort	Population	All	Combined autopsy or other official records (eg, medical, military, athletic body)	SCA and SCD	Multiple	Multiple	ND	11–29	M and F	4	Low
Koskenvuo et al[33] (1976)	Retrospective cohort	Known	ND	Combined autopsy or other official records (eg, medical, military, athletic body)	SCD only	Military	Military	No	18–24	M	6	Moderate
Maron et al[14] (1998)	Retrospective cohort	Population	Exertion	Autopsy reports	SCD only	Multiple	Scholastic	No	13–19	M and F	1	Moderate
Young et al[51] (1999)	Retrospective cohort	Population	Exertion	Autopsy reports	SCD only	Australian football	Competitive	No	15–37	M	3	Moderate
Drezner et al[7] (2005)	Survey	Population	ND	Facility event report (eg, school records)	SCA and SCD	Multiple	Elite	ND	17–24	M and F	0.5	Moderate
Maron et al[43] (2013)	Prospective cohort with database	Population	All	Combined media reports or autopsy and medical records	SCD only	Multiple	Scholastic	No	12–18	M and F	3	Moderate

Table 1. Continued From Previous Page

Study (Year)	Design	Population (Open) Versus Known (Closed) Cohort	Type of Cardiac Deaths	Method of Case Identification	SCA or SCD Reported	Category of Sport or Activity[a]	Level of Sport or Activity[a]	ECG Screened	Age, Range or Mean, y	Sex	Study Length, y	Risk of Bias
Toresdahl et al[52] (2014)	Prospective cohort	Known	All	Interview family or eyewitness	SCA and SCD	Multiple	Scholastic	No	14–19	M and F	11	Moderate
Harmon et al[10] (2016)	Prospective cohort with database	Population	All	Media reports	SCA and SCD	Multiple	Scholastic	No	14–19	M and F	10	Moderate
Grani et al[32] (2016)	Retrospective cohort with database	Population	Exertion	Autopsy reports	SCD only	Multiple	Multiple	Portion	10–39	M	7	Moderate
Maron et al[53] (2016)	Retrospective cohort	Population	All	Autopsy reports	SCD only	Multiple	Multiple	No	14–23	M and F	20	Moderate
Berge et al[39] (2018)	Retrospective cohort	Known	All	Media reports	SCA and SCD	Soccer	Elite	Yes	18–40	M	15	Moderate
Assanelli et al[35] (1995)	Prospective cohort	ND	ND	Medical records	SCA and SCD	Multiple	Multiple	Yes	Unclear	M and F	5	High
Jordaens et al[54] (1996)	Retrospective cohort	Population	ND	Media reports	SCD only	Cycling	Elite	ND	Unknown	M and F	2	High
Fuller et al[36] (1997)	Prospective cohort	Known	ND	Not reported	SCA and SCD	Multiple	Scholastic	Yes	<20	M and F	8	High
Chevalier et al[55] (2009)	Prospective cohort	Population	Exertion	Medical records	SCD only	Multiple	Multiple	No	<35	M and F	21	High
Drezner et al[8] (2009)	Survey	Population	ND	Facility event report (eg, school records)	SCA and SCD	Multiple	Scholastic	No	14–19	M and F	10	High
Maron et al[56] (2009)	Prospective cohort with database	Population	All	Combined media reports or autopsy and medical records	SCA and SCD	Lacrosse	Competitive	No	14–23	M and F	32	High
Solberg et al[57] (2010)	Retrospective cohort with database	Population	Exertion	Combined autopsy or other official records (eg, medical, military, athletic body)	SCD only	Multiple	Multiple	No	15–34	M	10	High
Steinvil et al[9] (2011)	Retrospective cohort	Population	ND	Media reports	SCA and SCD	Multiple	Competitive	Portion	Unclear	M and F	15	High
Duraković et al[31] (2012)	Retrospective cohort	Population	ND	Combined media reports or autopsy and medical records	SCD only	Multiple	Competitive	Portion	17–29	M	8	High
Biasco et al[38] (2013)	Retrospective cohort	Known	ND	Not reported	SCA and SCD	Soccer	Elite	Yes	23.6	M	5	High
Boden et al[58] (2013)	Prospective cohort with database	Population	ND	Combined eyewitness interview and medical or autopsy records	SCD only	American Football	Multiple	ND	14–25	M	6	High
Roberts and Stovitz[15] (2013)	Retrospective cohort	Population	Exertion	Insurance records	SCD only	Multiple	Scholastic	No	12–19	M and F	19	High
Maron et al[34] (2016)	Prospective cohort with database	Population	All	Combined media reports and autopsy or medical records	SCD only	Multiple	Competitive	ND	15–24	M and F	10	High
Santos-Lozano et al[41] (2017)	Retrospective cohort	Population	Exertion	Media reports	SCD only	Soccer	Elite	Portion	16–34	NR	21	High
Kucera et al[40] (2018)	Prospective cohort with database	Population	All	Combined eyewitness interview and medical or autopsy records	SCD only	American football	Competitive	No	<40	M	25	High
Maurice et al[37] (2018)	Survey	Population	Exertion	Facility event report (eg, school records)	SCA and SCD	Rugby	Competitive	No	Unknown	NR	1	High
Endres et al[59] (2019)	Retrospective cohort	Population	Exertion	Media reports	SCD only	Multiple	Multiple	No	6–17	M and F	27	High

Abbreviations: ECG, electrocardiogram; F, female; M, male; ND, not determined; NR, not reported; SCA, sudden cardiac arrest; SCD, sudden cardiac death.

[a] Athlete categories: *Elite* = professional or National Collegiate Athletic Association Division I athletes in the United States; *competitive* = athletes participating in organized sport with practices and competitions; *university* = athletes competing in all levels at a university setting; *scholastic* = competing for schools between middle and high school equivalents in the United States (approximately ages 12–19); *multiple* = combination of levels; *military* = active-duty military. One study involved firefighters.

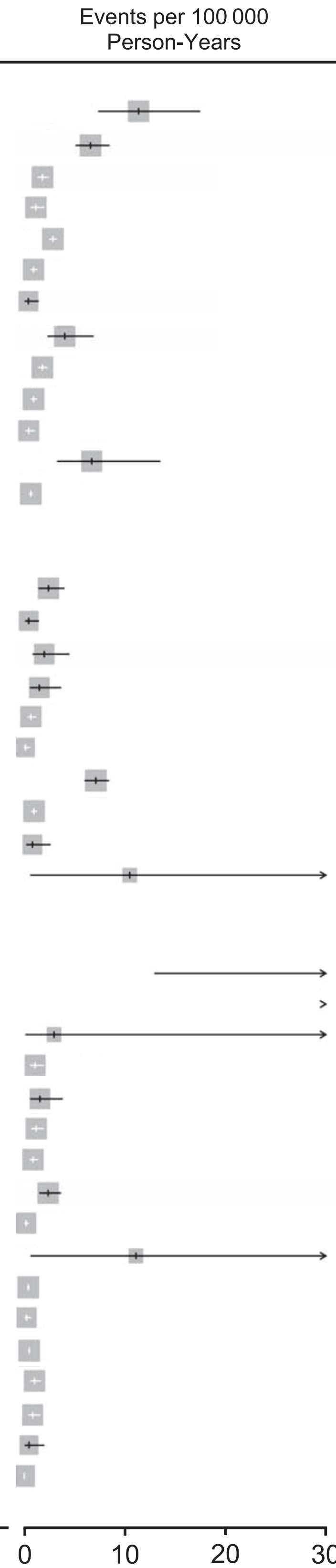
Table 2. Risk-of-Bias Table for Included Studies Reporting on Incidence Based on Customized Version of Risk of Bias in Prevalence Studies Tool[44]

Study	Numerator and Denominator	Definition of Cases	Study Period (>100 000 Person-Years)	Reliable Data-Collection Source?	Same Mode of Data Collection for All Sources	Was the Sampling Frame a Close Representation of the Target Population?	Was the Included Population a Close Representation of Relevant Variables (Age, Sex, etc)?	Nonresponse Bias or Follow-Up of Cohort (if applicable for survey study)[a]	Final Risk-of-Bias Determination
Koskenvuo et al[33] (1976)	Unclear	Unclear	Low	Low	Low	Low	Low	NA	Moderate
Phillips et al[18] (1986)	Low	Low	Low	Low	Low	Low	Low	NA	Low
Assanelli et al[35] (1995)	High	Unclear	High	Unclear	Unclear	Unclear	High	NA	High
Jordaens et al[54] (1996)	Unclear	Unclear	High	High	Unclear	Unclear	Unclear	NA	High
Fuller et al[36] (1997)	Unclear	Unclear	High	High	High	Low	Unclear	NA	High
Maron et al[14] (1998)	High	Low	Low	High	Low	Low	Low	NA	Moderate
Young et al[51] (1999)	High	Low	High	Low	Low	Low	Low	NA	Moderate
Eckart et al[42] (2004)	Low	Low	Low	Low	Low	Low	Low	NA	Low
Drezner et al[7] (2005)	Low	High	Low	Low	High	Low	Low	Low	Moderate
Corrado et al[30] (2006)	Low	Low	Low	Low	Low	Low	Low	NA	Low
Chevalier et al[55] (2009)	High	Unclear	Low	Low	Low	Low	Unclear	NA	High
Drezner et al[8] (2009)	High	Low	Low	Low	Low	High	Low	High	High
Maron et al[56] (2009)	High	Low	Low	Low	High	Low	High	NA	High
Holst et al[13] (2010)	Low	Low	Low	Low	Low	Low	Low	NA	Low
Solberg et al[57] (2010)	High	Low	Low	Low	Low	Unclear	Low	NA	High
Eckart et al[16] (2011)	High	Low	Low	Low	Low	Low	Low	NA	Low
Marijon et al[11] (2011)	Low	Low	Low	Low	Low	Low	Low	NA	Low
Steinvil et al[9] (2011)	High	High	Low	High	Low	Low	Low	NA	High
Duraković et al[31] (2012)	Unclear	Low	Low	Unclear	Low	Unclear	Unclear	NA	High
Biasco et al[38] (2013)	High	Unclear	High	Unclear	Unclear	Low	Low	NA	High
Boden et al[58] (2013)	High	Unclear	Low	Low	High	Low	Low	NA	High
Maron et al[43] (2013)	High	Unclear	Low	Low	Low	Low	Low	NA	Moderate
Roberts and Stovitz[15] (2013)	High	Unclear	Low	High	Low	Low	Low	NA	High
Risgaard et al[29] (2014)	Low	Low	Low	Low	Low	Low	Low	NA	Low
Toresdahl et al[52] (2014)	Low	High	Low	High	Low	Low	Low	NA	Moderate
Farioli et al[49] (2015)	Low	Low	Low	Low	Low	Low	Low	NA	Low
Harmon et al[1] (2015)	Low	Low	Low	Low	Low	Low	Low	NA	Low
Grani et al[32] (2016)	High	Low	Low	Unclear	Unclear	Low	Low	NA	Moderate
Harmon et al[10] (2016)	High	Low	Low	Low	High	Low	Low	NA	Moderate
Maron et al[34] (2016)	High	Low	Low	Low	High	High	High	NA	High
Maron et al[53] (2016)	Low	High	Low	Low	Low	Unclear	High	NA	Moderate
Smallman et al[17] (2016)	Low	Low	Low	Low	Low	Low	Low	NA	Low
Landry et al[12] (2017)	Low	Low	Low	Low	Low	Low	Low	NA	Low
Santos-Lozano et al[41] (2017)	Unclear	Low	Low	Low	High	Unclear	Unclear	NA	High
Berge et al[39] (2018)	Low	Low	High	High	Low	Low	Low	NA	Moderate
Kucera et al[40] (2018)	High	High	Low	High	High	Low	High	NA	High
Malhotra et al[50] (2018)	Low	Low	Low	Low	Low	Low	Low	NA	Low
Maurice et al[37] (2018)	Unclear	High	Low	Low	Unclear	Unclear	Low	Low	High
Endres et al[59] (2019)	High	High	Low	High	Low	Low	High	NA	High
Peterson et al[44] (2020)	Low	Low	Low	Low	Low	Low	Low	NA	Low

Abbreviation: NA, not applicable.

[a] This section was applicable only to survey projects.

Study	Events	Person-Years	Events per 100 000 Person-Years (95% CI)
Low risk of bias			
Phillips et al[18] (1986)	21	184 819.00	11.36 (7.41, 17.43)
Eckart et al[42] (2004)	64	969 231.00	6.60 (5.17, 8.44)
Corrado et al[30] (2006)	55	2 938 730.00	1.87 (1.44, 2.44)
Holst et al[13] (2010)	15	1 239 493.00	1.21 (0.73, 2.01)
Eckart et al[16] (2011)	298	10 250 000.00	2.91 (2.60, 3.26)
Marijon et al[11] (2011)	50	5 076 465.00	0.98 (0.75, 1.30)
Risgaard et al[29] (2014)	3	638 298.00	0.47 (0.15, 1.46)
Farioli et al[49] (2015)	14	342 877.00	4.08 (2.42, 6.89)
Harmon et al[1] (2015)	79	4 242 519.00	1.86 (1.49, 2.32)
Smallman et al[17] (2016)	63	6 425 421.00	0.98 (0.77, 1.26)
Landry et al[12] (2017)	7	1 379 574.00	0.51 (0.24, 1.06)
Malhotra et al[50] (2018)	8	118 351.00	6.76 (3.38, 13.52)
Peterson et al[44] (2020)	96	13 437 888.00	0.71 (0.58, 0.87)
Heterogeneity: χ^2_{12} = 396.59, P < .01			
Moderate risk of bias			
Koskenvuo et al[33] (1976)	16	660 000.00	2.42 (1.49, 3.96)
Maron et al[14] (1998)	3	651 695.00	0.46 (0.15, 1.43)
Young et al[51] (1999)	6	299 985.00	2.00 (0.90, 4.45)
Drezner et al[7] (2005)	5	330 736.00	1.51 (0.63, 3.63)
Maron et al[43] (2013)	13	1 930 504.00	0.67 (0.39, 1.16)
Toresdahl et al[52] (2014)	2	1 500 000.00	0.13 (0.03, 0.53)
Grani et al[32] (2016)	145	2 032 730.00	7.13 (6.06, 8.39)
Harmon et al[10] (2016)	69	6 974 640.00	0.99 (0.78, 1.25)
Maron et al[53] (2016)	3	361 841.00	0.83 (0.27, 2.57)
Berge et al[39] (2018)	0	4760.00	10.50 (0.66, 167.94)
Heterogeneity: χ^2_{9} = 262.35, P < .01			
High risk of bias			
Assanelli et al[35] (1995)	5	16 000.00	31.25 (13.01, 75.08)
Jordaens et al[54] (1996)	14	15 722.00	89.05 (52.74, 150.35)
Fuller et al[36] (1997)	0	16 782.00	2.98 (0.19, 47.63)
Chevalier et al[55] (2009)	12	1 096 240.00	1.09 (0.62, 1.93)
Drezner et al[8] (2009)	5	317 205.00	1.58 (0.66, 3.79)
Maron et al[56] (2009)	19	1 578 872.00	1.20 (0.77, 1.89)
Solberg et al[57] (2010)	23	2 597 204.00	0.89 (0.59, 1.33)
Steinvil et al[9] (2011)	22	923 077.00	2.38 (1.57, 3.62)
Duraković et al[31] (2012)	6	3 133 512.00	0.19 (0.09, 0.43)
Biasco et al[38] (2013)	0	4495.00	11.12 (0.70, 177.84)
Boden et al[58] (2013)	100	24 100 754.00	0.41 (0.34, 0.50)
Roberts and Stovitz[15] (2013)	4	1 666 509.00	0.24 (0.09, 0.64)
Maron et al[34] (2016)	842	165 705 417.00	0.51 (0.47, 0.54)
Santos-Lozano et al[41] (2017)	20	1 923 076.00	1.04 (0.67, 1.61)
Kucera et al[40] (2018)	10	1 175 000.00	0.85 (0.46, 1.58)
Maurice et al[37] (2018)	2	408 750.00	0.49 (0.12, 1.96)
Endres et al[59] (2019)	34	185 792 350.00	0.02 (0.01, 0.03)
Heterogeneity: χ^2_{16} = 950.39, P < .01			



Heterogeneity: χ^2_{39} = 2793.36, P < .001
Residual heterogeneity: χ^2_{37} = 1609.33, P < .001

Figure 2. Incidence rates of sudden cardiac death reported by included studies.

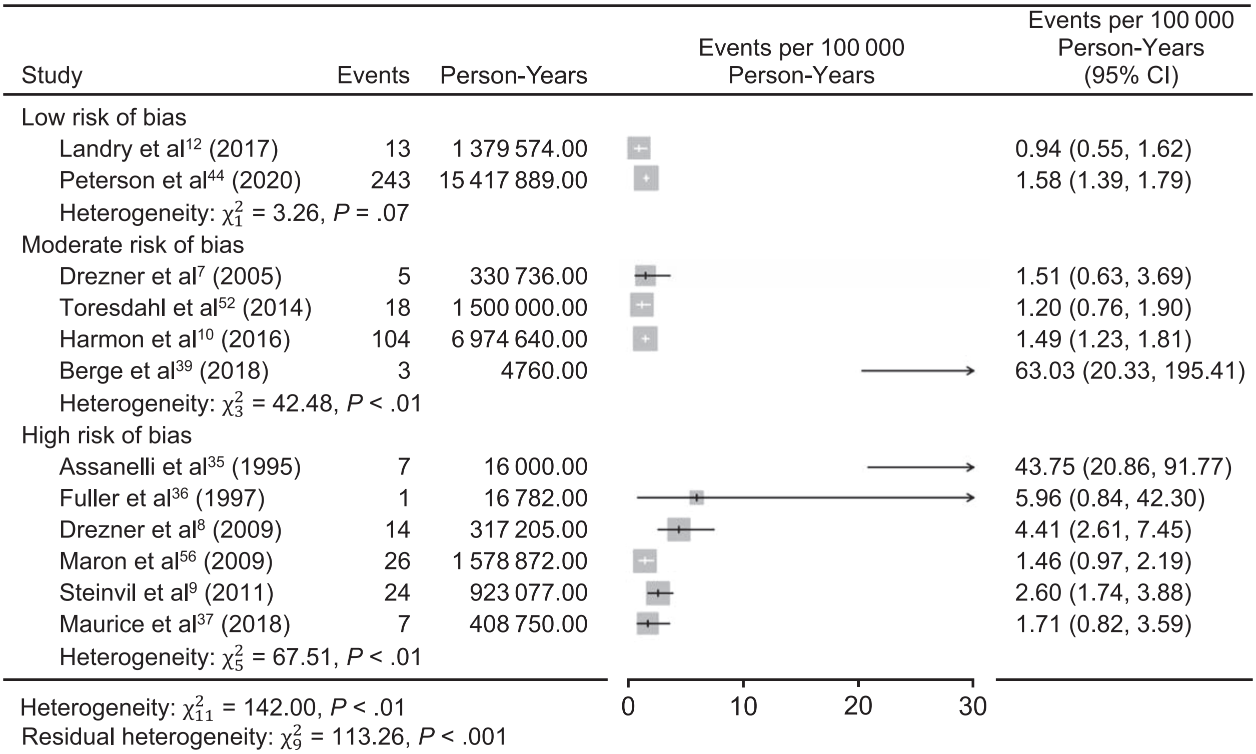


Figure 3. Incidence rates of sudden cardiac arrest reported by included studies.

We found only 2 low-ROB studies in which the authors reported episodes of SCA, and these data were not synthesized. Landry et al[12] conducted a retrospective, population-level study in a region of Ontario, Canada, and reported a rate of 0.94 (95% CI = 0.55, 1.62) SCAs per 100 000 athlete-years, whereas Peterson et al[44] conducted a prospective study of SCA in US high school and collegiate athletes and reported 1.58 (95% CI = 1.39, 1.79) SCAs per 100 000 athlete-years. The moderate- and high-ROB studies ranged from 1.20 to 63.03 SCAs per 100 000 athlete-years, with 5[7,10,37,52,56] providing point estimates at <2.00 and the remaining 5[8,9,35,36,39] with estimates between 2.60 and 63.03 per 100 000 person-years.

We did not perform synthesis of subgroups because of the small number of low-ROB studies providing subgroup data. Notable findings from low-ROB subgroups indicated higher

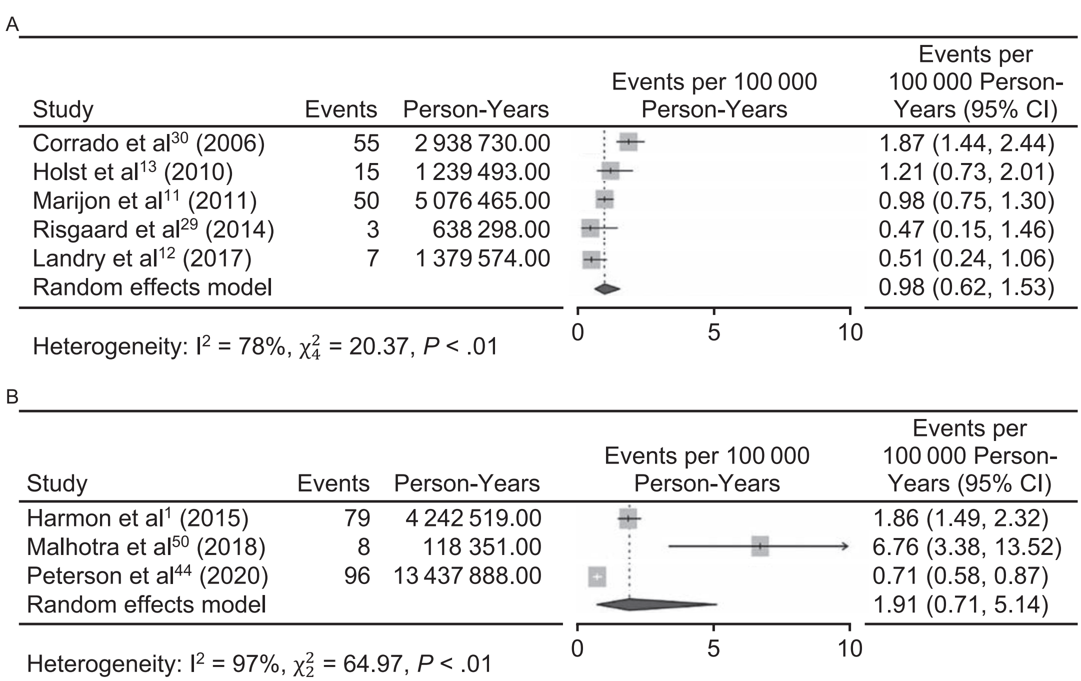


Figure 4. Meta-analyses of the incidence rate of sudden cardiac death in low risk-of-bias studies, A, at population levels and, B, in competitive athletes between the ages of 14 and 25 years.

rates of SCA and SCD in males than in females[1,44] with rates >3 times as high in males in both cases. Subgrouping and comparing athletes by race was difficult because of a lack of uniformity in reporting. The reported data in low-ROB studies indicated elevated rates of SCA and SCD in Black high school and university-level athletes[1,44] as well as military members[42] when compared with their White counterparts. In the 1 study of Hispanic athletes,[1] Black athletes were noted to have elevated rates in comparison. These data are similar to those in a high-ROB study, which reported elevated rates in non-White athletes when compared with White athletes.[34] Further narrative detail, as well as forest plot figures with results from individual studies on subgroups, including by individual sport and by level of sport, is supplied in Supplemental Material 5.

Visual assessment of the funnel plot (Supplemental Material 8) for publication bias showed asymmetry in the direction of larger studies with larger incidences. This finding is likely related to the heterogeneity in the included studies.

DISCUSSION

We believe this is the first systematic review of SCA and SCD in athletes and military members. Our analysis showed a substantial amount of heterogeneity in the published literature, with most papers demonstrating a moderate or high ROB. For studies judged to have a low ROB, meta-analysis of 3 published studies[1,44,50] in which the authors included young competitive athletes showed the incidence of SCD to be 1.91 (95% CI = 0.71, 5.14) per 100 000, whereas 5 studies[11–13,29,30] in which the authors included large national or regional populations of athletes had an incidence of 0.98 (95% CI = 0.62, 1.53) SCDs per 100 000 athlete-years. Authors of only 2 low-ROB studies reported extractable SCA details; Landry et al[12] described a point estimate of 0.94 (95% CI = 0.55, 1.62) per 100 000 athlete-years for athletes at all levels in a regional population-based study in Ontario, Canada, and Peterson et al[44] observed a point estimate of 1.58 (95% CI = 1.39, 1.79) SCAs per 100 000 athlete-years in high school and university athletes. Military studies[16–18,33,42,49] were not meta-analyzed but showed a range of estimates from 0.98 to 11.36 SCDs per 100 000 years.

We believe these findings in high-quality studies of athletes confirm the overall rarity of SCA and SCD in athletes. Based on our results, the rate of SCD appears to be <2 per 100 000 athlete-years in young competitive athletes. The authors[1,44] of recent high-quality studies that were done prospectively or using information garnered from prospectively collected databases in the United States who focused on competitive athletes at the high school and university levels identified rates of <2 per 100 000. Peterson et al[44] reported rates of SCA and SCD together, with a point estimate of 1.58 per 100 000, whereas Harmon et al[1] studied university-level athletes and reported an SCD rate of only 1.86 per 100 000. The authors of both articles included cases of SCA and SCD that occurred during (exertional) or not during (nonexertional) exertion. Criticisms of estimates excluding nonexertional cases have been made in the past[5] based on the belief that counting only deaths due to exertion underestimates the risks of SCA and SCD in the active young population. The estimates provided by the authors of these 2 studies included broad populations of male and female athletes as well as athletes of multiple ethnicities. An accounting of both SCA and SCD at the university level would likely provide an estimate higher than that of Harmon et al.[1] The authors of these publications suggested the rates of SCA and SCD in the population of competitive scholastic- and university-level athletes were greater than other estimates of <1 per 100 000.[3]

When we reviewed the included publications, it did appear that the incidence of SCD in military members may be more frequent than in athletes. The point estimates reported in the included studies ranged from 0.98[17] to 11.36[18] SCDs per 100 000 in the low-ROB military studies. When comparing the highest military point estimate for SCD from Phillips et al[18] with the lowest from Smallman et al,[17] we noted that Phillips et al[18] studied a 20-year cohort extending into the 1960s, whereas Smallman et al[17] studied a sample between 2005 and 2010. Considerable confounding is likely present when comparing the different military studies, including the proportion of female members, general health behaviors of the population such as tobacco use, and perhaps a more nuanced understanding of SCD in comparison with conditions that can cause sudden death (such as hyperthermia) based on the timing of the deaths.

When considering the results of low-ROB studies in which the authors focused on athletes participating in regular practices and competitions, we observed that the SCD estimate (1.91 per 100 000) was higher than that in population-based studies of athletes at all levels, including recreational (0.98 per 100 000). The explanations for this difference are likely multifactorial. The primary possibility exists that the risk of SCD is higher in competitive athletes than that estimated in population-level studies including recreational athletes. Other possible explanations reflect country populations in the population-based studies compared with those studies in which the authors focused on competitive athletes. The population-based studies were from Europe[11,13,29,30] (n = 4) and Ontario, Canada[12] (n = 1), where the population of Black athletes was likely lower than in the United States; 2[1,44] of the 3 studies[1,44,50] of competitive athletes were from the United States and contributed most of the population analyzed. If, as indicated by the high-quality studies[1,44] of competitive athletes in the United States, the rate of SCD in Black athletes is elevated versus other populations, this could lead to elevated rates of SCD in the United States in comparison with Europe and Canada. Also of note is that, of the population-based studies,[11–13,29,39] only Corrado et al[30] included both exertional and nonexertional deaths in athletes rather than exertional deaths only, whereas the authors of all 3 studies[1,44,50] in the competitive athlete analysis included all deaths in athletes, not only exertional. This fact probably led to an underestimation of the population-level point estimate for all athletes, including recreational athletes. In addition, the ages of participants in the population-level studies extended into the 30s, whereas those in the competitive athlete studies were in their teens and early 20s. One would expect this to increase the frequency of SCD related to coronary artery disease when compared with other conditions causing SCD in the younger athlete.[44] However, this fact did not appear influential enough to raise the rates in competitive athletes.

Although the overall rate of SCA and SCD appears relatively low, attention to subgroups of athletes suggests areas where rates may be consistently much higher. The rates reported in Black male athletes in basketball and American football were considerably different from their population estimates. Harmon et al[1] reported a rate of 1 SCD in Black male basketball players per 4380 athlete-years at the elite university level, and Peterson et al[44] reported a rate of SCA and SCD of 1 per 4810 athlete-years in university-level athletes at all levels and 2087 in athletes at the elite National Collegiate Athletic Association Division I level and reported a rate of 1 per 28 061 in Black American football athletes at all levels and 1 per 18 031 at the Division I level. The authors of 5 articles reported outcomes specifically in soccer athletes,[13,38,39,41,50] and the authors of 2 reported subgroups of soccer athletes.[1,44] Authors of the high-quality articles who reported SCD events indicated rates of 4.22 in US university athletes and 6.76 in UK professional athletes per 100 000 athlete-years, whereas Peterson et al[44] reported a far lower rate of SCA in US university athletes at 1.28 SCAs per 100 000 athlete-years. The variability in these results makes it somewhat difficult to interpret or understand the true risk associated with soccer in comparison with other sports.

The primary strength of our review lies in the breadth of the search, which enabled us to draw data from multiple, large population-level studies as well as studies in which the authors focused specifically on scholastic and collegiate athletes or military members. We believe that we have provided the most up-to-date and precise estimates of the population-level incidence in athletes of all types as well as in competitive athletes. We also believe that our narrative review of subgroups adds to the overall knowledge base about those with high or low risk levels. In this review, we also assessed the level of evidence published on the incidence of SCA and SCD.

Limitations of our review include substantial clinical and statistical heterogeneity in the published data as well as the overall small proportion of data judged to have a low ROB. Authors of many of the studies looked at only males or single sports, and those studies were judged to have a moderate or high ROB, tempering the robustness of their findings. Most of the data were drawn from studies in Europe and the United States, potentially limiting the applicability of our findings outside of these regions. Given the available resources and timing, not all included studies were dual screened or assessed for ROB. This lack of dual ROB assessment could have led to bias of a single reviewer's interpretation of the included studies. For the meta-analysis, we also combined studies of exertional deaths only and of death at any time among athletes, potentially underestimating the overall rate.

CONCLUSIONS

In this systematic review, we provided a comprehensive evaluation of the available data on SCA and SCD in active populations aged $\leq$40 years. The overall literature base displayed substantial clinical and methodologic heterogeneity, with most studies having a moderate or high ROB. In studies with a low ROB, our analysis of the SCD incidence showed it to be a rare occurrence in both population-level studies that included all levels of athletes at 0.98 (95% CI = 0.62, 1.53) SCDs per 100 000 athlete-years and focused studies of young competitive athletes between the ages of 14 and 25 years at 1.91 (95% CI = 0.71, 5.14) SCDs per 100 000. These estimates are generally consistent with those of the moderate- and high-ROB studies included. Our evaluation of the published literature suggests higher incidences of both SCD and SCA in males, Black athletes, and potentially military members versus athletes. We believe that the estimates presented here for broad populations of competitive athletes are not likely to be changed by further publications. We do propose that population-based studies may be improved by including events at all times compared with events that occurred only with exertion. As has been suggested previously,[6] a uniform reporting system of sudden deaths in the young active population would benefit our understanding of this condition and advance a more reliable understanding of the incidence of both SCA and SCD.

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