Evidence Map: Screening for cardiac conditions associated with sudden cardiac death in the young

Protocol

Produced by: Sheffield Evidence Network for Screening Synthesis (SENSS)

Produced for: UK National Screening Committee (UK NSC)

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Plain Language Summary

Sudden cardiac death (SCD) is the sudden and unexpected death of a person, caused by a problem with their heart. SCD can occur in the general population as well as in young athletes (non-competitive, competitive and elite), typically 34 years of age or younger. A number of conditions can cause SCD. In young individuals and young athletes, SCD is often due to structural heart problems or an electrical problem with the heart.

Screening of young people or young athletes has been proposed as a way to prevent sudden cardiac death in young people. This may identify heart conditions at an early stage before they cause symptoms. This would allow treatment to start earlier, which might prevent SCD. On the other hand, it is possible that screening may not be effective or may cause harm through unnecessary tests and treatments or through causing people to avoid exercise unnecessarily.

The UK National Screening Committee (NSC) last looked at the research evidence for screening for SCD in young people in 2019. The report concluded that there was not enough evidence to support screening. This was because there were uncertainties in how many young people each year were affected by sudden cardiac death; it was unclear whether tests could accurately detect heart conditions in young people without symptoms; and no studies were identified which met the inclusion criteria for whether screening young people reduced the risk of SCD.

This evidence map aims to summarise how much, and what type, of research evidence has become available since the previous report in 2019. This evidence map assesses three questions: 1) how many young people are affected by SCD; 2) how accurate screening tests are for identifying problems with the heart that may lead to SCD; and 3) whether screening reduces the risk of SCD or leads to other benefits or harms, compared with not screening.

Brief background

Sudden cardiac death (SCD) is sudden and unexpected death due to a problem with the heart. It is defined by the European Society of Cardiology (ESC) as "sudden natural death presumed to be of cardiac cause that occurs within 1 hour of onset of symptoms in witnessed cases, and within 24 hours of last being seen alive when it is unwitnessed; SCD in autopsied cases is defined as the natural unexpected death of unknown or cardiac cause."

SCD can occur in the general population as well as in young athletes, typically 34 years of age or younger. Sports and exercise-related SCD is SCD occurring during or within 1 hour of moderate- to high-intensity exercise. In young individuals and young athletes, SCD is often due to genetic disorders causing structural heart issues or abnormalities in the electrical activity of the heart, but can also be due to non-genetic disorders.

A review for the UK NSC was published in 2019;[1] searches were conducted in December 2018. This review identified evidence on incidence of SCD and sudden cardiac arrest, but noted that there was uncertainty in estimates of incidence. This review also identified studies assessing test accuracy of screening for conditions that may cause SCD; however, only data from athletic populations (rather than young general populations) were identified, and the majority of studies

lacked follow-up for individuals who screened negative, thereby preventing the calculation of key test accuracy outcomes. No studies were identified which compared clinical outcomes for individuals with a screen-detected cardiac abnormality versus non-screened individuals.

The UK NSC does not currently recommend systematic population screening of people under the age of 39 for cardiac conditions associated with sudden cardiac death.

Aims

The aim of this evidence map is to provide an overview of the volume and type of evidence that has become available since the 2019 UK NSC review,[1] relating to the incidence of SCD, test accuracy of screening to identify cardiac conditions associated with SCD, and clinical effectiveness of screening and interventions to prevent SCD, in young individuals aged 12 to 39 years. The review questions are as follows:

Question 1: What is the volume and type of evidence on the reported incidence of SCD in young individuals aged 12 to 39 years old?

Question 2: What is the volume and type of evidence on the accuracy of available screening tests to identify cardiac conditions associated with SCD in young individuals aged 12 to 39 years old?

Question 3: What is the volume and type of evidence on the effectiveness of interventions to prevent SCD in young individuals aged 12 to 39 years old with a screen-detected cardiac abnormality compared to non-screened individuals?

Methods

Search strategy

The search strategies below will be run on Ovid MEDLINE and translated for EMBASE and the Cochrane Library. We estimate that the total retrieval across all databases will be between 2.5x and 3x the numbers below; in the future, we plan to investigate whether it would be possible to streamline our processes by reducing the number of sources without missing any important studies.

Search strategy for Question 1

The search strategy for Question 1 combines the following search concepts: (sudden cardiac death or sudden cardiac arrest) AND (young people or athletes) AND incidence. Results were limited to English language and 2018 onwards.

Ovid MEDLINE(R) ALL <1946 to April 09, 2025>

1   Death, Sudden, Cardiac/   18969
2   (sudden cardiac death* or sudden cardiac arrest*).mp.   24594
3   1 or 2 33658
4   (young* or youth* or child* or adolescen* or teen* or student* or school or college).mp. or universit*.ti,ab.   5888687

5   (athlet* or sport* or runn* or marathon* or rugby or football* or soccer or cyclist* or gymnast* or tennis or basketball or swimmer* or rowing or rower* or baseball or hockey or dancer*).mp.   311950
6   4 or 5   6084223
7   incidence.mp. 1129369
8   incidence/   319234
9   7 or 8   1129369
10   3 and 6 and 9 1405
11   limit 10 to (english language and yr="2018 -Current")   **446**

Search strategy for Questions 2 and 3:

We propose to populate the map for Questions 2 and 3 with a single search as below. This combines the following search concepts: (sudden cardiac death or sudden cardiac arrest or cardiac conditions) AND (young people or athletes) AND screening, with a final "safety net" string (in line 15) to pick up any studies of cardiovascular screening in this population not already retrieved. Results were limited to English language and 2018 onwards.

Ovid MEDLINE(R) ALL <1946 to April 08, 2025>

1 Death, Sudden, Cardiac/ 18977
2 (sudden cardiac death* or sudden cardiac arrest*).mp. 24608
3 1 or 2 33672
4 (hypertroph* or HCM or arrhythmogenic right ventricular* or ARVC or cardiomyopath* or channelopath* or QT syndrome or LQTS or SQTS or Brugada syndrome or catecholaminergic polymorphic ventricular tachycardia or CPVT or progressive cardiac conduction defect* or early repolarisation syndrome or sodium channel disease or Wolff-Parkinson-White or WPW syndrome or Marfan syndrome or myocarditis).mp. 319555
5 arrhythmogenic right ventricular dysplasia/ or exp cardiomyopathy, hypertrophic/ or myocarditis/ or exp Cardiomyopathies/ or Channelopathies/ or *Heart Diseases/di 127389
6 brugada syndrome/ or exp long qt syndrome/ 13411
7 Wolff-Parkinson-White Syndrome/ 5710
8 4 or 5 or 6 or 7 346372
9 3 or 8 367414
10 (young* or youth* or child* or adolescen* or teen* or student* or school or college).mp. or universit*.ti,ab. 5888938
11 (athlet* or sport* or runn* or marathon* or rugby or football* or soccer or cyclist* or gymnast* or tennis or basketball or swimmer* or rowing or rower* or baseball or hockey or dancer*).mp. 311956
12 10 or 11 6084475
13 exp Mass Screening/ or screen*.mp. 1203749
14 9 and 12 and 13 4737
15 (screen* adj2 (cardiac or heart or cardiovascular)).mp. 3864
16 12 and 15 1401
17 14 or 16 5567
18 limit 17 to (english language and yr="2018 -Current") 1990

Inclusion criteria

Inclusion criteria for all three questions are provided in the table below.

Table: Inclusion criteria for evidence map for Sudden Cardiac Death

Question	1. Incidence of SCD in young individuals	2. Accuracy of screening tests to identify cardiac conditions associated with SCD	3. Effectiveness of screening and intervention to prevent SCD
Population	•Age 12-39 prioritised (include studies for age 1-39; exclude studies that include people aged <1 or >40 years)[a] •Asymptomatic prioritised •UK prioritised; if little data then include data from comparable countries (Europe, US, Canada, Australia, New Zealand)[b] **Exclude:** •Study cohorts with a known cardiac or cardiac-related condition •Cascade screening in family members of person with a target condition	•Age 12-39 prioritised (include studies for age 1-39; exclude studies that include people aged <1 or >40 years)[a] •Asymptomatic prioritised •UK prioritised; if little data then include data from comparable countries (see left) **Exclude:** •Study cohorts with a known cardiac or cardiac-related condition •Cascade screening in family members of person with a target condition	•Age 12-39 prioritised (include studies for age 1-39; exclude studies that include people aged <1 or >40 years)[a] •Screen-detected cardiac abnormality •UK prioritised; if little data then include data from comparable countries (see left) **Exclude:** •Study cohorts with a known cardiac or cardiac-related condition •Cascade screening in family members of person with a target condition
Stratification[c]	Where possible, stratify by: •Age, Ethnicity, Sex •General population i.e. non-athletes •Athletes (competitive, non-competitive, elite) •Underlying cause, if known (see target conditions under Q2)	Where possible, stratify by: •General population i.e. non-athletes •Athletes (competitive, non-competitive, elite)	Where possible, studies by: •General population i.e. non-athletes •Athletes (competitive, non-competitive, elite)
Intervention	-	-	•Screening and subsequent management strategies (as in identified studies)
Comparator	-	•None or different combinations of index tests	•Current standard of care (as in identified studies) i.e. no offer or receipt of screening •**Note:** studies must compare screened and non-screened groups
Index tests	-	•History-taking •Physical exam •12-lead electrocardiogram (ECG) •Mobile health devices (e.g. mobile phones, tablets, smart watches and other wearables)	-

Question	1. Incidence of SCD in young individuals	2. Accuracy of screening tests to identify cardiac conditions associated with SCD	3. Effectiveness of screening and intervention to prevent SCD
		•Genetic testing •Combinations of the above •Other available screening tests	
Reference standard	-	Any recognised ref standard e.g: •Autopsy reports •Genotyping •Testing for pathogenic variations	-
Outcomes	Incidence of: •Sudden cardiac death (SCD) •Sudden cardiac arrest (SCA) •Sudden cardiac arrest and/or death [for SCA, only include studies which sought to exclude cases unlikely to relate to SCD e.g. trauma and asphyxia] Note: Studies of cases occurring in specific locations or at specific times of day, such as at school, during working hours, or whilst playing sport, will be highlighted as such. **Exclude:** •Studies only reporting incidence of target conditions within an SCD/SCA cohort, rather than incidence in general population (these studies will be listed separately)	Test accuracy outcomes: •Sensitivity •Specificity •Positive predictive value (PPV) •Negative predictive value (NPV) •Likelihood ratios •Area under the curve (AUC)	Clinical outcomes: •Incidence of sudden cardiac arrest and/or death •Change in any relevant cardiac outcome e.g. arrhythmia symptoms •Effect on quality of life Harms: •Overtreatment •Anxiety •Disqualification from sports •Exercise avoidance
Target conditions	-	Potentially lethal CVD conditions, such as: Cardiomyopathies: •Hypertrophic cardiomyopathy (HCM) •Arrhythmogenic right ventricular cardiomyopathy (ARVC) / arrhythmogenic right ventricular dysplasia (ARVD) / arrhythmogenic cardiomyopathy (ACM) •Dilated cardiomyopathy (DCM) Channelopathies:	-

Question	1. Incidence of SCD in young individuals	2. Accuracy of screening tests to identify cardiac conditions associated with SCD	3. Effectiveness of screening and intervention to prevent SCD
		•Long QT syndrome (LQTS) •Brugada syndrome •Catecholaminergic polymorphic ventricular tachycardia (CPVT) •Progressive cardiac conduction defect (PCCD) •Short QT syndrome (SQTS) •Early repolarisation syndrome (ERS) •Sodium channel disease •Familial atrial fibrillation Other cardiac conditions: •Wolff-Parkinson-White (WPW) syndrome •Marfan syndrome •Myocarditis •Coronary artery anomalies •Premature coronary artery disease and familial hypercholesterolemia **Exclude:** •SCD due to non-cardiac conditions such as COVID-19 •SCD following surgical procedures •Studies which only report the frequency of specific ECG abnormalities rather than target conditions (consistent with 2019 review)	
Study designs	•Cohort studies •Systematic reviews of the above •(Other designs if none/few of the above)	•RCTs •Cohort studies •Cross-sectional studies •Systematic reviews of the above •(Other designs if none/few of the above, e.g. case-control / two-gate studies)	•RCTs •Quasi-experimental studies •Cohort studies •Systematic reviews of the above •(Other designs if none/few of the above)
Publication types[d]	•Full publications only (exclude conference abstracts) •Publications with results only (exclude protocols and trial registries)	•Full publications only (exclude conference abstracts) •Publications with results only (exclude protocols and trial registries)	•Full publications only (exclude conference abstracts) •Publications with results only (exclude protocols and trial registries)
Date limit	Since Dec 2018	Since Dec 2018	Since Dec 2018

Question	1. Incidence of SCD in young individuals	2. Accuracy of screening tests to identify cardiac conditions associated with SCD	3. Effectiveness of screening and intervention to prevent SCD
Language	English language	English language	English language

[a]The main age range of interest is age 12-39; however, in the 2019 UK NSC review, due to variability in age ranges across studies and because SCD incidence is broadly similar from age 1 to 19, studies including ages 1-39 were included while studies that include people aged <1 or >40 were excluded. The same criteria are used here.
[b]Includes: European Economic Area (EEA, i.e. 27 EU countries plus Iceland, Liechtenstein, Norway and Switzerland); United States, Canada, Australia, New Zealand.
[c]Stratification is not technically an inclusion criterion, but is included here for completeness.
[d]In line with NIHR-NSC Evidence Map Process Document.
RCT, randomised controlled trial; SCA, sudden cardiac arrest: SCD, sudden cardiac death.

Screening of Titles and Abstracts

Titles and abstracts will be screened for relevance by the reviewer team. The first 100 references for each search (Q1 search and Q2+3 search) will be screened by all reviewers, then checked for consistency of inclusion decisions in order to align interpretation of the inclusion criteria. If agreement is low then this process will be repeated. The remaining titles and abstracts will each be screened by a single reviewer (within a team of two to three reviewers). All included references will be checked for inclusion by a second reviewer.

Full texts will only be obtained and consulted where insufficient information is available from the abstract to either assess eligibility, or extract data (consistent with the NIHR-NSC Evidence Map Process Document). In cases where there is uncertainty about inclusion, a second reviewer will be consulted (or the UK NSC Evidence Team asked for advice).

Data Extraction

Data will be extracted from abstracts where possible. Full texts will only be checked where necessary to clarify unclear information from the abstract (consistent with the NIHR-NSC Evidence Map Process Document).

Data will be extracted by one reviewer and numerical data checked by a second reviewer.

Data extraction will focus on the following essential information for each study (as in Appendix 2 of the UK NSC Evidence Map template):
- Study type
- Objectives of the study
- Components of the study (e.g. PICO)
    - For Q1: Population (and N), country/setting.
    - For Q2: Population (and N), country/setting, index test, reference standard, target conditions (if reported).
    - For Q3: Population (and N), country/setting, intervention, comparator.
- Outcomes reported and brief results on these outcomes
    - For Q1: Incidence of sudden cardiac arrest and/or sudden cardiac death.
    - For Q2: Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratios, area under the curve.
    - For Q3: Incidence of sudden cardiac arrest and/or death, change in cardiac outcomes e.g. arrhythmia symptoms, effect on quality of life, overtreatment, anxiety, disqualification from sports, exercise avoidance.
- Conclusions of the study.

Depending on the number of studies, data will either be extracted directly into the UK NSC Evidence Map template Appendix 2 (structured summary per study), or be extracted initially into an Excel table for ease of extraction and to ensure consistency across studies, then into the structured summary per study.

Quality assessment

No formal quality assessment will be conducted (consistent with the NIHR-NSC Evidence Map Process Document). Any obvious quality issues evident from the data available in the abstracts will be highlighted through the narrative review of the studies.

Reporting

The evidence map will be constructed in accordance with the UK NSC Evidence Map template. This will include:
- Summary section and brief recommendations regarding further work
- Background and objectives
- Brief summary of the previous UK NSC review
- Aims and research questions
- Search methods and search results with PRISMA flow charts
- Summary of findings per question
- Conclusions
- Recommendations regarding further work
- Appendix 1 with details of search strategies and inclusion criteria
- Appendix 2 with structured summary of each included study
- References.

The "Summary of findings per question" will summarise the volume and type of evidence published since the previous UK NSC review in 2019 and the results of the included studies. This section will also briefly summarise the results and limitations of the evidence identified within the previous 2019 UK NSC review.

Outputs

The main output will be a report for the UK NSC as described above. We are happy to discuss further publication and dissemination activities with the UK NSC.

Project team

The project team will include:
- Project lead: Katy Cooper
- Systematic reviewers: Katy Cooper, Gamze Nalbant and Munira Essat
- Information specialist: Mark Clowes
- Statistical advice if required (for study interpretation): Sarah Ren.

The three systematic reviewers will undertake regular meetings and checks to ensure consistency of understanding and processes.

Timelines

Timelines for the evidence map are provided in the table below.

Table 6: Timelines for evidence map for Sudden Cardiac Death

Task	Timepoint	Date
Initial meeting	**Start**	**2 April 2025**
Search strategies agreed with UK NSC Evidence Team	End of Week 1	10 April 2025
Literature searches	End of Week 1	10 April 2025
Protocol to UK NSC Evidence Team for feedback	**End of Week 3**	**23 April 2025[a]**
Sifting titles/abstracts and selection of includable studies	Middle of Week 6	12 May 2025
Data extraction and production of structured abstracts per study	Middle of Week 8	23 May 2025
Report writing	End of Week 10	12 June 2025
Draft evidence map	**End of Week 10**	**12 June 2025**
Feedback from UK NSC Evidence Team	End of Week 11	19 June 2025
Updated evidence map	**End of Week 12**	**26 June 2025**
Feedback from Reference Group	tbc	tbc
Updated evidence map	tbc	tbc
Public consultation (3 months)	tbc	tbc
UK NSC Meeting	tbc	tbc
Updated evidence map	tbc	tbc
[a]Usually the protocol would be developed within 2 weeks. On this occasion we have requested 3 weeks to allow for bank holidays and staff annual leave.		

References

1.	UK National Screening Committee (UK NSC). Adult screening programme: sudden cardiac death. Screening for cardiac conditions associated with sudden cardiac death in the young: External review against programme appraisal criteria for the UK National Screening Committee. https://view-health-screening-recommendations.service.gov.uk/document/437/download. 2019.