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Sudden unexpected death in children with congenital heart defects

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Aims Congenital heart defects (CHDs) are the most common birth defects and are an important cause of death in children. The fear of sudden unexpected death has led to restrictions of physical activity and competitive sports. The aim of the present study was to investigate the rate of sudden unexpected deaths unrelated to surgery in children 2–18 years old with CHDs and, secondarily, to determine whether these deaths were related to cardiac disease, comorbidity, or physical activity.

Methods and results To identify children with CHDs and to determine the number of deaths, data concerning all 9 43 871 live births in Norway in 1994–2009 were retrieved from the Medical Birth Registry of Norway, the Cardiovascular Disease in Norway project, the Oslo University Hospital's Clinical Registry for Congenital Heart Defects and the Norwegian Cause of Death Registry. Survivors were followed through 2012, and information for the deceased children was retrieved from medical records at Norwegian hospitals. Among 11 272 children with CHDs, we identified 19 (0.2%) children 2–18 years old who experienced sudden unexpected deaths unrelated to cardiac surgery. A cardiac cause of death was identified in seven of these cases. None of the children died during physical activity, whereas two children survived cardiac arrest during sports.

Conclusion Sudden unexpected death was infrequent among children with CHDs who survived 2 years of age. Comorbidity was common among the children who died. This study indicates that sudden unexpected death in children with CHDs rarely occurs during physical activity.

Keywords Cardiology • Congenital heart defect • Sudden unexpected death • Mortality • Sport

Introduction

Congenital heart defects (CHDs) affect ~1 per 100 live births and are the most common birth defects.[1–3] Despite improved survival over the last 50 years, CHDs still represent an important cause of death in children.[4,5] Some children with CHDs die suddenly and unexpectedly.[6–9] The fear of sudden unexpected death has led to restrictions of physical activity and competitive sports in adolescents and adults with CHDs.[10–14] These recommendations are often extrapolated to use also in recreational sports and in children. The scientific justification for these policies is weak. Physical activity has positive health effects for patients with heart disease,[15,16] but reports indicate that children with CHDs are generally less physically active and have impaired motor competence.[17,18] The fears of parents and health professionals concerning sudden unexpected death may be one possible reason for these findings.

Norwegian national health registers and databases provide the opportunity to conduct nationwide population-based studies. In Norway, physical activity recommendations have been consistently liberal, and restrictions have primarily been placed on children with severe left ventricular outflow obstructions.

The aim of the present study was to investigate the rates of sudden unexpected death unrelated to surgery in children with CHDs who were older than 2 years of age born in Norway 1994–2009.

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The secondary aim was to determine whether these deaths were related to cardiac disease, comorbidity, or physical activity.

Methods

Classification of congenital heart defects

Congenital heart defects were defined as structural abnormalities of the heart or intrathoracic vessels with functional or potentially functional significance. Children with isolated cardiomyopathies and primary arrhythmias were not included. Congenital heart defects were classified as severe [heterotaxia, transposition of the great arteries (TGA), tetralogy of Fallot (TOF), double-outlet right ventricle, truncus arteriosus, interrupted aortic arch, atrioventricular septal defects, anomalous pulmonary venous return, hypoplastic left heart syndrome, coarctation of the aorta, valvular aortic stenosis, pulmonary valve atresia, tricuspid valve atresia, Ebstein's anomaly, and other complex defects] or non-severe [atrial septal defects, ventricular septal defects, minor valve malformation, venous malformation, pulmonary valve stenosis, unspecified CHDs including anomalies of the coronary arteries, and isolated patent ductus arteriosus (PDA)].[2]

Data sources

Data were retrieved from two research projects, 'Congenital Heart Defects in Norway—a nationwide study (CHDNOR)' and 'Mortality in children with Congenital Heart Defects', corresponding to the approvals from the Regional Ethics Committees. We were not allowed to link individual information between the two projects.

Among all live births in Norway 1994–2009, the total number of children with CHDs and the total number of children with CHDs who died 2–18 years old due to causes unrelated to cardiac surgery were determined in the CHDNOR. This nationwide research project, which has been previously described,[2] include non-identifiable medical data from (i) the *Medical Birth Registry of Norway*, which collects medical information on all births in Norway; (ii) the *Cardiovascular Disease in Norway (CVDNOR)* research project at the University in Bergen that has retrieved information on all patients with International Classification of Disease (ICD) codes related to cardiovascular diseases from all hospitals in Norway[19]; (iii) the *Oslo University Hospital's Clinical Registry for Congenital Heart Defects*, which contains information on all children with CHDs who have been examined or treated at Oslo University Hospital; and (iv) the *Norwegian Cause of Death Registry*, which contains death certificate information, including date and cause of death. The case ascertainment in CHDNOR was done by searching specific diagnostic codes for CHDs (van Mierop 100–120, 1002–7442, ICD-8 746.0–747.4, 759.0 ICD-9 745.0–747.4, 759.3, and ICD-10 Q20.0–Q26.9, Q89.3) in all data sources.[2]

To acquire individual medical information, data on children with CHD diagnoses born 1994–2009 who died 2–18 years old due to causes unrelated to cardiac surgery were retrieved from the *Oslo University Hospital's Clinical Registry for Congenital Heart Defects*, which was updated per 30 September 2014. Oslo University Hospital covered ~80% of the country until 2004, and since that time, it has served as a national centre for congenital heart defects in Norway. The clinical registry was updated due to this study with information from the *Norwegian Cause of Death Registry* and from other hospitals after inquiries were sent to all paediatric cardiologists in Norway. Announcements were also made in the patient organization's journal and web pages. We reviewed the medical records and death certificates of the included children.

Children with CHDs who survived cardiac arrest were also identified in the *Oslo University Hospital's Clinical Registry for Congenital Heart Defects* and were described by review of medical records.

Comorbidity

Information on chromosome aberrations were retrieved by using ICD codes (ICD-8 759.3–759.5, ICD-9 758.0–759.9, and ICD-10 Q82.1, Q90.0–Q99.9) and van Mierop codes (8000–8004, 8009–8025, and 8072). Extracardiac defects were also identified by ICD codes (ICD-8 740.0–745.9, 748.0–756.9, 759.8–759.9, ICD-9 740.0–744.9, 748.0–756.9, 759.0–759.9, and ICD-10 Q00.0–Q18.9, Q30.0–Q89.9) and van Mierop codes (8041–8051, 8066, 8074–8076, 8079, and 8099).

Definitions of events

Sudden unexpected death was defined as death occurring instantaneously or within 1 h of the onset of acute symptoms or signs. Deaths in children who suddenly and irrevocably collapsed and never regained consciousness after the event were defined as sudden unexpected death even if death occurred later than 1 h. Children with sudden unexpected deaths were presumed to have died a *sudden unexpected cardiac death* if there was no other evident cause and the clinical history and autopsy ruled out other possibilities. *Physical activity-related sudden unexpected death* was defined as non-traumatic sudden unexpected death that occurred during or within 1 h after engaging in moderate-to-high intensity exercise. *Operative mortality* was defined as all deaths that occurred during the hospitalization during which cardiac surgery was performed, regardless of the length of stay, or deaths occurring after discharge from the hospital within 30 days of the procedure.

Cardiac arrest was defined as cessation of cardiac mechanical activity as confirmed by the absence of a detectable pulse, unresponsiveness, and apnoea. Cardiac arrest survivors were identified by searching specific diagnostic (ICD-9 427.4, 427.5, and ICD-10 I46, I46.0, I46.1, I46.9, I49.0) and therapeutic codes.

Study population

All 9 43 871 live births in Norway 1994–2009 registered in the Medical Birth Registry of Norway comprised the study population. All children were followed to emigration, death, or the end of follow-up (31 December 2012).

Statistical analysis

Baseline characteristics were compared using the chi-squared test, *t*-test, or nonparametric tests, as appropriate. Mortality rates for different CHD types were compared with hazard ratios (HRs) with 95% confidence intervals, with adjustments for being part of multiple births (twins, etc.) and sex. The estimated rates of non-operative sudden unexpected cardiac death in children 2 years and older with severe/non-severe CHD refer to the recorded number of such deaths divided by the total number of observed person-years for each group, and are expressed per 1 00 000 person-years. The numbers of deaths were identified in the Oslo University Hospital's clinical registry for congenital heart defects while the numbers of person-years were calculated from the CHDNOR. Analyses were performed using STATA (version 13, StataCorp LP, College Station, TX, USA).

Ethics

The Regional Committee for Medical and Health Research Ethics in Western Norway approved 'Congenital Heart Defects in Norway—a nationwide study (CHDNOR),' and the committee of South East Norway approved the study. Individual informed consent was not required.

Role of the funding sources

The funders of the study had no involvement in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication. The

corresponding author had full access to all the data in the study and had the final responsibility for the decision to submit for publication.

Results

Among the 9 43 871 live births in Norway 1994–2009, CHDs were identified in 11 272 (1.2%) cases in the CHDNOR, and 2673 (23.7%) of these children had severe CHD. Through 31 December 2012, 842 (7.5%) of the children with CHD died at a mean age of 0.9 years (±2.3 years). More children ($n = 515$, 19.3%) with severe CHD died compared with children with non-severe CHD ($n = 327$, 3.8%), resulting in an adjusted HR of 5.6 (4.8–6.4), $P < 0.001$. Most deaths occurred during the first 2 years of life for both severe ($n = 466$, 90.5%) and non-severe ($n = 285$, 87.2%) CHD cases. The operative mortality rate was 7.3% ($n = 141$) for severe CHD and 2.2% ($n = 23$) for non-severe CHD. The total follow-up time for the 10 459 children with CHD who survived the first 2 years of life and did not die in relation to cardiac surgery was 1 10 528.7 person-years, with a mean follow-up time of 10.6 years (±4.5 years). Due to emigration, 106 (1.0%) children were lost to follow-up after 2 years of age. During the study period, 38 (1.4%) children diagnosed with severe CHDs and 40 (0.5%) children diagnosed with non-severe CHDs died 2–18 years old from causes unrelated to surgical procedures (*Figure 1A*). The clinical characteristics of the children who survived the study period and the children who died from non-surgical causes after 2 years of life are described in *Table 1*. During the study period, implantable cardioverter defibrillators were placed in only three children with CHDs who were born 1994–2009.

After an update of the *Oslo University Hospital's Clinical Registry for Congenital Heart Defects* with seven cases from other Norwegian hospitals, we were able to retrieve individual medical information for 71 children born 1994–2009 with CHD diagnoses who died 2–18 years old from causes unrelated to surgical procedures. This number corresponds to 91% of the reported deaths in the CHDNOR for the same period. After a systematic review of the medical records, five children were reclassified (two primary cardiomyopathies with minor septal defects and three operative deaths) (*Figure 1B*). Three children did not have CHDs. For the remaining 63 children, the median survival time was 5.5 years (lower quartile 2.9, upper quartile 9.8) from birth. Most deaths occurred in hospitals ($n = 39$, 62%). An infection was diagnosed in 26 (41%) children before death or at autopsy. None of the children had implantable cardioverter defibrillators.

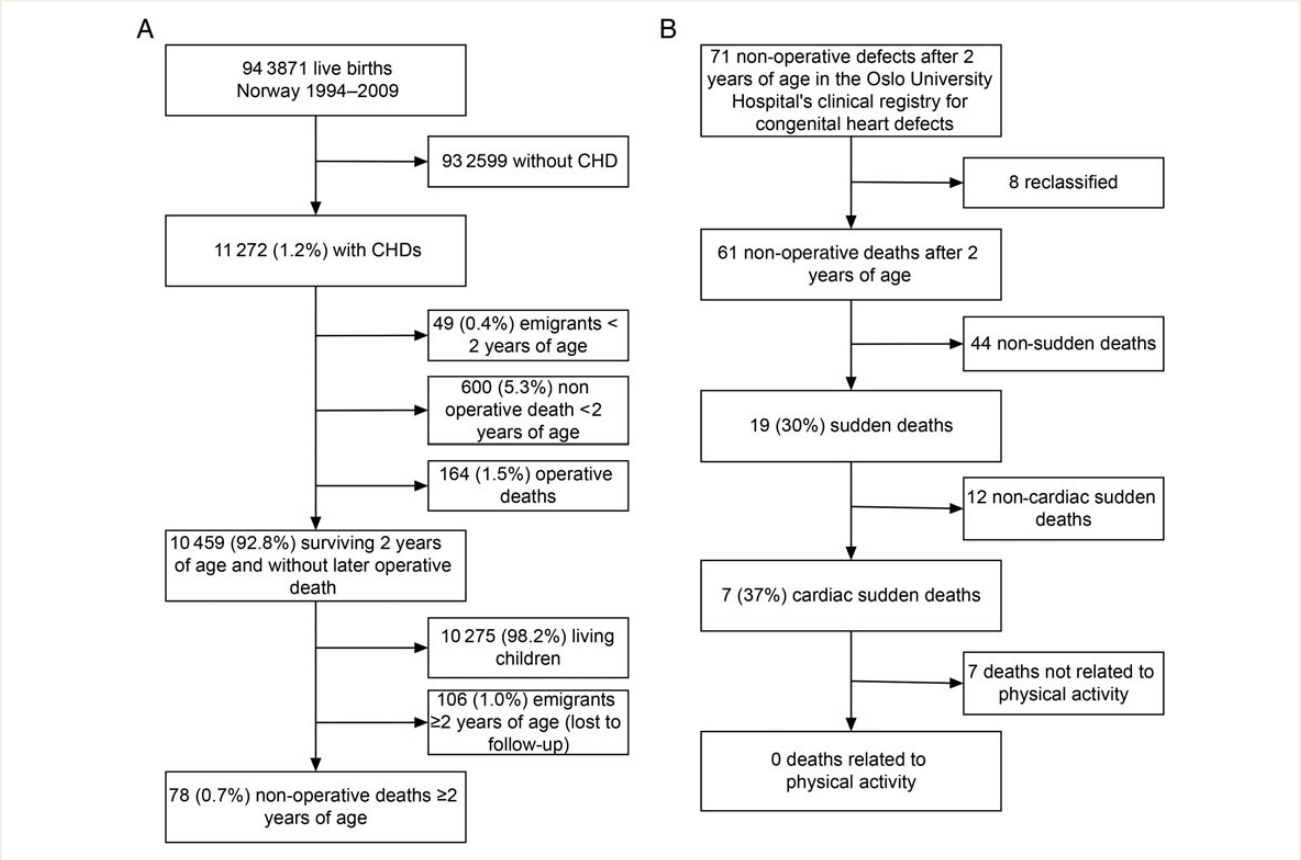

Figure 1 (*A*) Congenital heart defects in Norway 1994–2009. The number of live births with diagnosis of congenital heart defects and the number of deaths (in patients 2–18 years old) unrelated to cardiac surgery in Norway 1994–2009. (*B*) Sudden death. Circumstances of deaths who were unrelated to cardiac surgery in children 2–18 years old with congenital heart defects registered in the *Oslo University Hospital's Clinical Registry for Congenital Heart Defects*.

Table 1 Clinical characteristics

	Severe CHD			Non-severe CHD		
	Surviving children *N* = 2150 *n* (%)	Non-operative deaths in patients 2–18 years old *N* = 38 *n* (%)	*P*	Surviving children *N* = 8231 *n* (%)	Non-operative deaths in patients 2–18 years old *N* = 40 *n* (%)	*P*
Male sex	1257 (58)	25 (66)	0.36	3923 (48)	15 (38)	0.20
Multiple births	107 (5)	2 (5)	0.94	518 (6)	0 (0)	0.10
Extracardiac defects	571 (27)	18 (47)	0.004	1293 (16)	22 (55)	<0.001
Chromosomal aberration	404 (19)	11 (29)	0.11	535 (6)	15 (38)	<0.001
Preterm birth	279 (13)	7 (18)	0.32	1270 (15)	7 (18)	0.72
Small for gestational age	376 (17)	11 (29)	0.06	1119 (14)	10 (25)	0.03
Cardiac intervention	1757 (82)	35 (92)	0.10	1746 (21)	16 (40)	0.004
First cardiac intervention before 1 year of age	1483 (69)	28 (74)	0.73	740 (9)	7 (18)	0.800
Median age at first cardiac intervention (days)	56	49	0.53	488	493	0.06
Cardiac surgery	1684 (78)	30 (79)	0.68	987 (12)	11 (28)	0.003
Median survival time (days)		1698			2517	

Characteristics of children with CHDs surviving the study period and of children who died 2–18 years old from causes unrelated to cardiac surgery. Congenital Heart Defects in Norway 1994–2009.

Sudden unexpected deaths occurred in 8 of the 32 children with severe CHDs and 11 of the 31 children with non-severe CHDs who were identified in the *Oslo University Hospital's Clinical Registry for Congenital Heart Defects*. Twelve of the 19 sudden unexpected deaths occurred in children with known comorbidities (i.e. chromosomal aberrations or extracardiac malformations), and five children had an infection at the time of death. A probable cardiac cause of the sudden unexpected death was identified in six children with severe CHDs and one child with non-severe CHD (37% of sudden unexpected deaths). Four of the cardiac sudden deaths occurred in boys. The CHD diagnoses were TGA (two children), tricuspid atresia (two children), Ebstein's anomaly, TOF and PDA. Arrhythmias were noted in the medical records of all seven patients as the suspected cause of death. None of the children had been hospitalized due to arrhythmias or syncope earlier in life. Six of these seven children had undergone cardiac surgery. With the limitations mentioned below, the estimated rate of non-operative sudden unexpected cardiac death in children 2–18 years old with severe CHDs was 25 per 1 00 000 person-years and 1 per 1 00 000 person-years for children with non-severe CHDs.

During the study period, none of the deaths of the children with CHDs was associated with physical activity.

We identified two children with severe CHDs who survived a cardiac arrest after 2 years of age; these cases were unrelated to cardiac surgery. Both children had CHDs with a known increased risk of fatal arrhythmias. The cardiac arrests occurred during physical activity in both cases. Including these two sudden cardiac arrest survivors, the estimated rate of non-operative sudden unexpected cardiac death in children 2–18 years old with severe CHDs was 34 per 1 00 000 person-years and the estimated rate of sudden unexpected death related to physical activity in children 2–18 years old with CHDs was 2 per 1 00 000 person-years.

Discussion

In this nationwide cohort study, which included all live births in Norway 1994–2009, the non-operative mortality rate of children 2–18 years old with CHDs was low. Individual medical information was available for ~90% of these deaths. Review of the medical records disclosed a low frequency of cardiac sudden unexpected death, while comorbidity was common among the patients who died. In the children with CHDs surviving 2 years of age, we identified no death related to physical activities, whereas two children survived cardiac arrest during sports.

The reported incidence of sudden unexpected cardiac death in children and young adults without known heart disease ranges from 0.5 to 8 per 1 00 000 person-years.[9,20–26] We found a slightly higher incidence in children 2–18 years old with severe CHDs (25 per 1 00 000 person-years), while the incidence of sudden unexpected cardiac death in children 2–18 years old with non-severe CHDs (1 per 1 00 000 person-years) was in the lower range of these reports. The risk of sudden unexpected cardiac death in patients surviving surgery for CHDs has been estimated to be around 100 per 1 00 000 person-years and has been explained by myocardial scarring as a substrate for arrhythmias.[6,27–29] The risk appears to increase after the second post-operative decade and in patients with left heart obstructive lesions or cyanotic defects.[27] This finding could not be confirmed in our study because there were too few sudden unexpected deaths and a shorter follow-up time.

There are few studies concerning sudden unexpected death in children with CHDs. Polderman *et al.* identified patients younger than 19 years of age with sudden unexpected death and previously diagnosed heart disease in the Netherlands from 1990 to 2001.[6] The majority (76%) of the 150 included patients died of cardiac causes. In a Canadian study, Sanatani *et al.* described 80 sudden unexpected

deaths in children younger than 19 years with heart disease.[7] Arrhythmias were the most common cause of cardiac sudden death in both studies. In contrast to previous reports, we did not include children with cardiomyopathies or primary arrhythmic disorders, which may explain the lower number of arrhythmias. Our data do not allow for precise estimates of the risk factors for sudden unexpected death, but infections and comorbidity were frequently found in cases with sudden unexpected death.

Sudden unexpected deaths in young athletes receive much media attention and, thus, greatly impact the attitudes of the public and clinicians. The increased risk of sudden unexpected death during exercise among the general population has been described in several studies.[24,30] The incidence is not known with certainty, but it is reported to be ~1 per 2 00 000 young athletes per year.[31] Sudden deaths among previously healthy athletes are commonly caused by hypertrophic cardiomyopathy and anomalies of the coronary arteries.[24,32] Other CHDs account for a small fraction of these cases.[24] Sudden unexpected cardiac death during exercise in children with CHDs may theoretically occur because of thromboembolic complications, tissue rupture, and arrhythmias following post-operative scarring, myocardial ischaemia, haemodynamic overload, or desaturation. We are unaware of any reports concerning the frequency and causes of activity-related deaths in children with CHDs. In Norway, most children with CHDs have been advised to participate in regular physical activities. During the study period, <20 senior consultants at the tertiary level have been responsible for counselling of the families to children with CHDs. Although the recommendations for physical activity have been consistently liberal, we did not identify any activity-related sudden deaths. A possible explanation for the low number of sudden unexpected deaths among children with CHDs could be improved public skills in cardiac pulmonary resuscitation. However, only two cardiac arrest survivors were identified during the study period. Implantable cardioverter defibrillator use occurred infrequently and did not impact the study results. The two children who survived cardiac arrest during physical activity had CHDs with a known increased risk of serious arrhythmias. They encountered their events in school age, in spite of previous regular physical activity, and it was not possible to determine whether the cardiac arrests were provoked by activity or occurred incidentally. Even if these two episodes are taken into account, the risk of sudden unexpected death in relation to physical activity in children with CHDs was low in our study. Because of few events, our data do not allow for risk stratification, and restricted physical activity may still be warranted in select cases.

The main strengths of the present study are the large population from a national cohort of all children born in Norway 1994–2009 and the comprehensive follow-up. Some study limitations must be noted. We lack information concerning the circumstances of death in a small number of children who had never been recorded in the *Oslo University Hospital's Clinical Registry for Congenital Heart Defects*. Another limitation is the missing information about the level of physical activity. We do not know to what extent the children were exposed to intense cardiopulmonary activation. Restrictions from parents, teachers, and leaders of organized activities may hamper the level of activities. However, it is unlikely that all of these children had avoided potentially dangerous activity levels during organized sports, leisure activities, and free play. In addition, exercise tests are routinely performed to exhaustion in children with CHDs, with few adverse events and complications.[33] We also lack documentation of the contents of counselling provided by health professionals other than our knowledge of the national traditions. Finally, we must emphasize that the follow-up was for 3–18 years from birth and that the risk in adults with CHDs likely differs from the risk in children and youth.

In conclusion, sudden unexpected death was rare among children 2–18 years old with CHDs. Comorbidity was common among those children who died. None of the children in this 16-year national birth cohort of children with CHDs were reported to have died because of physical activity, whereas two children survived cardiac arrest during sports. Consequently, our findings indicate that sudden unexpected death in children with CHDs rarely occurs during physical activity. In our opinion, the benefits of physical activity in children with CHDs outweigh the low risk of sudden unexpected death.

Authors' contributions

J.J., T.F.: performed statistical analysis. J.J., N.Ø., H.H.: handled funding and supervision. J.J., L.E., N.Ø., G.S.T., T.F., P.H., G.D., A.H., H.H.: acquired the data. J.J., L.E., N.Ø., G.D., H.H.: conceived and designed the research. J.J.: drafted the manuscript. J.J., L.E., N.Ø., S.B., G.S.T., T.F., P.H., G.D., A.H., H.H.: made critical revision of the manuscript for key intellectual content.

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Conflict of interest: This study used data from the *Medical Birth Registry of Norway* and from the *Norwegian Cause of Death Registry*. The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by the *Medical Birth Registry of Norway* or by the *Norwegian Cause of Death Registry* is intended nor should be inferred.

References

1. Hoffman JI, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol* 2002;**39**:1890–1900.
2. Leirgul E, Fomina T, Brodwall K, Greve G, Holmstrom H, Vollset SE, Tell GS, Oyen N. Birth prevalence of congenital heart defects in Norway 1994–2009 – a nationwide study. *Am Heart J* 2014;**168**:956–964.
3. Øyen N, Poulsen G, Boyd HA, Wohlfahrt J, Jensen PK, Melbye M. National time trends in congenital heart defects, Denmark, 1977–2005. *Am Heart J* 2009;**157**: 467–473 e1.
4. Tennant PW, Pearce MS, Bythell M, Rankin J. 20-year survival of children born with congenital anomalies: a population-based study. *Lancet* 2010;**375**:649–656.
5. Wren C, Irving CA, Griffiths JA, O'Sullivan JJ, Chaudhari MP, Haynes SR, Smith JH, Hamilton JR, Hasan A. Mortality in infants with cardiovascular malformations. *Eur J Pediatr* 2012;**171**:281–287.
6. Polderman FN, Cohen J, Blom NA, Delhaas T, Helbing WA, Lam J, Sobotka-Plojhar MA, Temmerman AM, Sreeram N. Sudden unexpected death in children with a previously diagnosed cardiovascular disorder. *Int J Cardiol* 2004; **95**:171–176.
7. Sanatani S, Wilson G, Smith CR, Hamilton RM, Williams WG, Adatia I. Sudden unexpected death in children with heart disease. *Congenit Heart Dis* 2006;**1**:89–97.
8. Gajewski KK, Saul JP. Sudden cardiac death in children and adolescents (excluding Sudden Infant Death Syndrome). *Ann Pediatr Cardiol* 2010;**3**:107–112.
9. Winkel BG, Risgaard B, Sadjadieh G, Bundgaard H, Haunso S, Tfelt-Hansen J. Sudden cardiac death in children (1–18 years): symptoms and causes of death in a nationwide setting. *Eur Heart J* 2014;**35**:868–875.
10. Hirth A, Reybrouck T, Bjarnason-Wehrens B, Lawrenz W, Hoffmann A. Recommendations for participation in competitive and leisure sports in patients with congenital heart disease: a consensus document. *Eur J Cardiovasc Prev Rehabil* 2006;**13**: 293–299.
11. Pelliccia A, Zipes DP, Maron BJ. Bethesda Conference #36 and the European Society of Cardiology Consensus Recommendations revisited a comparison of U.S. and European criteria for eligibility and disqualification of competitive athletes with cardiovascular abnormalities. *J Am Coll Cardiol* 2008;**52**:1990–1996.
12. Takken T, Giardini A, Reybrouck T, Gewillig M, Hovels-Gurich HH, Longmuir PE, McCrindle BW, Paridon SM, Hager A. Recommendations for physical activity, recreation sport, and exercise training in paediatric patients with congenital heart disease: a report from the Exercise, Basic & Translational Research Section of the European Association of Cardiovascular Prevention and Rehabilitation, the European Congenital Heart and Lung Exercise Group, and the Association for European Paediatric Cardiology. *Eur J Prev Cardiol* 2012;**19**:1034–1065.
13. Longmuir PE, Brothers JA, de Ferranti SD, Hayman LL, Van Hare GF, Matherne GP, Davis CK, Joy EA, McCrindle BW, American Heart Association Atherosclerosis, Hypertension and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young. Promotion of physical activity for children and adults with congenital heart disease: a scientific statement from the American Heart Association. *Circ* 2013;**127**:2147–2159.
14. Budts W, Borjesson M, Chessa M, van Buuren F, Trigo Trindade P, Corrado D, Heidbuchel H, Webb G, Holm J, Papadakis M. Physical activity in adolescents and adults with congenital heart defects: individualized exercise prescription. *Eur Heart J* 2013;**34**:3669–3674.
15. Janssen I, Leblanc AG. Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. *Int J Behav Nutr Phys Act* 2010;**7**:40.
16. Fredriksen PM, Kahrs N, Blaasvaer S, Sigurdsen E, Gundersen O, Roeksund O, Norgaand G, Vik JT, Soerbye O, Ingjer E, Thaulow E. Effect of physical training in children and adolescents with congenital heart disease. *Cardiol Young* 2000;**10**: 107–114.
17. Pinto NM, Marino BS, Wernovsky G, de Ferranti SD, Walsh AZ, Laronde M, Hyland K, Dunn SO Jr, Cohen MS. Obesity is a common comorbidity in children with congenital and acquired heart disease. *Pediatrics* 2007;**120**:e1157–e1164.
18. Holm I, Fredriksen PM, Fosdahl MA, Olstad M, Vollestad N. Impaired motor competence in school-aged children with complex congenital heart disease. *Arch Pediatr Adolesc Med* 2007;**161**:945–950.
19. Sulo G, Igland J, Nygard O, Vollset SE, Ebbing M, Tell GS. Favourable trends in incidence of AMI in Norway during 2001–2009 do not include younger adults: a CVDNOR project. *Eur J Prev Cardiol* 2014;**21**:1358–1364.
20. Atkins DL, Everson-Stewart S, Sears GK, Daya M, Osmond MH, Warden CR, Berg RA, Resuscitation Outcomes Consortium Investigators. Epidemiology and outcomes from out-of-hospital cardiac arrest in children: the Resuscitation Outcomes Consortium Epistry-Cardiac Arrest. *Circulation* 2009;**119**:1484–1491.
21. Harmon KG, Asif IM, Klossner D, Drezner JA. Incidence of sudden cardiac death in National Collegiate Athletic Association athletes. *Circulation* 2011;**123**:1594–1600.
22. Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980–2006. *Circulation* 2009;**119**:1085–1092.
23. Holst AG, Winkel BG, Theilade J, Kristensen IB, Thomsen JL, Ottesen GL, Svendsen JH, Haunso S, Prescott E, Tfelt-Hansen J. Incidence and etiology of sports-related sudden cardiac death in Denmark – implications for preparticipation screening. *Heart Rhythm* 2010;**7**:1365–1371.
24. Meyer L, Stubbs B, Fahrenbruch C, Maeda C, Harmon K, Eisenberg M, Drezner J. Incidence, causes, and survival trends from cardiovascular-related sudden cardiac arrest in children and young adults 0 to 35 years of age: a 30-year review. *Circ* 2012;**126**:1363–1372.
25. Neuspiel DR, Kuller LH. Sudden and unexpected natural death in childhood and adolescence. *JAMA* 1985;**254**:1321–1325.
26. Driscoll DJ, Edwards WD. Sudden unexpected death in children and adolescents. *J Am Coll Cardiol* 1985;**5**(6 Suppl.):118B–121B.
27. Silka MJ, Hardy BG, Menashe VD, Morris CD. A population-based prospective evaluation of risk of sudden cardiac death after operation for common congenital heart defects. *J Am Coll Cardiol* 1998;**32**:245–251.
28. Nieminen HP, Jokinen EV, Sairanen HI. Causes of late deaths after pediatric cardiac surgery: a population-based study. *J Am Coll Cardiol* 2007;**50**:1263–1271.
29. Mondesert B, Khairy P. Implantable cardioverter-defibrillators in congenital heart disease. *Curr Opin Cardiol* 2014;**29**:45–52.
30. Corrado D, Basso C, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden cardiac death? *J Cardiovasc Med* 2006;**7**:228–233.
31. Maron BJ, Gohman TE, Aeppli D. Prevalence of sudden cardiac death during competitive sports activities in Minnesota high school athletes. *J Am Coll Cardiol* 1998;**32**: 1881–1884.
32. Maron BJ, Thompson PD, Ackerman MJ, Balady G, Berger S, Cohen D, Dimeff R, Douglas PS, Glover DW, Hutter AM Jr, Krauss MD, Maron MS, Mitten MJ, Roberts WO, Puffer JC. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation* 2007;**115**:1643–1455.
33. Rhodes J, Ubeda Tikkanen A, Jenkins KJ. Exercise testing and training in children with congenital heart disease. *Circulation* 2010;**122**:1957–1967.