Sudden Cardiac Death in Congenital Heart Disease: Repaired and Unrepaired

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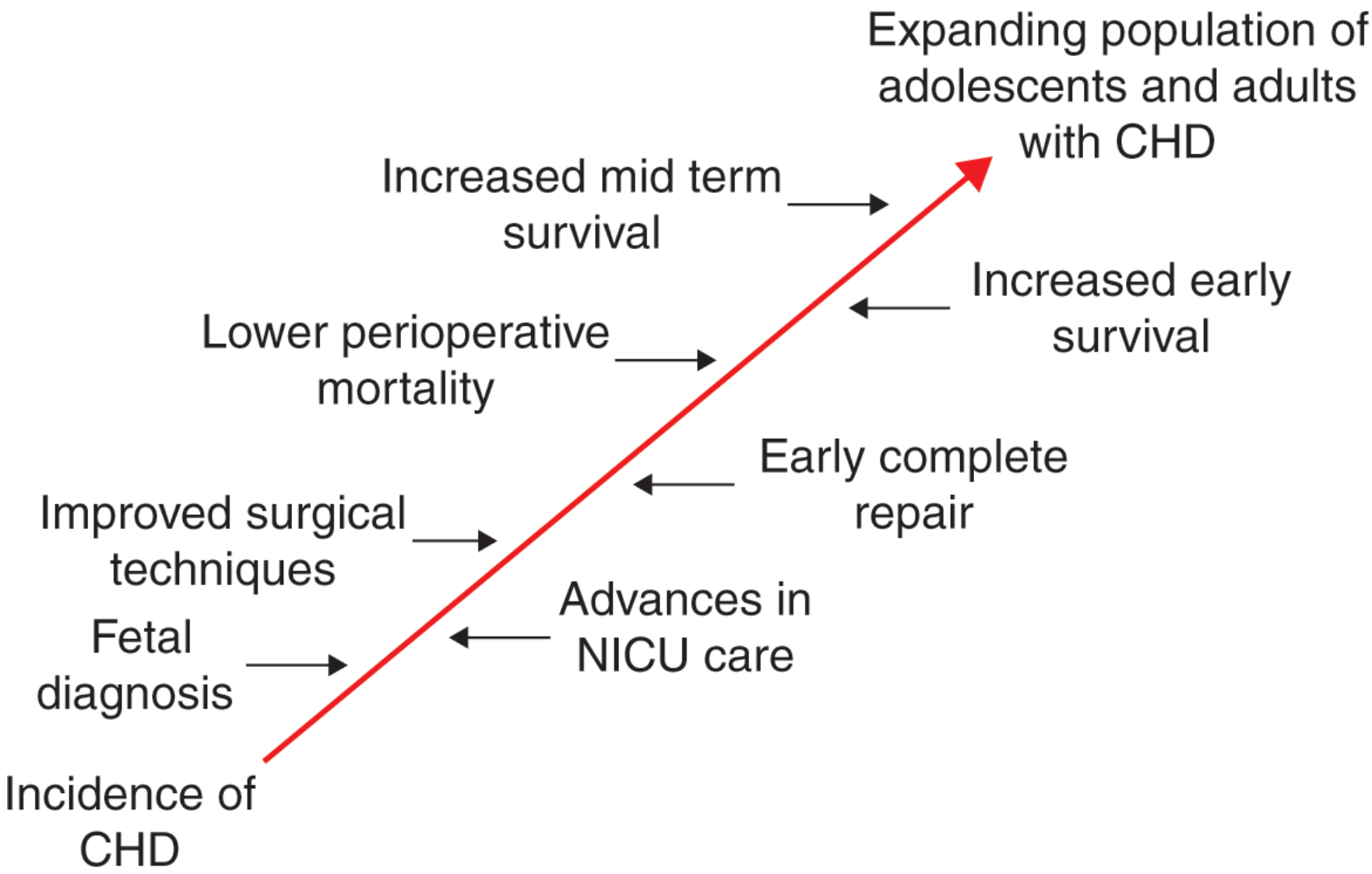
I have no disclosures

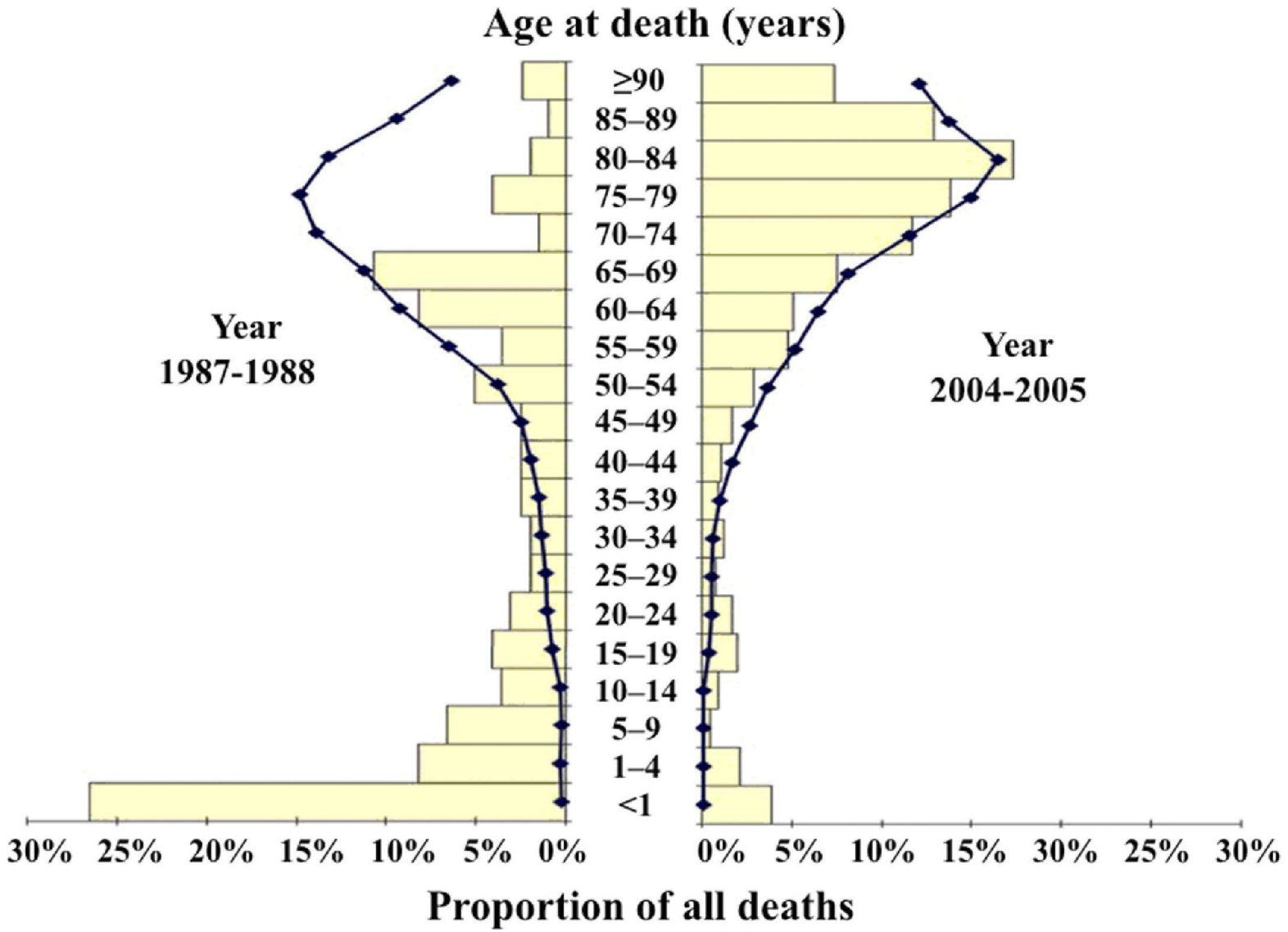
Outline

- Demographics of Congenital Heart Disease (CHD)
- Highlight the burden of sudden cardiac death (SCD) in CHD patients
- Discuss circumstances of SCD in CHD patients
- Risk stratification and prevention of SCD

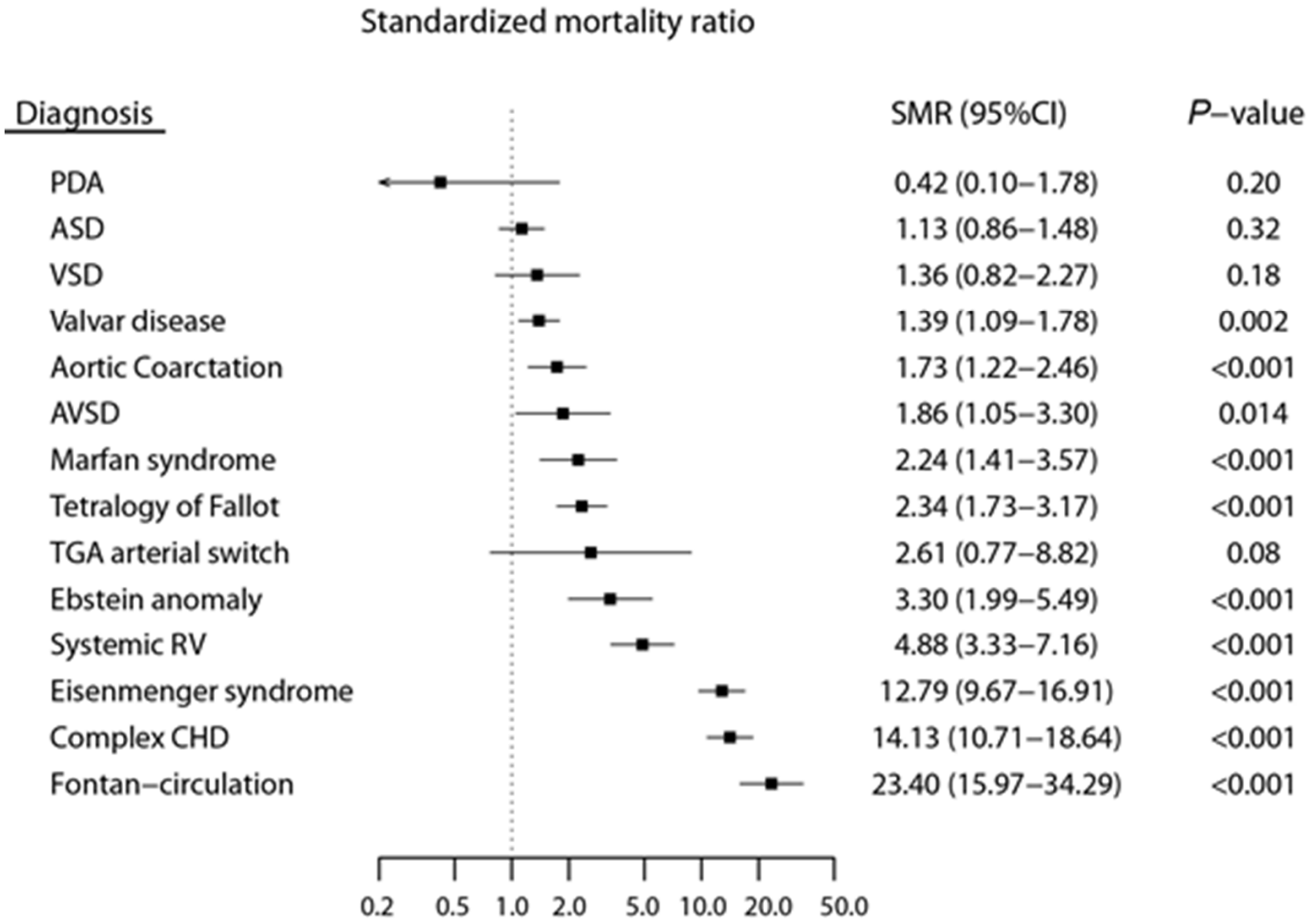
Pediatric to Adult Congenital Heart Disease



Changing Mortality in Congenital Heart Disease



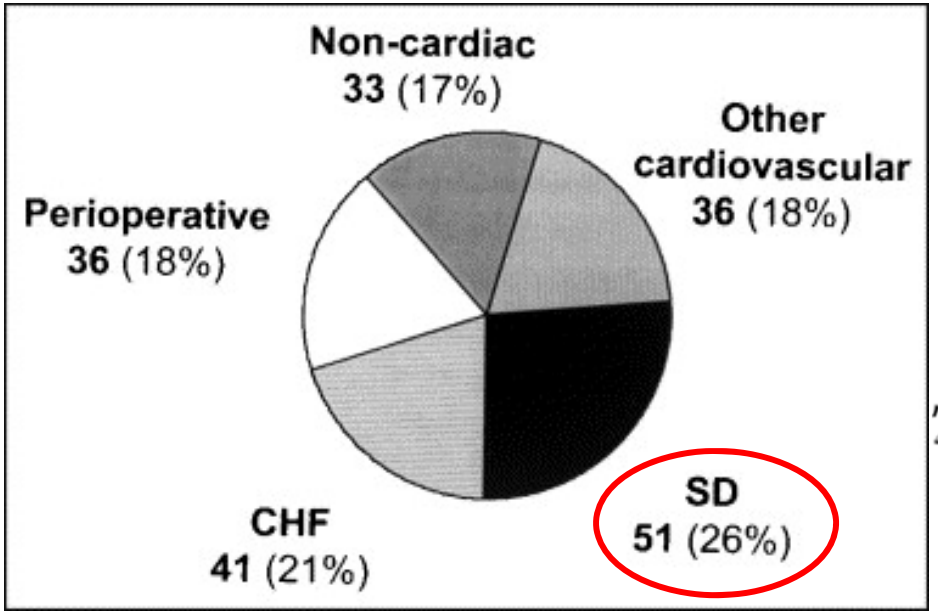
Paul Khairy et al. JACC 2010;56:1149-1157



Diller GP et al. Circulation. 2015 Dec 1;132(22):2118-25

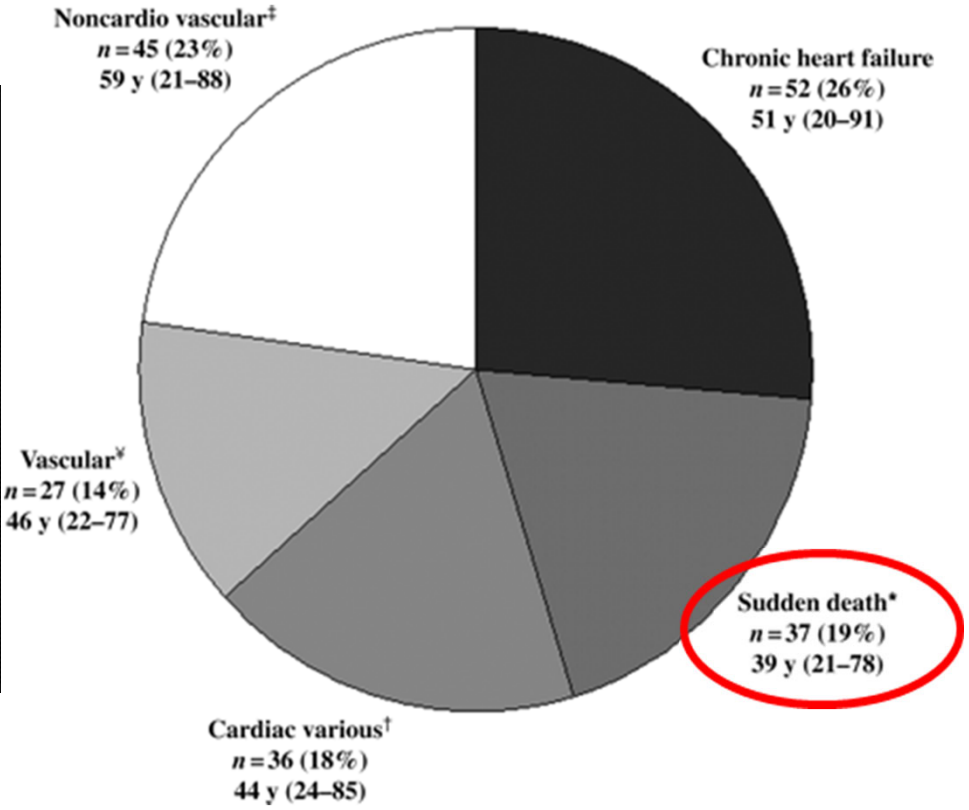
Mode of death in CHD patients

Univ. of Toronto
2609 Patients
197 Deaths



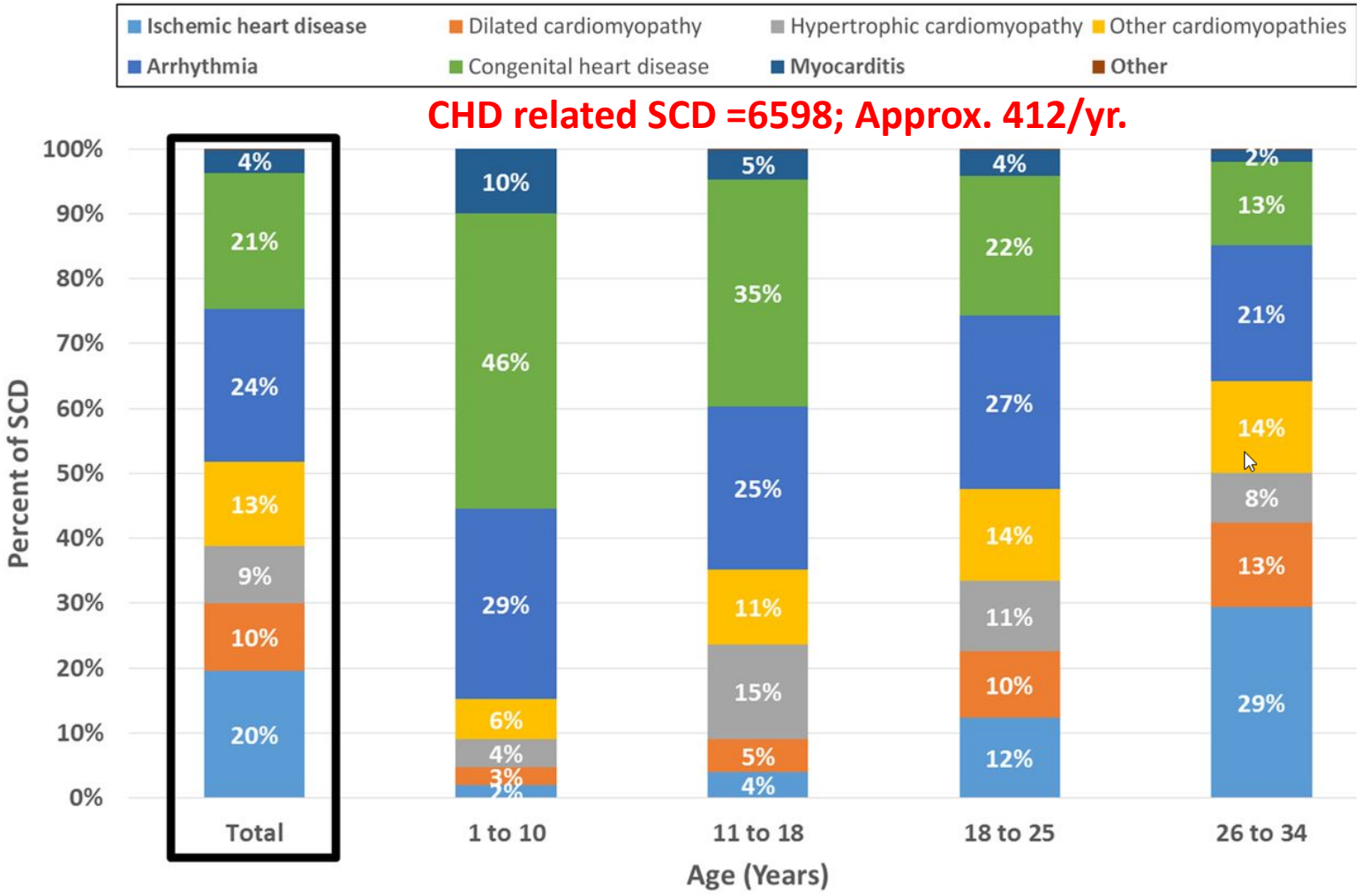
Oechslin EN et al Am J Cardiol 2000;86:1111-6

Dutch CONCOR Registry
6933 Patients
197 Deaths



Verheugt CL et al Eur Heart J 2010:31:1220-9

Causes of sudden cardiac death among children and young adults 1 to 34 years of age



Iqbal El-Assaad et al. Pediatrics 2017;140:e20171438

Study	Location	Types of patients	Patients (N)	Death (N[%])	Sudden Death (%)
Koyak et al. Circulation 2012	Multicentric	Repaired & unrepaired	25790	1189 (5.0)	19.0
Silka MJ et al. JACC 1998	Oregon (USA)	Repaired	3589	176 (4.9)	23.3
Nieminen et al. JACC 2007	Finland	Repaired	5919	582 (9.8)	14.9
Oechslin EN et al. AJC 2000	Canada	Repaired & unrepaired	2609	197(7.6)	25.9
Verheught CL et al EHJ 2010	Netherlands	Repaired & unrepaired	6933	197 (2.8)	19.0
Diller GP et al. Circulation 2015	UK	Repaired & unrepaired	6969	524(7.5)	7.0

Scope of the Problem

- Annual incidence of SCD in total CHD population 0.09%/yr.

(60-70 times higher than normal population)

Approximately 2000-2500 Sudden cardiac deaths

Approximately 3 million CHD patients

Silka MJ et al. J Am Coll Cardiol 1998;32:245-251
Yap SC and Harris L Expert Rev Cardiovasc Ther 2009;7:1605-20

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Sudden Cardiac Death in Adult Congenital Heart Disease

Zeliha Koyak, Louise Harris, Joris R. de Groot, Candice K. Silversides, Erwin N. Oechslin, Berto J. Bouma, Werner Budts, Aeilko H. Zwinderman, Isabelle C. Van Gelder and Barbara J.M. Mulder

Circulation. 2012;126:1944-1954; originally published online September 18, 2012;
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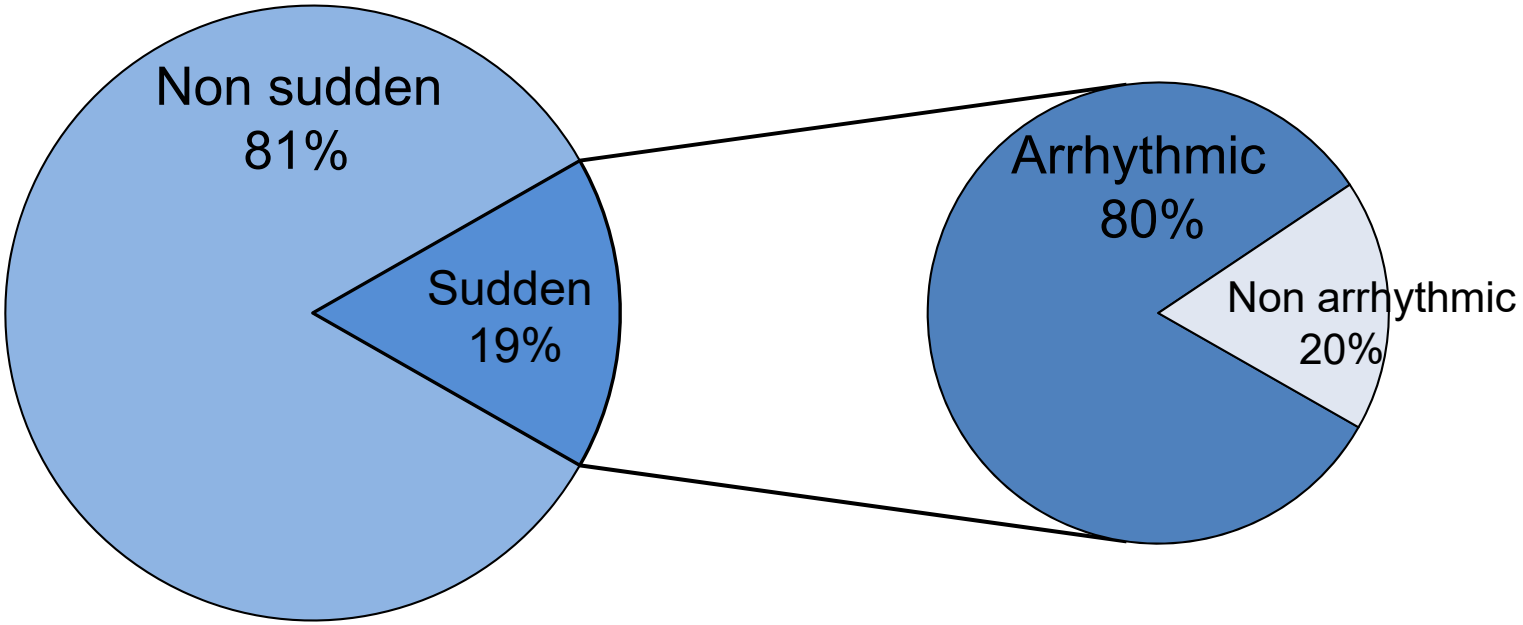
CONCOR	TCCCA	UZ Leuven
N=11,535	N~8,000	N~6255
25,790 ACHD patients from three registries		

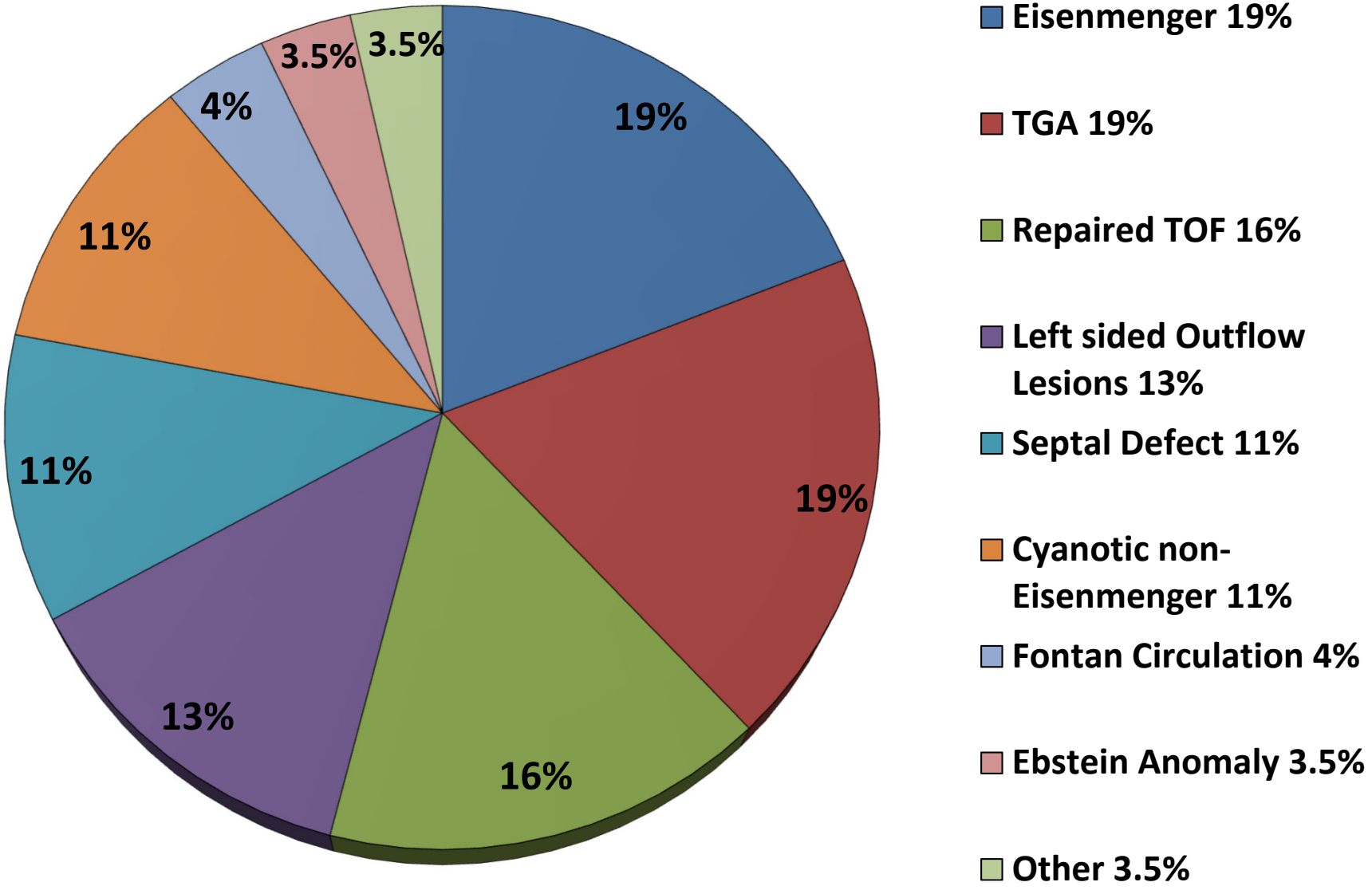
Total deaths=1189

N= 213 deaths

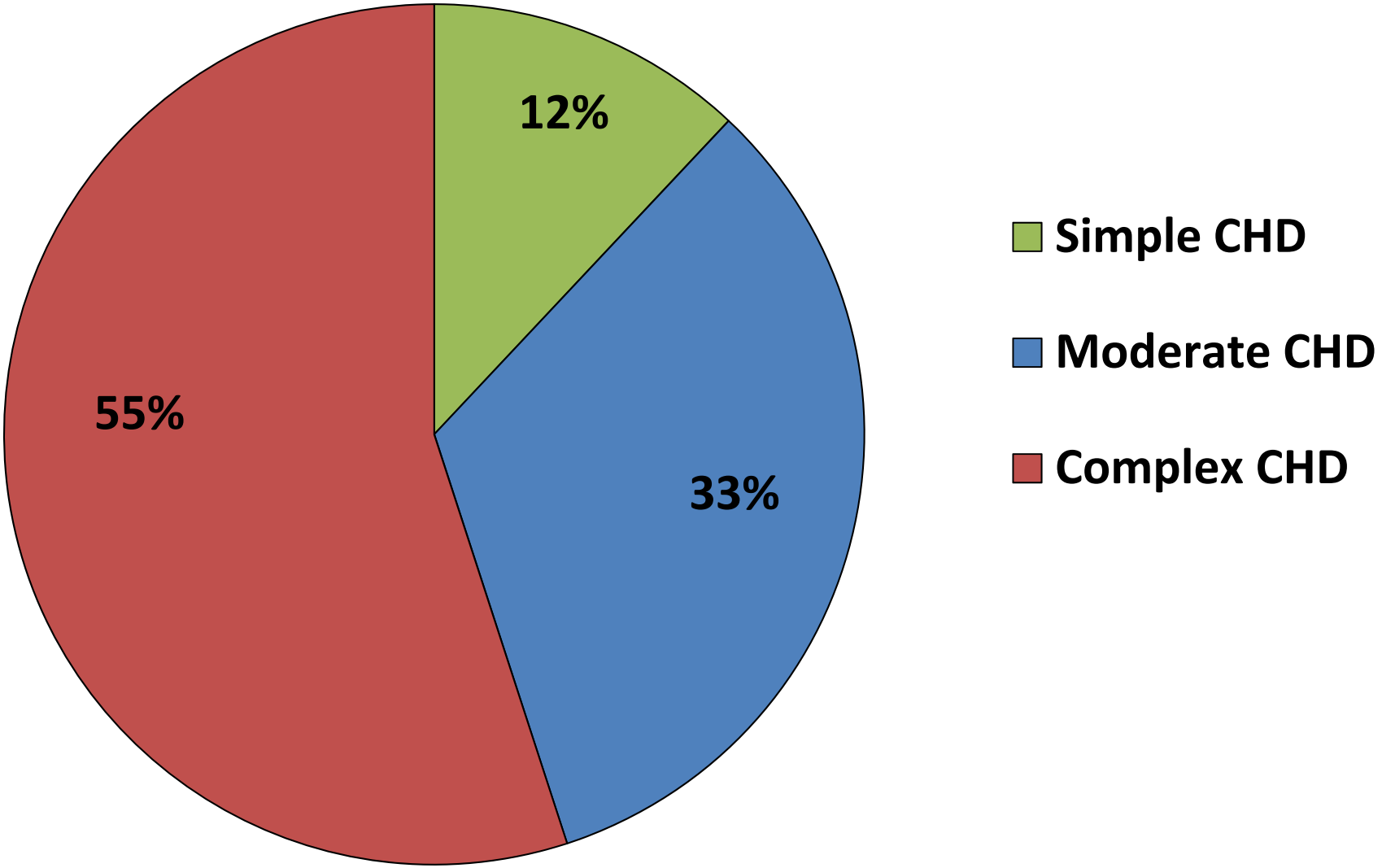


Causes of non-arrhythmic sudden death: aortic rupture(9%), cerebral (4%), pulmonary embolism (4%), myocardial infarction (2%), GI bleeding(1%)

SCD by CHD Lesion



SCD by Severity of CHD



Sudden Cardiac Death cases versus controls

- For each SCD case, 2 matched living controls

Variables	Cases (n=165)	Controls (n=310)	P value
NYHA functional class 3	40(24%)	17(5%)	<0.001
Heart Failure symptoms	62(38%)	42(14%)	<0.001
Documented SVT	66(40%)	77(25%)	<0.001
Atrial fibrillation/atrial flutter	57(35%)	58(19%)	<0.001
Sustained VT/VF	5(3%)	3(1%)	0.096
Non sustained VT	23(14%)	33(11%)	0.032

Clinical variables associated with SCD

Parameter	Odds Ratio	95% Confidence Intervals	P value
Supraventricular tachycardia (SVT)	**3.5**	1.5 - 7.9	0.004
Moderate to severe systemic ventricular dysfunction	**3.4**	1.1 - 10.4	0.034
Moderate to severe sub pulmonary ventricular dysfunction	**3.4**	1.1 - 10.2	0.030
Increased QRS duration (per 10-ms increase)	**1.34**	1.10 - 1.34	0.008
QT dispersion (per 10-ms increase)	**1.22**	1.22 - 1.48	0.008

Do the guidelines for ICD implantation fall short ?

ICD Indications	Consensus Statement		ESC Guidelines	
	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Class I	12 (7–19)	98 (95–99)	15 (10–21)	97 (94–99)
Class IIa	39 (22–59)	76 (63–86)	34 (18–54)	73 (60–84)
Class IIb (1)	16 (10–24)	92 (88–95)	15 (10–22)	92 (88–95)
Class IIb (2)	35 (26–44)	86 (81–91)	NA	NA
Any indication	41 (32–51)	83 (77–88)	35 (27–43)	85 (80–89)

CI indicates confidence interval; ESC, European Society of Cardiology; ICD, implantable cardioverter-defibrillator; and NA, not available.

Vehmeijer JT et al. Circ Arrhythm Electrophysiol. 2017 Jul;10(7)

Tetralogy of Fallot

Author	Patients	Date of Repair	Parameters
Gatzoulis et al. 2000	793	1958-1990's	• QRS duration, rate of change • Older age at repair • Pulmonary regurgitation
Khairy et al. 2008 (Selected patients with ICD)	121	1985-2001	• Prior palliative shunt • Inducible sustained VT • Non sustained VT • LVEDP >12 mmHg • Ventriculotomy incision
Diller et al. 2012	413	N/A	• LV longitudinal dysfunction • RV fractional area change
Valente et al. 2014	873	N/A	• RV hypertrophy • RV and LV dysfunction • Atrial tacharrhythmias

Estimated risk of all-cause mortality for 3 patients at 15 years

Patient Characteristics	Disease Severity Index	32nd Bethesda classification	NYHA	Ability Index	CHD Functional Index
25 yr. old woman: Ebstein Anomaly, moderate TR	Moderate 5%	Low 6%	Class I **4%**	Grade 2 **9%**	Class 3 8%
25 yr. old man: PA, VSD, Transposed GA, s/p extracardiac Fontan	Complex 18%	High 23%	Class I **4%**	Grade 2 9%	Class 4 **36%**
26 yr. old man: Aortic atresia, s/p Yasui, RV-PA conduit, s/p PPM/ICD	Complex 18%	Moderate **7%**	Class III-IV 44%	Grade 3 **51%**	Class 5 40%

Concept of "age equivalent"/ "loss of years"

	Patient's age (years)								
	20	**25**	**30**	**35**	**40**	**45**	**50**	**55**	**60**
ASD	25	26	32	38	42	47	52	57	61
Valvar disease	29	31	36	40	45	49	54	59	63
VSD	28	30	36	40	44	49	53	59	63
Aortic Coarctation	32	33	38	43	47	52	56	62	66
AVSD	33	34	39	44	48	52	57	62	66
Marfan syndrome	37	38	42	46	50	54	59	64	68
Tetralogy of Fallot	37	38	42	47	50	54	60	65	69
TGA arterial switch	38	39	44	48	52	56	61	66	70
Ebstein anomaly	42	43	47	51	54	59	63	68	72
Systemic RV	46	48	51	55	59	63	67	72	76
Eisenmenger syndrome	57	58	62	65	69	73	77	81	84
Complex CHD	58	59	63	67	70	74	78	82	85
Fontan	64	65	68	72	75	78	82	86	91

Age difference:
- >40
- 30-40
- 20-30
- 10-20
- 5-10
- 2-5
- <2

Values present relative age adjusted for predicted 5-years mortality. Colors reflect the difference between relative and actual age. For example a 40 year old Fontan patient has a mortality rate that is comparable to that of a 75 year old individual without CHD.

Diller GP et al. Circulation. 2015 Dec 1;132(22):2118-25

Estimated risk of all-cause mortality for 3 patients at 15 years

Patient Characteristics	Disease Severity Index	32nd Bethesda classification	NYHA	Ability Index	CHD Functional Index	"Equivalent Age"/loss of life years
25 yr. old woman: Ebstein Anomaly, moderate TR	Moderate 5%	Low 6%	Class I 4%	Grade 2 9%	Class 3 8%	Age 43: **loss of 18 years**
25 yr. old man: PA, VSD, Transposed GA, s/p extracardiac Fontan	Complex 18%	High 23%	Class I 4%	Grade 2 9%	Class 4 36%	Age 65: **loss of 40 years**
26 yr. old man: Aortic atresia, s/p Yasui, RV-PA conduit, s/p PPM/ICD	Complex 18%	Moderate 7%	Class III-IV 44%	Grade 3 51%	Class 5 40%	Age 59: **loss of 33 years**

Conclusions

- Sudden cardiac death is one of the **leading causes of death** in patients with congenital heart disease, especially in patients with repaired cyanotic and left heart obstructive lesions.
- Overall annual incidence of sudden cardiac death is estimated at **0.09% per year.**
- Identified risk factors have a high sensitivity, but a low predictive power due to a combination of a low event rate and moderate specificity.
- **Ventricular dysfunction** of the subaortic ventricle has gained increasing attention as a potential important risk factor for sudden cardiac death.
- Future studies will have to focus on **improving risk stratification** of patients with congenital heart disease for prophylactic ICD implantation.