Supplementary material

Chmielewski P, Świerczewski M, Foss-Nieradko B, et al. Clinical and genetic yield of familial screening after a sudden unexplained death at a young age. Pol Heart J. 2024.

Table S1. List of genes tested in Trusight Cardio panel

ABCC9	*CBL*	*FBN1*	*KCNE1*	*MYH11*	*RANGRF*	*TBX20*
ABCG5	*CBS*	*FBN2*	*KCNE2*	*MYH6*	*RBM20*	*TBX3*
ABCG8	*CETP*	*FHL1*	*KCNE3*	*MYH7*	*RYR1*	*TBX5*
ACTA1	*COL3A1*	*FHL2*	*KCNH2*	*MYL2*	*RYR2*	*TCAP*
ACTA2	*COL5A1*	*FKRP*	*KCNJ2*	*MYL3*	*SALL4*	*TGFB2*
ACTC1	*COL5A2*	*FKTN*	*KCNJ5*	*MYLK*	*SCN1B*	*TGFB3*
ACTN2	*COX15*	*FXN*	*KCNJ8*	*MYLK2*	*SCN2B*	*TGFBR1*
AKAP9	*CREB3L3*	*GAA*	*KCNQ1*	*MYO6*	*SCN3B*	*TGFBR2*
ALMS1	*CRELD1*	*GATAD1*	*KLF10*	*MYOZ2*	*SCN4B*	*TMEM43*
ANK2	*CRYAB*	*GCKR*	*KRAS*	*MYPN*	*SCN5A*	*TMPO*
ANKRD1	*CSRP3*	*GJA5*	*LAMA2*	*NEXN*	*SCO2*	*TNNC1*
APOA4	*CTF1*	*GLA*	*LAMA4*	*NKX2-5*	*SDHA*	*TNNI3*
APOA5	*DES*	*GPD1L*	*LAMP2*	*NODAL*	*SEPN1*	*TNNT2*
APOB	*DMD*	*GPIHBP1*	*LDB3*	*NOTCH1*	*SGCB*	*TPM1*
APOC2	*DNAJC19*	*HADHA*	*LDLR*	*NPPA*	*SGCD*	*TRDN*
APOE	*DOLK*	*HCN4*	*LDLRAP1*	*NRAS*	*SGCG*	*TRIM63*
BAG3	*DPP6*	*HFE*	*LMF1*	*PCSK9*	*SHOC2*	*TRPM4*
BRAF	*DSC2*	*HRAS*	*LMNA*	*PDLIM3*	*SLC25A4*	*TTN*
CACNA1C	*DSG2*	*HSPB8*	*LPL*	*PKP2*	*SLC2A10*	*TTR*
CACNA2D1	*DSP*	*ILK*	*LTBP2*	*PLN*	*SMAD3*	*TXNRD2*
CACNB2	*DTNA*	*JAG1*	*MAP2K1*	*PRDM16*	*SMAD4*	*VCL*
CALM1	*EFEMP2*	*JPH2*	*MAP2K2*	*PRKAG2*	*SNTA1*	*ZBTB17*
CALR3	*ELN*	*JUP*	*MIB1*	*PRKAR1A*	*SOS1*	*ZHX3*
CASQ2	*EMD*	*KCNA5*	*MURC*	*PTPN11*	*SREBF2*	*ZIC3*
CAV3	*EYA4*	*KCND3*	*MYBPC3*	*RAF1*	*TAZ*	

Table S2. Cardiovascular disorders associated with genes tested in Trusight Cardio panel according to the manufacturer's data sheet

Inherited Arrthymias							
Long QT syndrome (LQTS) — 16 genes							
KCNQ1	*KCNH2*	*SCN5A*	*ANK2*	*KCNE1*	*KCNE2*	*KCNJ2*	*CACNA1C*
CAV3	*SCN4B*	*AKAP9*	*SNTA1*	*KCNJ5*	*RYR2*	*KCNE3*	*CALM1*
Short QT syndrome (SQTS) — 4 genes							
KCNH2	*KCNQ1*	*KCNJ2*	*CACNA2D1*				
Brugada syndrome (BrS) — 14 genes							
SCN5A	*GPD1L*	*CACNA1C*	*CACNB2*	*KCNE3*	*SCN3B*	*KCNJ8*	*CACNA2D1*
KCND3	*RANGRF*	*HCN4*	*KCNH2*	*PKP2*	*ABCC9*		
Catecholaminergic polymorphic ventricular tachycardia (CPVT) — 6 genes							
RYR2	*CASQ2*	*KCNE1*	*KCNJ2*	*TRDN*	*CALM1*		
Cardiomyopathies							
Hypertrophic cardiomyopathy (HCM) — 48 genes							
MYBPC3	*MYH7*	*TNNT2*	*TNNI3*	*TPM1*	*MYL3*	*MYL2*	*ACTC1*
CSRP3	*FHL1*	*PRKAG2*	*MYPN*	*TTN*	*TCAP*	*TNNC1*	*KLF10*
JPH2	*ACTN2*	*GAA*	*MYH6*	*MYLK2*	*ANKRD1*	*SLC25A4*	*SOS1*
TRIM63	*VCL*	*CALR3*	*MYOZ2*	*COX15*	*NEXN*	*RAF1*	*CACNA1C*
CAV3	*CASQ2*	*DES*	*FXN*	*MYO6*	*ACTA1*	*GLA*	*PDLIM3*
BRAF	*LAMP2*	*PTPN11*	*MAP2K1*	*MAP2K2*	*CRYAB*	*KCNQ1*	*BRAF*
Dilated cardiomyopathy (DCM) — 51 genes							
LMNA	*MYH7*	*TTN*	*DSP*	*MYBPC3*	*TNNT2*	*BAG3*	*SCN5Aa*
RBM20	*DMD*	*TPM1*	*LDB3*	*DES*	*TNNI3*	*MYPN*	*MYH6*
TNNC1	*ANKRD1*	*TCAP*	*VCL*	*PLN*	*MURC*	*ACTC1*	*ACTN2*
DSG2	*CSRP3*	*FKTN*	*LAMA2*	*PRDM16*	*SGCD*	*TAZ*	*CRYAB*
NEXN	*DOLK*	*PKP2*	*ABCC9*	*ILK*	*LAMA4*	*TXNRD2*	*DNAJC19*
DSC2	*TMPO*	*GATAD1*	*EMD*	*LAMP2*	*PDLIM3*	*SGCB*	*JUP*
NPPA	*ACTA1*						
Arrhythmogenic right ventricular cardiomyopathy (ARVC) — 12 genes							
PKP2	*DSP*	*DSG2*	*DSC2*	*JUP*	*TTN*	*TMEM43*	*RYR2*
DES	*TGFB3*	*LMNA*	*SCN5A*				
Restrictive cardiomyopathy (RCM) — 9 genes							
TNNI3	*DES*	*MYH7*	*TNNT2*	*ACTC1*	*MYL3*	*MYL2*	*TPM1*
MYPN							
Left ventricular non-compaction (LVNC) — 10 genes							
MYH7	*MYBPC3*	*TAZ*	*TPM1*	*ACTC1*	*TNNT2*	*PRDM16*	*MIB1*
CASQ2	*DTNA*						
Noonan syndrome (NS) — 9 genes							
PTPN11	*SOS1*	*RAF1*	*KRAS*	*BRAF*	*CBL*	*NRAS*	*MAP2K1*
SHOC2							
Aortopathies							
Marfan syndrome (MFS) — 4 genes							
FBN1	*TGFBR2*	*TGFBR1*	*LTBP2*				
Loeys-Dietz syndrome (LDS) — 3 genes							
TGFBR2	*TGFBR1*	*FBN1*					
Familial aortic anuerysm (FAA) — 12 genes							
ACTA2	*FBN1*	*MYH11*	*TGFB2*	*TGFBR2*	*COL3A1*	*SMAD3*	*MYLK*

TGFBR1	*SLC2A10*	*NOTCH1*	*EFEMP2*				
Aortic valve disease (AVD) — 3 genes							
NOTCH1	*ELN*	*FBN1*					
Other cardiac diseases							
Familial hypercholesterolemia (FH) — 8 genes							
LDLR	*APOB*	*PCSK9*	*LDLRAP1*	*CETP*	*SREBF2*	*APOE*	*ABCG8*
Additional genes in ICCv2 panel							
CTF1	*FHL2*	*SCN2B*	*TRPM4*	*SCO2*			

Table S3. Comorbidities and cardiovascular risk factors in the screened relatives of sudden unexplained death victims

	All n = 87	Probands n = 39	Other n = 48	*P*-value
Coronary artery disease	3 (3%)	2 (5%)	1 (2%)	0.59
Hypertension	19 (22%)	12 (31%)	7 (15%)	0.12
Diabetes	5 (6%)	1 (3%)	4 (8%)	0.37
Prediabetes	12 (14%)	6 (15%)	6 (13%)	0.70
Dyslipidemia	27 (31%)	12 (31%)	15 (31%)	0.96
Obesity	17 (20%)	8 (21%)	9 (19%)	0.84
Body mass index, kg/m^2	25 [21-28]	25 [22-30]	25 [21-27]	0.61
Current smoking	10 (11%)	6 (15%)	4 (8%)	0.31

Number of subjects is expressed as n (%). Continuous variables are shown median and quartiles [Q1:25th–Q2:75th percentiles]. Probands denote those family members in whom the diagnosis of a cardiovascular disorder of probably genetic origin was either established or seemed most likely and who were selected for next generation sequencing

Table S4. Comparison of selected characteristics of the examined families and probands depending on the diagnostic yield

	All n = 39	Definite diagnosis n = 17	No diagnosis n = 20	*P*-value
Age at SUD of the reference victim, years	33 (7)	34 (6)	32 (9)	0.66

Minimal age at SUD in the family, years	32 (7)	33 (6)	31 (9)	0.63
≥2 SUDs in the family	15 (41%)	10 (59%)	5 (25%)	0.04
≥1 female SUD in the family	11 (28%)	6 (35%)	5 (25%)	0.49
≥2 female SUDs in the family	3 (8%)	3 (18%)	0	0.09
Number of screened relatives	2 [1-3]	2 [2-3]	1.5 [1-3]	0.39
≥2 screened relatives	23 (62%)	13 (76%)	10 (50%)	0.10
Number of screened I° relatives	1 [1-2]	1 [1-2]	1 [1-3]	0.96
Age of the proband, years	38 ± 14	38 ± 12	38 ± 15	0.84
Child of the reference SUD victim as the proband	15 (41%)	8 (47%)	7 (35%)	0.27
Presence of symptoms in the proband	24 (65%)	14 (82%)	10 (50%)	0.04
History of syncope in the proband	7 (19%)	4 (24%)	3 (15%)	0.68

Number of subjects is expressed as n (%). Continuous variables are shown as mean (standard deviation) or median [25^{th}–75^{th} percentile]. Legend: SUD, sudden unexplained death. The Reference victim denotes an individual whose death inclined the family to screening. Probands denote those family members in whom the diagnosis of a cardiovascular disorder of probably genetic origin was either established or seemed most likely and who were selected for next generation sequencing