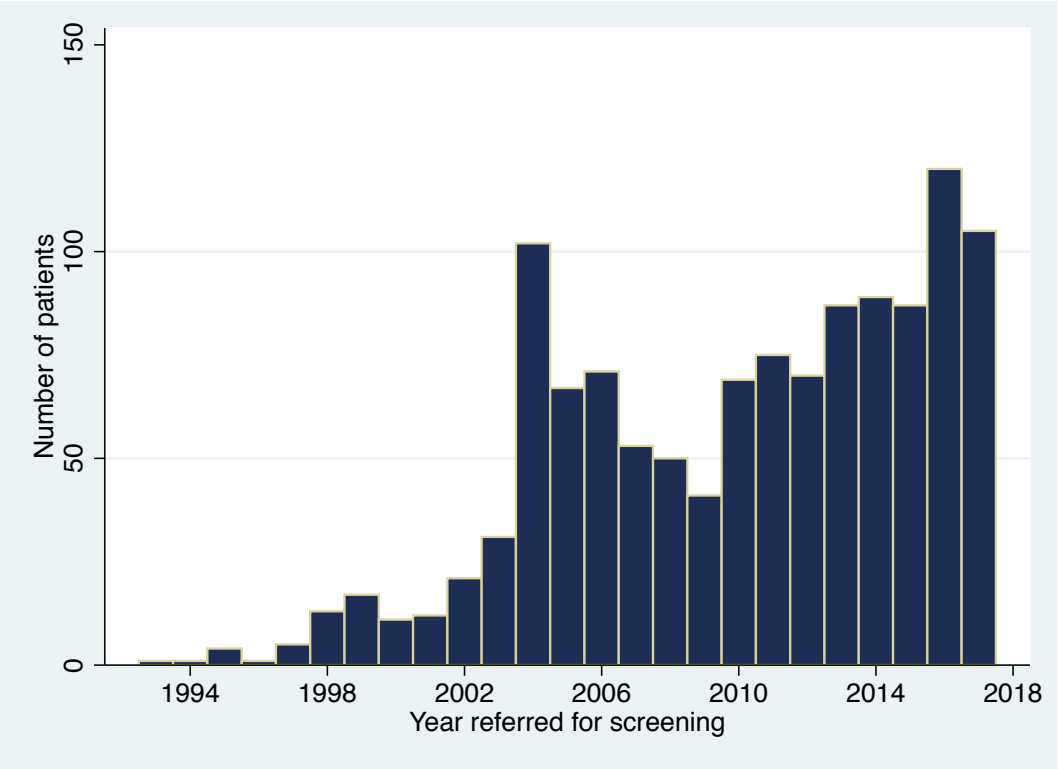
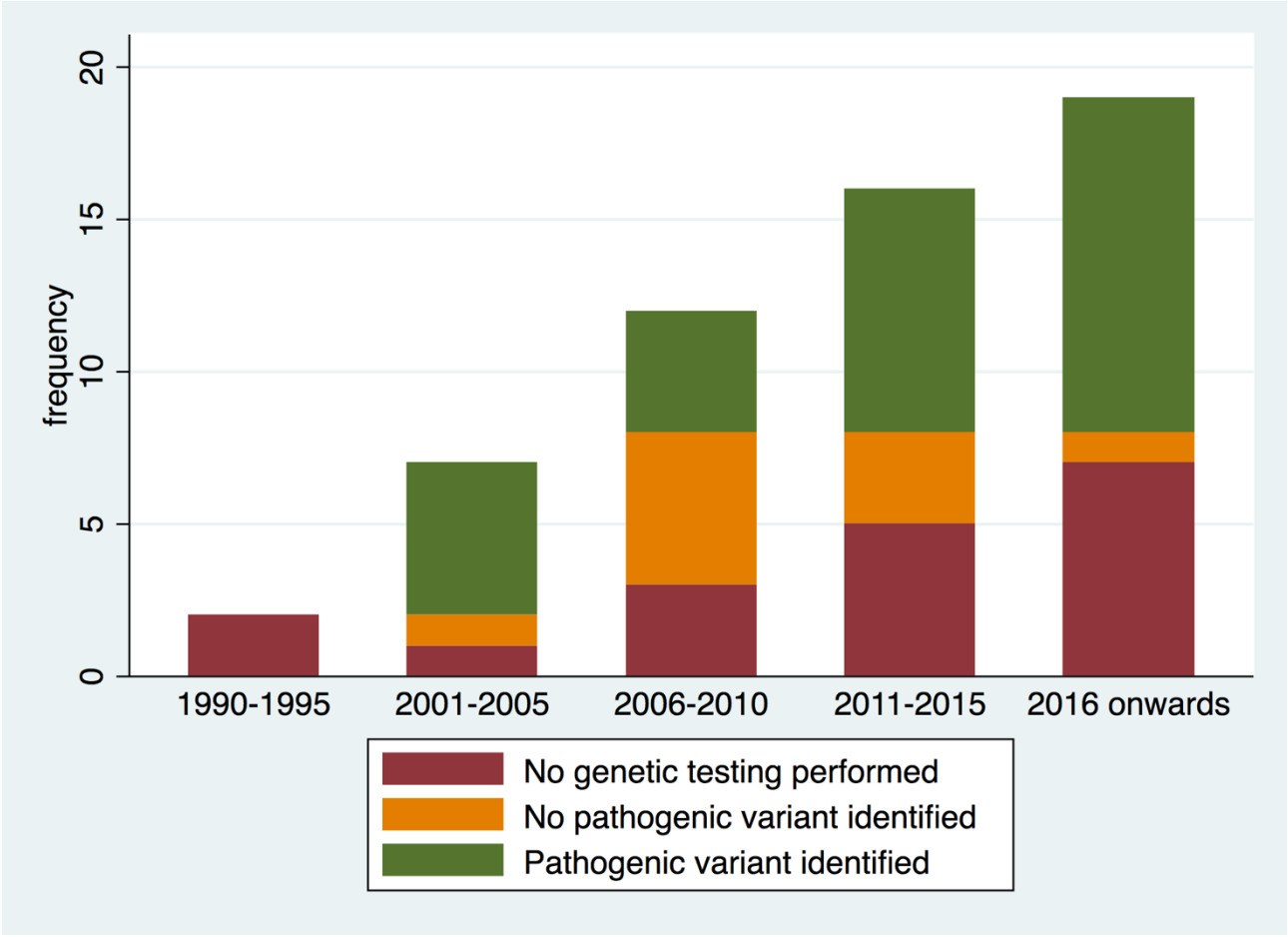
SUPPLEMENTAL MATERIAL

Supplementary Figure 1: Number of patients undergoing clinical screening by year



Supplementary figure 2: Result of genetic testing in patients with a diagnosis of HCM by era of diagnosis



Supplementary table 1: Re-classification of reported variants according to ACMG classification guidance.

Gene	Protein change	Nucleotide change	Previous pathogenicity classification	ACMG classification
MYBPC3	Arg943*	c.2827C>T	**PATHOGENIC**	**PATHOGENIC**
TPM1	Glu192Lys	c.574G>A	**PATHOGENIC**	**LIKELY PATHOGENIC**
MYBPC3		c.3752_3753delAT	**PATHOGENIC**	**VUS**
MYH7	Glu374Val	g.23899001T>A	**PATHOGENIC**	**VUS**
MYBPC3	Arg495Gln	c.1484G>A	**PATHOGENIC**	**PATHOGENIC**
MYBPC3		c.927-9G>A	**PATHOGENIC**	**PATHOGENIC**
PRKAG2	Asn247Ile		**PATHOGENIC**	**VUS**
MYH7	Arg723Gly	c.2167C>G	**PATHOGENIC**	**PATHOGENIC**
MYL2	Gly87Ala	c.260G>C	**PATHOGENIC**	**VUS**
TNNT2	Glu163del	c.487_489delGAG	**PATHOGENIC**	**VUS**
MYBPC3		1928-2A>G	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Trp792Valfs*41	c.2373_2374insG	**PATHOGENIC**	**PATHOGENIC**
TNNI3	Asp196Asn	c.586G>A	**PATHOGENIC**	**PATHOGENIC**
TNNI3 +DES	Lys206Gln Leu470PhE	c.616A>C c.1408C>T	**PATHOGENIC** **VUS**	**PATHOGENIC** **VUS**
TPM1	Glu192Lys	c.574G>A	**PATHOGENIC**	**LIKELY PATHOGENIC**
MYH7	Phe247Leu	c.739T>C	**PATHOGENIC**	**VUS**
MYH7 + FHOD3	Asn696Ser Arg638Trp	c.2087A>G Arg638Trp	**PATHOGENIC** **VUS**	**LIKELY PATHOGENIC** **VUS**
MYH7	Glu374Lys	g.23899001T>A	**PATHOGENIC**	**VUS**
TNNT2	Arg92Gln	c.275G>A	**PATHOGENIC**	**PATHOGENIC**
MYBPC3		c. 3491-2A>T	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Lys505*	c.1513A>T	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Glu258Lys	c.772G>A	**PATHOGENIC**	**PATHOGENIC**
MYH7	Lys847Glu	c.2539A>G	**PATHOGENIC**	**PATHOGENIC**
MYBPC3 + PLN	Glu542Gln Ile47fs	c. 1624G>C c.138dupT	**PATHOGENIC** **VUS**	**PATHOGENIC** **VUS**
MYBPC3	His390Metfs16	c.1168delC	**PATHOGENIC**	**PATHOGENIC**
MYH7	Met982Thr	c.2945T>C	**PATHOGENIC**	**LIKELY BENIGN**
MYBPC3	Arg1138His	c.3413G>A	**PATHOGENIC**	**LIKELY BENIGN**
MYH7	Arg721Lys	c.2162G>A	**PATHOGENIC**	**LIKELY PATHOGENIC**
MYH7	Thr449Asn	c.1346C>A	**PATHOGENIC**	**VUS**
MYBPC3 X2	Arg802Trp Ser858Asn	c.2573G>A	**PATHOGENIC**	**VUS** **VUS**

MYBPC3		c.1224-19G>A	**PATHOGENIC**	**PATHOGENIC**
MYH7	Gly741Trp	c.2221G>T	**PATHOGENIC**	**PATHOGENIC**
TNNT2	Asp86Tyr	c.256G>T	**PATHOGENIC**	**LIKELY PATHOGENIC**
TNNT2 + MYH7	Arg278Cys Asp239Asn	c.832C>T c.715G>A	**PATHOGENIC**	**PATHOGENIC** **VUS**
TNNT2	Arg92Leu	c.832C>T	**PATHOGENIC**	**PATHOGENIC**
MYH7	Arg453Cys	c.1357C>T	**PATHOGENIC**	**PATHOGENIC**
MYH7	Glu931del	2791_2793delGAG	**PATHOGENIC**	**VUS**
MYH7	Ala797Thr	c.2389G>A	**PATHOGENIC**	**PATHOGENIC**
MYBPC3 + TNNT2	Arg502Trp	c.1504C>T (c.341C>T)	**PATHOGENIC**	**PATHOGENIC**
MYBPC3 + FLNC	Leu2421His	c.927-2A>G c.7262T>A	**PATHOGENIC** **VUS**	**PATHOGENIC** **VUS**
MYH7	Arg442Cys	c.1324C>T	**PATHOGENIC**	**PATHOGENIC**
TNNT2	Arg148Gln	c.443A>G	**PATHOGENIC**	**VUS**
MYH7	Glu927Lys	c.2779G>A	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Ser871Glnfs*13	c.2610_2611insC	**PATHOGENIC**	**PATHOGENIC**
MYH7	Leu908Val	c.2722C>G	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Arg597Gln	c.1790G>A	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Arg502Trp	c.1504C>T	**PATHOGENIC**	**PATHOGENIC**
MYH7	Arg663His	c.1988G>A	**PATHOGENIC**	**PATHOGENIC**
MYH7	Leu889His	c.2666T>A	**PATHOGENIC**	**LIKELY PATHOGENIC**
MYH7	Ala335Thr	c.1003G>A	**PATHOGENIC**	**VUS**
MYBPC3 + TNNT2	Arg495Gln Arg285Cys	c.1484G>A c.853G>A	**PATHOGENIC** **VUS**	**PATHOGENIC** **VUS**
MYH7 + DES	Arg453Pro Thr76Profs*22	c.1358G>C c.226delA	**PATHOGENIC** **VUS**	**PATHOGENIC** **VUS**
MYH7	Asn817Lys	c.2451C>A	**PATHOGENIC**	**VUS**
MYBPC3	Glu1085Glyfs*104	c.3254delA	**PATHOGENIC**	**PATHOGENIC**
MYH7	Arg453His	c.1358G>A	**PATHOGENIC**	**PATHOGENIC**
MYH7	Glu958Lys	c.2872G>A	**PATHOGENIC**	**VUS**
MYBPC3	Ser871Alafs*8	c.2604_2605delTCinsA	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Pro699Glnfs*55	c2093delC	**PATHOGENIC**	**PATHOGENIC**
PRKAG2	Asn488lle	c.1463A>T	**PATHOGENIC**	**VUS**
MYH7	Gly741Arg	c.2221G>C	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Val758Ala	c.2273C>T	**PATHOGENIC**	**LIKELY PATHOGENIC**
TNNT2	Arg92Trp	c.274C>T	**PATHOGENIC**	**PATHOGENIC**
TNNT2	Arg278Cys	c.832C>T	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Arg502Gln	c.1505G>A	**PATHOGENIC**	**PATHOGENIC**
MYH7	Glu965Lys	c.2893G>A	**PATHOGENIC**	**LIKELY PATHOGENIC**
MYBPC3 + MYBPC3	Cys1266Tyr Gly5Arg	c.3797G>A c.13G>C	**PATHOGENIC** **VUS**	**VUS** **LIKELY BENIGN**
MYBPC3	Pro1243Arg	c.3728C>G	**PATHOGENIC**	**VUS**
MYBPC3	Tyr333*	c.999C>G	**PATHOGENIC**	**PATHOGENIC**
TNNI3	Arg162Gln	c.485G>A	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Arg495Gly	c.1483C>G	**PATHOGENIC**	**PATHOGENIC**
MYBPC3		C.927-9G>A	**PATHOGENIC**	**PATHOGENIC**

MYH7	Glu924Lys	c.2770G>A	**PATHOGENIC**	**PATHOGENIC**
MYH7	Tyr624Asn	c.1870T>A	**PATHOGENIC**	**VUS**
MYBPC3		1457+5G>C	**PATHOGENIC**	**PATHOGENIC**
MYBPC3 + FHOD3	Arg502Trp Arg637Gln	c.1504C>T	**PATHOGENIC** **VUS**	**PATHOGENIC** **VUS**
MYH7	Arg403Leu	1208G>T	**PATHOGENIC**	**PATHOGENIC**
MYH7	Arg403Gln	c.1208G>A	**PATHOGENIC**	**PATHOGENIC**
MYH7	Met515Thr	c.1544T>C	**PATHOGENIC**	**LIKELY PATHOGENIC**
MYBPC3	Gln969*	c.2905C>T	**PATHOGENIC**	**PATHOGENIC**
TNNT2	Arg92Trp	c.274C>T	**PATHOGENIC**	**PATHOGENIC**
MYBPC3		c.927-2A>G	**PATHOGENIC**	**PATHOGENIC**
ACTC1	Tyr296Asn		**PATHOGENIC**	**VUS**
MYBPC3	Tyr1251*	c.886T>A	**PATHOGENIC**	**PATHOGENIC**
MYBPC3		3190+5G>A	**PATHOGENIC**	**PATHOGENIC**
MIT1	m.4300A>G		**PATHOGENIC**	**VUS**
MYBPC3	Lys685Argfs	c.2054_2067+11del25	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Asp770Asn	c.2308G>A	**PATHOGENIC**	**PATHOGENIC**
MYBPC3 + MYH7	Arg502Trp Lys1459Asn	c.1504C>T c.4377G>T	**PATHOGENIC** **VUS**	**PATHOGENIC** **LIKELY BENIGN**
MYH7	(Asp900Glu)	c.2700T>A,	**PATHOGENIC**	**VUS**
MYH7	Arg719Gln	c.2156 G>A	**PATHOGENIC**	**PATHOGENIC**
TNNT2	Ile79Asn	c.236T>A	**PATHOGENIC**	**VUS**
MYBPC3		2326-36Del	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Trp1098*	c.3294G>A	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Pro960Leu		**PATHOGENIC**	**VUS**
MYH7	Val406Met	c.1216G>A	**PATHOGENIC**	**LIKELY PATHOGENIC**
MYBPC3+ MYBPC3 + CSRP3	 Glu165Asp Thr84Met	3330+5G>A c.495G>C c.251C>T	**PATHOGENIC** **VUS** **VUS**	**PATHOGENIC** **VUS** **VUS**
MYBPC3+ MYH7	Asp610Asn Arg787His	c.1828G>A c.2360G>A	**PATHOGENIC** **PATHOGENIC**	**LIKELY PATHOGENIC** **LIKELY PATHOGENIC**
TNNI3	Arg162Glu	c.485G>A	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Pro453Cysfs*21	c.1357_1358delCC	**PATHOGENIC**	**PATHOGENIC**
MYBPC3		c.927-2A>G	**PATHOGENIC**	**PATHOGENIC**
MYBPC3	Asp1076Valfs*6	c.3226_3227insT	**PATHOGENIC**	**PATHOGENIC**
MYH7	Arg723Cys	c.2167C>T	**PATHOGENIC**	**PATHOGENIC**
MYH7	Ala355Ser	c.1063G>T	**PATHOGENIC**	**PATHOGENIC**
MYBPC3		c.1624+4A>T	**PATHOGENIC**	**PATHOGENIC**
MYH7	Ala463Asp	c.1388C>A	**PATHOGENIC**	**LIKELY PATHOGENIC**
MYBPC3 + MYL3	Tyr373* Ala57Asp	c.170C>A	**PATHOGENIC**	**PATHOGENIC** **LIKELY PATHOGENIC**
MYBPC3		c.1457+5G>C	**PATHOGENIC**	**PATHOGENIC**
MYH7	Glu256Glu	c.767G>A	**PATHOGENIC**	**PATHOGENIC**
TNNT2	Glul83Lys	c.277G>A	**PATHOGENIC**	**PATHOGENIC**
MYH7	Val606Leu	c.1816G>T	**PATHOGENIC**	**LIKELY PATHOGENIC**

MYH7	Asp906Gly	c.2717A>G	**VUS**	**PATHOGENIC**
MYBPC3	Lys505del	c.1513_1515delAAG	**VUS**	**PATHOGENIC**
MYBPC3 + MYH7	Asp610Asn Arg787His	c.1828G>A c.2360G>A	**VUS**	**LIKELY PATHOGENIC** **LIKELY PATHOGENIC**
MYH7	Glu1293Lys	c.3877G>A	**VUS**	**LIKELY PATHOGENIC**
TNNT2	Glu83Lys	c.277G>A	**VUS**	**PATHOGENIC**
TPM1	Ser252Thr	c.755G>C	**VUS**	**LIKELY PATHOGENIC**
Titin	lle22436del	c.67308_67310delAAT	**VUS**	**VUS**
MYH7	Glu374Val	g.23899001T>A	**VUS**	**VUS**
MYBPC3	Ala833Val	c.2498C>T	**VUS**	**BENIGN**
ANKRD1	Arg78Ser	c.234A>T	**VUS**	**LIKELY BENIGN**
MYBPC3	Trp1086Arg	c.3256T>C	**VUS**	**VUS**
MYBPC3 + FLNC	(Arg766Trp)	c.3815-10T>G c.2296C>T	**VUS** **BENIGN**	**VUS** **LIKELY BENIGN**
SOS1	Ser1096Thr	c.3286T>A	**VUS**	**LIKELY BENIGN**
TPM1	Asn202Ser	c.605A>G	**VUS**	**VUS**
RAF1	Met224Arg	c.671T>G	**VUS**	**VUS**
MYBPC3	Trp486Gly	c.1456T>G	**VUS**	**VUS**
TTN	His4271Gln	c.12813C>A	**VUS**	**VUS**
SOS1	Val624Phe	c.1870G>T	**VUS**	**VUS**
TNNI3	Pro82Ser	c.244C>T	**VUS**	**LIKELY BENIGN**
MYBPC3	Arg1228Cys	c.3682C>T	**VUS**	**LIKELY BENIGN**

Duplicate variants identified in more than one family removed.

Supplementary table 2: Type of genetic testing performed in patients with a childhood diagnosis of hypertrophic cardiomyopathy by era.

	Type of genetic testing in those with phenotype		Size of genetic panel in genetic index case			
Year genetic testing performed	**Predictive testing**	**Panel testing**	**Sanger sequencing**	**Small NGS panel**	**Expanded NGS panel**	**Unknown size**
Pre 2000	-	-	-	-	-	-
2001-2005	1	1	-	1	-	-
2006-2010	4	5	7	3	-	2
2011-2015	-	1	2	2	-	1
2016 onwards	13	10	-	7	9	-
Unknown year of testing	4	-	-	-	-	6
	***22 (39%)**	**17 (30%)**	**9 (22.5%)**	**13(32.5%)**	**9(22.5%)**	**9 (22.5%)**

**3 patients underwent predictive testing for a previously classified pathogenic variant, which was subsequently re-classified as a VUS*