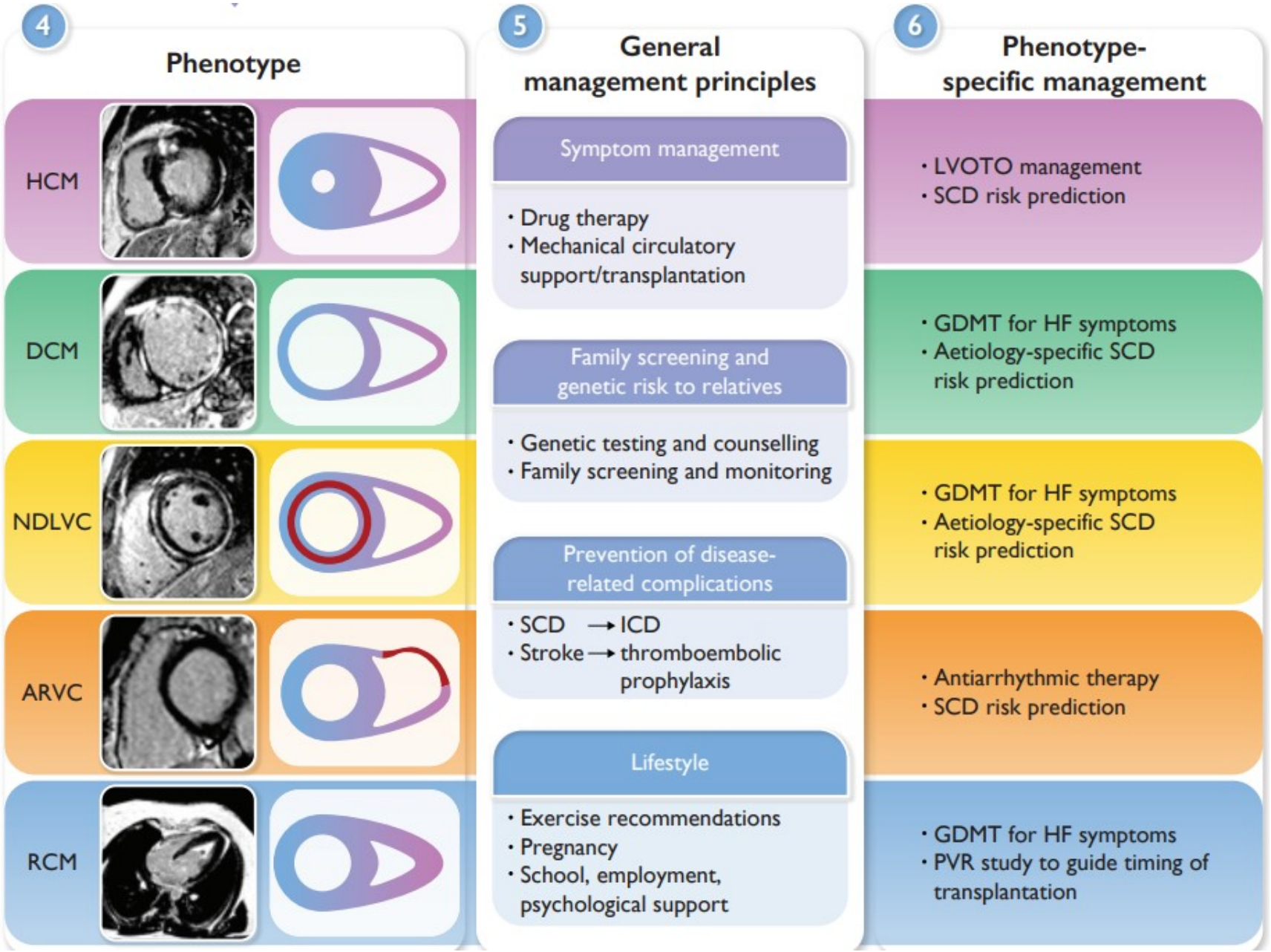
Markéta Adamová on behalf of WG
of Cardiogenetics in Czech Genetic
Society (SLG-ČSL JEP)

GENETIC BASIS FOR CARDIOMYOPATHY IN A REPRESENTATIVE COHORT IN THE CZECH REPUBLIC



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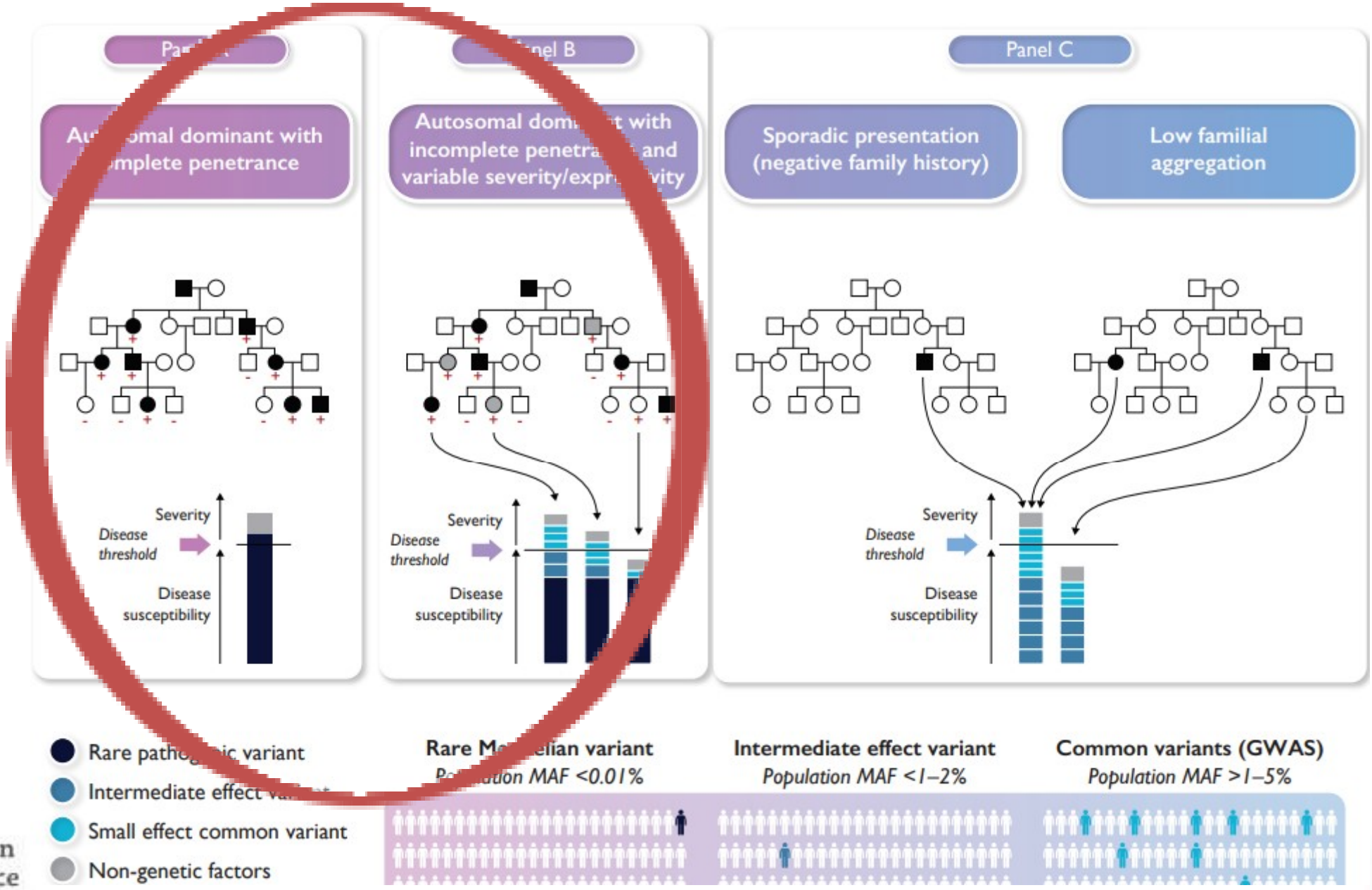
Arbelo et al. (2023)



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Arbelo et al. (2023)

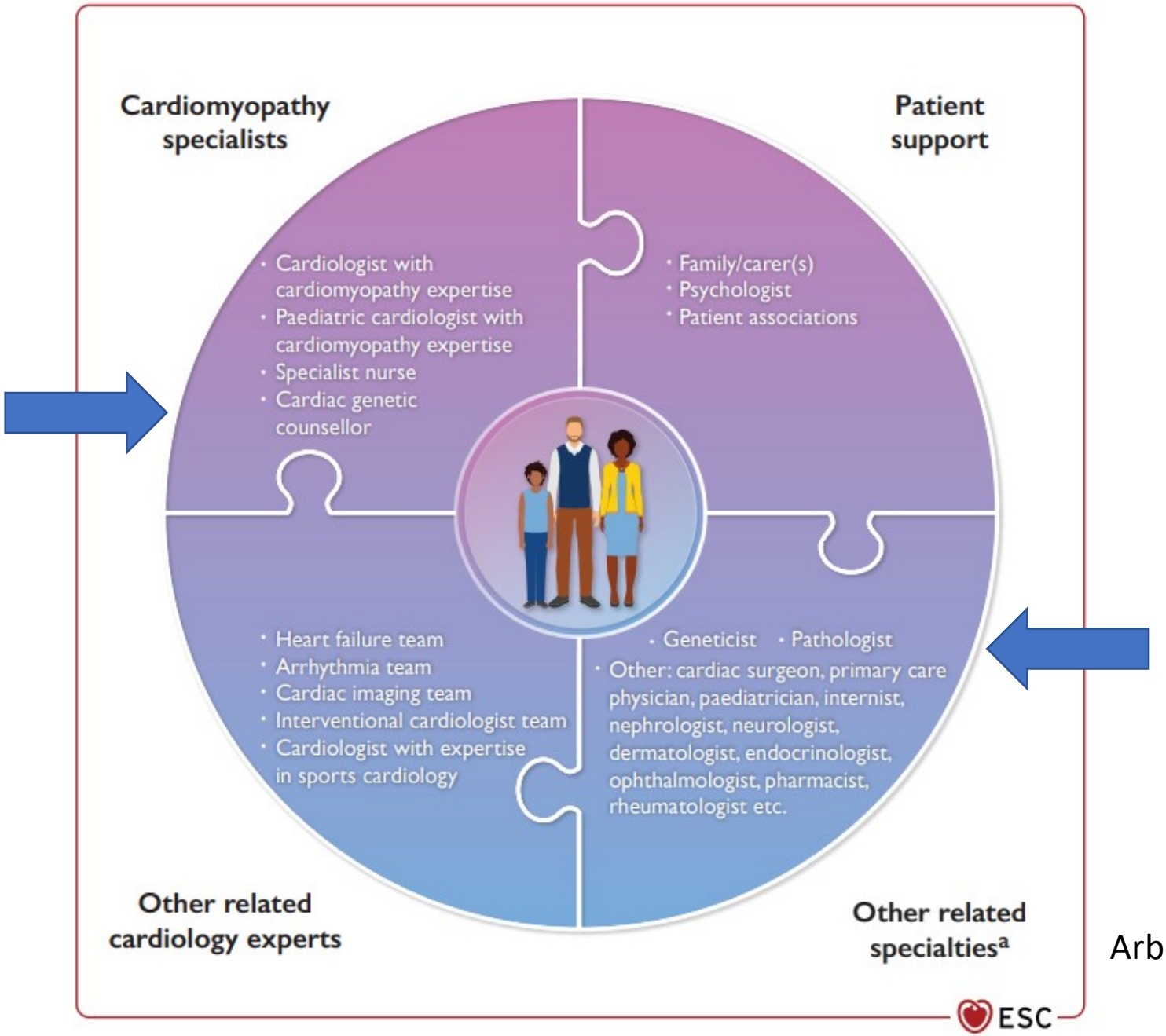

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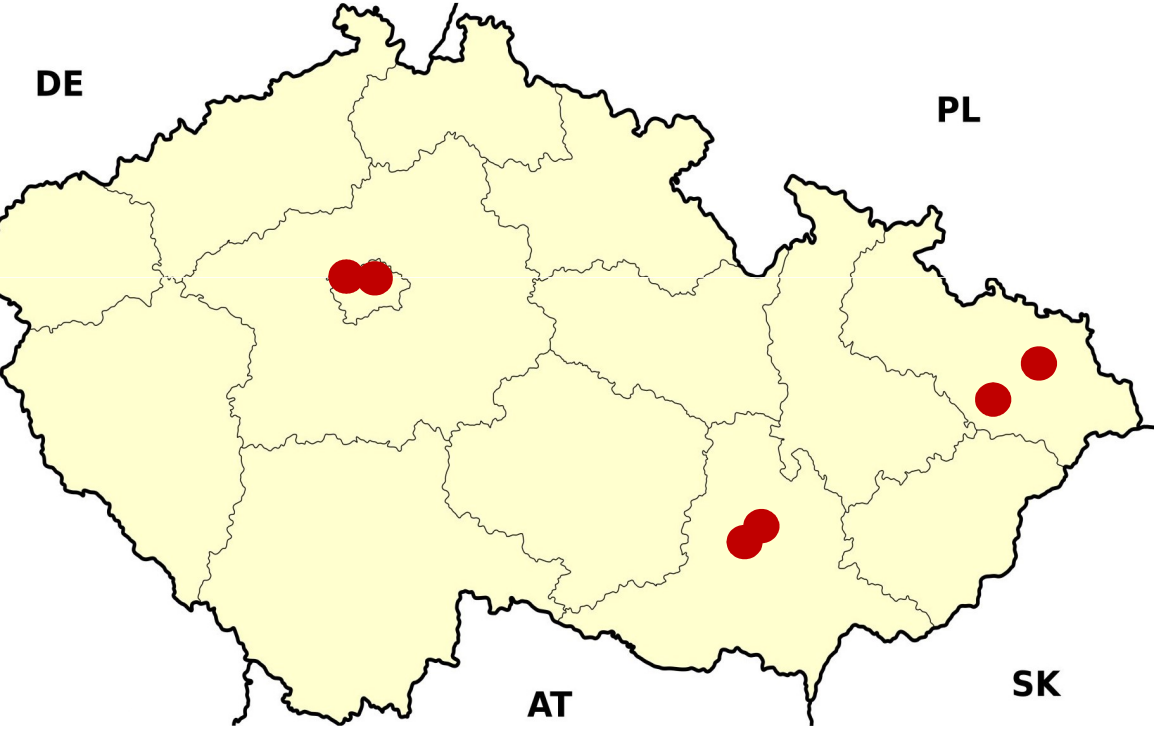
Figure 5 Multidisciplinary care of cardiomyopathies. [a]The list presented is not exhaustive and represents examples of specialties that often interact in the care of cardiomyopathy patients.

Working group of cardiogenetics within Czech Genetic Society (SLG-ČSL JEP)



Agel – Nový Jičín
FN Brno
Cytogenetic Laboratory - Brno
FN Motol
FN Ostrava
VFN Prague

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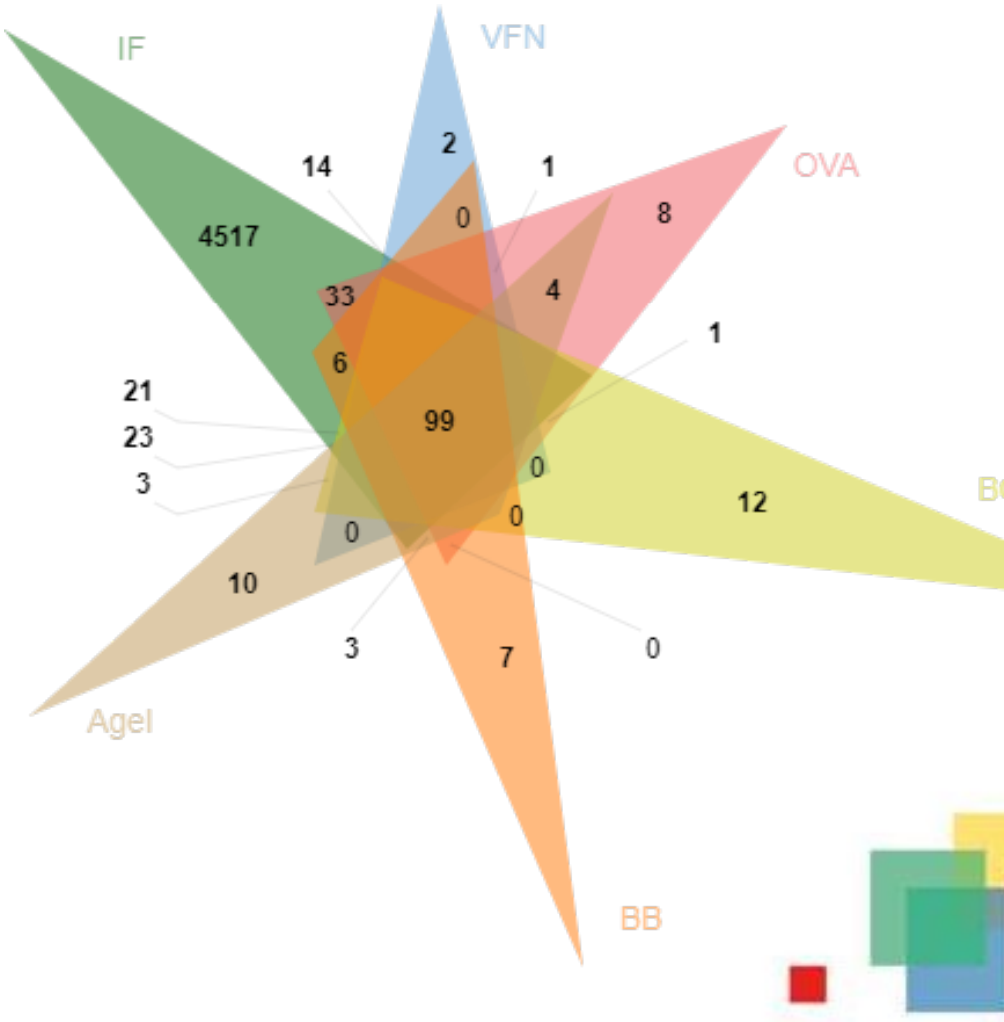
Methods: NGS – targeted panels, CES/WES

Performing laboratory	Method	Number of tested genes
FN Motol	WES/CES	19425/6300
FN Ostrava	NGS panel	253
Cytogenetic Laboratory - Brno	NGS panel	225
Agel - Nový Jičín	NGS panel	211
VFN Praha	NGS panel	180
1. LF UK	WES	18259
FN Brno	NGS panel	140

99 genes common to all laboratories



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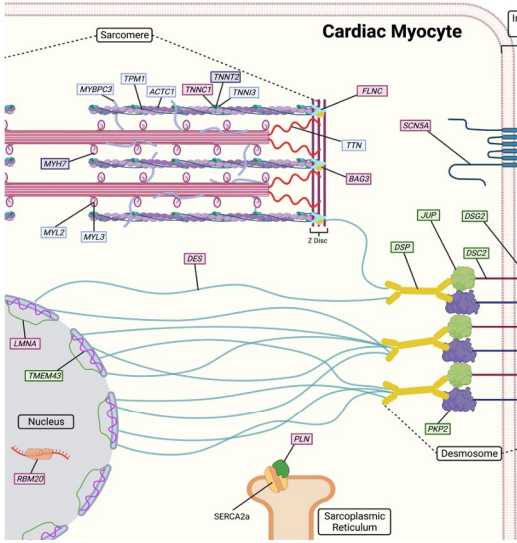
Genes with definite association with CMPs (according to ESC and ESHG guidelines)

Condition	Genes
HCM	*ACTC1, MYBPC3, MYH7, TNNT2, MYL2, MYL3, TNNI3, TPM1*
HCM Phenocopy	*GLA, FHL1, FLNC, LAMP2, PLN, PTPN11, RAF1, RIT1, TTR*
DCM	*DES, TTN, TNNT2, RBM20, MYH7, LMNA, FLNC, DSP, BAG3, PLN, SCN5A, TNNC1, TNNT2, JPH2, ACTC1, ACTN2,NEXN, TNNI3, TPM1, VCL, DMD*
ARVC	*PKP2, DSG2, DSC2, DSP, JUP, TMEM43, PLN, DES, FLNC*
RCM	*TNNI3, TNNT2, DES*



Hespe S. et al.

Arbelo et al. (2023), Hayesmoore et al. (2023)

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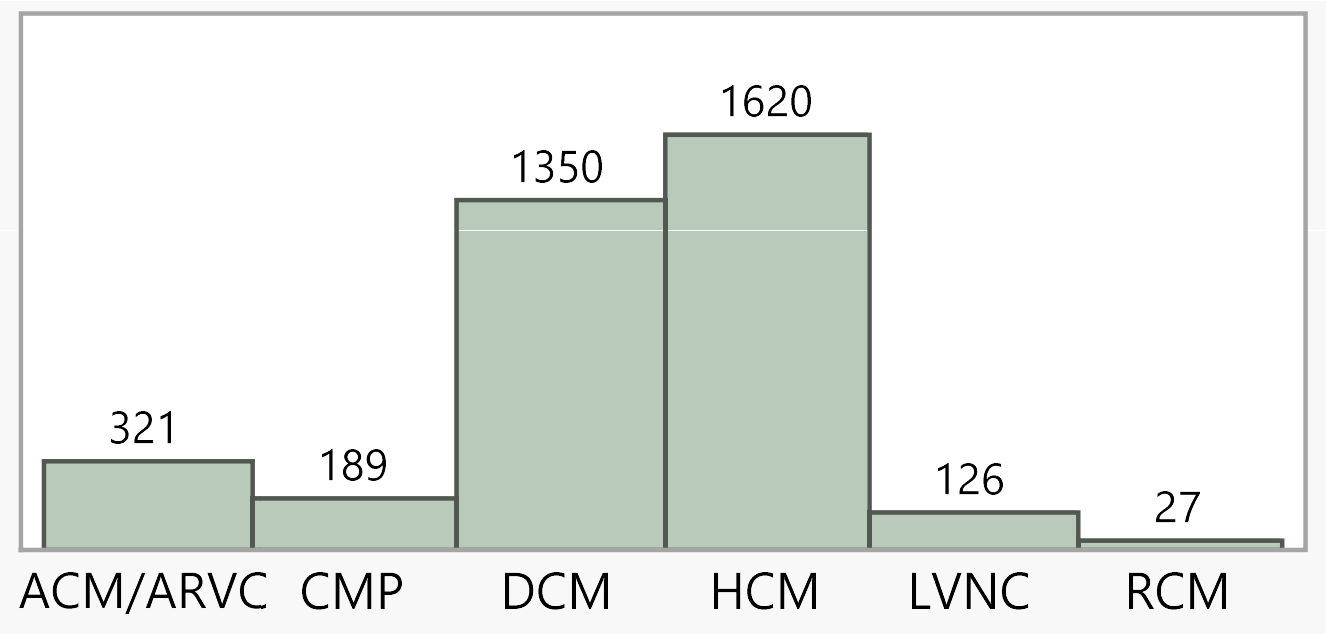
Czech patients in total 3633 with any CMPs

Probands	Count
Total	3633
Female	1202/3633 (33 %)
Male	2431/3633 (67 %)
Mean age	53 ± 17



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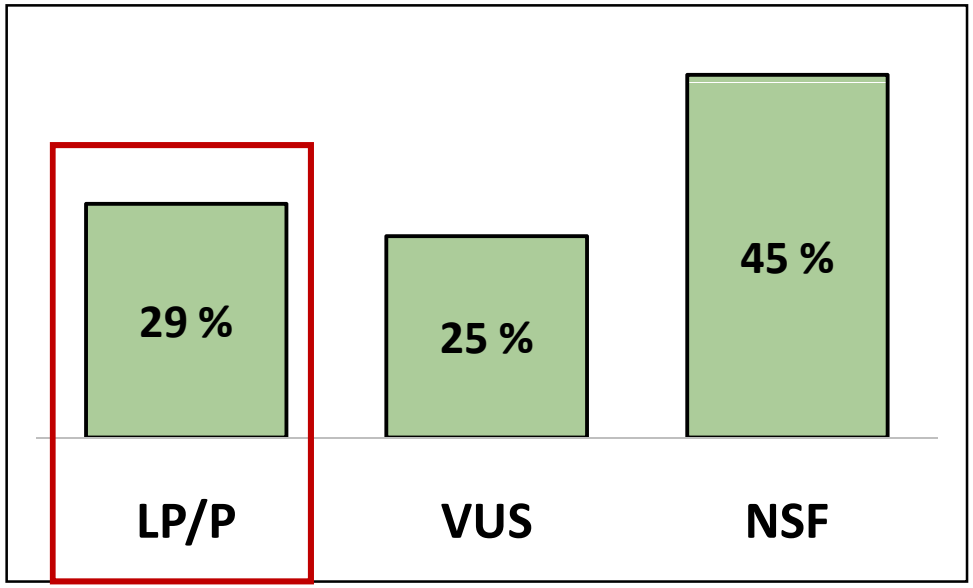
Genetic yield in all CMPs
(3633 probands/patients)



Gene	Count	(%)
MYBPC3	262	24.8
TTN	248	23.5
MYH7	150	14.2
PKP2	56	5.3
LMNA	34	3.2
DSP	29	2.7
FLNC	29	2.7
TNNT2	28	2.6
TNNI3	26	2.4
RBM20	17	1.6
SCN5A	14	1.3
TPM1	14	1.3

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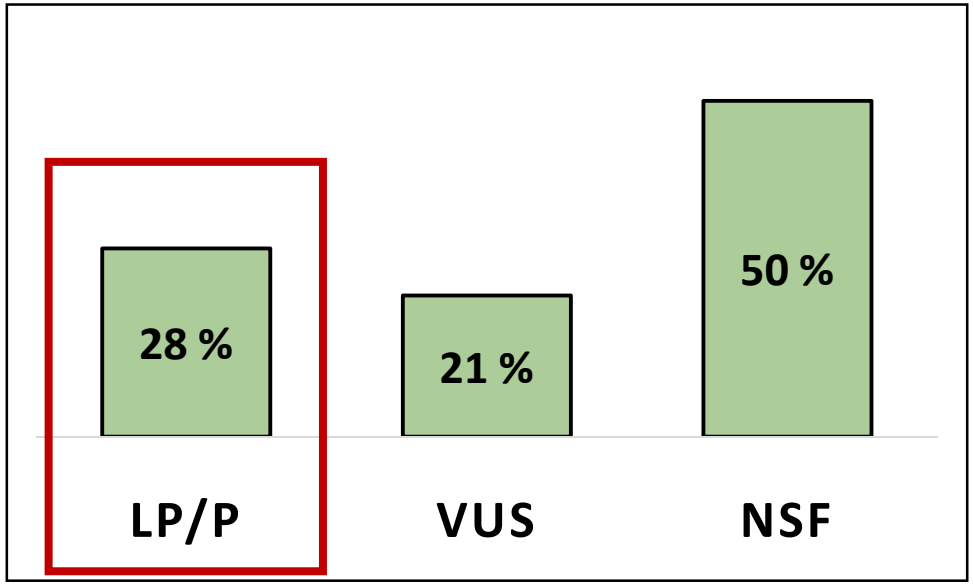
Genetic yield in HCM (1620 probands)



Gene	Count	(%)
MYBPC3	241	52.3
MYH7	112	24.3
TNNI3	16	3.4
TPM1	11	2.3
TNNT2	9	1.9
PTPN11	7	1.5
LAMP2	6	1.3
GLA	5	1.1
PRKAG2	5	1.1
TTN	5	1.1
MYL3	4	0.8
Total	461	

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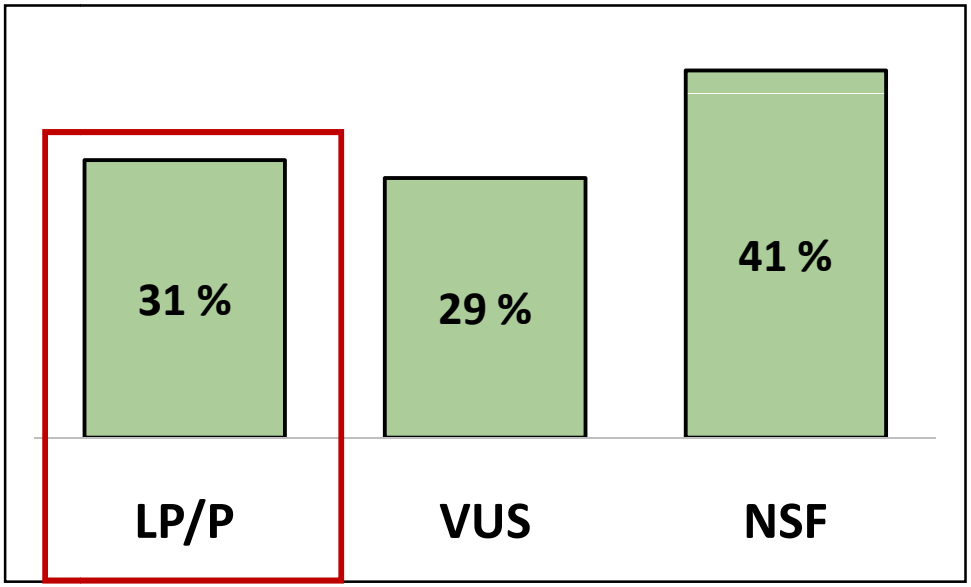
Genetic yield in DCM (1350 probands)

Gene	Count	(%)
TTN	214	51.9
LMNA	25	6.1
FLNC	19	4.6
MYH7	19	4.6
DSP	16	3.8
TNNT2	13	3.1
RBM20	12	2.9
BAG3	11	2.6
MYBPC3	11	2.6
NEXN	9	2.1
Total	412	



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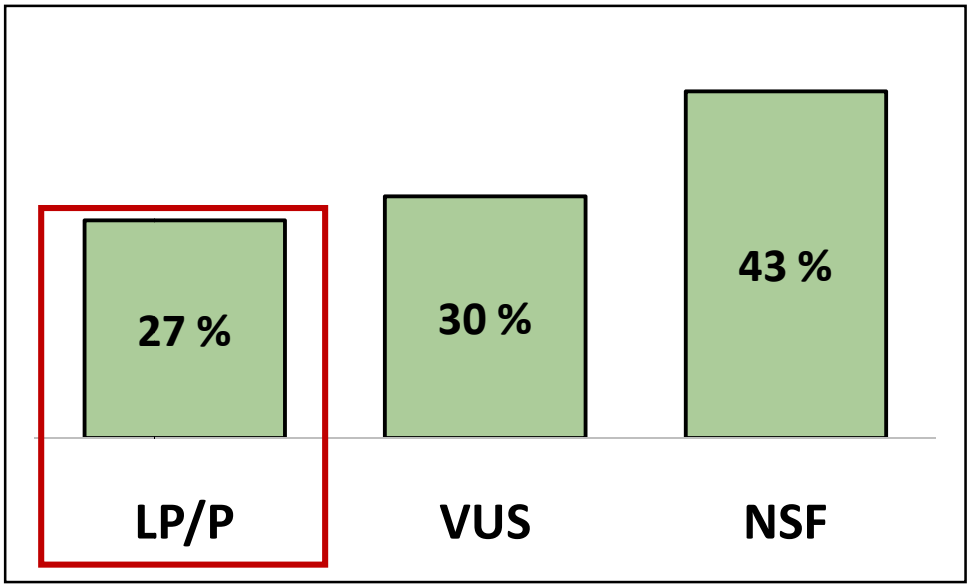
Genetic yield in ACM/ARVC (321 probands)

Gene	Count	(%)
PKP2	49	56.3
DSP	9	10.3
FLNC	4	4.5
TTN	4	4.5
LMNA	3	3.4
SCN5A	3	3.4
DSC2	2	2.3
DSG2	2	2.3
MYBPC3	2	2.3
MYH7	2	2.3
Total	87	



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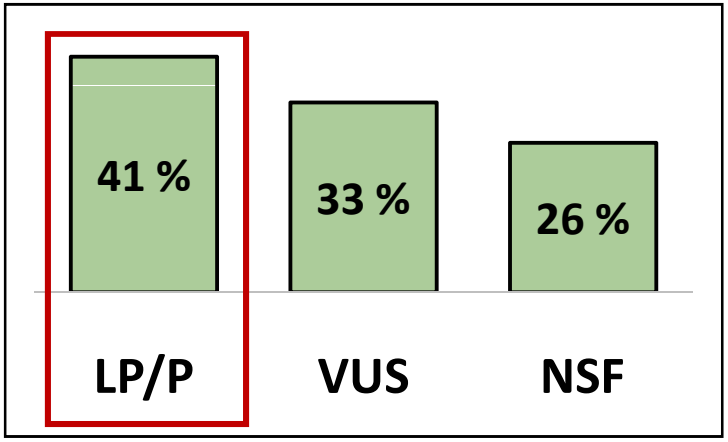
Genetic yield according to clinical diagnosis

RCM (27 probands), LVNC (126 probands)

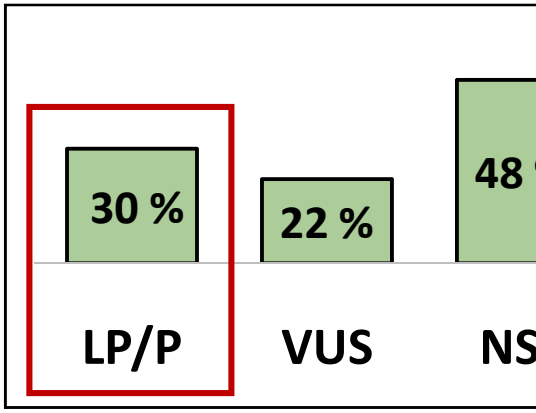
RCM

ne	Count	(%)
NI3	3	27.2
NT2	3	27.2
	1	9.1
C	1	9.1
BPC3	1	9.1
M1	1	9.1
	1	9.1
al	11	



LVNC

Gene	Count	(%)
MYH7	13	34.2
TTN	10	26.3
RBM20	3	7.8
OBSCN	2	5.2
RYR2	2	5.2
TNNT2	2	5.2
ACTC1	1	2.6
ACTN2	1	2.6
FLNC	1	2.6
GATA4	1	2.6
Total	38	



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MYBPC3: Frequent DNA variants in Czech population with regional distribution

Variant	Frequency
NM_000256.3(MYBPC3):c.3697C>T (p.Gln1233Ter)	80
NM_000256.3(MYBPC3):c.3190+5G>A	12
NM_000256.3(MYBPC3):c.977G>A (p.Arg326Gln)	11
NM_003476.5(CSRP3):c.208G>T (p.Gly70Trp)	11
NM_000256.3(MYBPC3):c.814C>T (p.Arg272Cys)	9
NM_000256.3(MYBPC3):c.1028delC (p.Thr343MetfsTer7)	9

NM_000256.3(MYBPC3):c.3697C>T (p.Gln1233Ter).....predominates in Moravian and Silesian regions

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Conclusions

- **First Czech national, pseudoanomized, representative cohort, studying the genetic architecture of heart failure (3633 patients).**
- **Interlaboratory cooperation is crucial for standardisation of variant analysis and the connection of family information among the molecular genetic laboratories.**
- **Genetic yield in CMPs is 29 %, most frequently mutated genes are *MYBPC3*, *TTN*, *MYH7* and *PKP2*.**
- **Genetic architecture reflects the special characteristic of our central European population, missing DNA variants in some genes** (eg.*TMEM43, JUP, VCL, TNNC1, MYL3*).

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K+E M

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Heart Diseases
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Thank you for your attention!