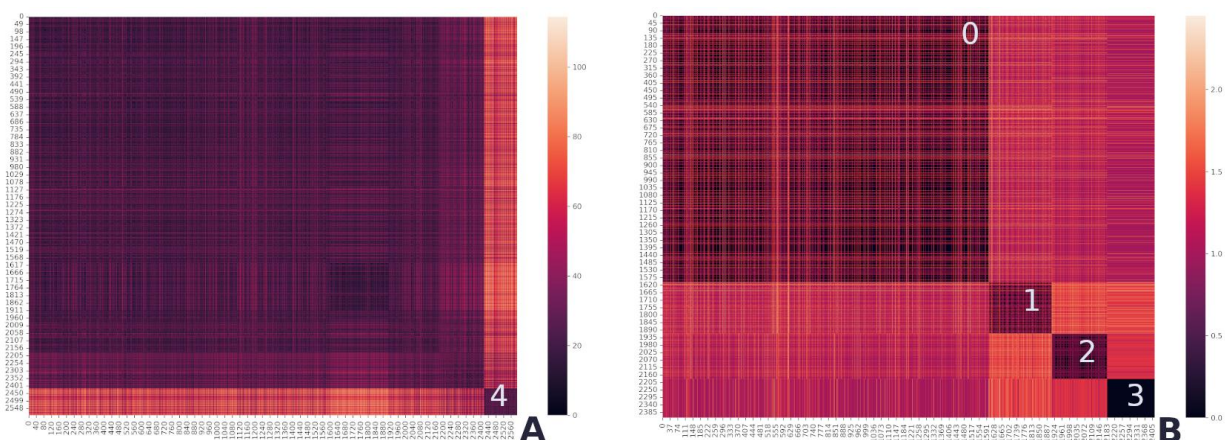


SUPPLEMENTARY DATA

# **Machine Learning-Based Decision-Making in Geriatrics: Aging Phenotype Calculator and Survival Prognosis**

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**Supplementary Figure 1.** Euclidean distance matrix for the first (A) and second (B) clustering steps.

**Supplementary Table 1.** Physical examination and laboratory testing results in different aging phenotypes (only significant).

Cluster	0	1	2	3	4	p-value (Kruskal test)
<b>Phenotype</b>	<b>Multimorbid frailty (n=1602)</b>	<b>Non-frail (n=309)</b>	<b>Metabolic frailty (N=272)</b>	<b>Cognitive frailty (N=234)</b>	<b>Functional frailty (n=175)</b>	
<b>Indicator</b>	Me [Q1-Q3]	Me [Q1-Q3]	Me [Q1-Q3]	Me [Q1-Q3]	Me [Q1-Q3]	
<b>Current health indicators</b>						
<b>Right hand grip strength</b>	13.00 [10.00 - 16.00]	13.00 [10.00 - 18.50]	13.00 [10.00 - 16.50]	10.00 [7.00 - 13.50]	7.50 [4.00 - 11.50]	4.9*10 <sup>-46</sup>
<b>Left hand grip strength</b>	12.00 [9.00 - 15.05]	13.50 [9.00 - 18.00]	12.00 [9.00 - 16.00]	9.00 [7.00 - 12.00]	6.25 [3.50 - 10.00]	1.3*10 <sup>-52</sup>
<b>Systolic blood pressure</b>	135.00 [126.00 - 146.00]	138.00 [127.00 - 150.00]	135.50 [127.00 - 148.75]	130.00 [120.00 - 150.00]	130.00 [110.00 - 140.00]	3.1*10 <sup>-5</sup>
<b>BMI</b>	25.50 [23.40 - 28.30]	24.80 [23.10 - 27.60]	26.60 [24.20 - 30.40]	25.15 [22.92 - 27.70]	24.20 [21.00 - 27.50]	1.7*10 <sup>-8</sup>
<b>Waist circumference</b>	92.00 [86.00 - 98.00]	92.00 [82.00 - 98.00]	95.00 [87.00 - 103.00]	89.50 [80.00 - 98.00]	90.00 [79.00 - 98.00]	2.1*10 <sup>-5</sup>
<b>13B-T (total bilirubin)</b>	8.90 [6.67 - 12.40]	10.50 [7.45 - 14.22]	8.25 [6.50 - 11.17]	8.90 [6.90 - 12.60]	8.30 [6.40 - 11.15]	6.8*10 <sup>-4</sup>
<b>1631NTP (NT-proBNP)</b>	621.50 [310.00 - 1489.00]	507.00 [256.00 - 1093.00]	546.50 [302.00 - 1130.75]	740.00 [390.00 - 1669.00]	787.00 [368.50 - 1774.75]	0.007
<b>16GLU (glucose)</b>	5.00 [4.50 - 5.60]	5.10 [4.60 - 5.70]	5.80 [5.00 - 7.57]	5.10 [4.70 - 5.70]	4.90 [4.50 - 5.70]	2.4*10 <sup>-20</sup>
<b>172INS (insulin)</b>	6.60 [4.60 - 10.17]	7.20 [4.90 - 11.10]	7.20 [4.93 - 11.53]	6.60 [4.40 - 11.20]	5.15 [3.60 - 8.72]	2.9*10 <sup>-4</sup>
<b>174S-C (IGF-1)</b>	99.40 [77.93 - 131.55]	105.75 [81.80 - 136.03]	109.80 [88.10 - 144.20]	99.70 [78.62 - 133.38]	90.85 [65.58 - 124.75]	2.6*10 <sup>-4</sup>
<b>18HBA1 (HbA1c (glycated haemoglobin))</b>	5.60 [5.40 - 5.90]	5.60 [5.40 - 5.90]	6.30 [5.70 - 7.15]	5.60 [5.30 - 5.80]	5.50 [5.30 - 5.80]	2.8*10 <sup>-44</sup>
<b>22CRE (creatinine)</b>	86.00 [72.25 - 105.75]	88.00 [75.00 - 108.00]	87.00 [72.00 - 105.75]	88.00 [73.00 - 109.00]	76.00 [61.00 - 100.25]	0.005

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<b>28TP (total protein)</b>	69.00 [64.00 - 74.00]	69.00 [65.00 - 74.00]	70.00 [64.00 - 74.00]	69.00 [66.00 - 74.00]	67.00 [61.00 - 71.00]	0.03
<b>29A1 (alpha-1-globulin)</b>	3.10 [2.80 - 3.50]	3.00 [2.70 - 3.30]	3.10 [2.80 - 3.50]	3.20 [2.80 - 3.60]	3.30 [3.00 - 3.70]	3.9*10 <sup>-5</sup>
<b>30TG (triglycerides)</b>	1.15 [0.89 - 1.48]	1.12 [0.89 - 1.54]	1.31 [0.96 - 1.81]	1.14 [0.87 - 1.49]	1.16 [0.84 - 1.49]	0.004
<b>32HDL (HDL)</b>	1.25 [1.05 - 1.53]	1.27 [1.01 - 1.57]	1.15 [0.94 - 1.45]	1.26 [1.07 - 1.51]	1.11 [0.96 - 1.36]	1.3*10 <sup>-5</sup>
<b>51FERR (ferritin)</b>	62.00 [32.00 - 112.50]	70.00 [36.50 - 121.00]	60.00 [30.00 - 115.00]	65.50 [34.25 - 118.50]	97.00 [41.00 - 175.00]	0.037
<b>53FT3 (free T3)</b>	3.60 [3.20 - 4.00]	3.70 [3.30 - 4.00]	3.50 [3.10 - 3.80]	3.60 [3.20 - 3.90]	3.40 [2.90 - 3.80]	1.2*10 <sup>-5</sup>
<b>5PLT (platelets)</b>	220.00 [183.00 - 266.75]	205.00 [171.75 - 244.50]	219.00 [177.00 - 278.00]	225.00 [184.00 - 279.00]	226.00 [181.00 - 274.00]	0.025
<b>8ALT (alanine transaminase)</b>	11.00 [9.00 - 15.00]	12.00 [10.00 - 16.00]	12.00 [9.00 - 16.00]	11.00 [8.00 - 15.00]	9.50 [7.00 - 14.00]	1*10 <sup>-4</sup>
<b>928VD3 (25(OH) D, vitamin D)</b>	9.00 [6.00 - 14.00]	11.00 [7.00 - 16.00]	9.00 [6.00 - 14.00]	8.00 [5.00 - 11.00]	7.00 [5.00 - 11.00]	5.1*10 <sup>-12</sup>
<b>9AST (aspartate aminotransferase)</b>	18.00 [15.00 - 21.00]	18.00 [16.00 - 21.00]	16.00 [14.00 - 20.00]	17.00 [15.00 - 22.00]	16.00 [14.00 - 19.00]	4.6*10 <sup>-6</sup>
<b>ALB-PF (albumin)</b>	38.40 [35.40 - 41.30]	39.50 [35.90 - 42.10]	38.80 [35.90 - 41.40]	38.40 [34.70 - 41.00]	35.00 [32.18 - 38.00]	3.8*10 <sup>-17</sup>
<b>ALB/CRU (urine albumin-creatinine ratio)</b>	22.00 [12.00 - 45.75]	23.00 [11.00 - 47.50]	34.00 [16.00 - 67.50]	31.00 [14.00 - 62.00]	35.00 [16.00 - 82.00]	0.007
<b>hsCRP</b>	2.69 [1.27 - 6.85]	2.29 [1.14 - 6.04]	2.9 [1.29 - 6.65]	2.59 [1.11 - 7.19]	4.19 [1.64 - 12.83]	0,044

**Supplementary Table 2. Pairwise phenotype comparison**

Cluster	0VS1	0VS2	0VS3	0VS4	1VS2	1VS3	1VS4	2VS3	2VS4	3VS4
<b>Indicator</b>	p-value of pairwise comparisons (Mann-Whitney U test) adjusted for multiple testing									
<b>MMSE</b>	1.3*10 <sup>-8</sup>	0.026	2.3*10 <sup>-121</sup>	1.5*10 <sup>-36</sup>	1.8*10 <sup>-10</sup>	5.2*10 <sup>-77</sup>	2.9*10 <sup>-34</sup>	1.1*10 <sup>-48</sup>	3.7*10 <sup>-15</sup>	1
<b>FAB</b>	1	1	8.6*10 <sup>-52</sup>	2.7*10 <sup>-42</sup>	0.36	5.7*10 <sup>-38</sup>	4.5*10 <sup>-32</sup>	6.7*10 <sup>-24</sup>	1.5*10 <sup>-22</sup>	1
<b>MNA</b>	0.77	1	1.1*10 <sup>-15</sup>	5.4*10 <sup>-41</sup>	1	2.3*10 <sup>-16</sup>	2.0*10 <sup>-33</sup>	8.9*10 <sup>-9</sup>	1.7*10 <sup>-27</sup>	6*10 <sup>-9</sup>
<b>Right hand hand grip strength</b>	1	1	1.6*10 <sup>-14</sup>	1.2*10 <sup>-34</sup>	1	2.8*10 <sup>-10</sup>	5.4*10 <sup>-25</sup>	4.2*10 <sup>-7</sup>	5.5*10 <sup>-21</sup>	2.4*10 <sup>-6</sup>
<b>Left hand hand grip strength</b>	1	1	8.5*10 <sup>-16</sup>	5.7*10 <sup>-38</sup>	1	4.1*10 <sup>-14</sup>	1.5*10 <sup>-30</sup>	2.3*10 <sup>-7</sup>	6.1*10 <sup>-23</sup>	1*10 <sup>-7</sup>
<b>SPPB</b>	5.6*10 <sup>-164</sup>	0.149	2.9*10 <sup>-23</sup>	2.2*10 <sup>-74</sup>	9.4*10 <sup>-95</sup>	1.6*10 <sup>-87</sup>	3.1*10 <sup>-74</sup>	6*10 <sup>-7</sup>	1.8*10 <sup>-45</sup>	2.1*10 <sup>-25</sup>
<b>Barthel</b>	4.4*10 <sup>-43</sup>	1	3.9*10 <sup>-22</sup>	2.2*10 <sup>-103</sup>	6.4*10 <sup>-35</sup>	1.7*10 <sup>-50</sup>	2.5*10 <sup>-73</sup>	1.4*10 <sup>-8</sup>	6.5*10 <sup>-69</sup>	9*10 <sup>-64</sup>
<b>IADL</b>	1.5*10 <sup>-27</sup>	1	1.6*10 <sup>-21</sup>	1.9*10 <sup>-79</sup>	3.4*10 <sup>-20</sup>	5*10 <sup>-35</sup>	4.3*10 <sup>-64</sup>	8*10 <sup>-9</sup>	2.6*10 <sup>-47</sup>	1.6*10 <sup>-15</sup>
<b>GDS-5</b>	0.617	1	6.5*10 <sup>-18</sup>	2.2*10 <sup>-37</sup>	0.002	6*10 <sup>-21</sup>	1.9*10 <sup>-35</sup>	2.4*10 <sup>-5</sup>	2.9*10 <sup>-19</sup>	5.5*10 <sup>-5</sup>

# SUPPLEMENTARY DATA

Assistance in social and everyday living scale	1.5*10 <sup>-18</sup>	1	7.1*10 <sup>-21</sup>	7.4*10 <sup>-95</sup>	1.9*10 <sup>-12</sup>	1.3*10 <sup>-34</sup>	2.3*10 <sup>-72</sup>	5.3*10 <sup>-10</sup>	1.1*10 <sup>-59</sup>	7.2*10 <sup>-42</sup>
Systolic blood pressure	1	1	1	1*10 <sup>-5</sup>	1	1	3.6*10 <sup>-5</sup>	1	0.001	0.075
Diastolic blood pressure	1	1	1	0.193	1	1	0.339	1	0.186	0.018
BMI	1	0.002	1	0.002	5.6*10 <sup>-4</sup>	1	0.962	0.007	2.8*10 <sup>-7</sup>	1
Waist circumference	1	0.09	0.068	1	0.047	1	1	1*10 <sup>-4</sup>	0.125	1
Total bilirubin	0.016	1	1	1	0.001	1	0.006	1	1	1
Homocysteine	1	1	0.01	1	1	0.006	1	7.8*10 <sup>-4</sup>	1	1
NT-proBNP	1	1	1	1	1	0.037	0.157	0.546	1	1
Glucose	1	1.7*10 <sup>-21</sup>	1	1	4.2*10 <sup>-9</sup>	1	1	9.3*10 <sup>-7</sup>	3.2*10 <sup>-8</sup>	1
Insulin	1	1	1	0.018	1	1	0.001	1	2.5*10 <sup>-4</sup>	0.422
IGF-1	1	0.027	1	1	1	1	0.054	1	0.001	1
HbA1c (glycated haemoglobin, Hb)	1	5.5*10 <sup>-41</sup>	1	0.068	7.5*10 <sup>-23</sup>	1	0.104	5.3*10 <sup>-24</sup>	5*10 <sup>-22</sup>	1
Creatinine	1	1	1	0.005	1	1	0.002	1	0.185	0.017
Total protein	1	1	1	0.024	1	1	0.011	1	0.249	0.074
alpha-1-globulin	1	1	1	0.028	1	0.012	1.2*10 <sup>-4</sup>	1	0.145	1
Triglycerides	1	4.7*10 <sup>-4</sup>	1	1	0.312	1	1	0.024	0.607	1
HDL	1	0.004	1	0.003	0.149	1	0.067	1	1	0.466
Ferritin	1	1	1	0.012	1	1	1	1	0.114	1
Free T3	1	1	1	0.001	0.03	1	1.6*10 <sup>-5</sup>	1	1	0.069
Platelets	0.038	1	1	1	1	0.020	0.605	1	1	1
Testosterone	6.7*10 <sup>-4</sup>	1	1	1	1.5*10 <sup>-5</sup>	0.043	8.2*10 <sup>-5</sup>	1	1	1
Alanine transaminase	1	1	1	0.004	1	1	6.6*10 <sup>-5</sup>	1	0.03	1
Vitamin D (25(OH) D)	0.004	1	0.01	4*10 <sup>-4</sup>	1	1.1*10 <sup>-7</sup>	2.4*10 <sup>-8</sup>	0.091	0.005	1
Albumin in the urine (concentration)	1	1	1	0.14	1	1	0.843	1	1	1ju
Aspartate aminotransferase	1	0.022	1	0.002	0.009	1	3*10 <sup>-4</sup>	1	1	0.674
Albumin	0.665	1	1	2*10 <sup>-14</sup>	1	0.229	1.7*10 <sup>-16</sup>	1	2.8*10 <sup>-12</sup>	2.6*10 <sup>-6</sup>
ALB/CRU (urine albumin-creatinine ratio)	1	0.047	1	1	1	1	1	1	1	1
hsCRP	1	1	1	0.025	1	1	0.0098	1	0.93	0.49
Monocytes, %	1	0.095	1	0.001	0.001	0.127	8.9*10 <sup>-6</sup>	1	1	1

# SUPPLEMENTARY DATA

**Supplementary Table 3.** Frequency of occurrence of the APOE genotypes

Genotype	Cluster 0 (1,602)	Cluster 1 (309)	Cluster 2 (272)	Cluster 3 (234)	Cluster 4 (175)	Entire sample	p-value (chi square)
ε2ε2	19 (1.2%)	6 (1.9%)	1 (0.4%)	3 (1.3%)	2 (1.1%)	31 (1.2%)	0.005
ε2ε3	228 (14.2%)	56 (18.1%)	40 (14.7%)	41 (17.5%)	33 (18.9%)	398 (15.3%)	
ε2ε4	18 (1.1%)	4 (1.3%)	3 (1.1%)	3 (1.3%)	5 (2.9%)	33 (1.3%)	
ε3ε3	1166 (72.5%)	218 (70.6%)	204 (75%)	144 (61.5%)	109 (62.3%)	1841 (70.8%)	
ε3ε4	165 (10.3%)	25 (8.1%)	23 (8.5%)	40 (1.3%)	26 (14.9%)	279 (10.7%)	
ε4ε4	6 (0.4%)	0 (-)	1 (0.4%)	3 (1.3%)	0 (-)	10 (0.4%)	

**Supplementary Table 4.** Results of logistic regression using APOE genotypes

Cluster	ε2		ε4	
	coef	p-value	coef	p-value
0	-0.2257	0.3	-0.1519	1
1	0.3008	0.47	-0.4823	0.2
2	-0.1286	1	-0.2805	1
3	0.1423	1	0.6885	0.001
4	0.2959	1	0.5721	0.07

**Supplementary Table 5.** Comparison of the socioeconomic backgrounds (only significant)

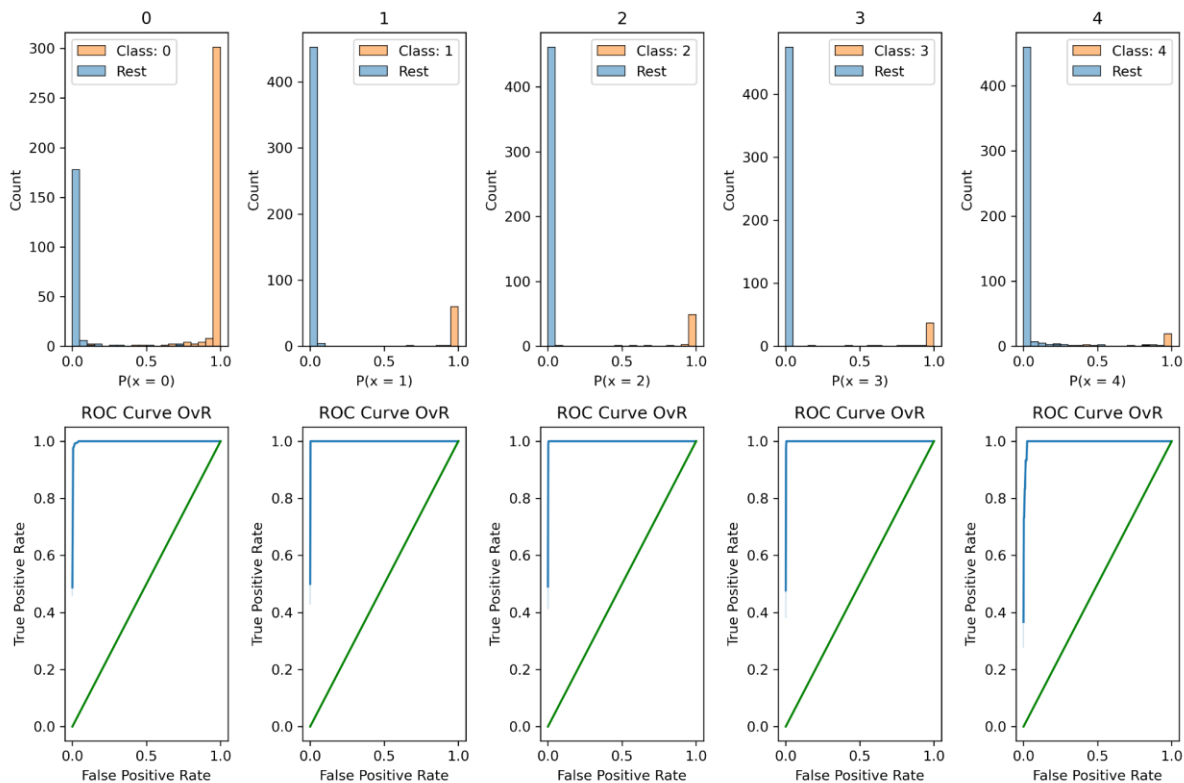
Cluster	0	1	2	3	4	p-value (chi square)	
<b>Phenotype</b>	Multimorbid frailty (n=1,602)	Non-frail (n=309)	Metabolic frailty (n=272)	Cognitive frailty (n=234)	Functional frailty (n=175)		
<b>Параметр</b>	n (%)	n (%)	n (%)	n (%)	n (%)		
<b>Lifelong residence</b>	Rural	87 (5.7%)	19 (6.7%)	6 (2.3%)	14 (6.8%)	22 (15.8%)	3*10-4
	Urban	1418 (94.3%)	264 (93.3%)	253 (97.7%)	191 (93.2%)	117 (84.2%)	
<b>Education</b>	Primary school or unfinished primary school	94 (5.8%)	27 (8.7%)	18 (6.6%)	35 (15.2%)	23 (13.2%)	3.46*10-7
	Middle school or unfinished middle school	197 (12.3%)	23 (7.4%)	36 (13.2%)	36 (15.6%)	28 (16.1%)	
	Complete high school	271 (17%)	46 (14.9%)	48 (17.7%)	56 (24.2%)	32 (18.4%)	
	Vocational school	135 (8.4%)	25 (8.1%)	15 (5.5%)	13 (5.6%)	4 (2.3%)	
	Training school	278 (17.4%)	38 (12.3%)	44 (16.2%)	30 (13%)	27 (15.5%)	
	Undergraduate	23 (1.4%)	3 (1%)	6 (2.2%)	1 (0.4%)	4 (2.3%)	
	Graduate	557 (35%)	140 (45.3%)	93 (34.2%)	55 (23.8%)	53 (30.5%)	
Postgraduate	43 (2.7%)	7 (2.3%)	12 (4.4%)	5 (2.2%)	3 (1.7%)		
<b>Occupation</b>	Primarily physical	370 (23.3%)	78 (25.6%)	62 (22.9%)	83 (35.8%)	54 (31.2%)	0.018
	Primarily intellectual	582 (36.7%)	120 (39.3%)	111 (41%)	71 (30.6%)	67 (39.6%)	
	Intellectual + physical	636 (40%)	107 (35.1%)	98 (36.1%)	78 (33.6%)	48 (28.4%)	
<b>Peak income</b>	Low	109 (7.2%)	26 (9.2%)	16 (6.2%)	32 (15.6%)	28 (20.3%)	1.6*10-9

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	Medium	1235 (82%)	201 (71%)	211 (81.5%)	153 (74.6%)	87 (63%)	
	High	162 (10.8%)	56 (19.8%)	32 (12.3%)	20 (9.8%)	23 (16.7%)	
<b>Lifelong hobby</b>	No	832 (56.1%)	182 (65%)	129 (49.6%)	140 (69.3%)	79 (58.1%)	0.002
	Yes	652 (43.9%)	98 (35%)	131 (50.4%)	62 (30.7%)	57 (41.9%)	

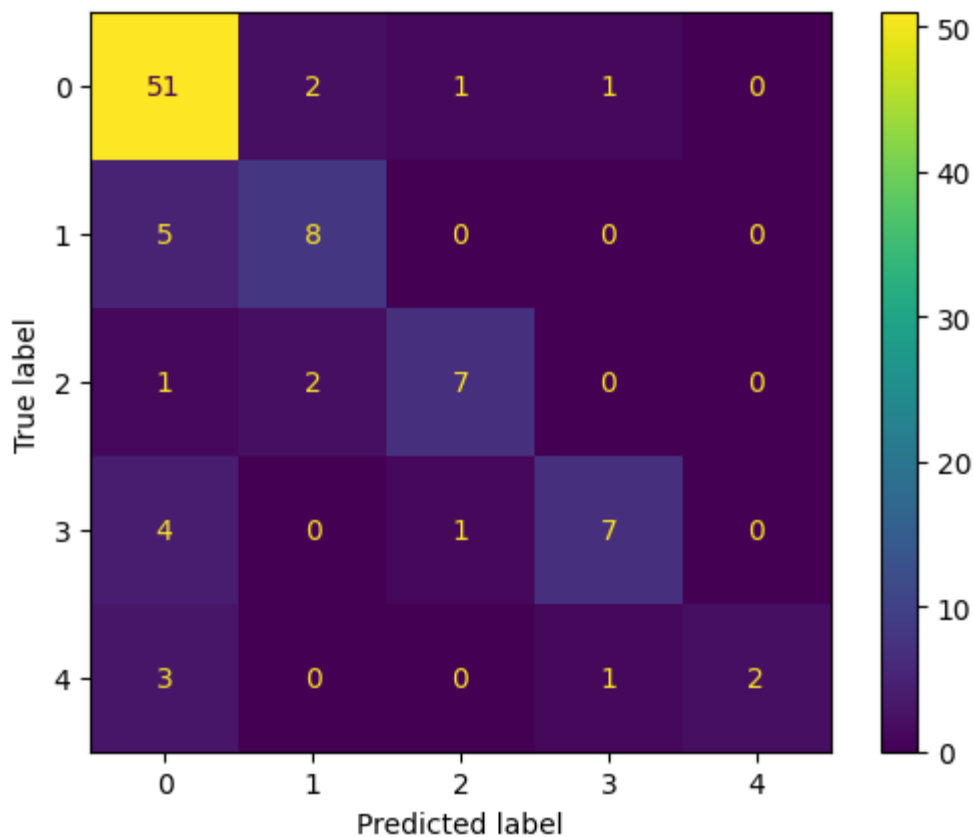
**Supplementary Table 6.** Effects of the background and socioeconomic background on the aging phenotype (based on logistic regression adjusted for age and sex).

Indicator	Non-frailty		Multimorbid frailty		Metabolic frailty		Cognitive frailty		Functional frailty	
	OR	p-val	OR	p-val	OR	p-val	OR	p-val	OR	p-val
Residence	1.21	1	0.84	1	2.94	0.319	0.92	1	<b>0.34</b>	<b>6.2*10<sup>-4</sup></b>
Graduate/un graduate	1.00	1	1.41	0.196	1.18	1	<b>0.58</b>	<b>0.013</b>	0.83	1
Intellectual work	0.95	1	1.19	1	1.19	1	0.7	0.504	1.08	1
High peak income	0.69	0.095	<b>1.72</b>	<b>0.041</b>	1.11	1	0.83	1	1.54	1
Low peak income	<b>0.59</b>	<b>0.01</b>	1.27	1	0.62	1	1.9	0.064	<b>2.65</b>	<b>7*10<sup>-4</sup></b>
Lifelong hobby	1.19	1	0.75	0.983	1.44	0.172	<b>0.53</b>	<b>0.006</b>	0.91	1



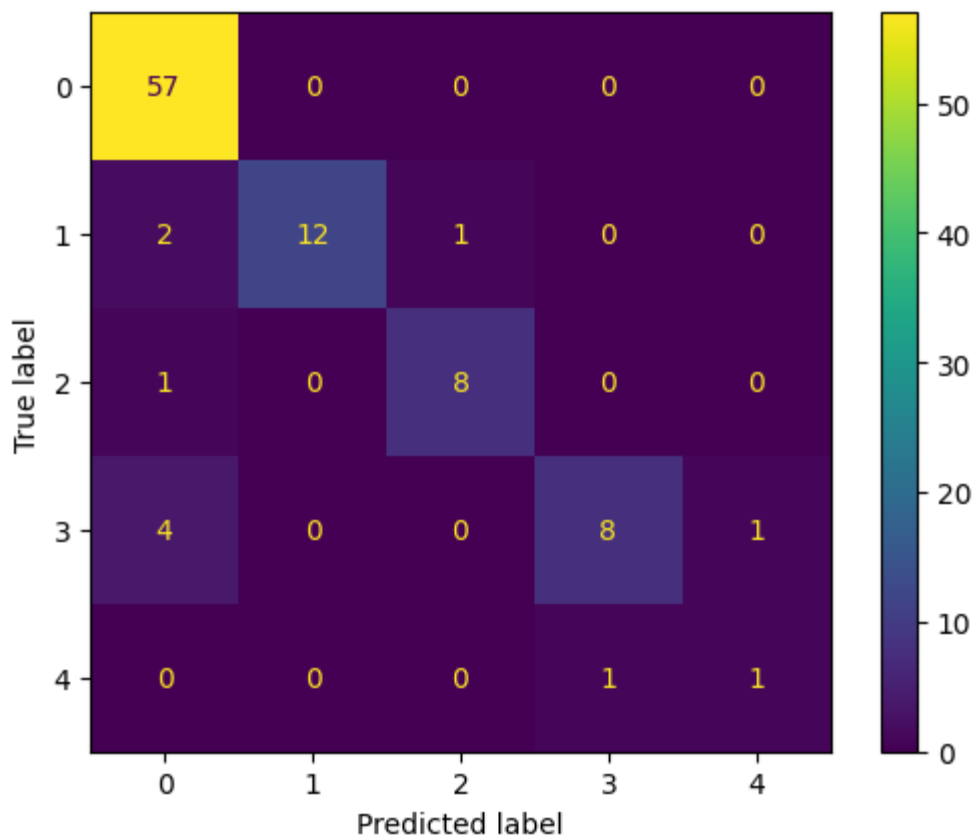
**Supplementary Figure 2.** Calculator quality assessment on the test set.

# SUPPLEMENTARY DATA



**Supplementary Figure 3.** Validation error matrix for geriatrician 1.

# SUPPLEMENTARY DATA



**Supplementary Figure 4.** Validation error matrix for geriatrician 2.