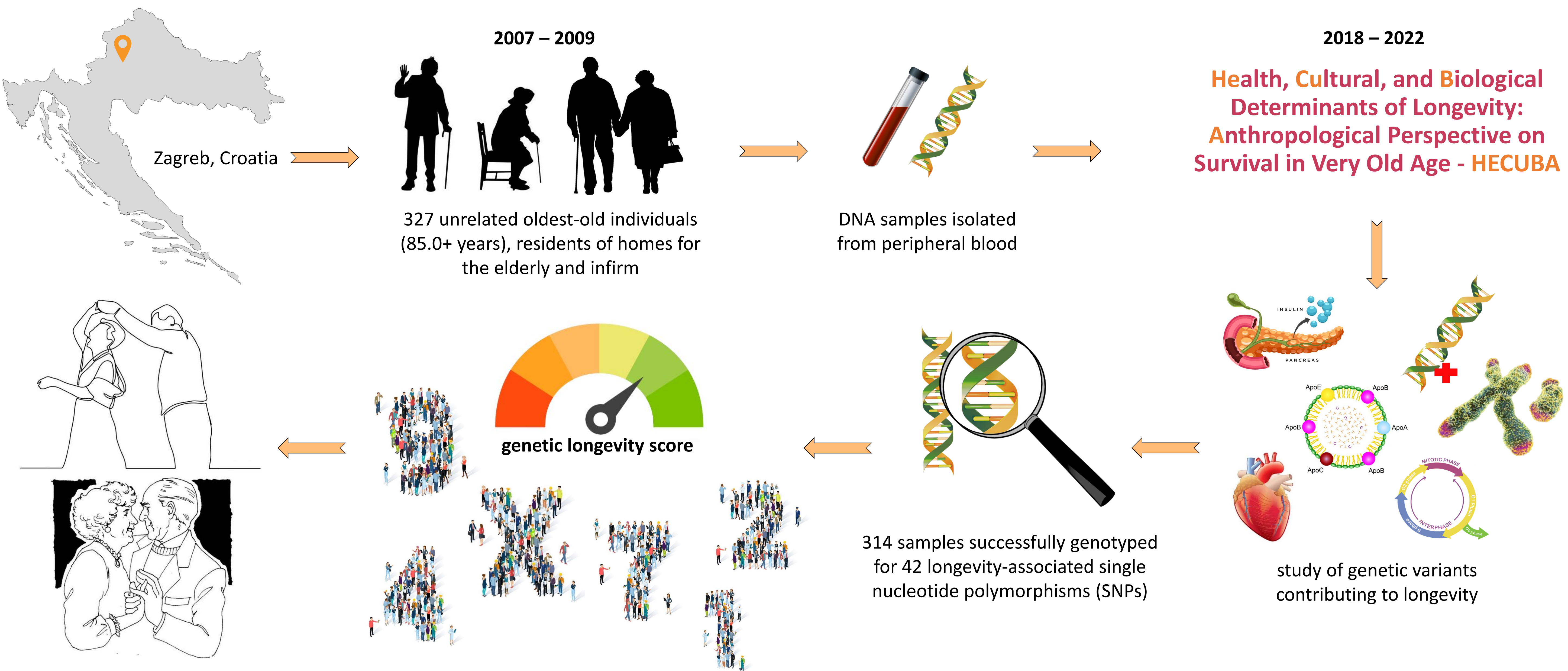# Genetic Longevity Scores for the Croatian population aged 85+

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2007 – 2009

Zagreb, Croatia

327 unrelated oldest-old individuals (85.0+ years), residents of homes for the elderly and infirm

DNA samples isolated from peripheral blood

2018 – 2022

Health, Cultural, and Biological Determinants of Longevity: Anthropological Perspective on Survival in Very Old Age - HECUBA

study of genetic variants contributing to longevity

genetic longevity score

314 samples successfully genotyped for 42 longevity-associated single nucleotide polymorphisms (SNPs)

Genetic longevity score

Genetic longevity score (GLS) is a sum of alleles related to human longevity across loci included in the best multivariate logistic model (Fig. 1). All the analyses were performed with two cut-off ages at death as dependent variables – 90.0 and 95.0 years – threshold ages for longevity and extreme longevity. Best models for predicting survival up to 90 and 95 years share only one locus, rs1042522 in the TP53 gene (Fig. 2). However, both models also point to the epsilon diplotypes of the APOE gene: one model to locus rs7412 and the other to locus rs429358.

Unweighted GLS (uGLS) was calculated by summing the coding values given to genotypes on all of the SNPs that made up the best model, and weighted GLS (wGLS) was calculated by summing the value of genotypes for each SNP multiplied by their respective odds ratio within the multivariate model (Table 1). There was no significant difference between sexes in mean values of any GLS. In order to test the reliability of GLS, additional statistical analyses were performed to evaluate the association between age at death and both uGLS and wGLS (Table 2). All four GLSs (uGLS90, wGLS90, uGLS95, wGLS95) were positively correlated with age at death (p<0.01). ROC curve analysis showed all four scores are predictive for reaching the longevity milestones. With area-under-curve (AUC) of 0.690, weighted GLS90 was shown to be the most predictive (Fig. 3 & 4).

Table 1. Descriptive statistics of unweighted and weighted genetic longevity scores for survival up to the ages of 90.0 and 95.0.

	Theoretical Maximum	Minimum	Maximum	Range	Mean	SD
uGLS90	18	1	15	14	7.869	2.551
uGLS95	10	1	9	8	4.379	1.510
wGLS90	36.232	1.330	29.271	27.941	14.337	5.132
wGLS95	25.104	2.703	22.599	19.896	11.112	3.732

Table 2. Correlation between age at death and calculated genetic longevity scores.

		uGLS90	wGLS90	uGLS95	wGLS95
Age at death	**Pearson correlation (r)**	0.159	0.178	0.215	0.211
	p	0.005	0.002	<0.001	<0.001
	Multiple regression (beta)	-0.132	0.143	0.188	-0.106
	p	0.513	0.011	0.001	0.734

coding of SNPs according to association with longevity

univariate logistic analyses with two cut-off ages at death

SNPs with p<0.2 → multivariate binary logistic regression model

9 SNPs explaining 20.5% of variance in survival beyond 90 years

5 SNPs explaining 9.3% of variance in survival beyond 95 years

genetic longevity score calculation
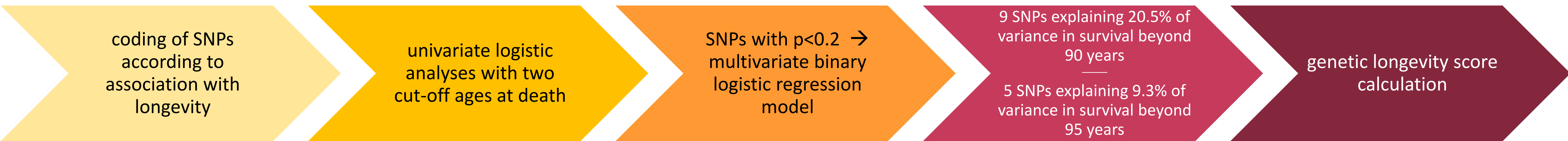
Figure 1. Statistical analyses preceding genetic longevity score calculation.

cut-off age 90.0

	O.R. (95% C.I.)
rs50871	1.072 (0.506 - 2.268)
rs9536314	1.575 (0.809 - 3.065)
rs1042522	1.752 (1.010 - 3.040)
rs1800629	1.898 (1.038 - 3.468)
rs17202060	2.024 (0.887 - 4.621)
rs16847897	2.280 (1.239 - 4.194)
rs2267723	2.128 (1.249 - 3.627)
rs12206094	2.332 (0.717 - 7.583)
rs7412	3.055 (1.230 - 7.587)

cut-off age 95.0

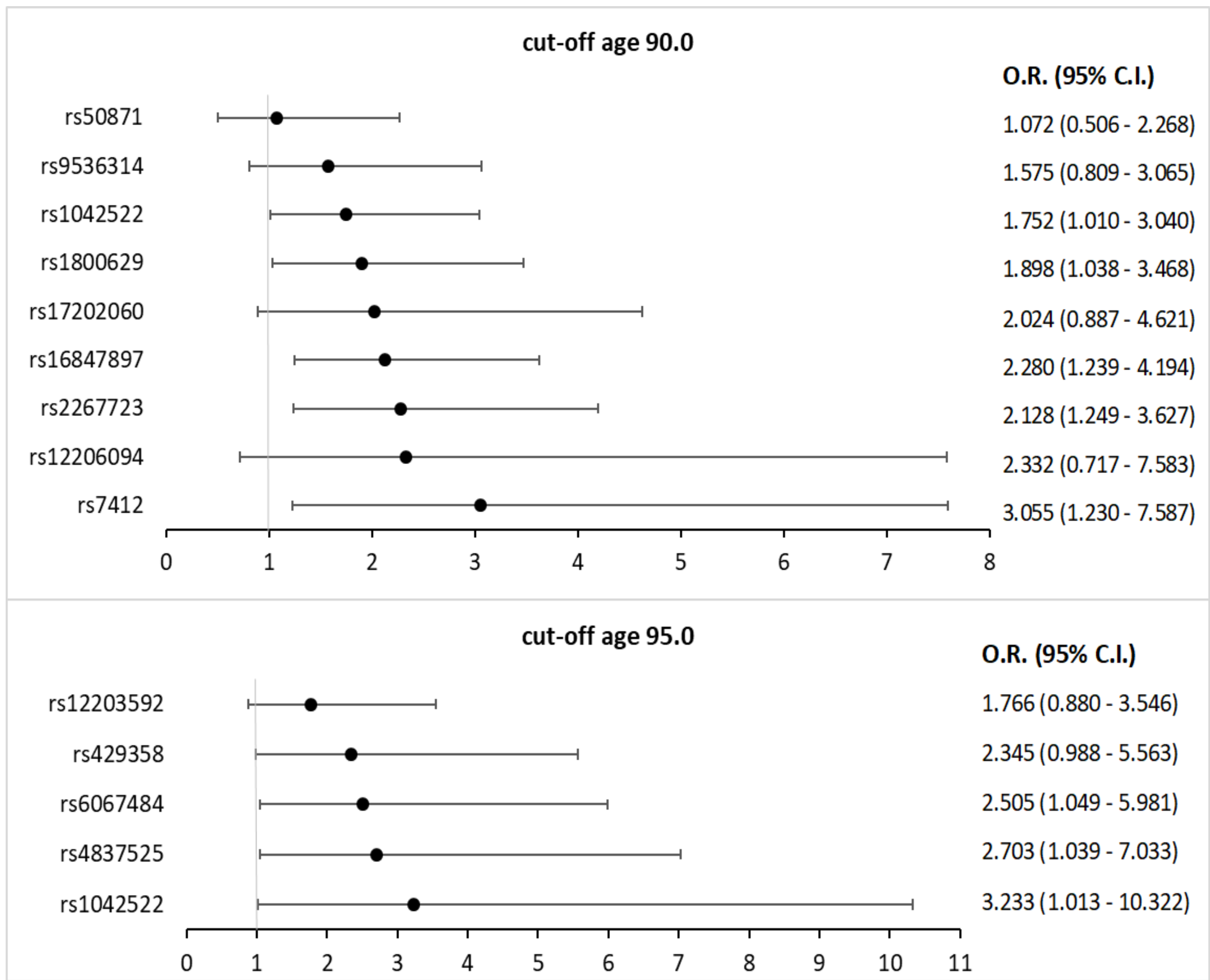|	O.R. (95% C.I.)
rs12203592	1.766 (0.880 - 3.546)
rs429358	2.345 (0.988 - 5.563)
rs6067484	2.505 (1.049 - 5.981)
rs4837525	2.703 (1.039 - 7.033)
rs1042522	3.233 (1.013 - 10.322)

Figure 2. The forest plot of SNPs positively (O.R. > 1) associated with longevity within two multivariate models.

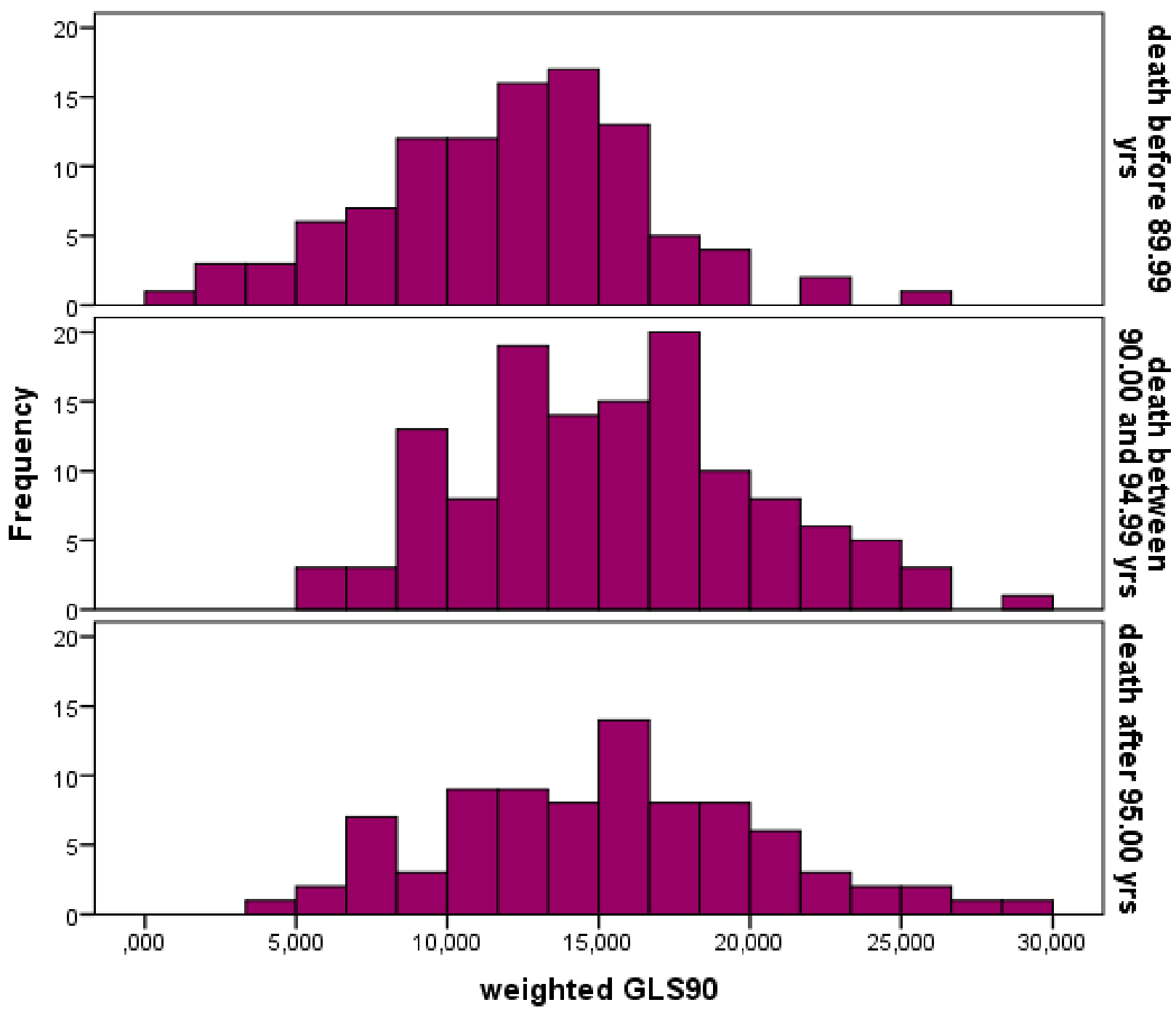**Figure 3. (left)** Distribution of wGLS90 in three age-of-death groups: <90.0, 90.0–94.99; 95.00+ years.
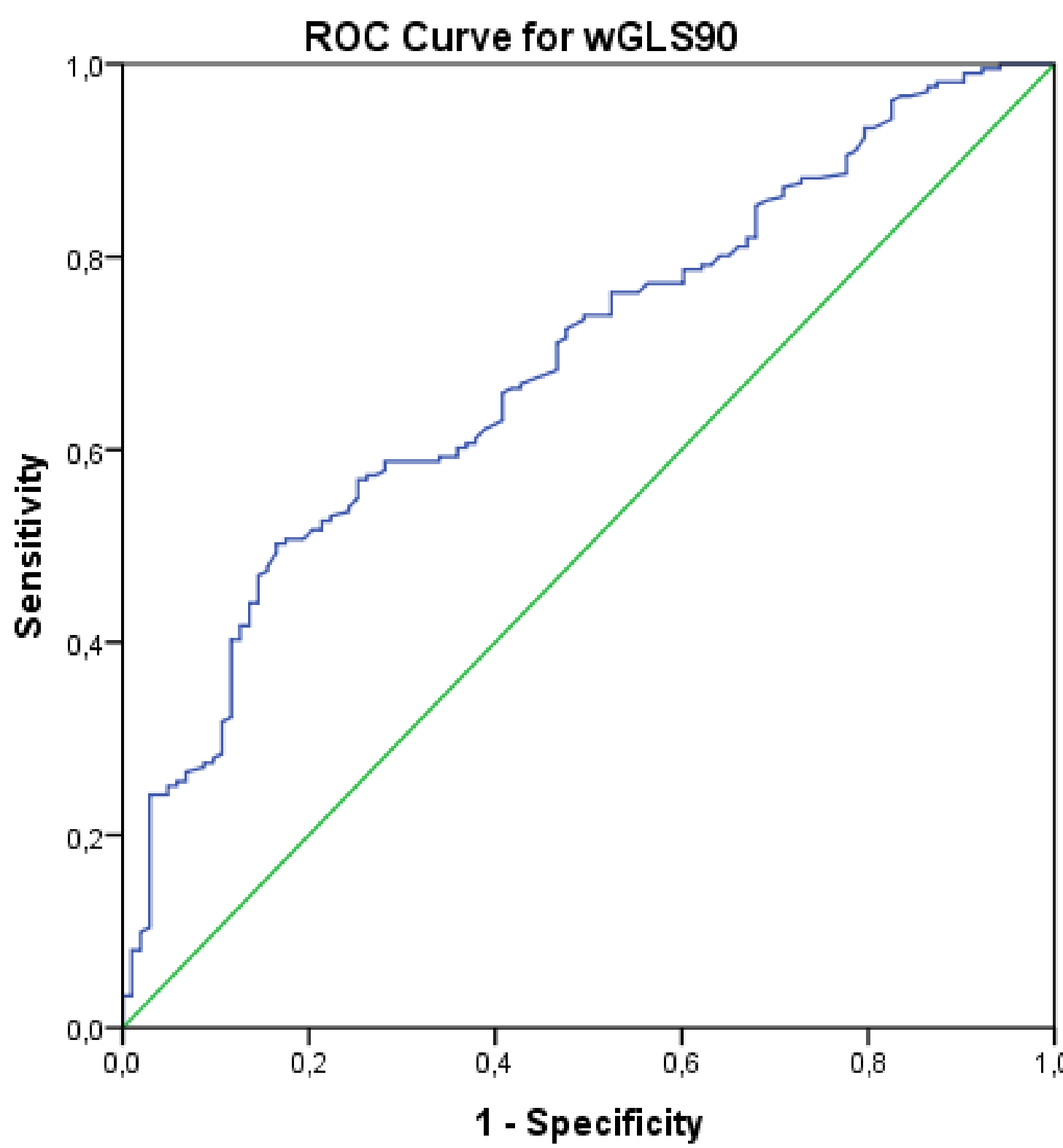
Figure 4. (right) Predictive power of wGLS90 depicted by a ROC curve (AUC=0.690).

ROC Curve for wGLS90

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No conflict of interest to disclose.

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