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“ASSOCIATION OF SNPs IN COAGULATION FACTOR GENES WITH ISCHAEMIC STROKE AMONG UKRAINIAN POPULATION”

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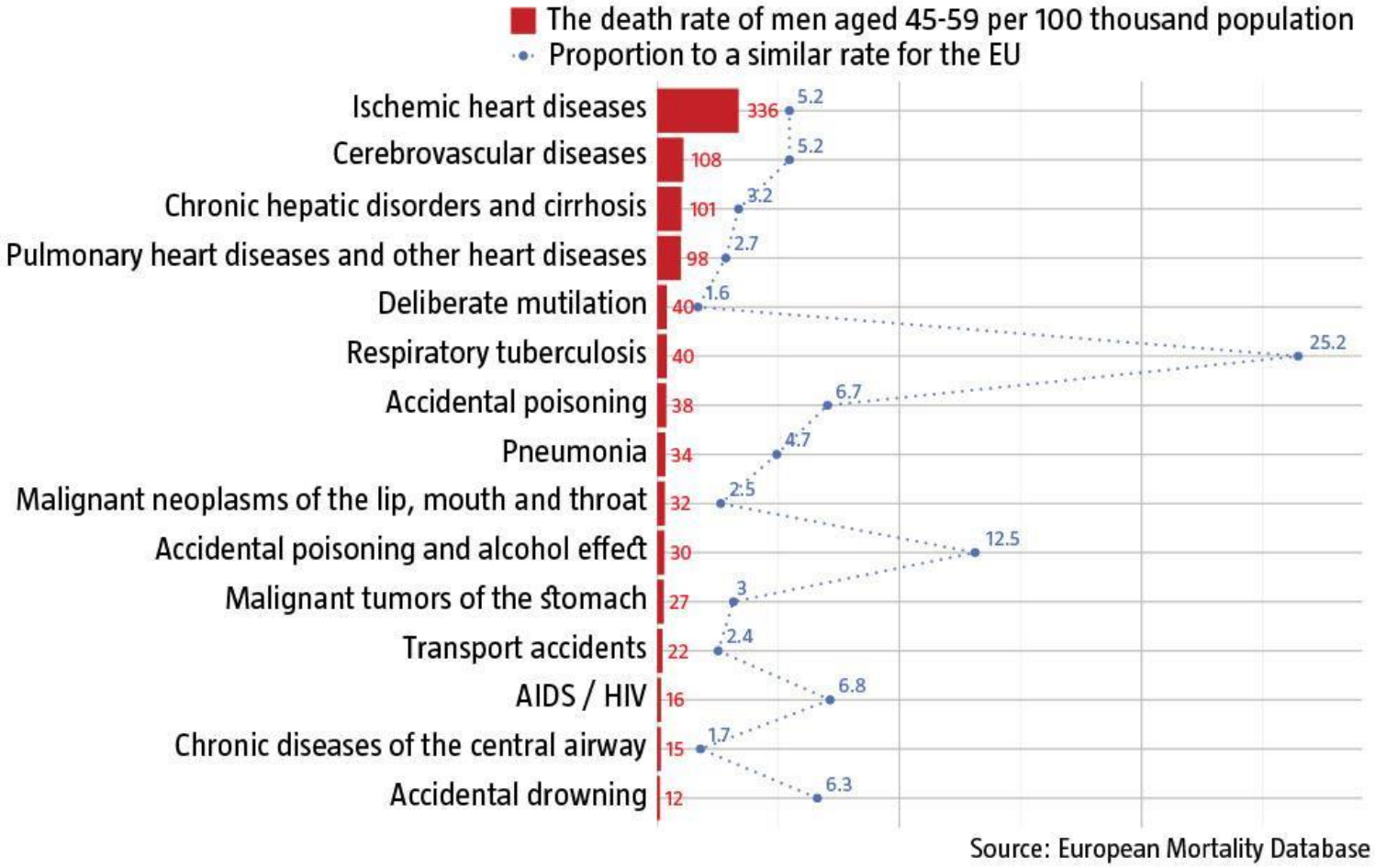
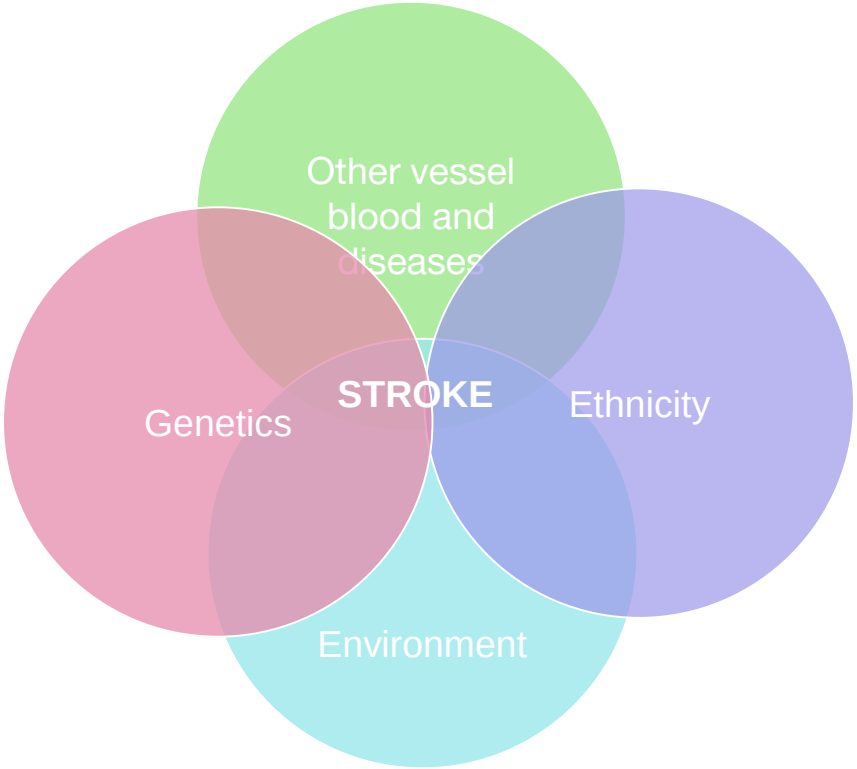
The main killers



Source: European Mortality Database

Stroke is a multifactorial disease



Aim

is to investigate the association of polymorphic variants of coagulation factor genes (***F2, F5, F7*, and *F13A1***) with the occurrence of ischemic strokes in the Ukrainian population.

spot the differences in minor allele frequencies between Ukrainian and other population

73 non-family patients with ischemic atherothrombotic stroke (37 men and 36 women, mean age 66.1 ± 10.3 years) and 88 neurologically healthy volunteers (19 men, 67 women, mean age 64.4). ± 11.6 years).

all relevant data was collected: biochemical profile, comorbidity, lipid profile, common ischemic stroke risk factors, physical activity, alcohol and smoking
(including the number of cigarettes per day).

Ген, SNP	Генотип	UA *N*, (%)	EUR *N*, (%)	AMR *N*, (%)	AFR *N*, (%)	EAS *N*,(%)	SAS *N*, (%)
F2	GG	82 (97)	81,7 (98,4)	81(97,4)	83 (100)	83 (100)	83 (100)
rs1799963 (G/A)	GA	2 (3)	1,3 (1,6)	1,9 (2,3)	0	0	0
	AA	0	0	0,2 (0,3)	0	0	0
χ2 значення			0,35	0,02	0,01	0,01	0,01
F5	GG	76 (92)	82 (98)	81,3 (98)	83 (100)	83 (100)	81,1 (97,7)
rs6025 (G/A)	GA	7 (8)	1,6 (1,9)	1,7 (2)	0	0	1,9 (2,3)
	AA	0	0,17 (0,1)	0	0	0	0
χ2 значення			*17,8*	*17,3*	0,6	0,6	*14,4*
F7	CC	69 (83)	66 (79,5)	44 (77)	84,8 (77)	75,4 (90)	38 (47)
rs6046 (C/T)	CT	14 (17)	15,5 (18,6)	12,4 (21,6)	23 (21)	7,6 (10)	37 (46)
	TT	0	1,5 (1,9)	0,8 (1,4)	1,3 (2)	0	6 (7)
χ2 значення			1,8	*14,3*	*7,8*	5,6	*45,4*
F13A1	GG	38 (46)	48,3 (58)	63,9 (77)	64,5 (77,7)	83 (100)	39 (47)
rs5985 (G/T)	GT	37 (45)	29,2 (35)	17,9 (22)	17,5 (21)	0	38 (46)
	TT	8 (9)	5,4 (7)	1,2 (1)	1 (1,2)	0	5,9 (7)
χ2 значення			5,5	*69,4*	*81,5*	*24,4*	0,8

"Comparative analysis of Ukrainian (UA), European (EUR), mixed American (AMR), African (AFR), East (EAS) and South Asian (SAS) populations "

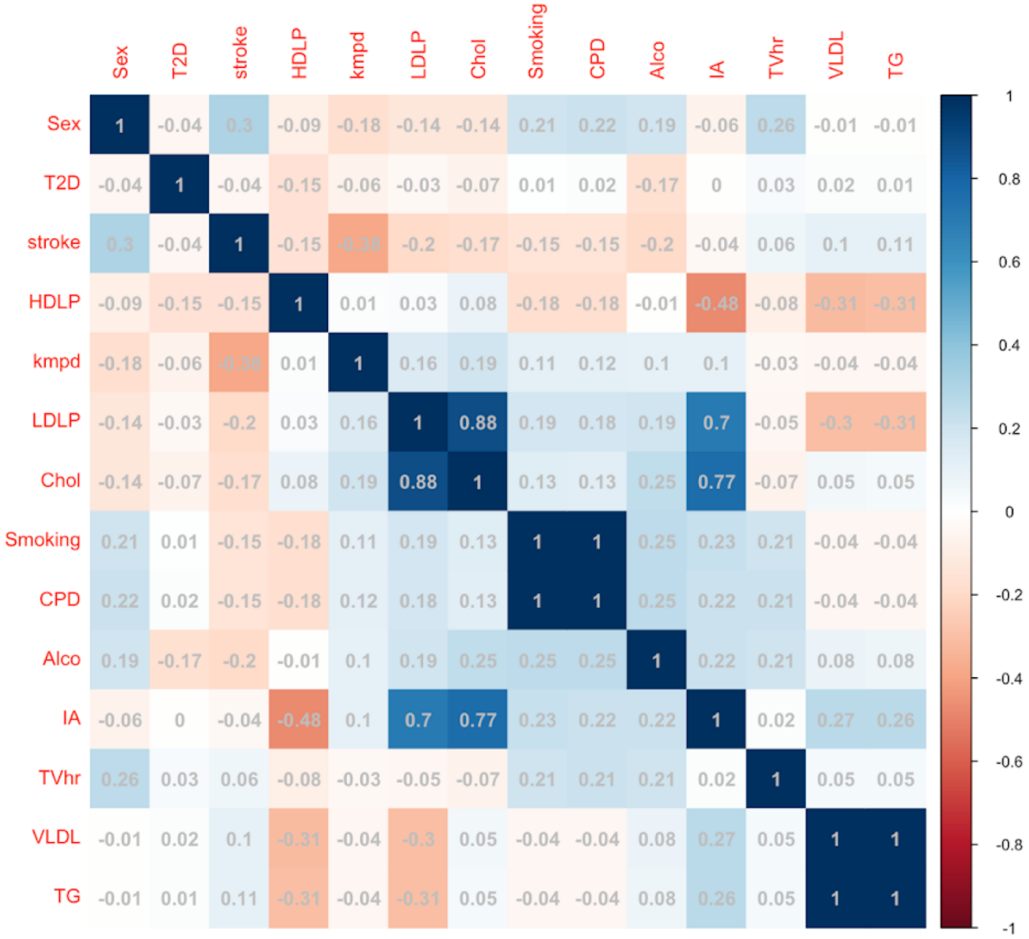
Italics and underlining highlight the results that exceed the calculated value - 3.84- for 1 degree of freedom, at p = 0.05.

Data is given according to the 1000 Genomes project

Results of multinomial logistic regression between polymorphisms and cases of ischemic stroke

Gene	SNP	OR	95%CI	*P*- value*
F2	*rs1799963*A*	*1.27*	*0.2- 9.2*	*0.2*
F5	rs6025*A	0,52	0.13-2.08	0.035
F7	rs6046*T	0,92	0.39-2.18	0.049
F13A1	rs5985*T	1,26	0.64-2.45	0.034

Calculated with Quanto statistical power of the association study between the locus with a minor allele frequency of 15% and stroke without consideration of interaction with non-genetic risk factors with OR = 1.5 reaches only 37%, with OR = 2.0 - 75%.



Correlation matrix between non-genetic factors and ischemic stroke.

Blue means a **positive correlation** between factor and ischemic stroke, **red - negative**.

Correlation coefficients from 1 to -1 are indicated in gray.

T2D - diabete type 2; HDLP - high density lipoproteins; kmpd - kilometres per day; LDLP - low density lipoproteins; Chol - cholesterol; CPD - cigarettes per day; IA - atherogenic index; TVhr - hours per day watching TV; VLDL - very low-density lipoprotein; TG - triglycerides

Association of non-genetic factors and ischemic stroke

Factor	OR	95%CI	*P*-value
Smoking	0,37	0.13-1.09	0.0097**
Alcohol abuse	0,4	0.19-0.84	0.013*

OR were calculated with generalized linear regression

Discussion

Gene, SNP	Genotype	Our study *N*, (%)	Tatarsky et all., *N*, (%)
F2	GG	82 (97%)	81,7 (98,4%)
	GA	2 (23%)	1,3 (1,6%)
rs1799963 (G/A)	AA	0	0
χ^2			*0,35*
F5	GG	76 (92%)	82 (98%)
	GA	7 (8%)	1,6 (1,9%)
rs6025 (G/A)	AA	0	0,17 (0,1%)
χ^2			17,8

According to preliminary data of J. Casas (Casaset.all 2004), the risk of ischemic stroke increases **1.33** times with heterozygous carriers of **G1691A** polymorphism (Factor V Leiden), in our case the risk of heterozygotes was **1.25**. This confirms the association of ischemic strokes with Leiden factor polymorphism rs6025.

For heterozygotes by **G10976A** coagulation factor FVII polymorphism, the risk of stroke increased **0.92** times, which is close to **0.73** reported in the cohort study of N. Zakai (Zakai et. All 2011).

We confirm the increased risk of ischemic stroke by ~ 40% among participants who abused **alcohol** or **smoked.**

Conclusions

Statistically significant association between the cases of atherothrombotic ischemic strokes and SNPs in the genes of coagulation factors FV, FVII and A1 of the FVIII polypeptide (gene *F13A1*) was detected.

Odds ratios between polymorphisms and disease were calculated. Analysis of non-genetic factors confirmed the relationship between ischemic strokes, smoking, and alcohol abuse in the Ukrainian population