



*FAMILIAL HYPERCHOLESTEROLEMIA
MUTATIONS
IN CZECH POPULATION
AND IN CZECH PATIENTS
WITH ACUTE CORONARY SYNDROME*

**J.A. Hubáček
J. Piňha, V. Adámková**

**IKEM
Praha**



Familial hypercholesterolemia

- (was believed to be...) **Autosomal dominant disorder**
- **High plasma cholesterol and ApoB, low TG**
- **Tendon xantomas**
- **Premature atherosclerosis**
- **Homozygotes –**
 - **Premature death (3rd decade)**
- **Prevalence ??**





FH prevalence around the World



Population	Prevalence
General population	~ 1 : 500
French Canadian	1 : 270
Christian Lebanese	1 : 85
Tunisia	1 : 165
South African Afrikaners	1 : 72 - 1 : 100
South African Ashkenazi Jews	1 : 67
Copenhagen study	1 : 210
Review (cca 8 000 000 s.)	1 : 311

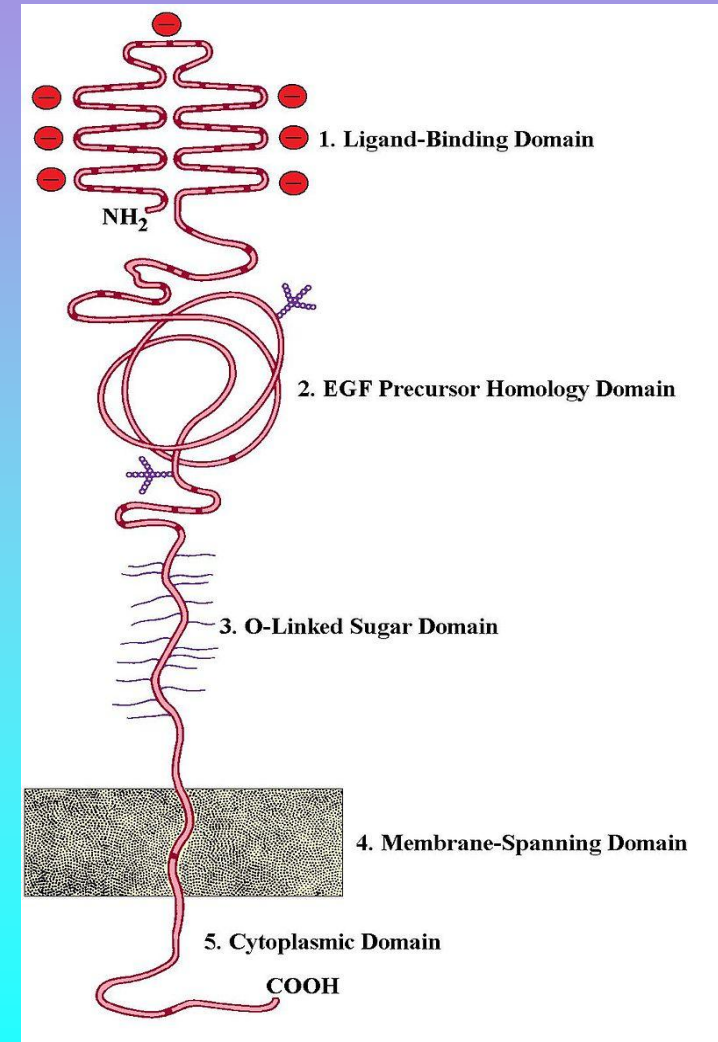
(no population/ethnicity without FH detected...)

?? FH prevalence in CZ population ??



Mutations leading to FH

- Majority of patients – LDL receptor
 - APOB
 - PCSK9
 - Oligogenic FH
 - Polygenic FH
 - GRS / PRS
- LDLr gene
- Hundreds of mutations
- <http://www.ucl.ac.uk/ldlr>
 - different severity





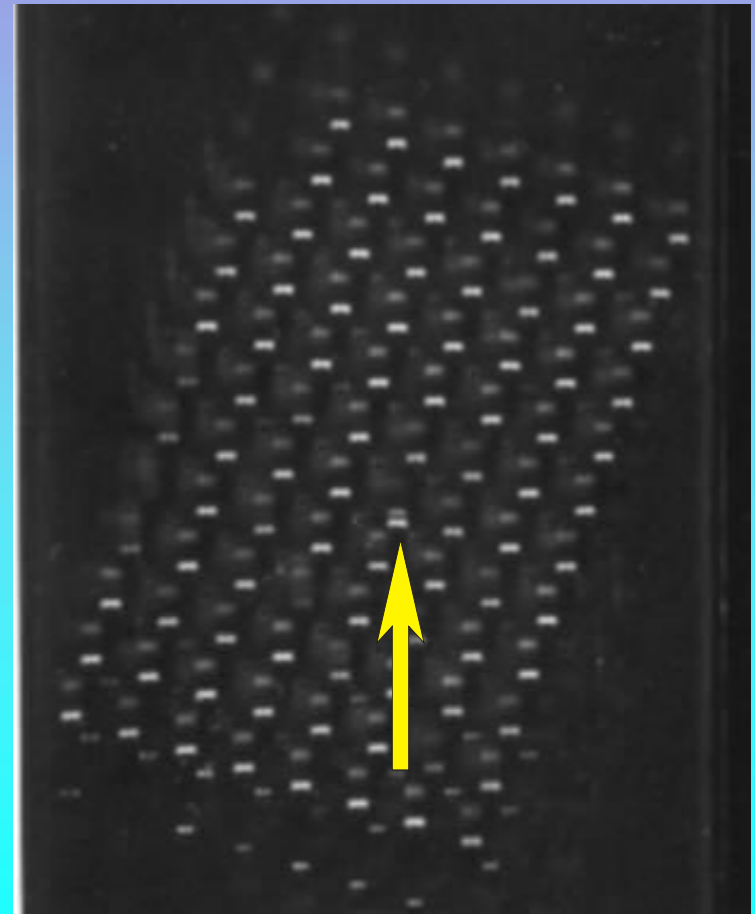
Methods

- LDL-R Asp266Glu
- LDL-R Gly592Glu
- APOB Arg3527Gln/Trp

- 9 100 subjects

- ~ 6 000 post-MONICA
- ~ 3 100 ACS patients

(Tichý et al., 2012)





FH mutations ACS / post-MONICA

■ LDL-R Asp266Glu

■ N = 7 / 12

38 / 9100

1:148 / 1:535

■ LDL-R Gly592Glu

■ N = 3 / 2

(1:60/1:210)

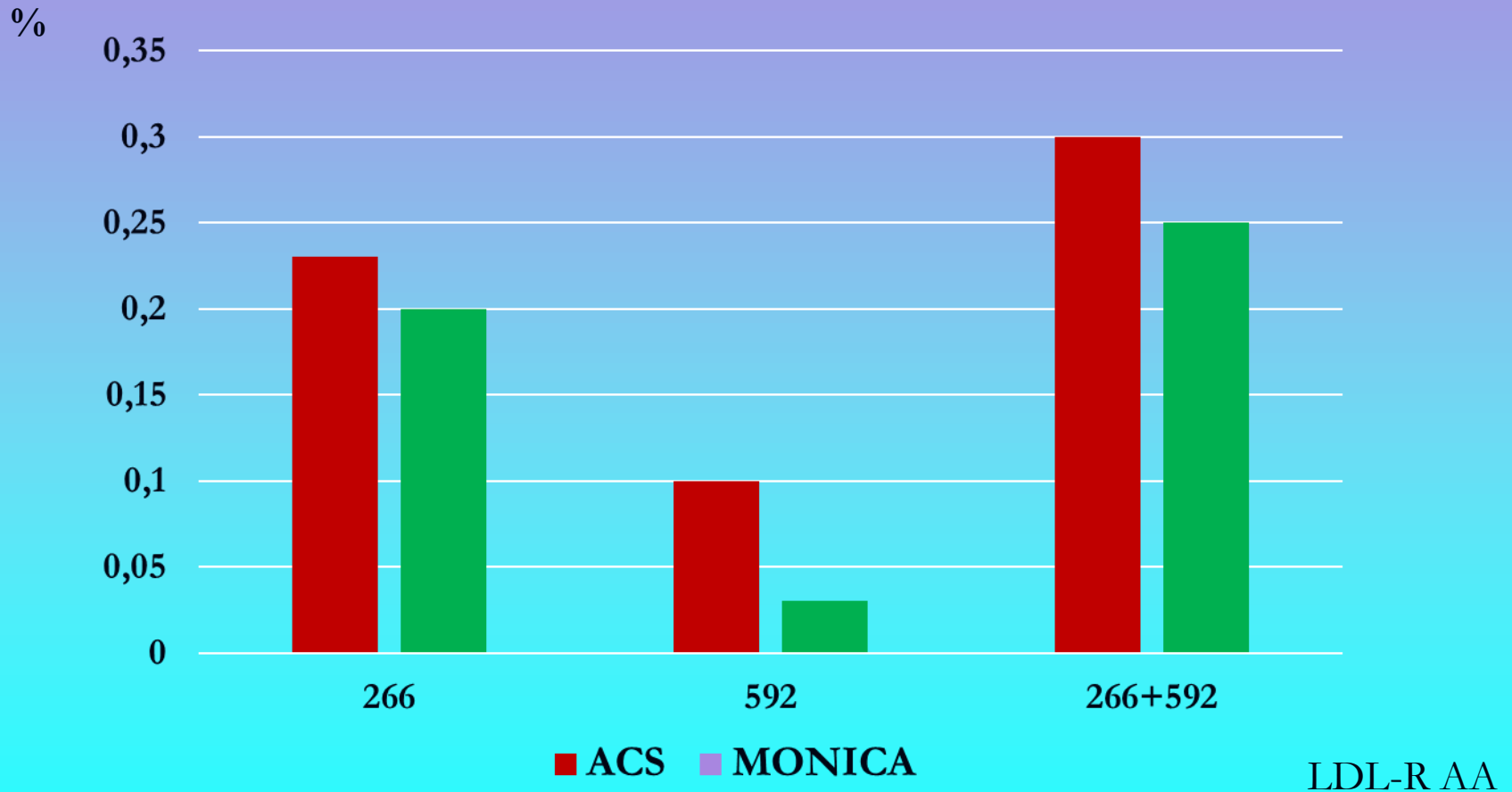
■ APOB Arg3527Gln/Trp

■ N = 11 / 3

ACS below 40 years
~ 25 %



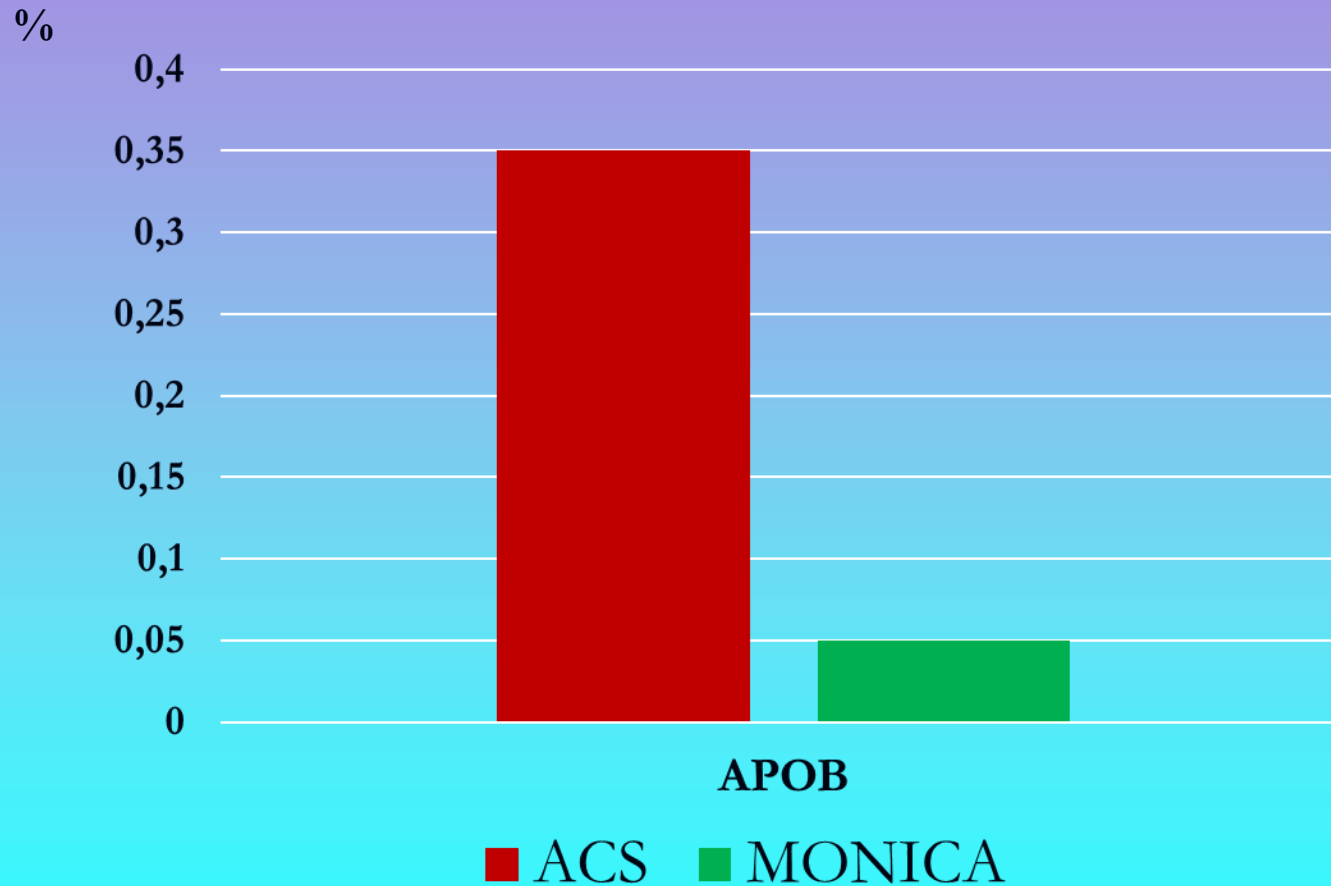
LDL-R mutations in population and ACS patients



P 0,21 - 0,80



APOB mutations in population and ACS patients



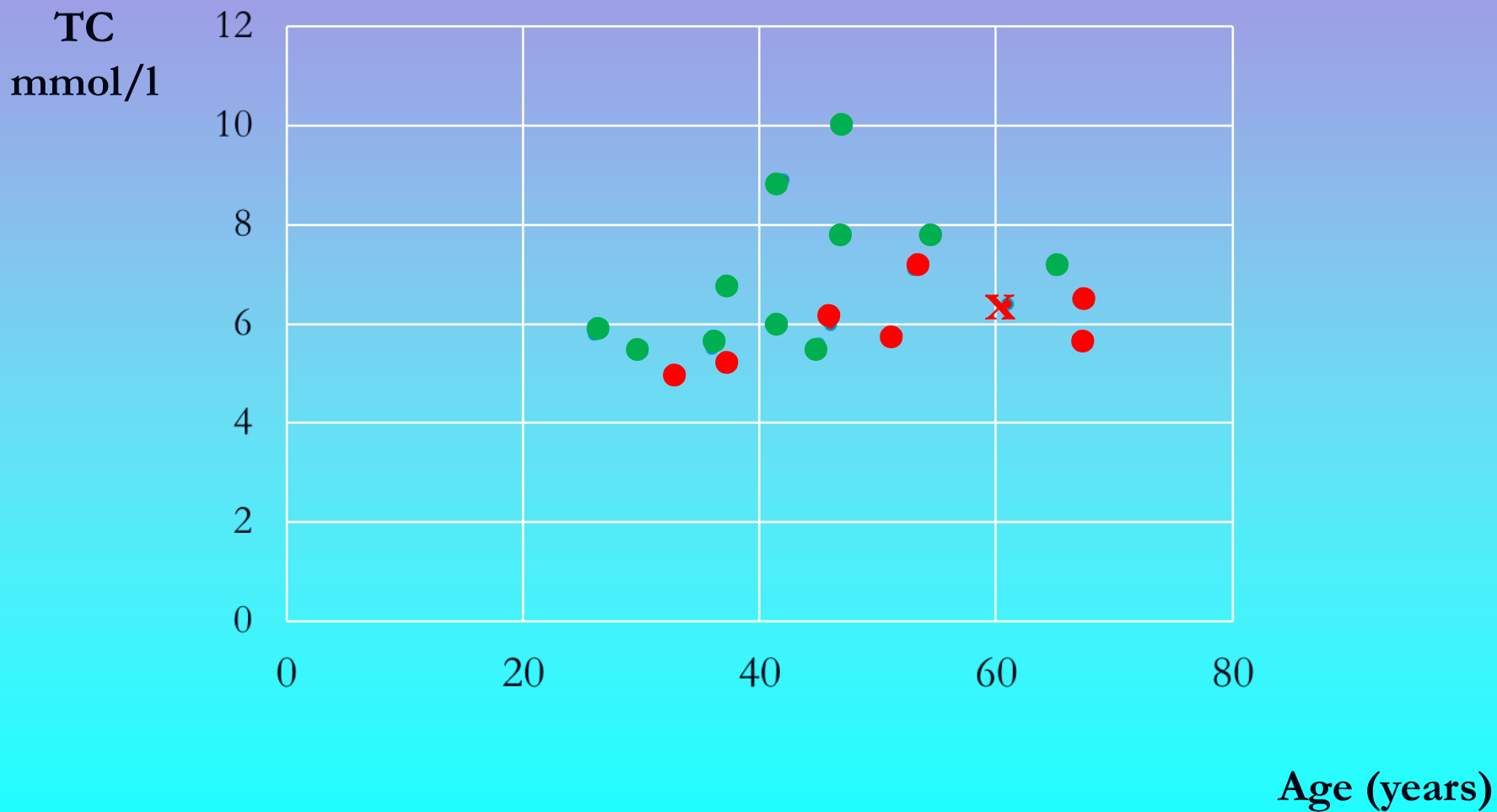
P < 0,0005

OR (95%CI) = 7.1 (2.0-25.5)



Age, TC and LDL-R/266 mutation ACS/post-MONICA

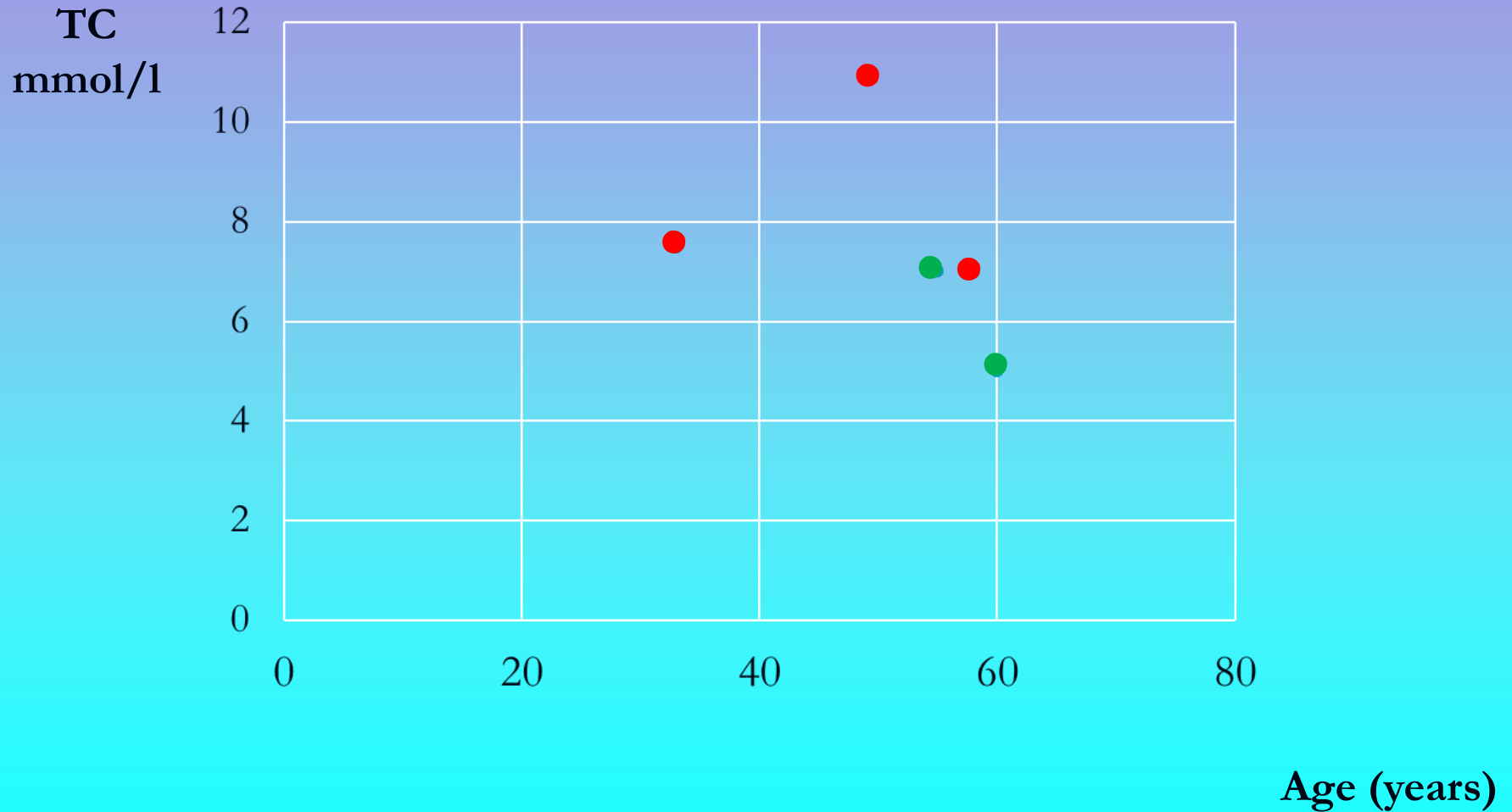
IKE
M





Age, TC and LDL-R/592 mutation ACS/post-MONICA

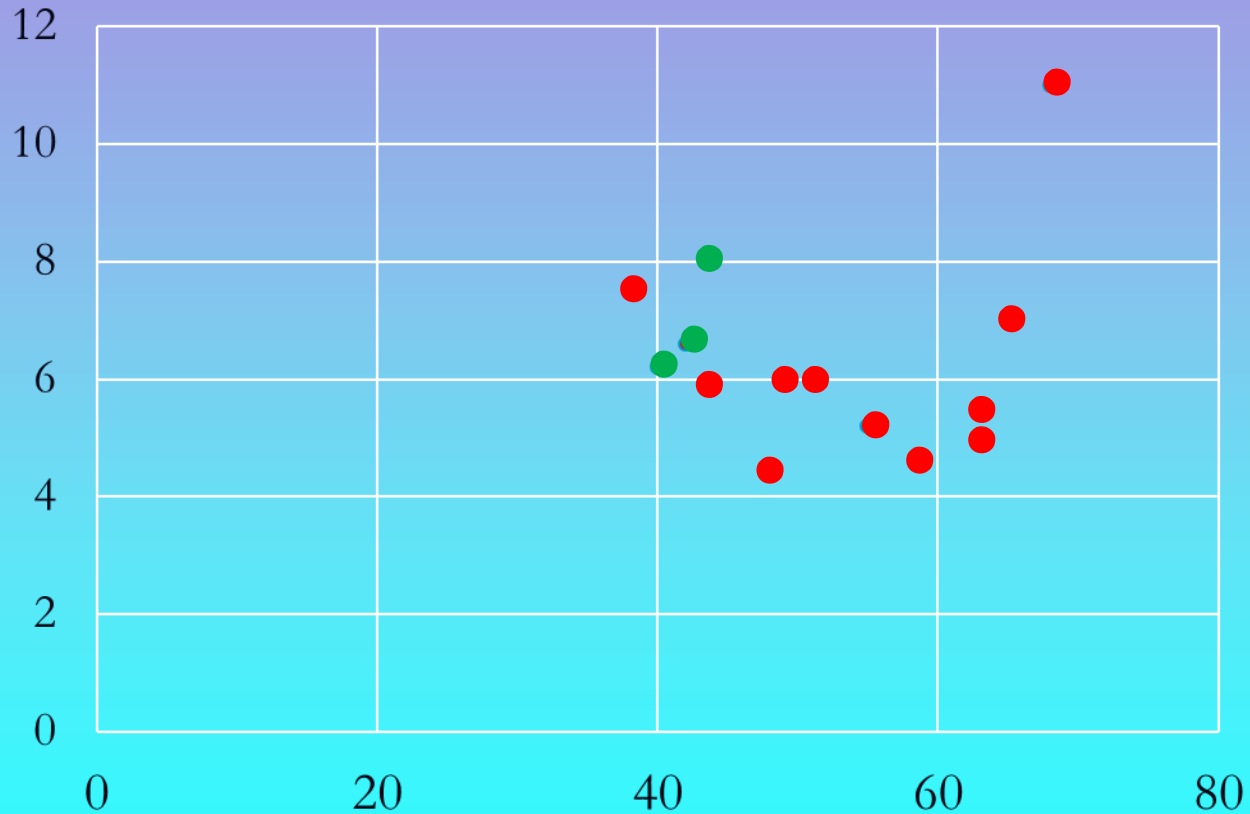
IKE
M





Age, TC and APOB mutations ACS/post-MONICA

TC
mmol/l



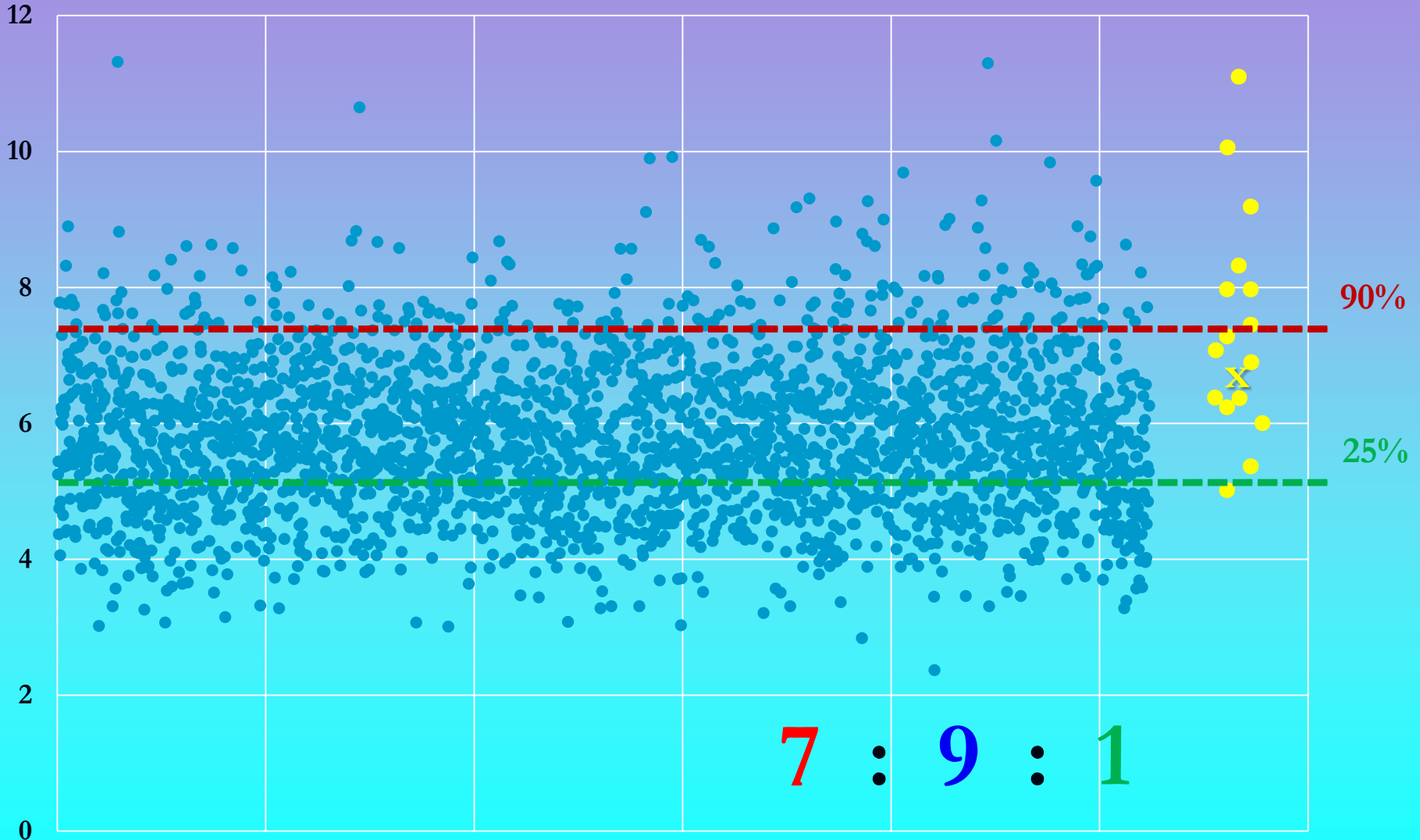
Age (years)



TC and FH mutations in population (post-MONICA)

IKE
+E
M

mmol/l





Conclusions

- Unrecognised FH subjects in the Czech population
- Prevalence much higher than 1 : 500
- Mutation in APOB more severe than in LDL-R ?

Complicated and heterogeneous clinical picture

- ...without CVD events...
- ...without high TC...
- ...although with high TC, without premature CVD event...



Thanks for your attention!

IKE
+E
M

