

What about rare Alleles?

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Genotype – Level – Risik

MM

M/Z

Z/Z

90 - 200

50 - 100

<50

Non-Smoker:
Very low

Smoker:
10% – 20%

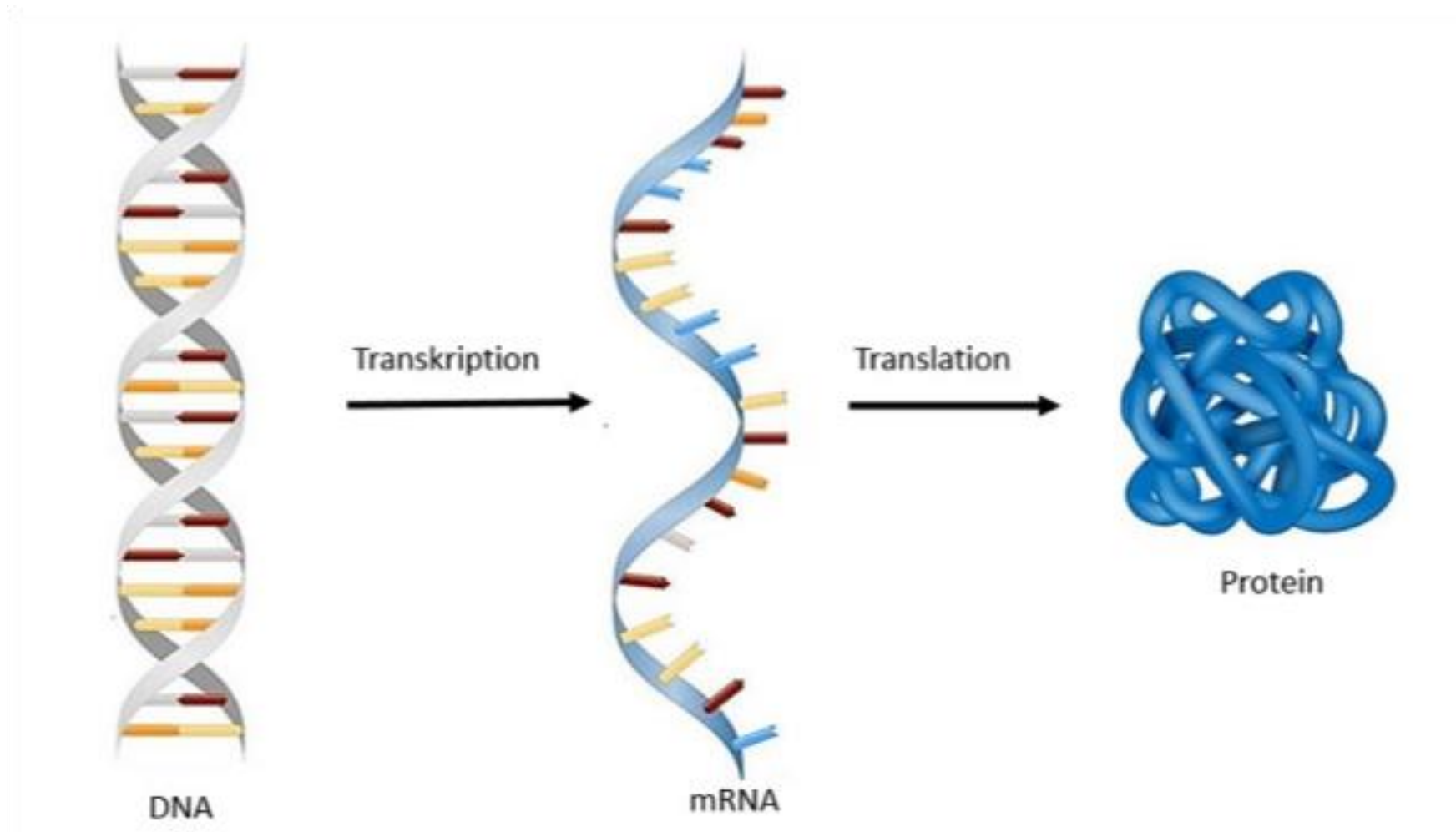
Non-Smoker:
Normal

Smoker:
Mildly Raised

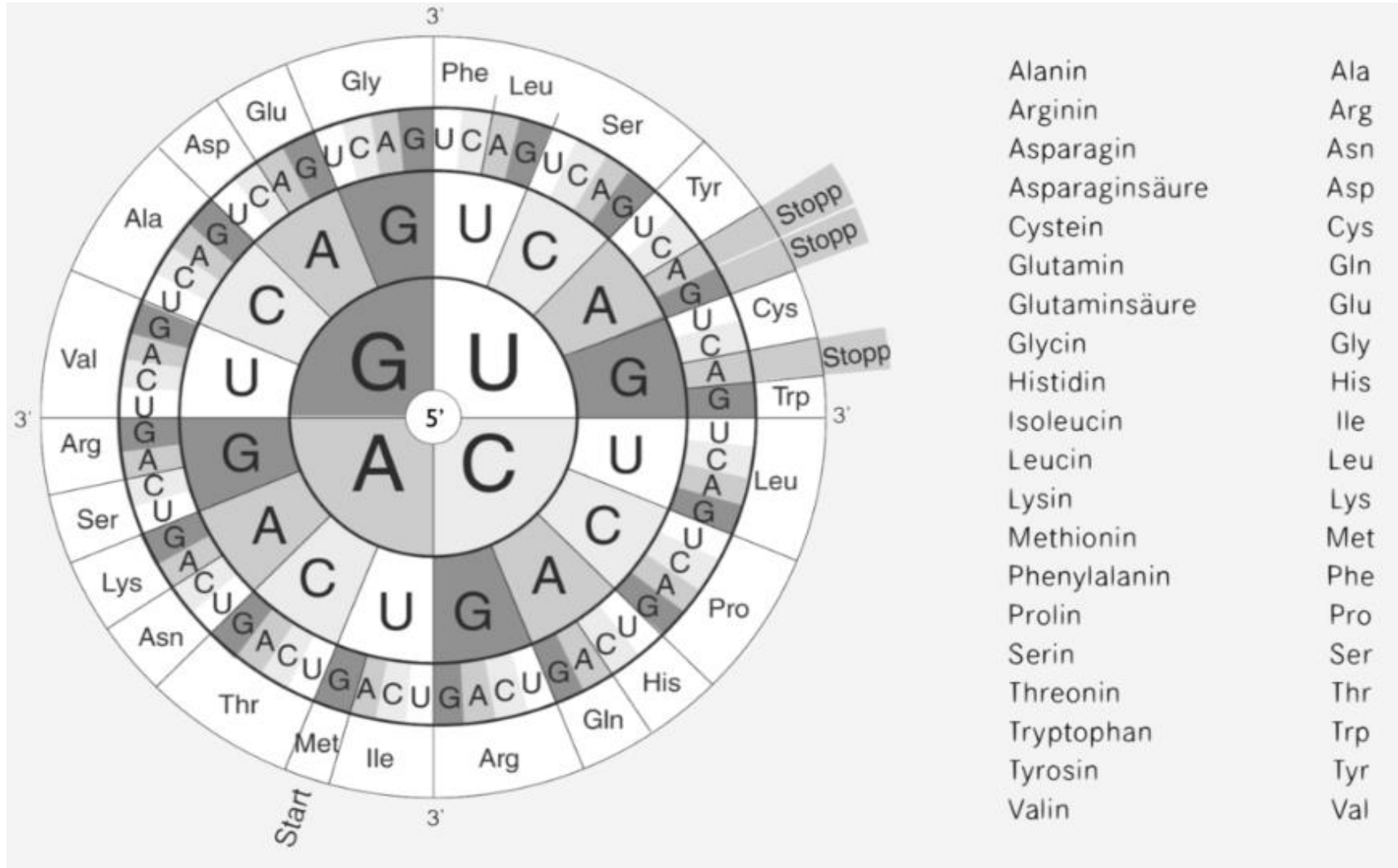
Non-Smoker:
Markedly Raised

Smoker:
Extremely Raised

Genes to Proteins

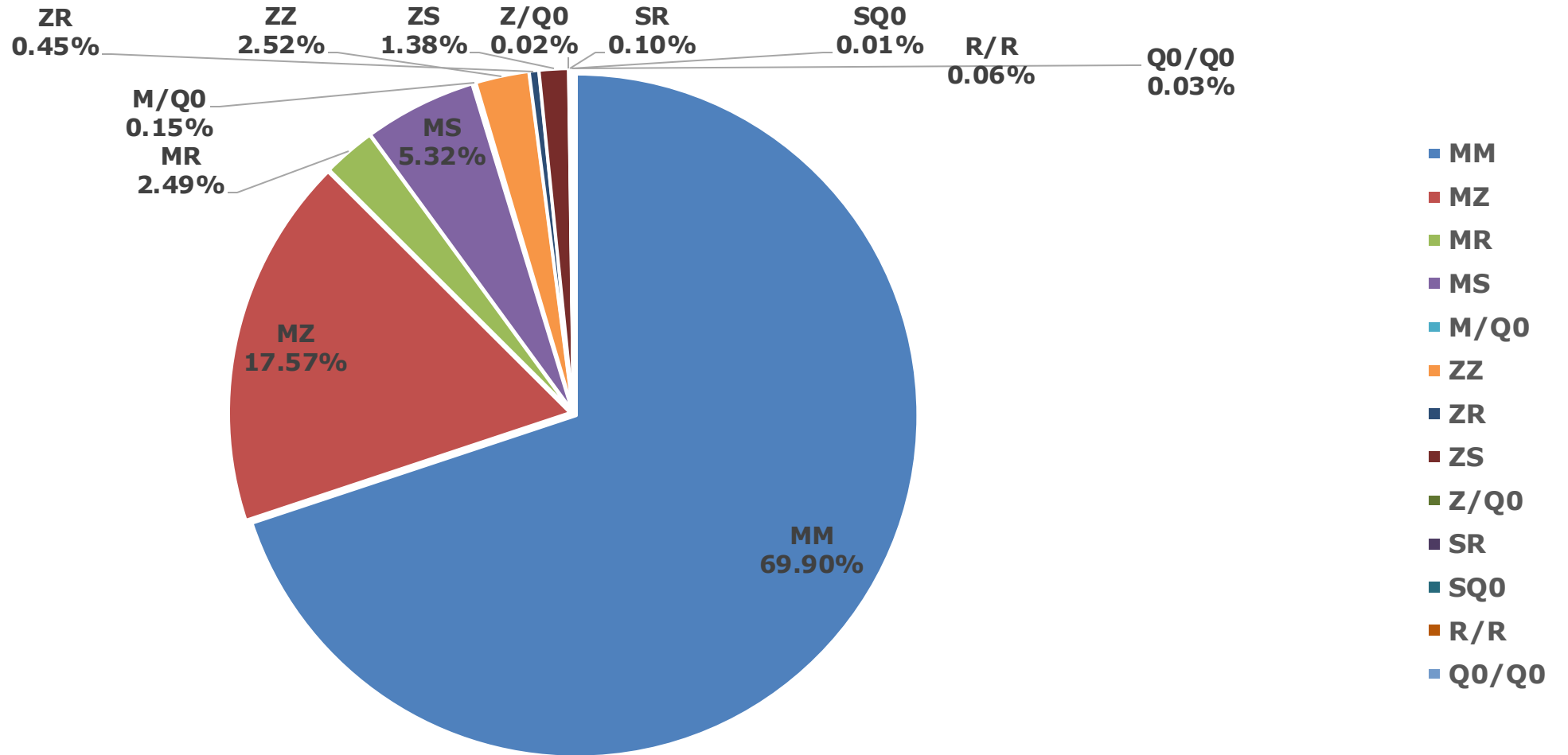


Three Base Pairs code for one Amino Acid (Building Block for Proteins)

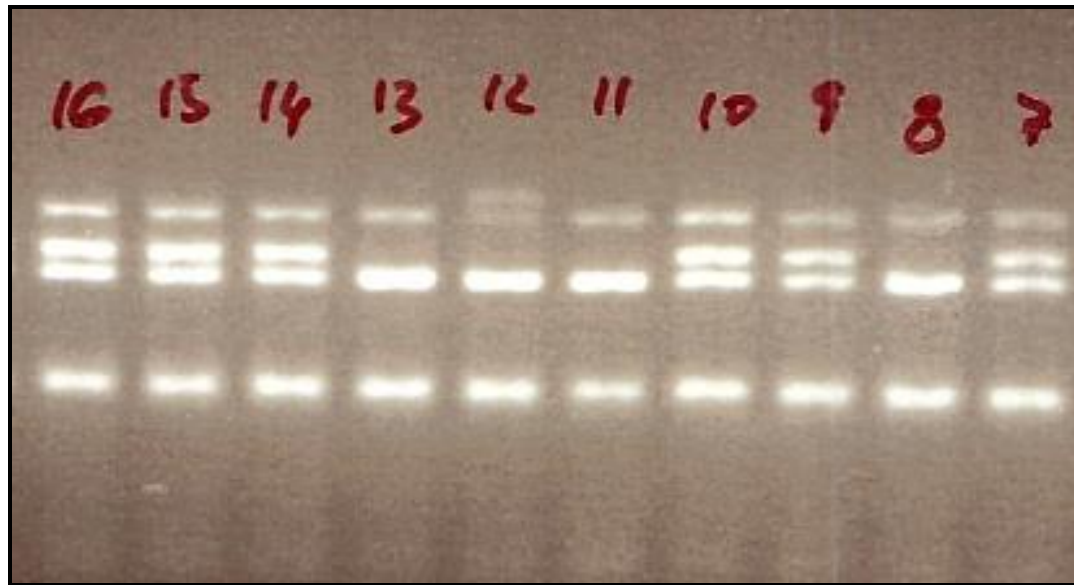




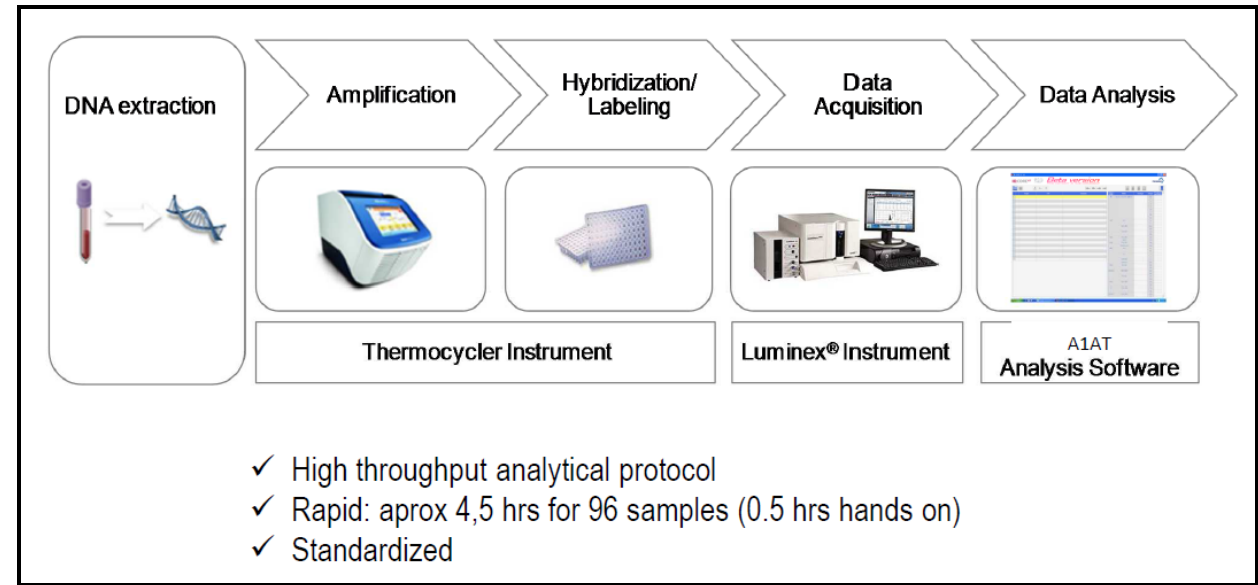
Status in 2024



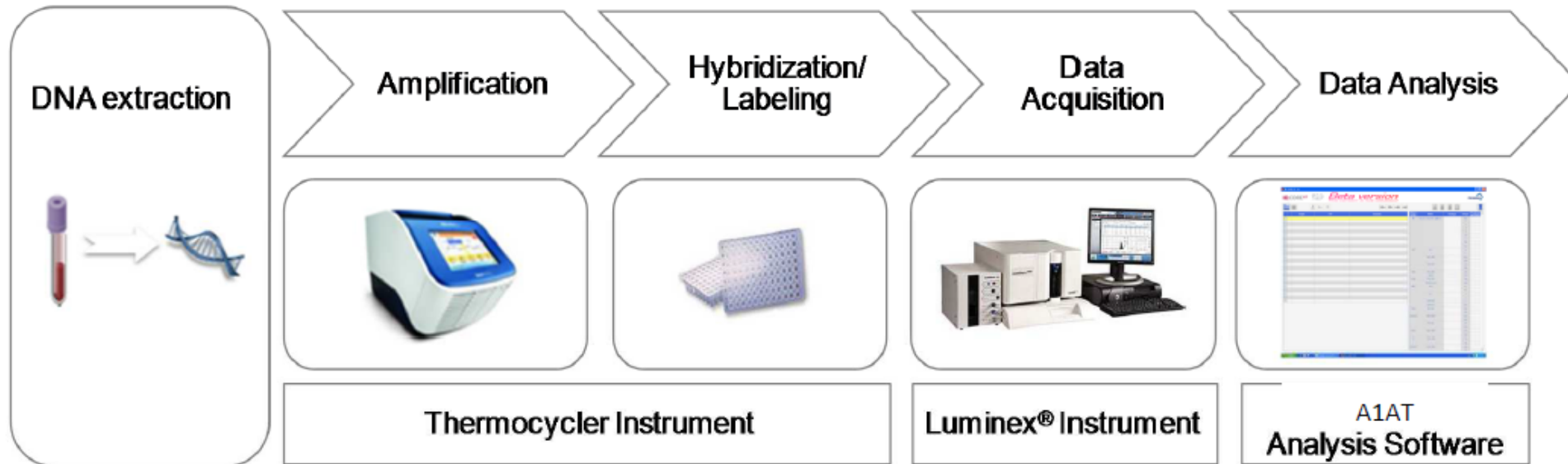
Why is that so?



2 Mutationen (S und Z)



14 Mutationen (S and Z)



- ✓ High throughput analytical protocol
- ✓ Rapid: aprox 4,5 hrs for 96 samples (0.5 hrs hands on)
- ✓ Standardized

	Allelic variant	Associated Alleles
A1AT Genotyping	RefSeq: NM_00112770.1	



14 „frequent“ Mutations in one Take

A1009	c.839A>I	PI*Y barcelona
A1010	c.863A>T	PI*S
A1011	c.1096G>A	PI*Z
A1012	c.1130_1131insT	Q0*Mattawa, Q0*Ourem
A1013	c.1156_1157insC	Q0*Clayton, Q0*Saarbruecken
A1014	c.1178C>T	PI*M heerlen



Ferrarotti *et al.*
Orphanet Journal of Rare Diseases (2024) 19:82
<https://doi.org/10.1186/s13023-024-03069-1>


Orphanet Journal of
Rare Diseases

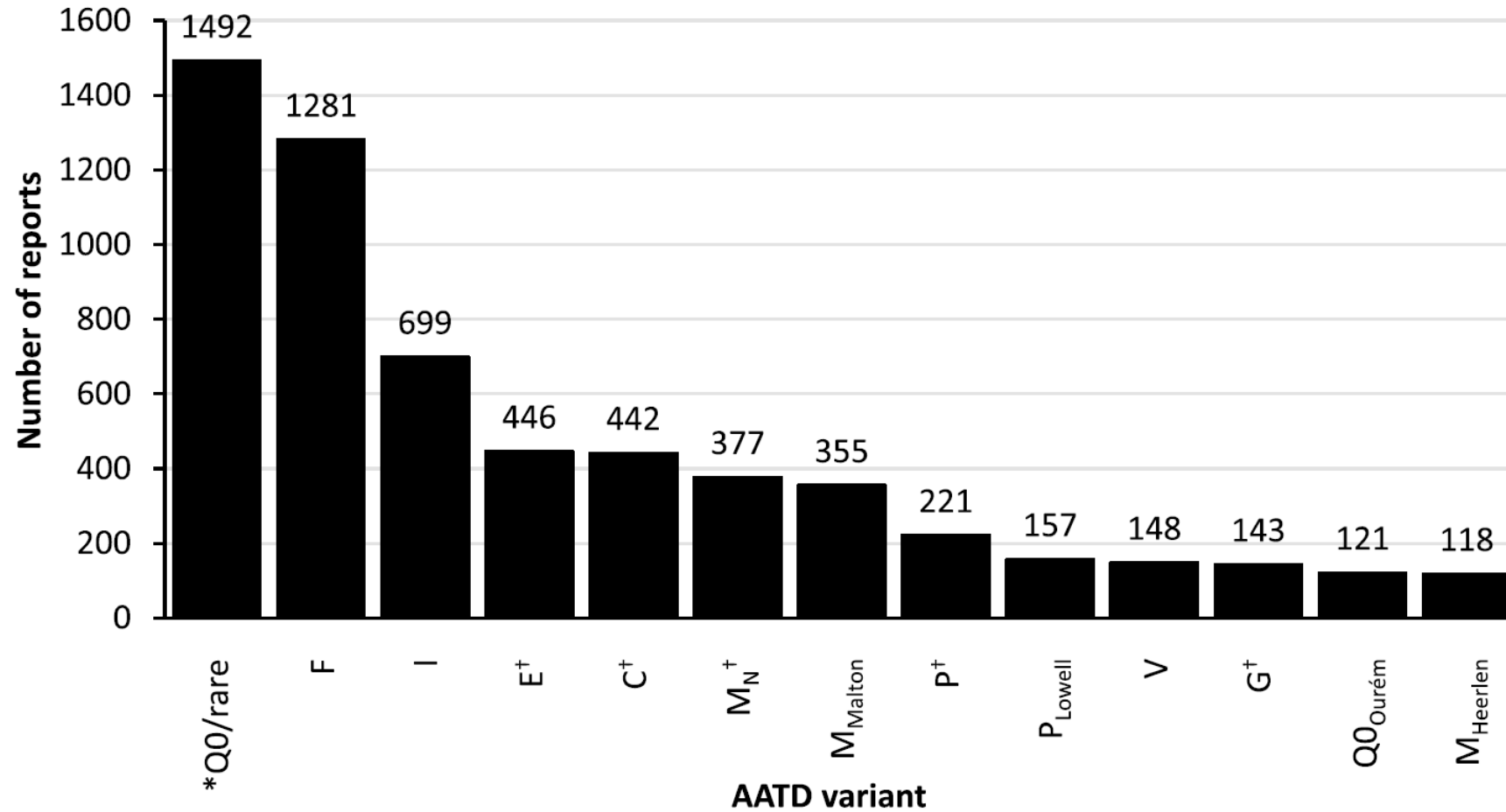
REVIEW

Open Access

Rare variants in alpha 1 antitrypsin deficiency: a systematic literature review

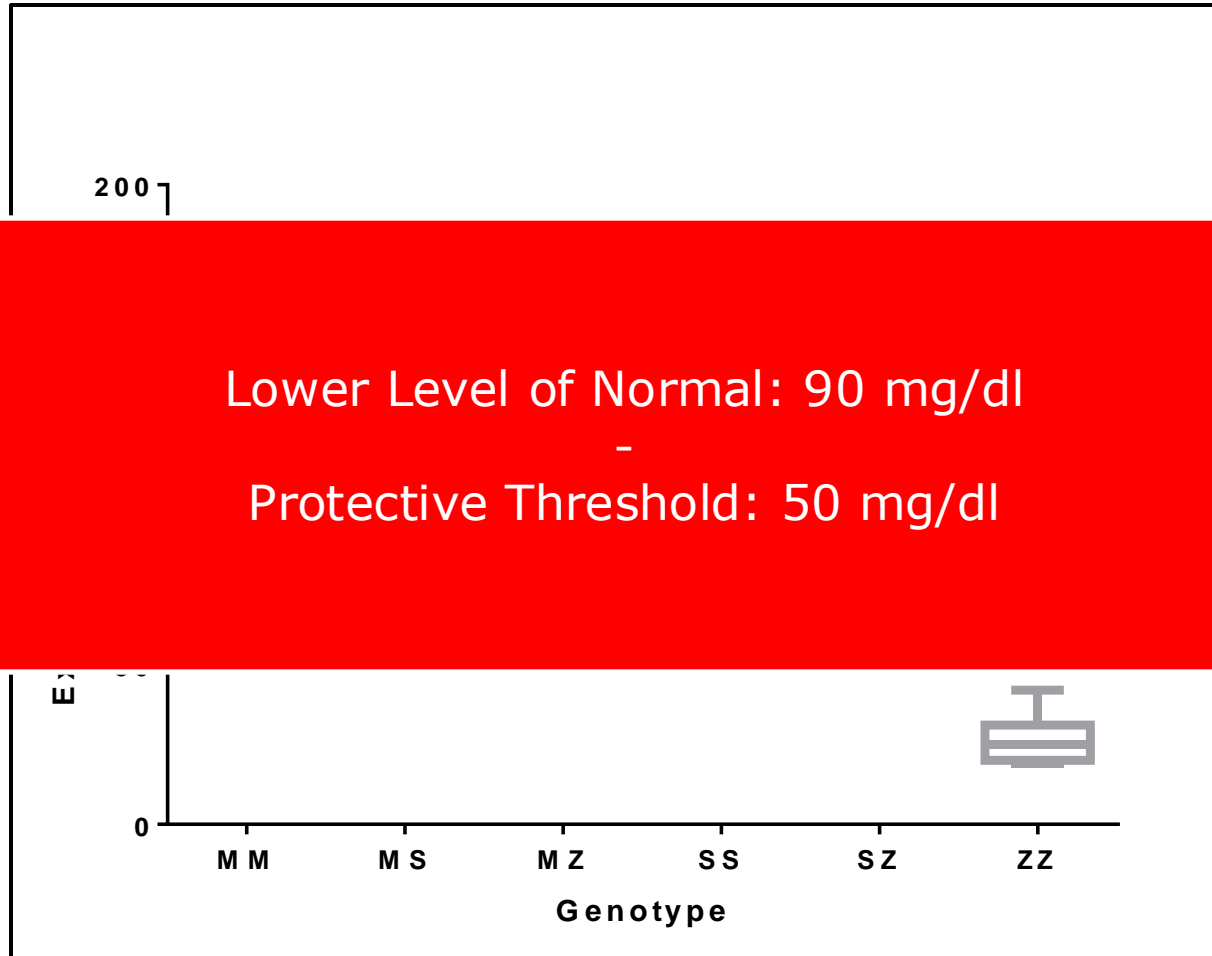


Ilaria Ferrarotti^{1*} , Marion Wencker² and Joanna Chorostowska-Wynimko³

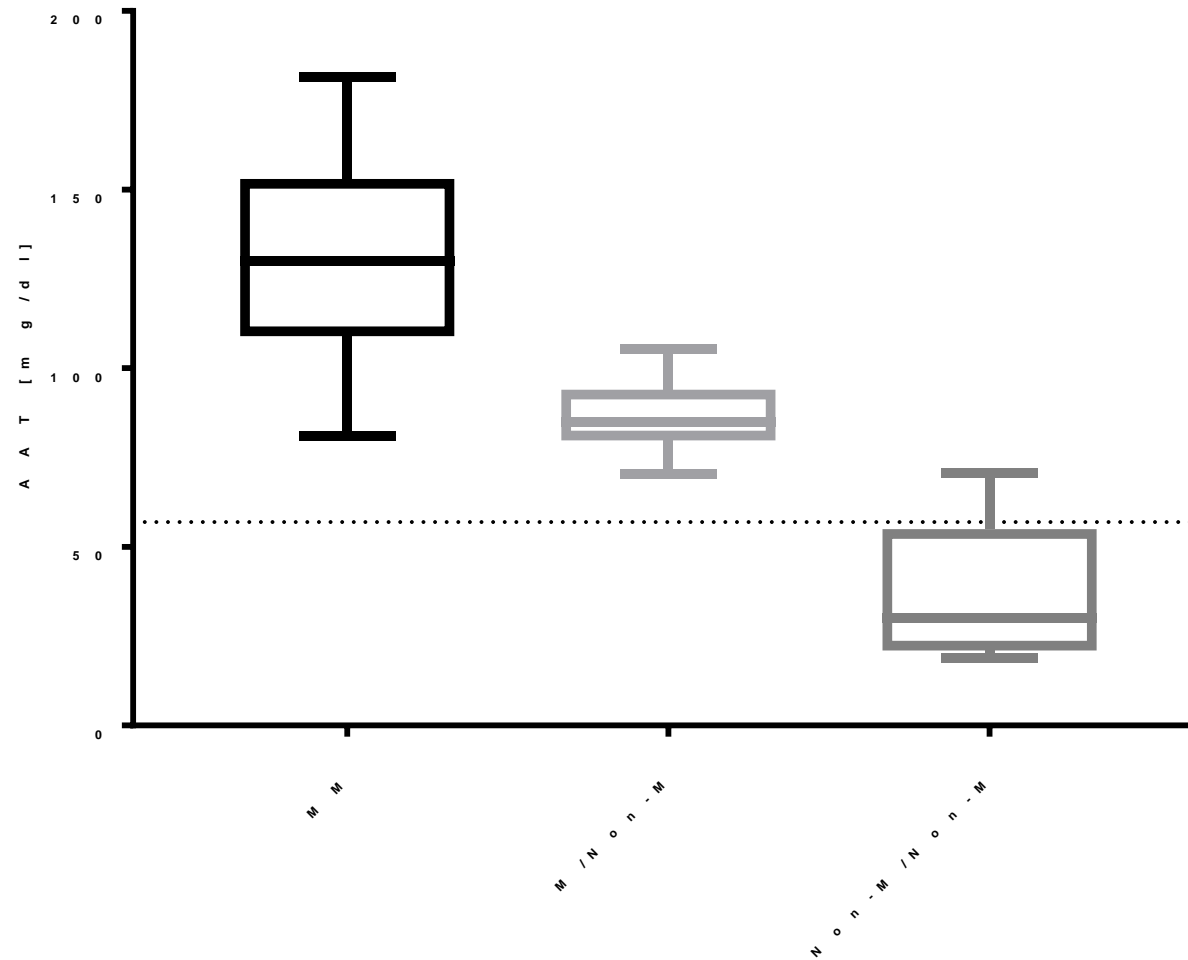




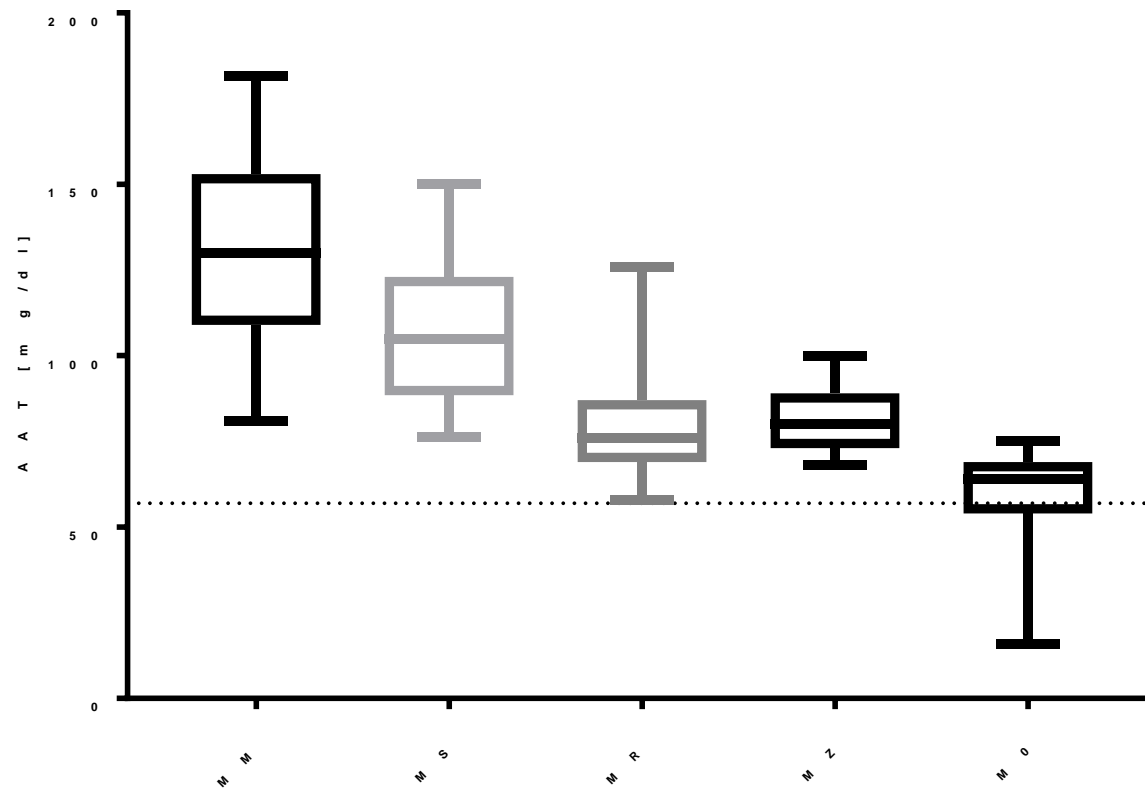
Serum Level and Genotype



From Z to Non-M

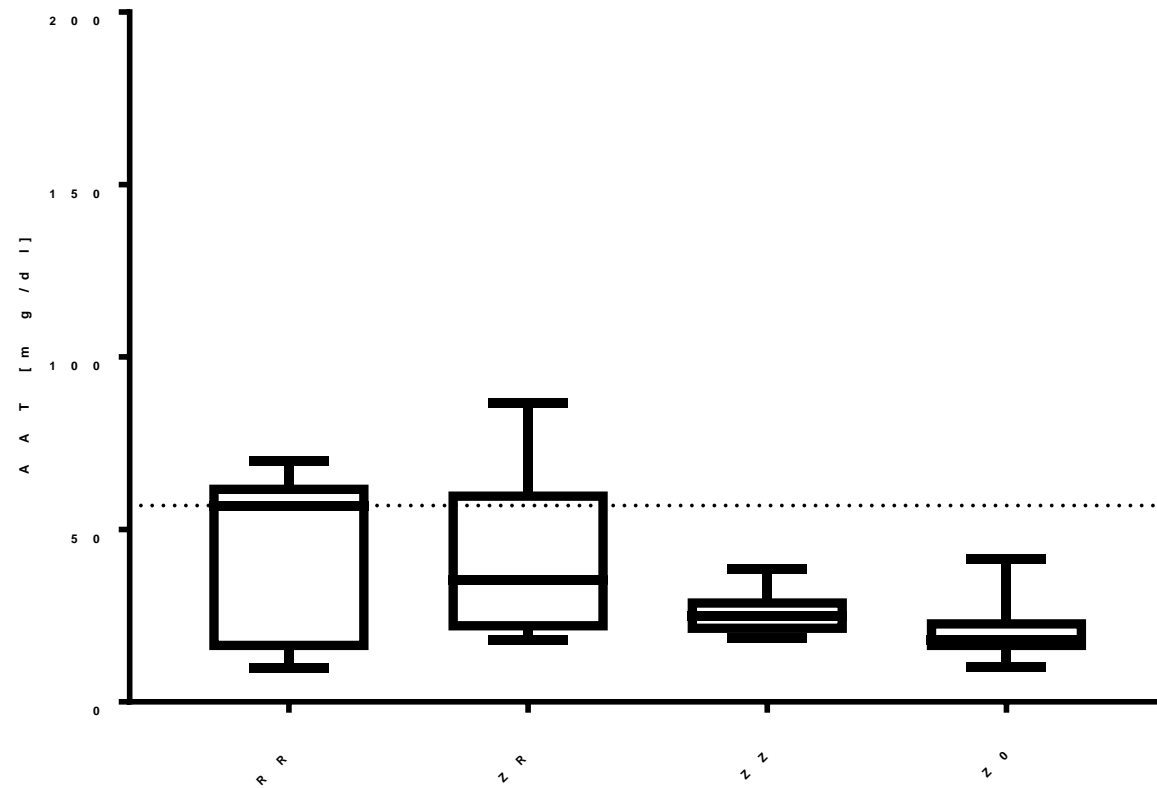


One non-M



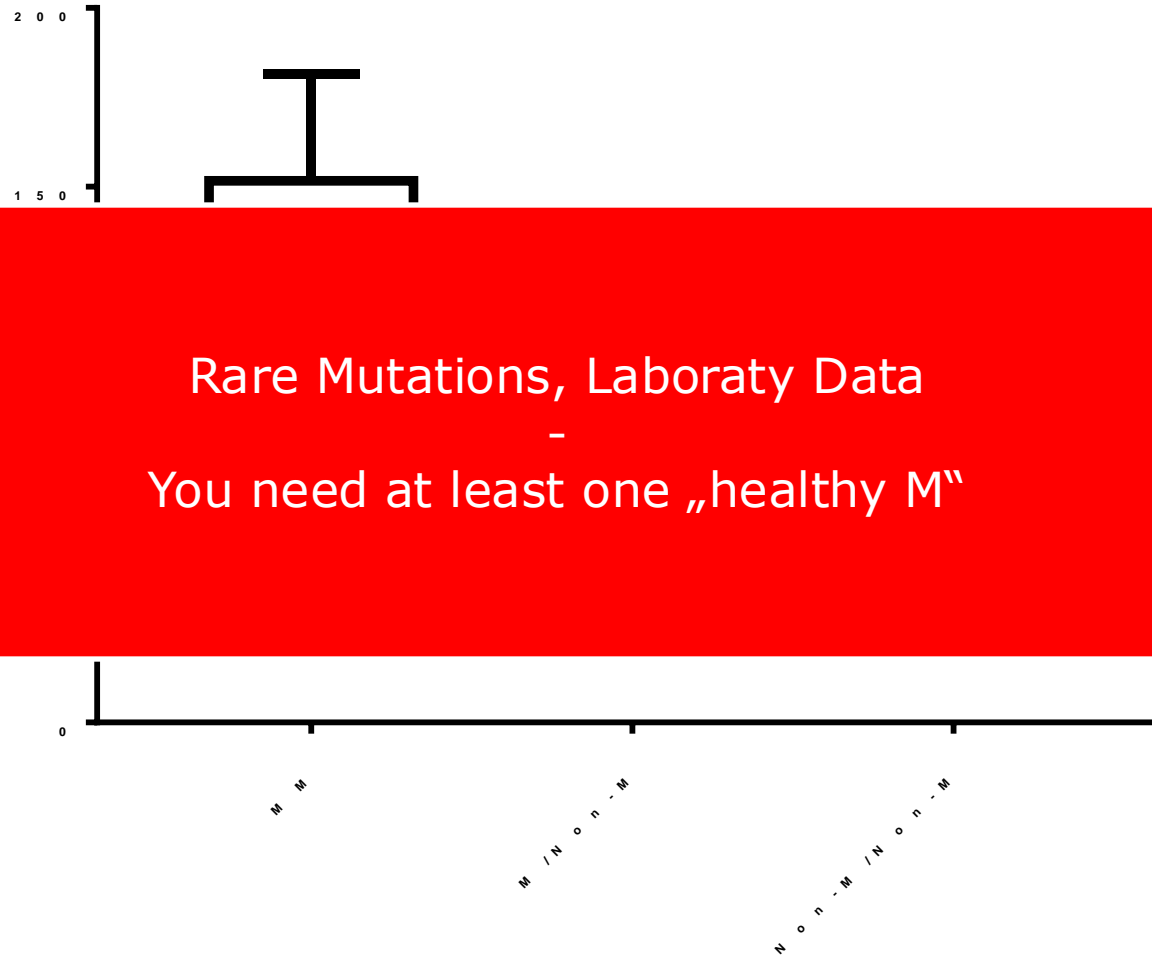


Two non-M





From Z to Non-M



MM

M/Non-M

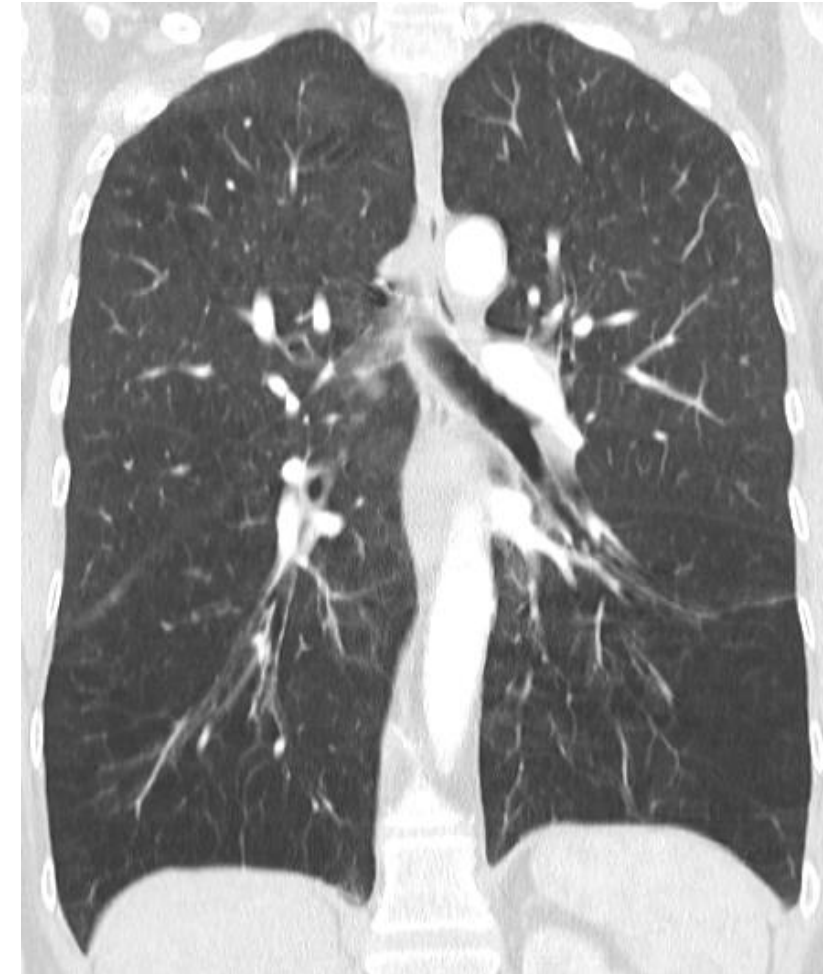
Non-M/Non-M

90 - 200

50 - 100

<50

- 52 year old male
- Symptoms
 - Dyspnoea on exertion
 - Chronic bronchitis
 - No known allergies
- More to know
 - Otherwise healthy
 - 15 py (1980 – 1985)
- Lung function
 - Moderate obstruction
 - Diffusion mildly impaired



- Analysis
 - Serum level: 0,35 g/l
 - Genotype Pi*MZ
 - Methods:
Looked for S und Z-Mutation



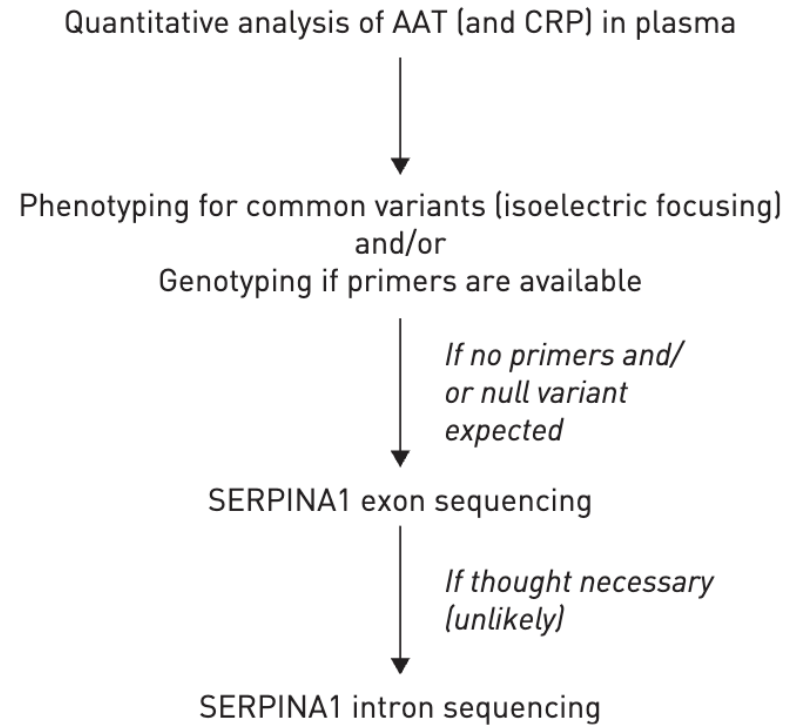


FIGURE 1 Algorithm for laboratory testing of α 1-antitrypsin deficiency (AATD). This algorithm describes the current practice of how members of the task force treat patients with AATD and is not provided as a general recommendation. AAT: α 1-antitrypsin; CRP: C-reactive protein.

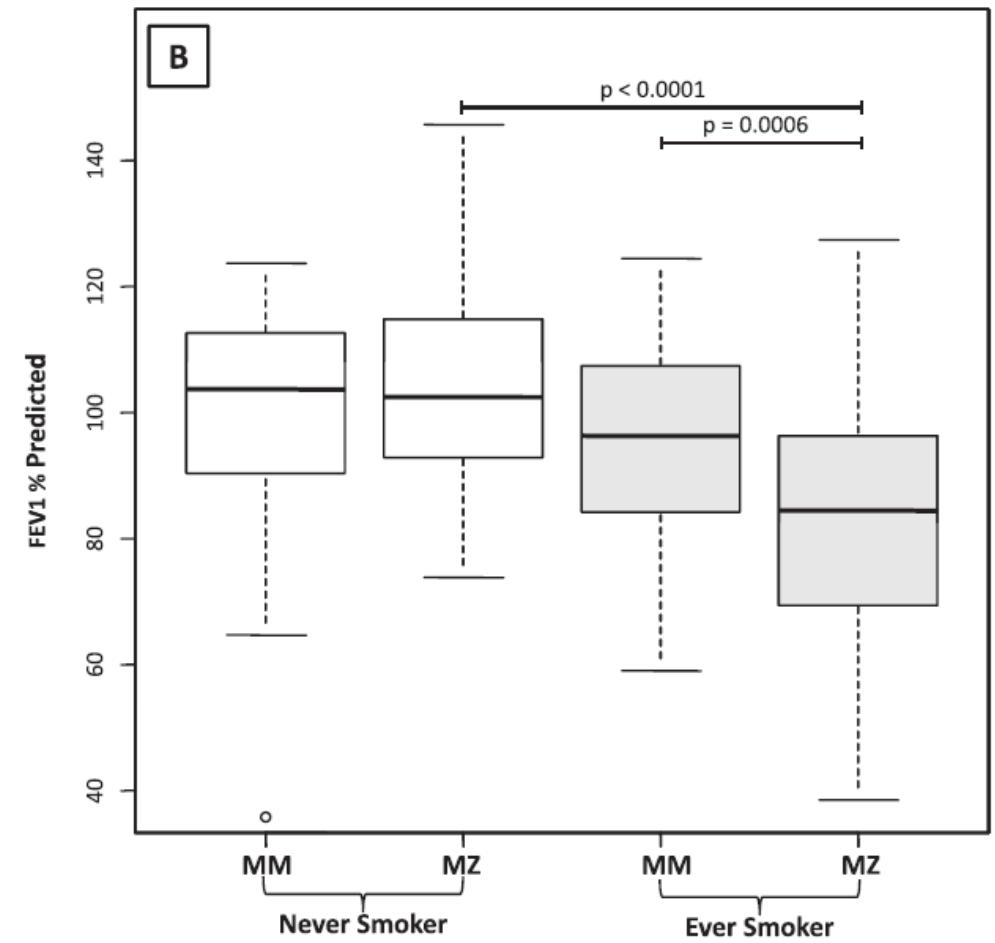
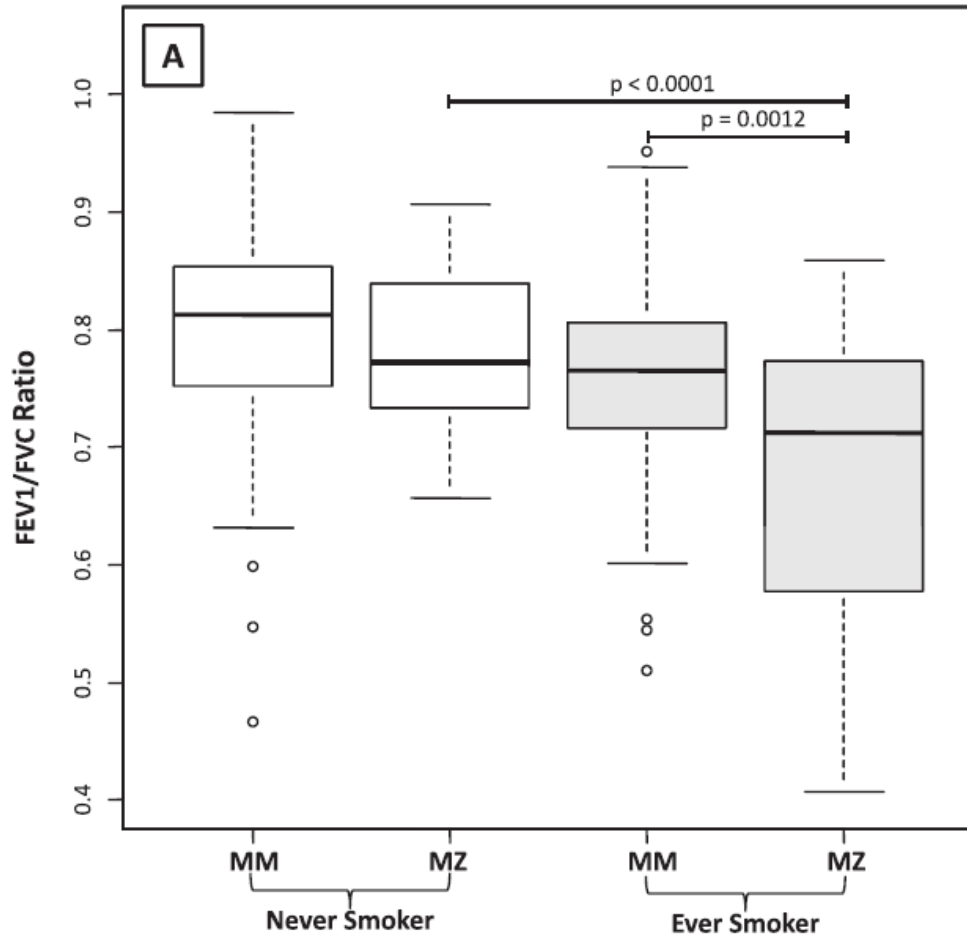
- Analysis

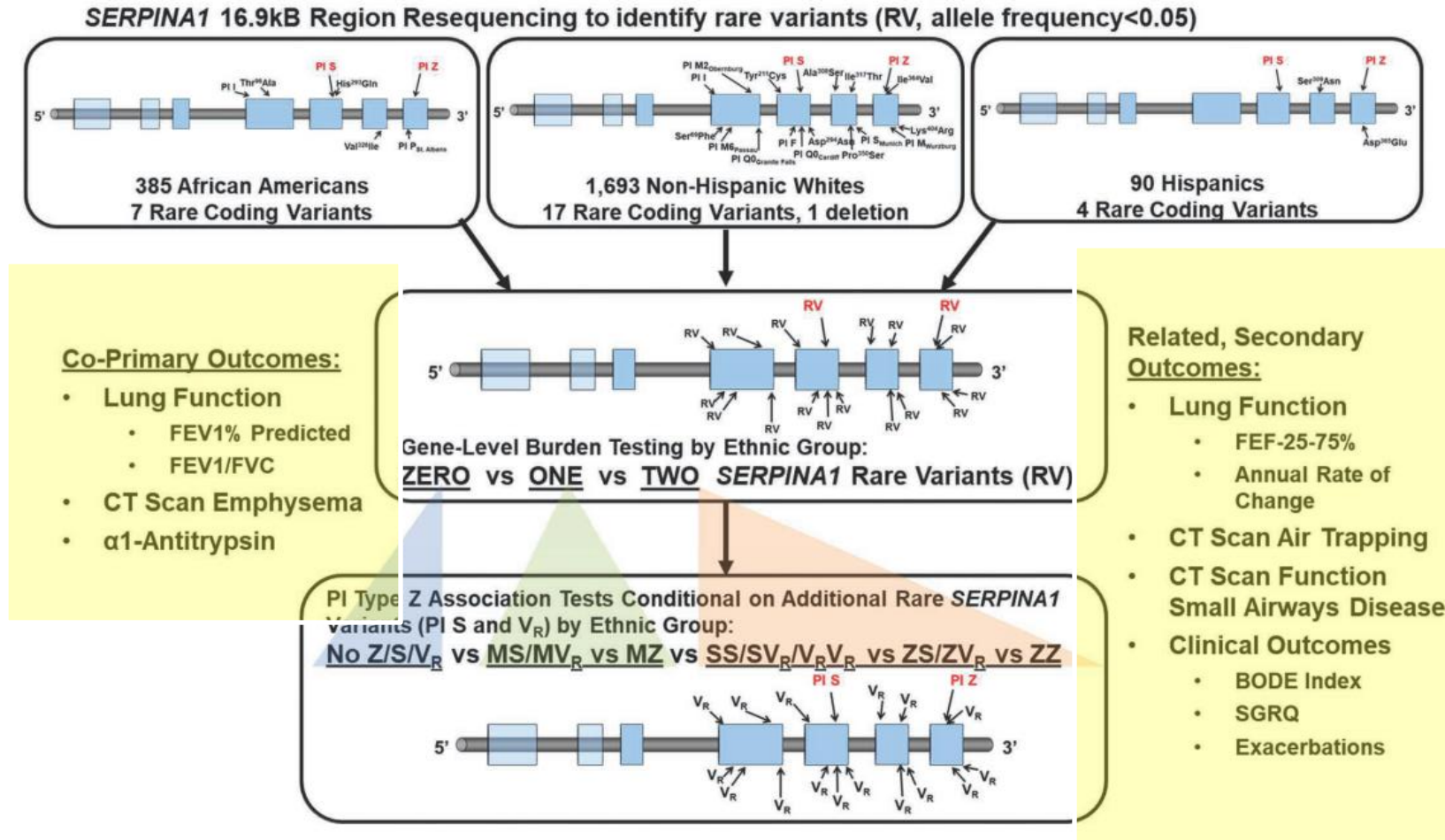
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- Genotype Pi*MZ
- Methods:
Looked for S- und Z-Mutation

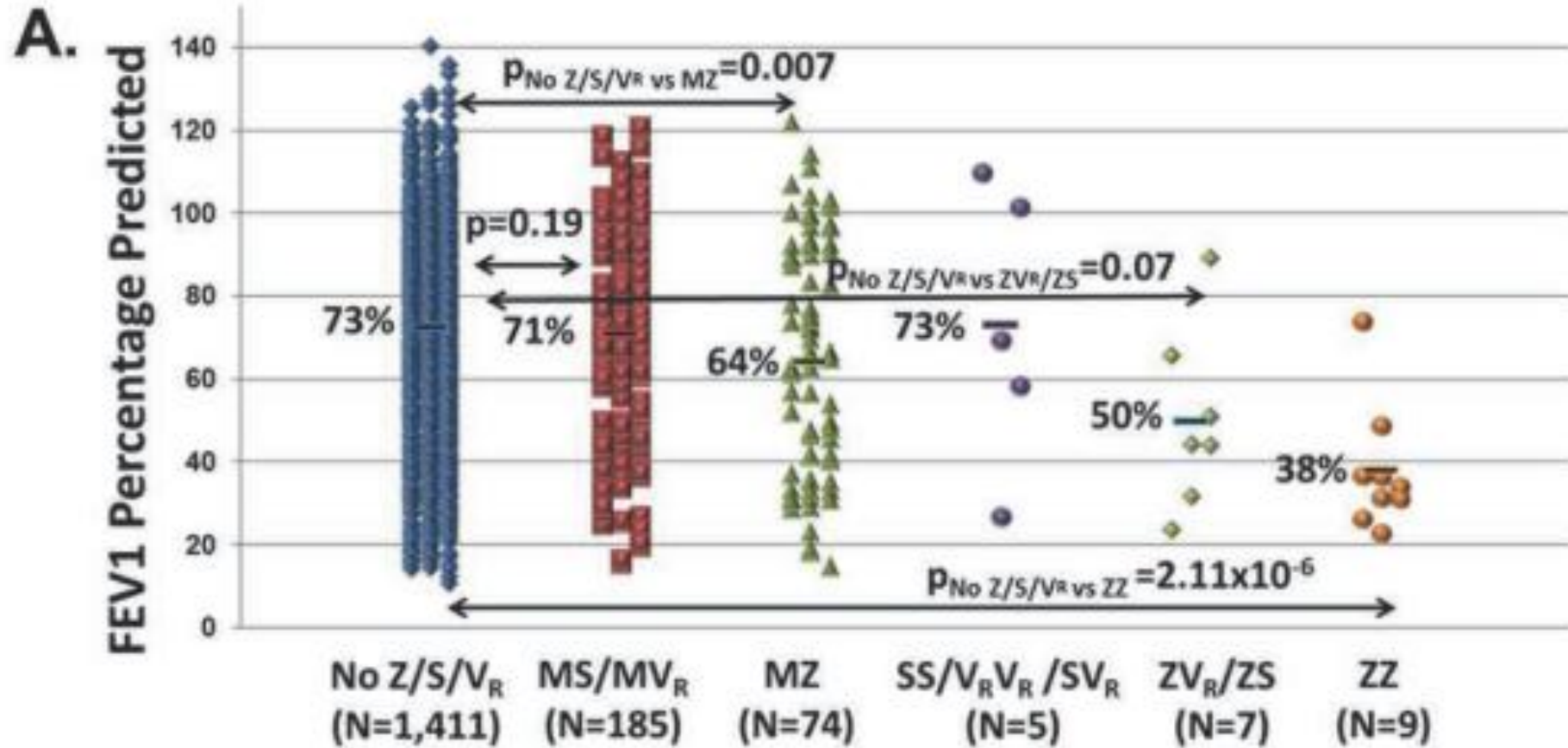
- Sequencing

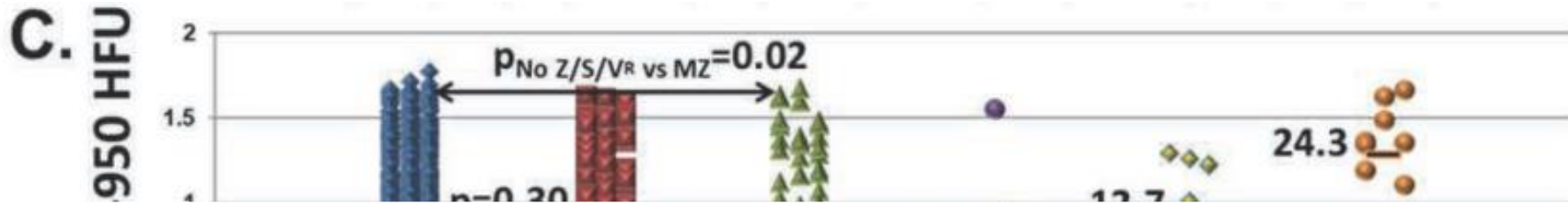
- Pi*Z/M_{Heerlen}
- Serum level 0,25 g/l





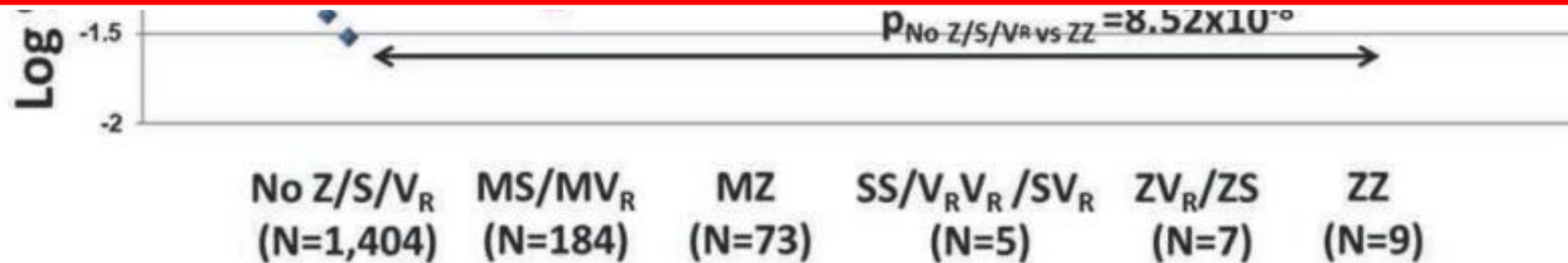






Rare Mutations, Clinical Data

-
You need at least one „healthy M“
Two „non-M“ likely cause Problems



A Simplification Genotype – Level – Risik

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non-M/non-M

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Thanks for listening