ERNDIM

QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM

Common DPT sample

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ERNDIM Workshop, 4th September 2018

Athens, Greece

Common DPT sample

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Clinical picture provided with the sample:

This female patient was referred at the age of 18 years with suspicion for multiple sclerosis based on MRI scan. Since the age of 5 years mental retardation and cognitive impairment was observed.

Urine was collected at the age of 20 years.

Sample referral information

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20 years old woman

- mental retardation
- cognitive impairment

Diagnosis

dihydropyrimidine dehydrogenase (DPD) deficiency

Diagnosis confirmation dihydropyrimidine dehydrogenase (DPD) deficiency

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Enzymatic analysis in fibroblasts

strongly decreased DPD activity

0.03 nmol/mg/h (ref. values 0.06-2.60)

Mutation analysis of *DPYD* gene

compound heterozygosity for prevalent mutation c.1905+1 G>A in intron 14 and mutation c.1057C>T (p.Arg353Cys) in exon 10

- prevalent mutation c.1905+1 G>A leads to skipping of exon 14 located immediately upstream of the mutated splice donor site

Analyses have been performed by Lab. Genetic Metabolic Diseases AMC in Amsterdam, Netherlands.

Dihydropyrimidine dehydrogenase deficiency

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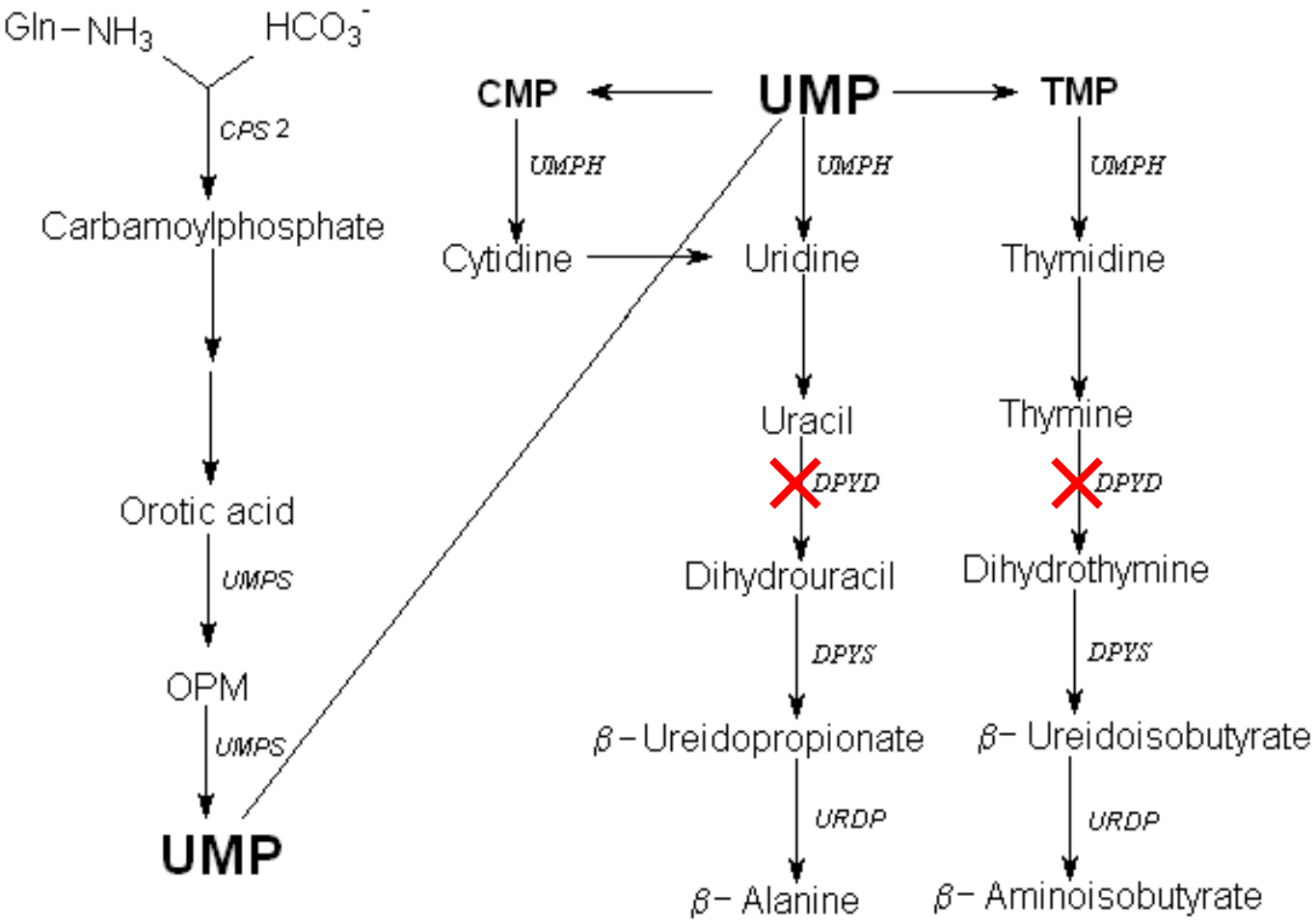

5-Fluorouracil toxicity

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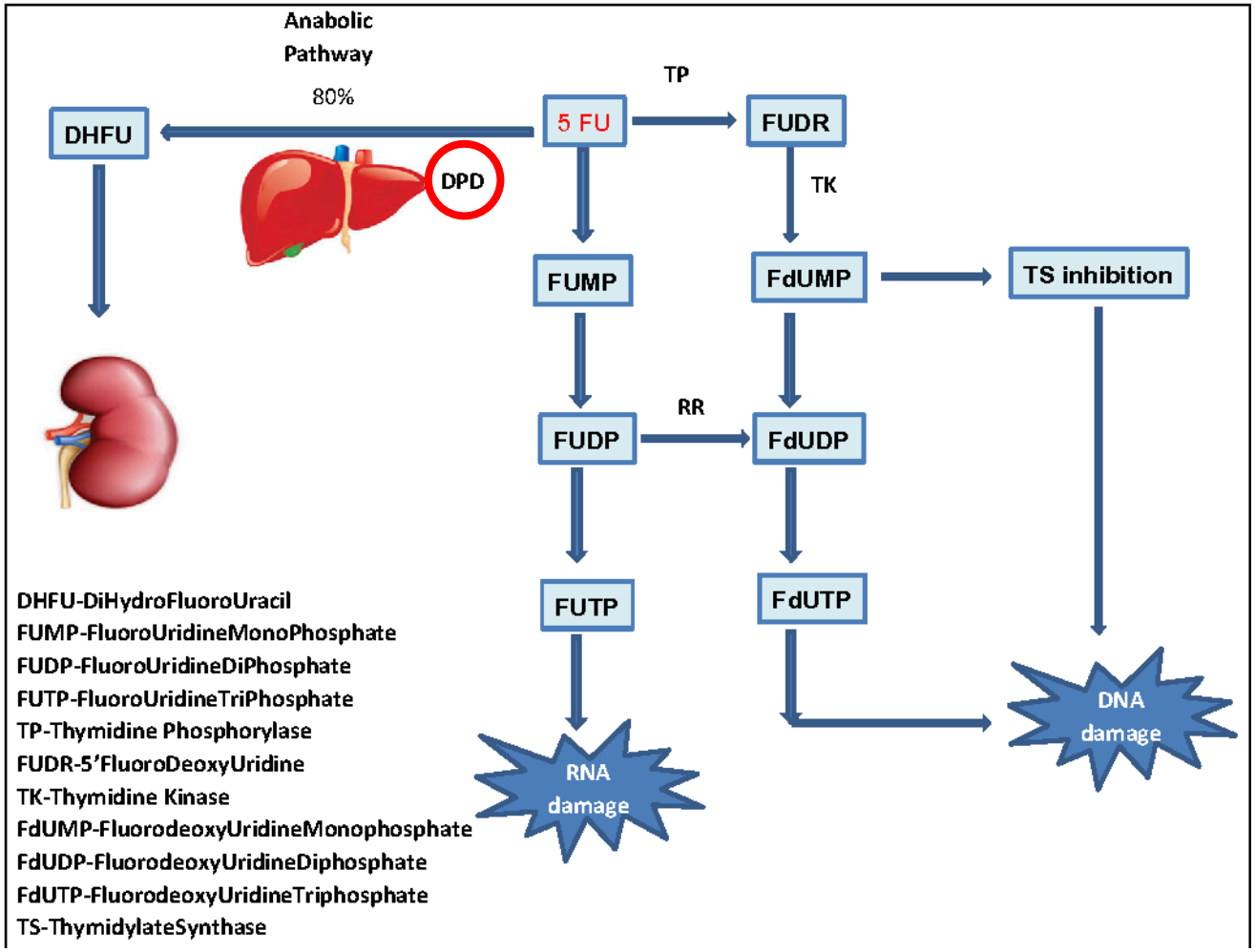

Kodali S, Bathini V, Rava P, Tipirneni E: J Gastrointest Cancer 48. 2017

DPT Centers

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• Czech Republic	21 labs (1 no answer)
• France	25 labs
• Netherlands	21 labs
• Switzerland	22 labs
• United Kingdom	21 labs
• Reports	109 labs

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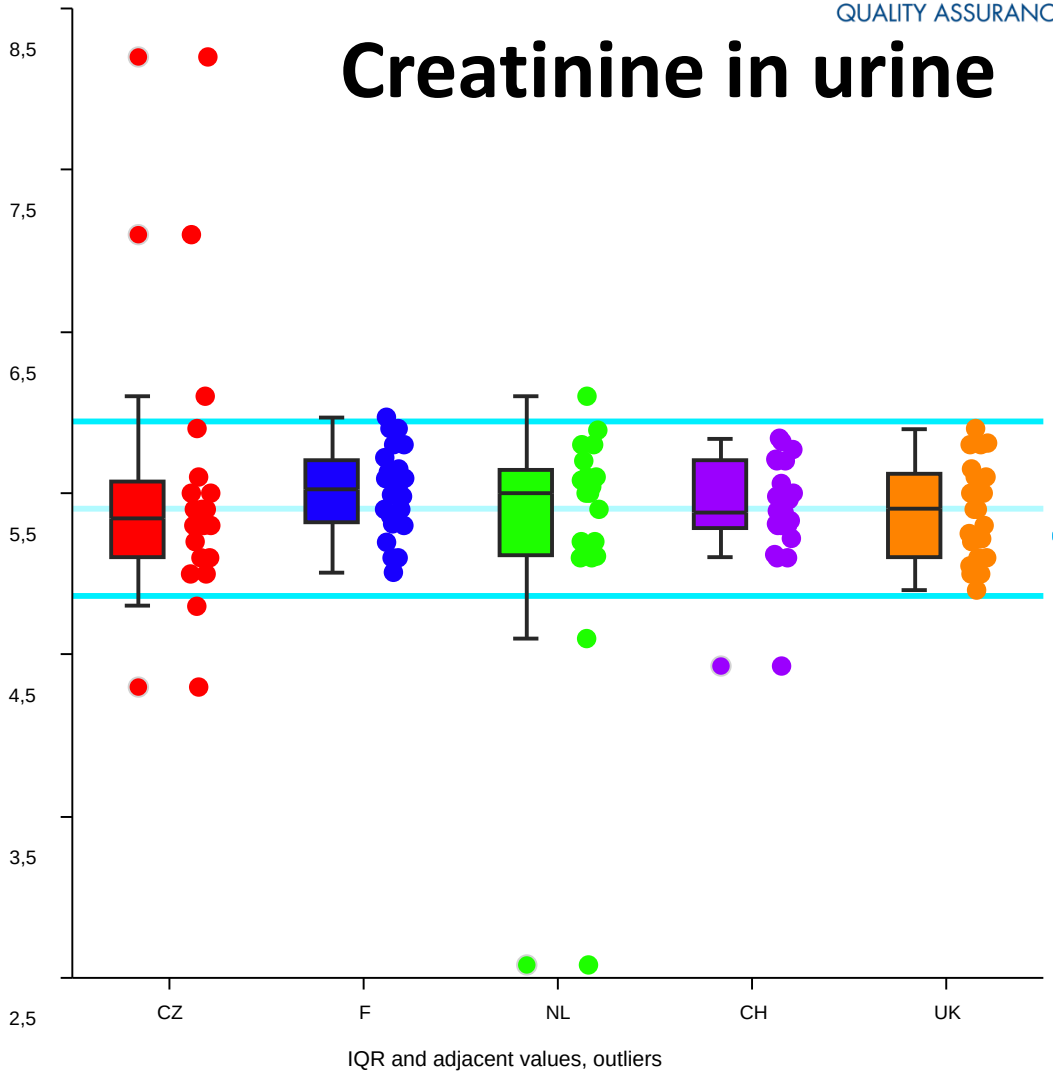

5,4 mmol/l

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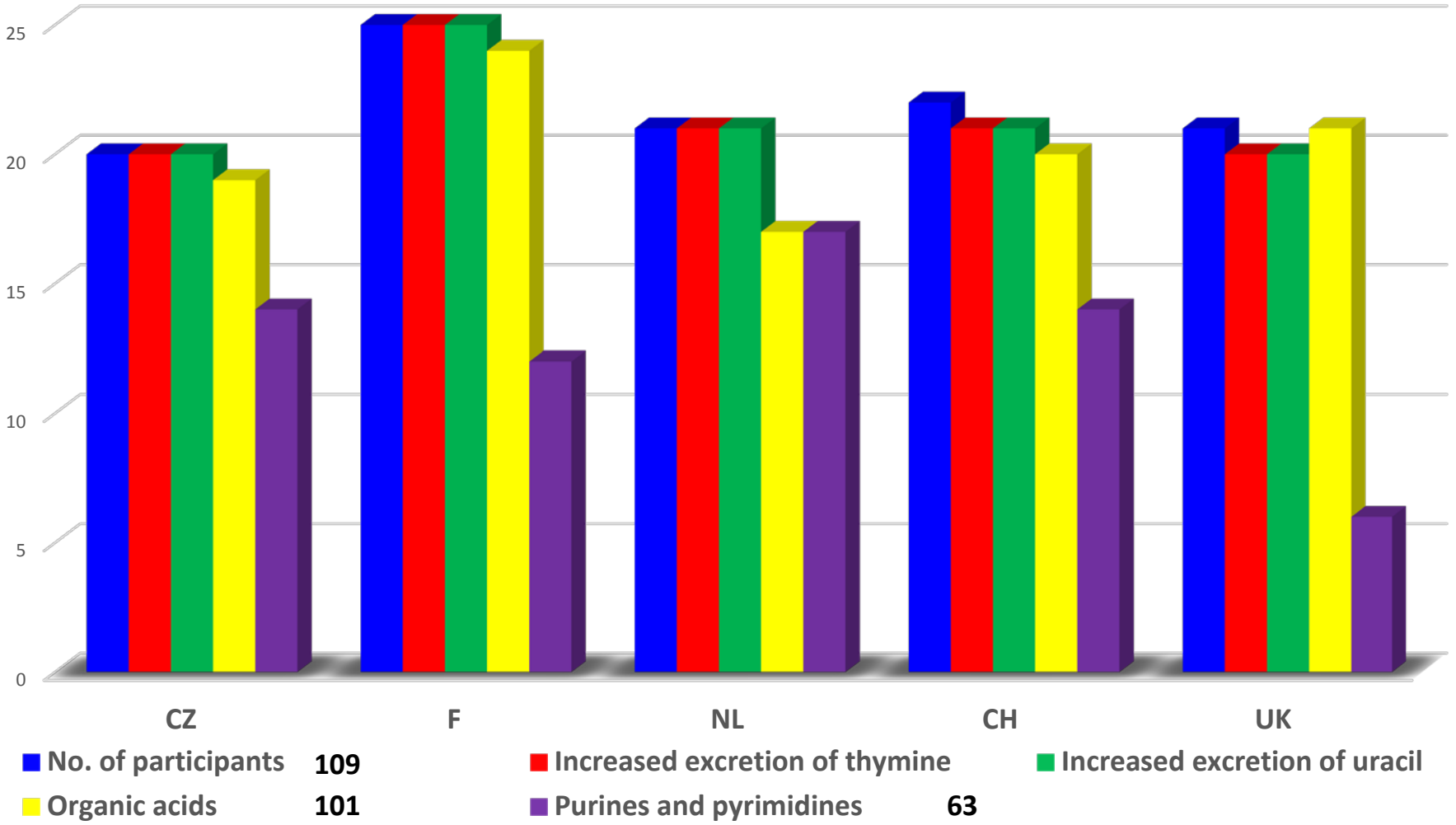

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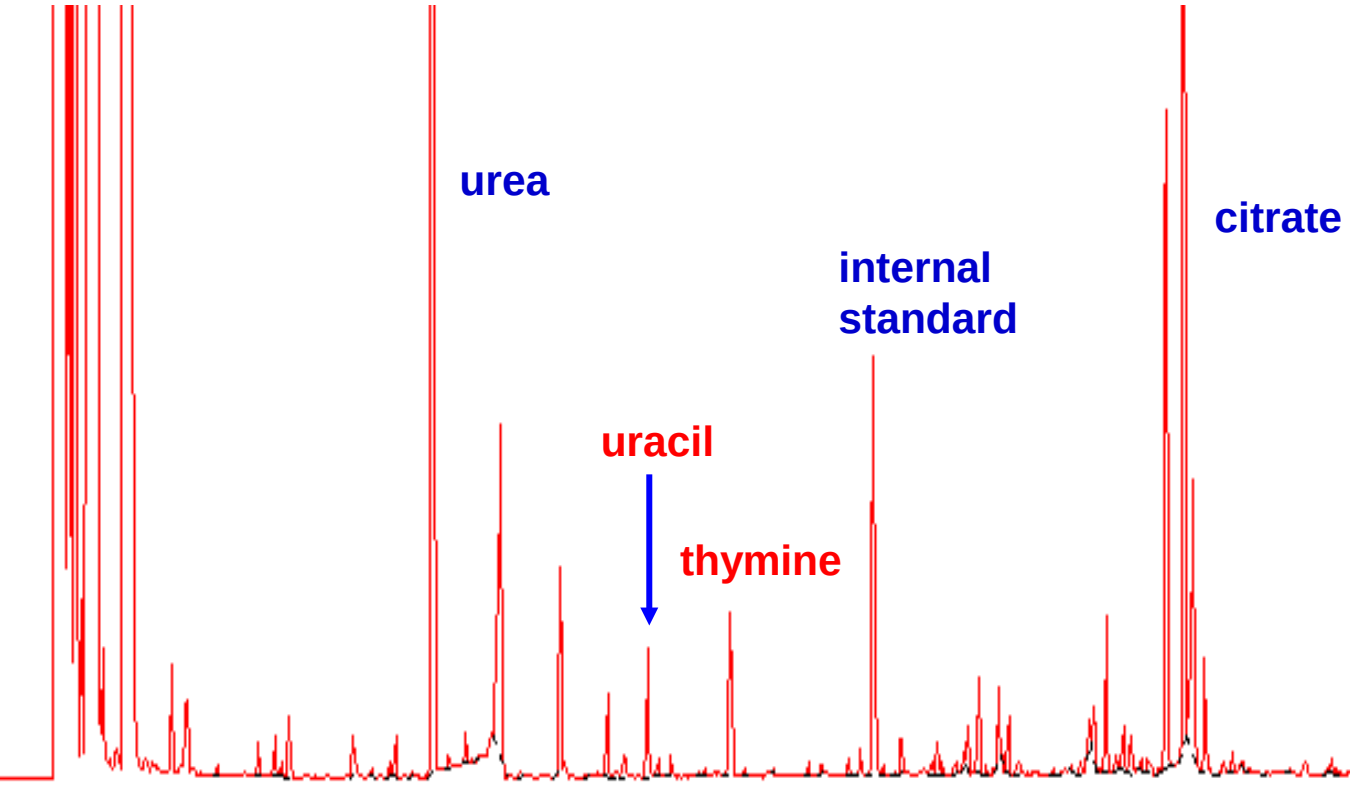
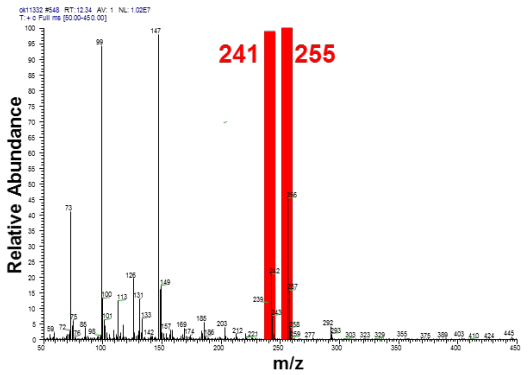
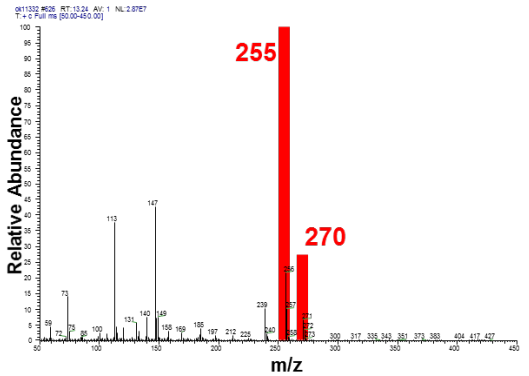
GC/MS analysis of organic acids



uracil 2tms



thymine 2tms



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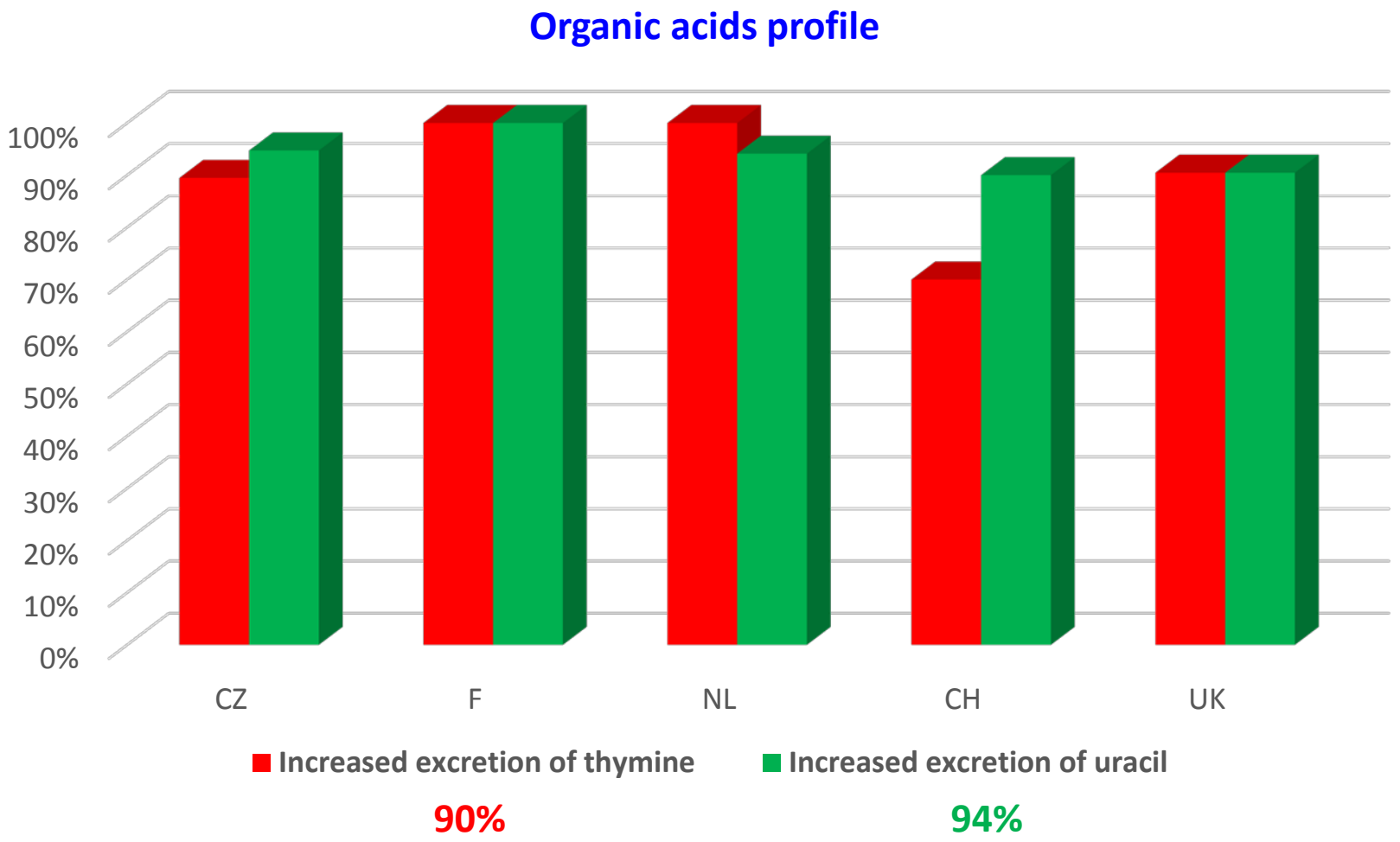

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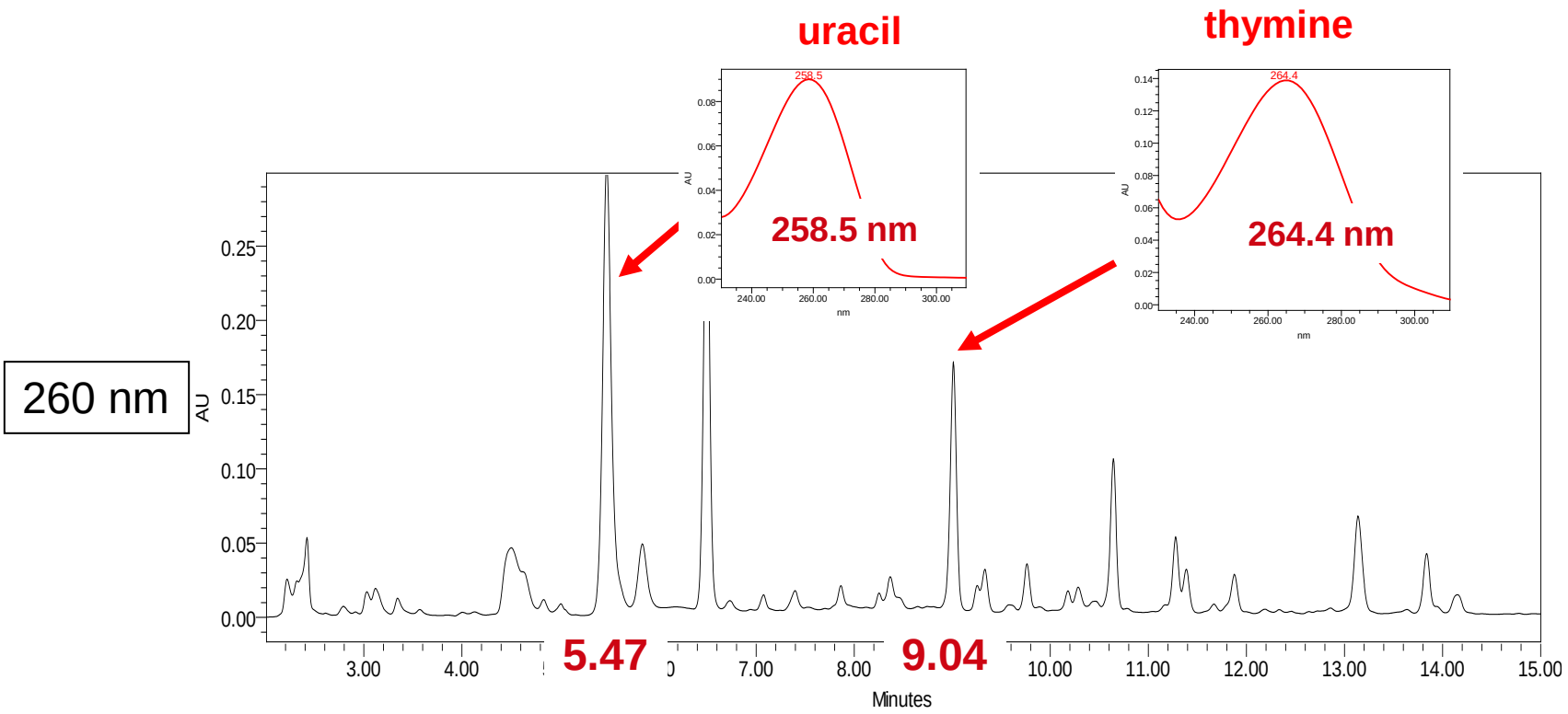
HPLC-UV analysis of purines and pyrimidines



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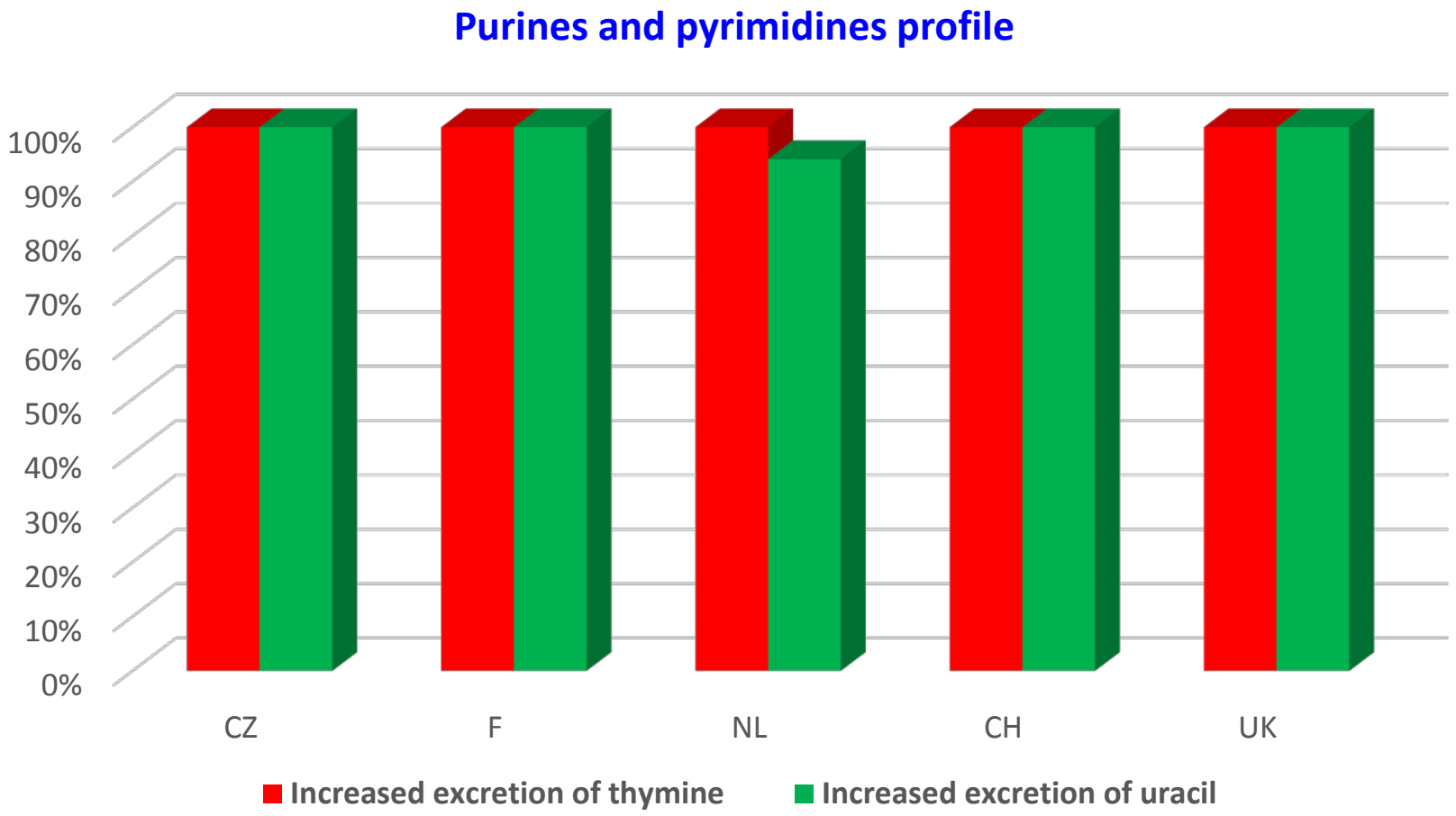

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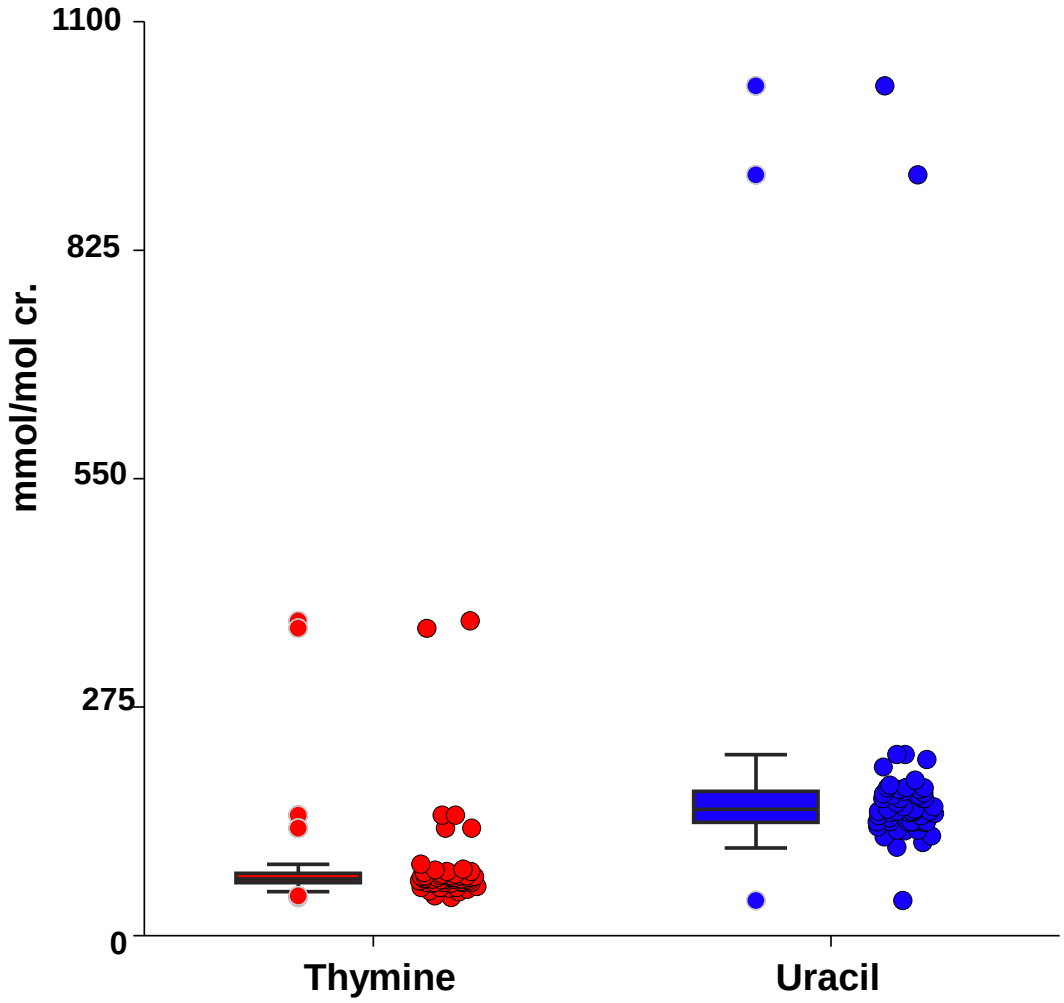

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Scoring of analytical performance

- increased excretion of thymine **1 point**
- increased excretion of uracil **1 point**

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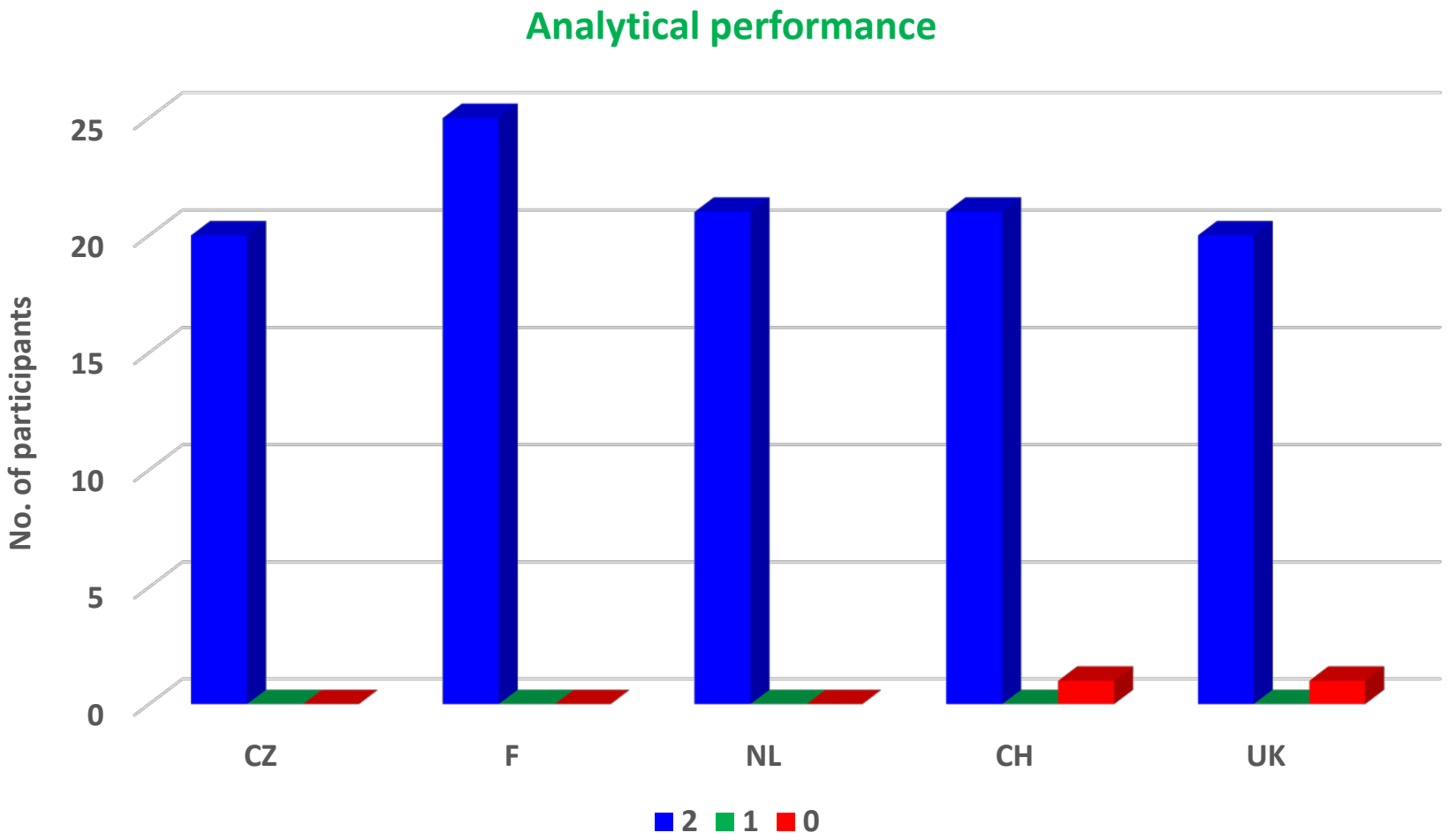

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Interpretation and recommendation

dihydropyrimidine dehydrogenase deficiency

n = 104 95% 2 points

+ enzyme assay of DPD activity in fibroblasts/lymphocytes (57)

+ mutation analysis of the *DPYD* gene (101)

+ information about 5-fluorouracil toxicity (47)

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Interpretation and recommendation

dihydropyrimidine dehydrogenase deficiency

n = 2 **1 point**

without recommendation of enzyme assay and mutation analysis

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Interpretation and recommendation

dihydropyrimidine dehydrogenase deficiency and cerebrotendinous xanthomatosisn n = 1 **1 point**

+ mutational analysis of the *CYP27A1* and *DPYD* genes

no specific diagnosis

n = 1 **1 point**

+ recommendation to carry out P/P analysis

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Interpretation and recommendation

congenital disorders of glycosylation

n = 1 **0 points**

+ serum glycosylated transferrin

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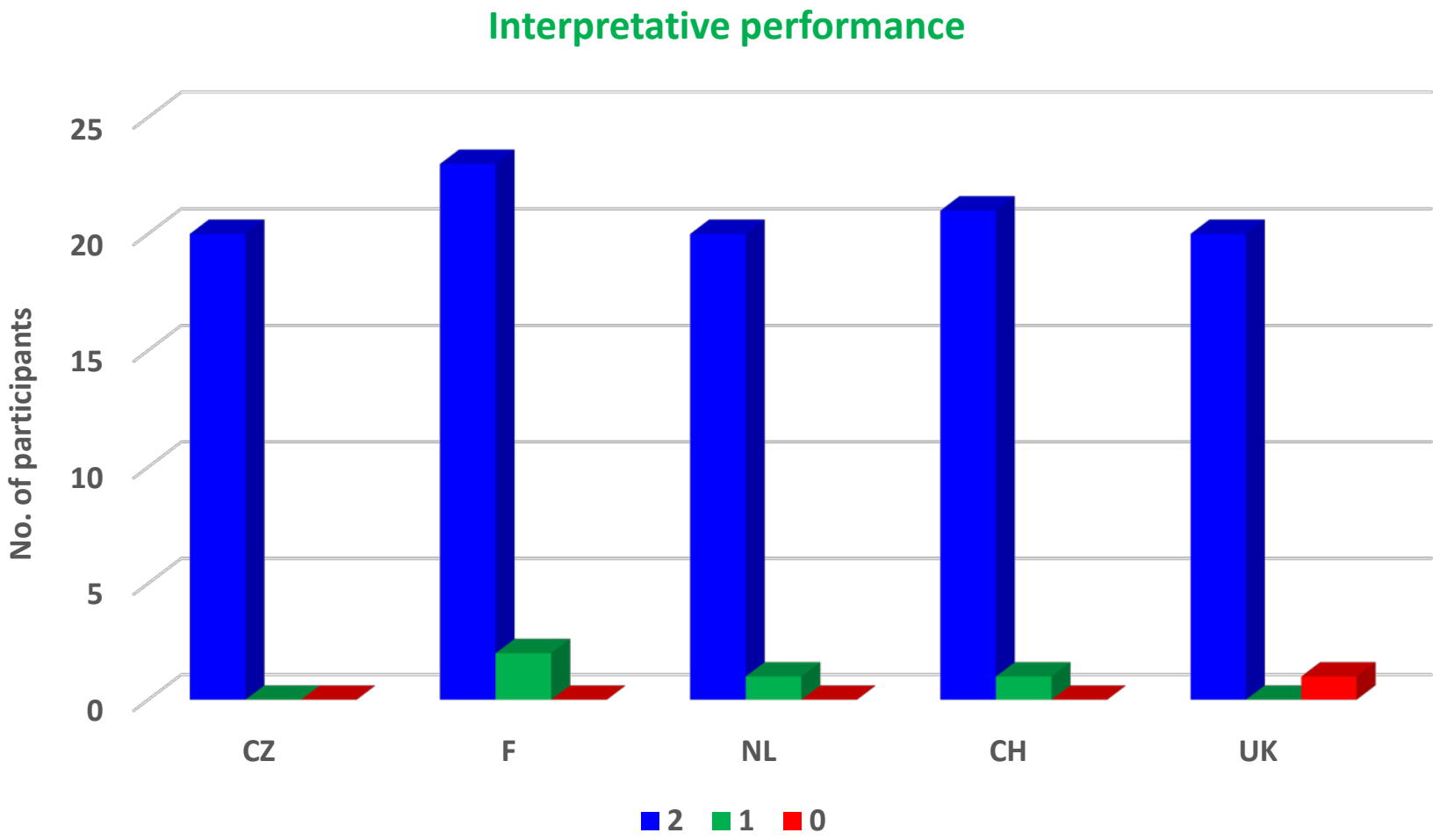

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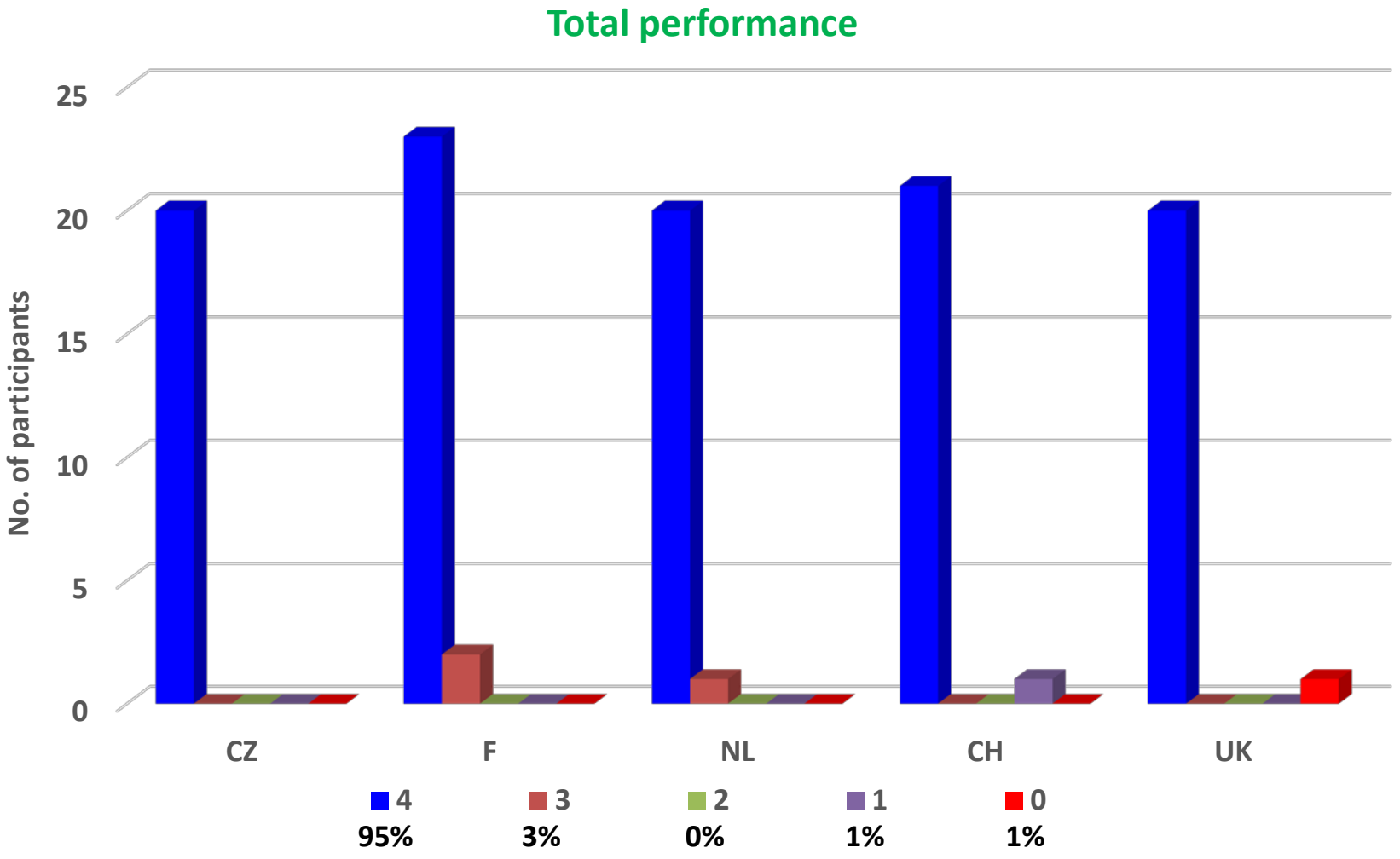

Summary

- **easy DPT sample with good proficiency scores**
- **increased excretion of thymine and uracil can be detected in profile of organic acids**
- **2/109 participants did not detect elevated excretion of uracil and thymine**


Thank you
for your attention!