DPT Common Sample 2024

Malonyl-CoA decarboxylase deficiency

(malonic aciduria)

03.09.2024

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Quality Assurance in Laboratory Testing for IEM

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30 years of ERNDiM
1994–2024

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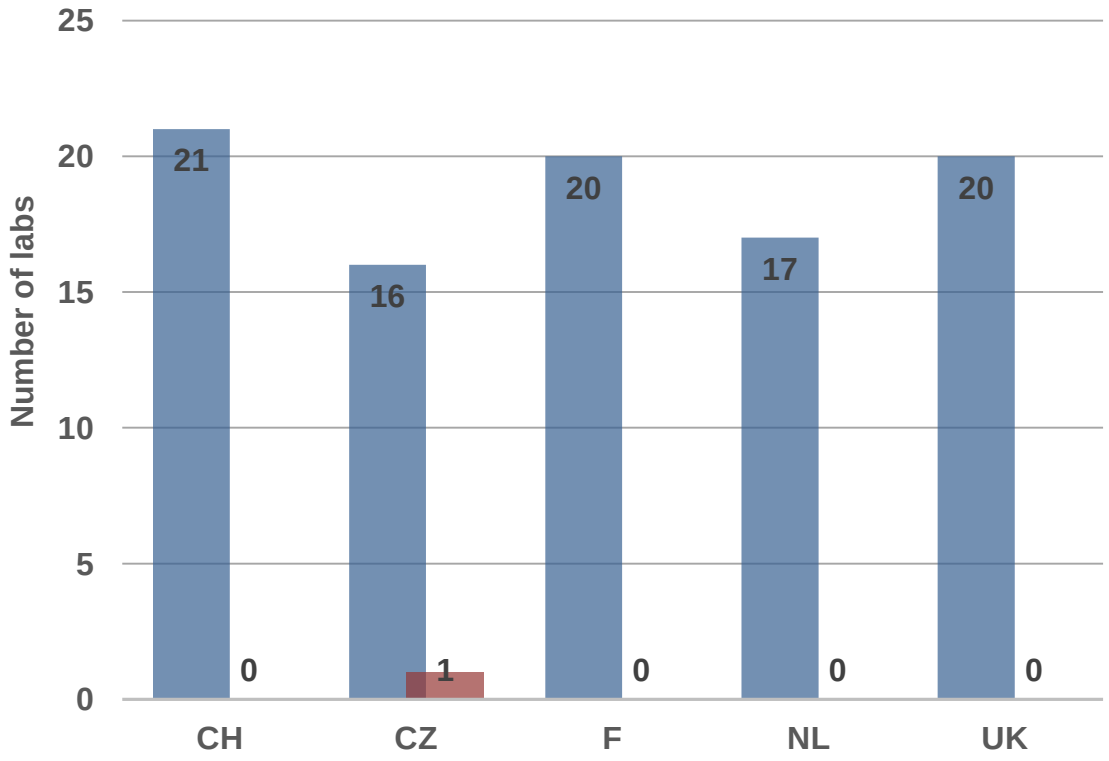
DPT 2024 Sample A – Common Sample

- Urine sample provided by Inselspital Bern University Hospital – DPT Center Switzerland
- Sample sent across the five DPT centers (CH, CZ, F, NL, UK).
- Returns received from all but one participants.



Total = 94 responders

Clinical information

Clinical information provided with the sample

- Diagnosed by family screening after sudden infant death of brother at 5 months of age in the context of an intercurrent viral infection. Dilated cardiomyopathy, normal development
- age at diagnosis: 3 years, current age 15 years

Further information about the patient

- Cognitive performance below average, mild learning disability → patient now integrated in special education
- Patient overweighted, treated with precautionary measures to avoid catabolic state
- Carnitine substitution

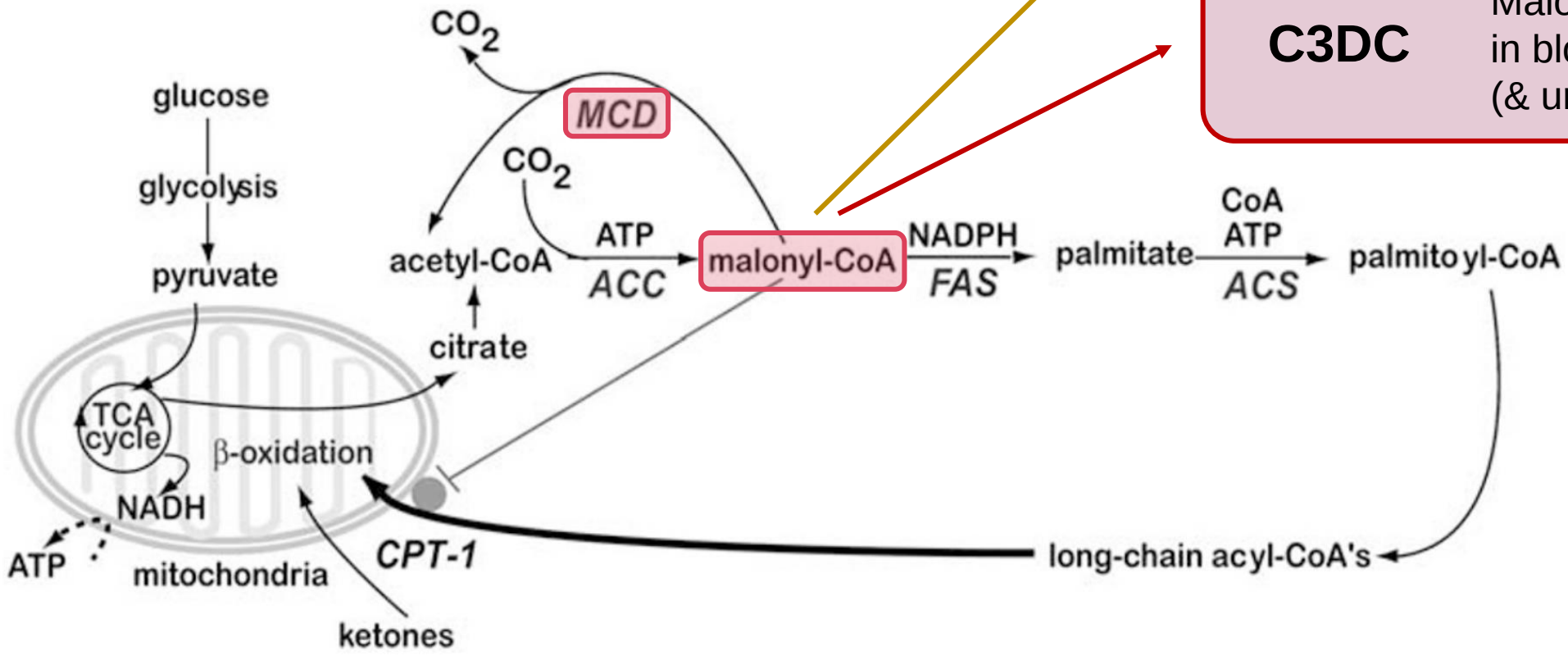
Diagnosis

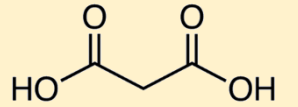
- Malonyl-CoA decarboxylase deficiency (OMIM #248360) → malonic aciduria

Malonyl-CoA decarboxylase deficiency

- Malonyl-CoA decarboxylase (MCD) regulates the levels of cellular malonyl-CoA
- Malonyl-CoA is both a substrate for fatty acid synthase (FAS) and an inhibitor of CPT1, so of fatty acid oxidation

  → **metabolic switch** between anabolic and catabolic fatty acid oxidation





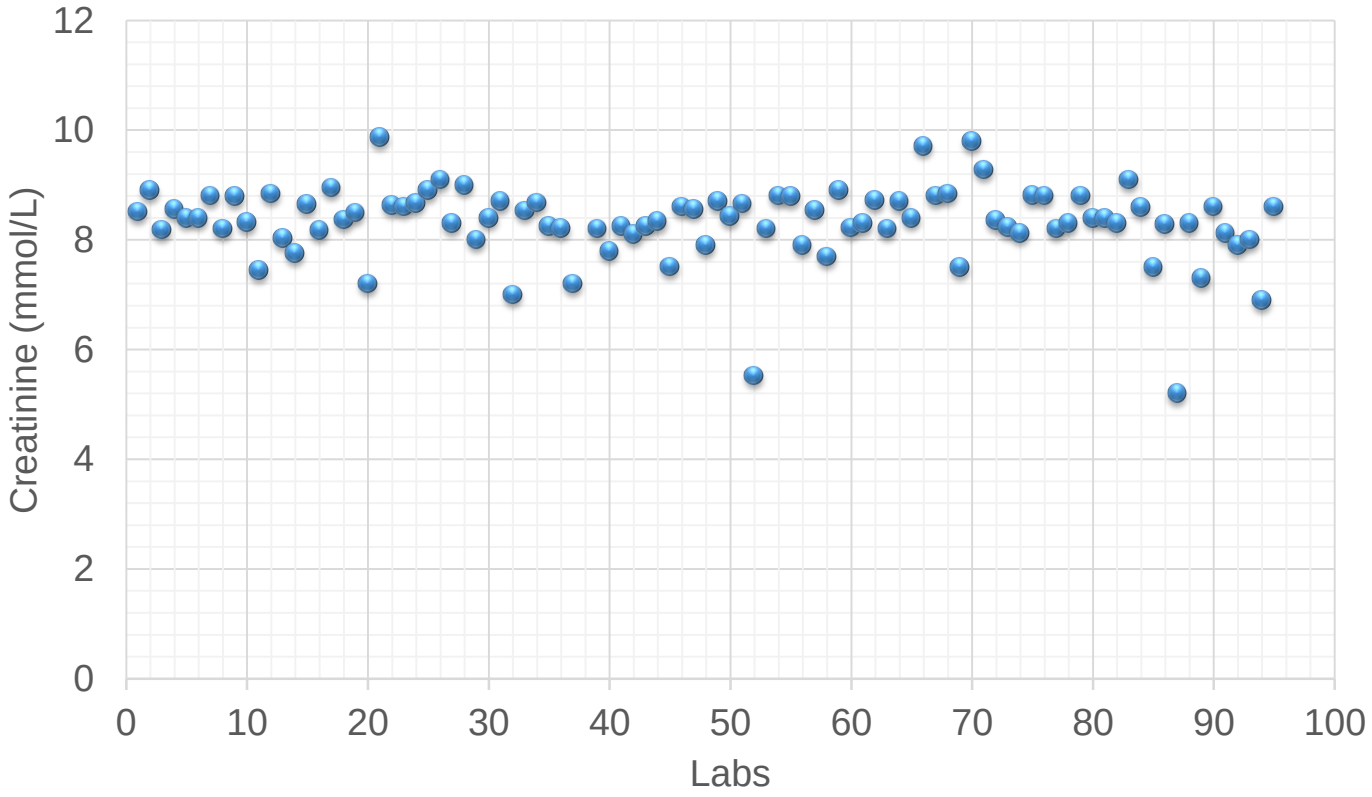
Malonic acid in urine

C3DC Malonylcarnitine in blood (& urine)

https://www.nature.com/articles/onc2009160

DPT 2024 common sample: RESULTS

Creatinine in urine



Creatinine:
Mean value = 8.3 mmol/L
SD = 0.7

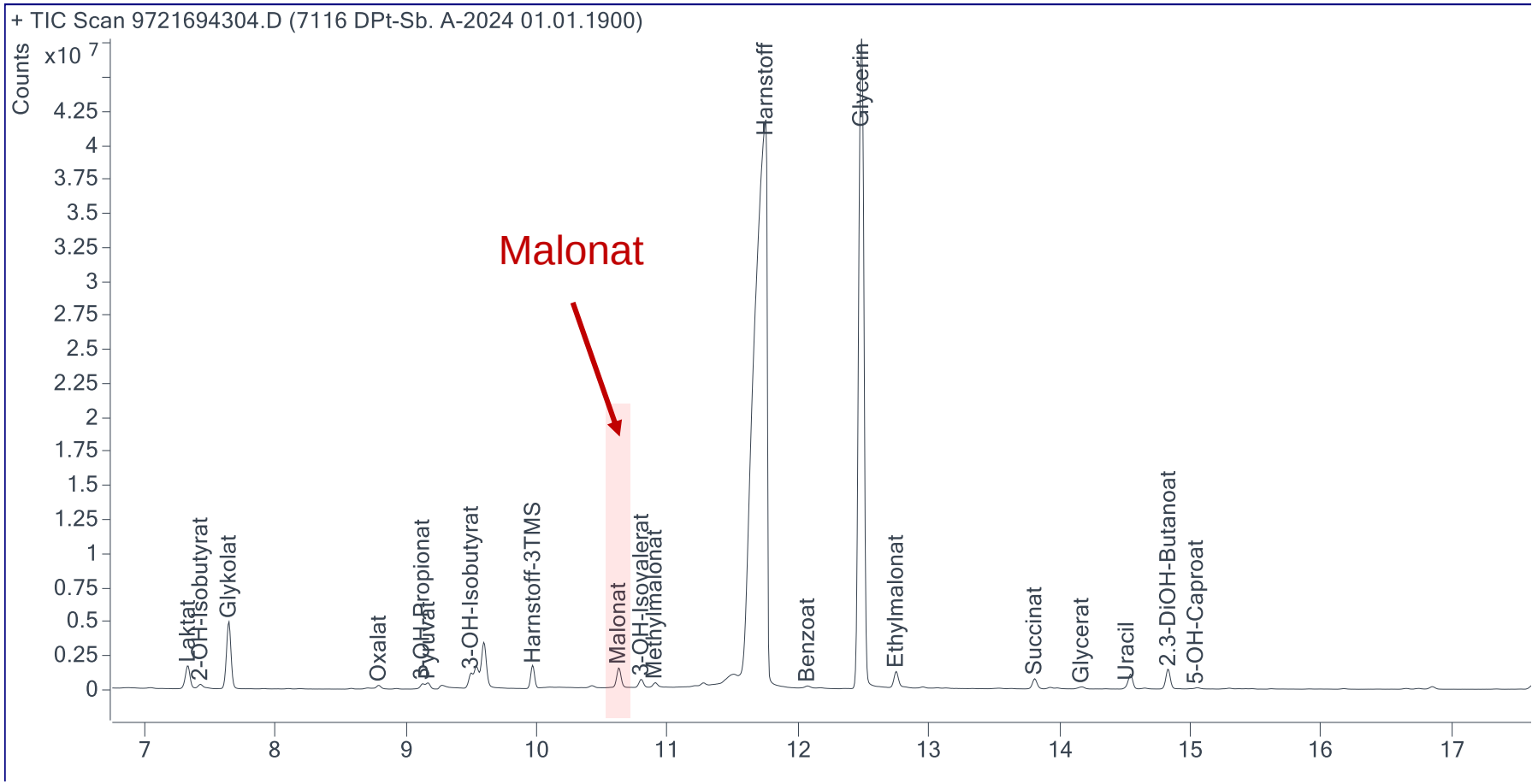
Scoring System

Analytical performance	2 points
Interpretation	2 points
	4 points

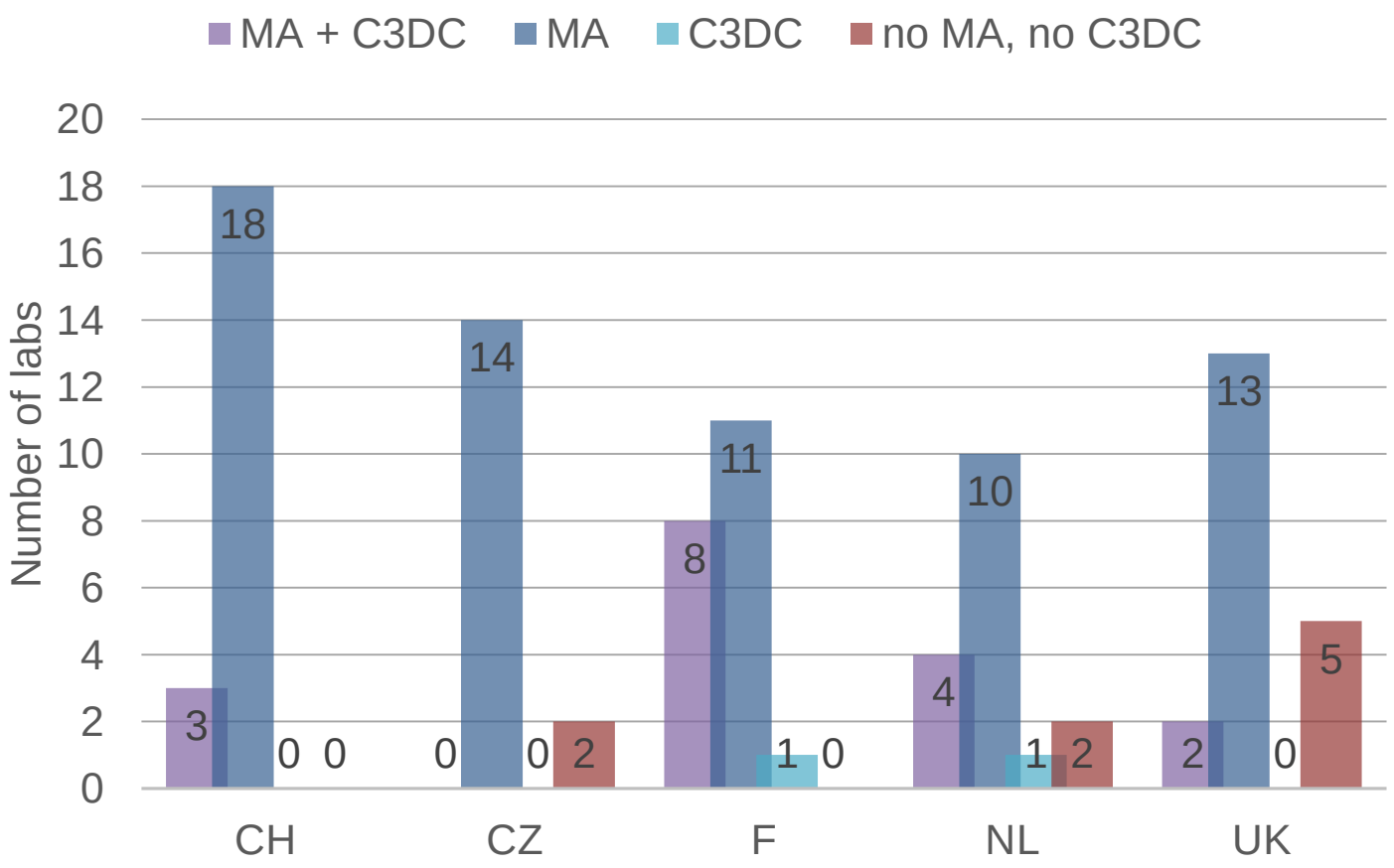
Analytical performance

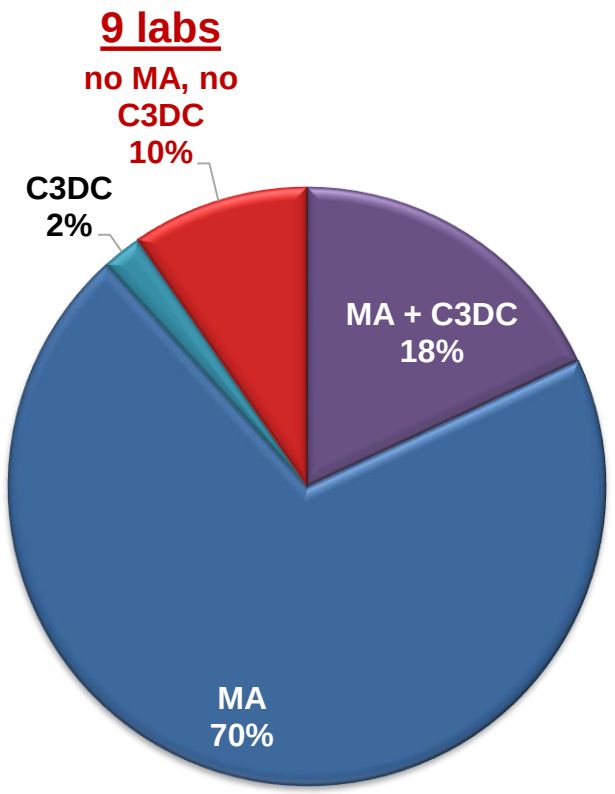
Scoring

Detection of increased concentration of **malonic acid** or **C3DC-Carnitine** was scored **2 points**.



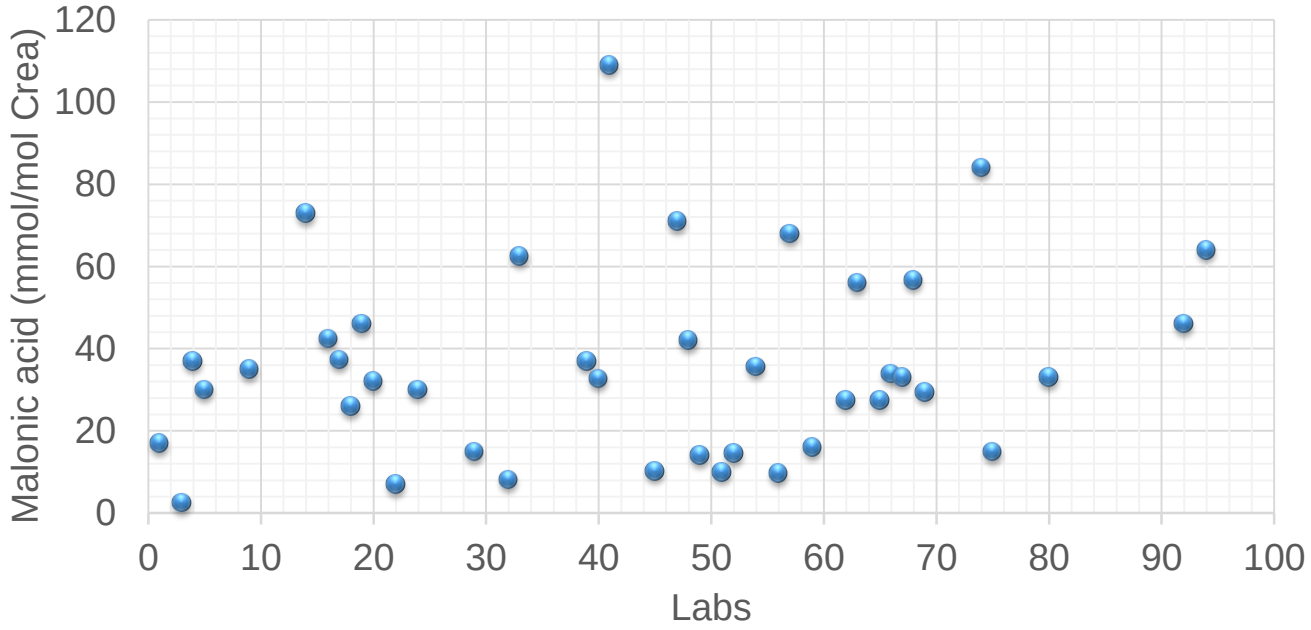
Analytical performance (n=94 labs)



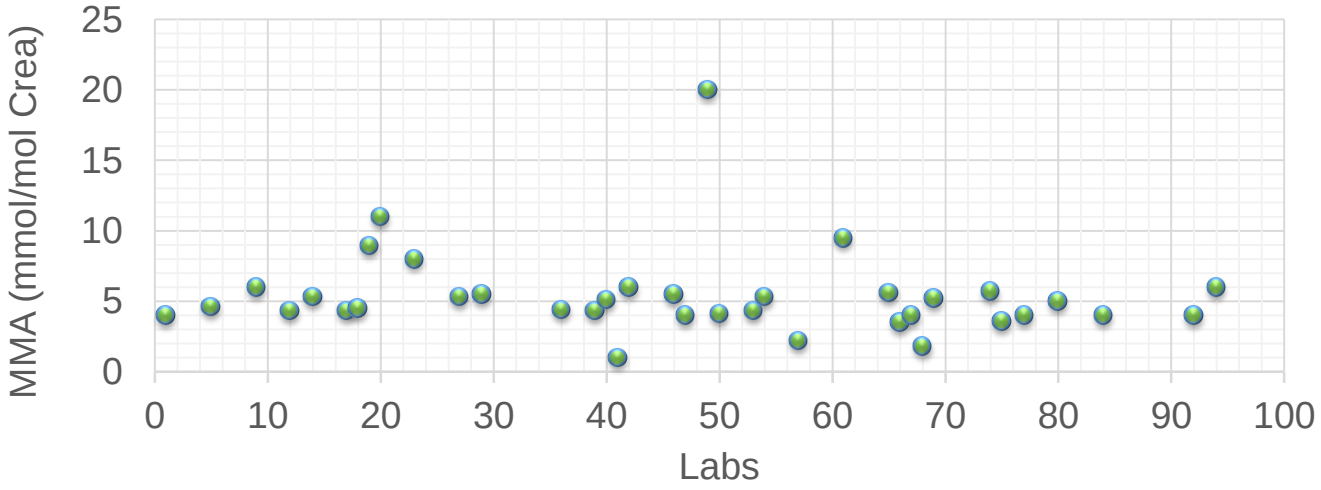


Analytical proficiency = 90%

Analytical performance

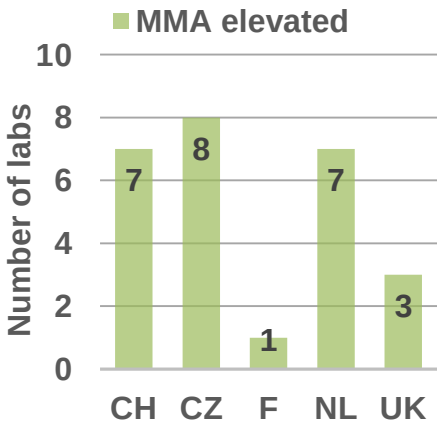


Malonic acid
Mean = 36 mmol/mol crea
SD = 23



Methylmalonic acid
Mean = 5 mmol/mol crea
SD = 3

→ 26 labs reported elevated MMA



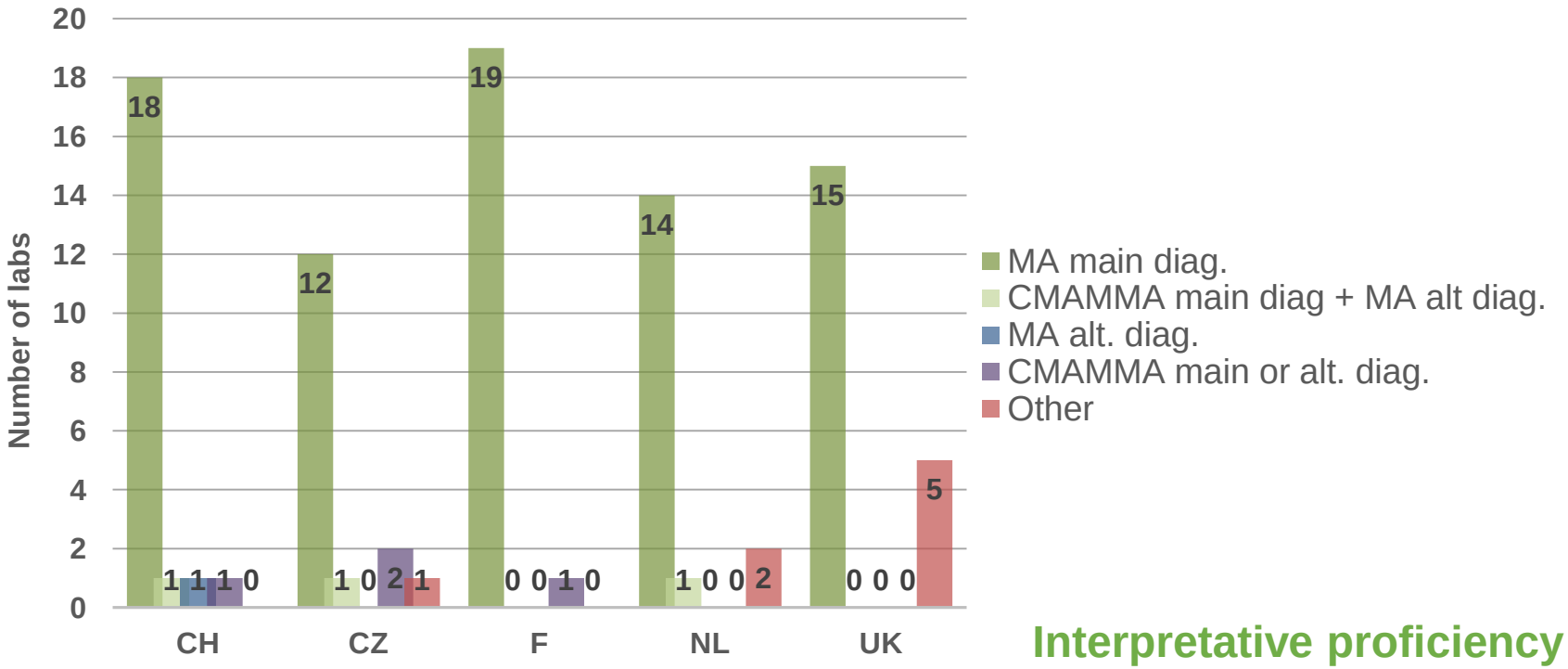
Interpretative performance

Scoring

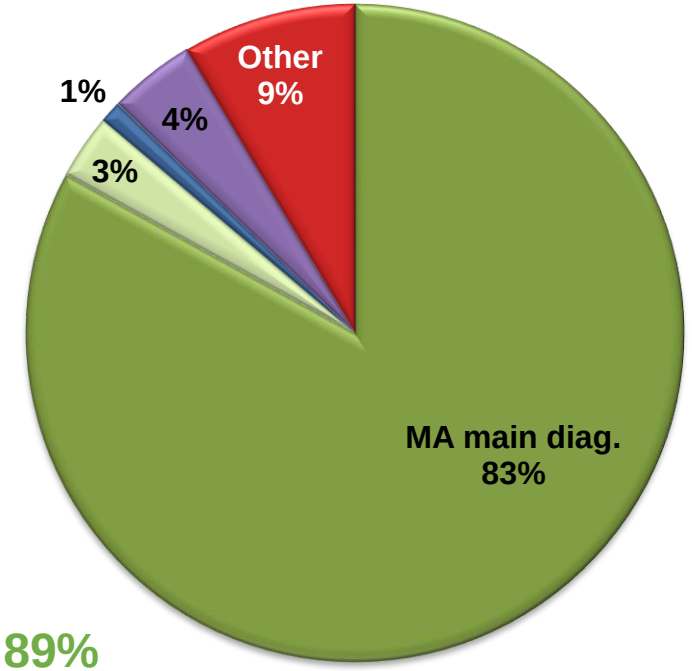
- Malonyl-CoA decarboxylase deficiency / malonic aciduria as main diagnosis was scored 2 points. As alternative diagnosis it was scored 1 point.
- Combined malonic and methylmalonic aciduria (CMAMMA) as main or alternative diagnosis was scored 1 point.

Other diagnosis

- No abnormality detected
- Fatty acid oxidation not ruled out
- MMA without homocystinuria
- Barth syndrome



8 labs



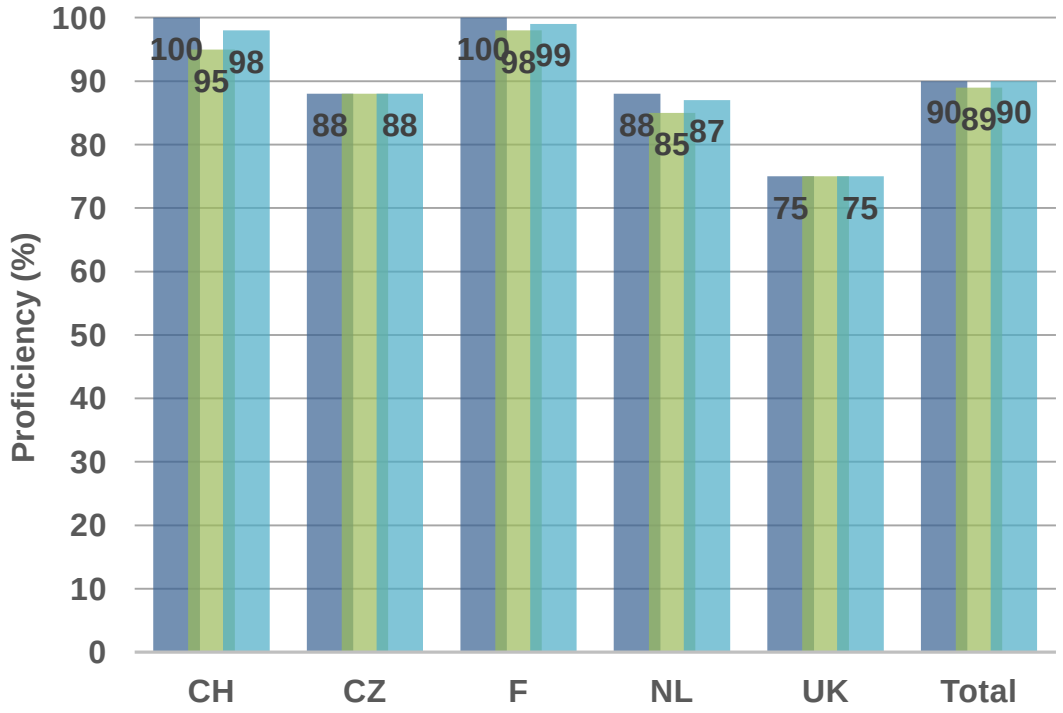
Interpretative proficiency = 89%

Overall impression and conclusion

- Good overall proficiency of 90% for an ultra-rare diagnosis (few cases reported)
- Concentration of malonic acid was relatively low but reflect what has been found in literature.
- Better proficiency in some scheme than others

26-104 mmol/mol Cr

J.M. Zhang et al., Brain & Development, https://doi.org/10.1016/j.braindev.2024.07.001



Thank you !

Acknowledgements

- Dr. med. Dr. phil. nat. Matthias Gautschi
- All other centers that provide samples

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