



DPT Schemes

Common sample 2015

Cystathionine beta-synthase
(CBS) deficiency

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Patient information

- ▶ 34 year-old woman, with normal psychomotor development, investigated because of phlebitis at the age of 30 (under oestrogens)
- ▶ Urine provided by Dr Marie-Hélène Read, from CHU Caen, France

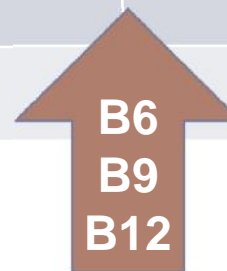


Case report

- ▶ 34 year-old woman
- ▶ Normal psychomotor development
- ▶ Phlebitis at the age of 30 (under oestrogens)
- ▶ No clinical manifestations before (except thyroidectomy and dust mites allergy)

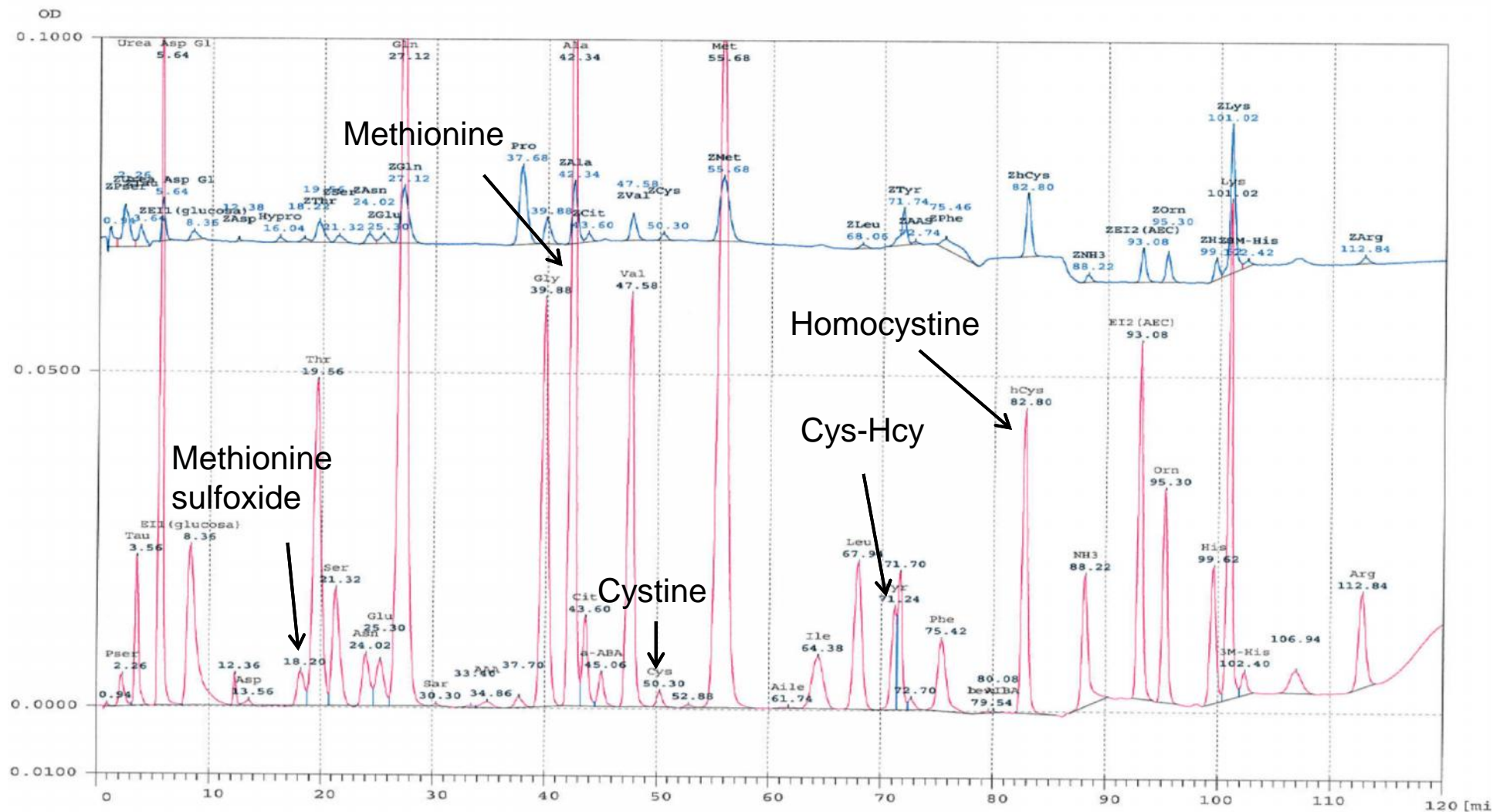
Investigation in plasma

	05 Jan 2015	21 jan 2015	29 Jan 2015	Reference values
Total hcy	330	280	10.7	<12
Homocystine	67	82	NM	<1
Methionine	160	552	22	14 - 38
Cystine	7	7	NM	28 - 75
Vit B12	97			135 - 470
Folates	8,4			7 - 45



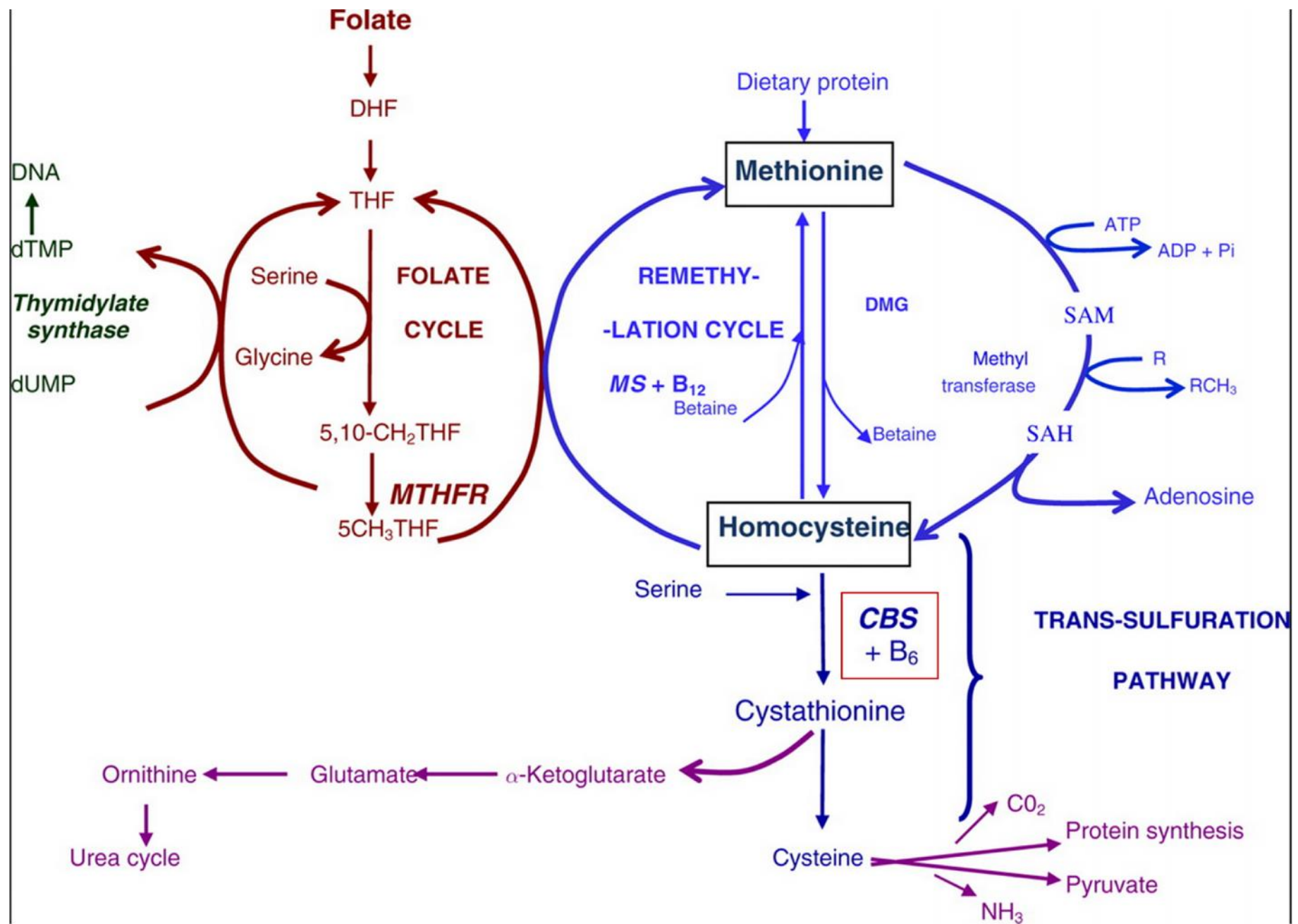
NM: not measured

Amino acids (Aminotac Jeol®)



Case report : CBS deficiency

- ▶ **Urines sent to DPT participants were urines at diagnosis (21 January 2015)**
- ▶ Spontaneously, the patient had a high protein diet (134 g/j)
- ▶ She felt much better (less anxiety and irritability) with vitamin supplementation and a normoproteic diet (80 g/j)
- ▶ Mutation analysis: compound heterozygous for 2 already described mutations in *CBS* gene
 - ▶ c.146C>T (p.Pro49Leu): B6 responsive
 - ▶ c.374G>A (p.Arg125Gln)
- ▶ No measurement of CBS activity has been performed



DPT centres

▶ Czech Republic	20 labs
▶ France	23 labs
▶ Switzerland	21 labs
▶ The Netherlands	20 labs
▶ United Kingdom	23 labs
▶ Total	107 labs (107 responders)

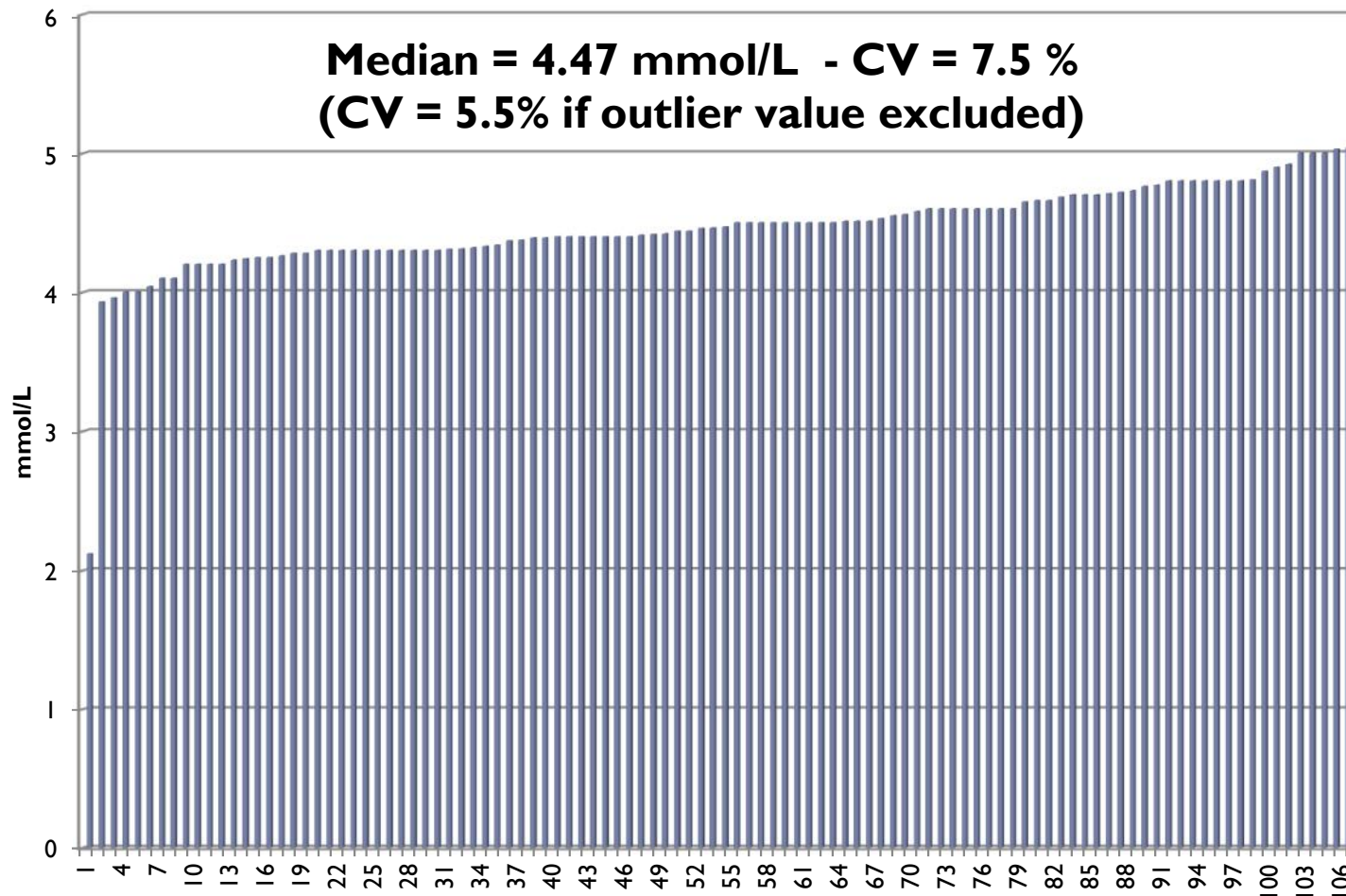
Creatinine determination

Centre	Median	Mean	Coefficient of variation
Czech Republic	4.53	4.49	5.1 %
France	4.50	4.55	5.5 %
Switzerland	4.41	4.49	5.1 %
The Netherlands	4.47	4.36	13.2 %
United Kingdom	4.40	4.43	5.9 %
All centres	4.47	4.46	7.5 %

Interlab CV 2014 Special Assay urine = 5.6 % (n = 122)

Interlab CV 2014 Quantitative organic acids = 5.2 % (n = 67)

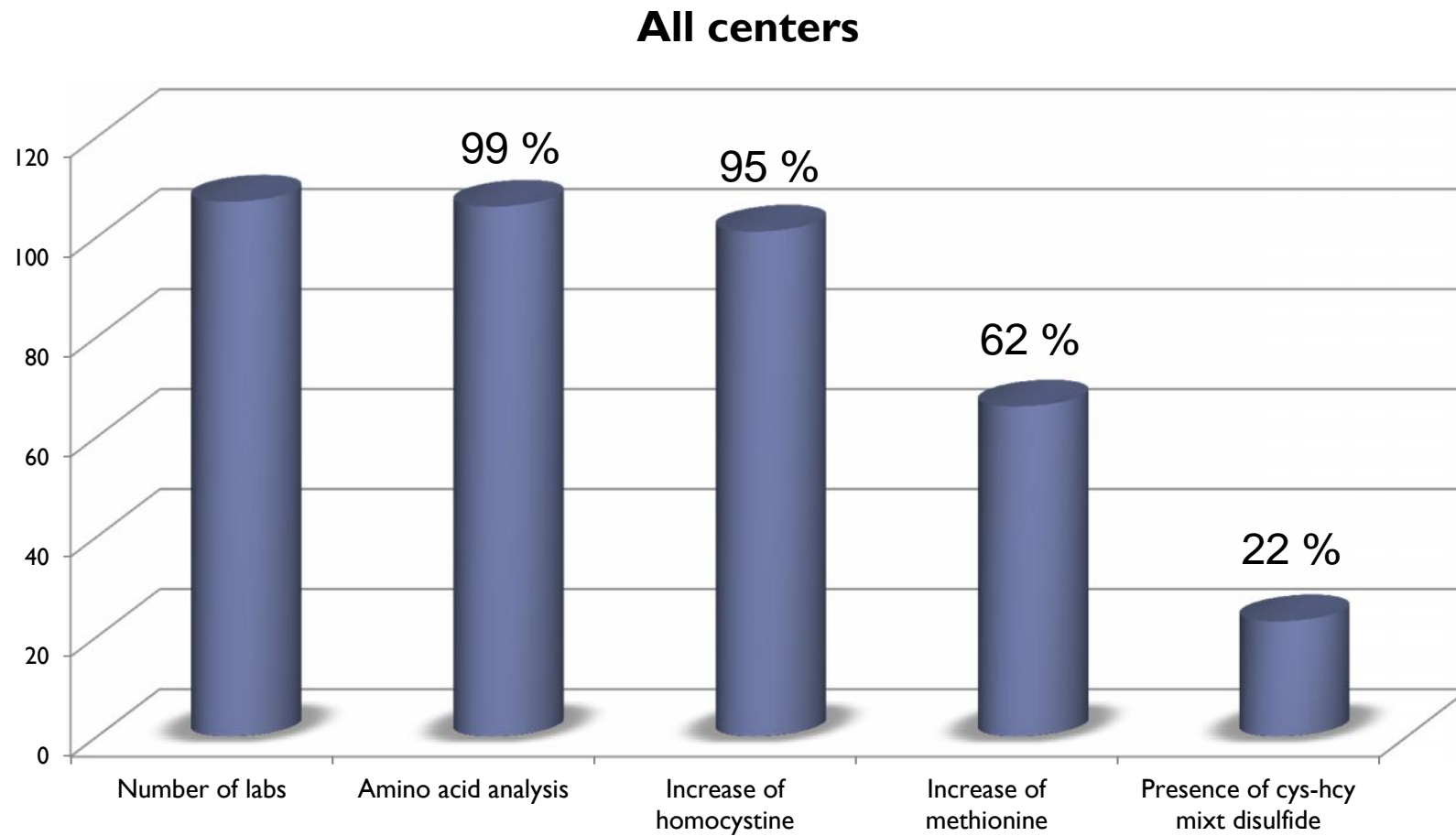
Creatinine determination (mmol/mol creat)



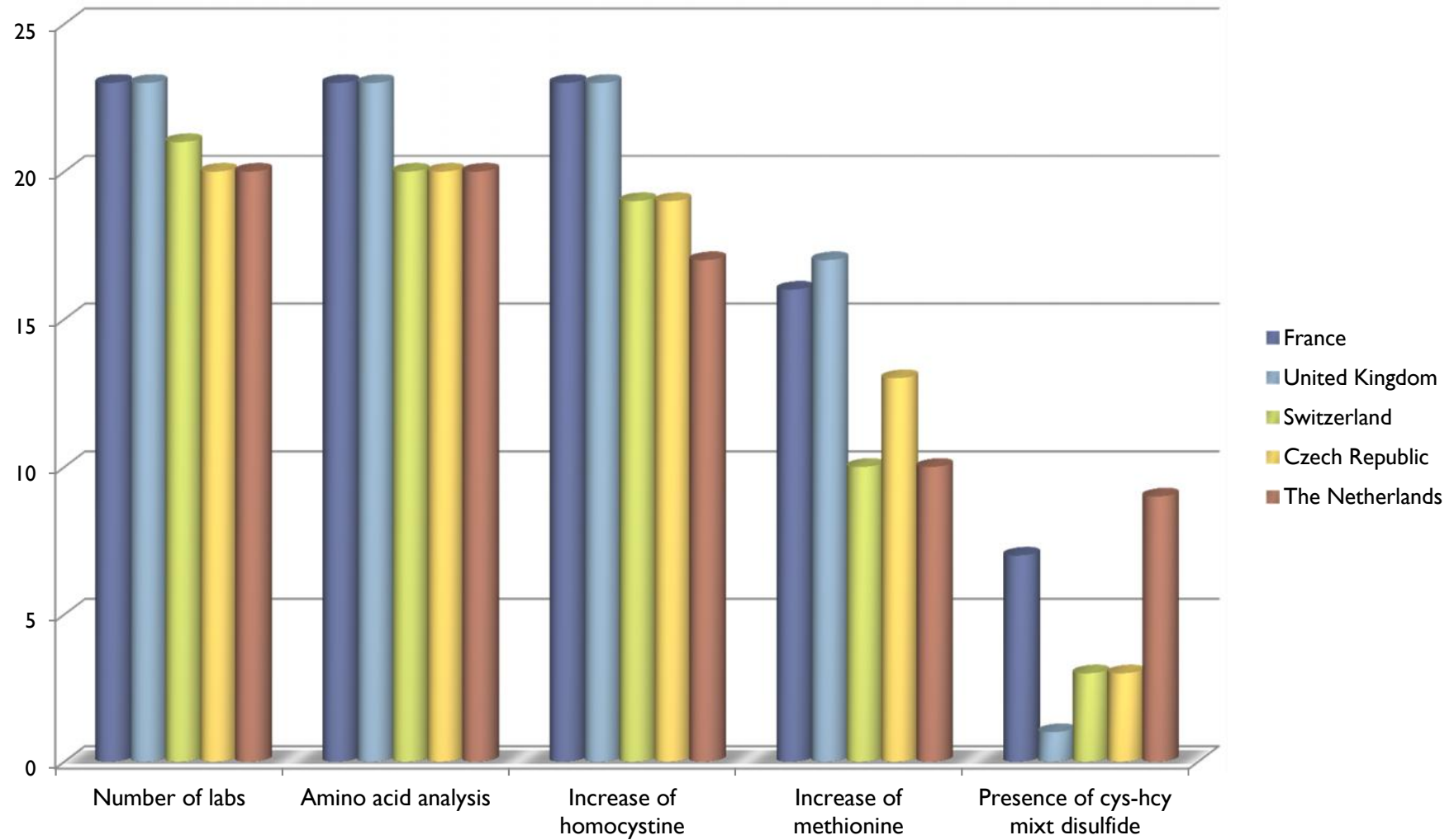
Amino acid determination

DPT centre	Number of labs	Test performed	%
Czech Republic	20	20	100 %
France	23	23	100 %
Switzerland	21	20	95 %
The Netherlands	20	20	100 %
United Kingdom	23	23	100 %
Total	107	106	99 %

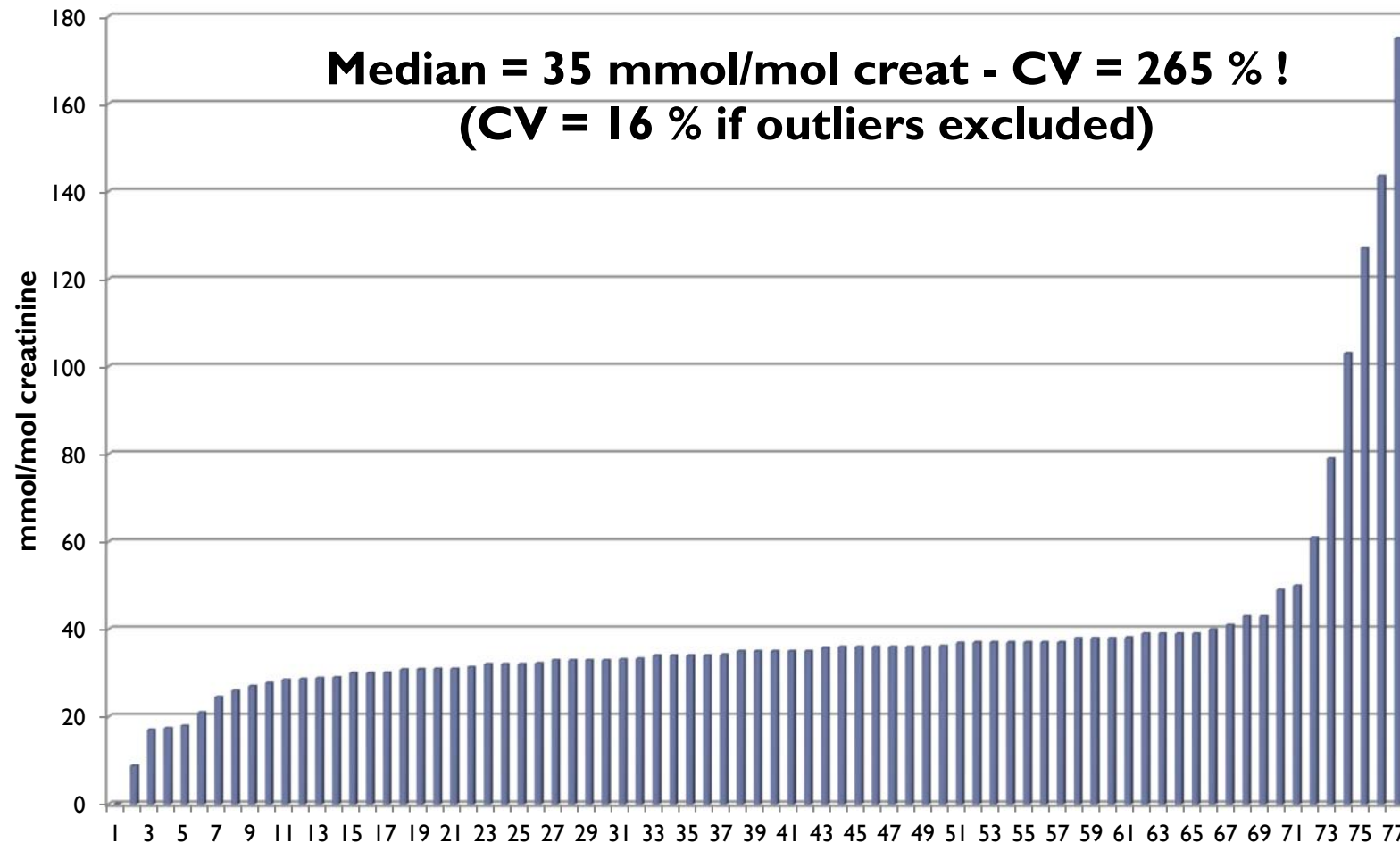
Amino acids



Amino acids



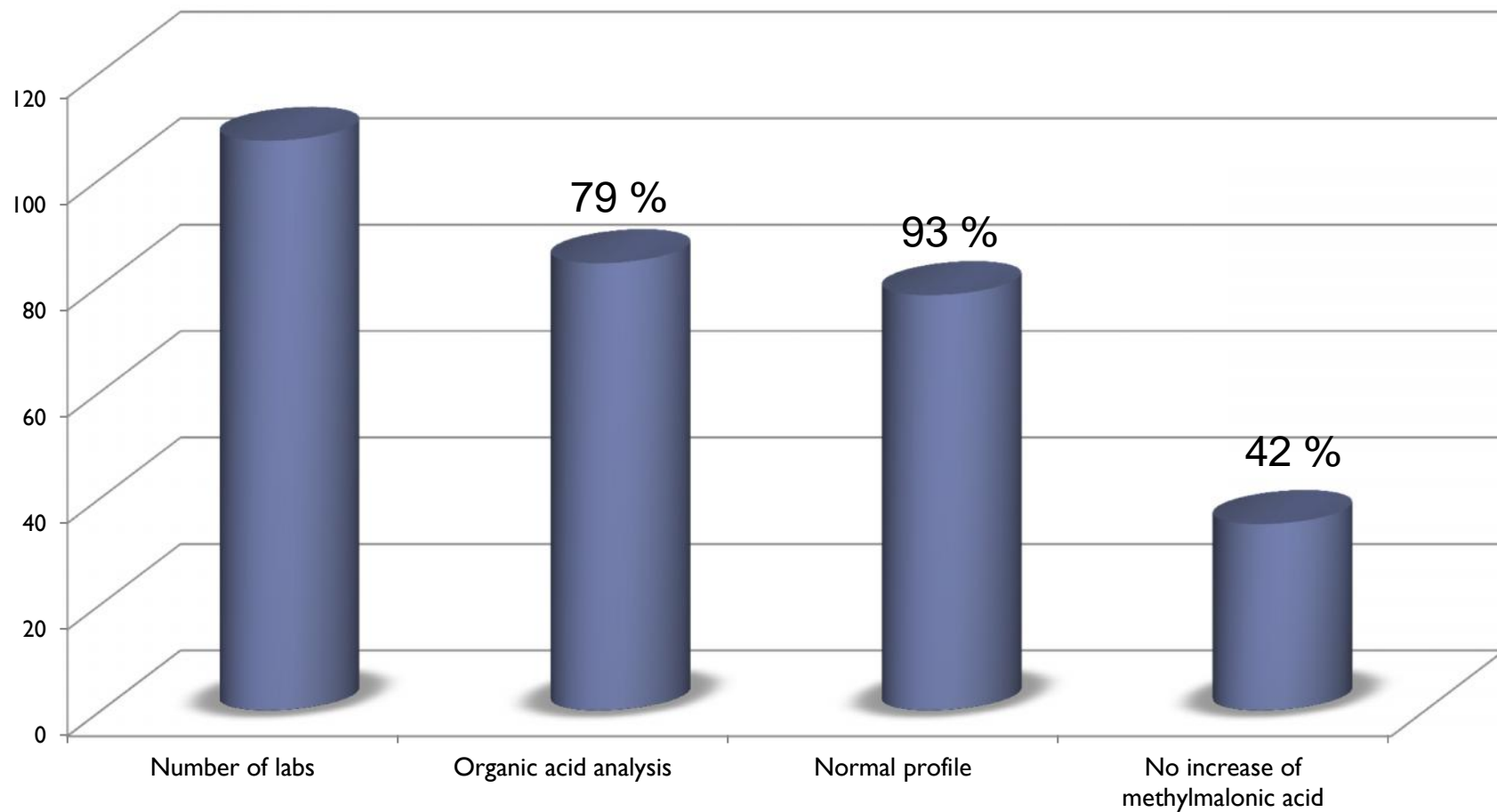
Homocystine (mmol/mol creat)



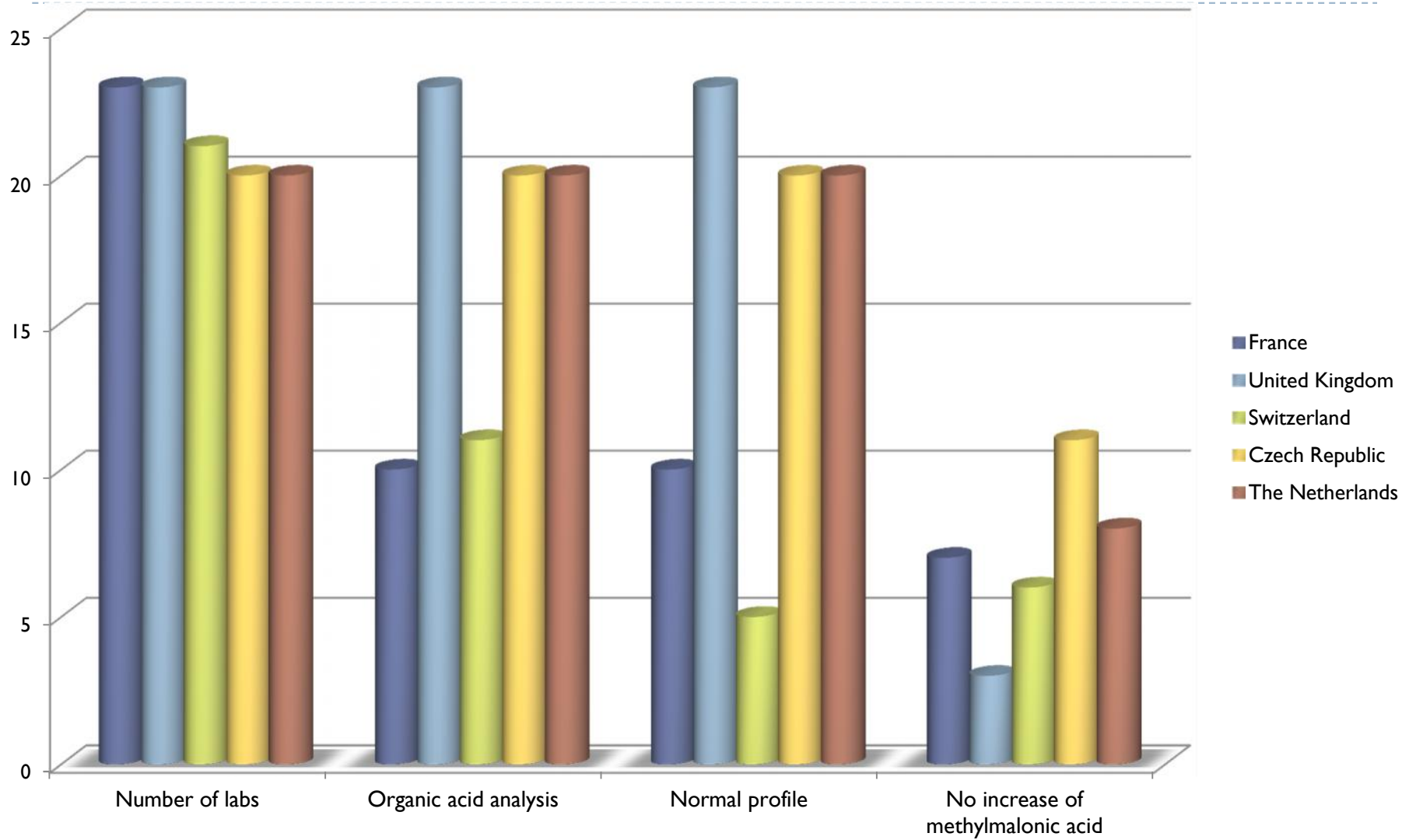
One wrong value excluded : 829 mmol/mol creat

Organic acids

All centers

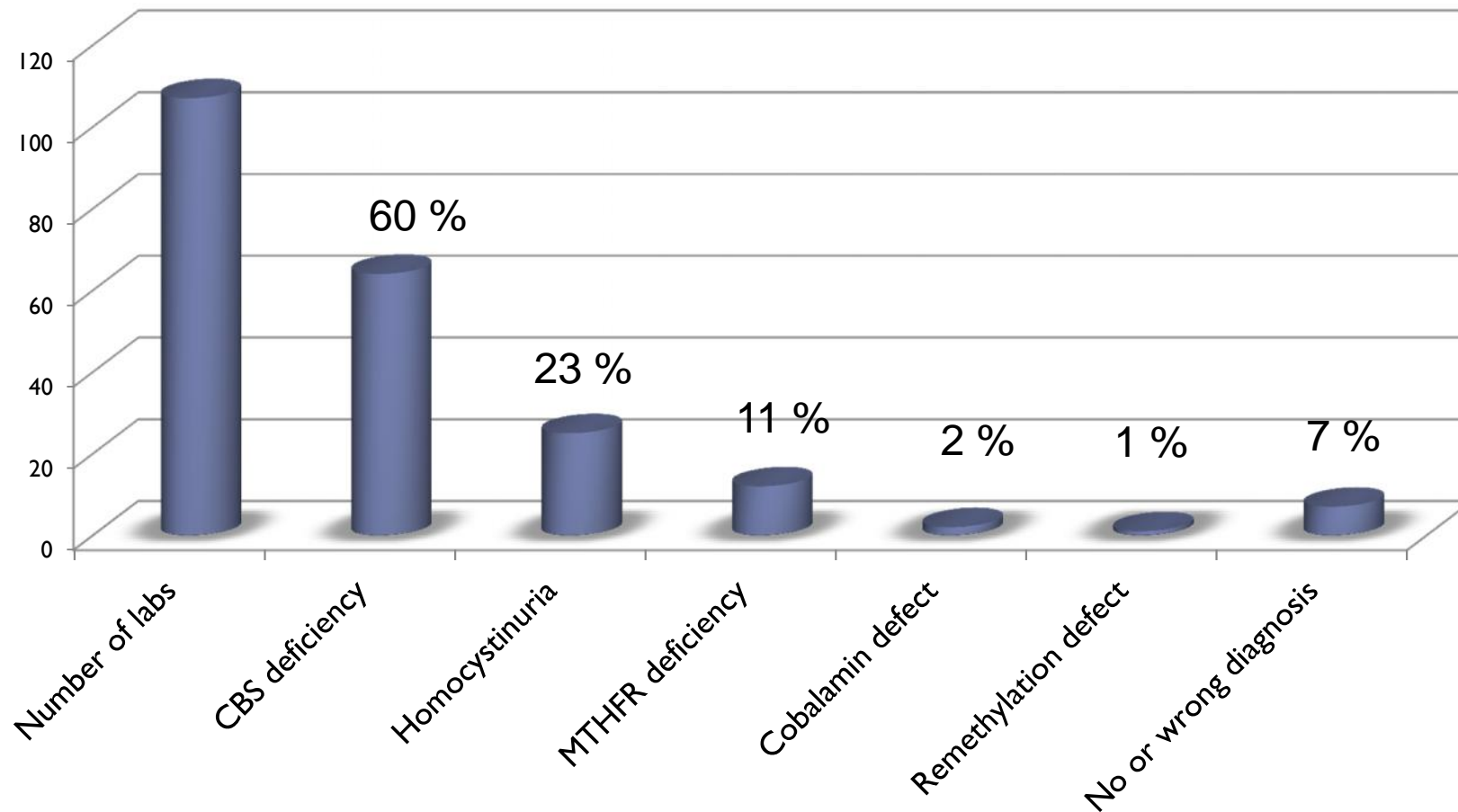


Organic acids

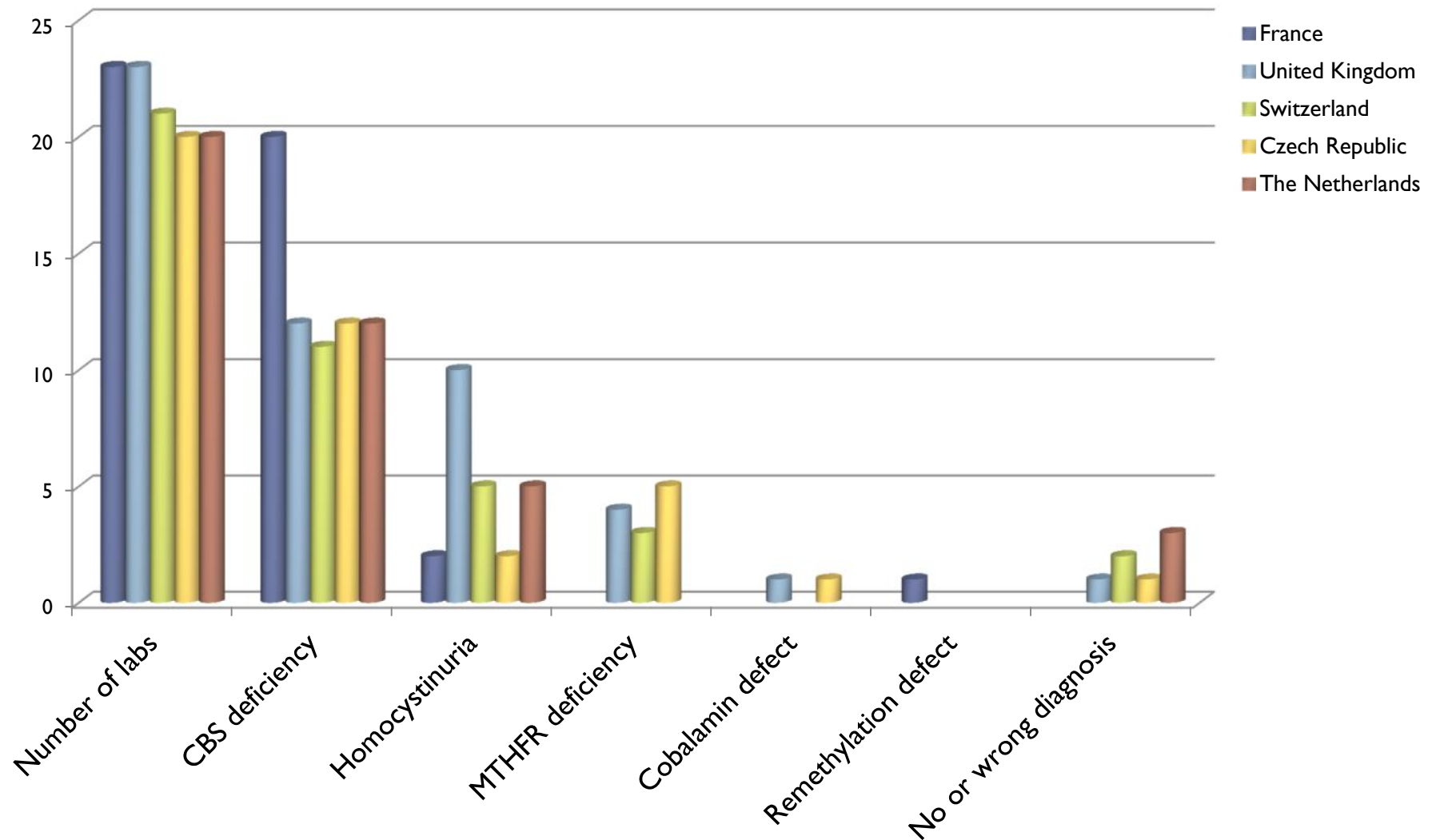


Interpretation of results

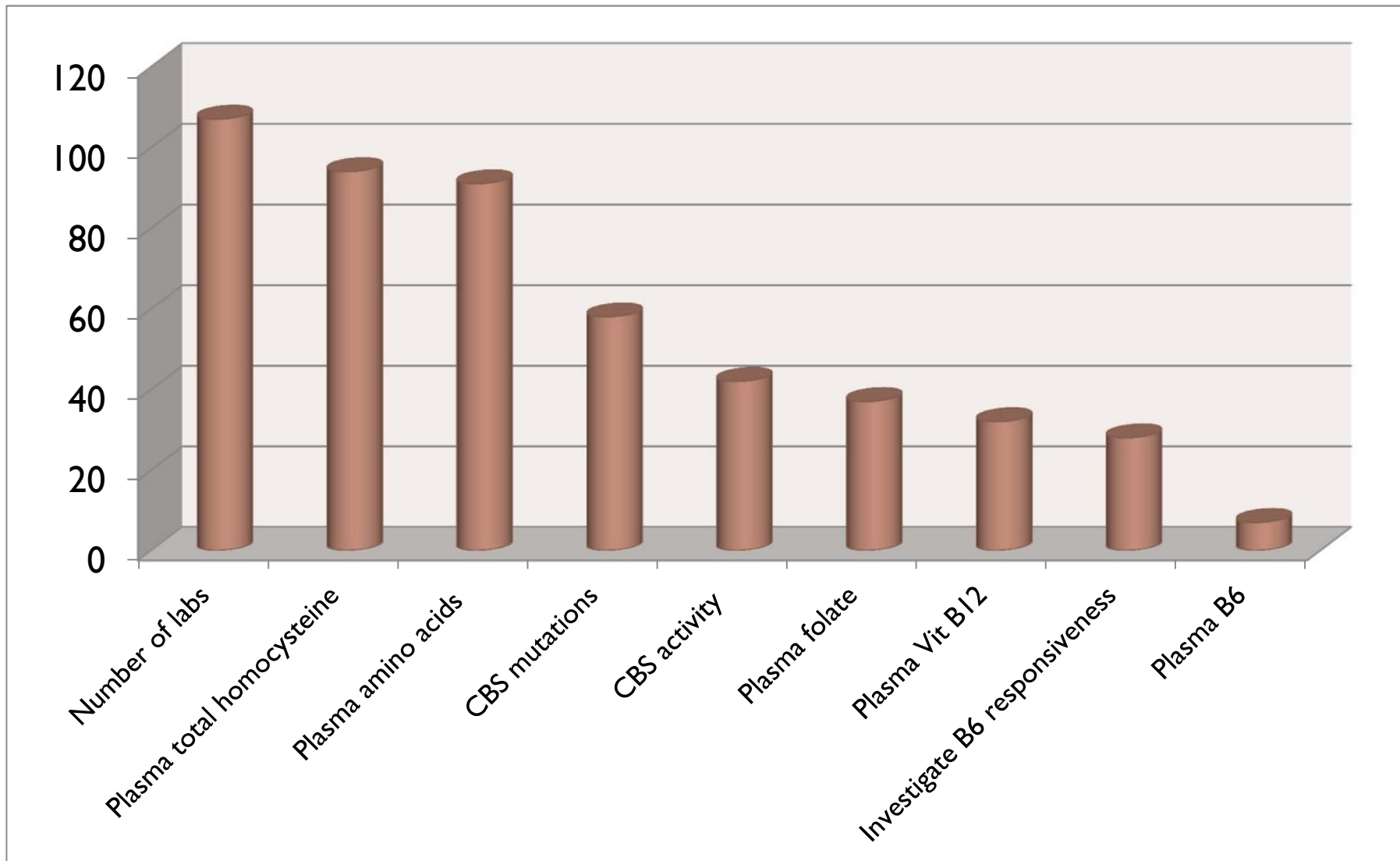
All centers



Interpretation of results



Recommendations



Scoring

■ Analytical performance

- ▶ Increase of homocystine (or homocysteine) |
- ▶ Increase of methionine and/or normal organic acid
and /or normal methylmalonic acid |

■ Interpretation of results

- ▶ Cystathionine beta-synthase deficiency |
(as first or alternative diagnosis) 2
- ▶ Homocystinuria |
(without precision or MTHFR def. or cobalamine defect)

Scoring

DPT Centre	Analytical (%)	Interpretation (%)	Total (%)
Czech Rep.	85 %	75 %	80 %
France	96 %	93 %	95 %
Switzerland	71 %	76 %	74 %
Netherlands	83 %	83 %	83 %
UK	98 %	91 %	95 %
All centres	89 %	86 %	87 %

Conclusion

- ▶ Although urine is not the best biological fluid to diagnose CBS deficiency
- ▶ Analytical performance was satisfactory
 - ▶ Some labs have too high reference values for methionine
- ▶ Interpretation of results
 - ▶ Lack of precision
 - ▶ Some labs were confused by the absence of psychomotor retardation
- ▶ Recommendations were correct for those who reached the diagnosis