HCL
LYON UNIVERSITY HOSPITAL

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Quality Assurance in Laboratory Testing for IEM

DPT Common Sample 2025

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Clinical information

- Clinical information provided: “15-year-old boy. Dysmorphic features, scoliosis, size -1.5 SD, normal intellectual development. Under treatment.”

- Normal pregnancy and delivery
- From 2 months to 6 years of age : frequent upper airways infections
- 1 year : height +3 SD
- 3 years : pectus carinatum
- 10 years
  - Scoliosis with platyspondyly
  - Dorsal kyphosis
  - Narrow cervical canal
  - Decrease in visual and hearing acuity

Clinical information

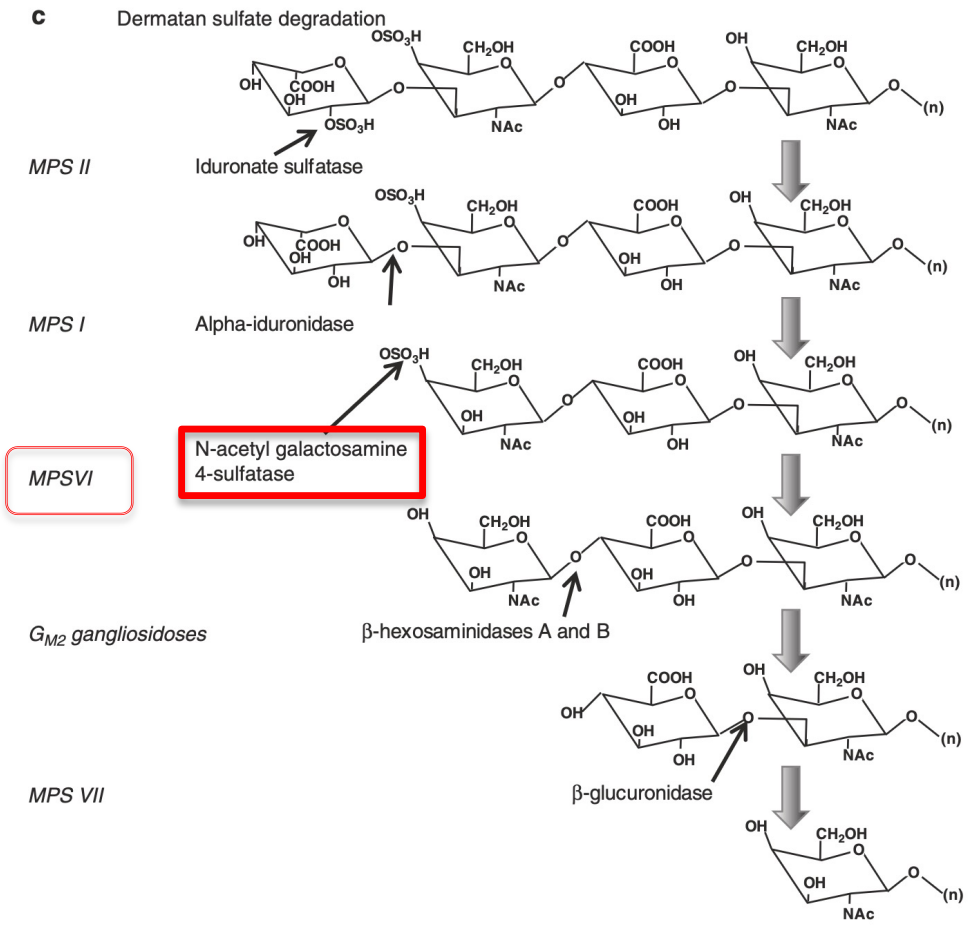
- 15 years
  - Normal intellectual development
  - Arthrodesis T10-T12
  - Height: -1.5 SD
  - Urinary MPS analysis because of spine abnormalities and dysmorphic features
  - Diagnosis of MPS VI confirmed by measurement of arylsulfatase B activity in leucocytes and mutation analysis of *ARSB* gene
- Since then, he is receiving enzyme replacement therapy every week

Mucopolysaccharidosis type VI

- Maroteaux-Lamy syndrome is a rare autosomal recessive LSD (birth prevalence : 1/625 000*)
- Due to arylsulphatase B deficiency (*ARSB* gene)
- Wide phenotypic spectrum (S Jones, F Wijburg, Inborn Metabolic Diseases – Diagnostic & Treatment, 2016)
  - Usual signs: short stature, dysostosis multiplex, degenerative joint disease
  - Frequent signs: cardiac valve disease, hearing loss, obstructive sleep apnoea, corneal clouding, carpal tunnel disease, and inguinal or umbilical hernia
  - Possible signs: cervical cord compression, communicating hydrocephalus, optic nerve atrophy and blindness
- Arylsulphatase B (N-acetylgalactosamine 4-sulphatase): lysosomal enzyme, removes 4-sulfate groups from the non-reducing end of chondroitin 4-sulfate and dermatan sulphate, and thereby regulates their degradation

* https://www.orpha.net/pdfs/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf

Mucopolysaccharidosis type VI

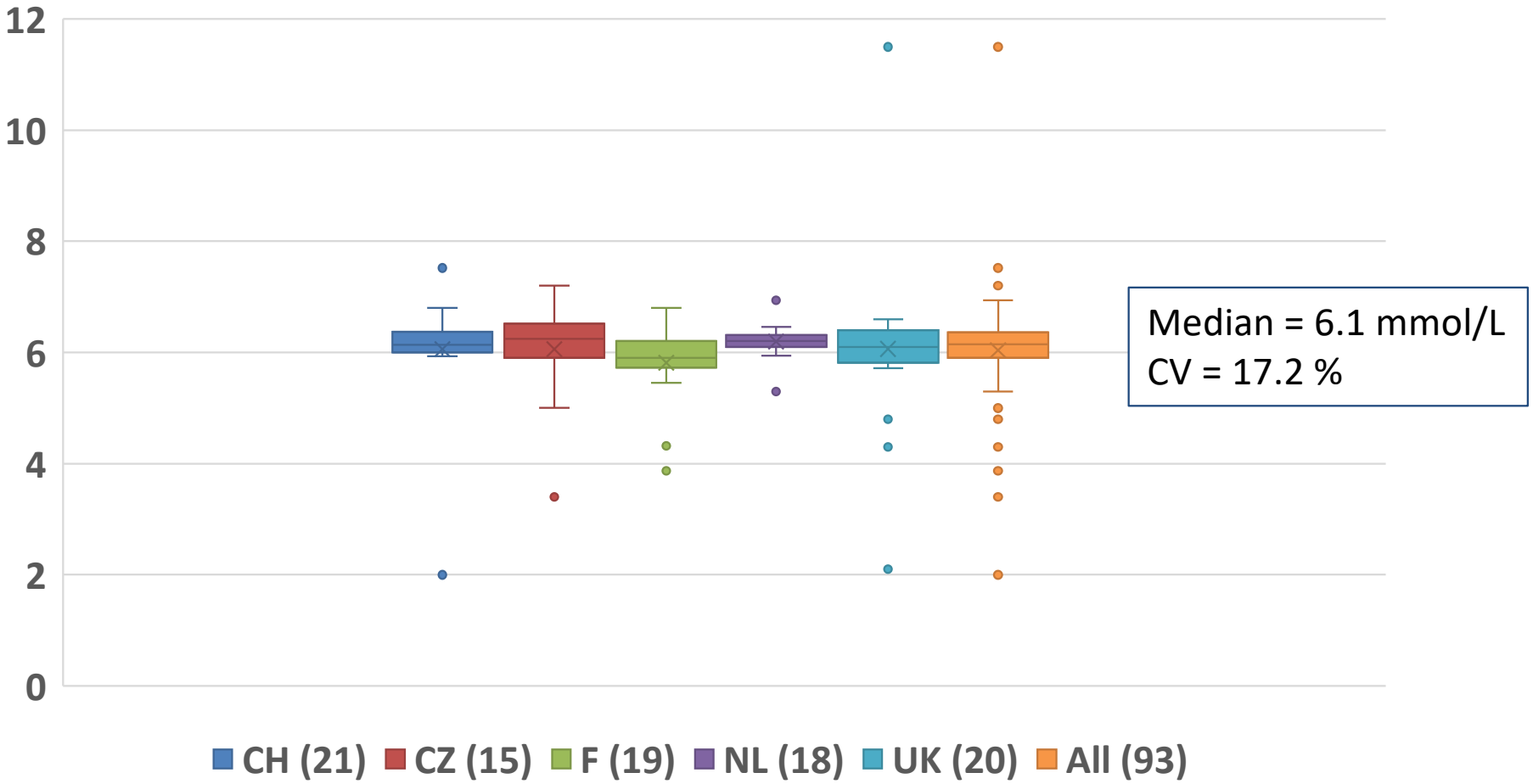


From Parenti & Giugliani, Physician's Guide to the Diagnosis, Treatment,and Follow-Up of Inherited Metabolic Diseases, 2022

Participants

• DPT CH (Switzerland)	21 participants
• DPT CZ (Czech Republic)	15 participants
• DPT F (France)	19 participants
• DPT NL (Netherlands)	18 participants
• DPT UK (United Kingdom)	20 participants
• **Total**	**93** participants

Creatinine (mmol/L)



Mucopolysaccharides quantification

- **81 / 93 participants** (87%)
- Methods
  - **DMB*** **72**
  - Alcian blue 3
  - Harmine 2
  - Other or ? 4

*Dimethyl methylene blue

- **Increase in GAGs** **68 / 81** (84%)

In our hands (DMB): 8.1 g/mmol creat (controls: 0.9 – 6)

- Can normal results be explained ?
  - Not dependent of the method used
  - Problem of control range ?

  With the same result and the same method, some participants concluded that quantification was elevated, while others concluded that quantification was normal
  - Wrong creatinine (high level): at least 1 lab

Mucopolysaccharides fractionation

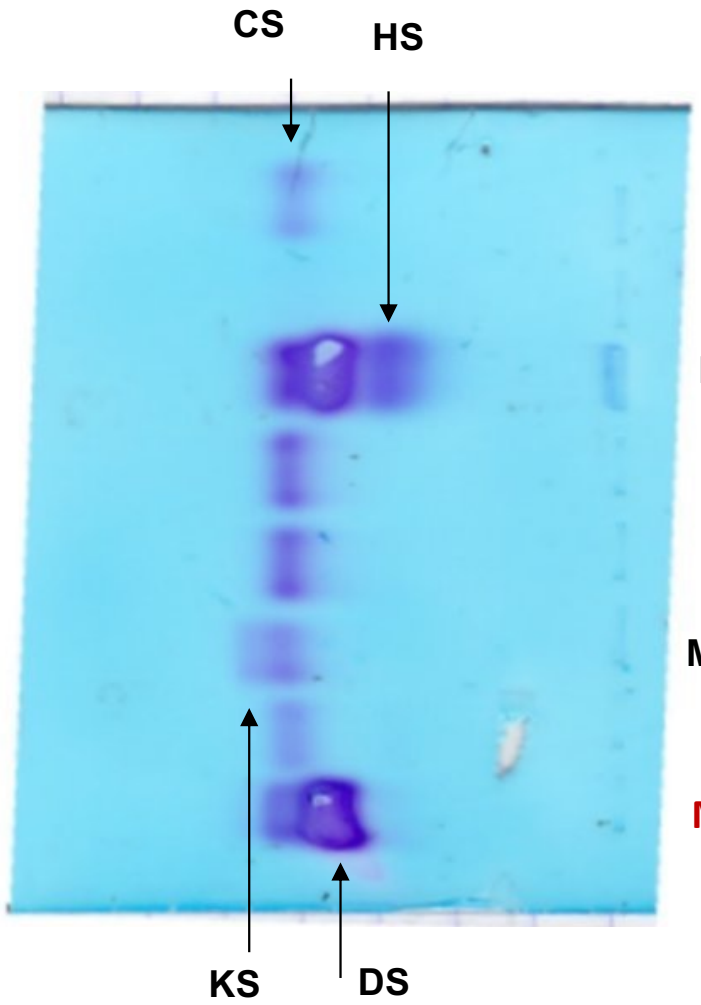
- **83 / 93 participants** (89%)
- Methods
  - **1D-electrophoresis** **38**
  - 2D-electrophoresis 13
  - LC-MS/MS 6
  - TLC 6
  - HPTLC 1
  - LC-MS 1
  - Other or ? 18

Increase in

- **Dermatan sulphate** **73** **(88%)**
- Chondroitin sulphate 25 (30%)
- Heparan sulphate 22 (26%)
- Keratan sulphate 4 (5%)

Identification (or not) of dermatan sulphate is not method dependent

1D-Electrophoresis



Hurler (MPS I)

Morquio (MPS IV)

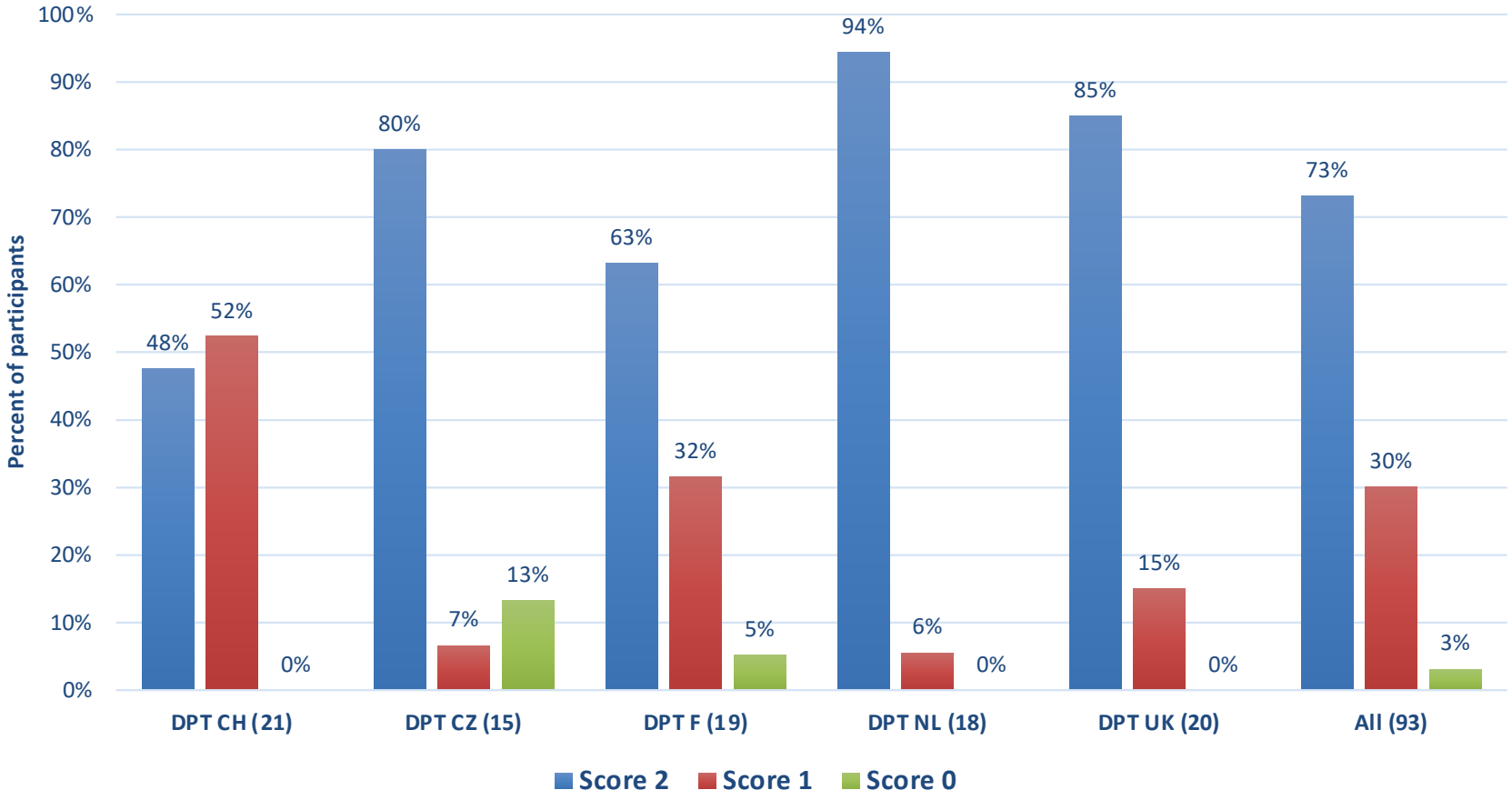
Maroteaux-Lamy (MPS VI)

KS: keratan sulphate
CS: chondroitin sulphate
DS: dermatan sulphate
HS: heparan sulphate

Analytical scoring

- Increase of dermatan sulphate : score 2
- Increase of GAGs quantification, without fractionation : score 1
- GAGs fractionation indicative of an incorrect mucopolysaccharidosis : score 1

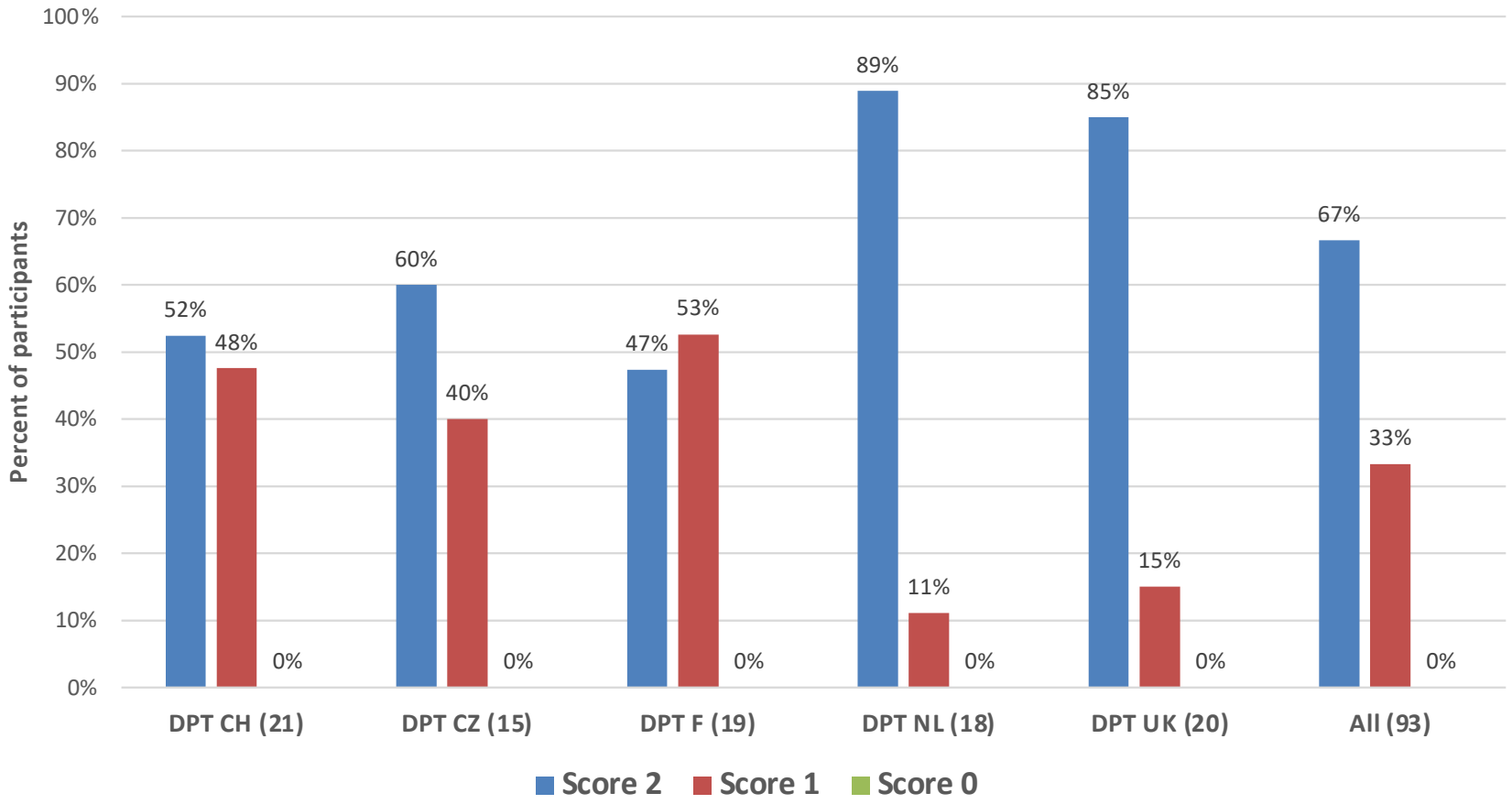
Analytical interim scores



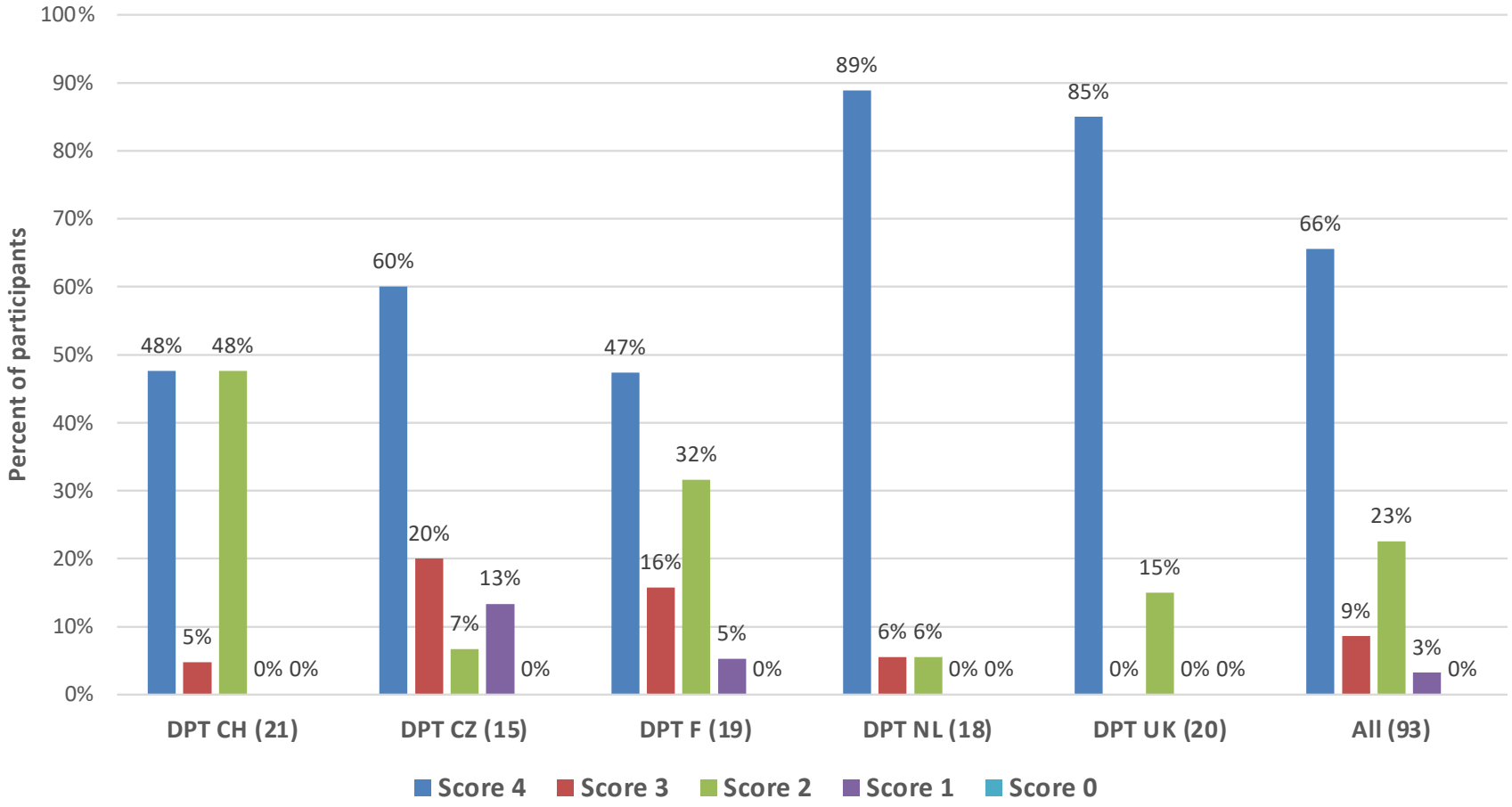
Interpretation scoring

- MPS VI as main diagnosis : score 2
- Other or unspecified mucopolysaccharidosis : score 1
- Diagnosis of mucopolysaccharidosis based on clinical information : score 1

Interpretation interim scores

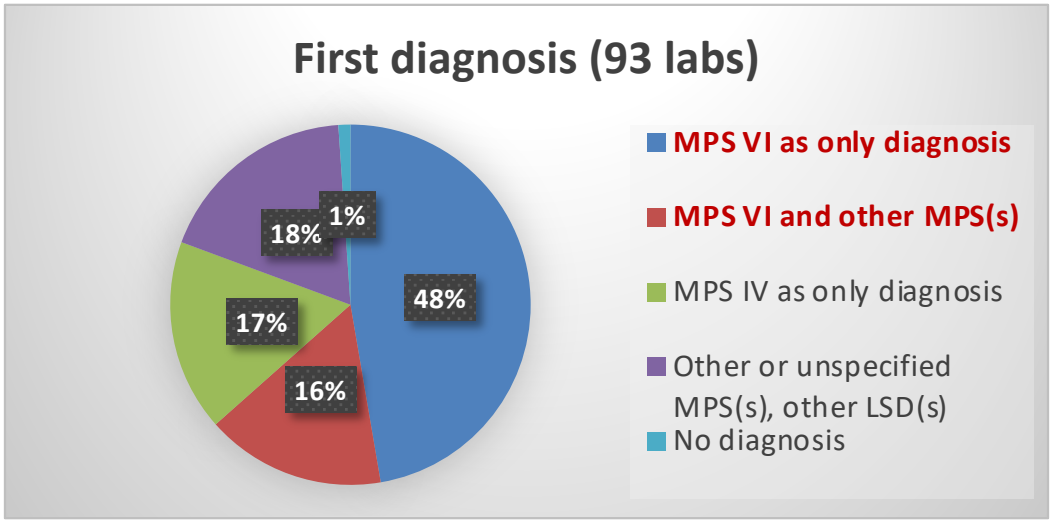


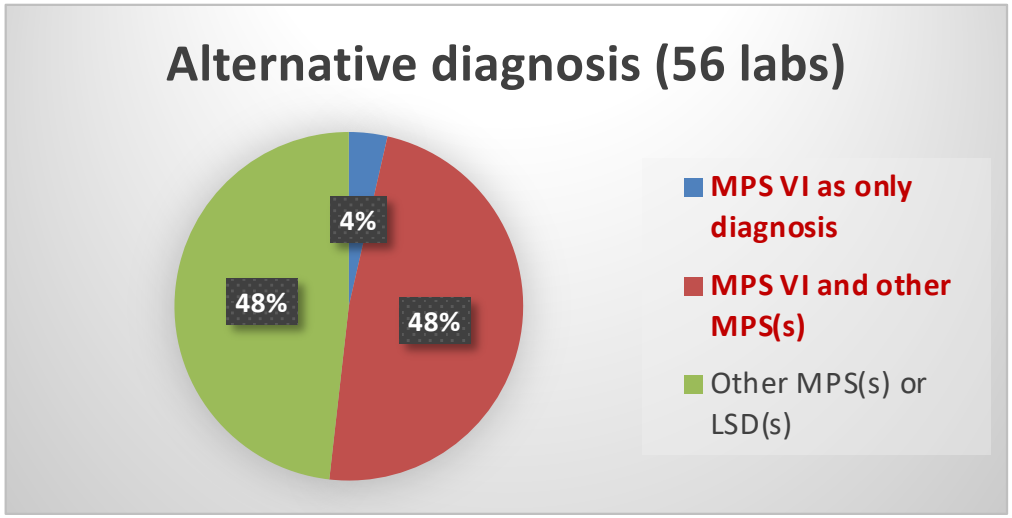
Overall interim scores



Conclusion

- Challenging sample: LSD, treated patient, but significant increase in abnormal metabolites
- Good analytical performance
  - 88 % participants who performed GAGs fractionation reported an increase in dermatan sulphate
  - 84 % participants who performed GAGs quantification reported an increase in GAGs
  - Only 3 participants did not get any mark
- Satisfying interpretation: no labs with no marks





Thank you for your attention !