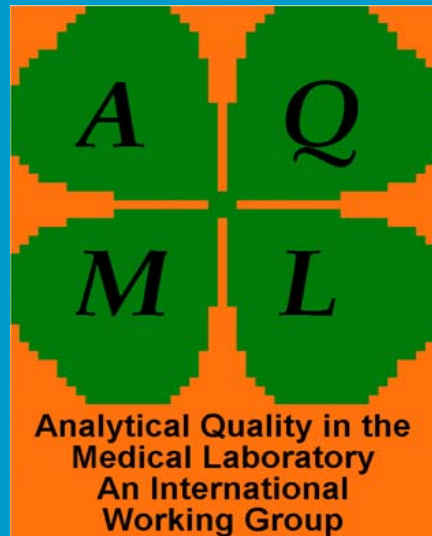


Theoretical Aspects of the Concept of Sharing Common Reference Intervals

Per Hyltoft Petersen



Workshop on Common Reference Intervals

Saturday, August 10

Iceland 2002



Overview

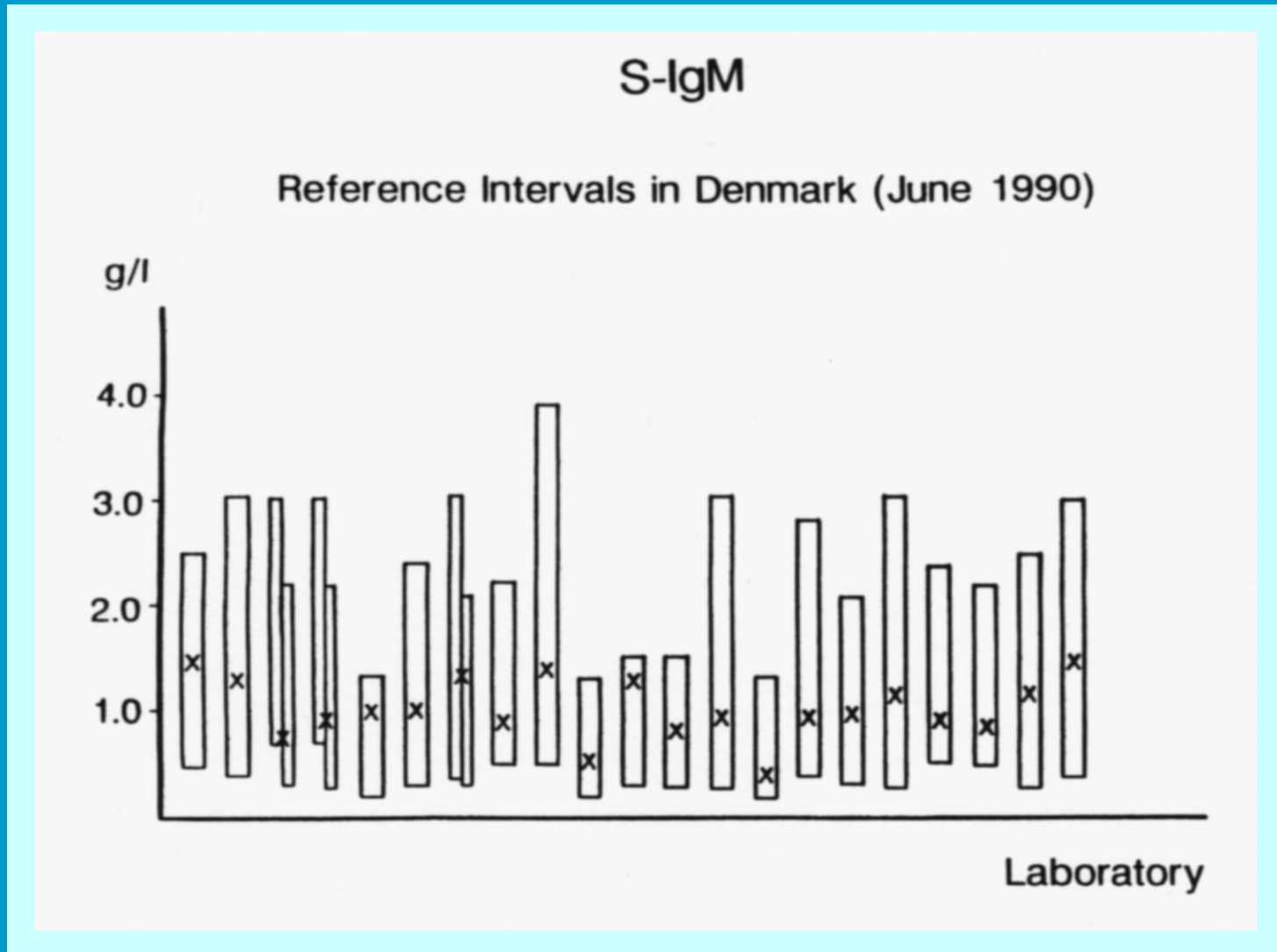
- The need for common reference intervals
- Cooperation
- Prerequisites for establishing common reference intervals
- Acceptance by the users

The need for common reference intervals

Laboratories in the same countries/cities present different reference intervals for same quantities (components)

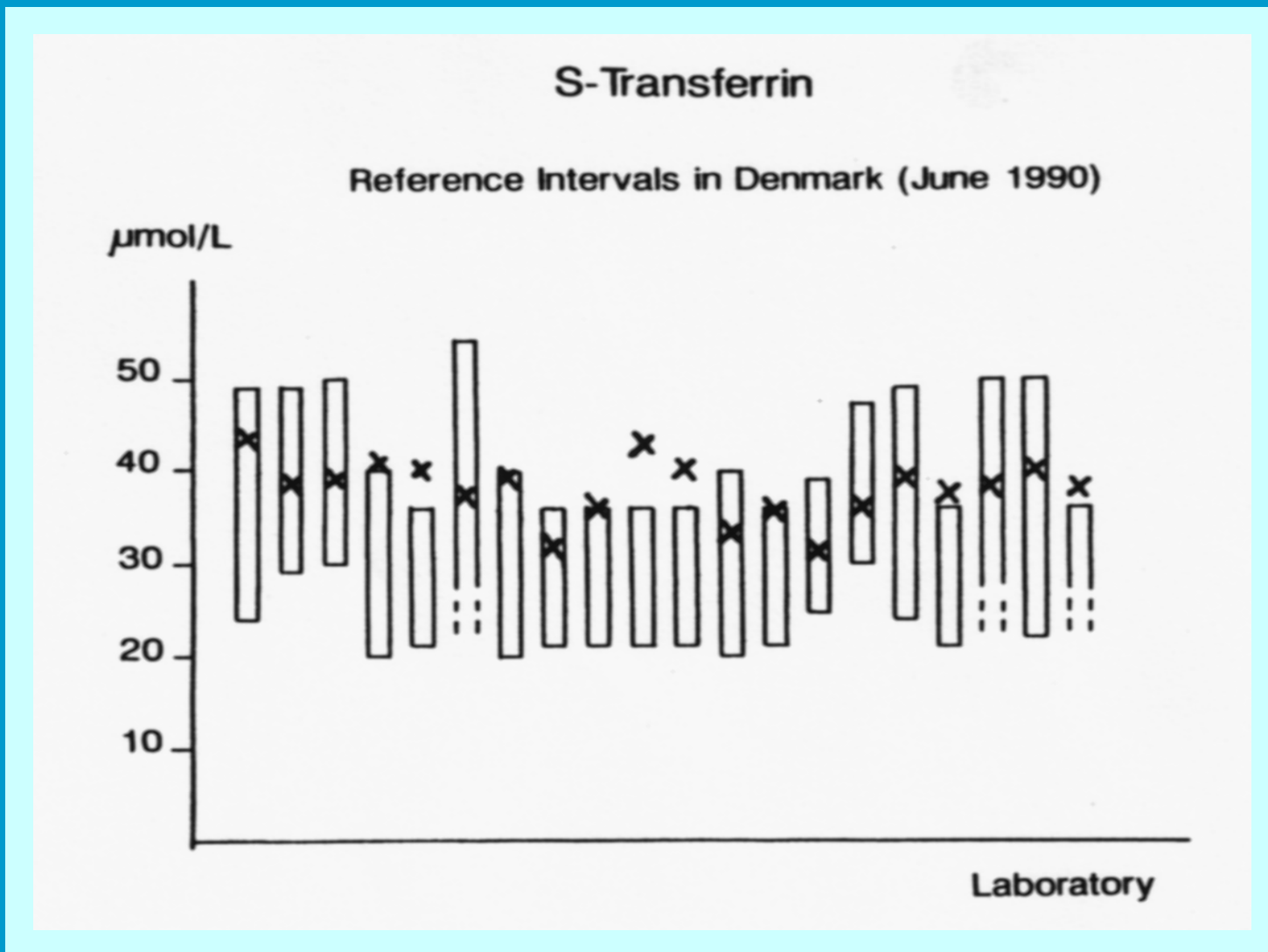
- The society do not understand why
- The profession cannot give acceptable explanation
- It is not evidence based

Reference intervals in 1990



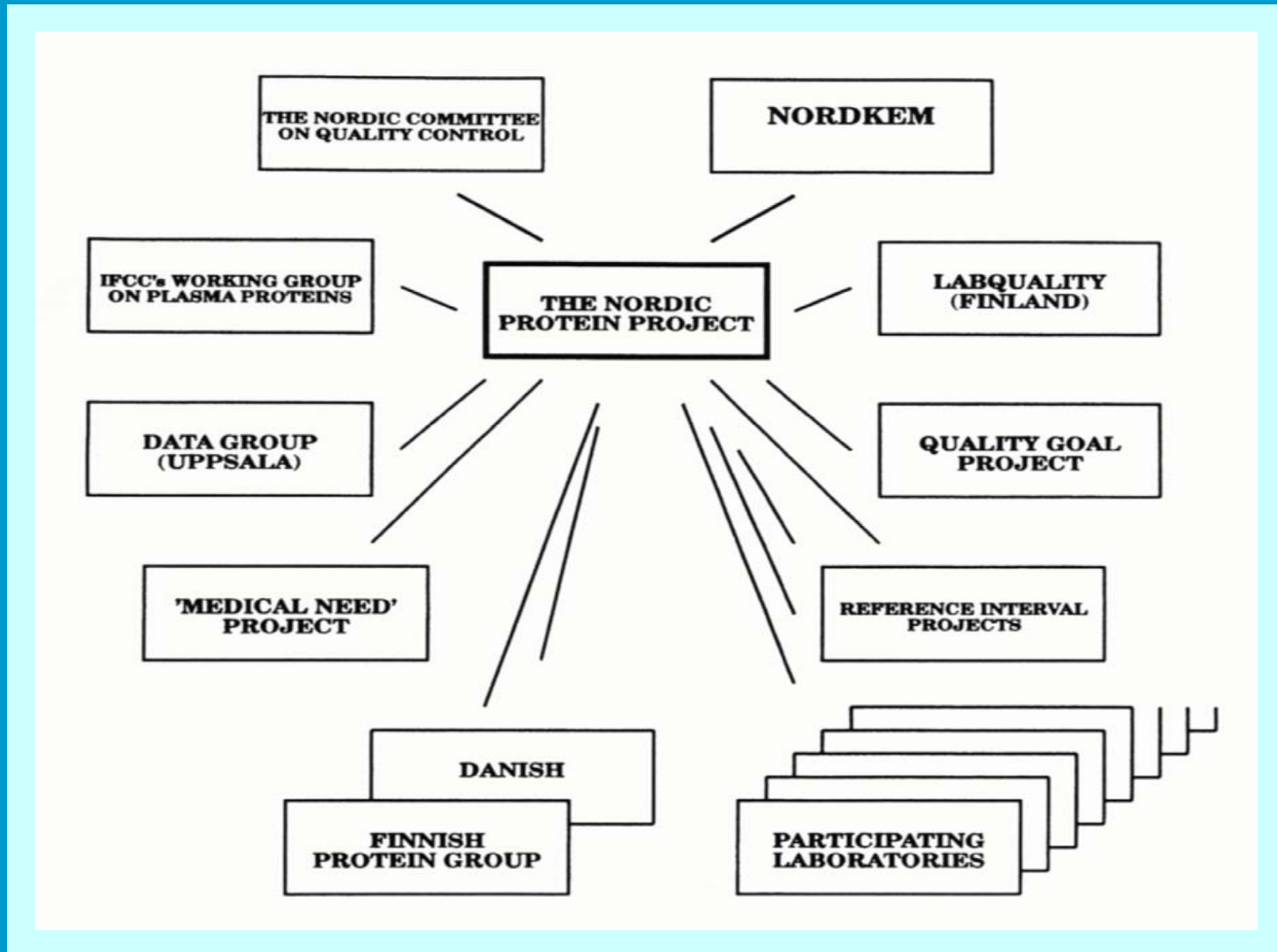
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Reference intervals in 1990



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Example of cooperation



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Prerequisites for establishing common reference intervals

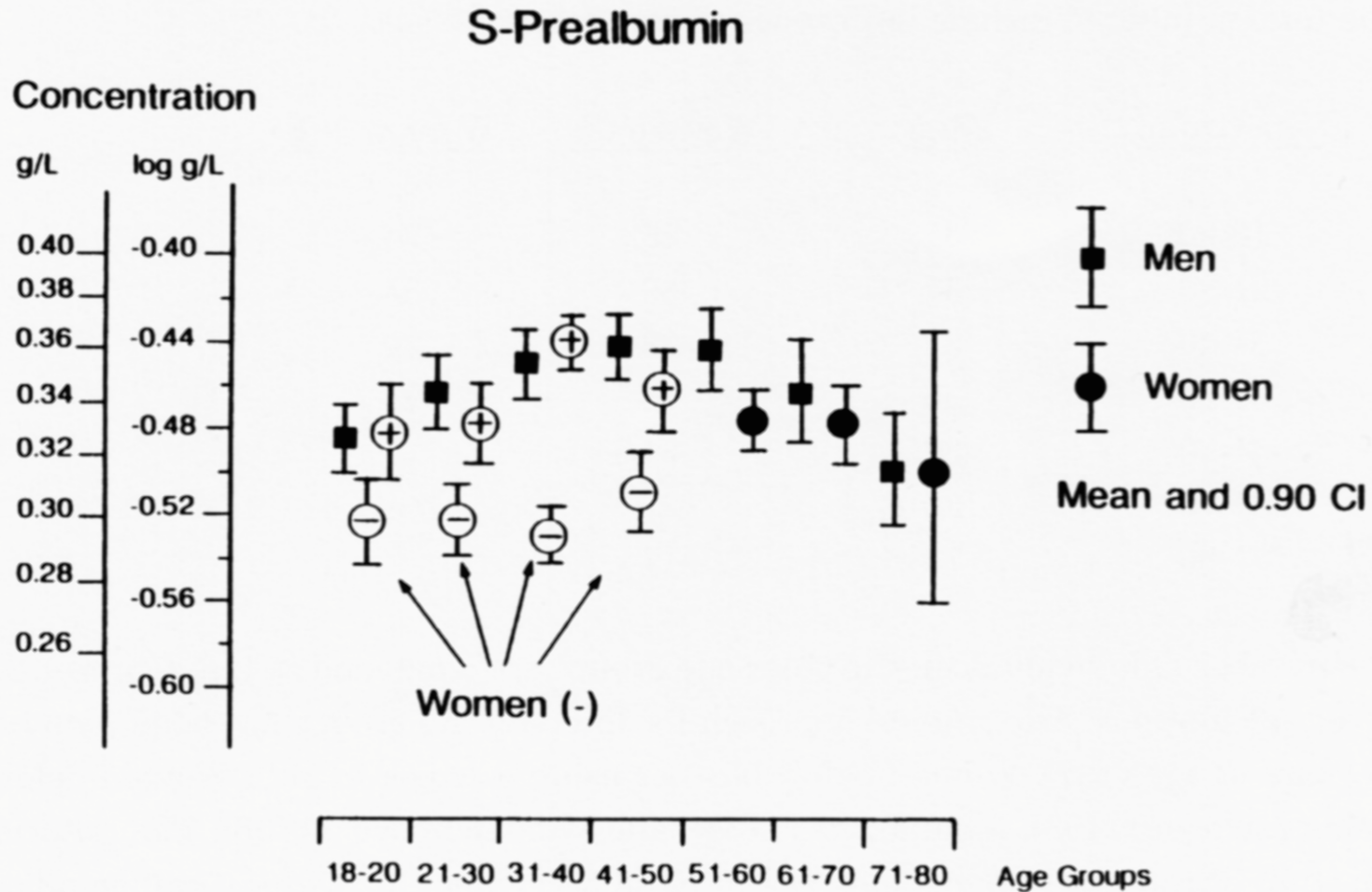
- Homogeneous reference populations
- State of health must be defined and stated
- Optimum sampling and storage conditions
- The quantity (component) must be well defined
- The values must be traceable to a reference
- Bias (and imprecision) must be acceptable
- The analytical quality must be controlled

Prerequisites for establishing common reference intervals

The reference populations:

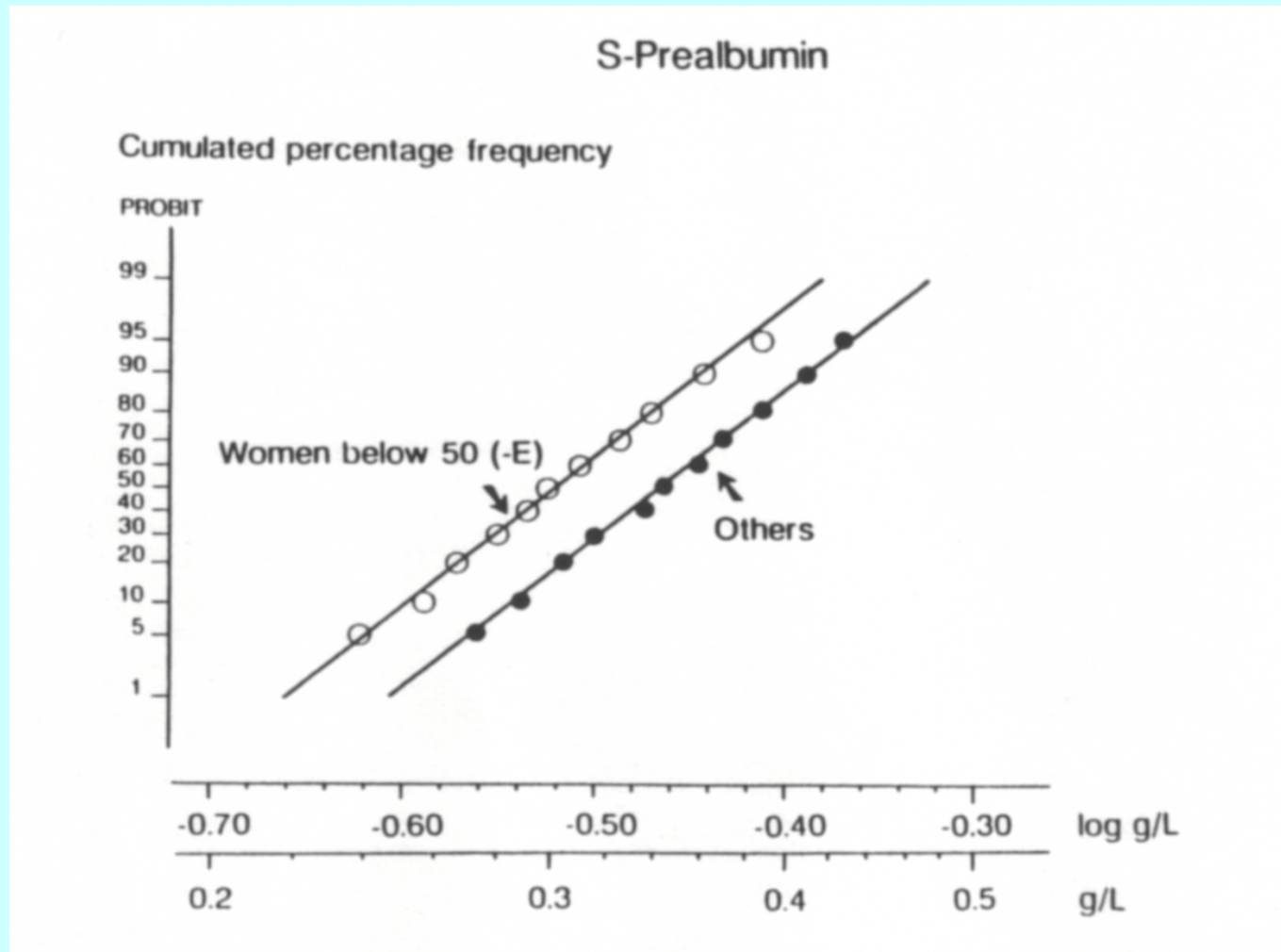
- Homogeneous reference populations
- Racial/ethnic/age/gender differences
- Genetic heterogeneity within groups
- Environmental conditions
- Definition of the state of health

Example: S-Prealbumin



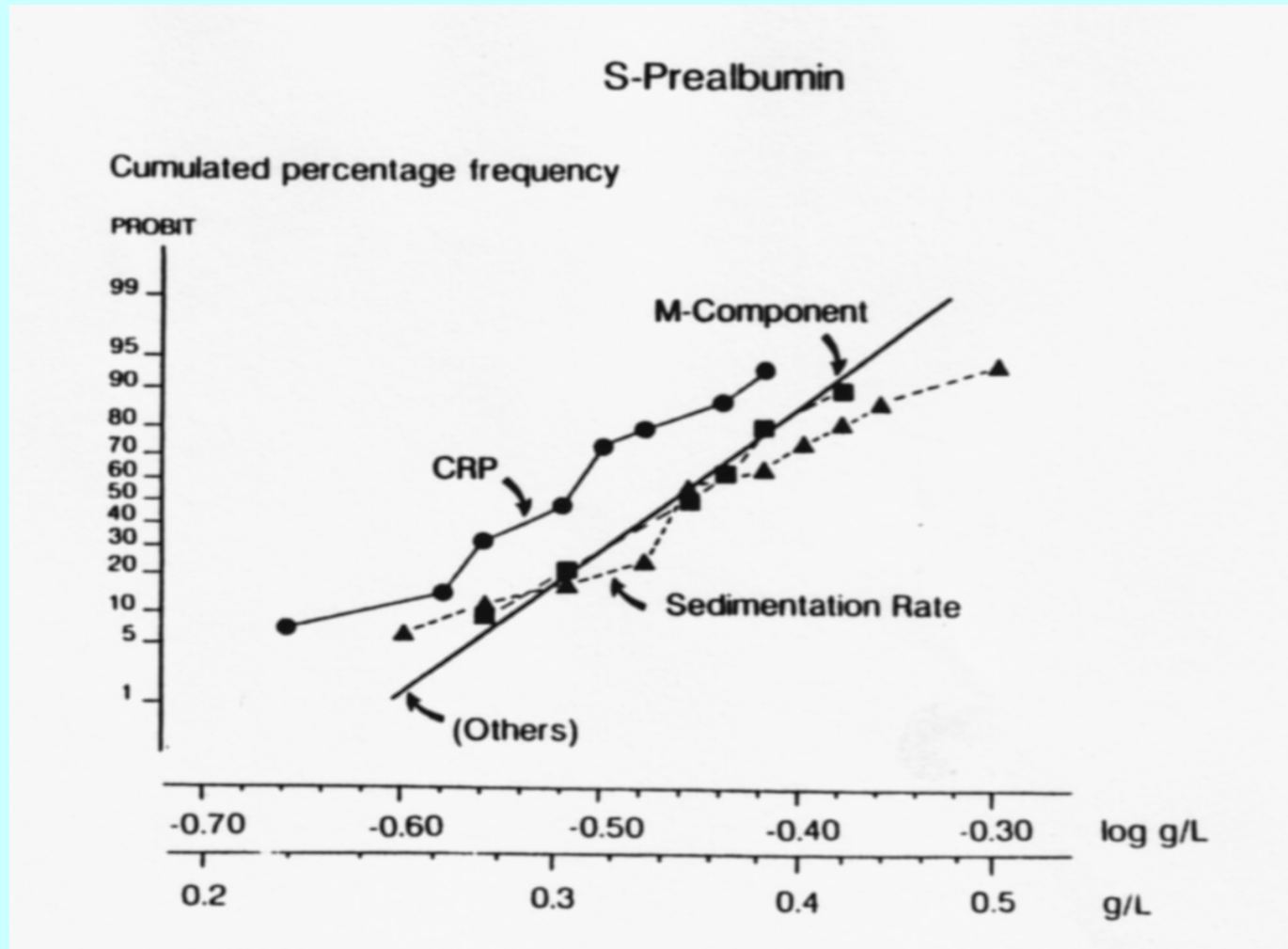
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Example: S-Prealbumin



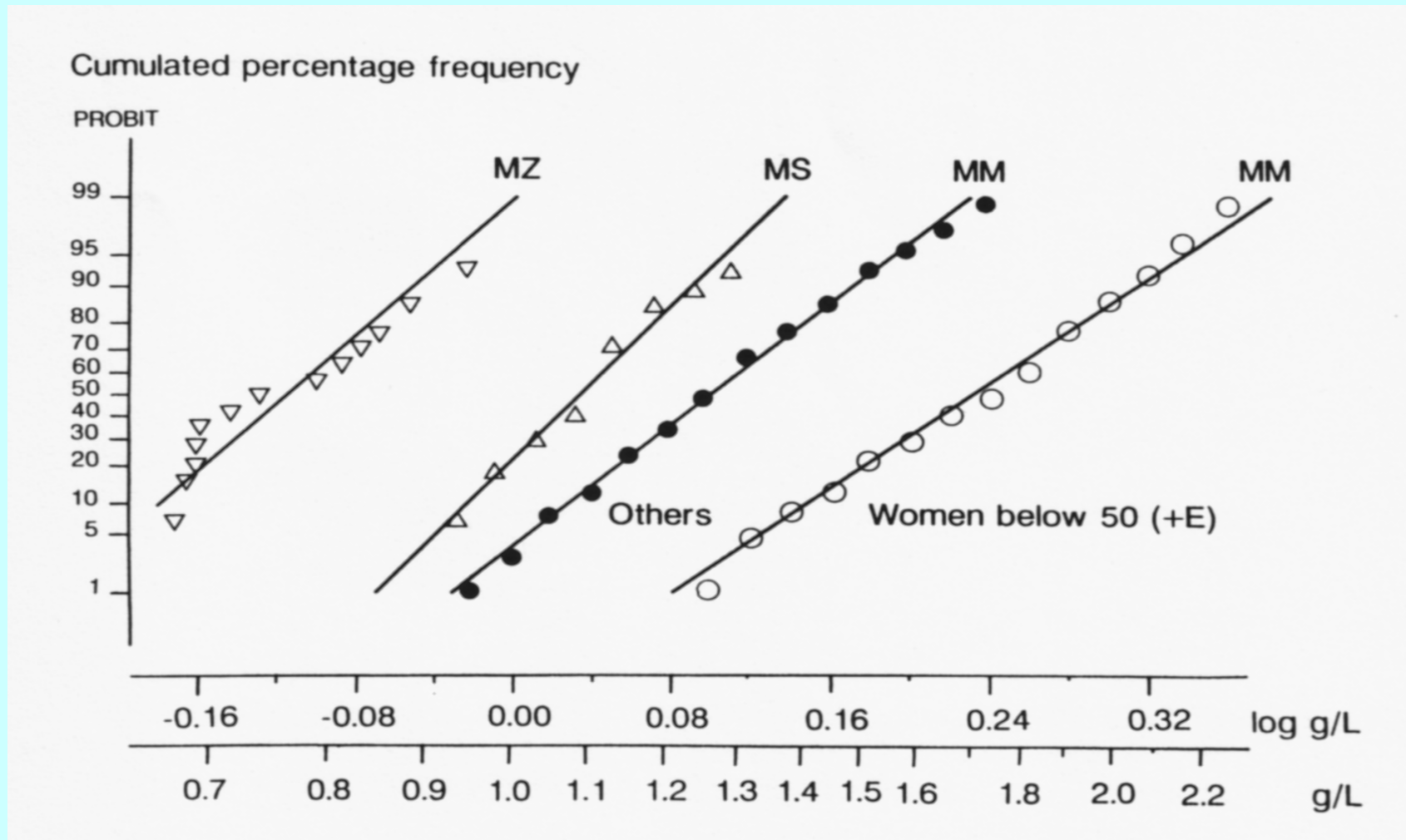
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S-Prealbumin, rule out criteria



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S-Antitrypsin, subgroups



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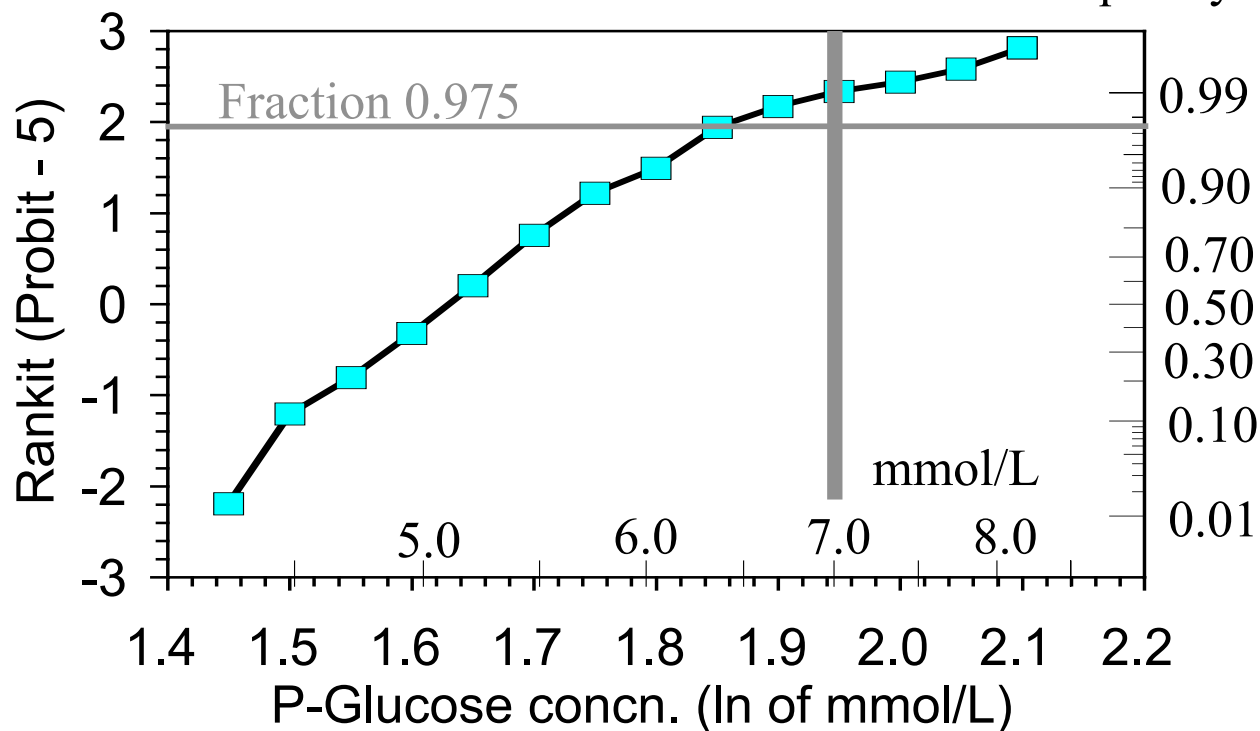
Example: P-Glucose

P-Glucose

Distribution(s) of Reference Values

Including HbA_{1c} > 6.3

Cumulated Frequency



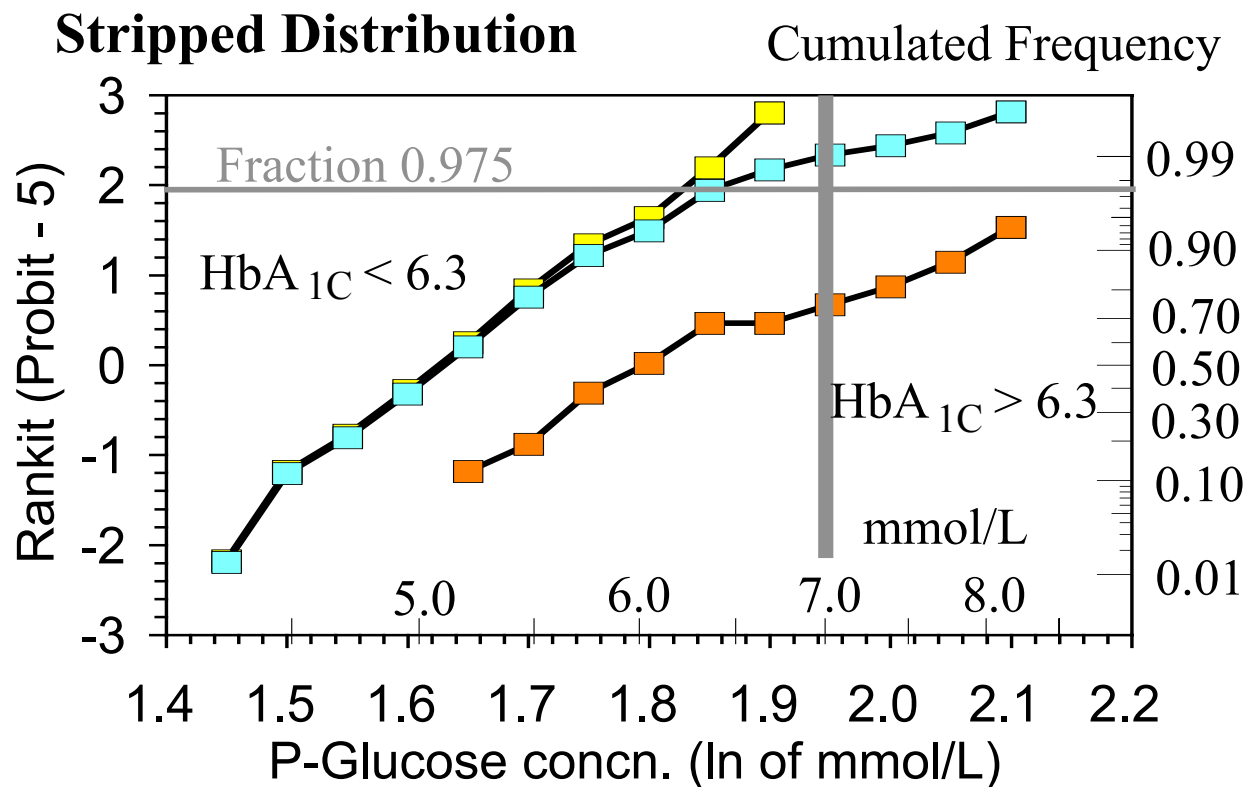
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Example: P-Glucose

P-Glucose

Distribution(s) of Reference Values



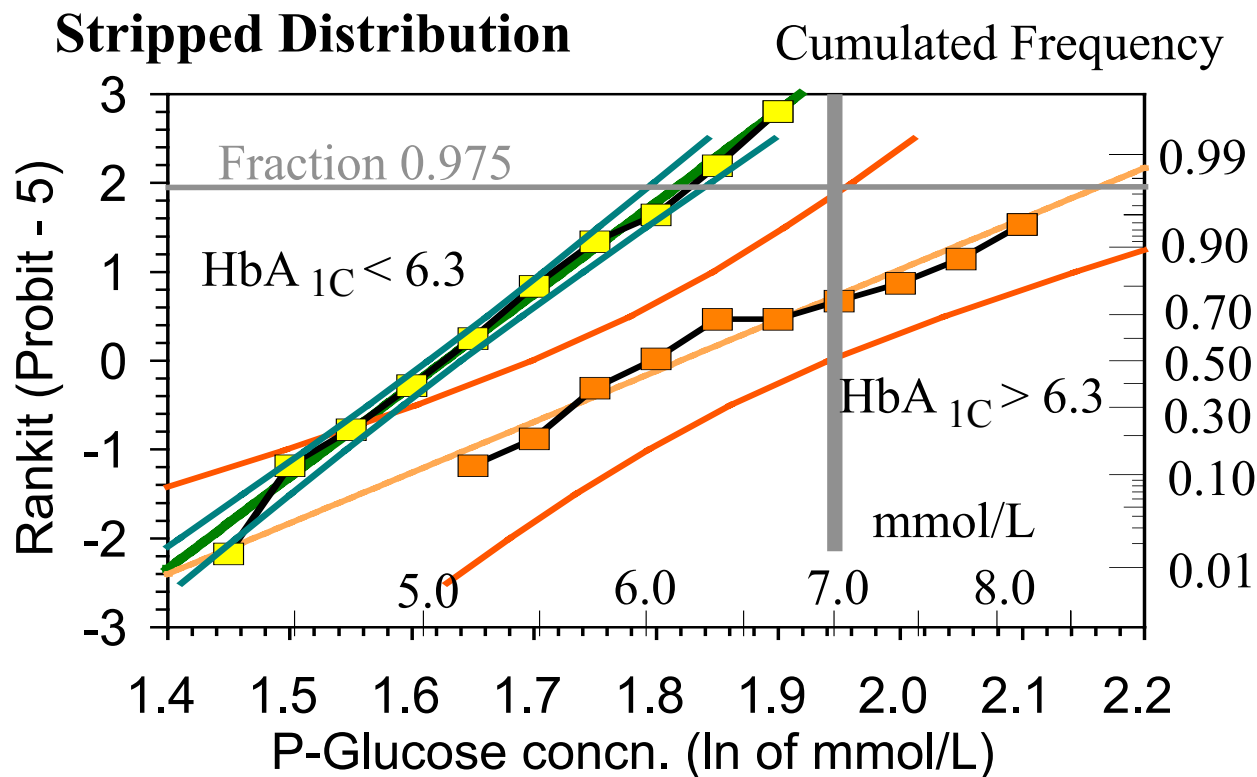
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Example: P-Glucose

P-Glucose

Distribution(s) of Reference Values



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Analytical prerequisites

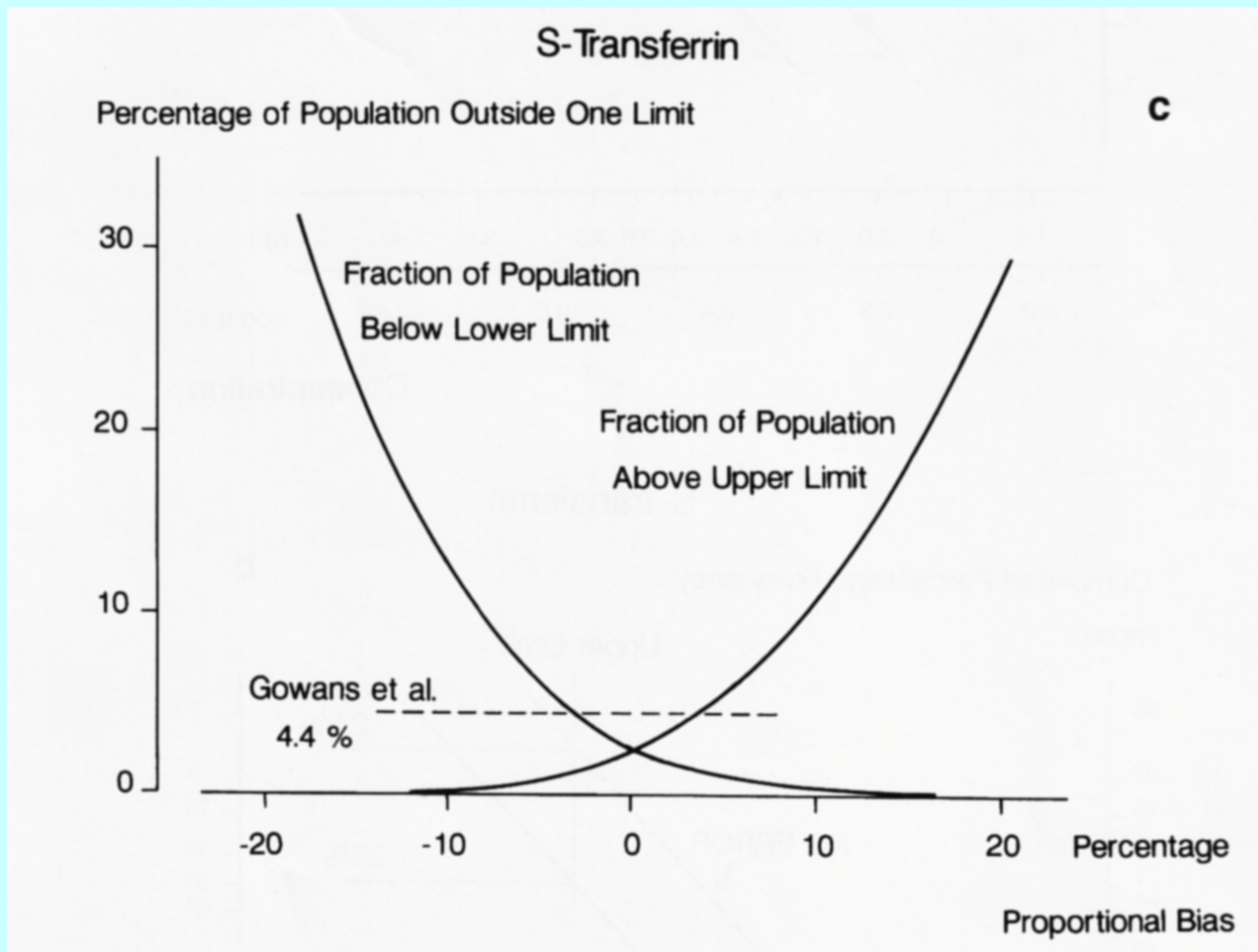
During establishment of the common reference intervals

- **Well defined standardisation**
- **Good specificity/interference**
- **High trueness (low bias)**
- **High precision (low imprecision)**
- **Documentation of the good quality**

Using the common reference intervals

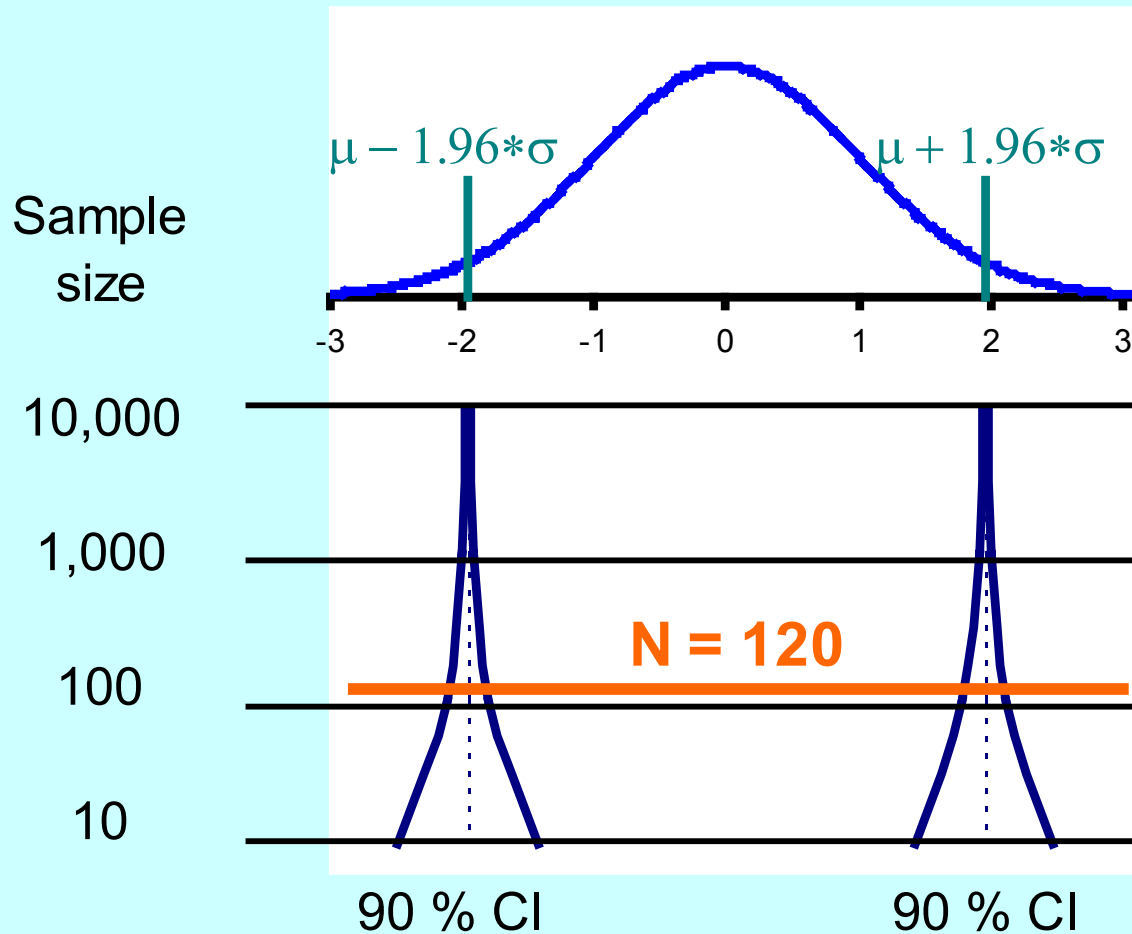
Documented analytical quality within the analytical quality specifications

Effect of analytical bias



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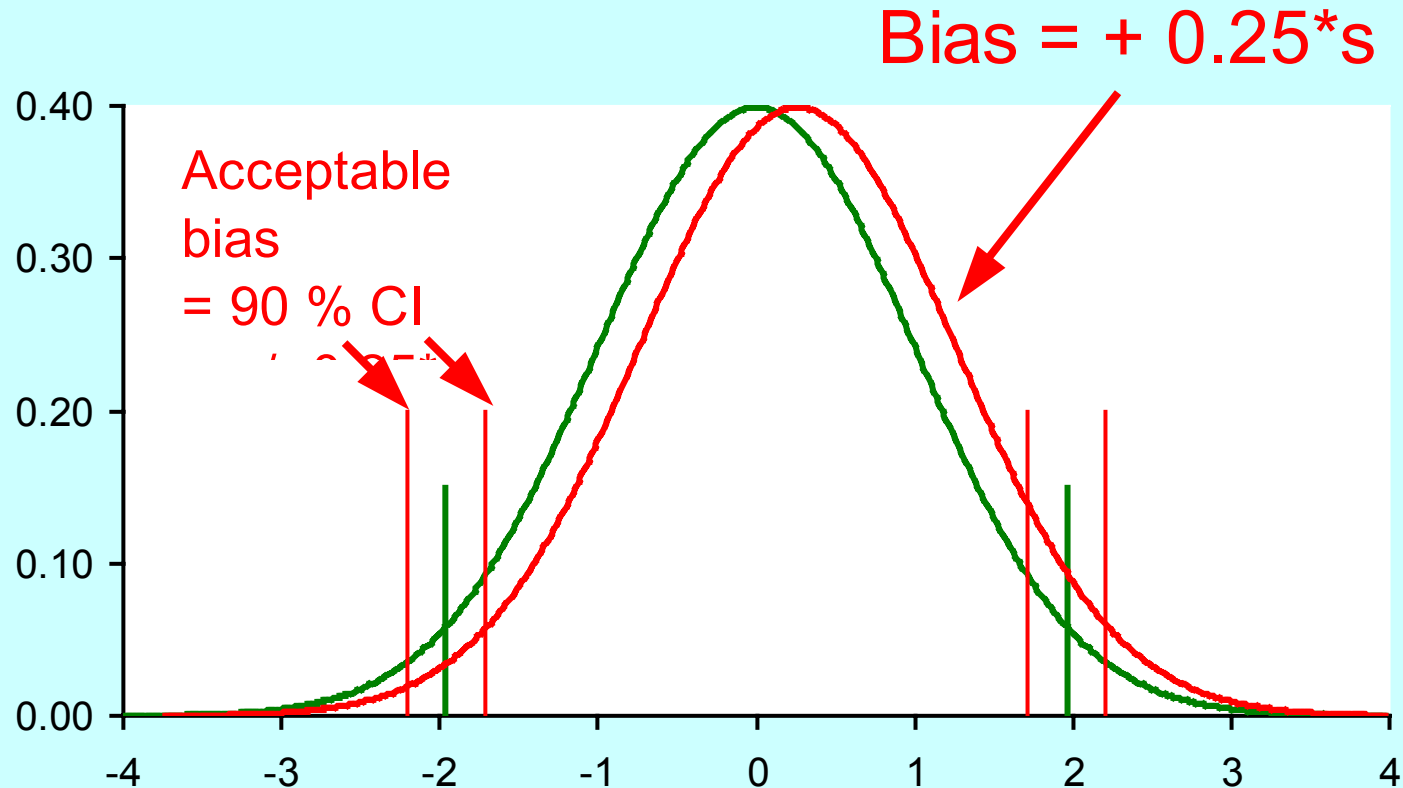
Sample Size and Confidence Intervals



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Confidence Intervals and Acceptable Bias

Effect of Bias



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Quality Specifications for Bias

Specifications for Bias:

Gowans et al. (1988)

$$| \text{Bias} | < 0.25 * CV_{\text{Population}}$$

Acceptance by the users ?

- Are the reference intervals reliable ?
- Will they last for many years ?
- How can we be sure that our calibration is the same ?
- We must change our laboratory book

Summary

- The need for common reference intervals
- Cooperation
- Prerequisites for establishing common reference intervals
- Acceptance by the users