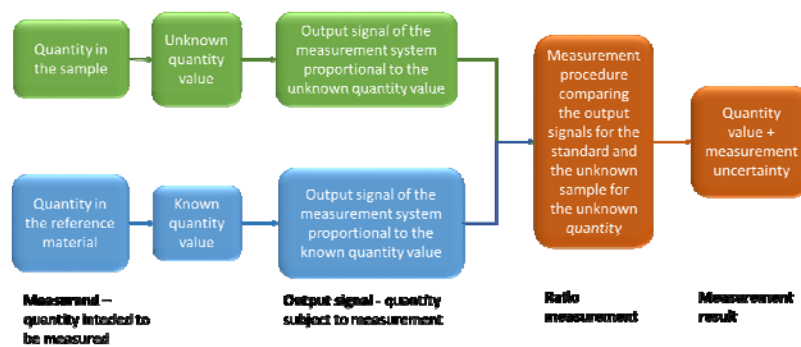


# Measurement and Diagnostic Uncertainty in Laboratory Medicine

Elvar Theodorsson







## Measuring means comparing



## Comparing in chemistry

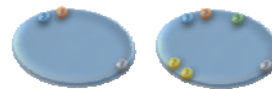
- Based on physical properties
- Prone to “influence quantities”

## Influence quantities 1(2)

- The presence of “matrix factors” 
- Inability to produce the substance in a pure form that can be weighed 
- Molecular heterogeneity, e.g. transferrin, LH, FSH, TSH 
- Detection of different epitopes 

## Influence quantities 2(2)

- Lack of knowledge of which epitopes of molecules are medically most relevant, e.g. most substantial biological activity or best diagnostic properties
- Changes in posttranslational modification of molecules e.g. LH and FSH during the ovarian cycle



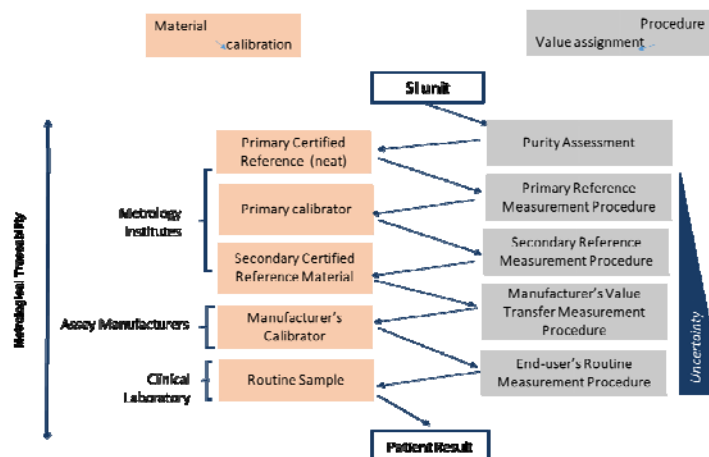
## Establishing traceability 1(2)

- Specify the measurand
- Choose a suitable
  - Measurement procedure
  - Model equation
- Demonstrate by validation that
  - That all significant influence quantities have been taken into account in the model equation
  - The measurement conditions are adequate

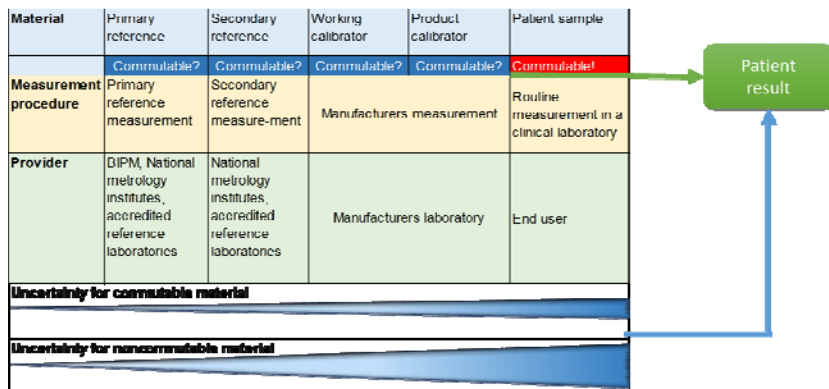
## Establishing traceability 2(2)

- Establish traceability for each influence quantity
  - Choose appropriate reference standards
  - Calibrate using these standards
- Evaluate the uncertainty

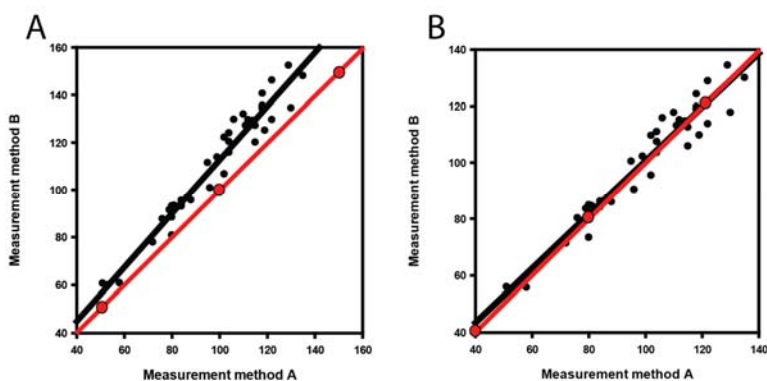
## Representative Measurement Traceability Chain



## Influence quantities in the traceability chain

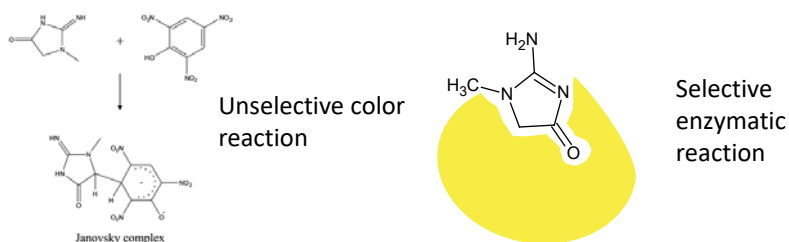


## Commutability



## Selectivity VIM 3 - 4.13

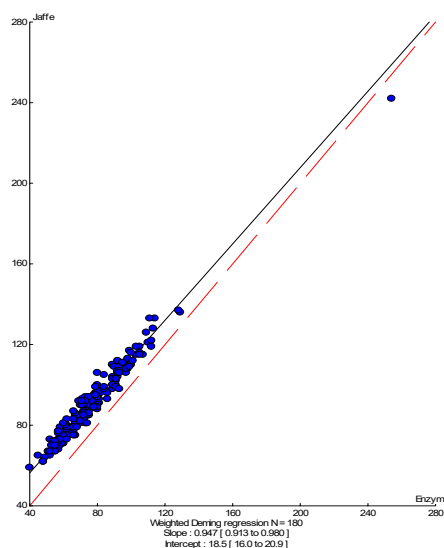
"Property of a measuring system used with a measurement procedure, whereby it provides measured quantity value for one or more such that the values of each measurand are independent of other measurands or other quantities in the phenomenon, body, or substance being investigated."



Comparison of the concentration of creatinine in 180 plasma samples measured using Jaffe and enzymatic methods

$$\text{Jaffe} = 0.947 * \text{Enzymatic} + 18.5$$

$$\text{Enzymatic} = \frac{\text{Jaffe}}{0.947} - 18.5$$



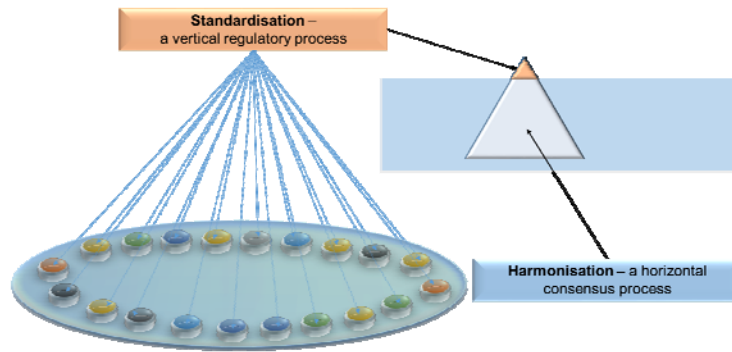
## Success stories in standardization in laboratory medicine 1(2)

- Molecules with simple molecular structures, LC/GC MS, ion-selective electrodes
- Standardization of methods for measuring enzymatic activity
- Enzymatic methods for measuring substances earlier measured by non-specific colorimetric procedures (e.g. creatinine)

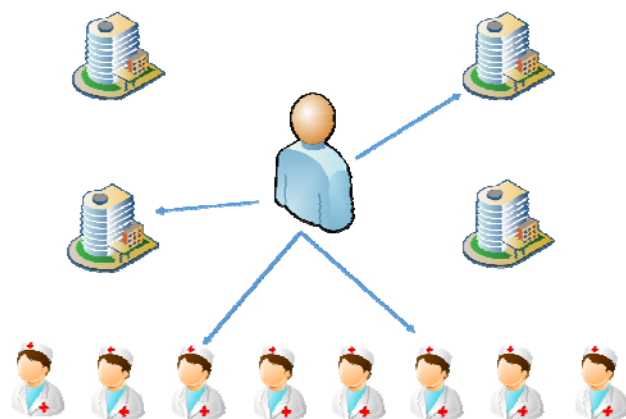
## Success stories in standardization in laboratory medicine 2(2)

- Cholesterol measurements
- Glycated hemoglobin
- Carbohydrate-deficient transferrin

# Standardisation vs harmonisation

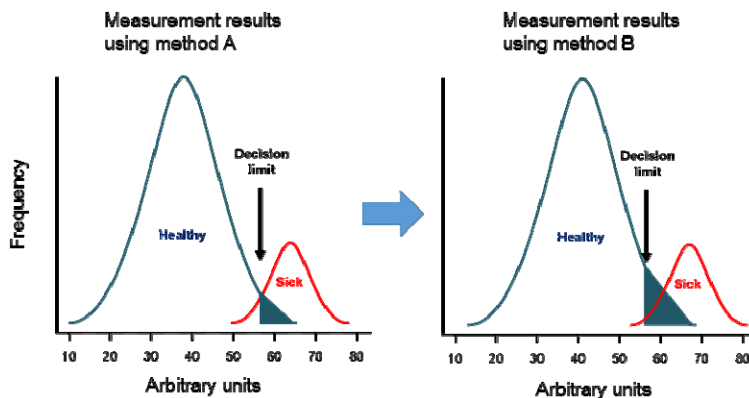


# Levels of diagnosis and monitoring

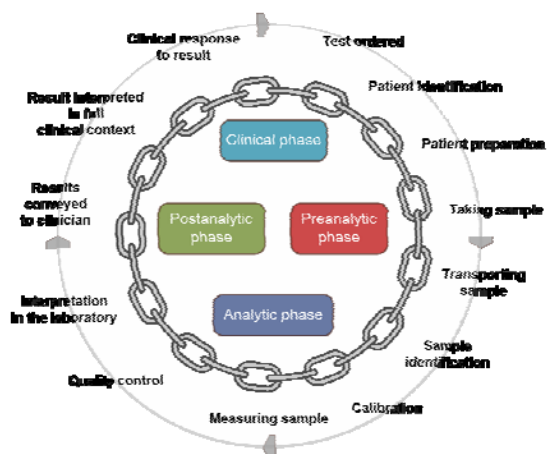




## Medical consequences of bias

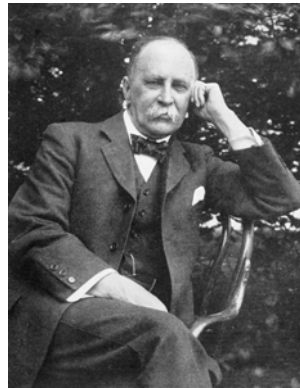


## The testing chain in laboratory medicine

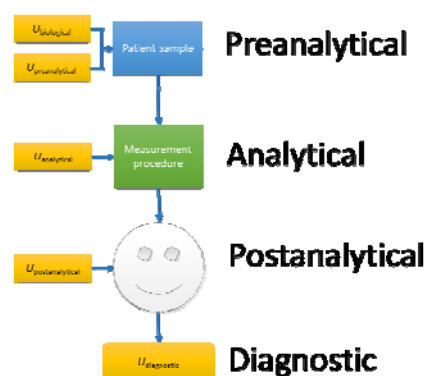


## “Medicine is a science of uncertainty and an art of probability”

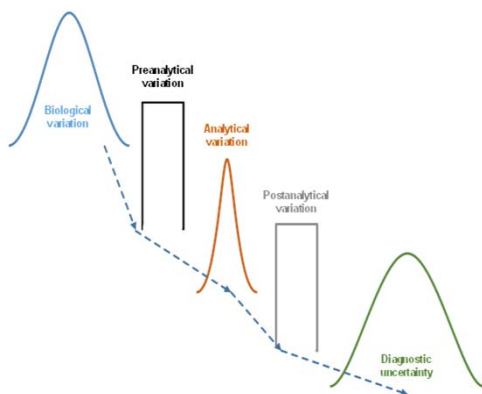
- Quotation from Dr. William Osler (1849.1919)
- Work in medical laboratories depends on the same metrological principles as work in other laboratories, but is also focused on reducing and handling numerous other uncertainties.



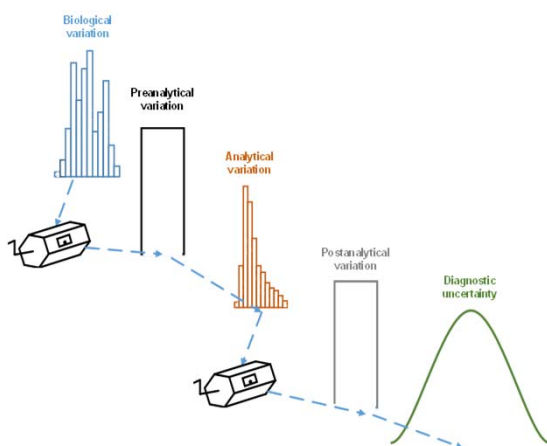
## Uncertainty components



# Monte-Carlo



# Resampling



## Ulysses syndrome

- The ill effects of too extensive diagnostic investigations conducted because of a false-positive result in the course of routine laboratory screening, diagnostic and monitoring procedures



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