The role of EQA for reliable post-analytical software
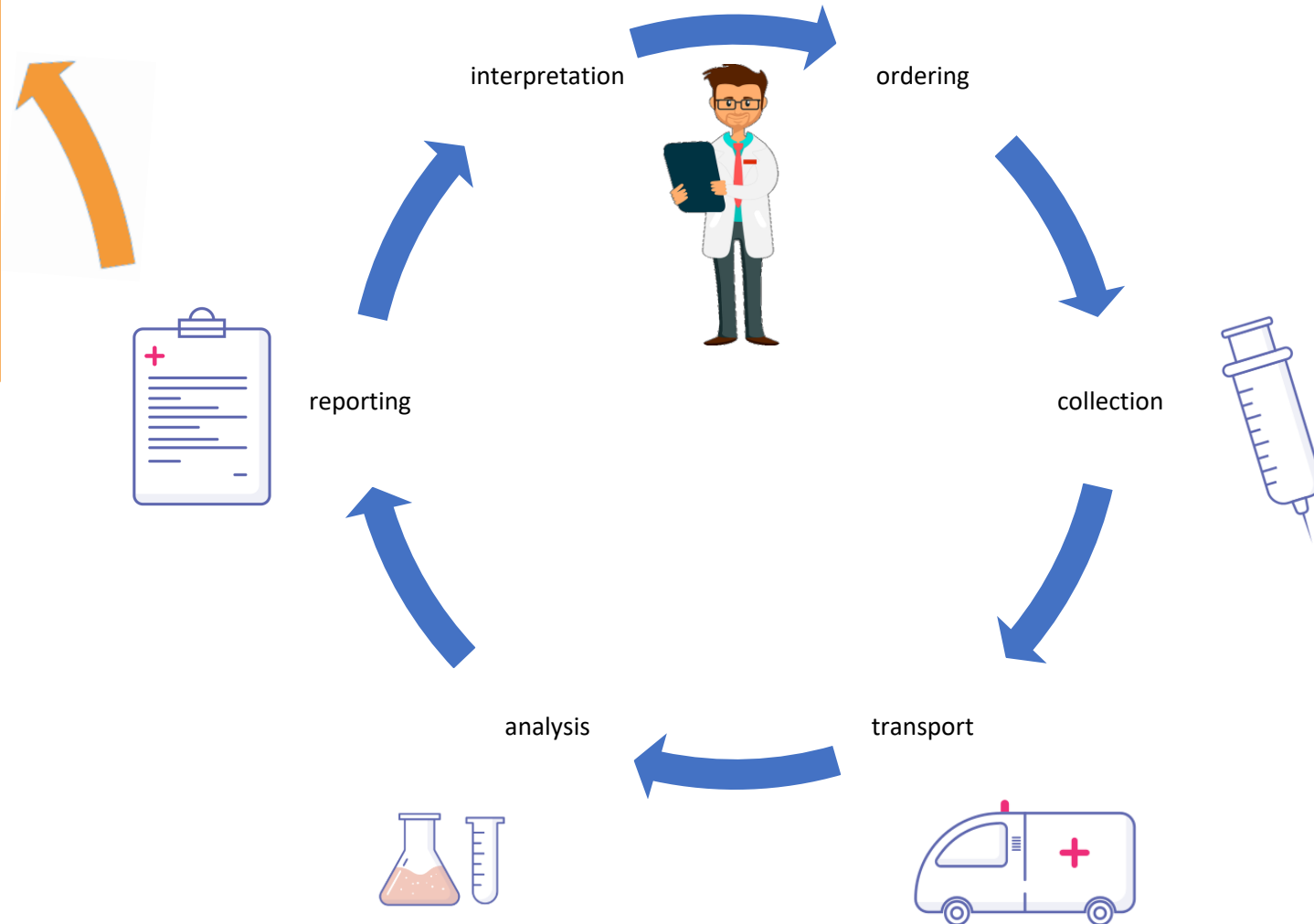
Andreas Bietenbeck

Medical Director MVZ Ärztliche Laboratorien München-Land Germany

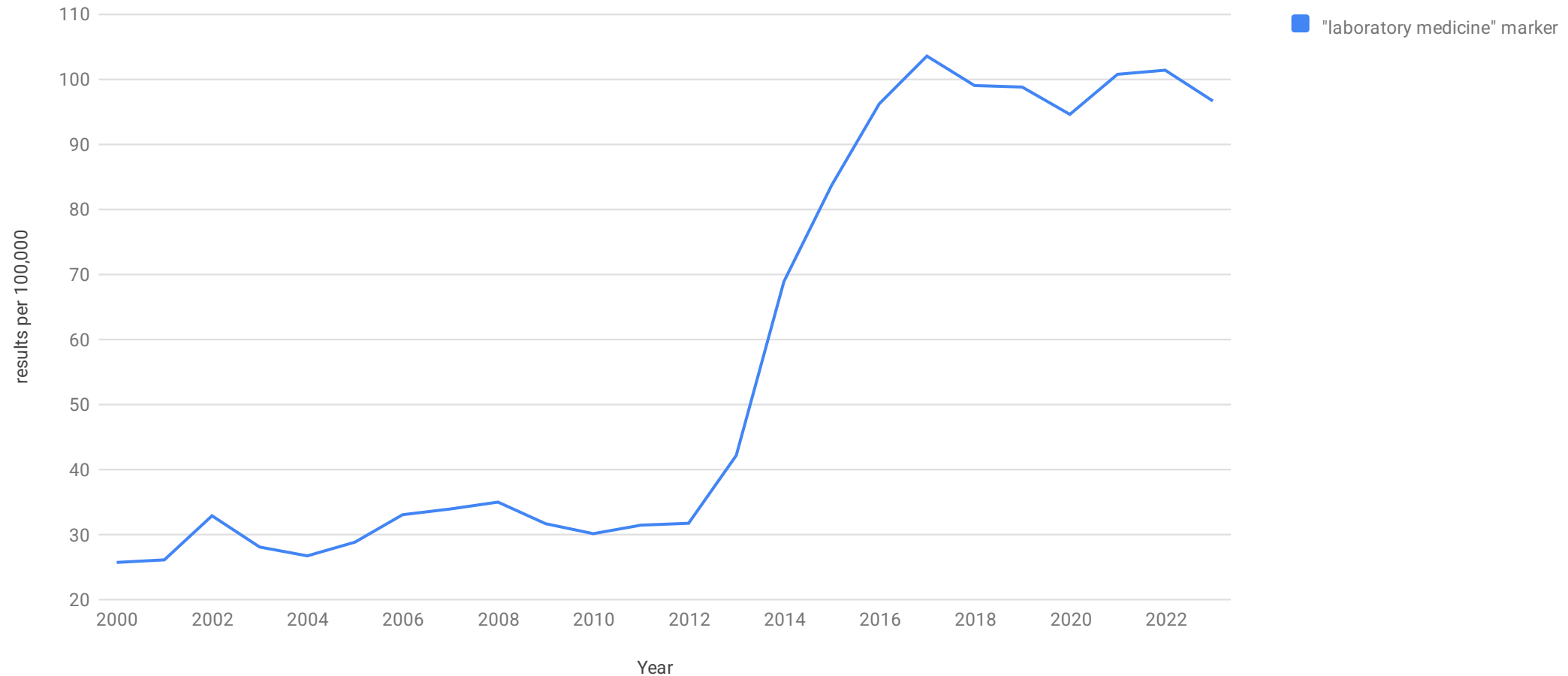lab@bietenbeck.net

Post-analytical software is needed

- Detection of high risk patients
- Interpretation of complex data
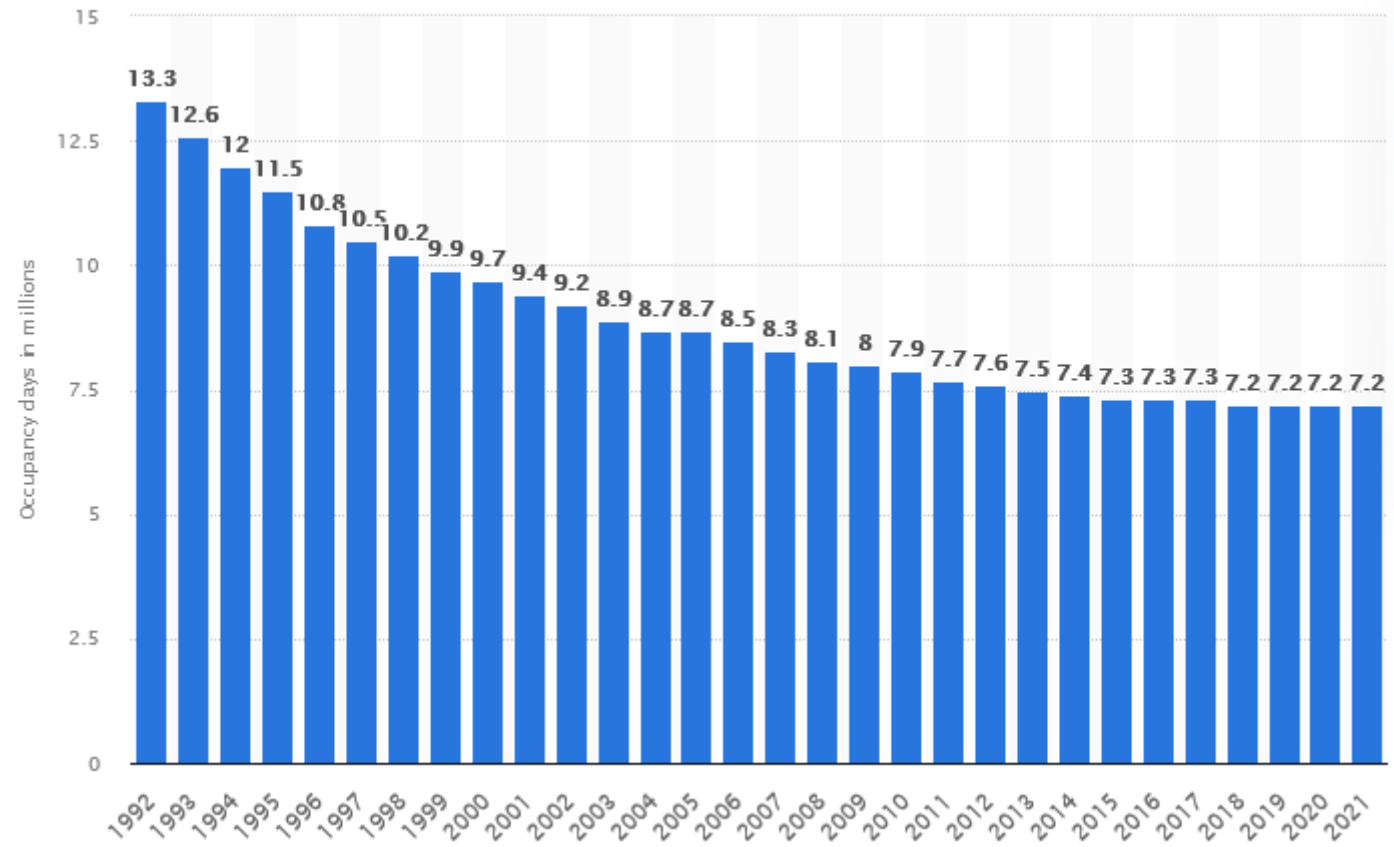- Diagnostic support
- ...

adapted from Gungoren *CCLM* 2023

interpretation

ordering

collection

transport

analysis

reporting

EQALM

Laboratory medicine discovers more markers

EQALM

Results per 100,000 citations in PubMed
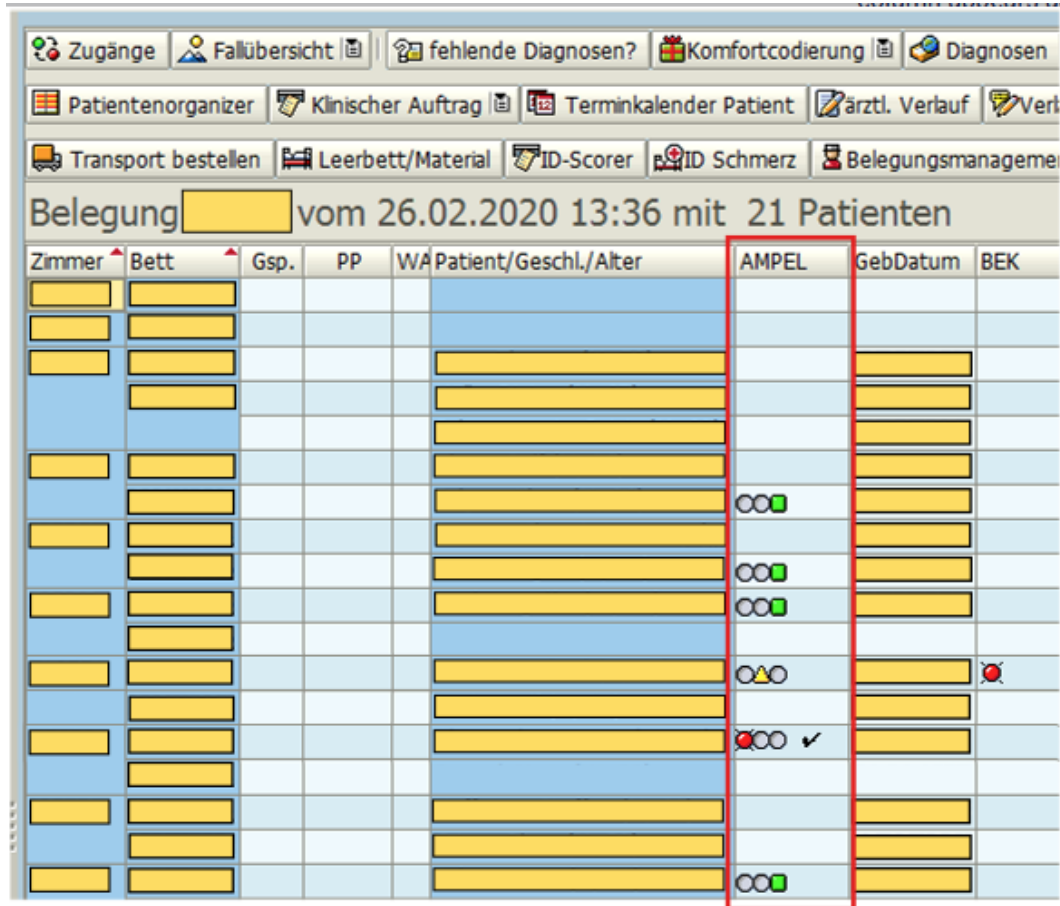proportion for each search by year, 2000 to 2023

results per 100,000

110
100
90
80
70
60
50
40
30
20

2000 2002 2004 2006 2008 2010 2012 2014 2016 2018 2020 2022

Year

■ "laboratory medicine" marker

Cost pressure increases

Working age population decreases

Canada 2022 **65.6** · France 2022 **61.5** · Germany 2022 **63.8** · Israel 2022 **59.8** · Italy 2022 **63.5** · Japan 2022 **59.4** · Sweden 2022 **62.2** · United Kingdom 2022 **64.0** · United States 2022 **64.8**

OECD
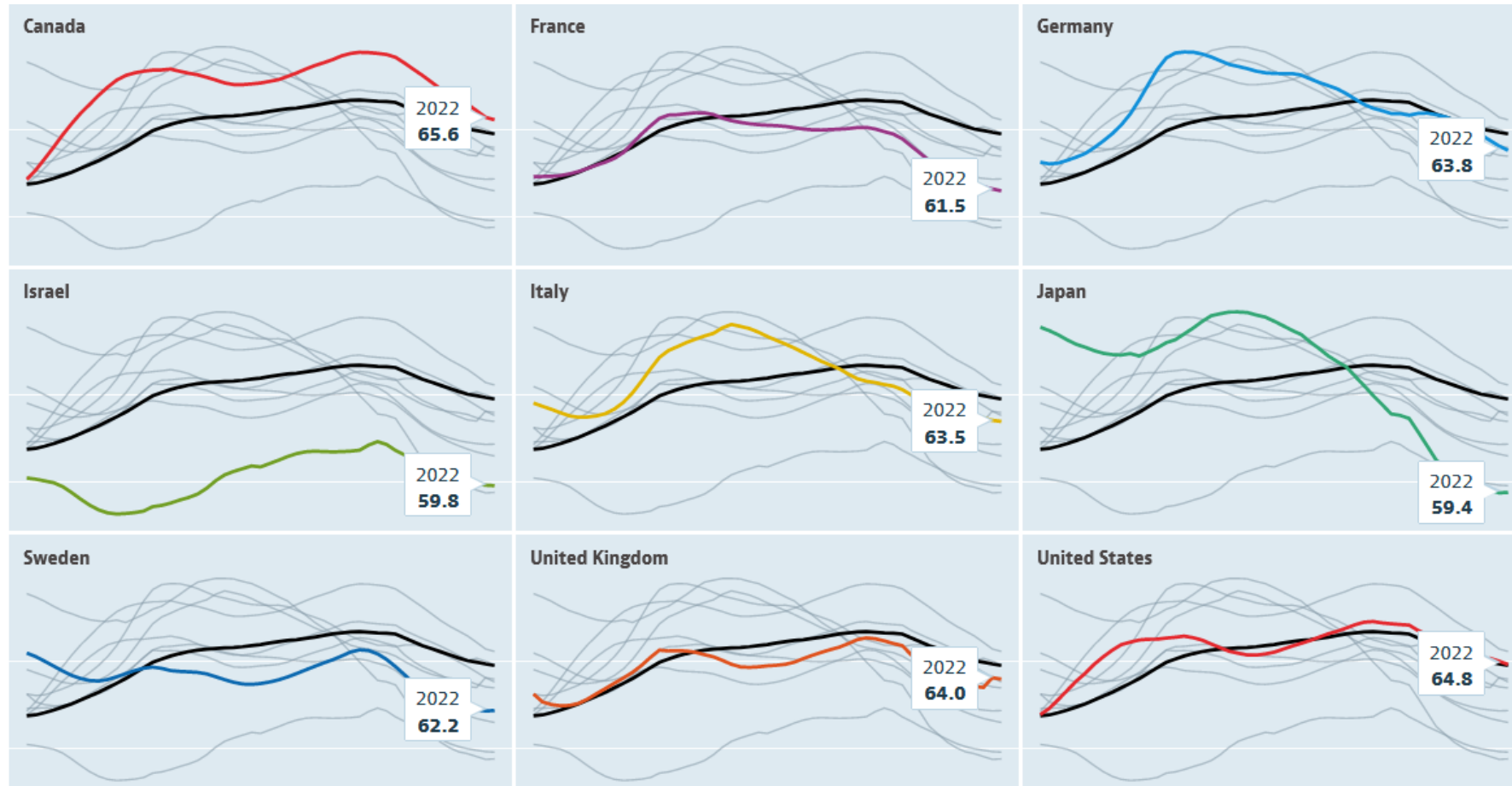
Software with different complexity
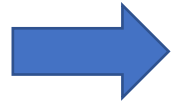

Costa et al. JMIR Med 2021

Master et al. Clin Chem 2023

Software is expensive to build but cheap to run

CRP by XY in Serum
PCT by AB in Serum

CRP by XY in whole blood
PCT by CD in Serum

CRP by Z in Serum
PCT by CD in Serum

CRP
PCT

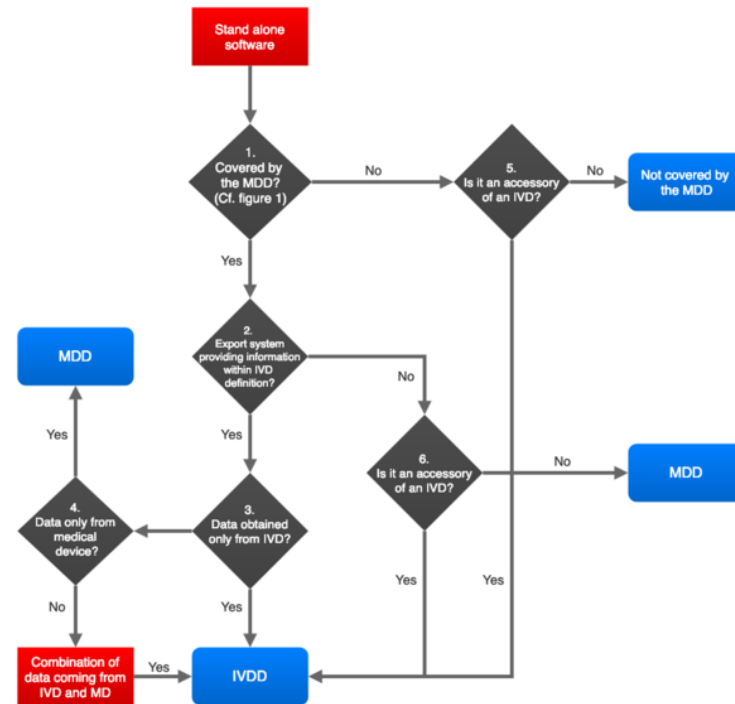# Requirements for software usable with diverse measurements

- Measurements need to produce a comparable result for a comparable patient
  - Approximately the same bias
  - Approximately the same imprecision

Not needed:

- harmonized reference interval

- harmonized units

- (Traceability)

Legal requirements lengthen software development

Flowchart for EU guideline MEDDEV 2.1/6 on IVD software (from Johner „Correctly classifying IVD software")

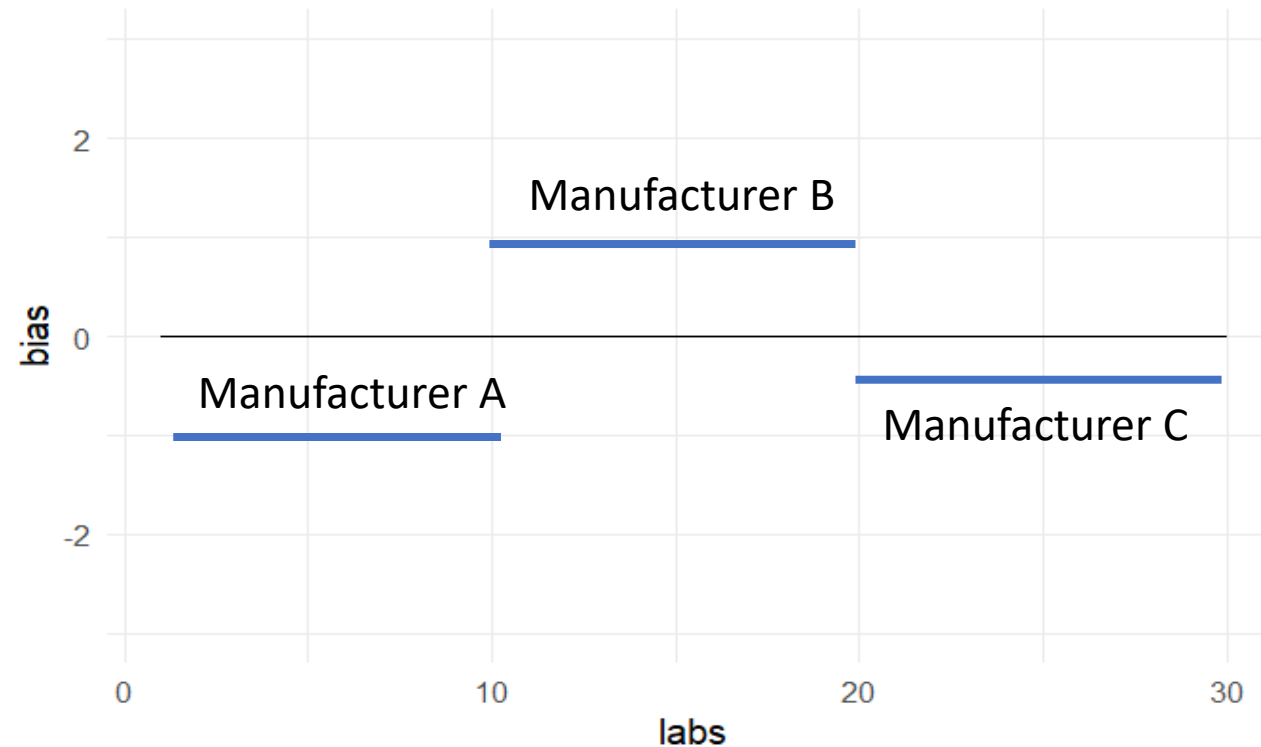- Software development and implementation need long-term stability

Ideal world

- Traceable measurement

- Commutable material

- reference method procedure as target value
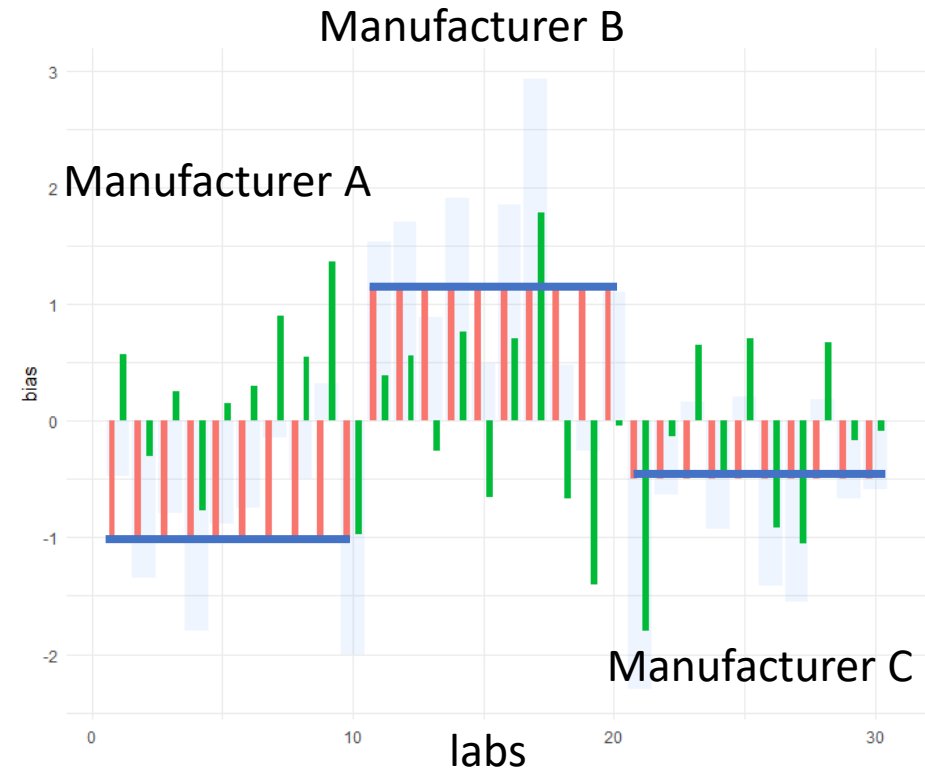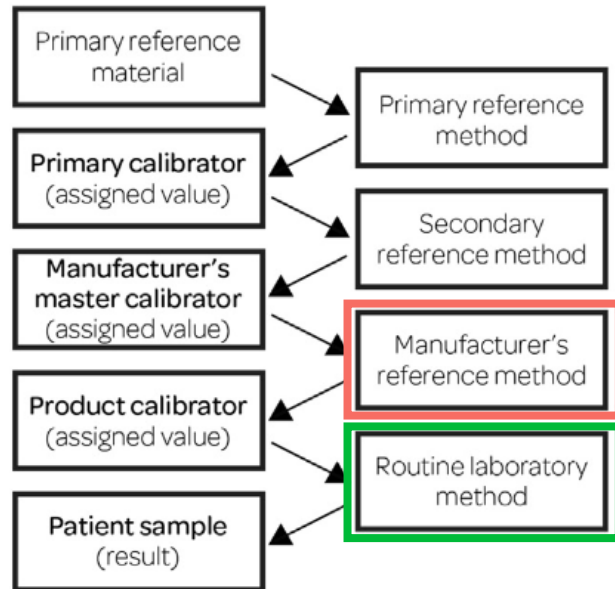
$\Rightarrow$ Comparability of results

$\Rightarrow$ Long-term stability

Peer groups with consensus values for non-commutable samples

- Robust central tendency (median, "algorithm A") as target value (ISO 13528)

Consensus values also compensate manufactures' bias

EQAs with consensus values are easy to pass

- True value 5, bias 0

- Target value 5

- Imprecision 0.5 => CV 10%

- True value 5, bias 5

- Target value 10

- Imprecision 0.5 => CV 5%

$\Rightarrow$ consensus values for "peer groups" can impede comparability of results

$\Rightarrow$ Long-term stability not guaranteed

$\Rightarrow$ Error budget for consensus values should be smaller than for reference method values to account for bias of the peer group

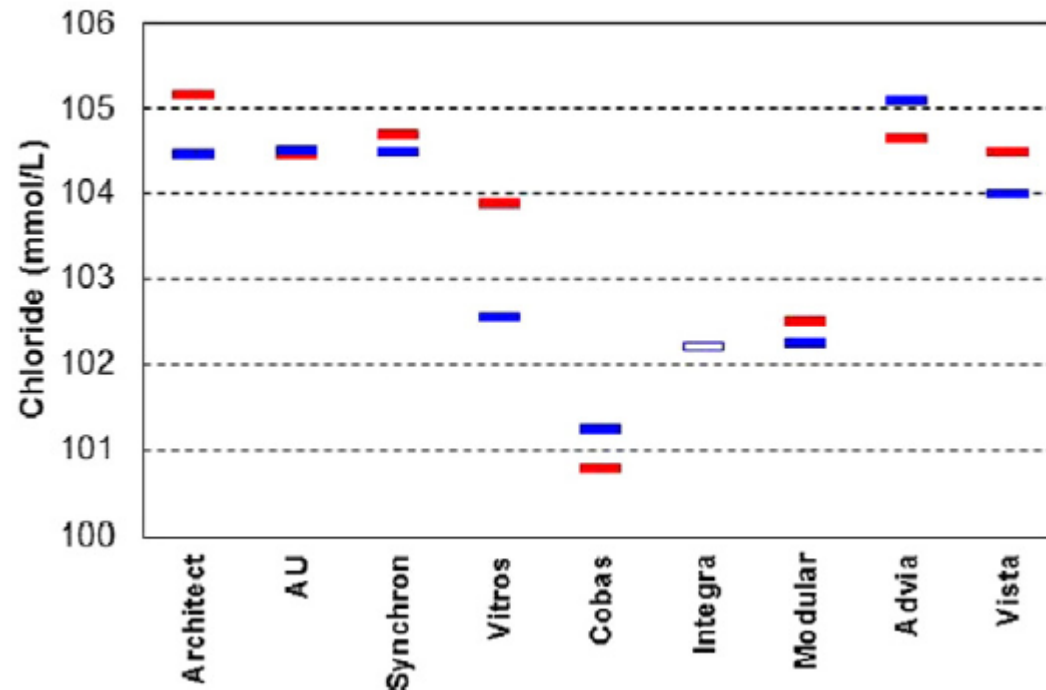# Better logistics can expand use of patient material
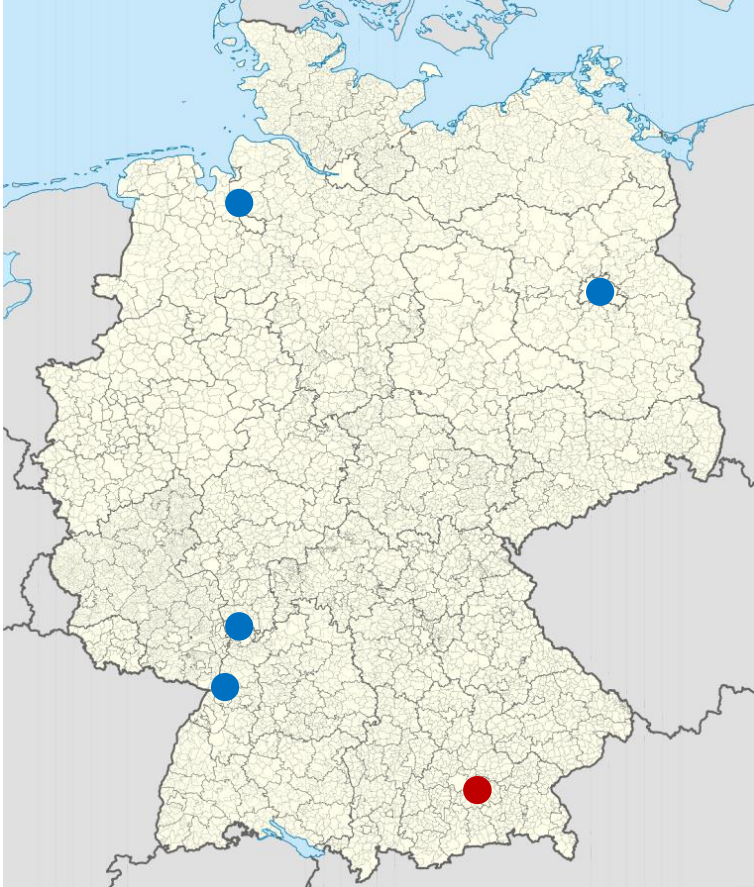
- Commutability guaranteed

- Smaller batches?

- Evaluation more complex?

- Limited range of target values ?

⇒focus on comparability

⇒Hard to guarantee long-term stability

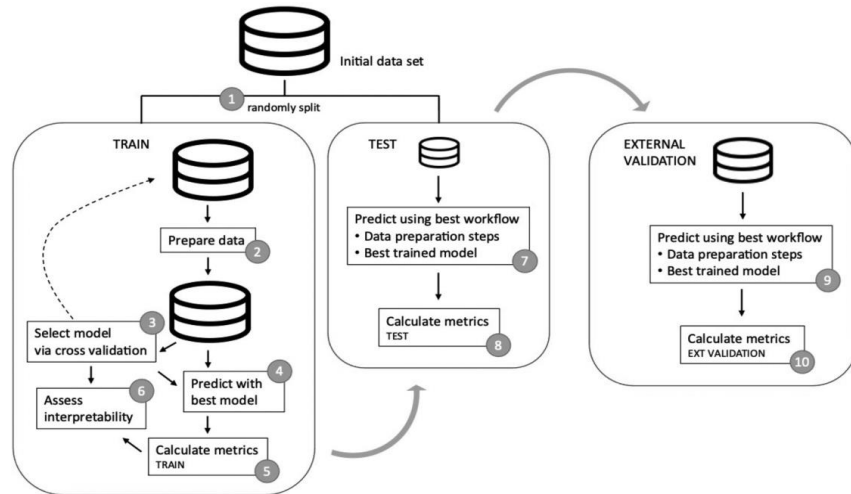# Data-driven QC can supplement traditional EQA

„Percentiler", Goossens et al., Clin Chim Acta 2015

- comparability ?
- long-term stability ?

Different test formats can have very different performance characteristics
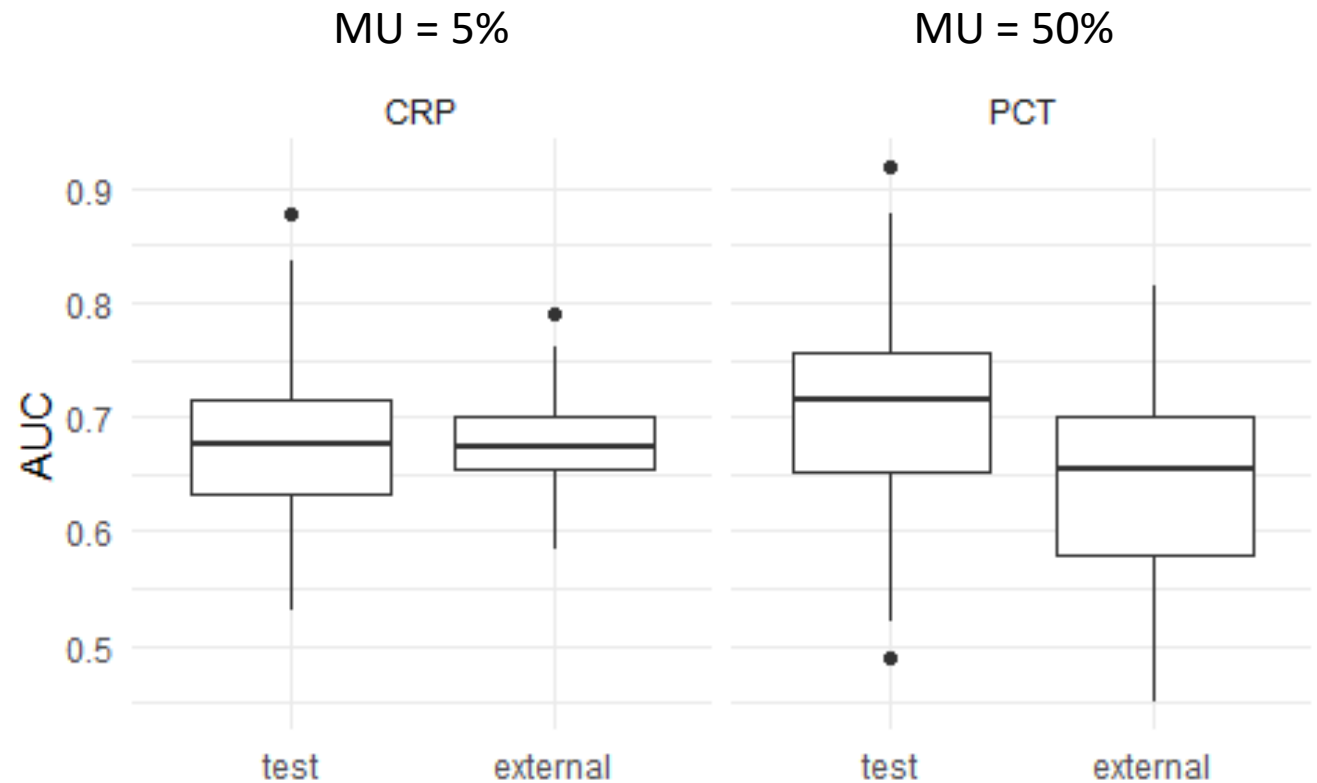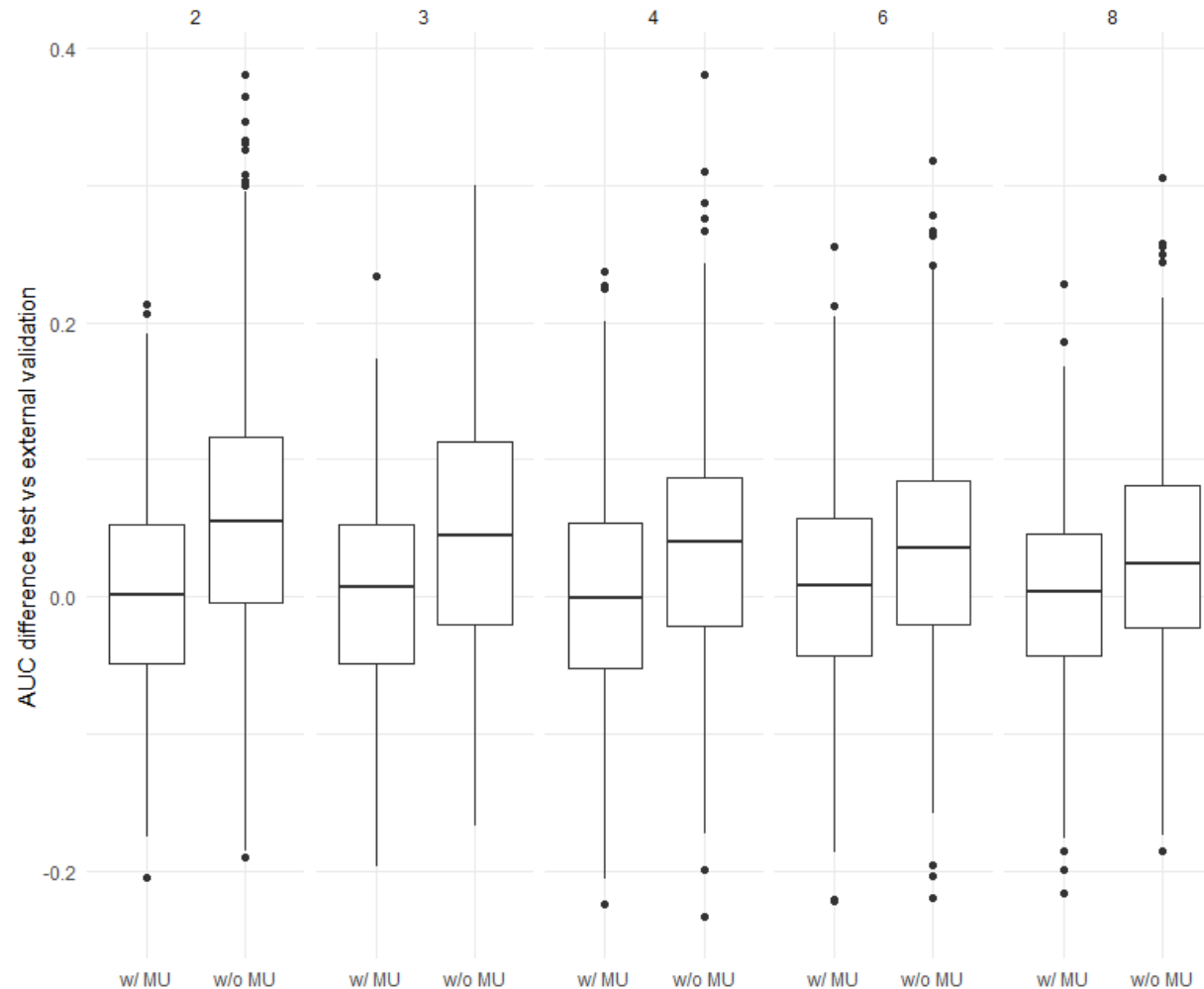
Simulation: Can Measurement Uncertainty (MU) provide the necessary information?
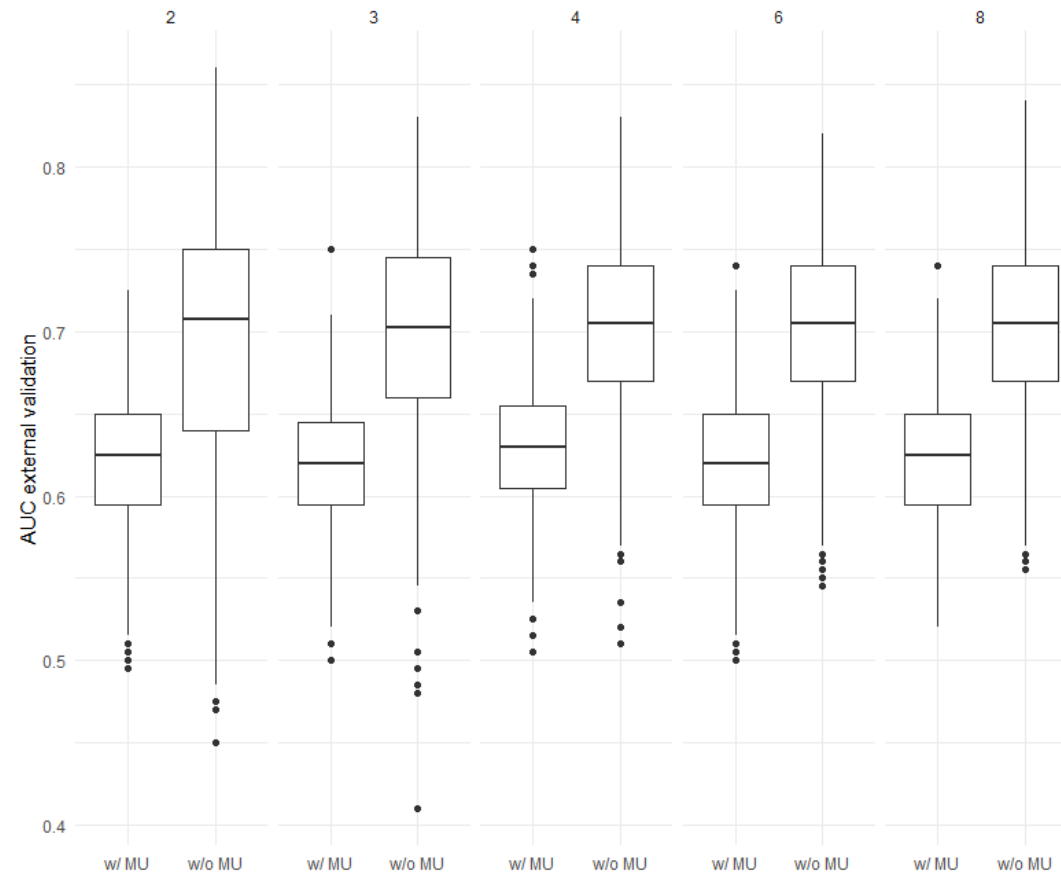

MU = 5%

MU = 50%

Master et al. Clin Chem 2023

When MU is included algorithms perform reliable even on new data sets

... but with MU included overall performace is considerably worse

- Post-analytical software is increasingly needed to interpret laboratory results.

- Comparable laboratory measurements with long-term stability facilitate development of post-analytical software.

- EQA schemes based on consensus values accounting for manufactures' bias, schemes with patient material and fast logistics and data-driven EQA schemes can foster comparability (and long-term stability) of measurements.

Thank you for your attention