Determination of lot-to-lot variability of reagents

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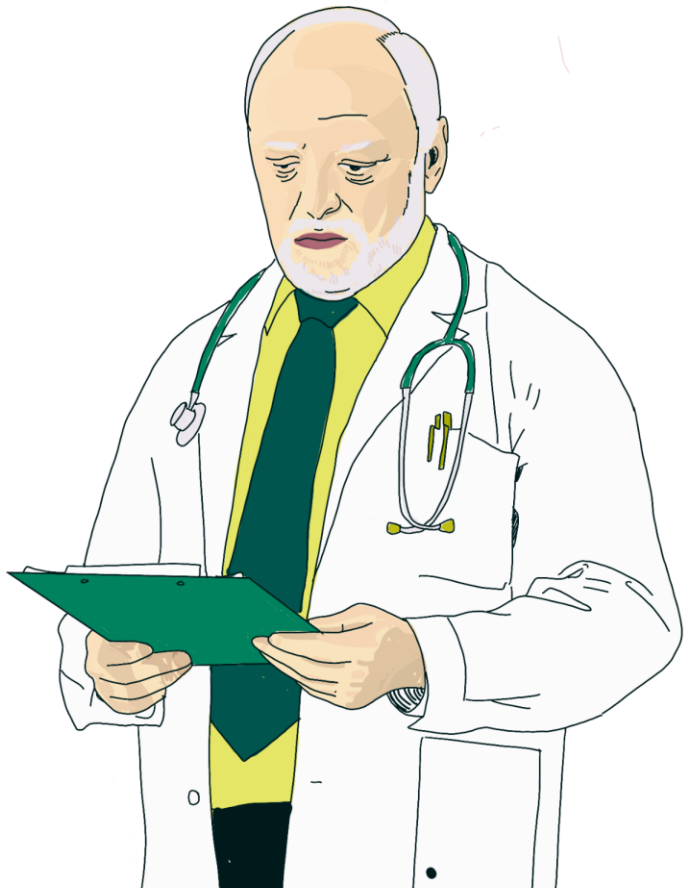
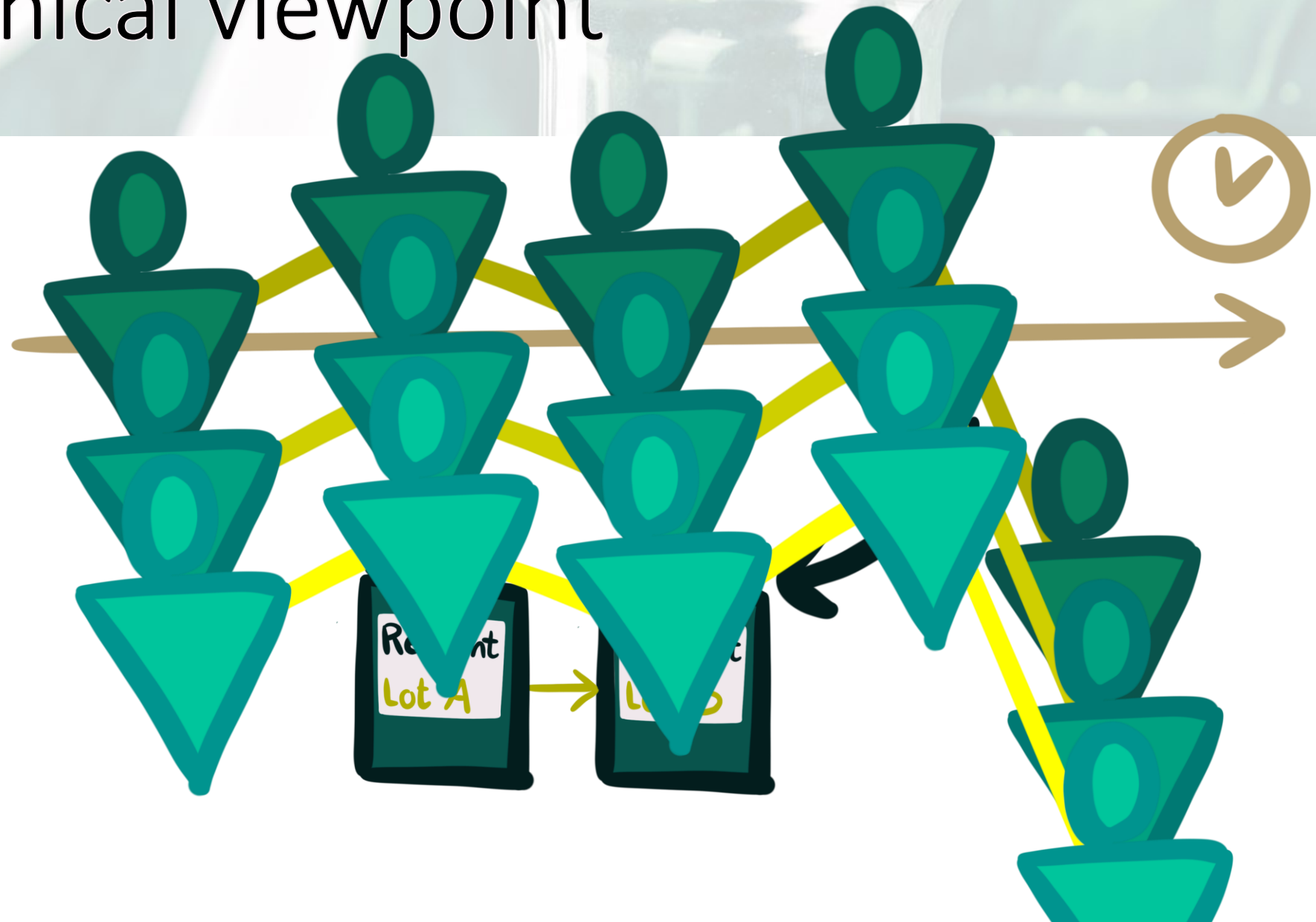
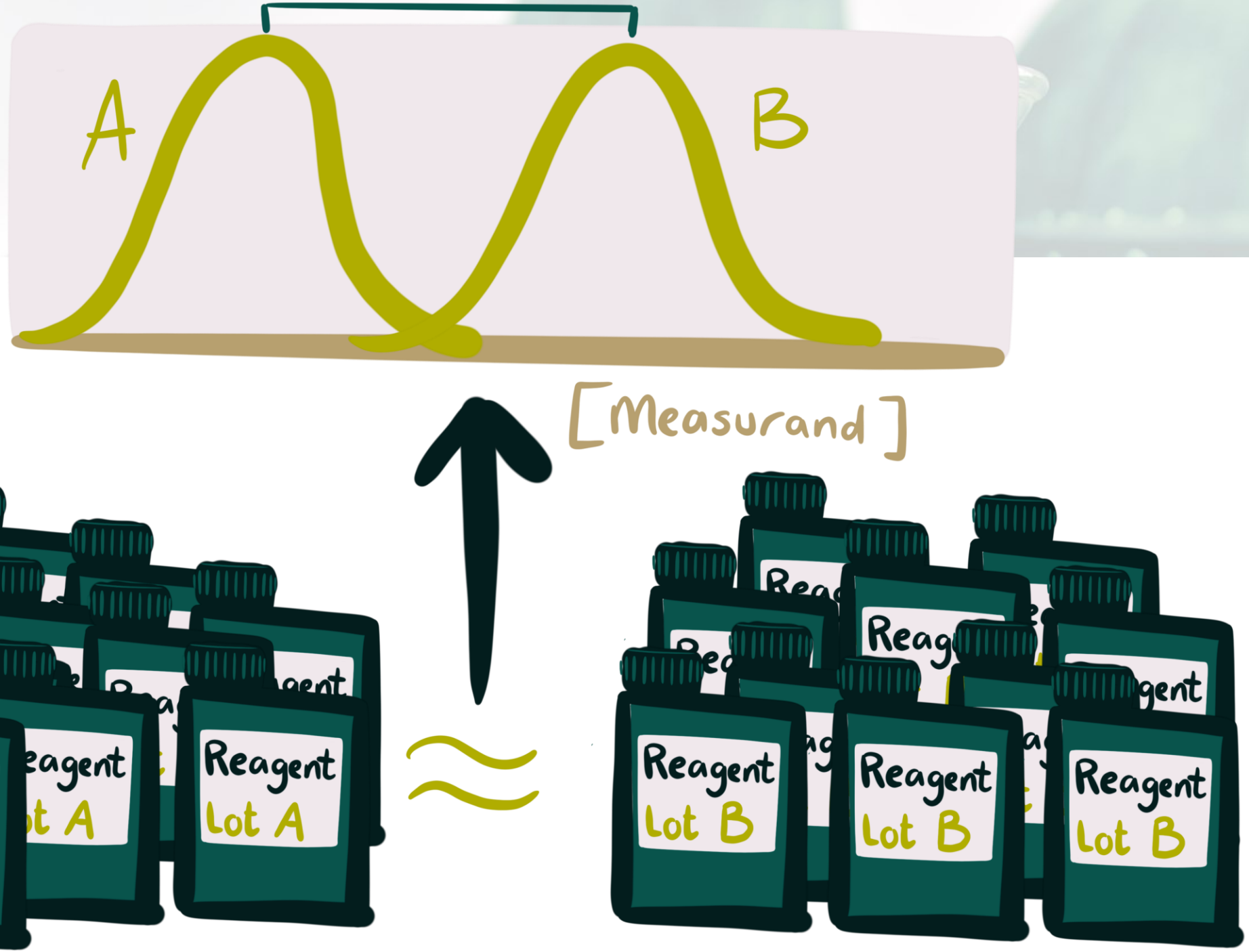
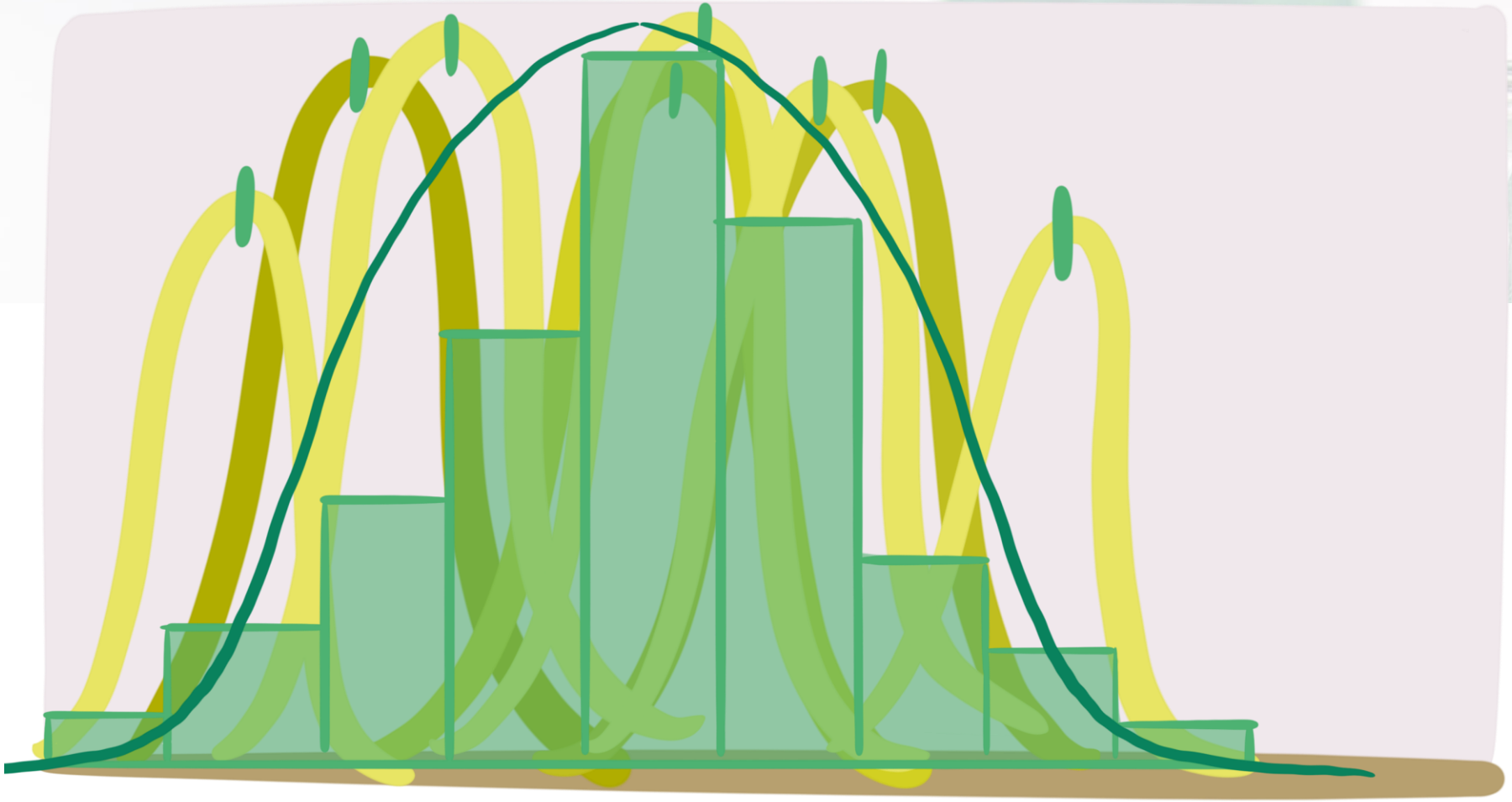
From a clinical viewpoint






A
B
[Measurand]
Reagent Lot A
Reagent Lot A
Reagent Lot A
Reagent Lot B
Reagent Lot B
Reagent Lot B



mean within lot

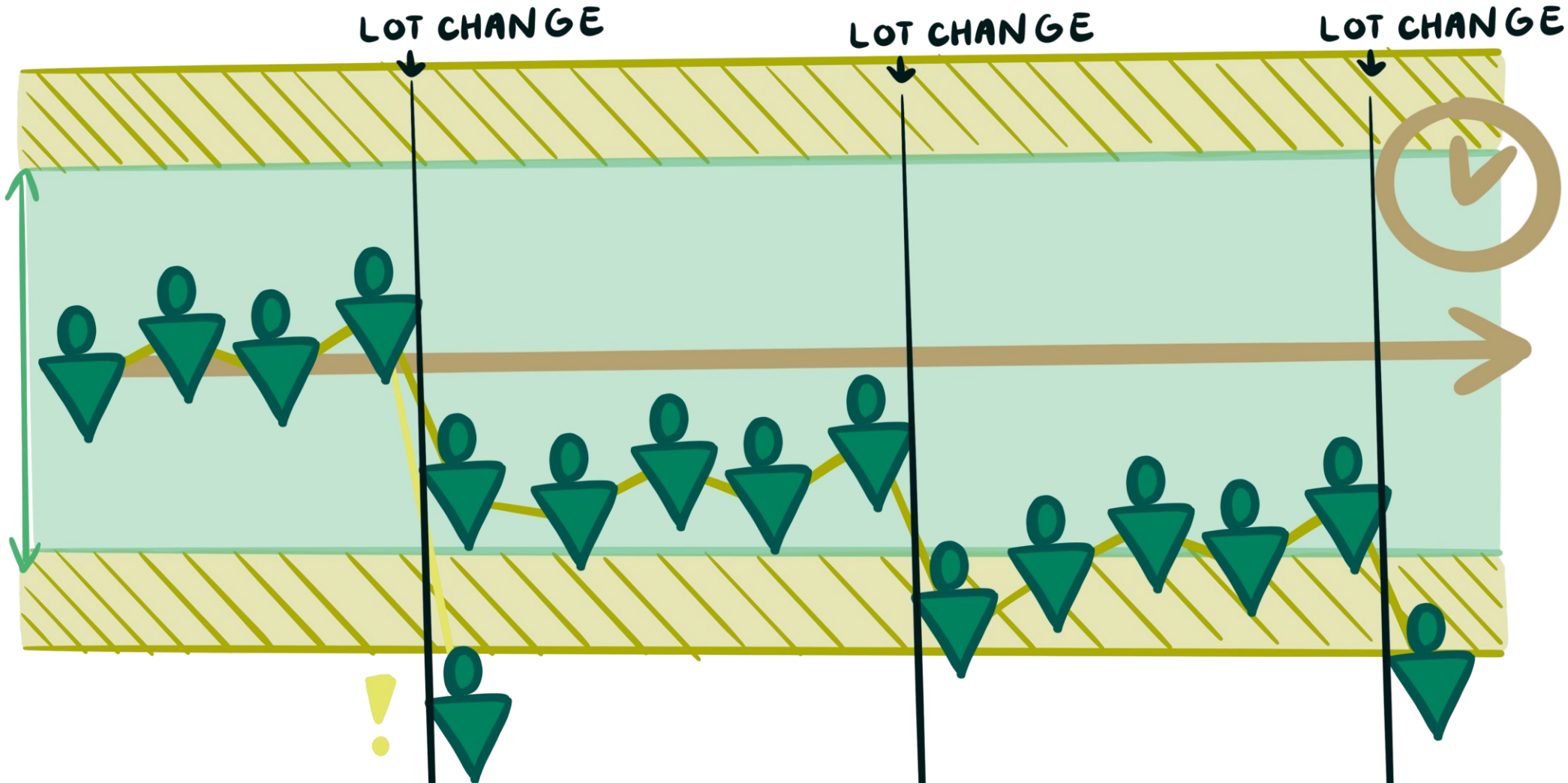
LTLV

LONG-TERM VARIATION

A, B, C, n

[Measurand]

Effect of LTLV?



Allowable LTLV – the theorem

EFLM Paper

Marith van Schrojenstein Lantman, Hikmet Can Çubukçu, Guilaine Boursier, Mauro Panteghini, Francisco A. Bernabeu-Andreu, Neda Milinkovic, Pika Mesko Brguljan, Solveig Linko, Duilio Brugnoni, Ruth O'Kelly, Christos Kroupis, Maria Lohmander, Luděk Šprongl, Florent Vanstapel and Marc Thelen*, on behalf of the European Federation of Clinical Chemistry, Laboratory Medicine EFLM Working Group Accreditation, ISO/CEN standards WG-A/ISO

An approach for determining allowable between reagent lot variation

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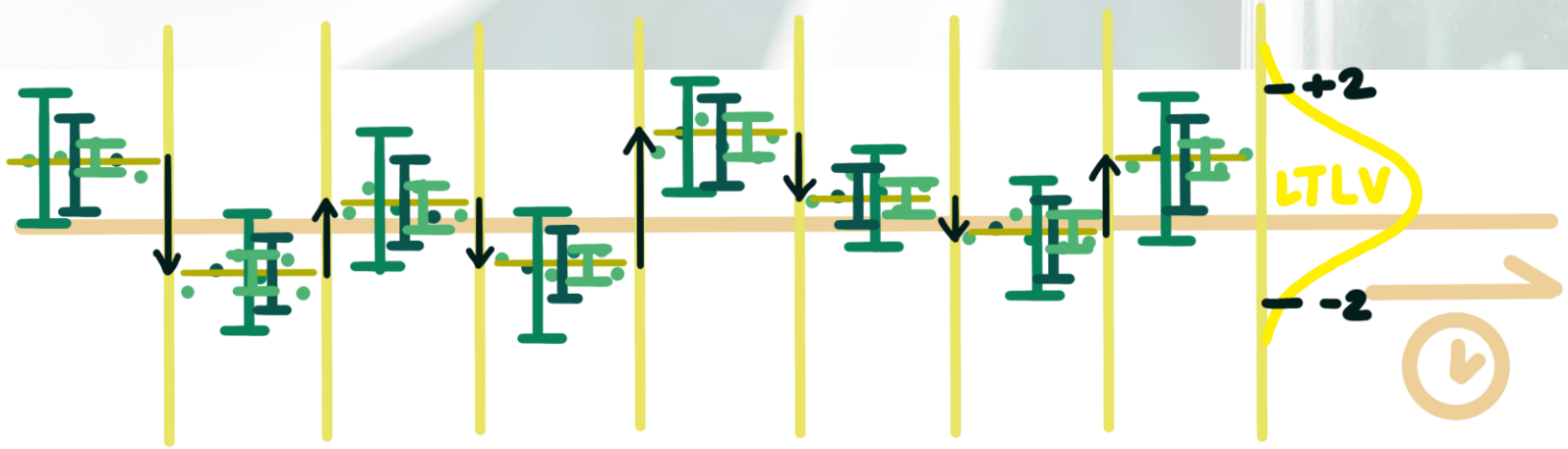
that are manageable vs. those that are not. One of the aspects that may influence u_{Rw} is the momentary significant bias caused by shifts in reagent and/or calibrator lots, which, when

Allowable LTLV – the theorem



$u_{brlot} \leq \frac{u_{wrlot}}{\sqrt{n}}$, n ↓ 1-6

| = lot change

• = ▽ (n=1) • = ▽ (n=2) • = ▽ (n=6)

— = average (▽)

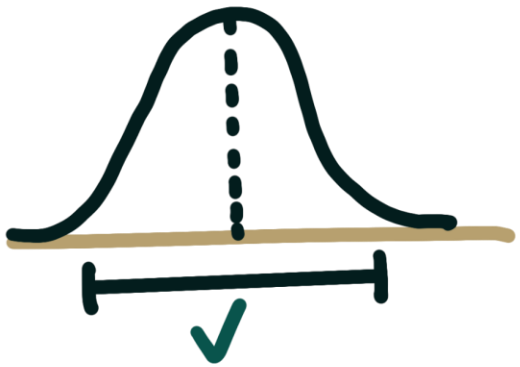
I = confidence (n=1) (n=2) (n=6) ≥ ↑↓ = LTLV change

$$u_{brlot} \leq \frac{u_{wrlot}}{\sqrt{n}}$$

1. combine with MU-formulas

- $APS \geq \sqrt{u_{RW}^2 + u_{cal}^2}$
  - $u_{RW} = \sqrt{u_{brlot}^2 + u_{wrlot}^2}$
  - $u_{brlot} \leq \frac{\sqrt{APS^2 - u_{cal}^2}}{\sqrt{n+1}}$ $\xrightarrow{u_{cal} = ?}$ $u_{brlot} \leq \frac{APS}{\sqrt{n+1}}$

2. Determine acceptability criteria

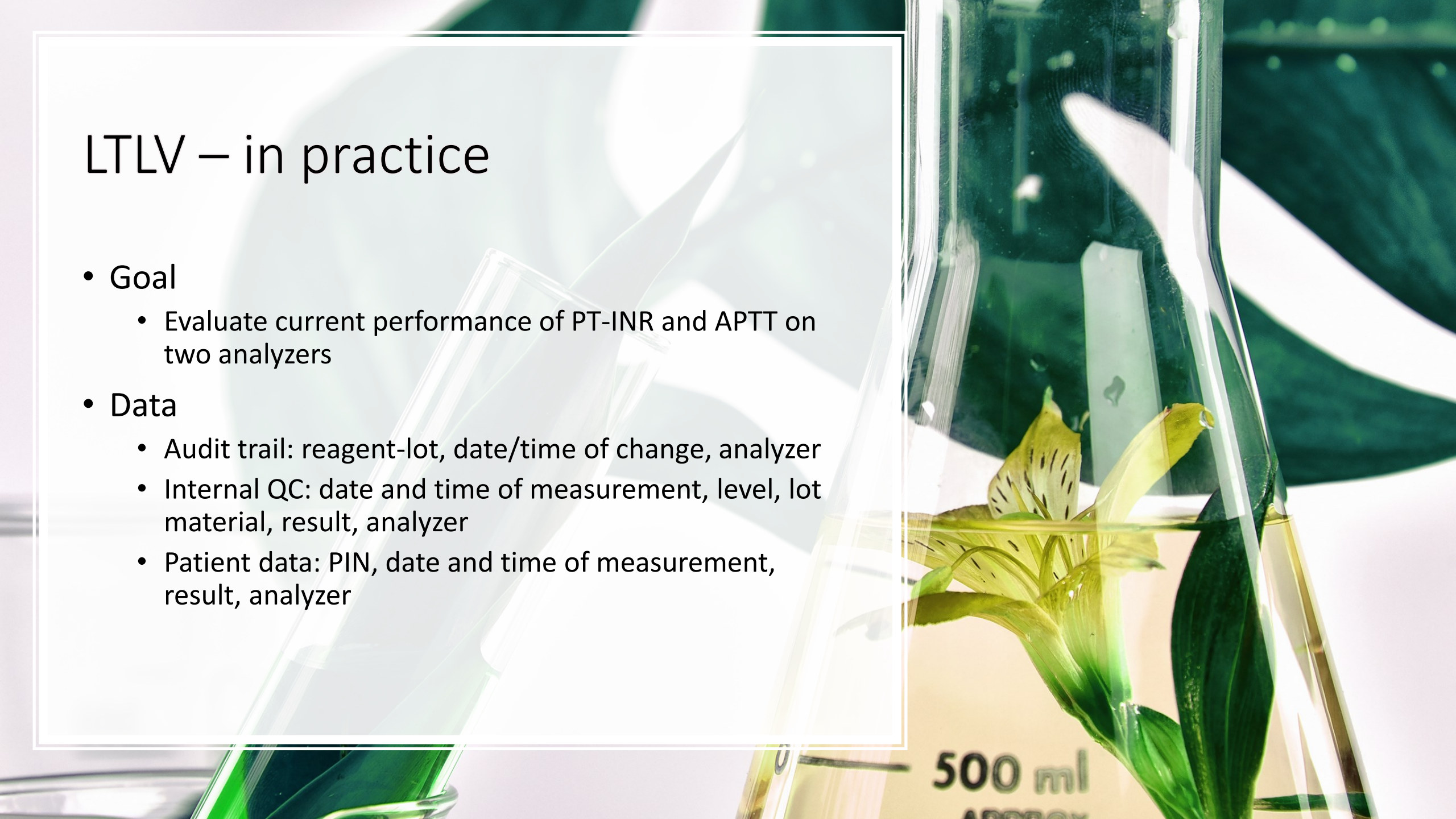


→ SD

- Accept new lot?
- current LTLV?
- QC design

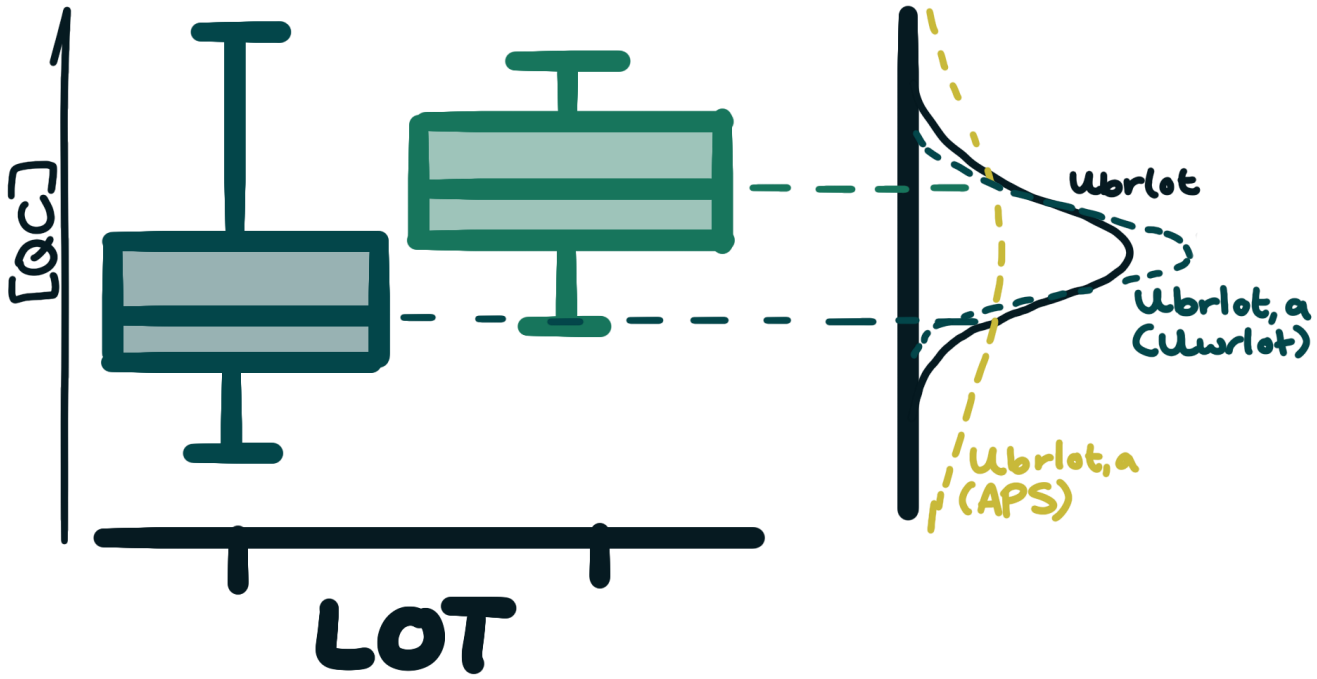
LTLV – in practice

- Goal
  - Evaluate current performance of PT-INR and APTT on two analyzers
- Data
  - Audit trail: reagent-lot, date/time of change, analyzer
  - Internal QC: date and time of measurement, level, lot material, result, analyzer
  - Patient data: PIN, date and time of measurement, result, analyzer

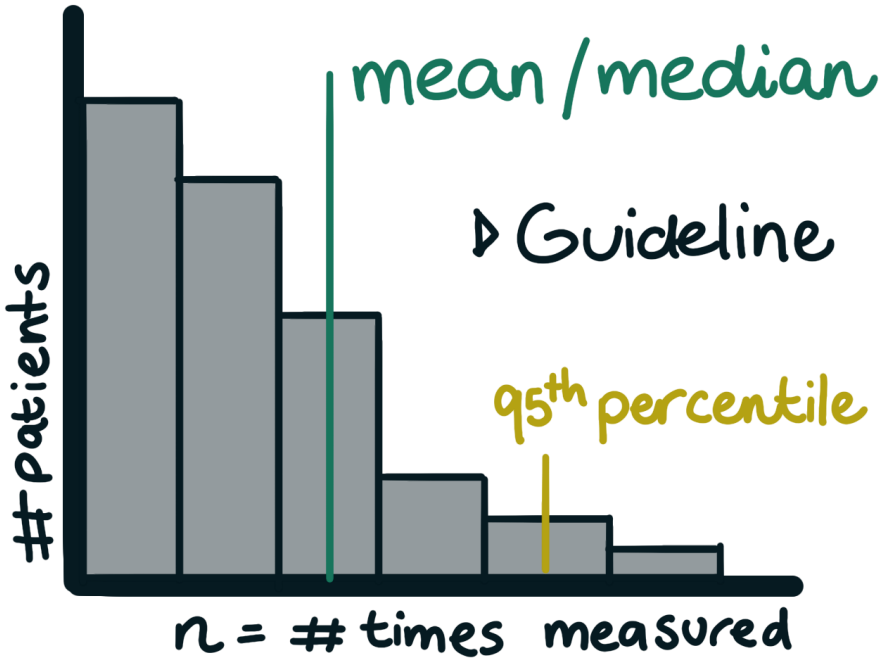


Methods

- Reagent lot x QC



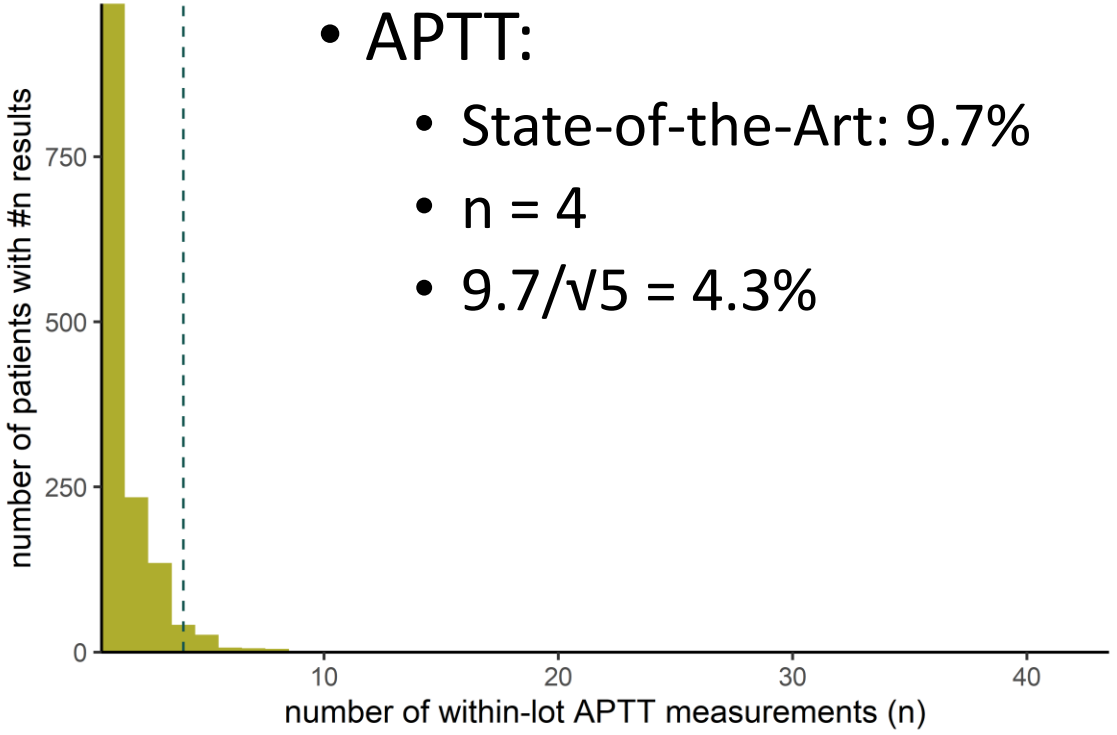
- Reagent lot x Patient



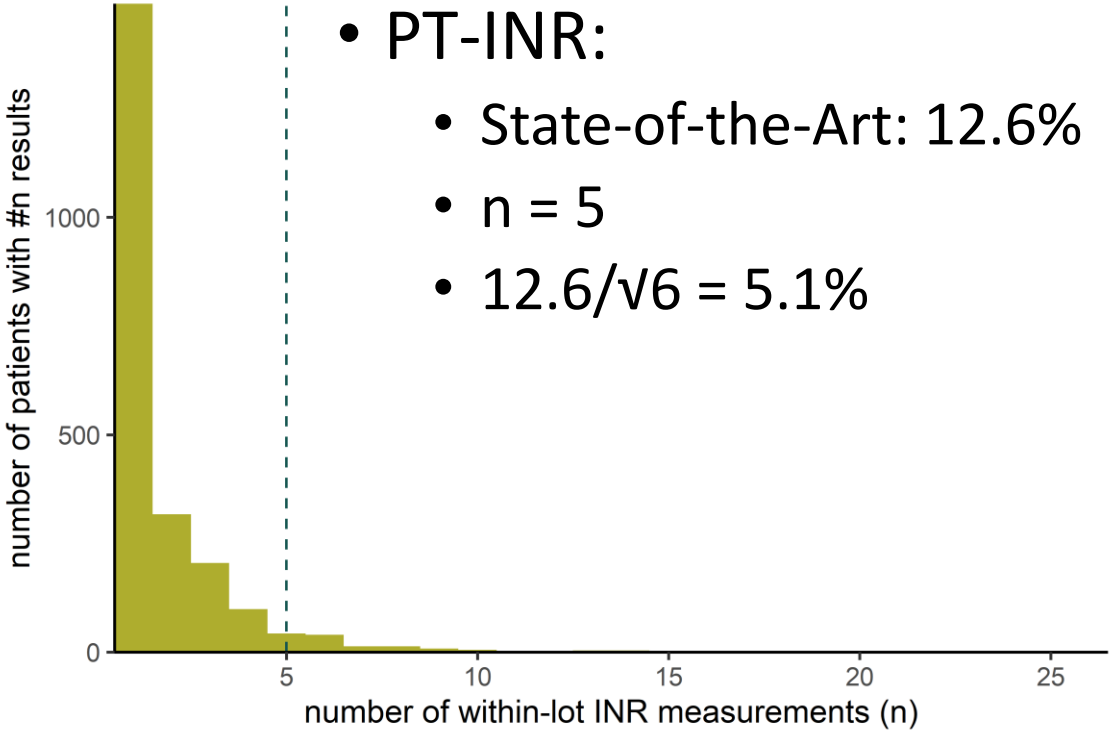
Allowable APS-based-LTLV

$$u_{brlot} \leq \frac{APS}{\sqrt{n+1}}$$

- APTT:
  - State-of-the-Art: 9.7%
  - n = 4
  - 9.7/√5 = 4.3%



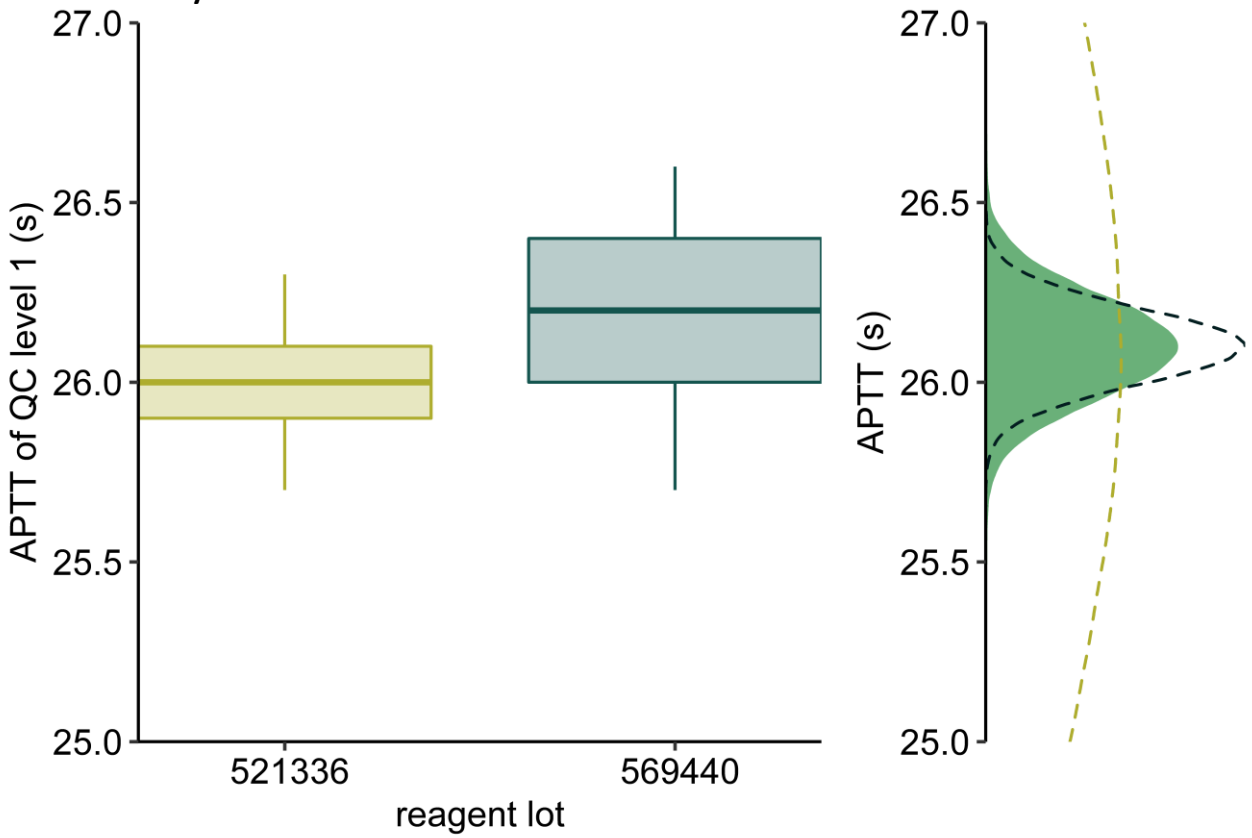
- PT-INR:
  - State-of-the-Art: 12.6%
  - n = 5
  - 12.6/√6 = 5.1%



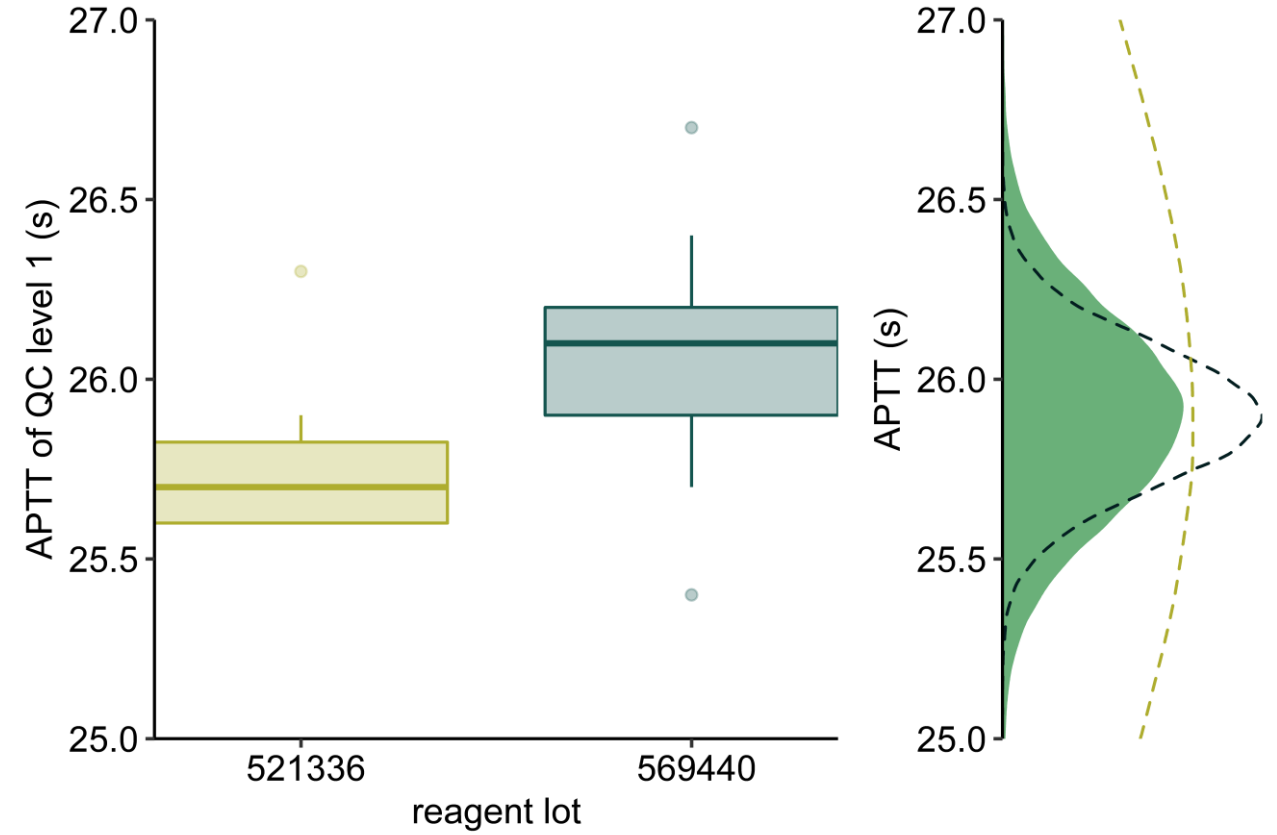
In practice: if urw << APS, then ubrlot < uwrlot/ sqrt(n)!

APTT – QC level 1

Analyzer 1

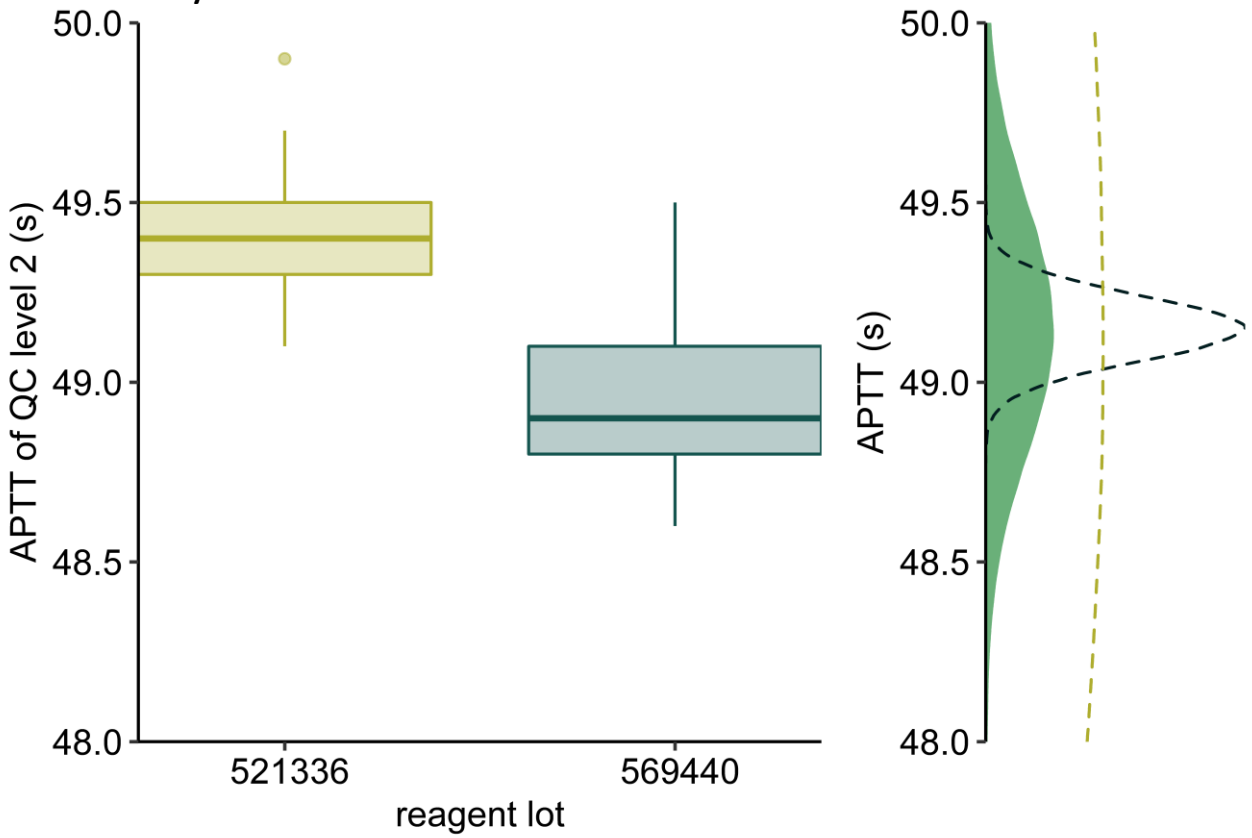


Analyzer 2

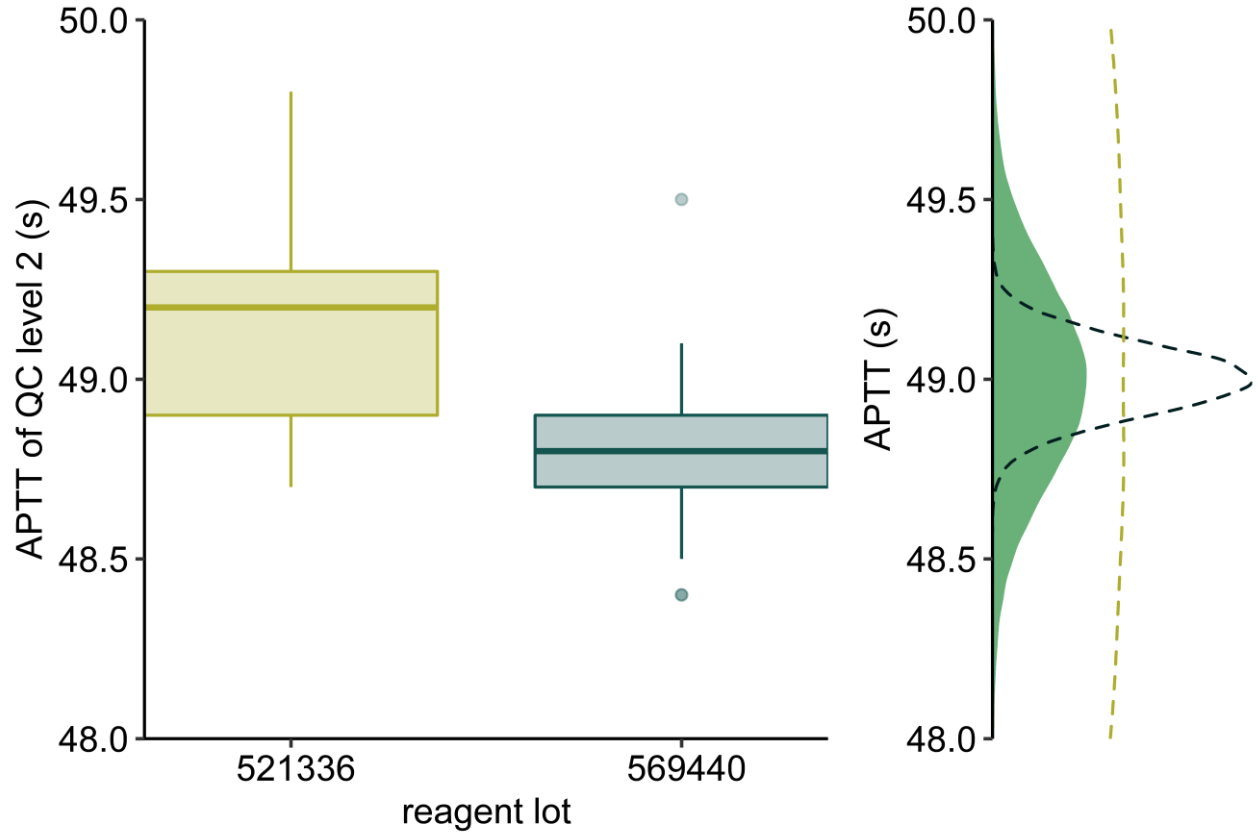


APTT – QC level 2

Analyzer 1

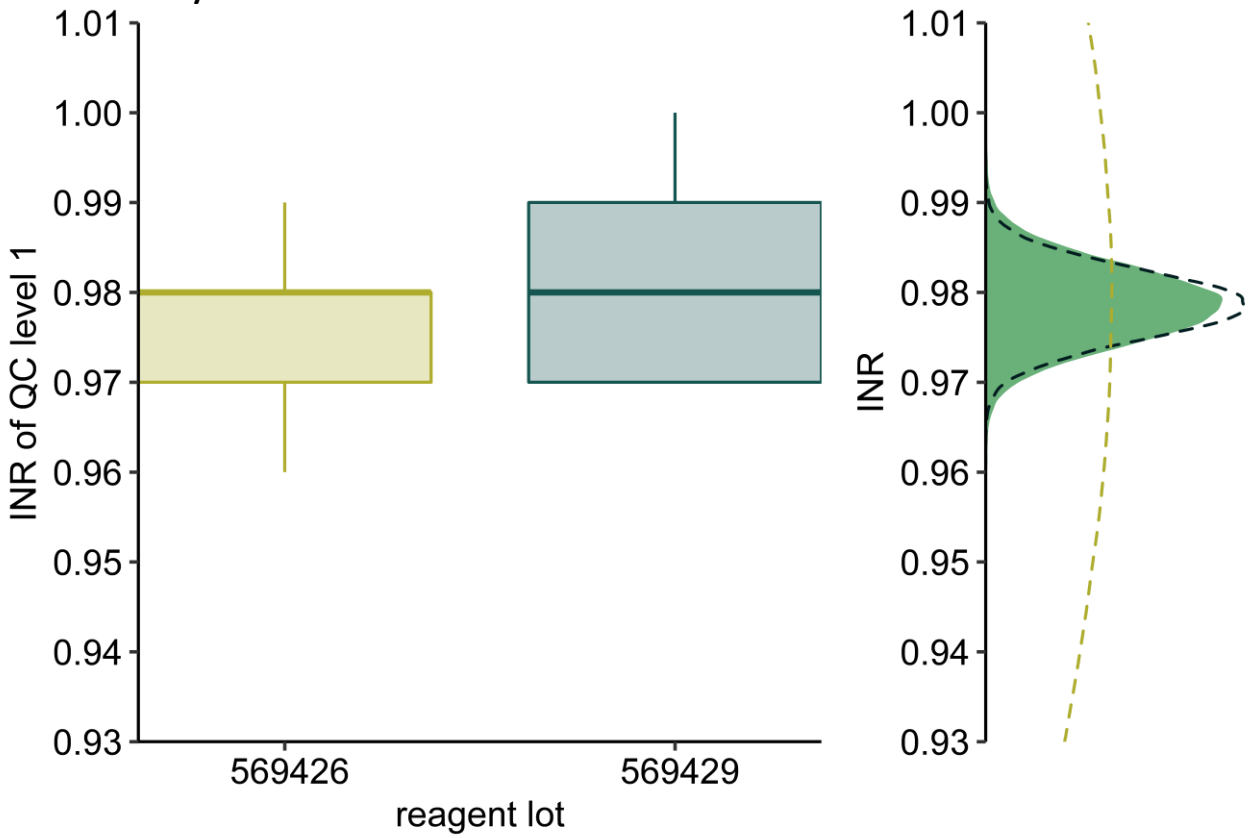


Analyzer 2

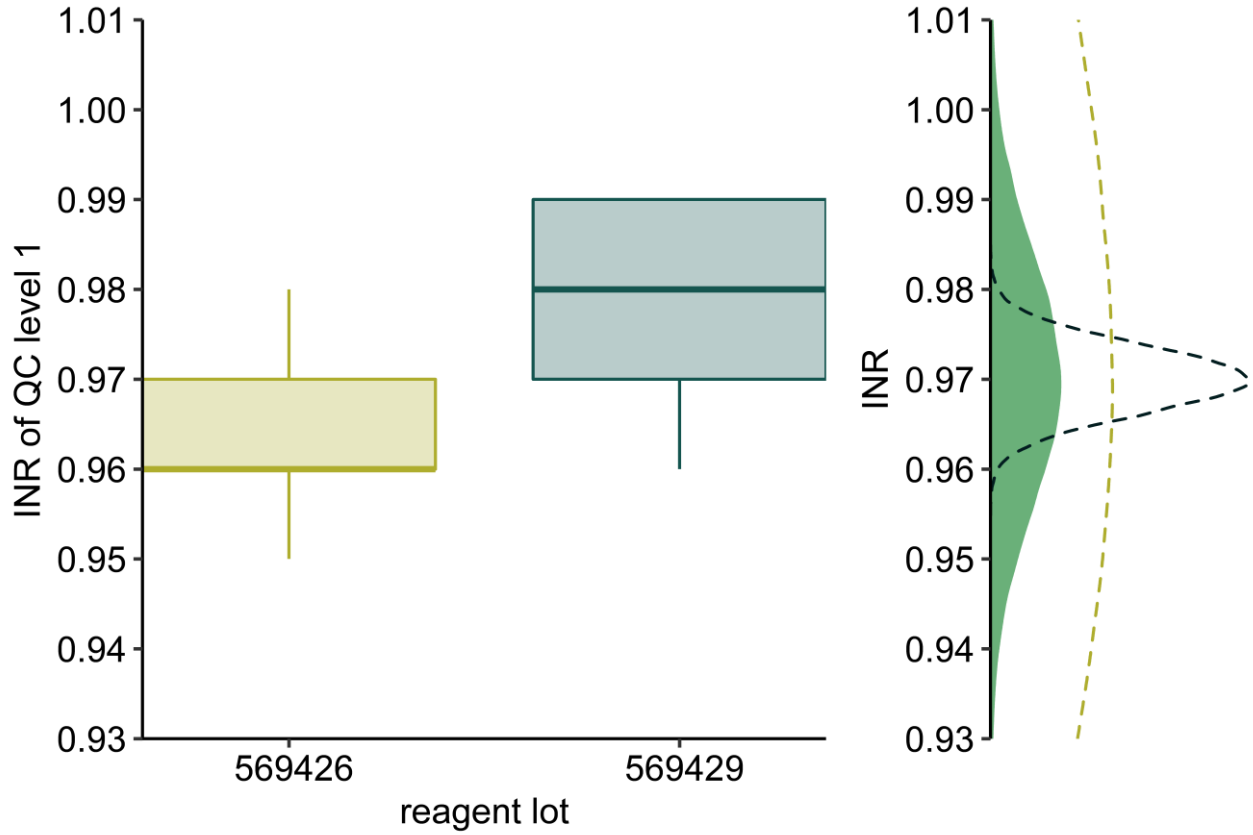


PT-INR – QC level 1

Analyzer 1

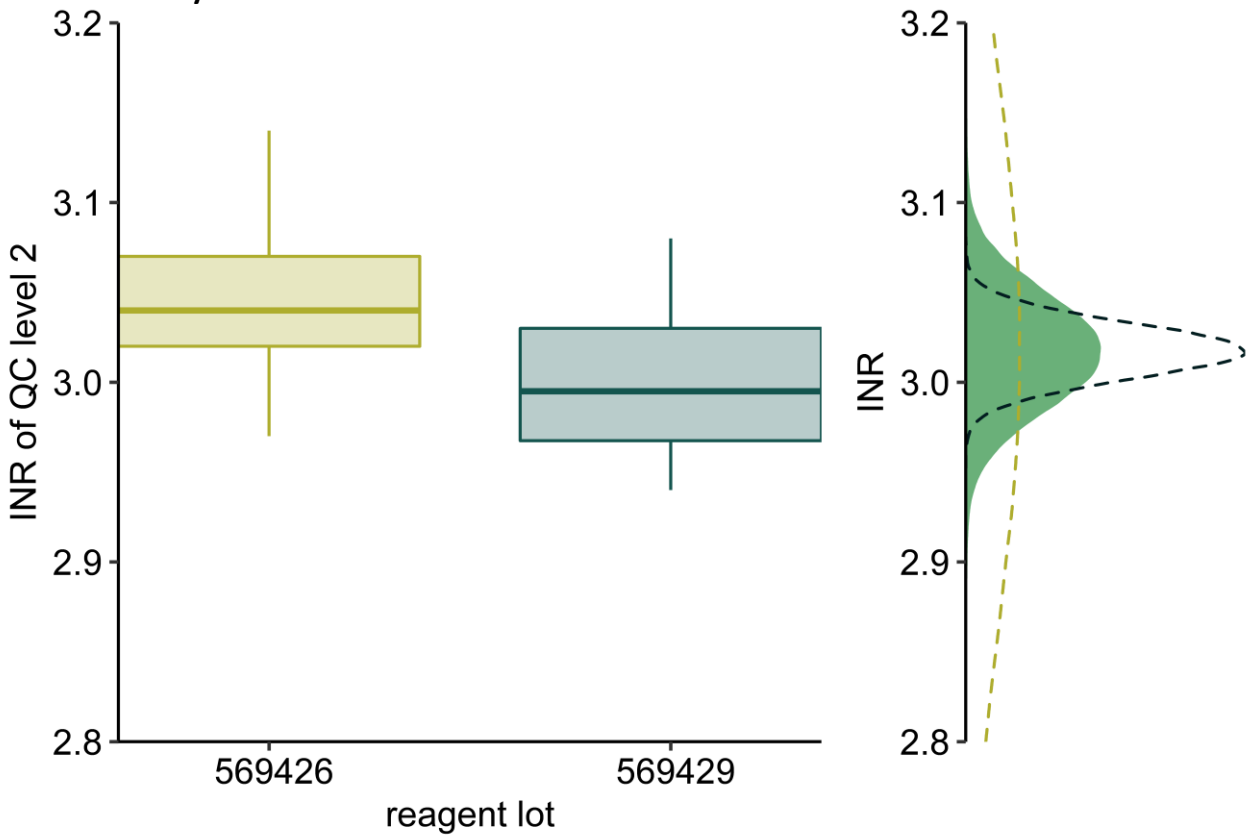


Analyzer 2

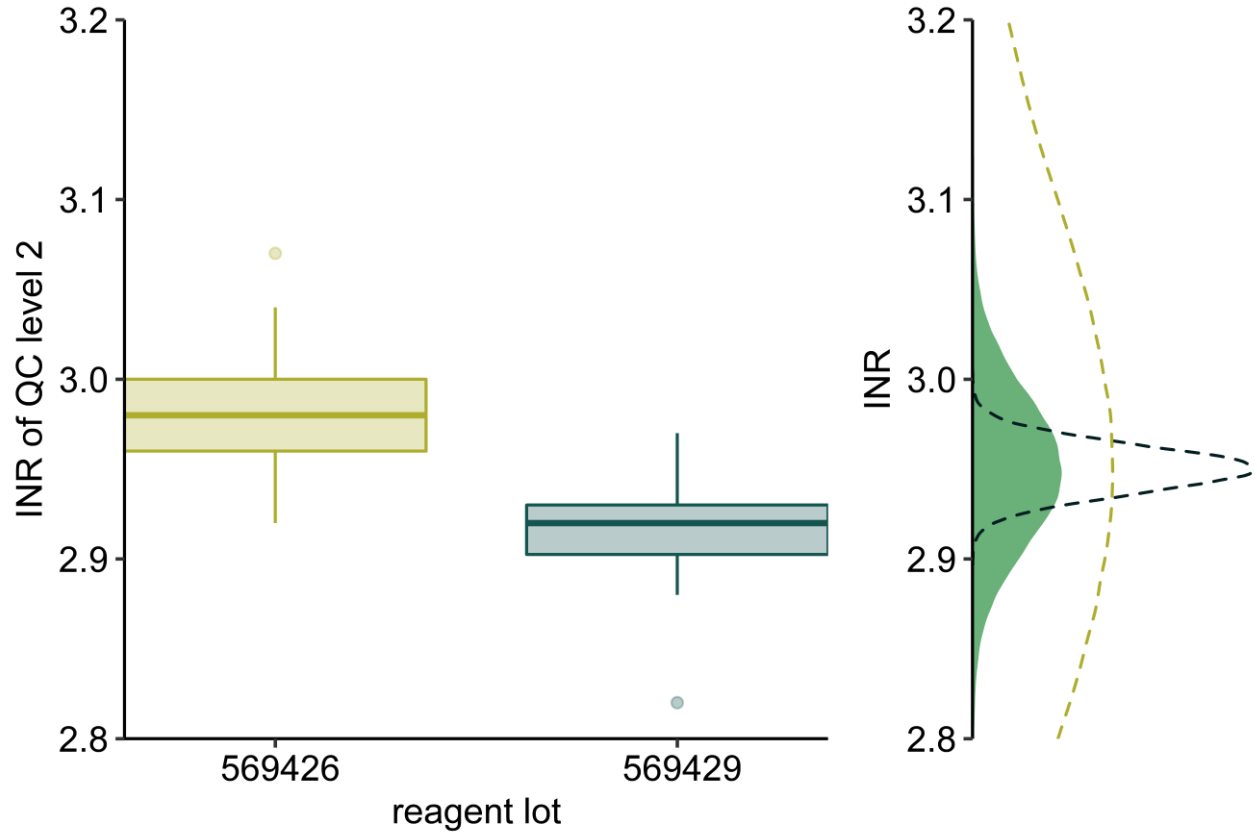


PT-INR – QC level 2

Analyzer 1



Analyzer 2



Conclusion

- Although LTLV meets APS-based criteria, within-lot precision can still cause significant shifts
  - Effect of continuous improvement over time
- Evaluating LTLV may give insight into integral analytical quality
  - Between-analyzer variation
  - Procedures on data-storage and management
- LTLV may cause adverse clinical decisions

Important notes

- Use of materials
  - Use of appropriate materials (IQC component II)
    - Pooled material → stability?
    - Third-party-QC-material → commutable?
  - Retention time of data

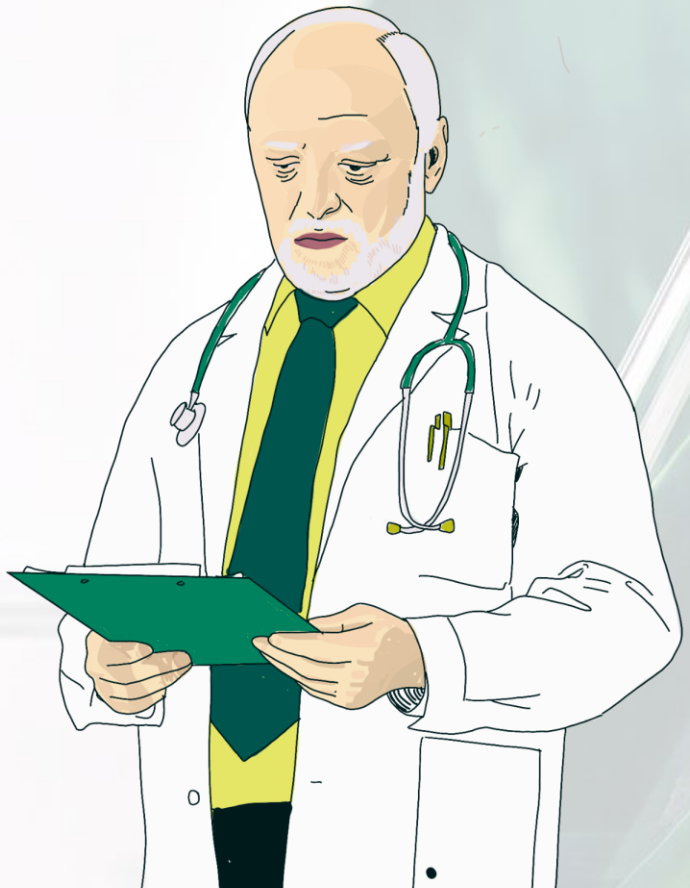
- Improve LTLV
  - Reduce n to increase proportion assigned to between-reagent lot variation
  - Thorough acceptance testing process, overarching multiple reagent lots

- First-lot-syndrome: accuracy of first lot is often overestimated

- Ideally LTLV is established by IVD, monitored by laboratories

Reporting back to the clinician

- Inform doctors when shifts occur!
  - What can they expect?



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- You!

SKML
Stichting Kwaliteitsbewaking
Medische Laboratoriumdiagnostiek

Result Laboratorium

Radboudumc
university medical center

Thank you for your attention! I’m happy to answer questions ☺