The importance of reagent lot registration in EQA

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2 examples

EQA schemes for point-of-care testing (POCT)

1. Urine-albumin:creatinine ratio (ACR)

2. International normalized ratio (INR)

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Example 1: EQA for POCT ACR

- Control material
  - Pooled urine from persons with normal and increased excretion of albumin
  - Stored frozen (-80 Celcius), thawed on distribution day
  - Homemade by Noklus
  - Two samples per survey
- Peer group target values
- Afinion AS 100 Analyzer (Alere)
- Surveys from 2009 to 2015
  - 1 per year from 2009 to 2012
  - 2 per year from 2013 to 2015

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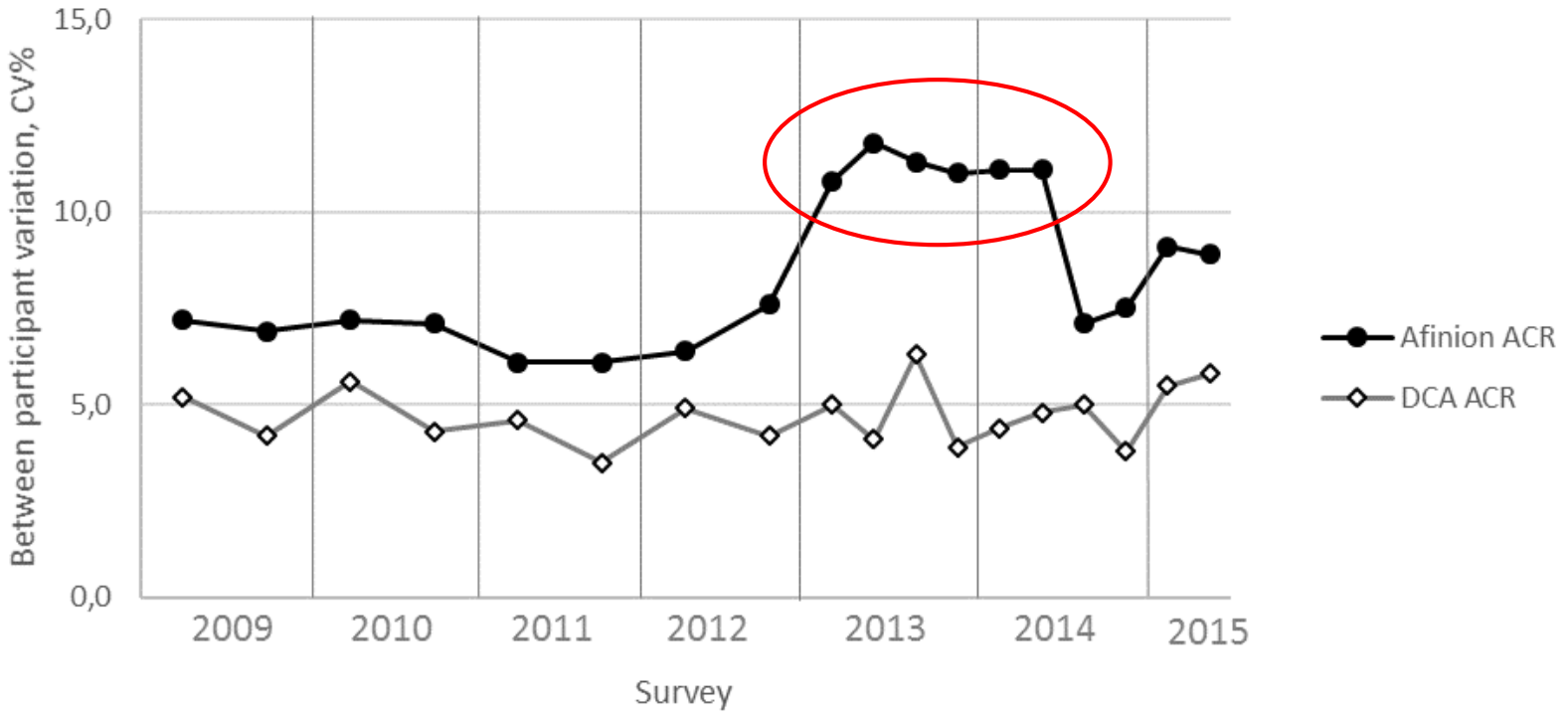
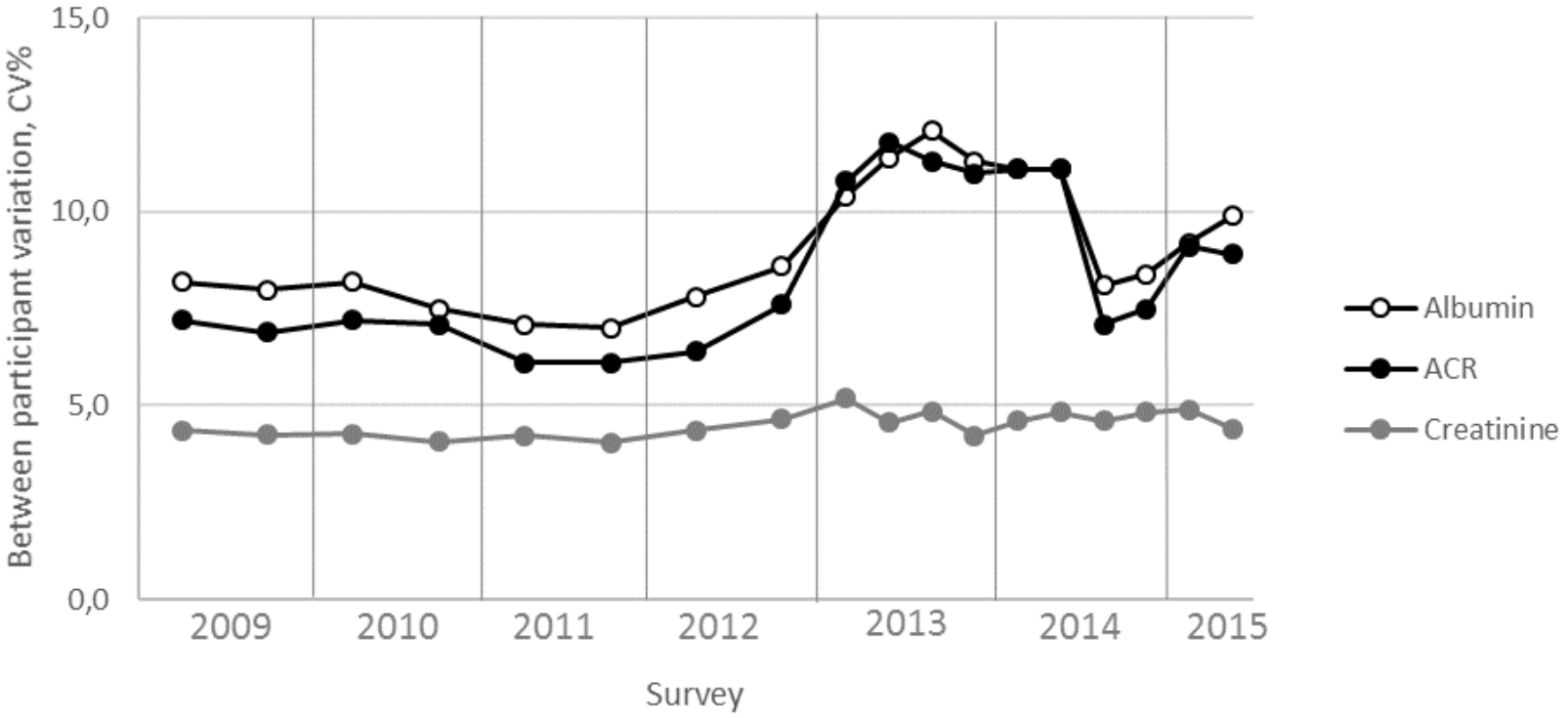
Between participate variation (CV%)



Afinion: Increased CV in 3 consecutive surveys

CV% Afinion



The problem: Albumin

Afinion u-albumin reagent lot

- Is the increased CV caused by lot-to-lot variation?

- Reagent lots used by n>5 participants were investigated
- Review of different reagent lots from 2009 to 2015

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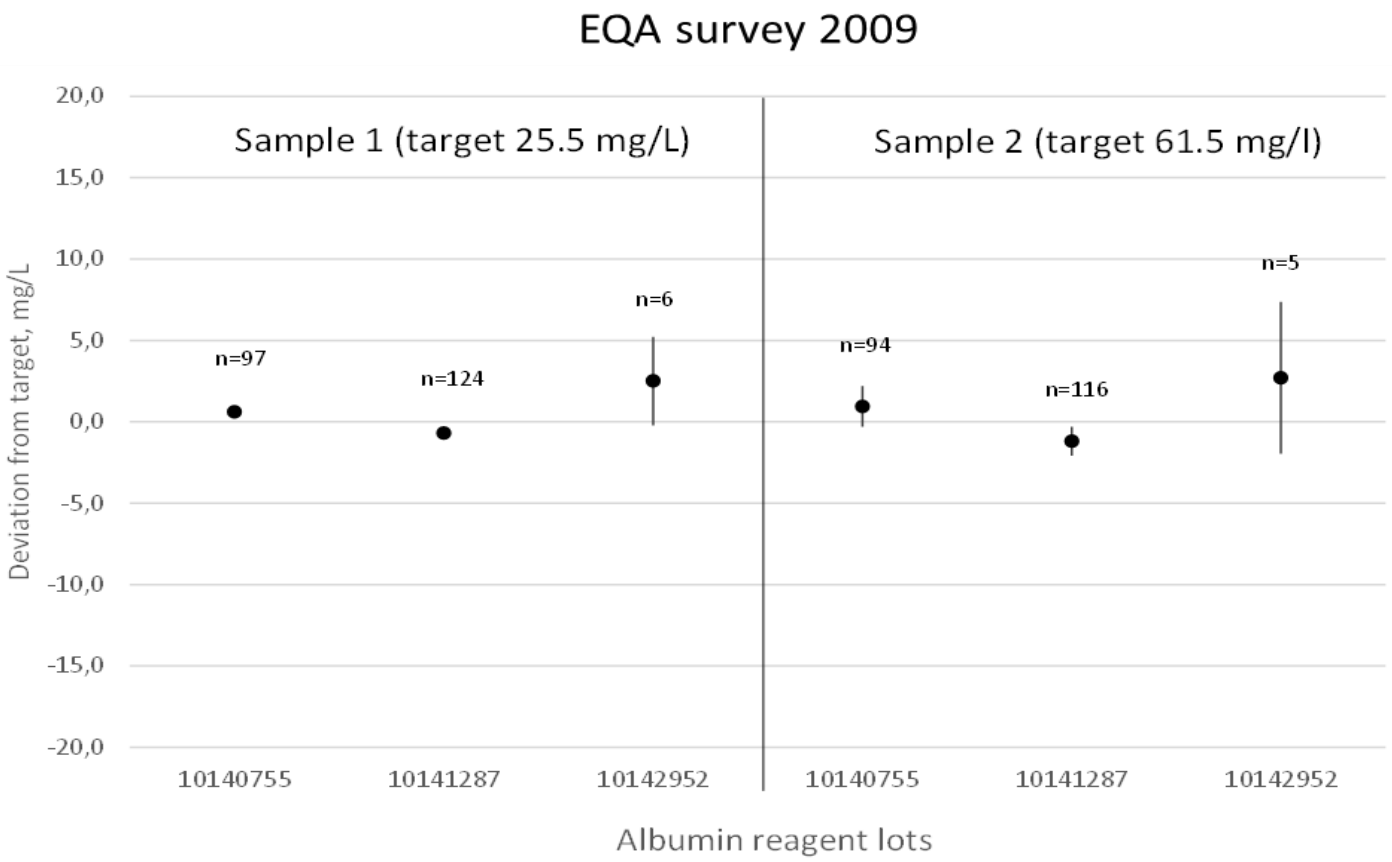
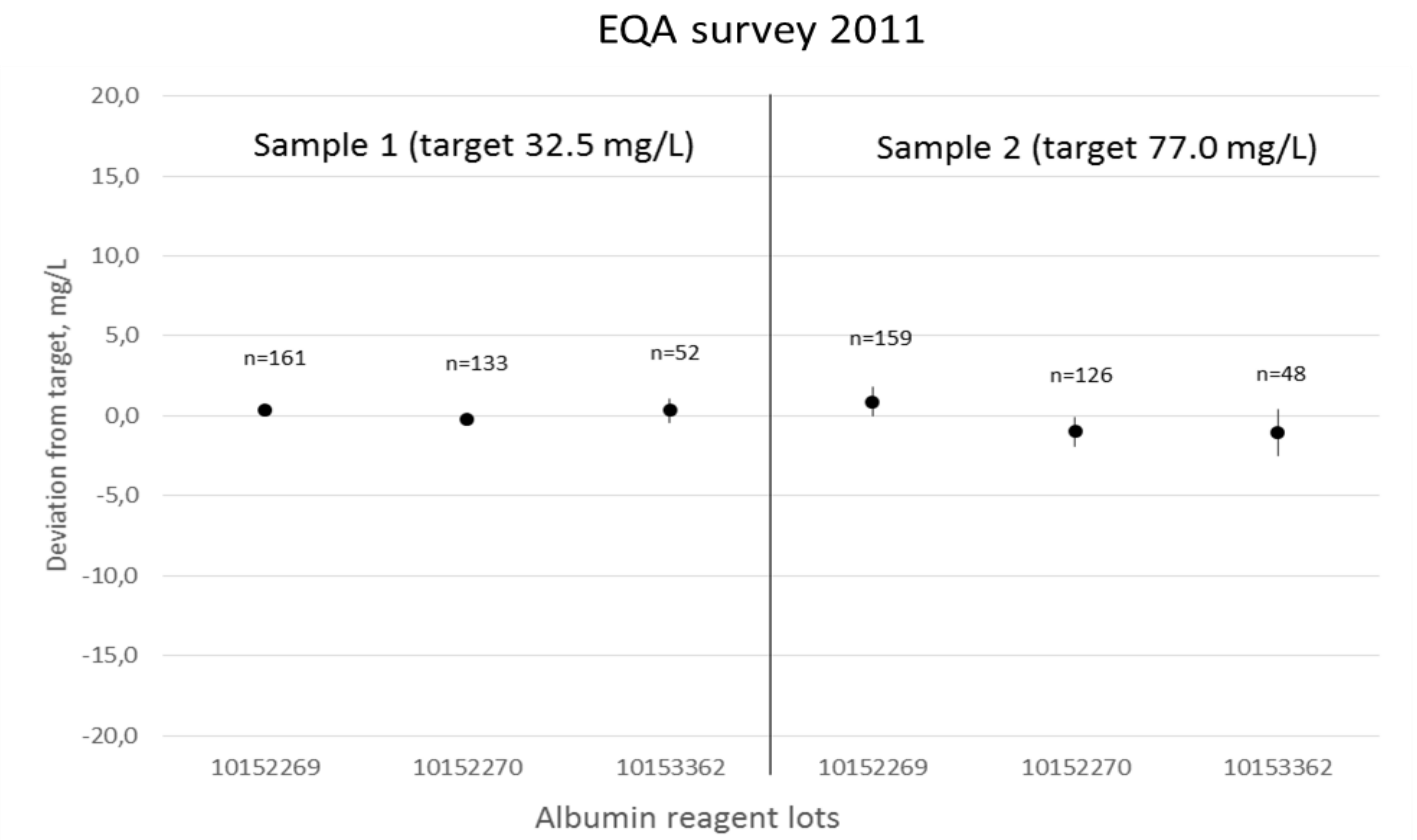
Lot-to-lot variation 2009



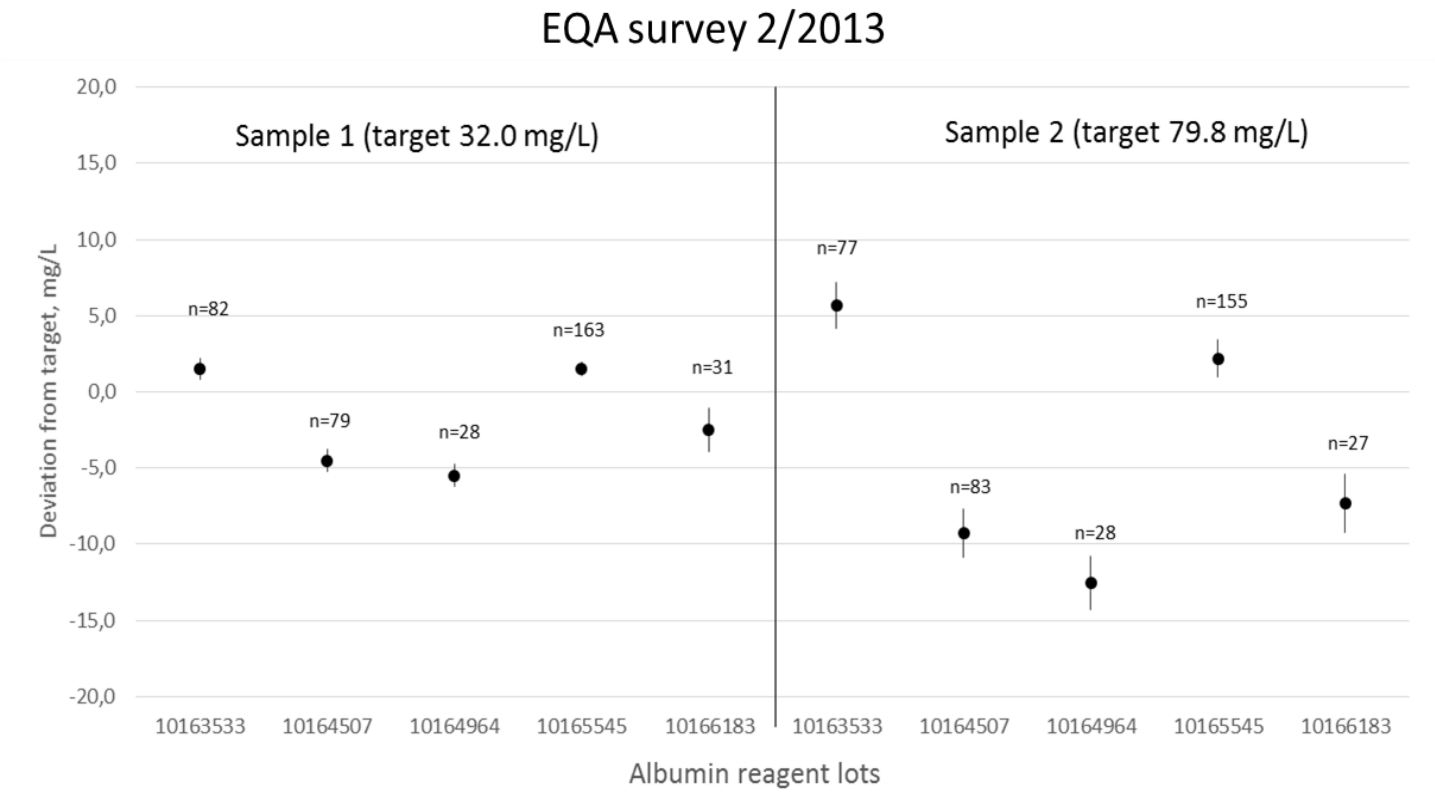
No differences between reagent lots

Lot-to-lot variation 2011



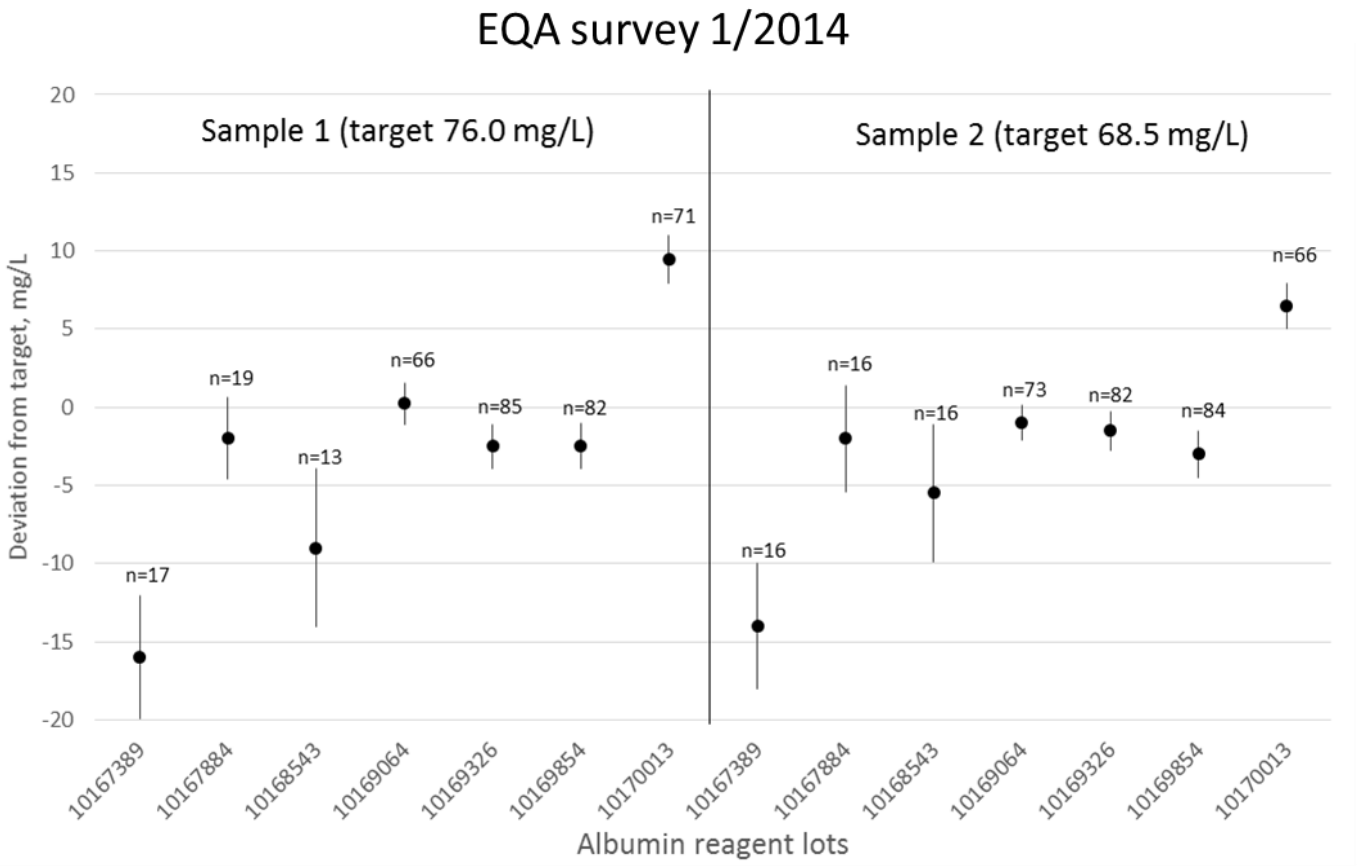
No differences between reagent lots

Lot-to-lot variation 2013



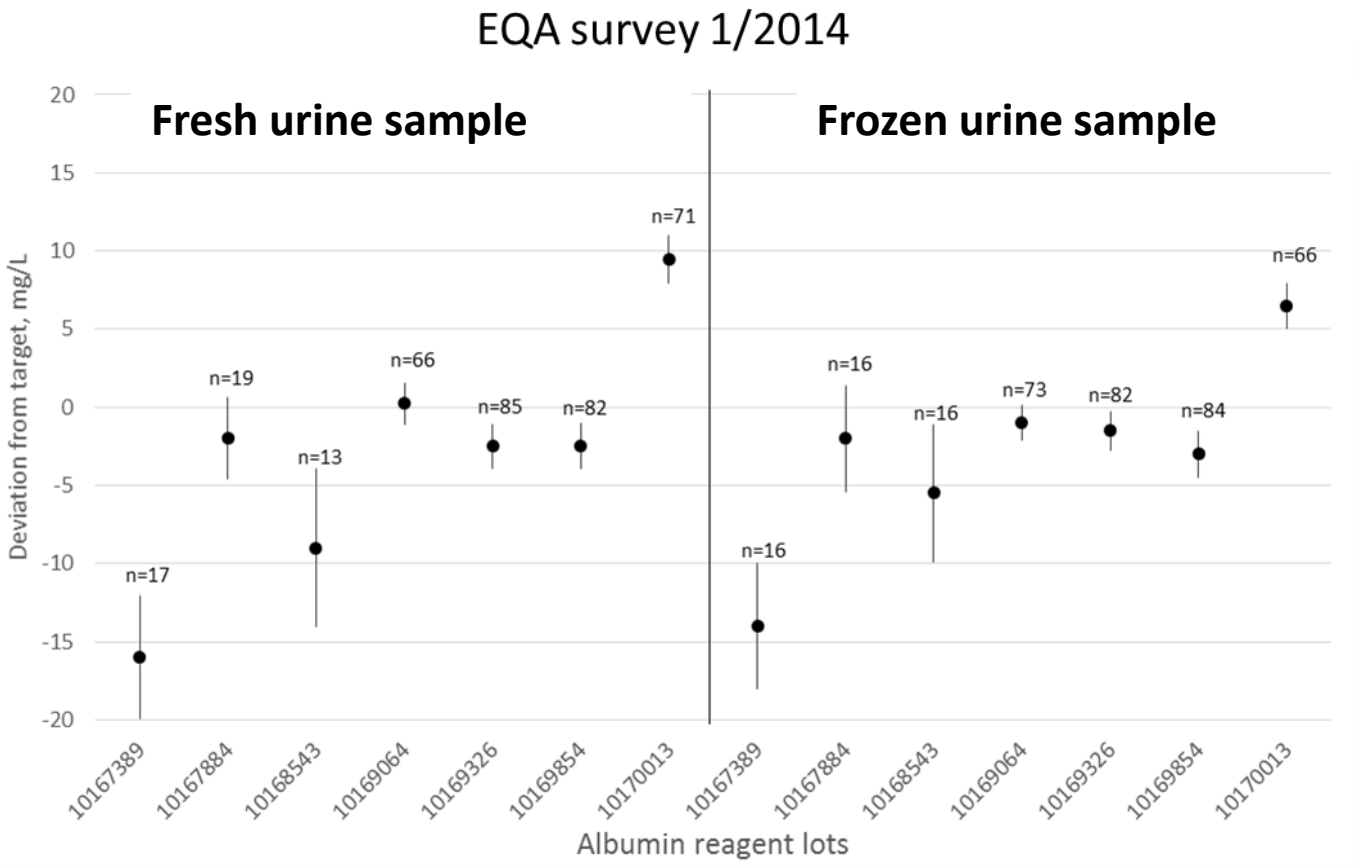
Differences between reagent lots

Lot-to-lot variation 2014



Differences between reagent lots

Lot-to-lot variation 2014



Same lot differences in fresh urine samples

Summary example 1 (ACR)

- The lot differences could explain the increased CV seen in 3 consecutive surveys for Afinion
- The lot differences was also valid for patient samples
- The participants and manufacturer (Alere) where informed about these findings
- Manufacturer: the reagents had not been stored adequately due to a change in warehouse
- When this was corrected both lot variation and CV decreased (but there was still lot differences)

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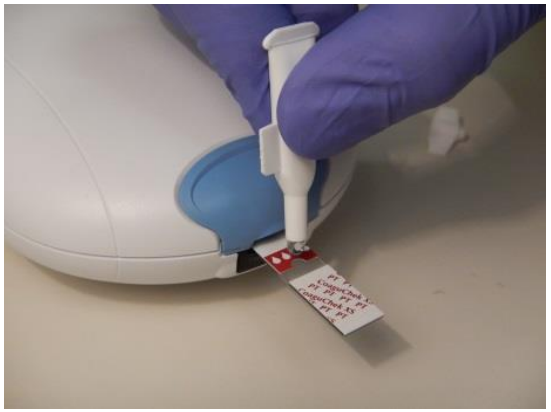
Example 2: EQA for POCT INR

- CoaguChek (Roche), n=1500
  - XS, XS Plus, XS Pro
- Control material
  - Liquid pooled human plasma from patients on anticoagulation treatment with warfarin
  - Nordic Haemostais (Sweden)
  - Two samples, twice a year
- Peer group target values
- Surveys from 2014 to 2016



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Target values CoaguChek

Same batch of control material in all surveys

Survey	Sample 1	Sample 2
1/2014	2,20 INR	2,80 INR
2/2014	2,40 INR	-
1/2015	2,40 INR	3,20 INR
2/2015	2,30 INR	2,95 INR
1/2016	-	2,70 INR

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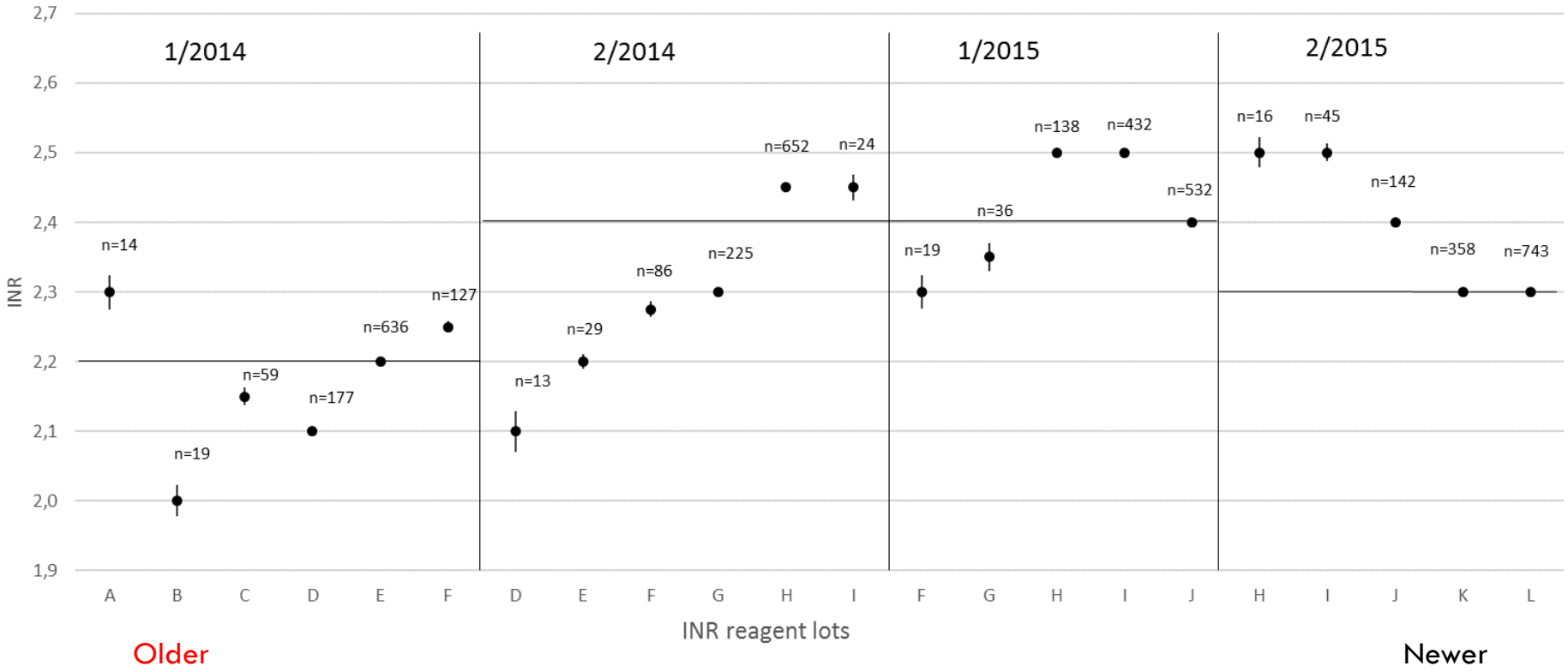
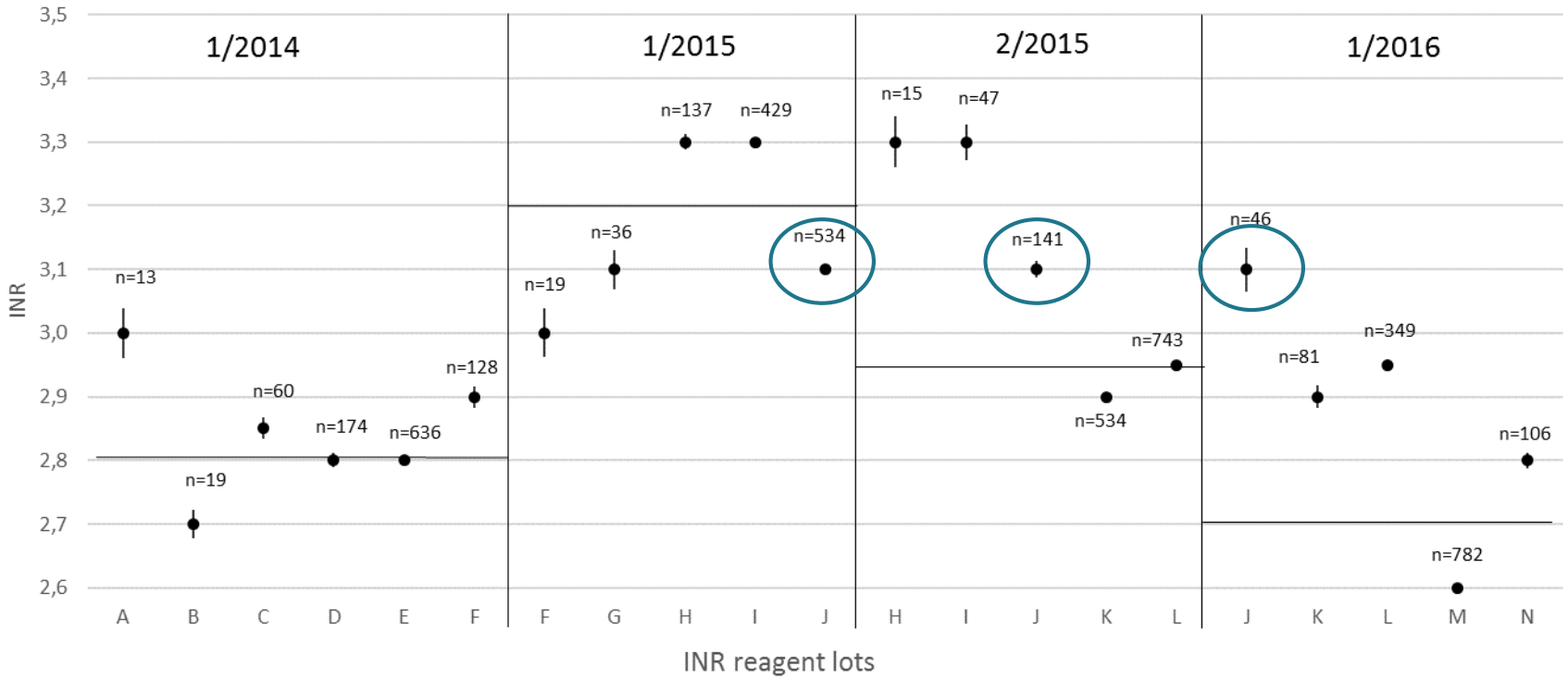
Lot-to-lot variation (Sample 1)



Lot G

Lot H

Lot-to-lot variation (Sample 2)



Lot G

Lot H

Split sample EQA scheme

- Noklus has offered this scheme since 2014
- For the most commonly used POCT INR methods
- Aim is to evaluate the accuracy and bias of the POCT methods
- This example: The split sample results were used to evaluate if the commercial EQA material gave the same lot-to-lot differences as native patient samples
- CoaguChek
  - Approx. 100 capillary samples analyzed by 25 GP offices
  - Venous citrated blood samples sent to Noklus and analyzed on a designated hospital INR method

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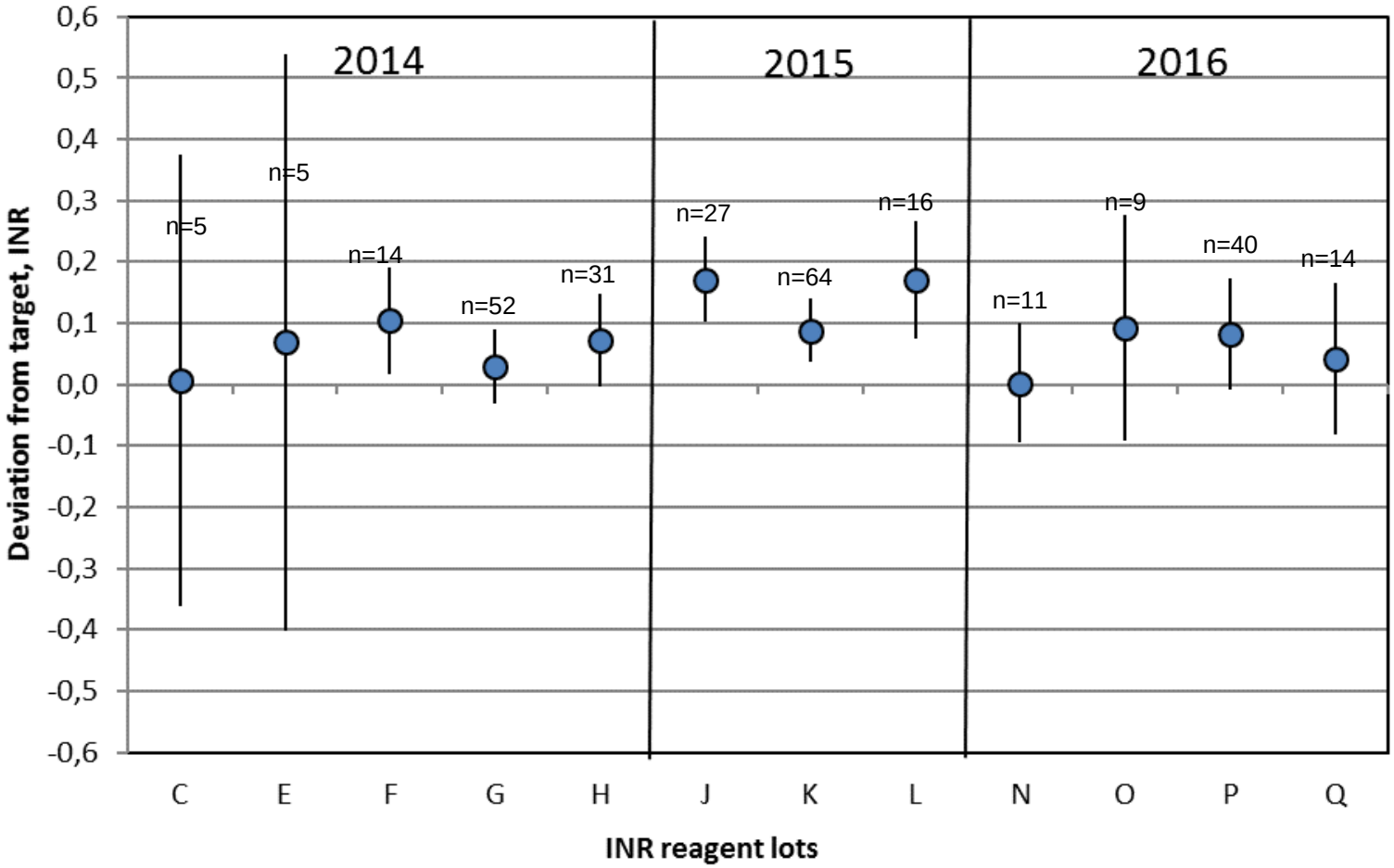
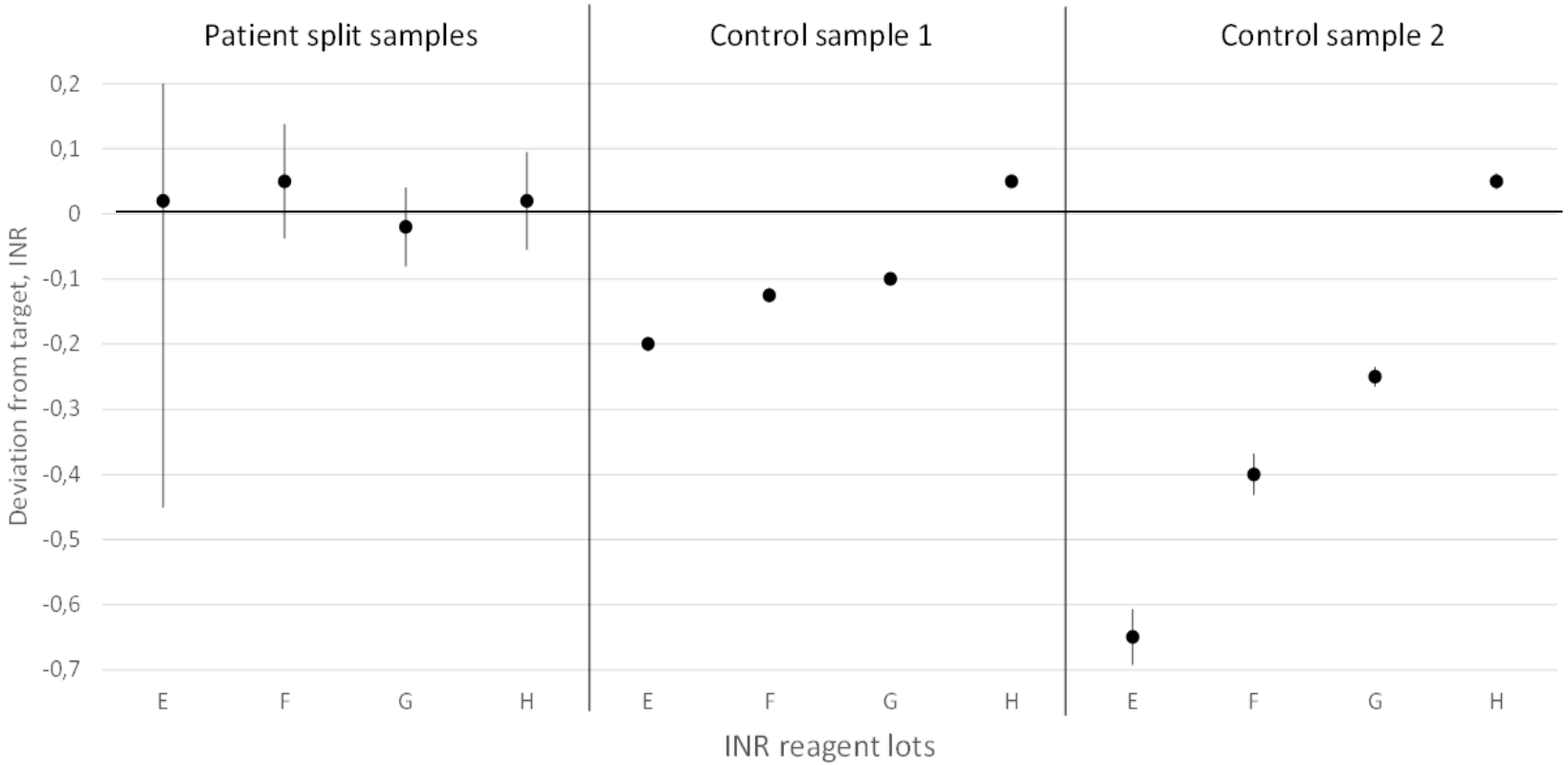
Lot-to-lot variation (patient samples)



Survey 2/2014: The same 4 reagent lots (E-H) were analyzed both with native patient samples and with control samples



Summary example 2 (INR)

- Large reagent lot differences were seen using the commercial EQA material
- Small or no reagent lot differences were seen using native patient samples (i.e. the EQA material was not “commutable between reagent lots”)
- The lot differences were important for correct interpretation of the EQA result
- The lot differences were given both to the participants and to the manufacturers (Nordic Haemostasis and Roche)

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Conclusion

- Results from different reagent lots can give helpful information
  - to the participants in the troubleshooting process, explaining a deviant EQA result
  - for the EQA provider to explain the survey results
  - for the reagent manufacturer (e.g. stability, calibration)
- Information whether lot-to-lot variation found in EQA schemes also affect patient samples should be given
  - Avoid using EQA material that is not commutable between reagent lots

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