Testing for Albuminuria Today's Reality

KDIGO
Controversies Conference
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Urinary Albumin

- Albumin filtered at the glomerulus is biochemically modified by lysosomal enzymes
- This results in the excretion of intact albumin (1%) and albumin-derived fragments (< 10 kDa)
- Antibody based assays recognize intact albumin

Microalbuminuria (Types 1 and 2 Diabetes)

- An established, early indicator of incipient nephropathy (early 1980's)
- Early treatment (guided by annual measurement) can slow or prevent progression to persistent albuminuria and E-SRD (2000-2002)
- Identifies those at increased risk of cardiovascular disease

Microalbuminuria

- Predicts risk for cardiovascular disease
  even in subjects without diabetes or hypertension
  (1990-2002)

- HOPE study – every 0.4 mg/mmol increase in A:CR increased adjusted hazard of major CV events by 5.9% (95% CI – 4.9% - 7.0%)

“the clinical decision levels for albuminuria have been set and applied without regard to the analytical method that is being used in the determinations”

Critical Tests and Clinical Guidelines

Clinical guidelines frequently direct clinicians to take actions on the basis of a given test result

The underlying assumption is that lab tests are consistently accurate and precise and that lab to lab variation in the testing and reporting of these analytes is negligible

The Impact of Laboratory Error

- Clinical laboratories trigger 75% of medical decisions
- Inaccurate test results, incorrect diagnosis
- Incorrect treatment, unnecessary treatment
- Negative impact – triage, trending, EMR, outcome assessments, missed opportunities for prevention
- Redundant testing

The Impact of Calibration Error in Medical Decision Making

Calibration error systematically skews all test results for a given test

Medical decisions made on the basis of this test result will also be skewed

Calcium calibration errors cost the US Health Care system $60 - $199 million annually

(NIST Planning report 04-1: The Impact of Calibration Error in Medical Decision Making)

What about urinary albumin?

Guidelines

What sample should be tested?

- random spot urine
- timed collection
- 24 hour collection
- first morning collection

Guidelines

What test should be ordered?

rapid test (primary care)

albumin:creatinine ratio

albumin concentration

albumin excretion rate

total protein excretion rate

Guidelines

What is the cut-off (albumin:creatinine ratio) ?

3.4 mg/mmol/L

2.5 mg/mmol/L (males)
3.5 mg/mmol/L (females)

1.8 mg/mmol/L (males)
2.5 mg/mmol/L (females)

Guidelines

How should albuminuria (microalbuminuria ?) be confirmed ?

3 positive within a month

2 confirmed without delay

2 out of 3 positive within a 3-6 month time interval

“when it comes to measuring albumin in urine - labs are like boats on a lake – everyone is paddling but no one knows where the dock is”

The problem

- Albumin assays in urine are not standardized
- Primary and secondary reference materials are unavailable
- A suitable reference method has yet to be identified and credentialed

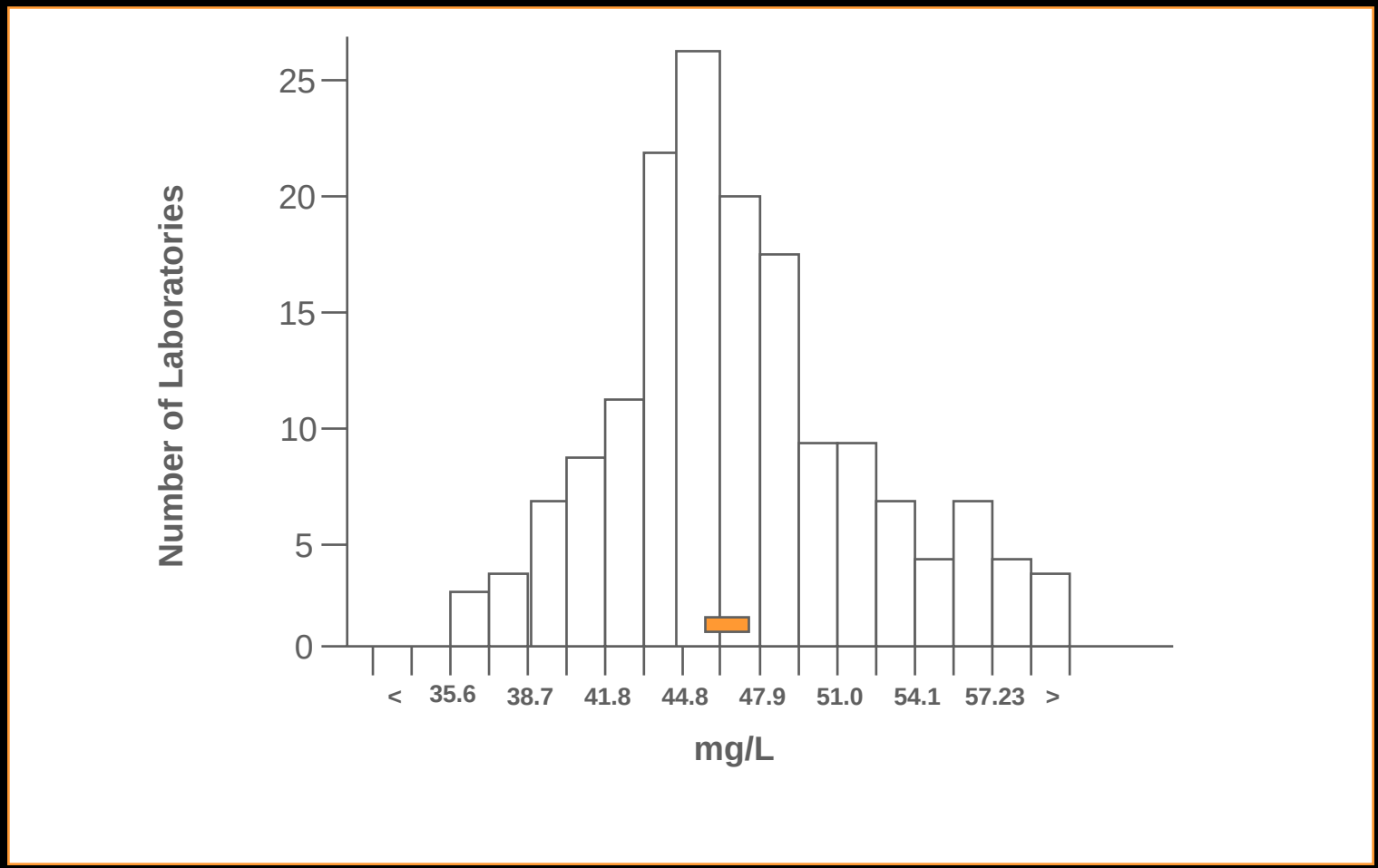
Albuminuria –Testing by Dip Stick

(Assigned Value - 85 mg/L)

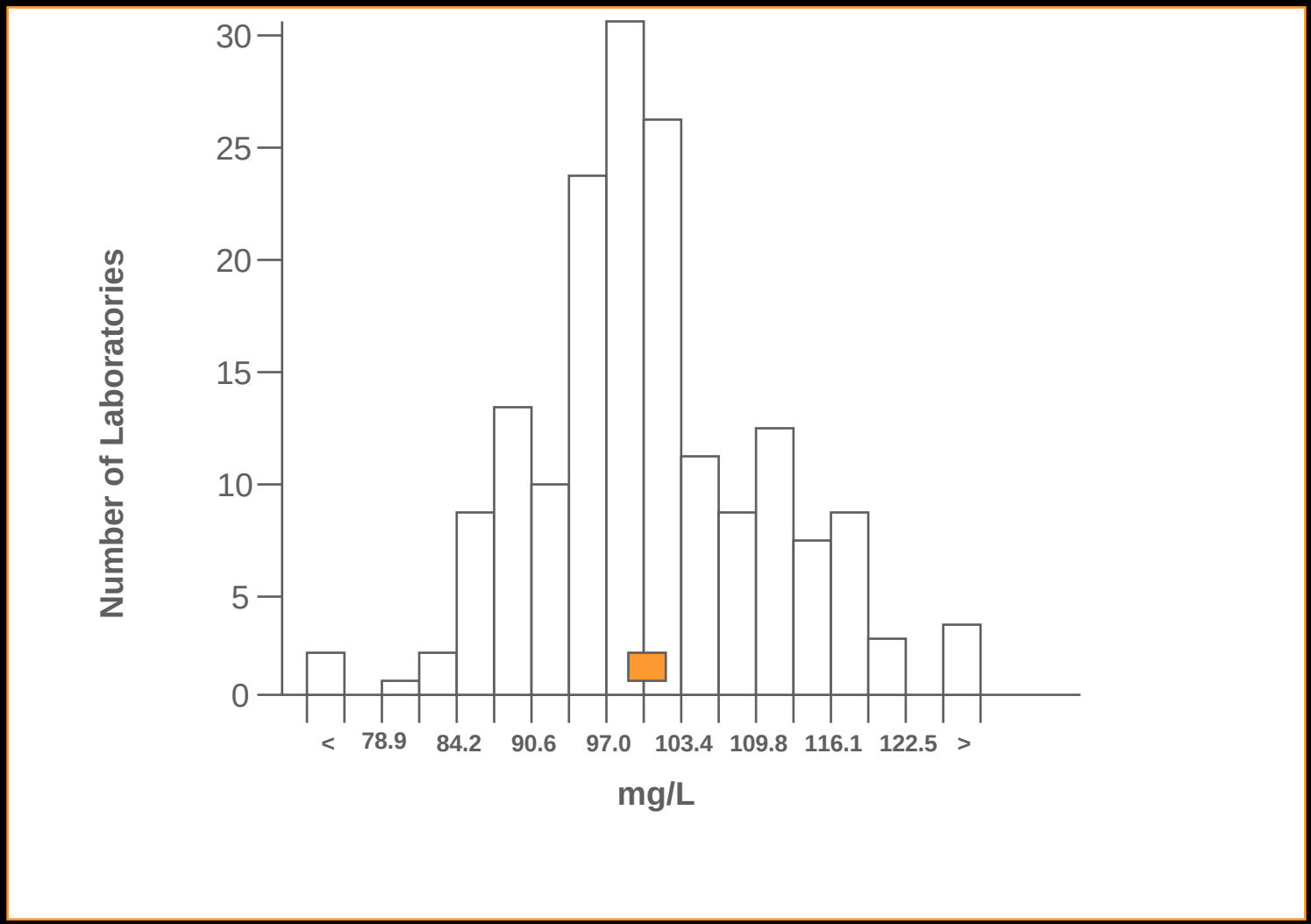
Value Reported (mg/L)	Program A Labs (%)	Program B Labs (%)
0	0	1
10	0	0
20	0	30
30	35	13
50	18	44
80	47	13
100	0	0

Urinary Albumin
(N = 160)

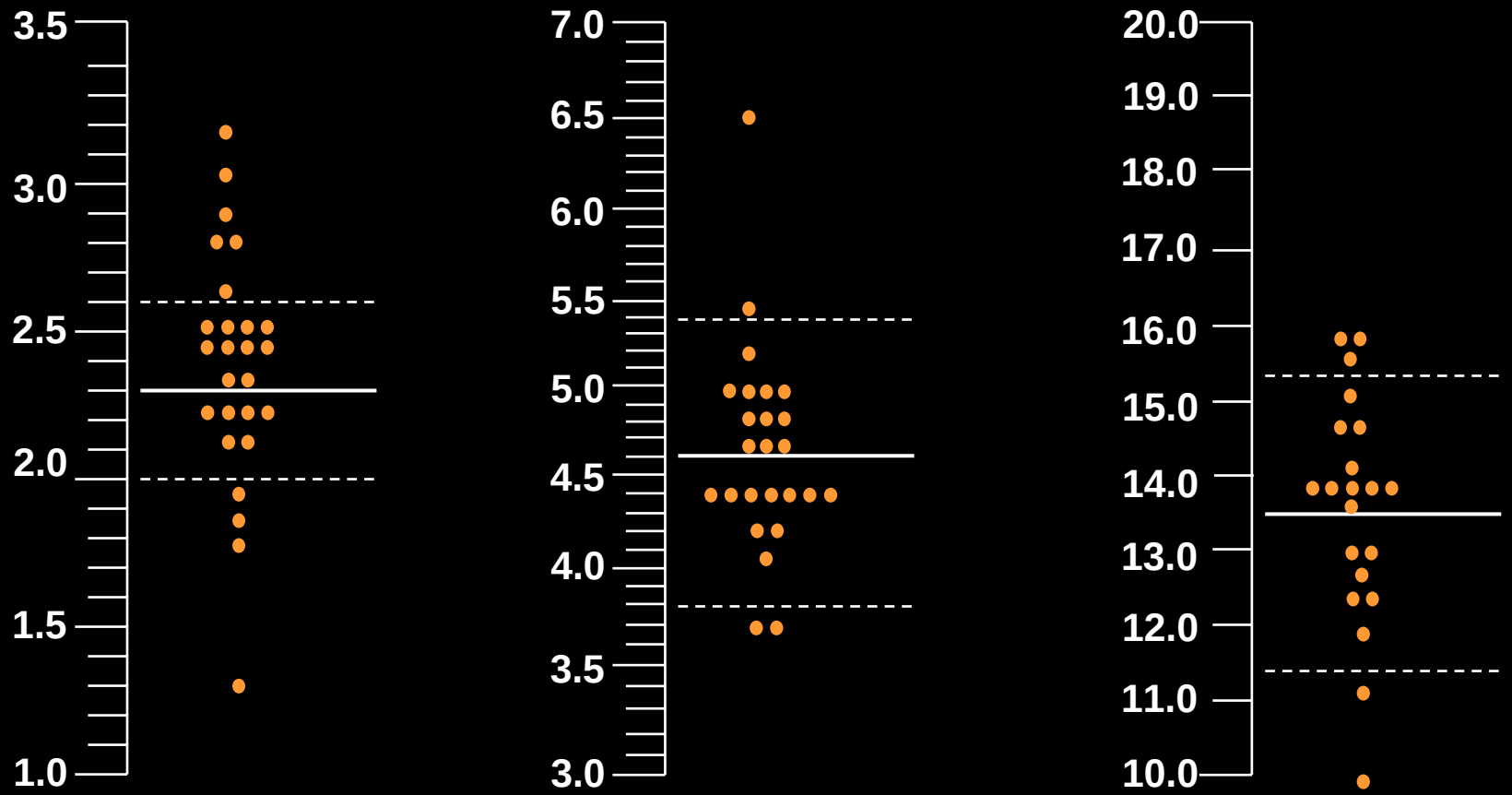
AMM = 46.4; SD=4.1; CV% = 9.0
(Randox - RIQAS Program)



Urinary Albumin
(N=160)
AMM = 100.2; SD = 8.5; CV%=8.5
(Randox – RIQAS Program)



Albumin:Creatinine (mg/mmol)
(QMPLS – 2005.01)



Albumin Concentration (17.6 mg/L)

Albumin Concentration (43.3 mg/L)

Albumin Concentration (116 mg/L)

Performance Assessment Criteria
Quantitative - Urine

(RV = Peer group mean)

Albumin	+/- 30% or 3 SD	+/-10 mg/L or 25%	+/-10 mg/L or 30%	+/-10 mg/L or 25%	+/- 3 SD	+/- 2.5 SD
Creatinine		+/-30 mg/dL or 15%	+/- 2 SD	+/- 3 SD	+/- 3 SD	+/- 0.3 mg/dL or 17%
Albumin : Creatinine Ratio	Not Assessed	Not Assessed	+/- 2 SD	+/- 3 SD	Not Assessed	+/- 2.5 SD

“As long as you are consistently wrong – you get a PASS ”

What level of analytical precision is needed ?

Albumin:creatinine ratio – within subject biological variation is approximately 30%

Analytical CV should be 0.5 x CV (within)

or 15%

Current methods operate with CV's ranging from 10% to 35%

What is needed ?

- Select the best test for standardization
- Establish and credential a suitable reference method
- Make available primary/secondary reference materials

What is needed ?

- Validate and transfer the reference method to a RM network (JCTLM)
- Provide pre and post analytical guidelines for standardizing the ordering and reporting of this test
- Use standardized methods for establishing reference intervals and target levels for treatment

What is needed ?

- Establish medically relevant performance goals for clinical laboratories that are reporting this test

- Monitor the analytical performance of this test in multi-centered research studies through the use of a common EQA/IQC program until such time as the test is standardized

Thank you

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