

CDC's Clinical Standardization Programs

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CDC Standardization Programs address clinical and public health needs for accurate and reliable measurements

- *Endocrine Society JCEM 2010;95:4541-48*
“deficiencies in these (testosterone) assays...threaten the health of those patients whose medical care relies upon its accurate measurement”
- *American Urology Association. www.auanet.org, 2013*
“This (inaccuracy in testosterone tests) leads to diagnostic and management dilemmas...”
- *Endocrine Society JCEM 2013;98:1376-87*
“the care of patients across the life span is hampered by the lack of availability of sensitive, precise, and specific estradiol assays.”
- *Institute of Medicine 2011*
“A single individual might be deemed (vitamin D) deficient or sufficient, depending on the laboratory where the blood is tested.”



CDC's Clinical Standardization Programs improve the laboratory diagnosis and detection of selected chronic diseases

Program Goals:

- Improve the accuracy of laboratory measurements for selected disease biomarkers
- Provide technical support to agencies and organizations working to improve the accuracy and reliability of clinical laboratory measurements

CDC's programs perform each step in the standardization process to effectively improve laboratory measurements

Develop and Maintain
Reference System



Establish Metrological
Traceability



Verify "End-User"
Test Performance

REFERENCE LABORATORY SERVICES

Provide reference value assignments to materials used in clinical and research laboratories

STANDARDIZATION SERVICES

Assist individual participants with calibration and maintenance of accuracy

PERFORMANCE MONITORING SERVICES

Assess measurement performance in patient care and research

CDC's programs perform each step in the standardization process to effectively improve laboratory measurements

Develop and Maintain Reference System

Target value assignments by Hormones, Vitamin D and Lipid Reference Laboratories
incl. Cholesterol Reference Method Laboratory Network (CRMLN)



Establish Metrological Traceability

Certification of performance through HoSt, VDSCP, and CRMLN



Verify "End-User" Test Performance

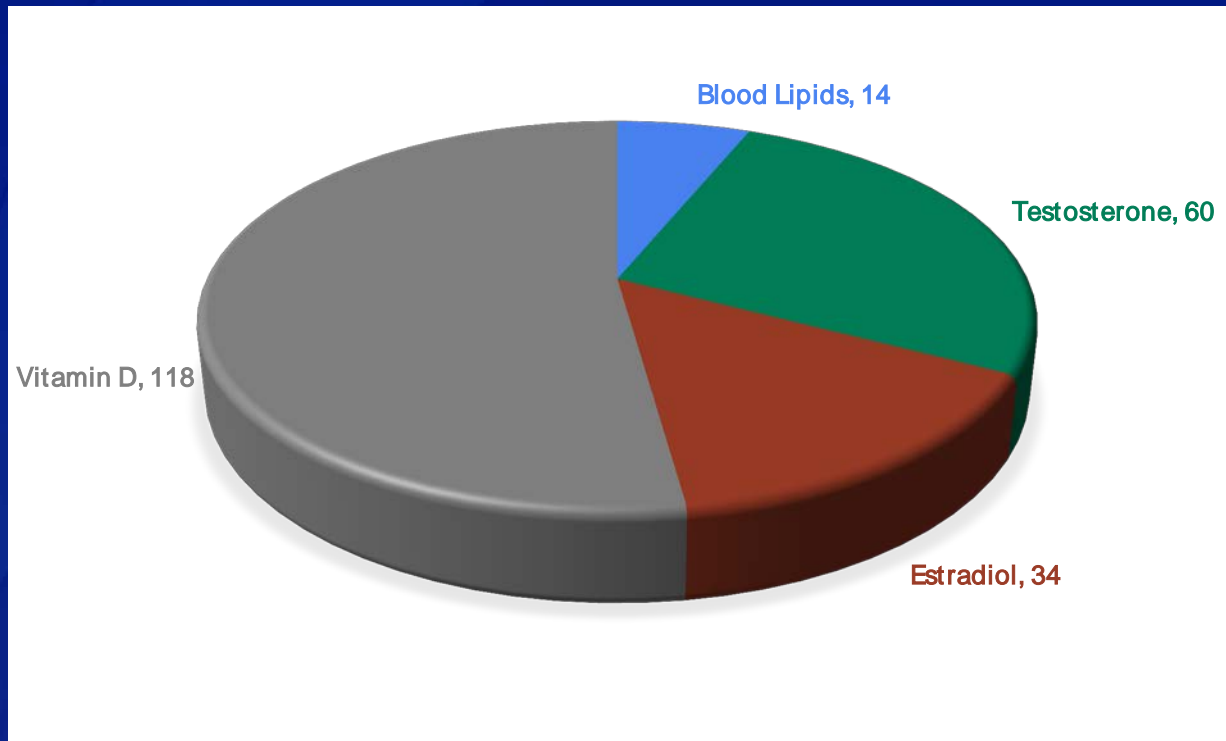
Performance monitoring through Lipids Standardization Program (LSP), accuracy-based EQA/PT programs, accuracy-based blind QCs in research studies

CDC operates several reference measurement procedures and continuously develops new procedures

Analytes	Methodology
Testosterone	HPLC/MS/MS
Estradiol	HPLC/MS/MS
25-Hydroxyvitamin D	HPLC/MS/MS
Total Cholesterol	GC/MS and Abel Kendall
Triglycerides	GC/MS
HDL-Cholesterol	UC/Abel Kendall
LDL-Cholesterol	UC/Abel Kendall
Glucose	UPLC/MS/MS in development
Thyroid Hormones	
Parathyroid Hormone	

CDC reference laboratory assigns target values to over 200 sera per year

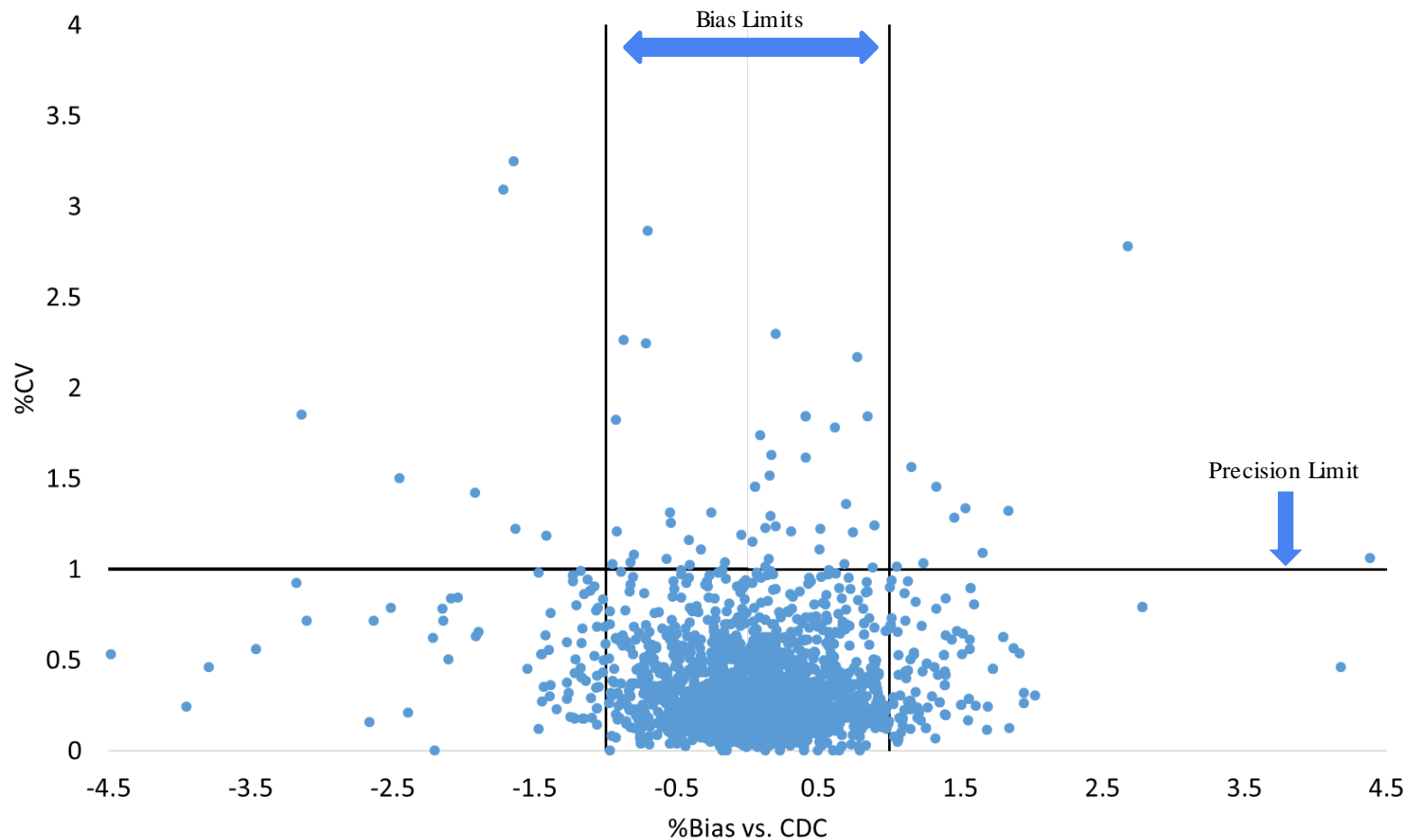
Average annual number of sera with target values by analyte



Blood Lipids: total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides
Vitamin D: 25-OH-Vitamin D3, 25-OH-Vitamin D2

Cholesterol Reference Method Laboratory Network (CRMLN) maintains highly accurate and precise reference measurements for over 10 years

Total Cholesterol CV vs. Bias Plot 2002 - 2015



CDC Performance Certification Programs are performed with individual donor specimens

CDC suggests a two phase process for performance evaluation and certification

Phase 1

Performance assessment and adjustment using single-donor samples with known reference values

Phase 2

HoSt and VDSCP:
Quarterly performance monitoring with 10 blinded single-donor samples provided by CDC

CRMLN:
Performance assessment with at least 40 single-donor samples provided by the manufacturer

Performance evaluation based on CLSI document EP 9 using performance criteria suggest by the clinical and laboratory communities

CDC Standardization Programs provide unique services to support laboratories improve measurement performance

CDC HoSt Program and VDSCP

Panel of 40 single-donor serum samples

- Avoids potential problems related to commutability frequently observed in pooled/altered serum
- Enables thorough evaluation of measurement performance across relevant concentration ranges
- Allows for identification of the sources for bias (calibration vs. non-specificity)

Replicate measurements

- Provides information on imprecision in addition to bias

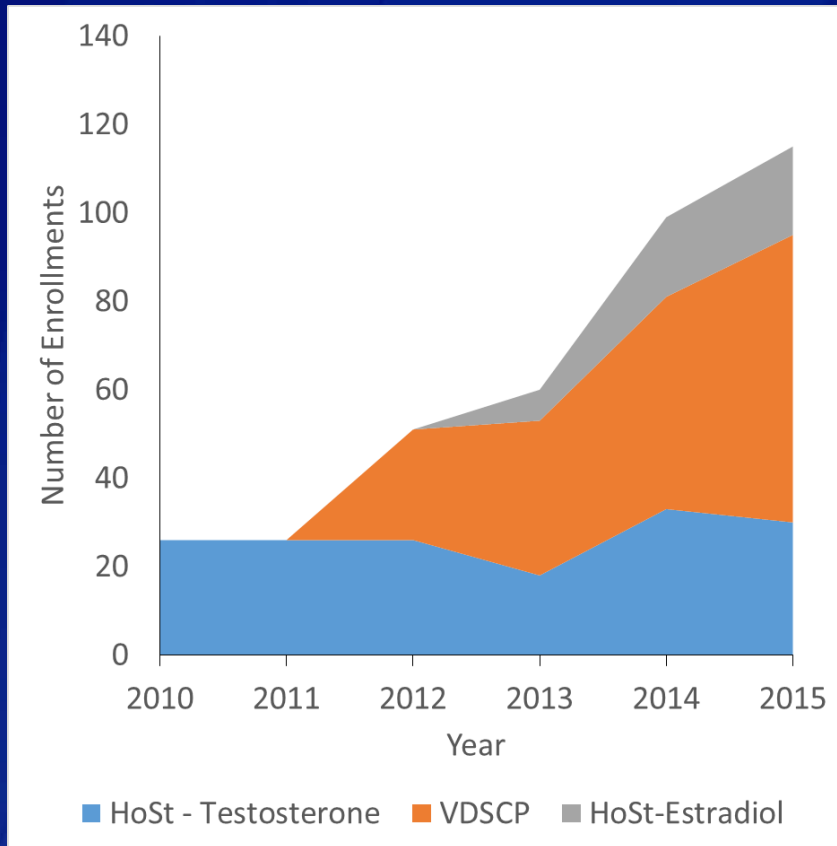
Quarterly and yearly assessments/certifications

- Allows timely detection of changes in accuracy (quarterly)
- Verifies performance over time (yearly)

Support to participants

- Minimizes other sources of error (i.e. clerical errors)
- Customization of analyte concentration to cover the reportable range of the assay

CDC's Standardization Programs is increasing in size and scope



Participation in the CRMLN Certification remained constant over the past 5 years

Average Annual Participation:

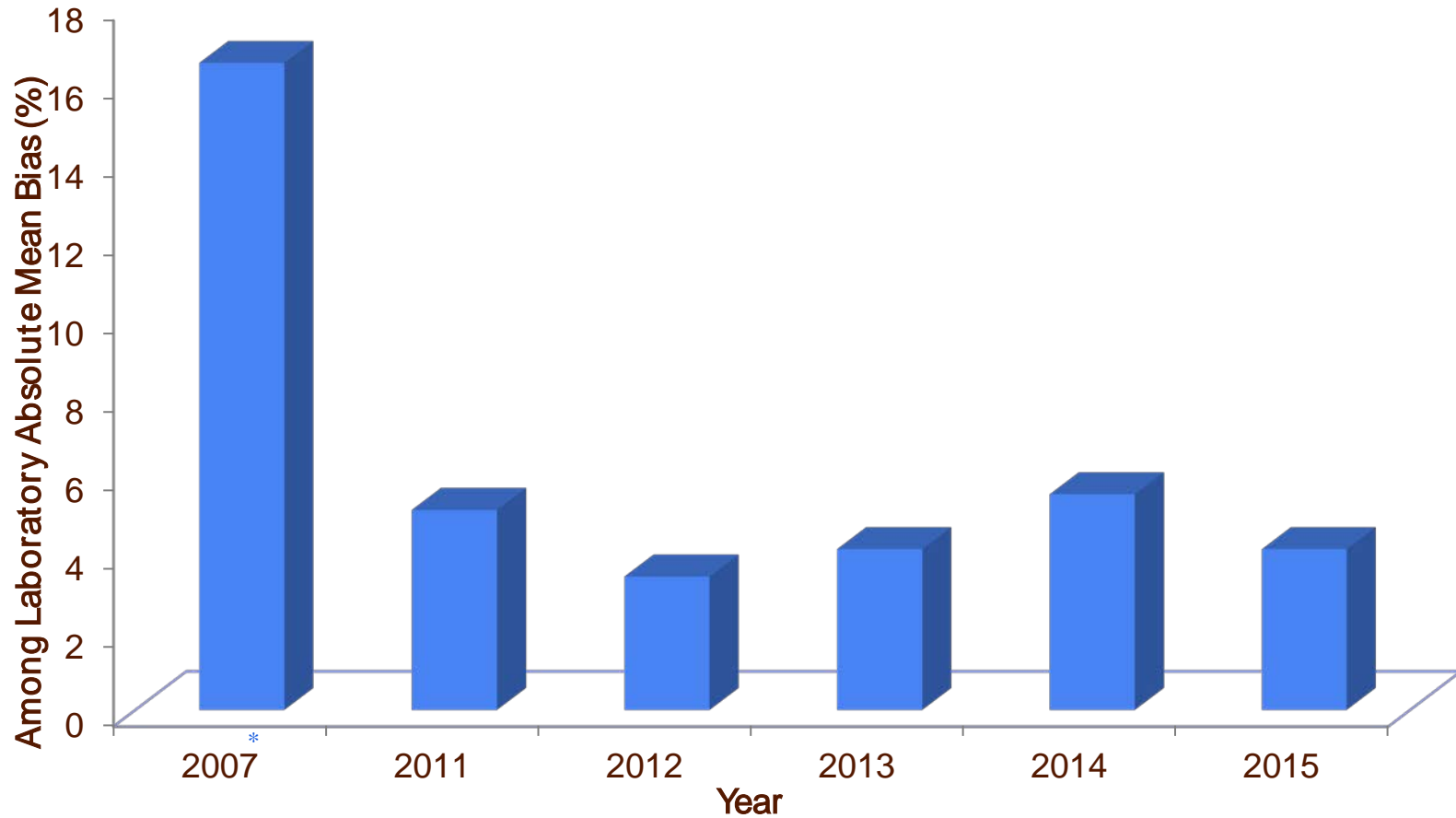
Manufacturers: 37

Systems/Assays: 110

Laboratories: 200

CDC's Standardization Programs issue over 1,000 performance evaluations each year

Calibration bias of testosterone measurements improved since the start of the CDC HoSt Program



*MS assays only

CDC supports PT/EQA providers with their surveys and monitors measurement performance of survey participants

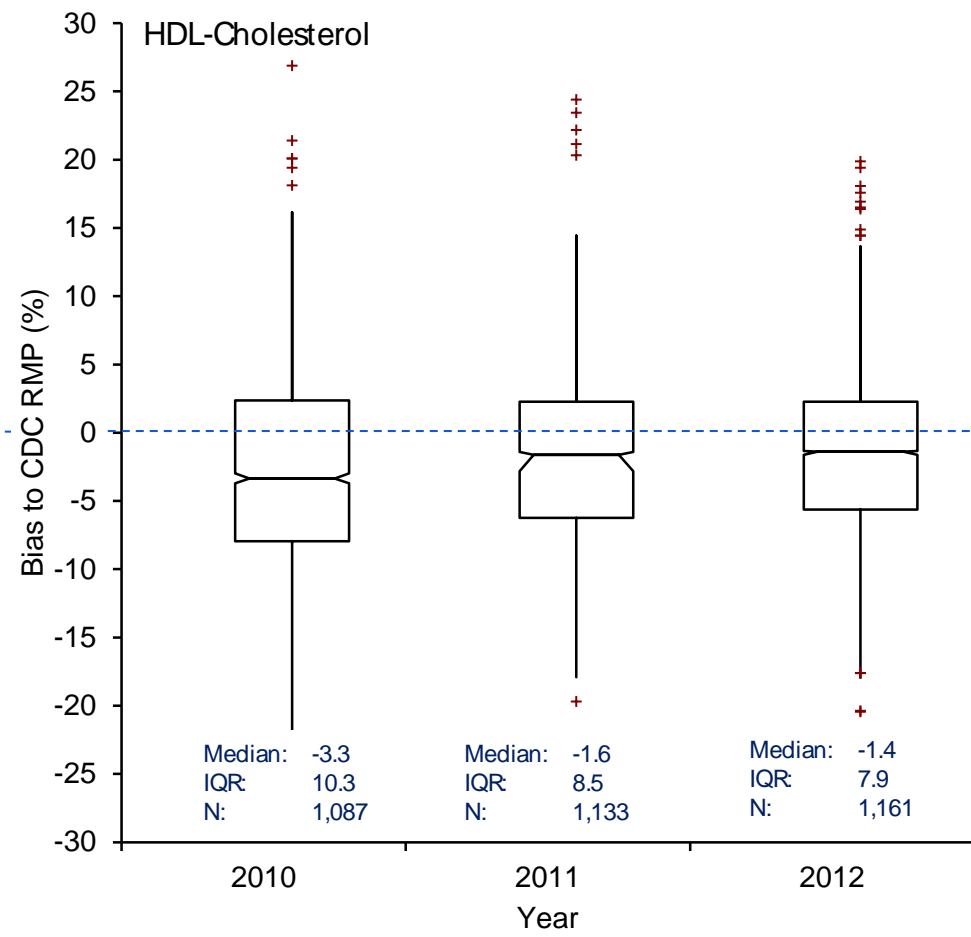
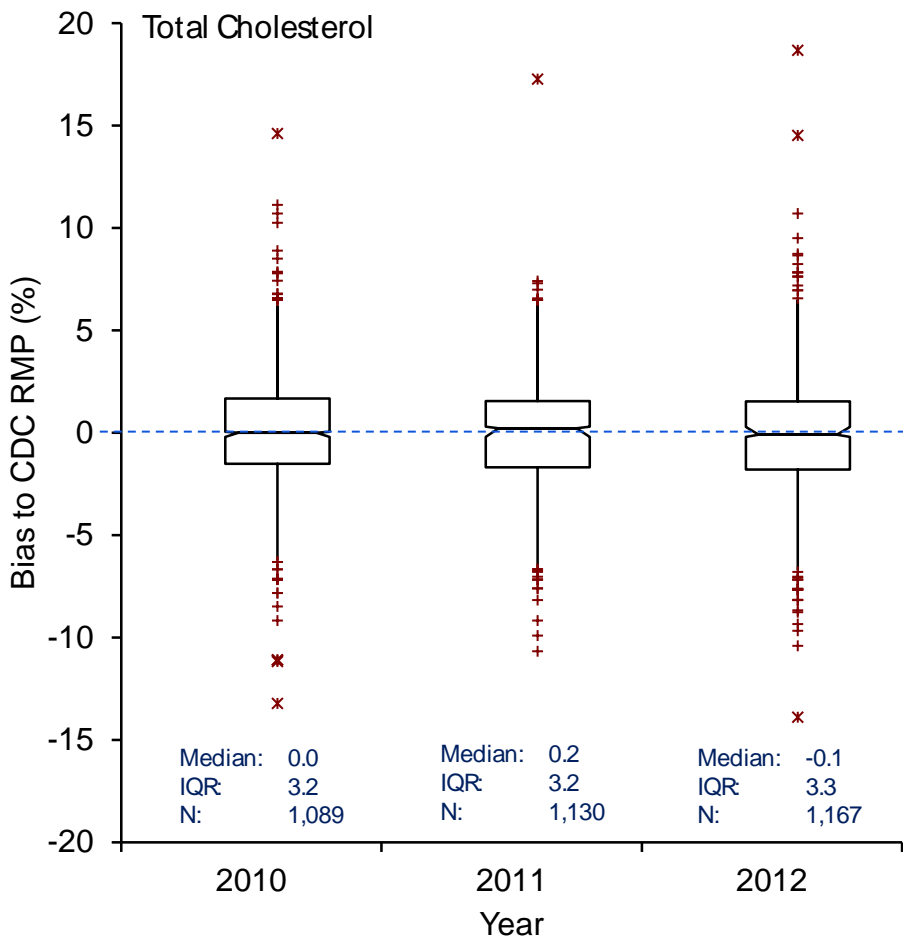
CDC is assigning target values for accuracy-based PT/EQA surveys conducted by the following organizations:

- ❑ College of American Pathologist (CAP)
- ❑ Royal College of Pathologists of Australasia (RCPA)
- ❑ New York State Department of Health



Total and HDL-cholesterol measurements performed in patient care are highly accurate with very small variability

CAP ABL Survey Bias Distribution by Year

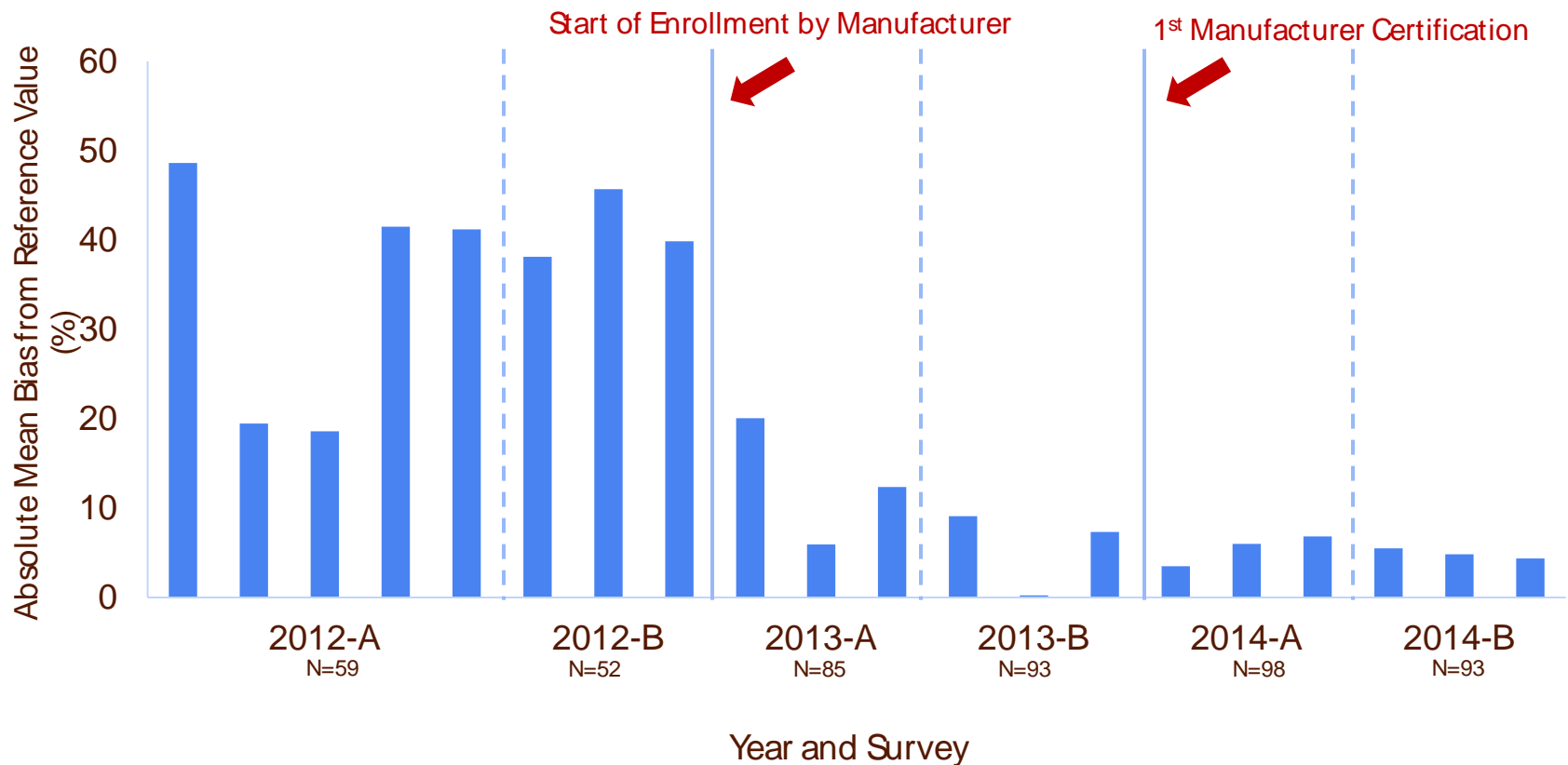


Interquartile range is well within the total allowable error of 7.9%

Interquartile range is well within the total allowable error of 11.6%

Certification of manufacturers leads to improved measurement accuracy in patient care

Absolut mean bias observed in CAP-ABVD samples measured by several clinical laboratories using the same immunoassay



CDC Standardization Program continues to improve clinical laboratory testing by increasing its program activities

- Provide new panels of 120 individual single-donor samples with reference target values for advanced performance testing
- Include individual sample bias in addition to overall mean bias in performance evaluation
- Add samples from patients with certain diseases to sample sets used in performance evaluation
- Conduct ad-hoc interlaboratory and commutability studies using the CDC Standardization Programs infrastructure



CDC supports other organizations working on improving the accuracy and reliability of clinical tests

Organization	Project/Activity
International Federation of Clinical Chemistry and Laboratory Medicine (IFCC)	Standardization of Parathyroid Hormone Guideline Development (Commutability)
National Glycohemoglobin Standardization Program (NGSP)	Standardization of HbA1c
Diabetes Technology Society (DTS)	Post-market Surveillance Program for Glucose Monitors
Clinical and Laboratory Standards Institute (CLSI) and International Standards Organization	Standards and Guideline Development
JCTLM and National Institute for Standards and Technology (NIST)	Reference Systems
American Association of Clinical Chemistry	Harmonization Initiative Universal Sample Bank Project

Partnership for the Accurate Testing of Hormones (PATH) supports and promotes standardized hormone tests for better healthcare and research

PATH is a stakeholder organization

- Consists of clinical, medical and public health organizations
- Promotes accurate tests and appropriate use of hormone tests through
 - Education
 - Advocacy
 - Technical Support

www.hormoneassays.org

PATH Members

American Association for Clinical Chemistry

American Association of Clinical Endocrinologists

Androgen Excess/PCOS Society

American Society for Bone and Mineral Research

American Society for Reproductive Medicine

American Urological Association

Association of Public Health Laboratories

College of American Pathologists

Centers for Disease Control and Prevention

Endocrine Society

Laboratory Corporation of America

National Institute of Health/NICHD

North American Menopause Society

Pediatric Endocrine Society

International Andrology Society

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American Association of Clinical Chemistry

Endocrine Society

Thank you

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<http://www.cdc.gov/labstandards/hs.html>

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Visit: www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info

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