NATIONAL ASSOCIATION OF
CHRONIC DISEASE DIRECTORS
Promoting Health. Preventing Disease.

CLINICAL STANDARDIZATION

Improving the diagnosis, detection and treatment of chronic diseases through standardization

What is standardization?

Clinical standardization programs improve the diagnosis, treatment and prevention of chronic diseases through accurate and reliable laboratory testing.

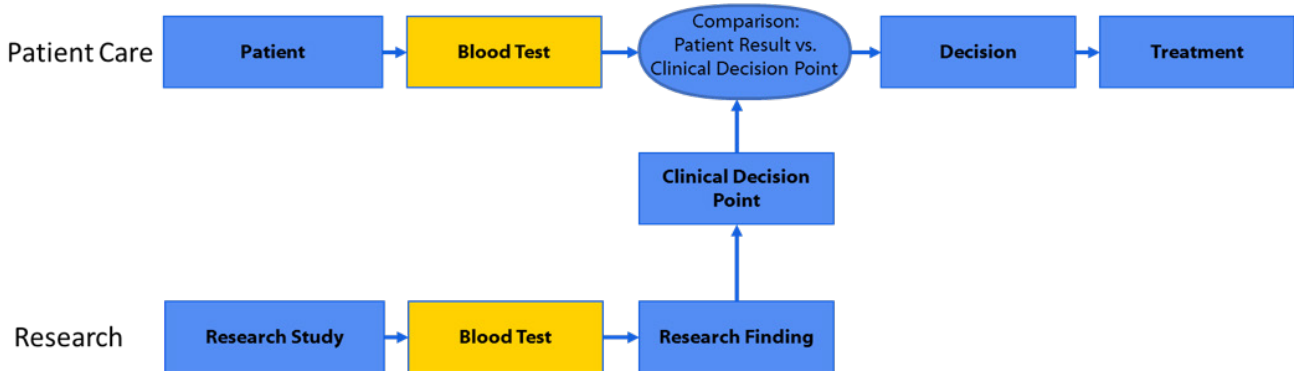
Clinical standardization programs harmonize clinical tests so that results are accurate and comparable over time and across methodologies and laboratories.

Accurate and reliable chronic disease biomarker measurements are critical for patient care and to conduct clinical research effectively. Standardization offers accurate and reliable laboratory testing for use in clinical diagnosis, treatment, and public health decisions. Standardization minimizes variability in patient testing and clinical trial outcomes. Without standardization, inaccurate measurements can cause incorrect diagnosis, unneeded medical procedures and repeat testing, and inappropriate treatment.

Effective, evidence-based patient care and public health require laboratory measurements that are accurate and harmonized.

In clinical practice, measurement results from a patient's blood test often are compared to clinical decision points to identify whether blood biomarker levels are normal or of concern. Based on this comparison, the healthcare provider decides how to treat a patient. The clinical decision points are obtained from research studies, in which blood tests were done to determine biomarker levels.

The diagram below illustrates how blood tests in research and patient care are connected to clinical decision making.



The Institute of Medicine investigated several research studies and found that people with vitamin D levels (expressed as 25-Hydroxyvitamin D) below 30 nmol/L can be at risk of deficiency relative to bone health. Health care providers may use this value as a clinical decision point for comparison with a patient's vitamin D level. A patient with vitamin D levels below this decision point might be considered deficient and get treatment.

Some tests are not sufficiently accurate to correctly assess a patient's health or success of treatment.

For example, Vitamin D measurements on the same patient may be different when measured in different laboratories (https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/).

The clinical and laboratory communities identified important biomarkers that need harmonization to improve the diagnosis, treatment, and prevention of major chronic diseases that affect many people in the U.S.

The table below provides some examples of biomarkers currently being addressed.

Biomarkers	Disease/Health Conditions
Total cholesterol, HDL-cholesterol, LDL-cholesterol, Total glycerides, Lipoproteins	Cardiovascular diseases
Vitamin D, Parathyroid hormone	Osteoporosis and bone health
Estradiol, testosterone, sex hormone binding globulin	Certain cancers and pituitary disorders
Thyroid hormones, Thyroid stimulating hormones	Child and developmental health, hypothalamus disorders

Standardization of chronic disease biomarker tests helps to ensure that patients are diagnosed and treated consistently whenever the test is done.

Who benefits from laboratory standardization?

Doctors, public health officials, researchers, and patients

Doctors

Doctors can diagnose and treat patients more effectively with accurate tests that allow the use of evidence-based clinical guidelines.

Researchers

Researchers can compile and compare testing data across laboratories and studies to formulate evidence-based patient guidelines and public health policies.

Benefits of Standardized Measurements

Patients

Patients can be assured of the accuracy of their clinical tests, thus giving them confidence in disease prevention treatment recommendations.

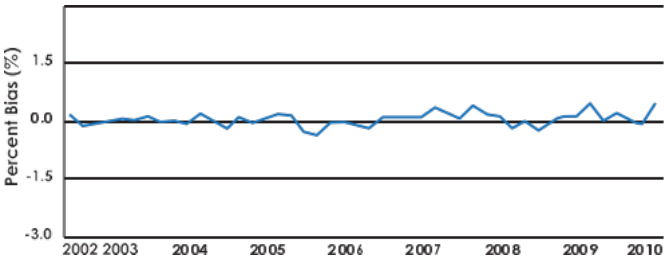
Public health officials

Public health officials can evaluate public health impact with reliable monitoring of biomarkers in populations over many years, even if testing methods and equipment changes.

Laboratory standardization creates and maintains accurate and comparable research, patient, and public health data. This allows for the rapid transfer of research findings to clinical and public health practice and facilitates the interpretation of public health data.

As an example, standardization efforts by the Centers for Disease Control and Prevention (CDC) for cardiovascular biomarkers impact doctors, public health officials, researchers, patients, and payers.

For doctors



CDC's Cholesterol Reference Method Laboratory Network (CRMLN) assures accurate testing of an estimated 300 million cholesterol tests performed in patient care annually in the U.S. and enables doctors to better diagnose patients at risk of cardiovascular disease.

Source: *CDC Lipid Standardization Program*

For patients

Reliable testing and treatments help increase screening rates and public awareness. An economic analysis of the CDC Lipid Standardization Program (LSP) and the CDC Cholesterol Reference Method Laboratory Network (CRMLN) found that LSP and CRMLN have prevented more than 340 thousand deaths since their inception and resulted in annual estimated health care savings of $1.53 billion and about 13,500 life-years gained annually.

Source: *Prev Chronic Dis 2011;8(6):A136*

For researchers

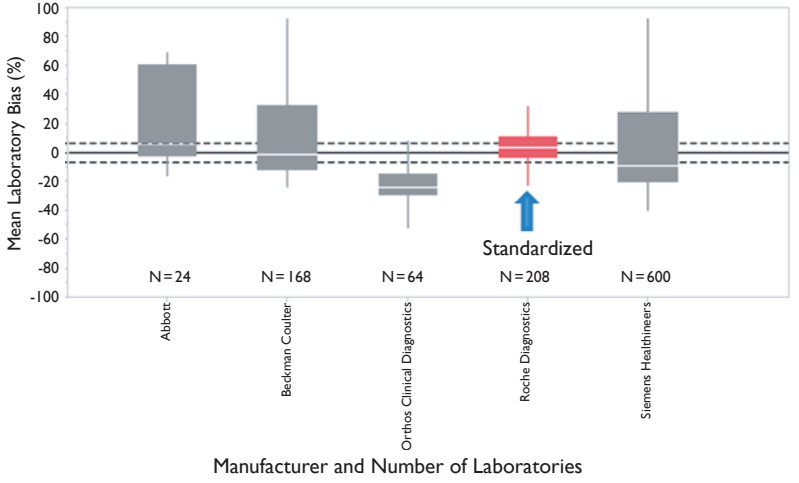
The standarized clinical and epidemiology studies enable researchers to develop and implement evidence-based clinical guidelines. The National Institute of Health's National Cholesterol Education Program developed guidelines for identifying individuals with high blood cholesterol levels using studies from CDC's Lipid Standardization Program.

Source: *JAMA 2001;285:2486-2407*

For more information on CDC's clinical standardization programs, visit: **cdc.gov/labstandards**

CDC also provides the Hormone and Vitamin D Standardization Certification Program to improve the diagnosis of polycystic ovary syndrome, certain cancers, and other diseases of hormone excess and deficiency. The program assists in providing more accurate and precise hormone measurements used in patient care and research, specifically testosterone, 25-hydroxyvitamin D, and estradiol. For example, CDC's Hormone Standardization program recently helped harmonize normal reference ranges for testosterone concentrations in men using data from four American and European cohorts. These reference ranges are now being applied in clinical practice (J Clin Endocrinol Metab., 2018).

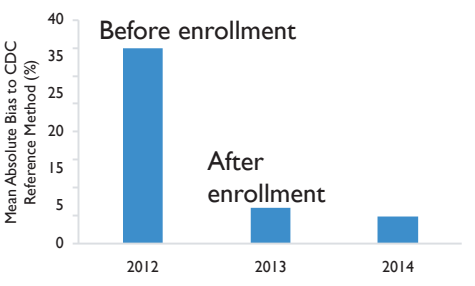
Tests standardized by programs such as CDC's Clinical Standardization Programs show higher accuracy and comparability in patient care than non-standardized tests. (Example: CDC Hormones Standardization Program [HoSt].)



Clin Chim Acta. 2017;469:31-36

Test manufacturers enrolling in programs such as CDC's Clinical Standardization Programs notably improve their accuracy and reliability. (Example: CDC Vitamin D Standardization Certification Program [VDSCP].)

For more information on CDC's clinical standardization programs: **cdc.gov/labstandards**



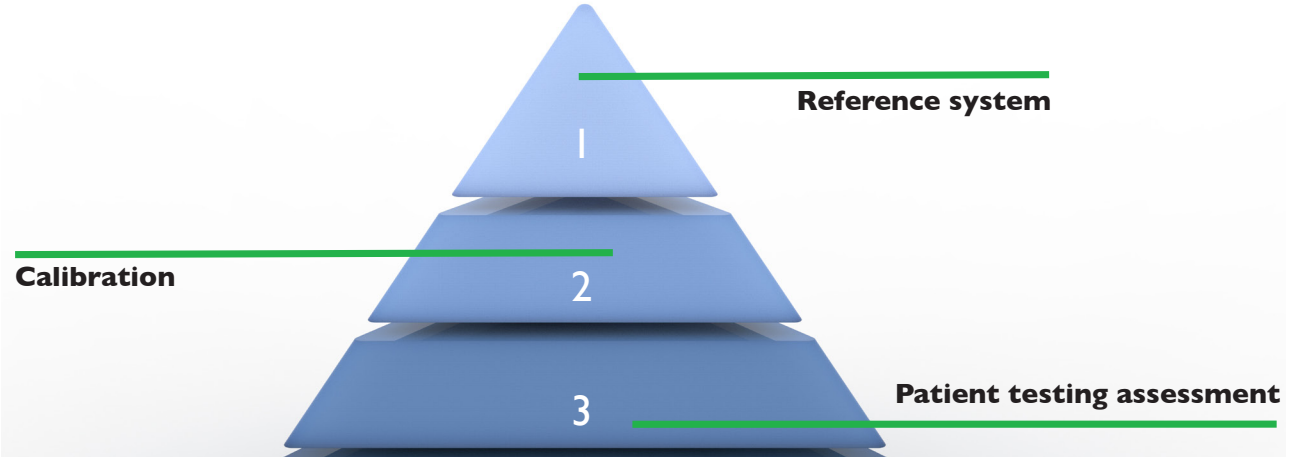
How does standardization work?

The three steps for reliable standardization:

A reference laboratory helps improve clinical measurements made in many laboratories, in turn improving the diagnosis of more patients.

The two most important characteristics of a good clinical chemistry test are accuracy and precision.

Both are achieved by making patient measurements traceable to one common reference system.



The Three-Step Standardization Process

Reference System

In the first step of standardization, a reference laboratory establishes a system of reference methods and reference materials. Reference methods are highly accurate, precise, and often traceable to the standards created by organizations such as the National Institute of Standards and Technology. Reference laboratories use these reference methods to assign concentrations to blood samples used for calibration and verification.

Calibration

In the second step of standardization, clinical tests are calibrated using the blood samples evaluated in the first standardization step.

Standardization laboratories, like those operated in CDC's Hormone Standardization Program, Vitamin D Standardization Certification Program, and Cholesterol Reference Method Laboratory Network, calibrate and assess analytical performance of laboratory-developed tests and test manufacturers. They also assist manufacturers and laboratories in improving test performance, so that clinical tests meet the accuracy and precision needed in patient care and public health. Laboratory-developed tests and test manufacturers that meet performance goals are certified as standardized.

Verify Test Performance

In the third step of standardization, the accuracy and reliability of patient testing is monitored to assess whether the improved test performance achieved in step two led to improved patient testing.

For example, CDC monitors testing performed in patients enrolled in epidemiological studies and clinical trials through their Lipid Standardization Programs and Accuracy-based Monitoring Program. By collaborating with organizations such as the College of American Pathologists and other proficiency testing or external quality assessment programs, CDC can monitor testing performed in patient care and research.

Services

To laboratories, test manufacturers, researchers, and doctors

Standardization programs such as CDC's provide services to laboratories, test manufacturers, researchers, and doctors in all three steps of the standardization process.

Reference System

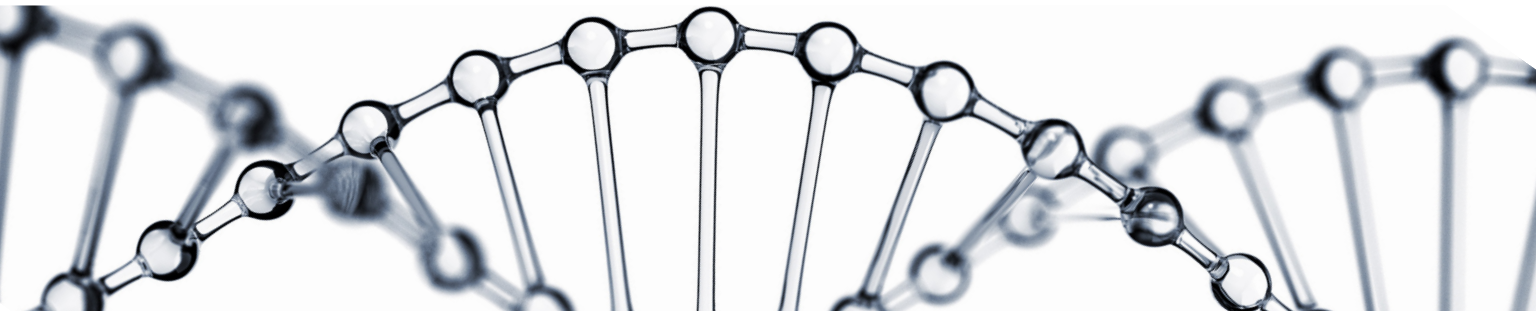
- Assign target values to serum-based materials for use as calibrators and controls.
- Aid laboratories and test manufacturers in achieving accurate and precise measurements.
- Perform research to identify and improve problems in clinical testing measurements.

Calibration

- Assure the accuracy and precision of clinical tests.
- Provide materials and technical assistance with test calibration.
- Certify tests that meet performance goals needed for optimal patient care.

Patient testing assessment

- Provide accuracy-based control blood samples to research laboratories to monitor and certify the accuracy and precision of measurements performed in clinical trials and other research studies.
- Assign target values to proficiency testing and external quality assurance programs, enabling clinical laboratories the ability to assess their measurement accuracy.
- Conduct focused studies to assess test performance and evaluate serum materials for their suitability as calibrator and control.



Additional Resources

The Partnership for the Accurate Testing of Hormones (PATH)

• hormoneassays.org

PATH is a stakeholder organization that consists of public and private clinical, medical, and public health organizations. PATH promotes the use of standardized tests through educating health care providers and the public and providing technical support.

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
• The Endocrine Society
• Laboratory Corporation of America
• National Association of Chronic Disease Directors
• National Institutes of Health, National Institute of Child Health and Human Development
• North American Menopause Society
• Pediatric Endocrine Society (formerly known as Lawson Wilkins Pediatric Endocrine Society)
• International Andrology Society
• Siemens
• Roche

CDC Laboratory and Quality Assurance Programs

• cdc.gov/labstandards/overview.html

The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC)

• ifcc.org

The Joint Committee for Traceability in Laboratory Medicine (JCTLM)

• bipm.org/en/committees/jc/jctlm/

National Institute for Standards and Technology (NIST)

• nist.gov

The World Health Organization (WHO)

• who.int

About NACDD

The National Association of Chronic Disease Directors (NACDD) and its more than 7,000 members seek to improve the health of the public by strengthening leadership and expertise for chronic disease prevention and control in states, territories, and at the national level. Established in 1988, in partnership with the U.S. Centers for Disease Control and Prevention, the NACDD is the only membership association of its kind serving and representing every state and U.S. territory's chronic disease division.

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