

## ASCLS Mission:

The mission of ASCLS is to make a positive impact in health care through leadership that will assure excellence in the practice of laboratory medicine.



## Resources:

AACC Lab Tests Online. Reference Ranges and What They Mean. <https://labtestsonline.org/articles/laboratory-test-reference-ranges>

ClinLab Navigator. Reference Ranges. <http://www.clinlabnavigator.com/reference-ranges.html>

CLSI. Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; *Approved Guideline - Third Edition, CLSI document EP28-A3c*. Wayne, PA: Clinical and Laboratory Standards Institute, 2008 (Oct 2010 corrected version)

Edwards, Nancy & Baird, Carol. (2005). Interpreting laboratory values in older adults.. *Medsurg nursing : official journal of the Academy of Medical-Surgical Nurses*. 14. 220-9; quiz 230.

Higgins, Chris. (2009). An introduction to reference intervals (1) - some theoretical considerations. *Acute Care Testing.org*. <https://acutecaretesting.org/en/articles/an-introduction-to-reference-intervals-1--some-theoretical-considerations>

Jones, Graham & Barker Antony (2008). Reference Interval. *Clin Biochem Rev*. 29(Suppl 1), S93-S97. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2556592/>

For additional information on specific laboratory tests visit *Lab Tests Online* <https://labtestsonline.org/>

Please contact your testing laboratory for information on individual laboratory test reference intervals or support on this topic.

**Your Safety and Service Experience  
Are Important To Us!**

## Laboratory Patient Safety Tips:

## Using a Laboratory Reference Interval (Range) for Result Interpretation

## Information For Providers



## What is a Reference Interval?

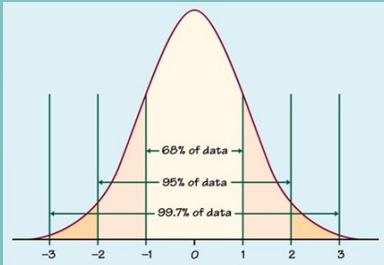
It is a statistical range of expected values set by the testing laboratory which identifies lower and upper limits of a population for a specific test (e.g. apparent healthy population or separate intervals for different sub-populations such as age, sex, reproductive status, race, etc.). Reference intervals provide a relevant population-based interval to assist in clinical interpretation of the test.

-Note: 'Reference Interval' is the current accepted terminology but may also be referred to as 'reference range' or 'normal range' in some settings or discussions.

## How are Reference Intervals Developed?

A laboratory is required to establish or verify its test reference intervals based upon evidence. There are three main methods to establish or validate a reference interval:

1. **Establish an internal reference interval study** using standard published procedures and statistical analysis to determine the central 95% of the population. For specifics contact your testing laboratory.



2. **Adopt a published reference interval** from reputable literature, other laboratories, manufacturers, etc. through statistical analysis and an accuracy assessment of a population.

3. **Utilize a consensus reference interval** determined by medical experts (e.g. American Diabetes Association, American Heart Association) for test results obtained during large clinical studies related to specific patient or disease populations, which may require accuracy of the laboratory test method in comparison to the clinical studies.

## Common Variables that May Affect Reference Interval Interpretation:

- Age, sex, and race
- Specimen type (e.g. plasma, urine)
- Time of collection (e.g. cortisol)
- Duration of collection (e.g. 2, 12, 24-hour urine collections)
- Fasting vs. non-fasting (e.g. glucose)
- Health status (e.g. pregnancy, chronic disease)
- Individual medical decision limits due to a pre-existing disease or identified abnormality (e.g. cholesterol, HbA1c)

## Common Factors that May Cause an Abnormal Result in a Normal Patient:

- Individual variability
- Biological variability
- Statistical variability
- Laboratory-to-laboratory variation may be caused by:
  - Geographic location
  - Operating conditions
  - Test method, instrumentation, reagents, interfering substances, analytical detection limits, etc.
- Pre-analytical factors
  - Specimen collection and type
  - Patient preparation (i.e. fasting, dietary restrictions, etc.)
  - Specimen processing, transportation, and storage
  - Specimen integrity (e.g. hemolysis, clotting, lipemia)
  - Medications and over-the counter supplements

## Reference Interval Considerations

- Reference intervals published for apparent healthy adult populations may have limitations for specific sub-populations. Additional considerations should be made when using reference intervals to evaluate special populations. Examples include:
  - Birth through adolescence: physiological growth and development variations
  - Elderly: age-related physiological changes, prevalence of comorbidities, medications, etc.
  - Transgender patients: transition status and/ or therapies may cause variations
  - Intersex individuals, or those with disorder or difference of sexual development (DSD): reference intervals may vary
- A result falling **within** the reference interval may not rule-out disease, especially in the early stages of disease.
- A result falling **outside** the reference interval may not indicate disease.
- A patient result that shifts within a reference interval may be an early indicator of disease.

## What if a Patient's Test Result is Outside the Reference Interval?

Complete routine patient evaluation based on medical and family history, physical exam, current treatment, and new signs and symptoms. Additional considerations:

- Did the patient comply with test preparation requirements (e.g. fasting, stopping medications)?
- Did the patient disclose all medications and over-the-counter supplements that may interfere with the laboratory assay (e.g. biotin, herbal supplements)?
- Could a pre-analytical or technical variable (during collection, transport, storage, or analysis) have affected the test results?

*Contact the testing laboratory with any clinical concerns, potential assay limitations, and reference interval or interpretation questions related to the test result. Your inquiries and questions help assure quality testing and patient outcomes.*

