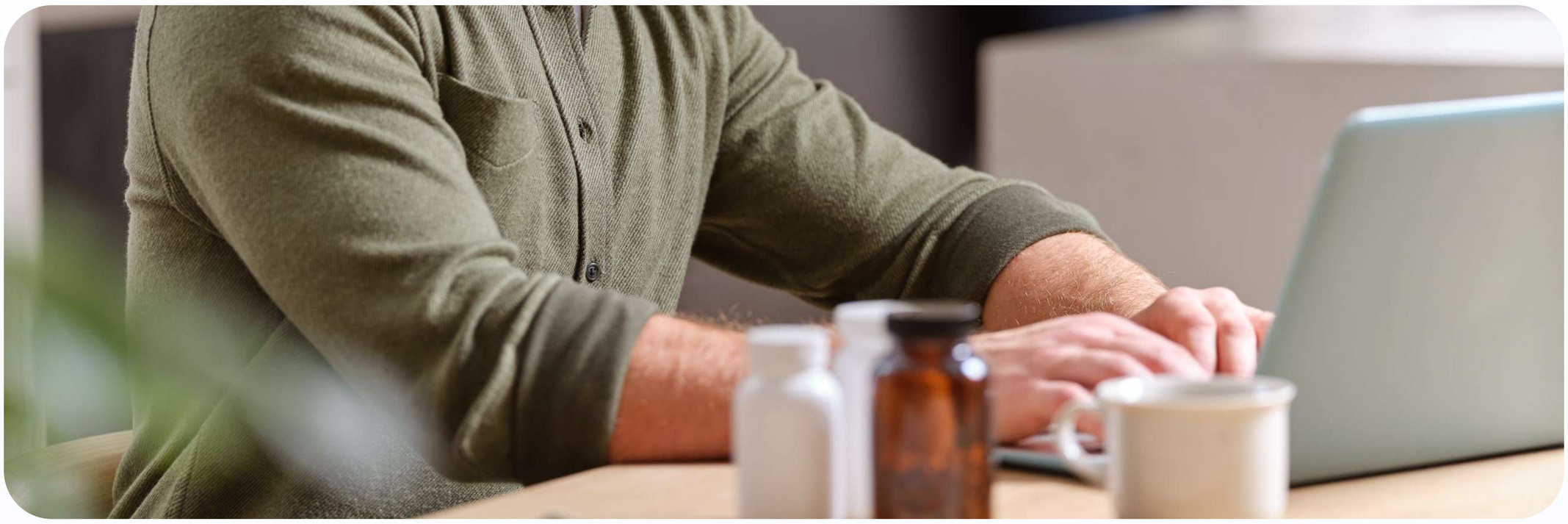


The basics of lab testing

Lab testing is an essential resource in a medical practitioner's toolkit and is used to inform approximately 70–80% of all clinical decisions. (Katayev 2010)(Rohr 2016)(St. John 2020) Many integrative practitioners use lab testing as a strategy to get patients invested in their health plan and boost treatment adherence by taking the time to adequately explain results and show progress in outcomes over time. (Bailey 2021)

Lab work can also be very useful for monitoring a patient's condition. Decision-making on the modification, maintenance, or discontinuation of treatment can be greatly aided by repeat lab testing at certain intervals after treatment has begun.

US regulatory environment

In partnership, the Food and Drug Association (FDA) and the Centers for Medicare and Medicaid Services (CMS) handle the regulatory oversight of lab tests and the laboratories that conduct and analyze tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA'88). The FDA oversees the manufacturing, clearance or approval, marketing, and post-market surveillance of tests intended for commercial distribution. In contrast, the CMS has duties related to the quality assurance of laboratory practices. (FDA 2021a)

From a regulatory standpoint, all diagnostic tests are either considered in vitro diagnostics (IVDs) or laboratory-developed tests (LDTs). Under the CLIA'88, the FDA primarily regulates IVDs and CMS primarily manages LDTs, (Genzen 2019)(Graden 2021) which are sometimes referred to as "homebrew" tests. (CMS 2013)(Genzen 2019)

Often, LDTs are developed when there is an unmet clinical need for innovation in an area of medicine and patient care. Though the classification as an IVD or LDT does not mean that one test type will be of higher quality or more accurate than another, (Kim 2018) there are differences in how these test types can be made available to patients.

Summarized differences between regulatory environments for IVDs and LDTs (FDA 2014)

Requirements	IVD	LDT
Intended for commercial distribution	✓	✗
Risk-based classification	✓	✗
FDA pre-market review	✓	✗
Test registration	✓	✗
Labeling review	✓	✗
Evidence for marketing claims	✓	✗
Lab quality and personnel assessments	✓	✓
Manufacturing quality assessments	✓	✗
Analytical testing validity	✓	✓
Clinical testing validity	✓	✗
Pre-market testing review	✓	✗
Regulatory review results publicly available	✓	✗
Mandatory adverse event reporting	✓	✗
Mandatory recalls can be issued	✓	✗

Types of tests

There are several different mediums available for lab testing that may require the collection of samples, including blood, saliva, stool, and urine. Genetic tests are also common and may require the collection of samples.

Type	When is it typically used?	Example
Single marker	• When a practitioner only needs information on specific markers • When there are financial considerations	Testing thyroid stimulating hormone (TSH) and/or free T3
Panels	• When a collection of markers may be needed for a more comprehensive assessment • When there is a financial bundling advantage compared to individually recommending multiple single markers	Thyroid panel testing: TSH, free T4, free T3, and total T3
Kits	• When a test can be performed by the patient at home, offering convenience or other logistical advantages	4-point saliva cortisol

Diagnostic versus functional tests

Diagnosis and monitoring of many conditions tend to be based on evidence from blood testing, (Clarke 2016) with some notable exceptions such as routine urinalysis for urinary tract infections or stool testing for parasites.

Many whole person medicine providers frequently refer to certain saliva or urine tests as functional medicine tests. The difference between these tests and conventional tests is not typically described in the research literature. However, many functional tests are considered direct-to-consumer tests because they can be accessed

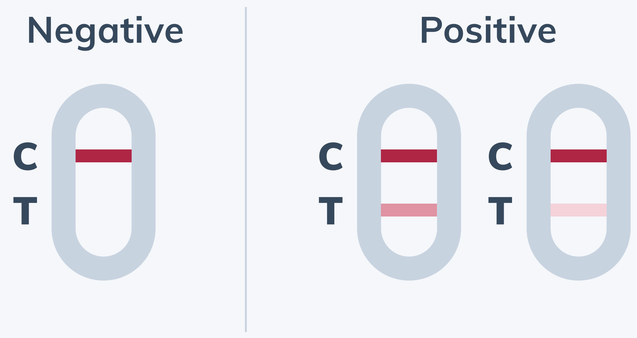
without a healthcare provider's prescription in some states. (Galior 2020) Though not an exhaustive list, some common functional medicine tests include:

- Comprehensive stool analyses for gut bacteria, yeast, parasites, pathogens, and various metabolic markers
- Genetic testing via saliva (legality varies by state)
- Heavy metals and neurotransmitters via urine
- Hormone levels via saliva and urine
- IgG food sensitivity testing via blood

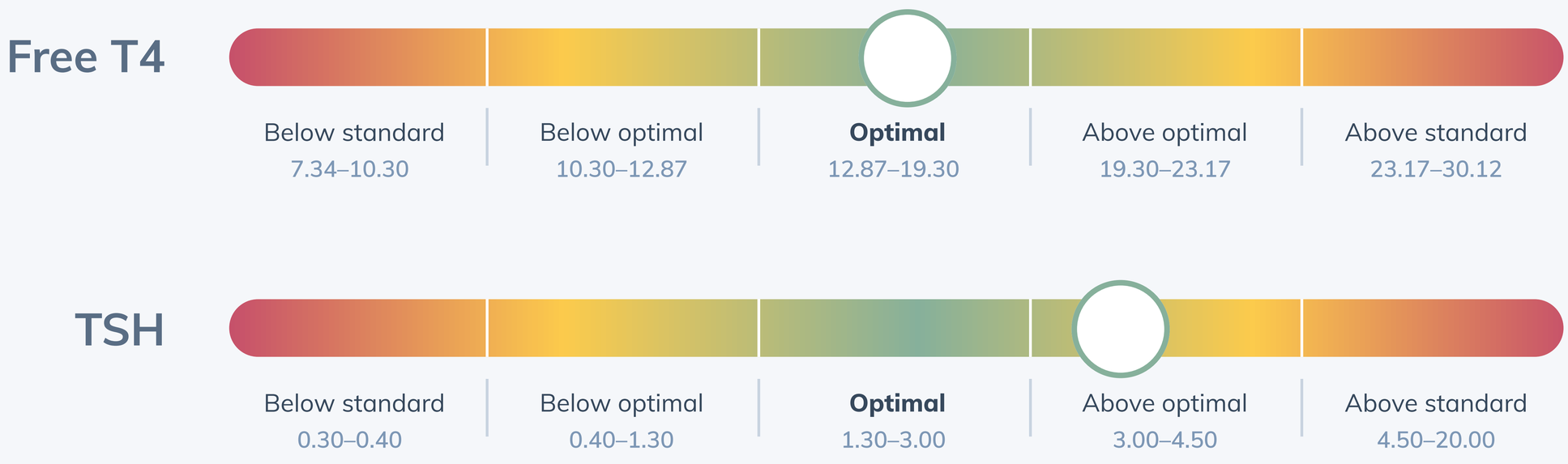
Types of results

The way results are reported varies based on the type of test. Some may be compared to reference ranges, while others may yield a binary or a graded result. Most commonly, tests come back with a number, a unit of measurement, and a corresponding reference range to indicate what a “normal” range should be for this result.

Binary results example: Testing for the presence of H. pylori



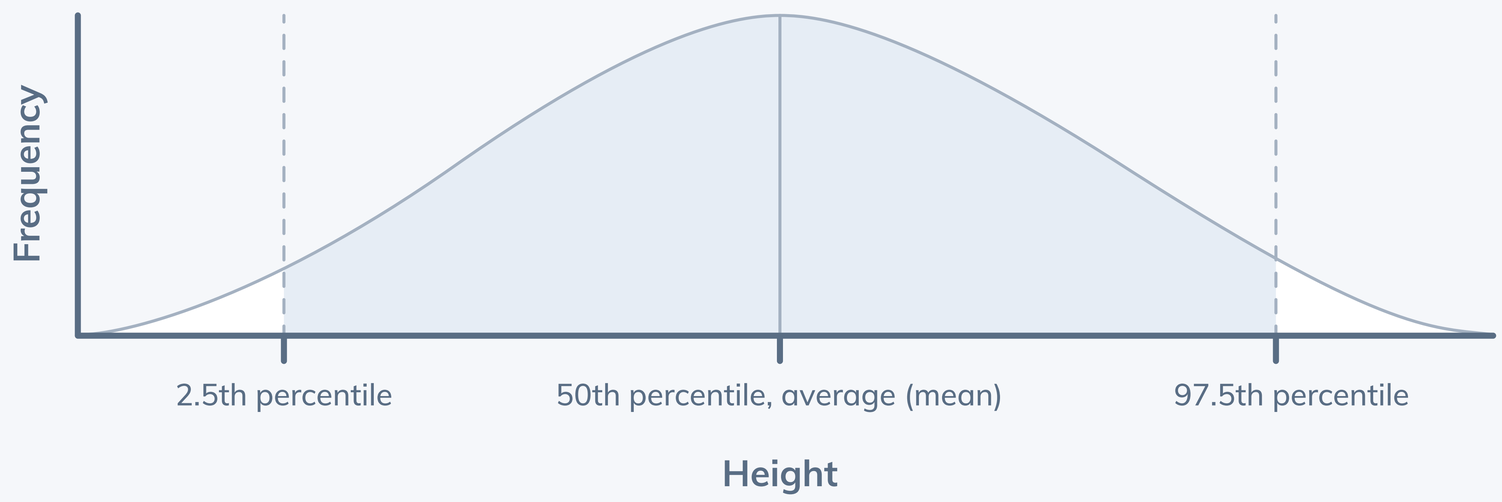
Graded results example: Thyroid hormone levels



Diagnostic versus functional intervals

Reference ranges are typically developed from percentiles of a surveyed population. For example, when setting a reference range, a population of people classified as healthy (i.e., people with no known health conditions, especially in regard to the particular marker) may all have their blood collected and the levels of a particular marker analyzed. The results are then typically represented through a bell curve.

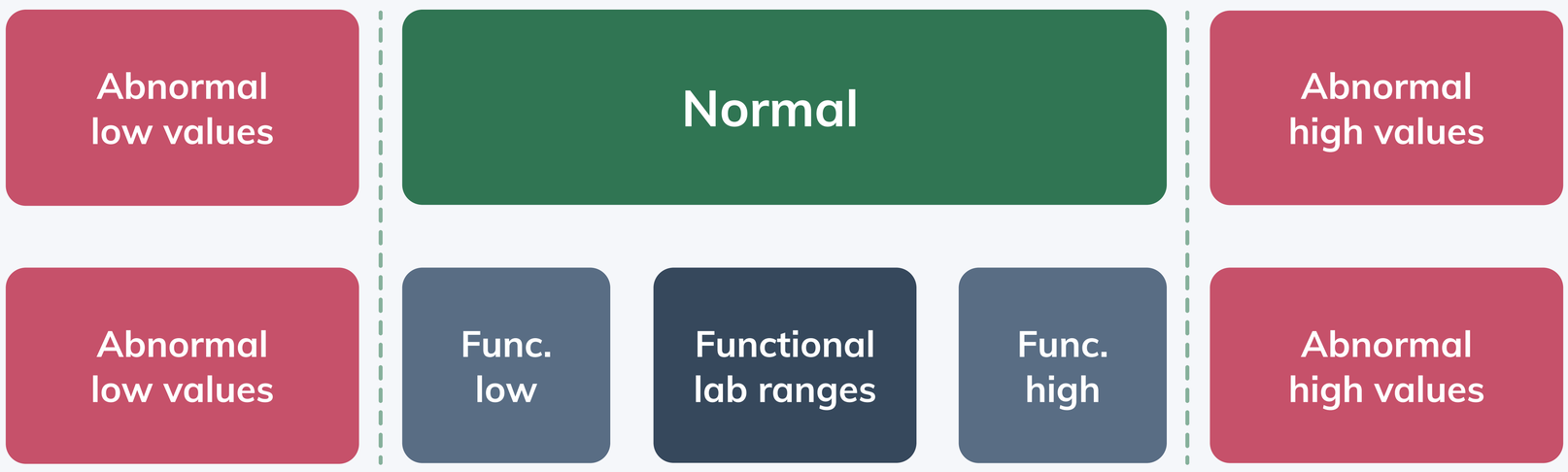
Reference range percentiles



Typically, the bottom 2.5% (i.e., 2.5th percentile) and top 2.5% (i.e., 97.5th percentile) of the population are excluded as statistical outliers. (Jones 2008) Such people would be the highest and lowest in the range and may not be representative of where an average person's marker "ought" to be for normal or better health.

Some practitioners will use more narrow reference ranges. These may be termed "functional (medicine) reference ranges," as opposed to the more traditional "diagnostic reference ranges." These ranges may be based on large research studies, or they may be based on anecdotal evidence, clinical practice experience, or other information.

Diagnostic and functional range results



Commonly offered tests

Marker grouping	Popular (blood-based) markers
Cardiovascular	• Fasting blood glucose • Hemoglobin A1C (HbA1C) • High-density lipoprotein-cholesterol (HDL-C) • Low-density lipoprotein-cholesterol (LDL-C) • Non-HDL-C • Total cholesterol • Triglycerides (TG)
Electrolytes	• Bicarbonate • Calcium • Chloride • Magnesium • Phosphate • Potassium • Sodium
Hematology	• Complete blood count (CBC) • Ferritin
Inflammation	• C-reactive protein (CRP) • Erythrocyte sedimentation rate (ESR) • Fibrinogen • Highly-sensitive C-reactive protein (hs-CRP)
Kidneys	• Creatinine • Estimated glomerular filtration rate (eGFR)
Liver	• Alanine aminotransferase (ALT) • Alkaline phosphatase (ALP) • Aspartate aminotransferase (AST) • Bilirubin • Gamma-glutamyl transferase (GGT)
Men’s health	• Follicle-stimulating hormone (FSH) • Free testosterone • Luteinizing hormone • Total testosterone

Commonly offered tests (continued)

Marker grouping	Popular (blood-based) markers
Nutritional	• 25-Hydroxyvitamin D (Vitamin D3) • Vitamin B12
Thyroid	• Free T3 (fT3) • Free T4 (fT4) • Thyroid-stimulating hormone (TSH)
Urinalysis	• Bilirubin • Blood • Glucose • Ketones • Leukocytes • pH • Protein • Nitrites • Specific gravity
Women’s health	• Beta-human chorionic gonadotropin (b-hCG) • Estradiol • FSH • LH • Progesterone

(Horton 2018) (Medline n.d.)

Access to labs through Fullscript

Lab testing can be an extremely valuable tool for integrative practitioners, but it also can be complicated to get started. Through Fullscript, practitioners now have centralized access to lab tests as well as professional-grade supplements, making practicing integrative medicine easier than ever. This means less time spent on administrative tasks and more time personalizing treatment plans to patient needs.

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