

Normal Values and Their Pitfalls (Prof. Dr. Alfred Hager)

The clinical interpretation of Cardiopulmonary Exercise Testing (CPET) hinges on comparing results with established **normal values**. Historically, this involved calculating the "percentage predicted" based on the mean of healthy subjects. Modern methodology emphasizes calculating the **z-score (SDS)** within the Normal Range (STD from the mean)). For data that exhibit a skewed distribution (such as SpO₂, BNP, AST, ALT, and GGT), the sophisticated **LMS System** (developed since 1964) is employed to apply corrections (L, M, S) for a more accurate z-value calculation.

A major **pitfall** is the reliance on reference values that are severely dependent on the characteristics of the population from which they were derived. Clinicians must account for crucial variables, including **age, sex, body mass and height, race, economic status, smoking status, medication, and disease**. For calculating accurate reference values related to **sex**, it is suggested that hormonal status at puberty be used. Clinicians must also decide how to report VO₂peak, whether as ml/min/kg, ml/min, or as a percentage of predicted.

While general reference ranges exist, **disease-specific thresholds** are often more relevant for diagnosis and risk assessment. These thresholds are typically derived from **ROC analysis**, optimizing the **Youden index** (sensitivity + specificity - 1). An example is the **Breathing Reserve (BR)**: while BR is rarely below 10% in healthy subjects (suggesting ventilatory disease), a threshold of 33% in heart failure patients may indicate concomitant COPD. It is important to note that the formula for calculating BR varies across systems. The clinical imperative is to interpret reference values with care, focusing on treating the patient rather than solely the numerical values.