# Controversies in Laboratory Medicine with special views to clinical hematology

Edited by:

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# Introduction

- The appropriate ordering and interpreting of laboratory tests is an essential element of a physician's clinical skills.
- Along with history taking, physical examination, and the thoughtful use of imaging techniques, the clinical laboratory is a major tool in the clinician's armamentarium.

# Introduction

- The introduction of sophisticated quality improvement techniques into the clinical arena has evolved substantially in the past decade.
- It makes sense to integrate the changes that we make in our daily practice of medicine with quality improvement changes in the clinical laboratory in order to maximize the functionality of both areas for the safety and quality of care for our patients.

# Introduction

- For that reason, I was delighted to be asked to contribute to this controversial topic as an opportunity to improve communication between the disciplines of the practice of clinical medicine and clinical laboratory medicine.

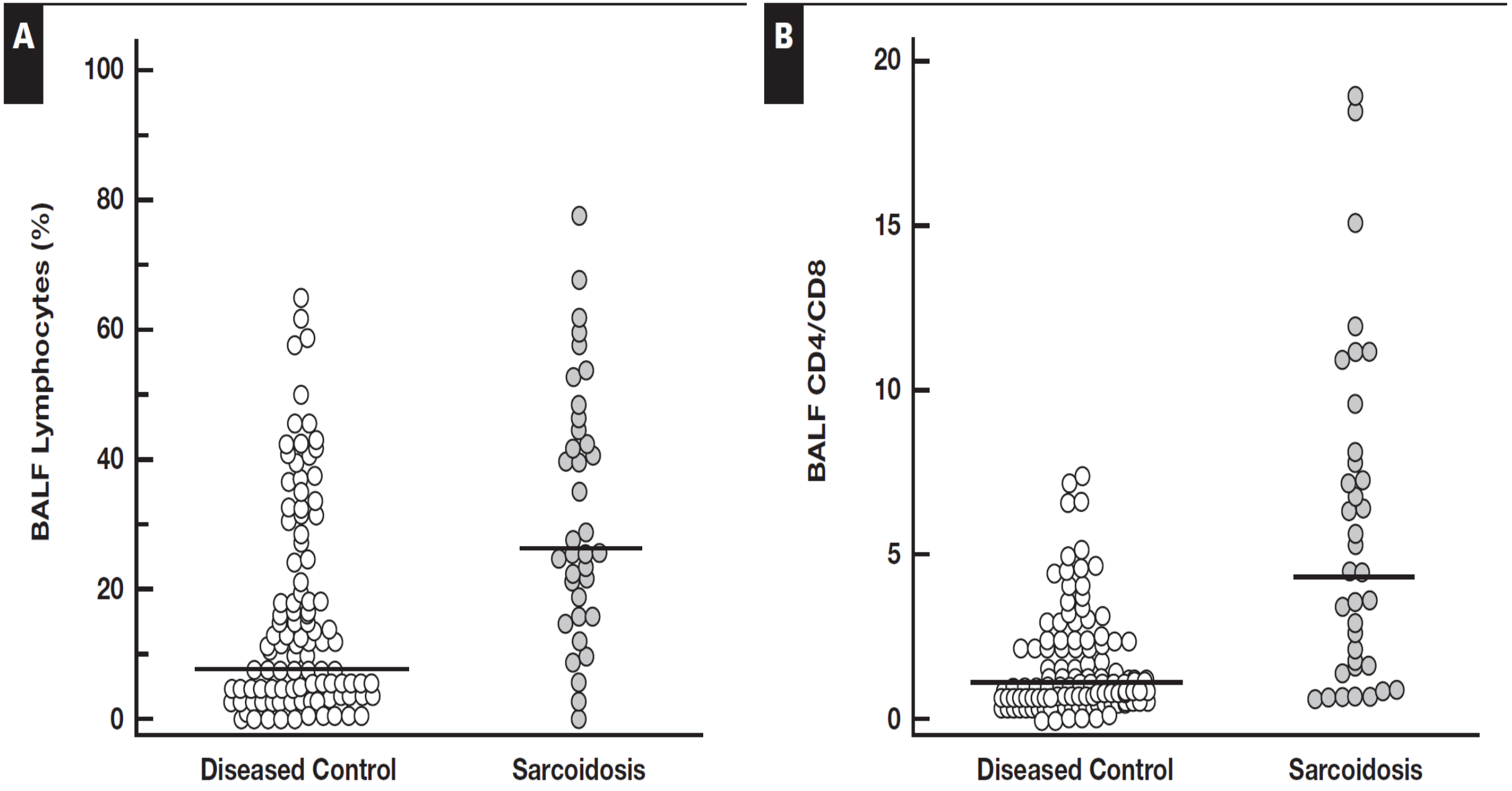
# Failure to Provide Useful Information to Help Interpret a Test Result

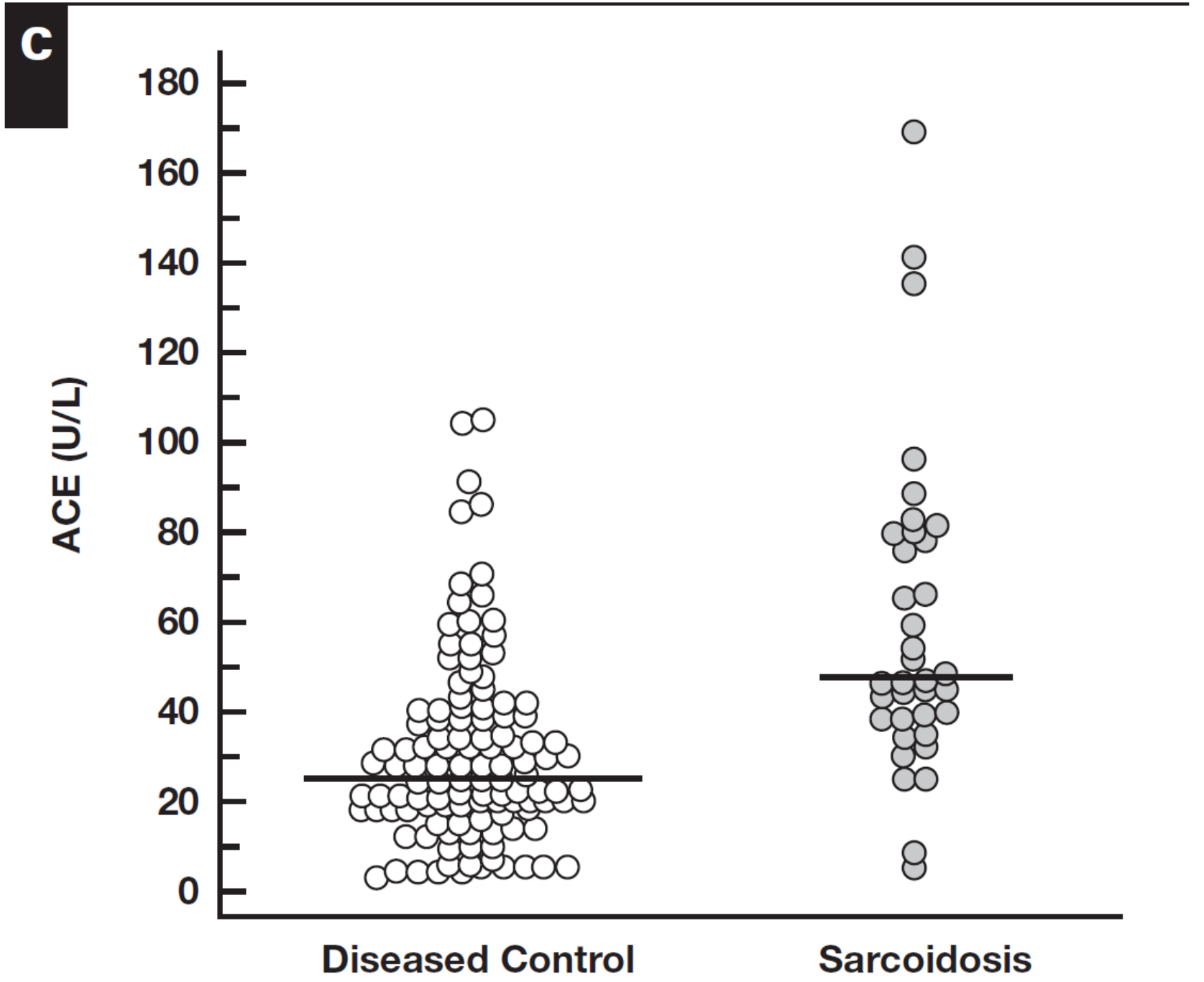
- You provide normal ranges for test results,
- But you do not provide ***likelihood ratios of the test results***.
  - very valuable for the ordering physician in
  - enabling her/him to know how much the odds of disease change with those specific results.
- provide would be feedback as to thoughtless test-ordering practices, such as ordering multiple tests when 1 test would suffice.

**Table 1**
**Clinical Characteristics of the Studied Population (n = 153)***

| | Patients With Pulmonary Sarcoidosis (n = 36) | Control Patients (n = 117) |
|---|---|---|
| Sex (M/F) | 21/15 | 65/52 |
| Diagnosis (No. of patients) | | |
| Sarcoidosis (biopsy proven) | 35 | — |
| Löfgren syndrome | 1 | — |
| Other interstitial lung disease | — | 51 |
| Infection | — | 23 |
| Tuberculosis | — | 5 |
| Malignancy | — | 16 |
| Autoimmune disease | — | 7 |
| Vascular disease | — | 6 |
| Hypereosinophilic syndrome | — | 3 |
| Other | — | 6 |
| Laboratory tests, median (IQR) | | |
| BALF lymphocytes (%)† | 27.0 (17.5-46.0) | 8.0 (3.5-22.5) |
| BALF CD4/CD8† | 4.55 (1.69-8.05) | 1.13 (0.73-2.27) |
| ACE, U/L† | 48 (39-80) | 27 (19-40) |

ACE, angiotensin-converting enzyme; BALF, bronchoalveolar lavage fluid; IQR, interquartile range.


A
BALF Lymphocytes (%)
100
80
60
40
20
0
Diseased Control
Sarcoidosis
B
BALF CD4/CD8
20
15
10
5
0
Diseased Control
Sarcoidosis


C
180
160
140
120
100
80
60
40
20
0
ACE (U/L)
Diseased Control
Sarcoidosis

# Optimum Cutoff Values for Individual Laboratory Tests

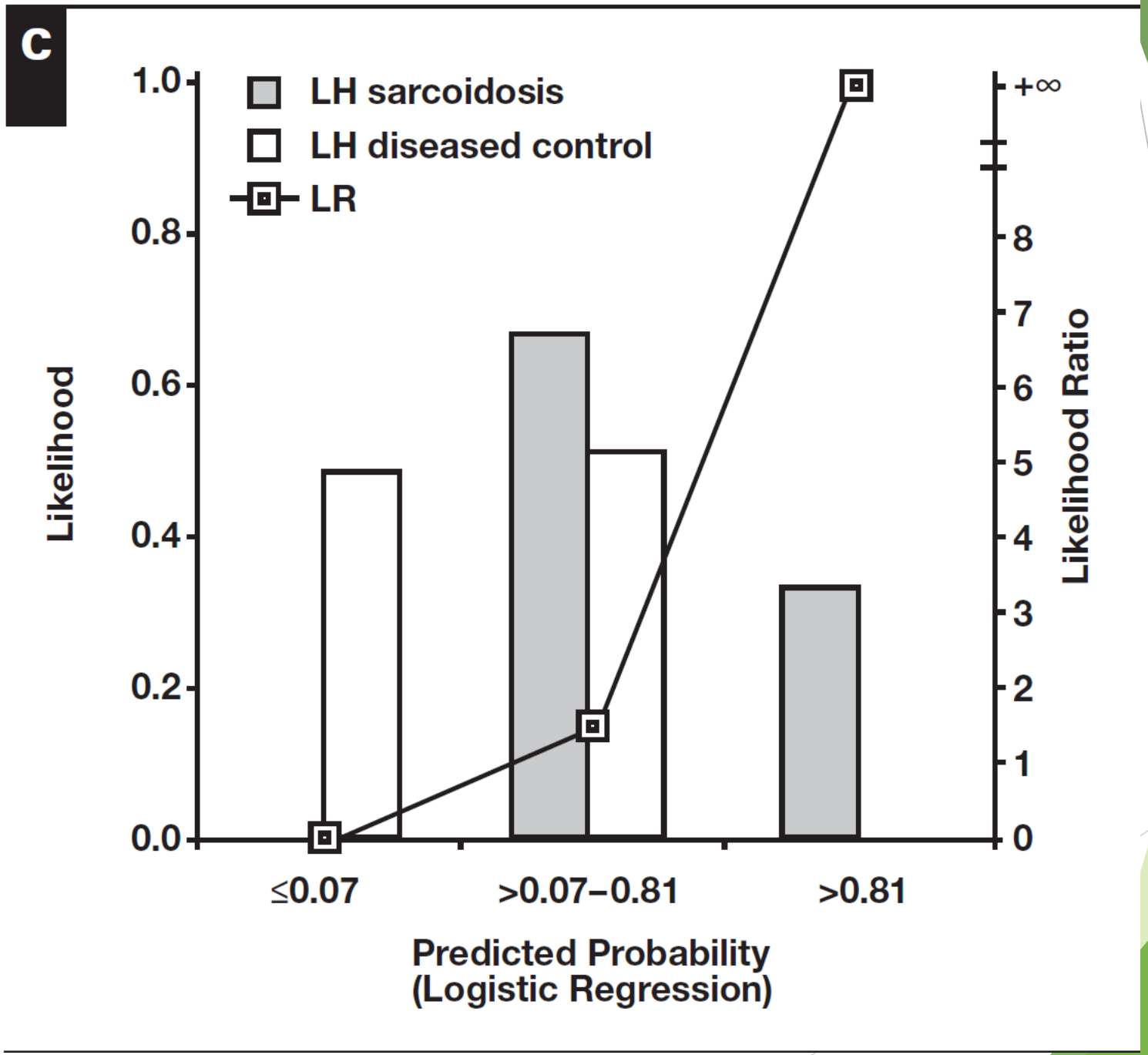
| Laboratory Test | Cutoff Value* | Sensitivity (%) | Specificity (%) |
|---|---|---|---|
| BALF lymphocytes (%) | 18.0 | 75.0 | 73.5 |
| BALF CD4/CD8 ratio | 2.62 | 66.7 | 82.1 |
| Serum ACE (U/L) | 34 | 83.3 | 66.7 |

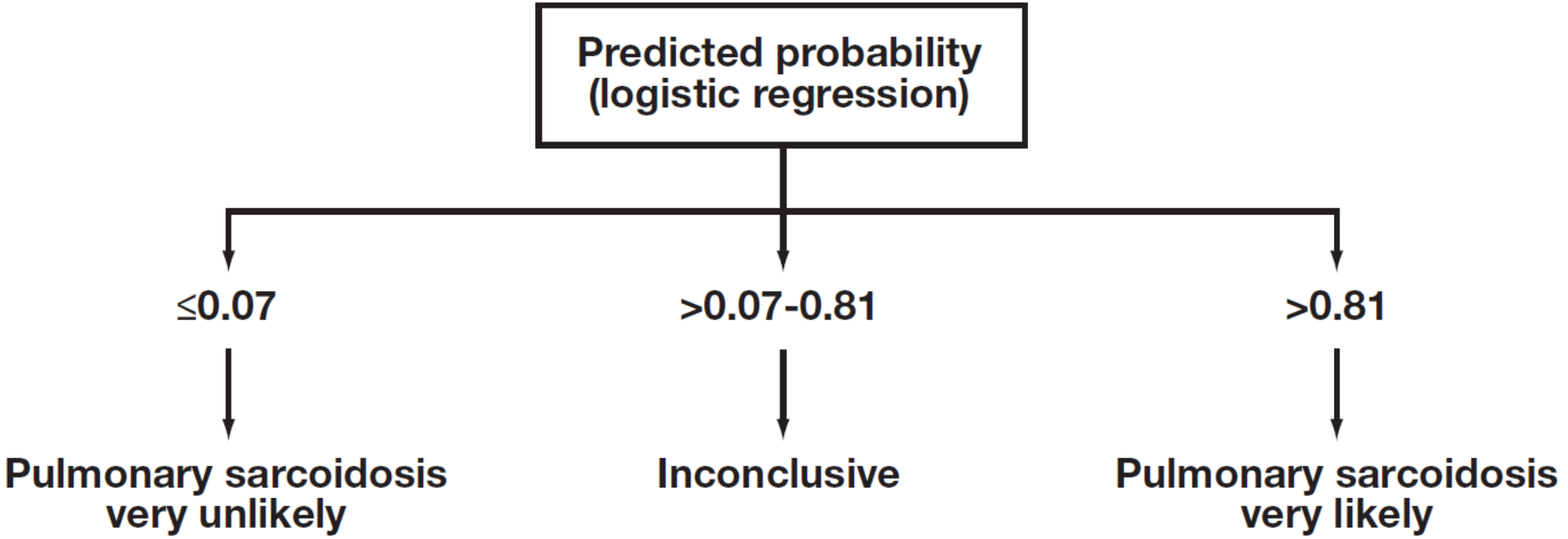
## Overview of LRs as a Function of the Percentage and CD4/CD8 Ratio of BALF Lymphocytes and Serum ACE Activity

| Test Result Interval | Patients With Pulmonary Sarcoidosis (n = 36) | Control Patients (n = 117) | LR (95% CI) |
|---|---|---|---|
| BALF lymphocytes (%) | | | |
| ≤5.5 | 2 | 42 | 0.16 (0.04 to 0.61) |
| 5.5-46 | 25 | 70 | 1.16 (0.89 to 1.51) |
| >46 | 9 | 5 | 5.85 (2.09 to 16.34) |
| BALF CD4/CD8 | | | |
| ≤0.69 | 0 | 28 | 0.00 (0.00 to 0.93) |
| 0.69 – 5.19 | 19 | 85 | 0.73 (0.52 to 1.01) |
| 5.19 – 7.45 | 7 | 4 | 5.69 (1.77 to 18.33) |
| >7.45 | 10 | 0 | +∞ (3.89 to +∞) |
| Serum ACE (U/L)* | | | |
| ≤25 | 2 | 55 | 0.12 (0.03 to 0.46) |
| 25-71 | 23 | 57 | 1.31 (0.96 to 1.78) |
| >71 | 11 | 5 | 7.15 (2.66 to 19.22) |

# Multivariable Logistic Regression Analysis: Overview of Constant* and Regression Coefficients

| Variable | Regression Coefficient | SE | *P*† |
|---|---|---|---|
| % BALF lymphocytes | 0.03 | 0.01 | .0263 |
| BALF CD4/CD8 ratio | 0.38 | 0.10 | .0002 |
| Serum ACE | 0.03 | 0.01 | .0008 |


C
LH sarcoidosis
LH diseased control
LR
Likelihood
1.0
0.8
0.6
0.4
0.2
0.0
Likelihood Ratio
+∞
8
7
6
5
4
3
2
1
0
≤0.07
>0.07–0.81
>0.81
Predicted Probability
(Logistic Regression)


Predicted probability
(logistic regression)
≤0.07
>0.07-0.81
>0.81
Pulmonary sarcoidosis
very unlikely
Inconclusive
Pulmonary sarcoidosis
very likely

# Standardization of Reference Ranges and Units of Measurement

- Because tests may be done with different techniques and/or different reagents, depending on the institution, reference ranges for “normals” can differ substantially.
- Although this may not be a problem for physicians who only practice in 1 setting, many physicians practice in multiple settings with multiple clinical laboratories.
- This, of course, is a setup for a poor quality and safety environment.

# Standardization of Reference Ranges and Units of Measurement

- An excellent example => use of the international normalized ratio (INR), created by the WHO, in reporting the prothrombin time (PT) in anticoagulated patients.
- This has become the widely accepted standard of care because clinicians and pathologists recognized the marked improvement over the widely variable PT.

# Standardization of Reference Ranges and Units of Measurement

- Similarly, when laboratories report results with different metrics, it can be confusing to clinicians and potentially dangerous for patients.
- For example, some laboratories report in millimoles per liter, whereas others report in milligrams per deciliter.
- Clinicians tend to get comfortable with particular measurements and the normal ranges associated with them, and it can become difficult to translate meaningfully from one unit to another.

# Standardization of Reference Ranges and Units of Measurement

- For example, as a cardiologist, a cholesterol level of 270 mg/dL catches my eye, whereas a level of 7.0 mmol/L doesn't.
- Yet, I quickly got used to using the INR over the PT, so if clinical laboratories agreed to standardize measurements for quality or safety reasons, I could get over it!

# Performance of the Wrong Test

- This can often be the result of an unclear order, but if the lab guesses wrong, it can be very frustrating for the clinician or patient.
- Should the lab guess or contact the ordering physician to clarify the order?
- Again, clear communication on both ends would minimize this. Computer physician (provider) order entry (CPOE), although it may have its own inherent problems, should eliminate this particular problem.

# Miscellaneous

- Other minor irritating issues may include
  - changes in …… without notification or explanation
    - reference range,
    - assay methodology, or
    - specimen requirements
  - turnaround times that are perceived as too slow;
  - and failure to recognize that a test was ordered stat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