

Multi-dimensional diagnosis of intramammary infections: a 3-herd evaluation

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Introduction

The 1947 2 x 2 table:

- a) disease conditions are either D- or D+, and
- b) (considering a “gold standard”) test results are either true or false

	D+	D-
T		
F		

Consequences and implications:

- a) Continuous data are converted into discontinuous categories (e. g., D+, D-), which results in ***D+/D- overlapping*** → a systematic loss of diagnostic efficacy;
- b) All D+ cases (all infections) are grouped together, **as if all infections were similar**;
- c) **Time is not considered** (infections are treated as if they were *instantaneous events*) → prognosis cannot be made.
- d) Because test *predictive values depend on prevalence*, **there is a problem about what “true” or “false” means** (“gold standards” may produce *false results*, e.g., a negative culture with 1×10^6 SCC/ml).

Goals, method and materials

Goals: to **build and evaluate an alternative approach** that

- i) *prevents D+/D- overlapping*,
- ii) if present, may *detect ≥ 2 D+ categories*,
- iii) *estimates the time* elapsed since initiation of the infection,
- iv) is *insensitive* to *variations in prevalence*,
- v) is *data-driven* (neither assumes nor defines anything), and
- vi) facilitates *data quality assessments*.

Method: determination of *disease stages* by

- a) considering (up to 20) *microbial and leukocyte* indicators,
- b) *partitioning* population (herd) data into any number of subsets through an open-ended system that stops when 3 criteria are met: (i) subsets display a *distinct data distribution*, (ii) each subset shows *similar data range for >2 indicators*, and (iii) *different* data ranges are observed *across subsets*;
- c) analyzing subsets of contrasting profiles.

Variables:

Mammary gland quarter milk samples, investigated in terms of:

- a) *whole leukocyte count* (as estimated by the SCC),
- b) *leukocyte differential counts*, and
- c) *microbial cultures*.

Populations

Longitudinal and experimental study

Study 0 (n=6, US)

Cross-sectional studies (all: n=1184)

Study I (n=120, US)

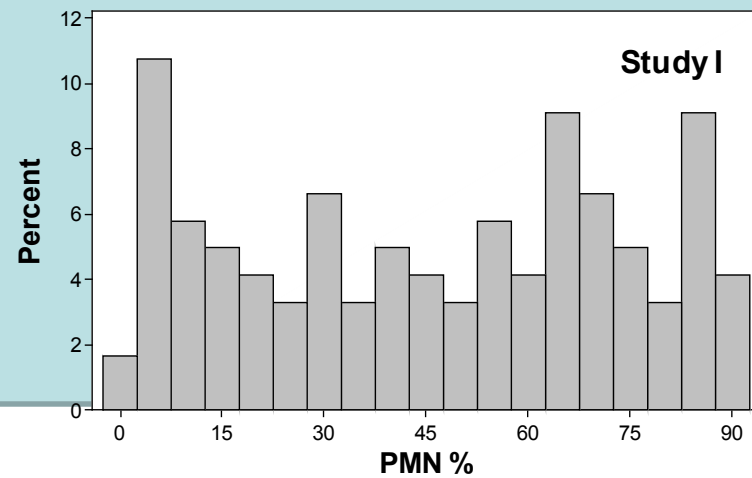
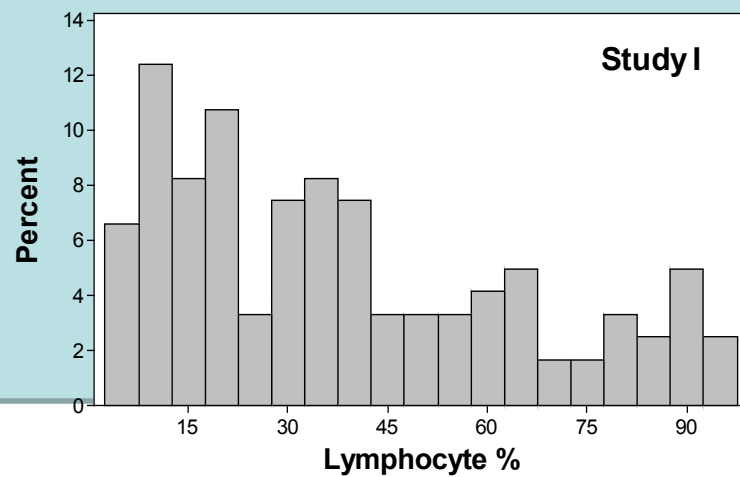
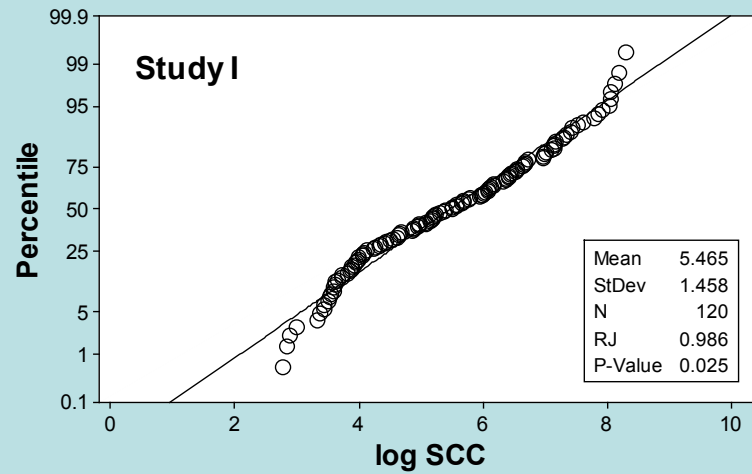
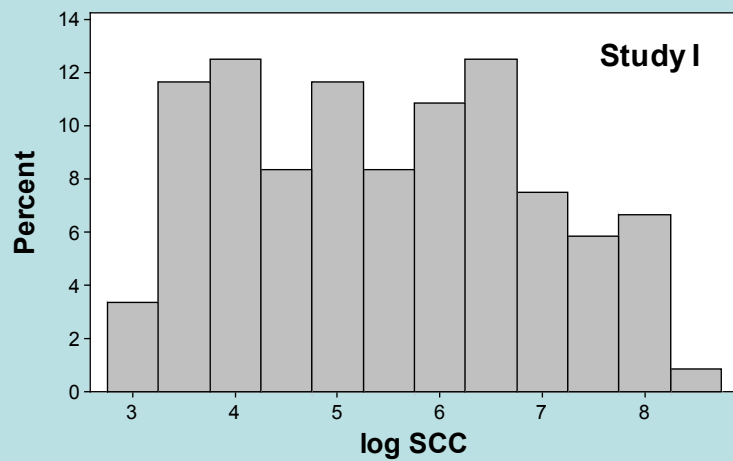
Study II (n=500, US)

Study III (n=484, Israel)

[Study IV (n=80, Germany)]

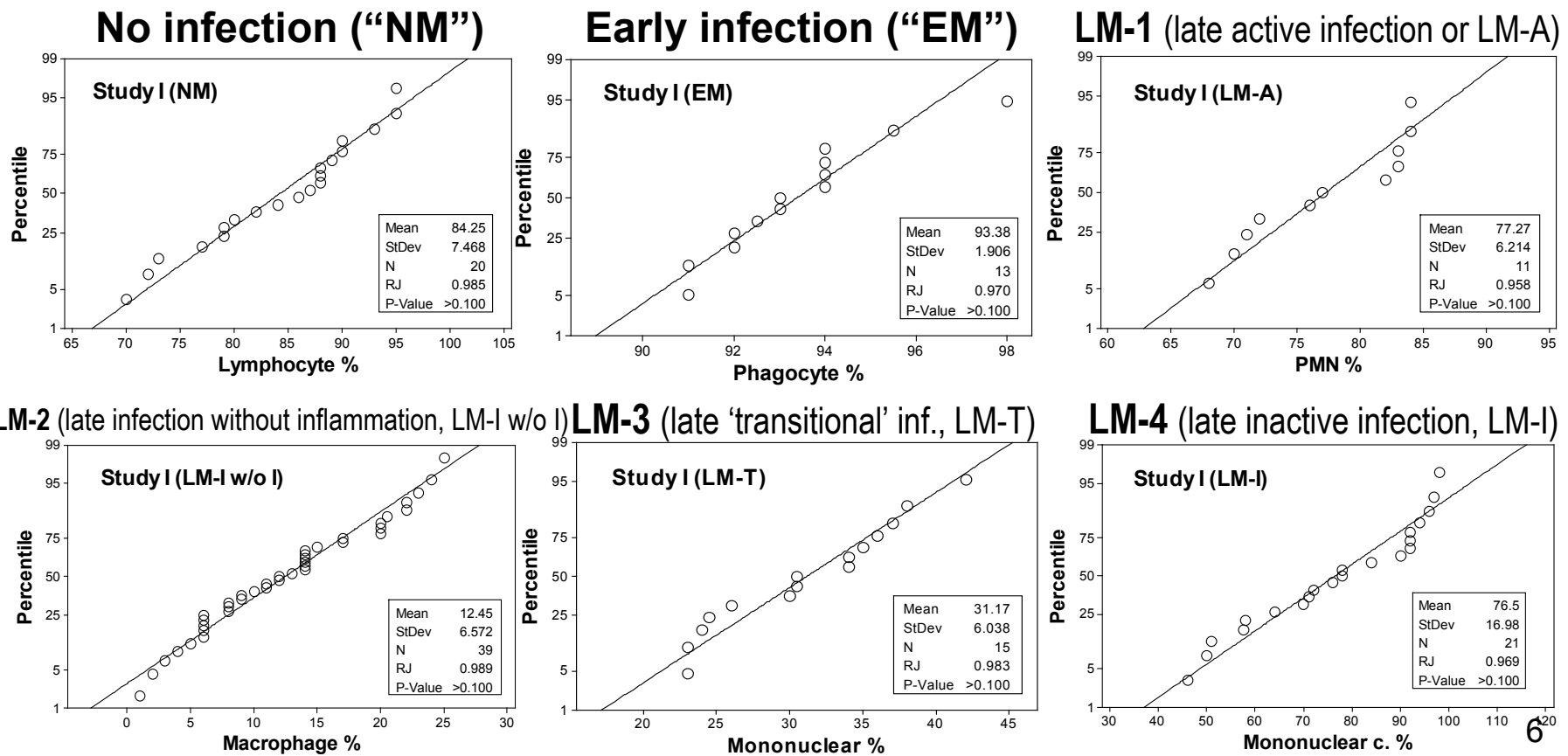
Results

Regardless of which indicator was considered, the distribution of each dataset (herd) was **not linear**.



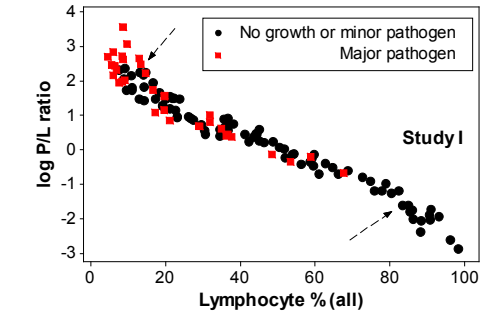
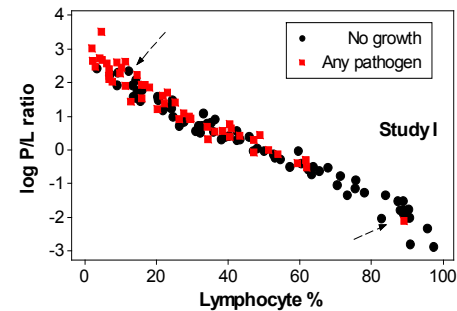
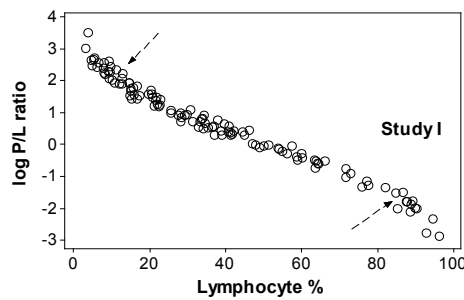
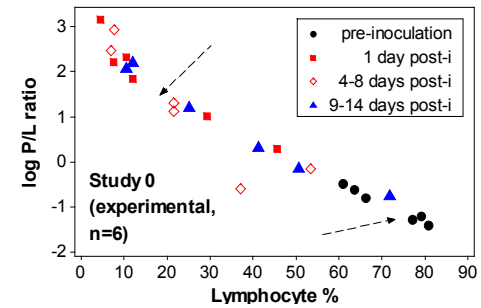
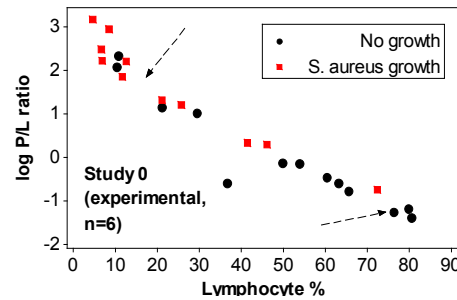
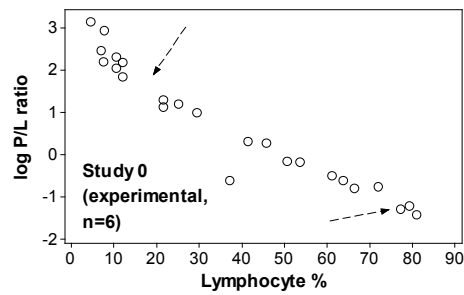
Results-II

However, when each dataset (herd) was **fragmented** into **subsets** that (internally) showed similarities while (across) differed in at least 2 indicators, up to **6 linearly distributed subsets** were found. Based on the literature, tentative descriptors were assigned: 1 “early” and 4 “late” mastitis stages.



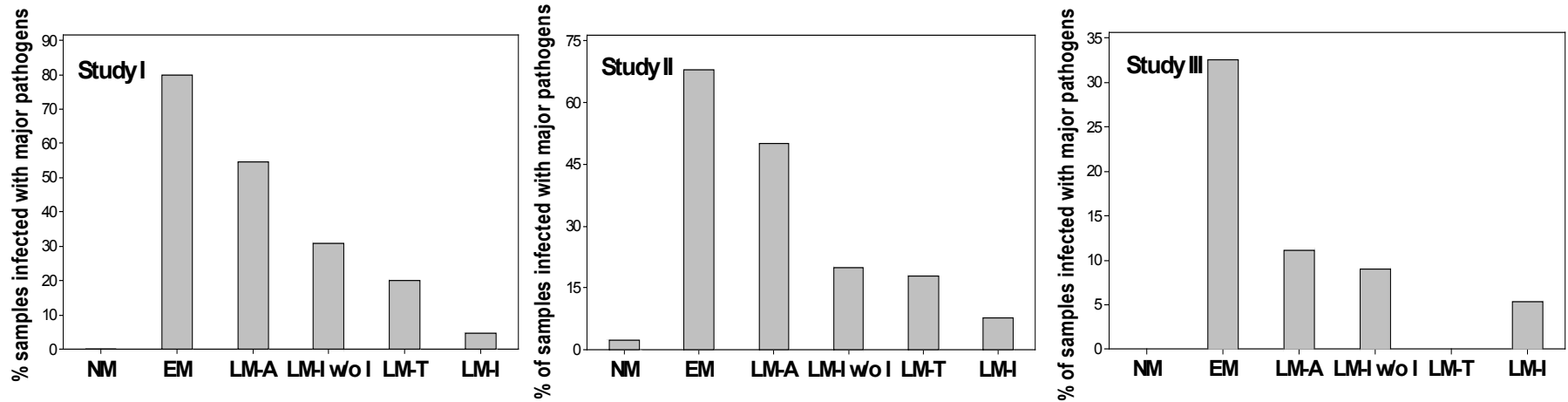
Results III. In 3-D plots, all populations showed the same pattern:

- a) 2 inflection points,
- b) **major pathogens on one end**, no infection on the opposite end.



The 4 studies showed 5% -27% prevalence to major pathogens.

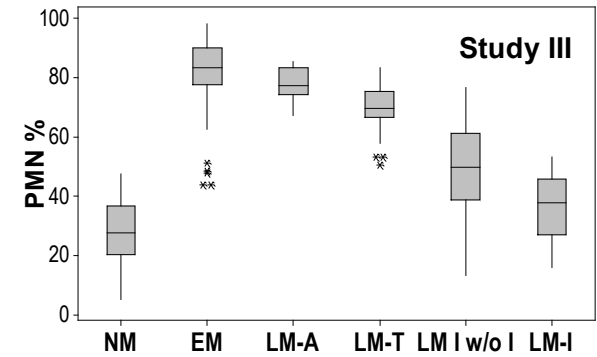
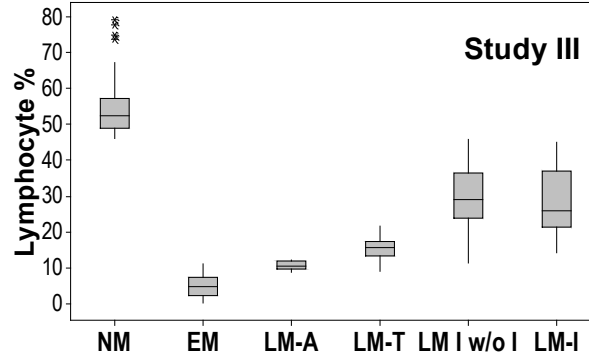
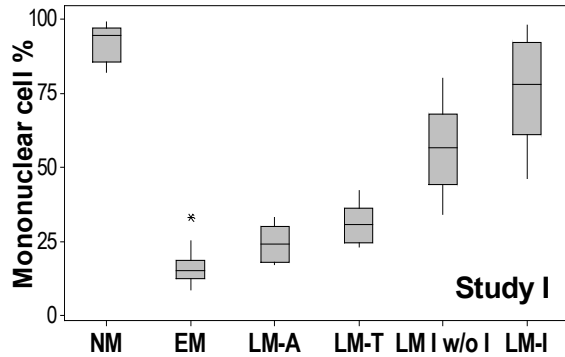
Results IV



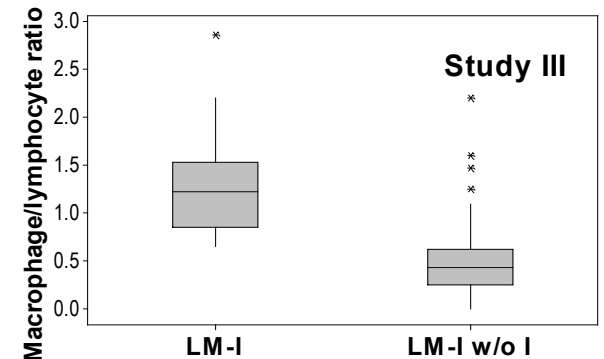
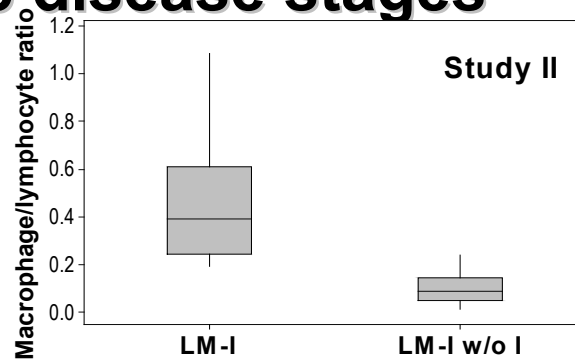
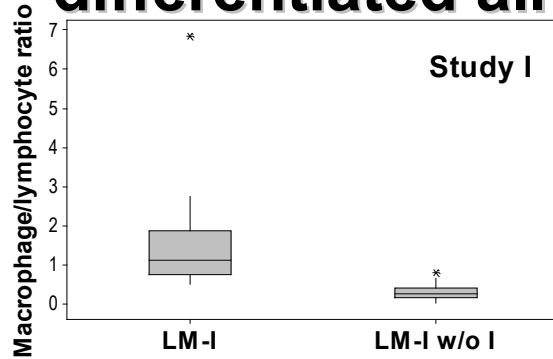
Microbial profiles *differed* across subpopulations (disease stages): EM showed the highest % of major pathogen + cultures; LM-I the lowest.

Results V

No indicator differentiated all subsets.

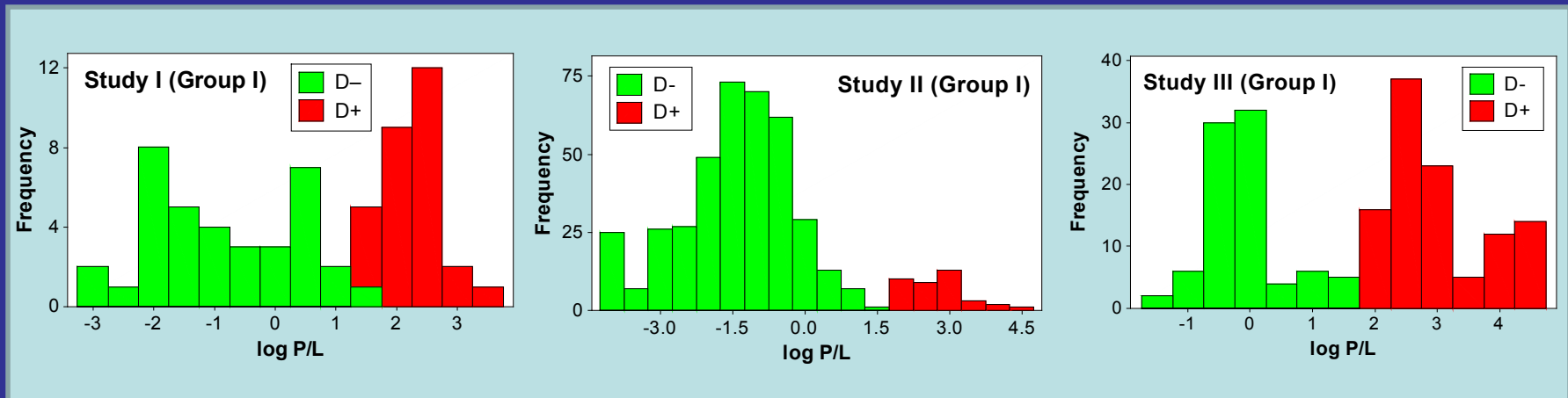


However, using > 2 indicators, leukocyte indicators differentiated all 6 disease stages



Results VI

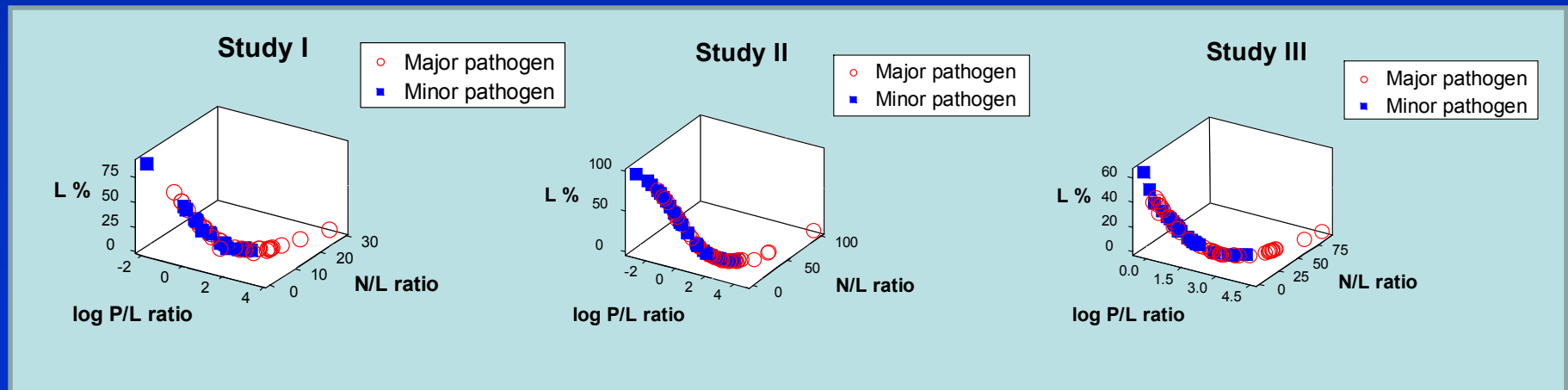
By *merging* subsets of *contrasting* profiles (NM, LM-I, EM, LM-A), D+/D- data overlapping was prevented.



- How accurate was this system?
 - After 4 populations were evaluated, the partitioning-oriented (disease stage-based) method was at least 6.4% more accurate than the non-partitioned alternative method.

Results VII

- **How sensitive** is it to differences in prevalence?
 - While the tested populations showed up to **11-fold differences in prevalence** (from 2.5% to 27.5%, for major pathogens), this approach was at least **93.1% accurate to detect D+ and D-**
- **Even without microbiological results, D+ may be suspected** (earlier decisions, e.g., animal isolation can be implemented) .



Summary

- By measuring up to 15 leukocyte and 3 microbial indicators, population (herd) data can be separated into *disease stages*.
- By considering the *relative time* (“inflammatory time”, e.g., “early”) associated with each disease stage, a *prognosis can be facilitated* (e.g., if “late ‘inactive’ mastitis” → recovery, e.g., it does not require treatment).
- *New* subsets (the “late mastitis without inflammation”, a subset associated with major pathogens but no or minor inflammation) can be *detected*.
- By analyzing subsets that reveal *contrasting profiles*, D+/D- data overlapping is reduced → *increased diagnostic accuracy*.

Dank u wel!

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