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Validation of a Novel Host Response Based Assay for Diagnosis of Acute Infectious Etiology in Febrile Children: A Blinded Retrospective Observational Study

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Introduction

Bacterial and viral infections are often clinically indistinguishable in young children with fever without source or pneumonia, leading to inappropriate management and antibiotic misuse. Bacterial-induced host proteins, such as C-reactive protein (CRP) and procalcitonin (PCT) are often used in the decision process, but often lack sensitivity and specificity. Ideally, a test combining bacterial <u>and</u> viral markers into a simple predictive score would be valuable in the clinical decision making of febrile children.

Recently, a study showed that the combination of 2 viral- (**TRAIL** and **IP-10**) and 1 bacterial-induced host proteins (**CRP**), weighted one to the other through a computerized algorithm to generate a probability of bacterial or viral infection, resulted in an impressive discriminative capacity [1].

The objective of this study was to compare the sensitivity, specificity and predictive values of this new ELISA test (ImmunoXpert™) to PCT and CRP in the serum of children with fever without source and pneumonia.

Methods

We studied serum samples collected prospectively from children (0-16y) with fever without source[2] and pneumonia[3]. Infection etiology was determined by three independent physicians, based on clinical and laboratory investigation (blood, CSF and urine culture, NPA viral PCR, chest X-ray, PCT).
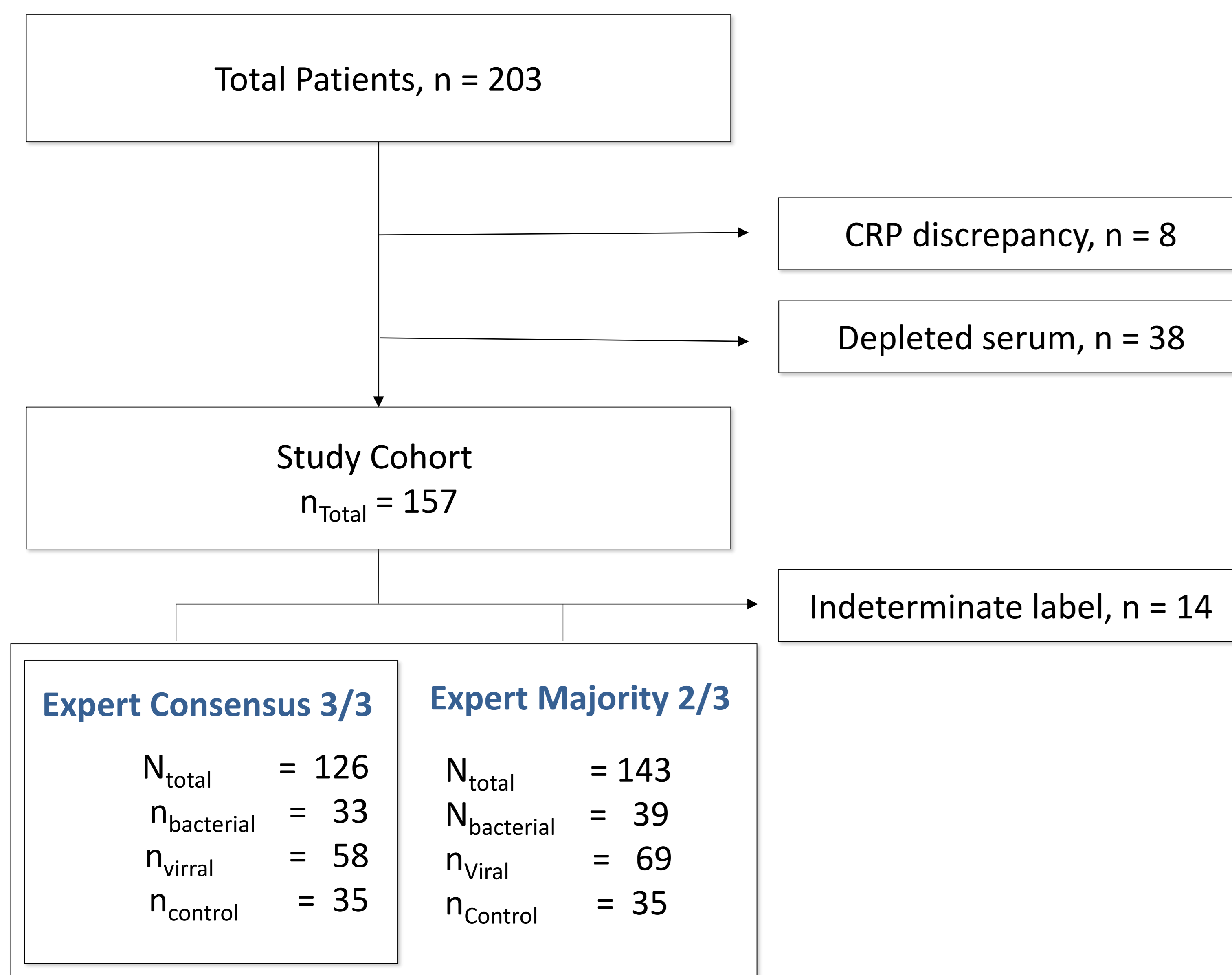
ImmunoXpert™ assay prediction accuracy was blindly compared to expert opinions and evaluated using sensitivity and specificity and predictive values.
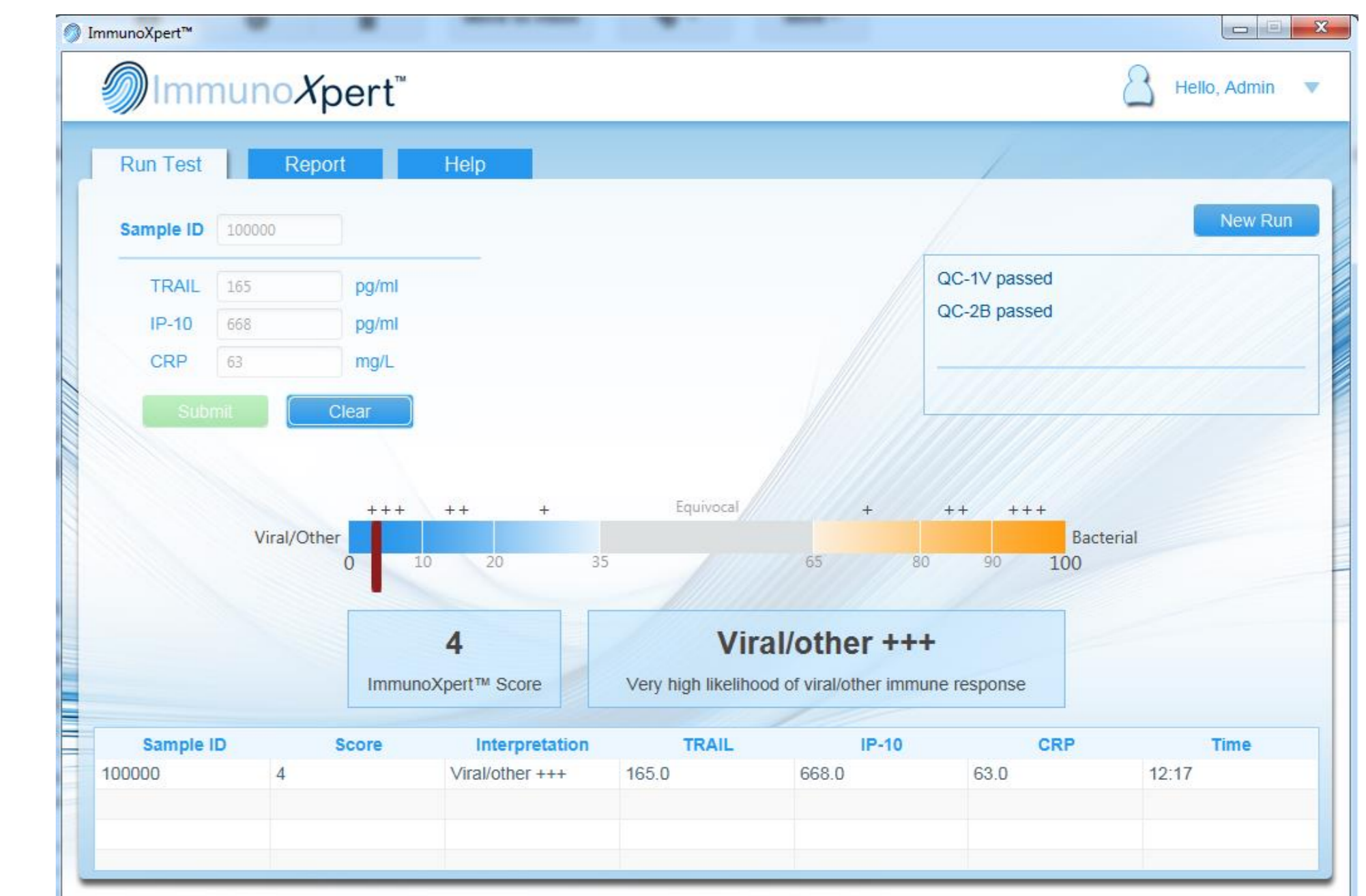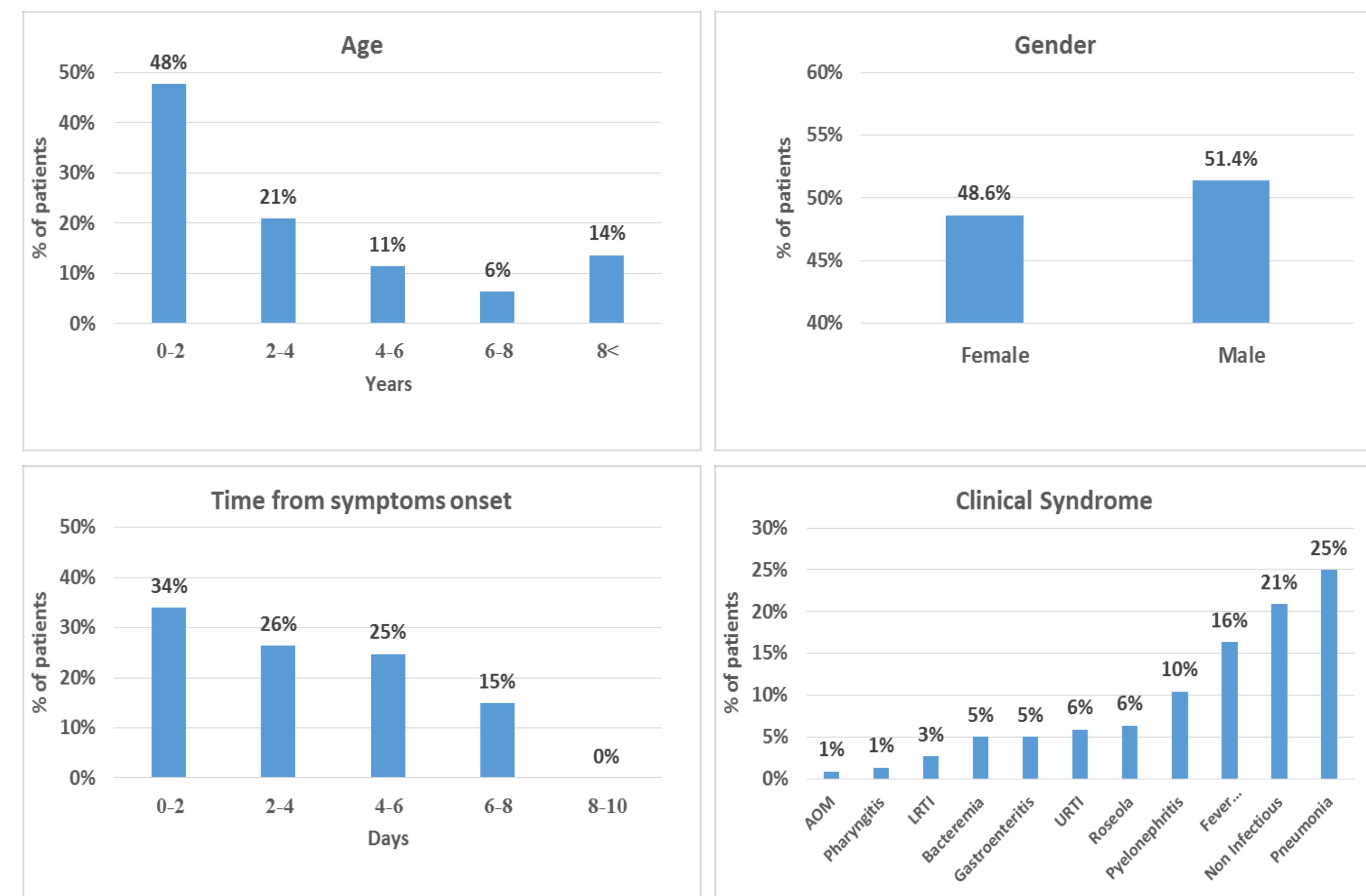

Example of a prediction score for a viral etiology based on the serum value of TRAIL, IP-10 and CRP
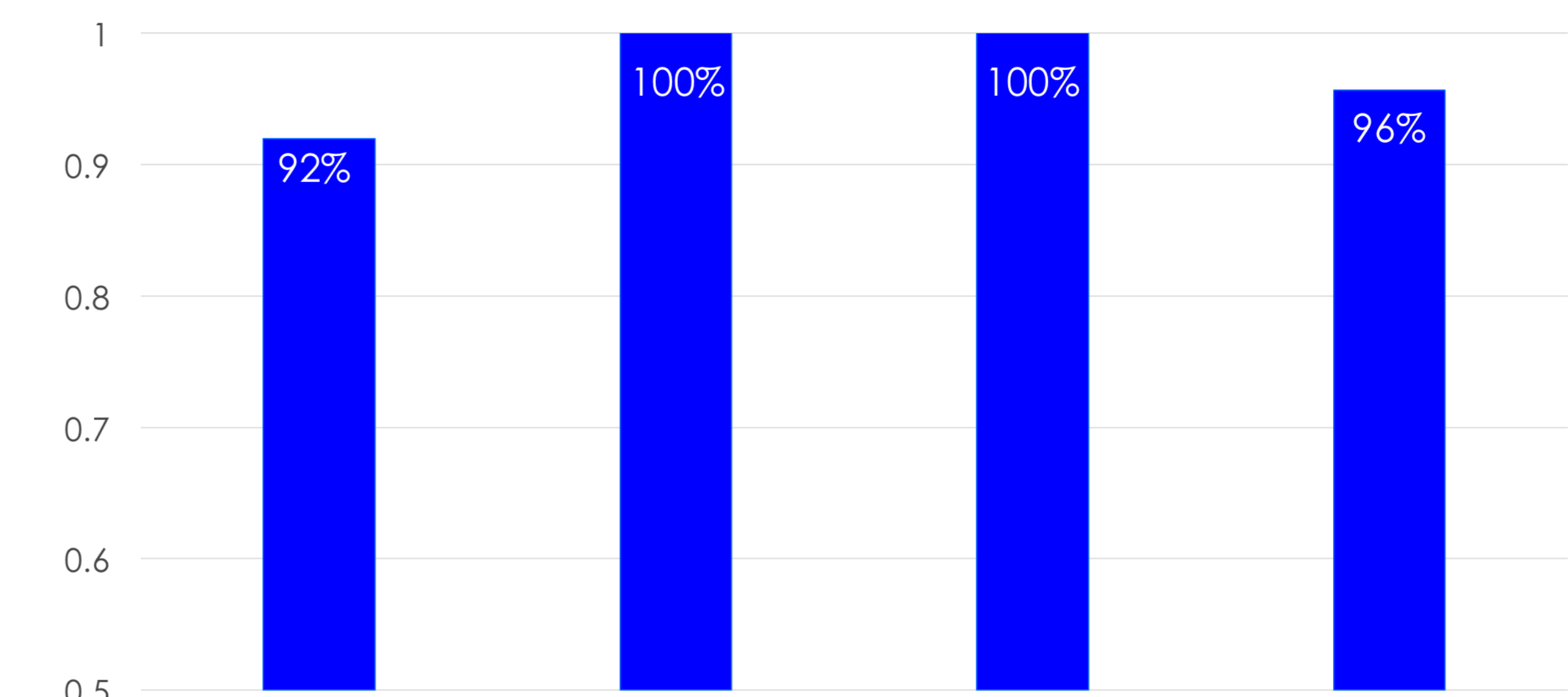
Results

Flowchart

Total Patients, n = 203 → CRP discrepancy, n = 8 → Depleted serum, n = 38

Study Cohort n$_{Total}$ = 157 → Indeterminate label, n = 14

Expert Consensus 3/3
N$_{total}$ = 126
n$_{bacterial}$ = 33
n$_{virral}$ = 58
n$_{control}$ = 35

Expert Majority 2/3
N$_{total}$ = 143
N$_{bacterial}$ = 39
n$_{Viral}$ = 69
n$_{Control}$ = 35

Patient characteristics

Age: 0-2 48%, 2-4 21%, 4-6 11%, 6-8 6%, 8< 14%

Gender: Female 48.6%, Male 51.4%

Time from symptoms onset (Days): 0-2 34%, 2-4 26%, 4-6 25%, 6-8 15%, 8-10 0%

Clinical Syndrome: AOM 1%, Pharyngitis 1%, LRTI 3%, Bacteremia 5%, Gastroenteritis 5%, URTI 6%, Roseola 6%, Pyelonephritis 10%, Fever... 16%, Non infectious 21%, Pneumonia 25%

ImmunoXpert: Bacterial vs. Viral
(Majority agreement n= 108)

92%, 100%, 100%, 96%

Comparison with other biomarkers
(Majority agreement n= 108)

Sensitivity, Specificity, PPV, NPV — ImmunoXpert, CRP 20, PCT 0.5
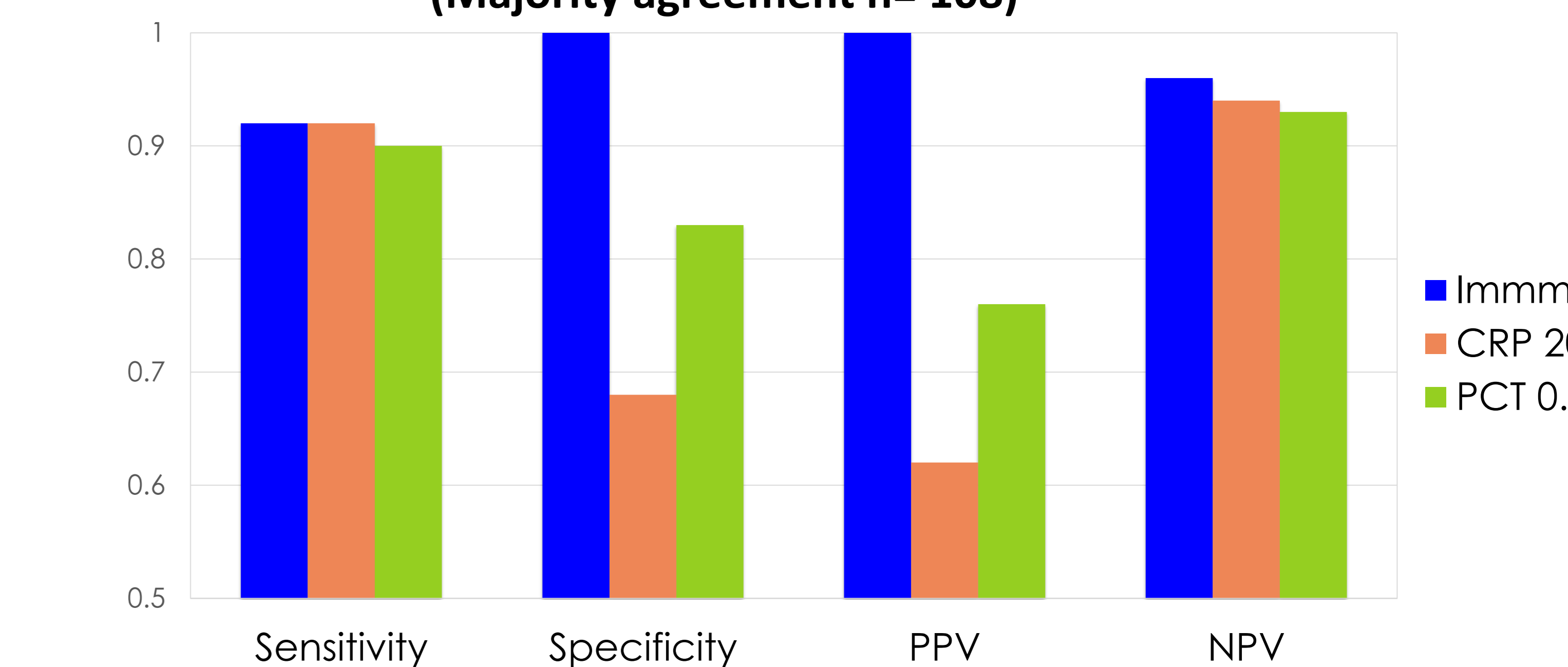
Conclusions

The evaluated ImmunoXpert™ assay, which combines both bacterial- and viral-induced host-proteins, was an accurate predictor of bacterial versus viral etiologies in children with fever. It added a diagnostic value over routinely used biomarkers and could potentially support effective management of febrile children while reducing unnecessary diagnostic tests and antibiotic misuse.

Prospective studies are still needed in specific febrile diseases such as meningitis, pneumonia, lower respiratory tract infection to a further validate this assay.

References

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