Appendix 3 (as supplied by the authors): Definition of the target zone of accuracy and generation of study objectives

Step 1: Set a priority between sensitivity and specificity and provide rationale

Sensitivity [X] or Specificity []

Rationale: clinicians do not want to miss group A *Streptococcus* (GAS) cases that could transmit the bacterium to other individuals and/or lead to complications.

Step 2: Define a minimally acceptable value for sensitivity and provide rationale

Minimally acceptable sensitivity = 85%

Rationale: Several clinical experts consider that diagnostic strategies for sore throat in children should be at least 80-90% sensitive [1-4].

Step 3: Define a minimally acceptable value for specificity and provide rationale

Minimally acceptable specificity = 85%

Rationale: Assuming a population of a 100 children with pharyngitis and a GAS prevalence of 35%, a diagnostic strategy with 85% sensitivity would lead to 30 prescriptions for antibiotic therapy for 100 patients. We aim to identify a diagnostic strategy that could reduce the antibiotics consumption (baseline ≥60%) [5-7]. If we set the maximum acceptable antibiotics prescription rate to 40%, then the maximum acceptable number of antibiotics prescribed for GAS-negative patients would be 10 for 65 patients, for a specificity of 85%.

Step 4: Clearly define study objectives

We aimed to identify a CPR-based selective testing strategy that would be at least 85% sensitive and 85% specific. We tested this by assessing whether the one-sided rectangular 95% confidence region for (sensitivity, specificity) lies entirely within the pre-specified target zone of accuracy [8].

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