

# ESTIMATING THE BURDEN OF PNEUMOCOCCAL PNEUMONIA AMONG ADULTS

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## INTRODUCTION

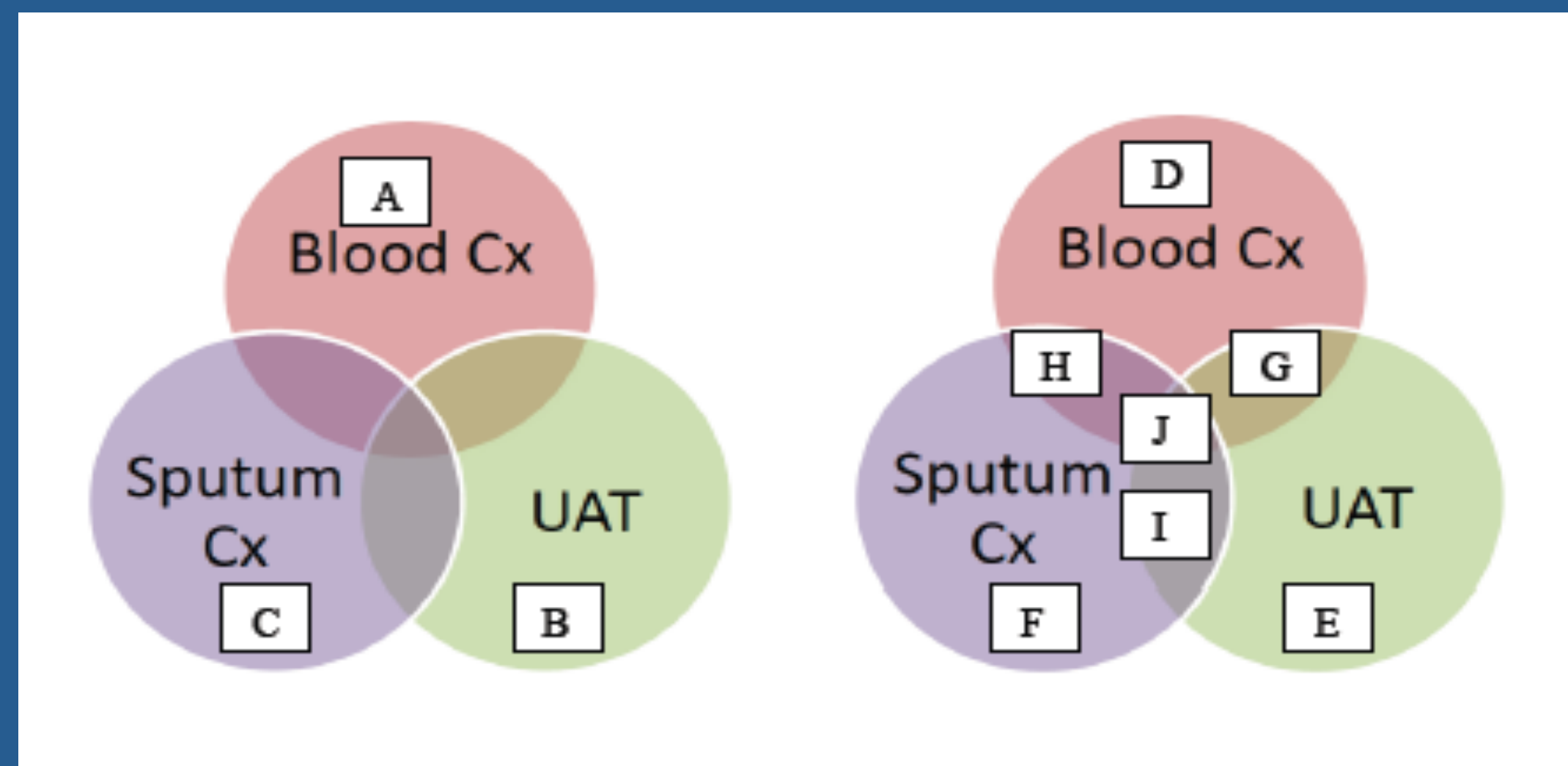
- Community-acquired pneumonia (CAP) causes significant morbidity and mortality and a large proportion is potentially attributable to pneumococcus.<sup>1</sup>
- In 2000, in children <5 years old, an estimated 14 million cases and 750,000 deaths from pneumococcal pneumonia occurred;<sup>2</sup> however, the adult burden is not well characterized.
- Diagnostic tests for non-bacteremic pneumococcal pneumonia are limited; thus, most etiology studies measure only the incidence of invasive or bacteremic disease.
- Through a comprehensive review and meta-analysis of studies utilizing the BinaxNOW<sup>®</sup> *S. pneumoniae* urinary antigen test (UAT), blood cultures, and sputum cultures, we sought to better understand the relationships between bacteremic pneumococcal pneumonia, non-bacteremic pneumococcal pneumonia, and all-cause CAP.
- The intention is to apply these parameters to a comprehensive review of bacteremic pneumococcal disease among adults in order to project the global disease burden in adults.

## METHODS

### Strategy

- We performed a comprehensive literature search to identify papers that compare the diagnostic yield of blood cultures, sputum cultures, and the Binax UAT.
- We contacted authors of potentially relevant studies to obtain information on the numbers of patients undergoing each diagnostic test, the numbers of positive test results, and the overlaps in positive results among the three methods of detection (Figure 1).

Figure 1. The relationship in diagnostic test yield of blood culture, sputum culture, and the Binax *S. pneumoniae* urine antigen test



### Definitions and Outcome Measures

- The total CAP population (N) included only those with radiographic pneumonia.
- Pneumococcal pneumonia: CAP and at least one of the three positive laboratory tests.
- Bacteremic pneumococcal pneumonia: CAP and a blood culture positive for pneumococcus (A/N).
- Non-bacteremic pneumococcal pneumonia: CAP and a sputum culture positive for pneumococcus and/or a positive Binax UAT, without a blood culture positive for pneumococcus: (E+F+I)/N
- The proportion of CAP attributable to pneumococcus: (A+E+I+F)/N
- The ratio of non-bacteremic to bacteremic pneumococcal pneumonia: (E+I+F)/A
- The additional contribution of the Binax UAT to blood and sputum culture: (E/N)
- The proportion of pneumococcal pneumonia that is bacteremic: A/(A+E+I+F)

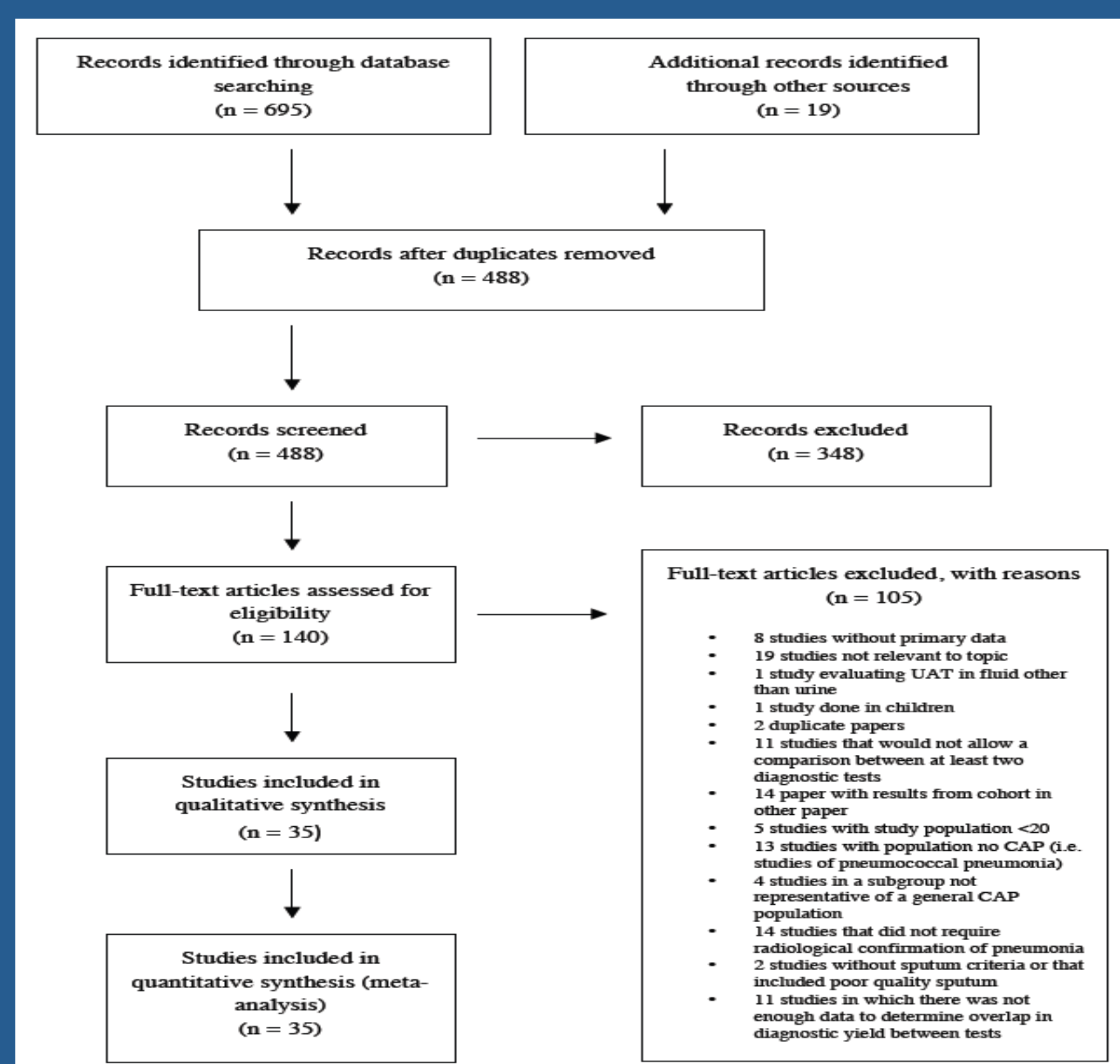
### Statistical Analysis

- The proportions were estimated using a random effects meta-analysis.
- The ratio of non-bacteremic to bacteremic pneumococcal pneumonia was estimated using a nonparametric bootstrap approach.

## RESULTS

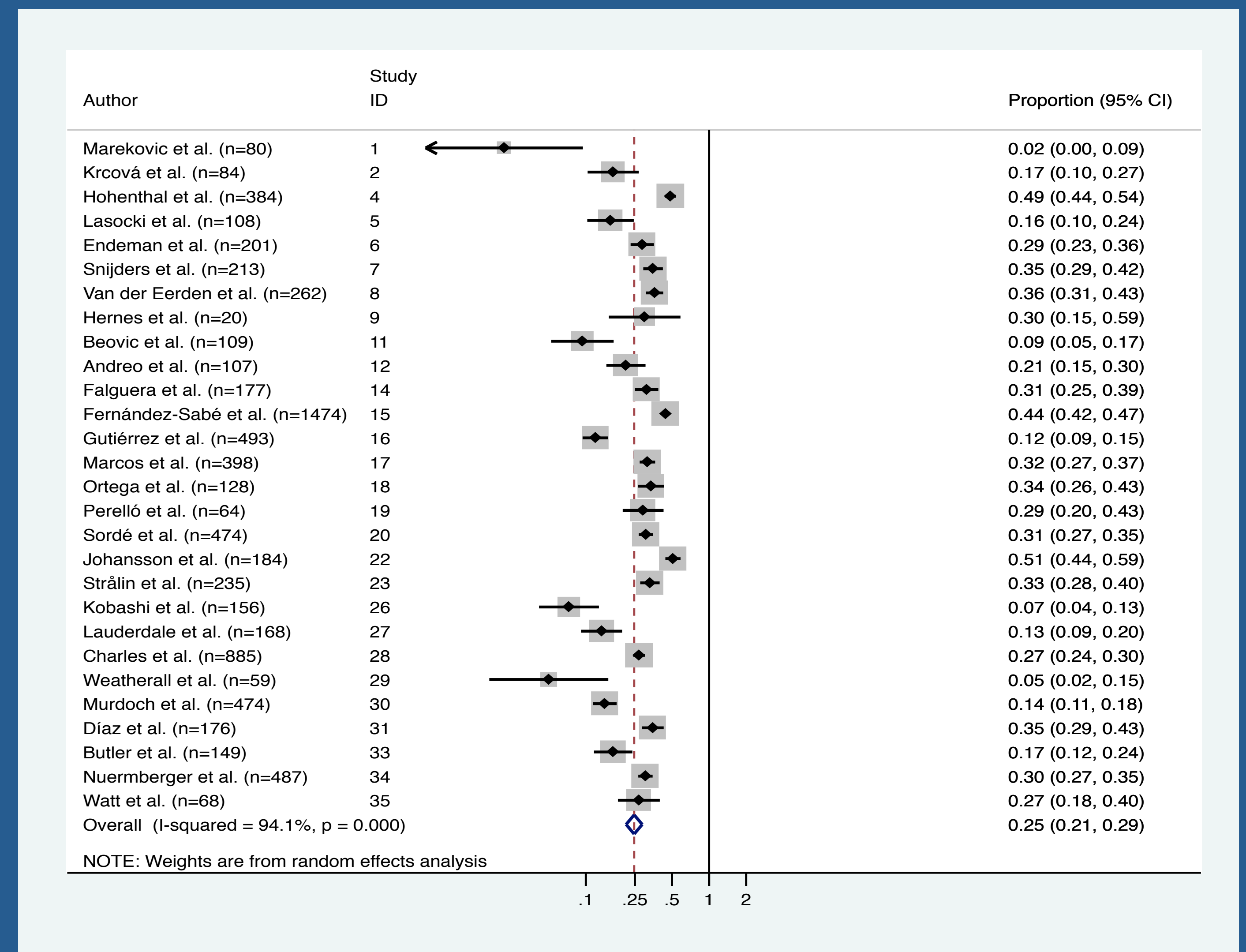
- A comprehensive literature search and hand searching of citation lists from other relevant published studies yielded 469 articles; 35 were ultimately included in the analysis (Figure 2).

Figure 2. Flow Diagram for the Selection of Studies



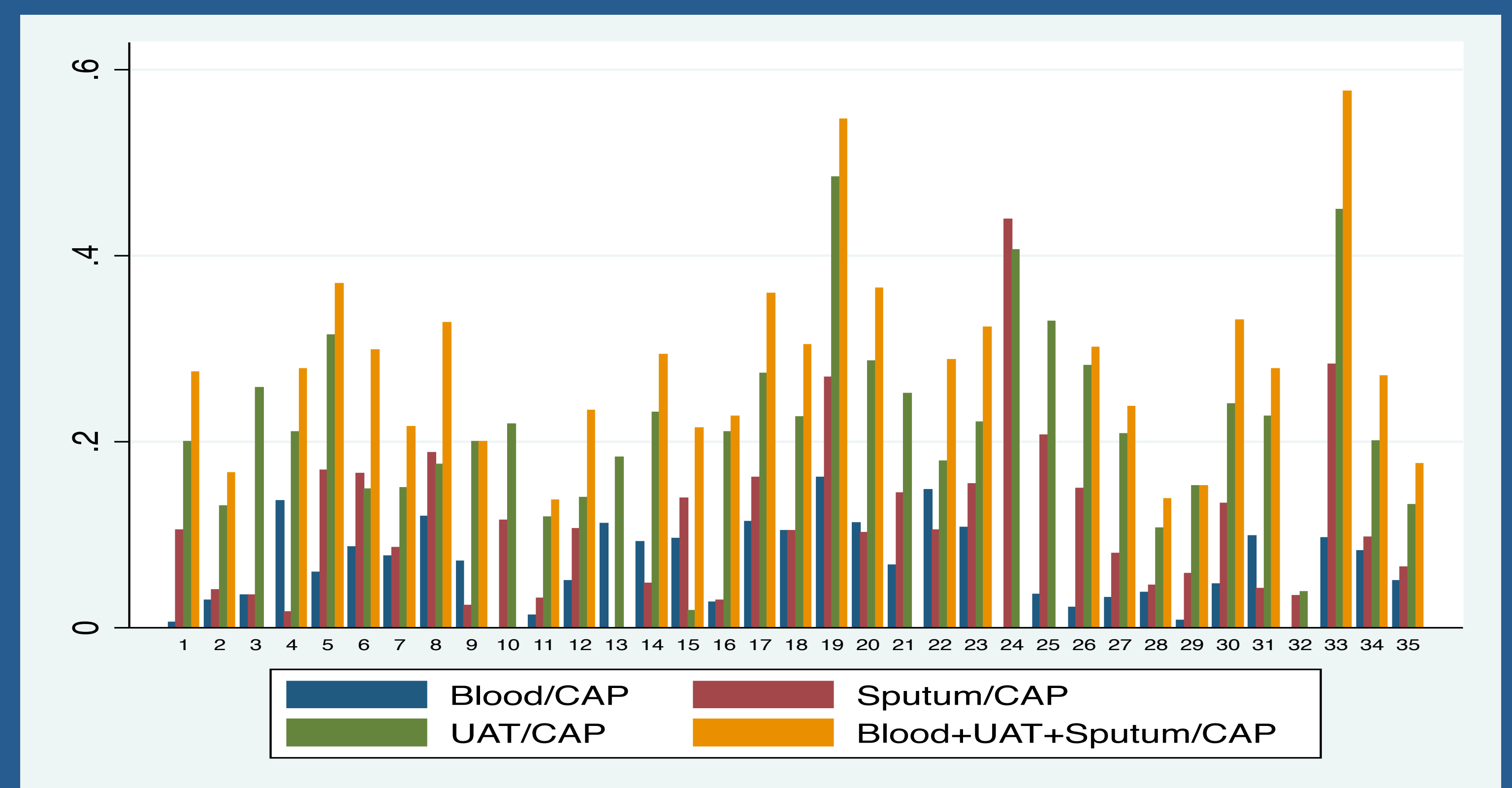
- The majority of studies came from resource-rich countries.
- The estimated ratio of non-bacteremic to bacteremic pneumococcal pneumonia was 3.75 (95% CI: 2.51-5.59).
- The proportion of pneumococcal pneumonia that was bacteremic to be 24.7% (95% CI: 21.2%-28.7%) (Figure 3), providing a ratio of non-bacteremic to bacteremic pneumococcal pneumonia of 3.05 (95% CI: 2.48-3.72).

Figure 3. Forest Plot for the Proportion of Pneumococcal Pneumonia Identified as Bacteremic



- The estimated proportion of CAP attributable to pneumococcus was 27.5% (95% CI: 24.1%-31.3%). The proportion of CAP identified as pneumococcus varied by diagnostic test. It was smallest with blood cultures and greatest with the Binax UAT (Figure 4).
- The Binax UAT diagnosed an additional 11.3% (95%CI: 9.5-13.4%) of CAP beyond that identified by blood and sputum culture alone

Figure 4. Proportion of CAP attributable to Pneumococcus



## CONCLUSION

- For every case of bacteremic pneumococcal pneumonia, there are at least 3 additional cases of non-bacteremic pneumococcal pneumonia. This result was observed using two unique statistical methods.
- Additional studies from resource-poor countries would be helpful in assuring the validity of this result in these areas.
- This ratio can be applied to global estimates of invasive pneumococcal disease or bacteremic pneumococcal pneumonia in adults in order to better estimate the overall burden of disease.
- At least one-quarter of CAP cases are likely attributable to pneumococcus.
- The Binax UAT may identify an additional 11% of CAP cases with an etiology of pneumococcal pneumonia. This might be considered in etiology studies among adults in the resource-limited countries in which only blood cultures and sputum studies are utilized.

## REFERENCES

- Fine MJ, Smith MH, Carson CA, et al. Prognosis and outcomes of patients with community-acquired pneumonia: a meta-analysis. JAMA 1995;274:134-141.
- O'Brien KL, Wolfson LJ, Watt JP, et al. Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates. Lancet 2009;374:893-902.

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