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A novel host-protein assay outperforms routine parameters for distinguishing between bacterial and viral lower respiratory tract infections☆

Michal Stein [a,*], Shelly Lipman-Arens [b], Kfir Oved [c], Asi Cohen [c], Ellen Bamberger [c,d,e], Roy Navon [c], Olga Boico [c], Tom Friedman [c,f], Liat Etshtein [c], Meital Paz [c], Tanya M. Gottlieb [c], Or Kriger [b], Yura Fonar [e], Ester Pri-Or [c], Renata Yacobov [b], Yaniv Dotan [d,e], Amit Hochberg [b], Moti Grupper [d,e], Irina Chistyakov [d,e], Israel Potasman [d,e], Isaac Srugo [d,e], Eran Eden [c], Adi Klein [b]

[a] Infectious Diseases Unit, Hillel Yaffe Medical Center, Hadera, Israel
[b] Department of Pediatrics, Hillel Yaffe Medical Center, Hadera, Israel
[c] MeMed Diagnostics, Tirat Carmel, Israel
[d] Bnai Zion Medical Center, Haifa, Israel
[e] Technion-Israel Institute of Technology, Haifa, Israel
[f] Rambam Medical Center, Haifa, Israel

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ABSTRACT

Bacterial and viral lower respiratory tract infections (LRTIs) are often clinically indistinguishable, leading to antibiotic overuse. We compared the diagnostic accuracy of a new assay that combines 3 host-biomarkers (TRAIL, IP-10, CRP) with parameters in routine use to distinguish bacterial from viral LRTIs. Study cohort included 184 potentially eligible pediatric and adult patients. Reference standard diagnosis was based on adjudication by an expert panel following comprehensive clinical and laboratory investigation (including respiratory PCRs). Experts were blinded to assay results and assay performers were blinded to reference standard outcomes. Evaluated cohort included 88 bacterial and 36 viral patients (23 did not fulfill inclusion criteria; 37 had indeterminate reference standard outcome). Assay distinguished bacterial from viral LRTI patients with sensitivity of 0.93 ± 0.06 and specificity of 0.91 ± 0.09, outperforming routine parameters, including WBC, CRP and chest x-ray signs. These findings support the assay's potential to help clinicians avoid missing bacterial LRTIs or overusing antibiotics.

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1. Introduction

Lower respiratory tract infections (LRTI), primarily pneumonia and bronchitis, are the third leading cause of death worldwide (WHO | The top 10 causes of death). The incidence of LRTIs in Europe is 30 million, greater than diabetes mellitus (2 million) and malignant neoplasms (2.4 million) combined, and leading to 230,000 deaths, and over 1 million hospitalizations (The burden of lung disease – ERS; WHO | Global burden of disease; Gibson et al., 2013; Welte et al., 2012). The attendant economic burden of community acquired pneumonia alone is estimated at €10.1 and $10 billion annually in Europe and the United States respectively (Jain et al., 2015; Welte et al., 2012). A major challenge to effective management of LRTI patients is the clinical difficulty of distinguishing bacterial from viral infections (Craig et al., 2010). Unfortunately, while routine tests like blood, urine, throat and cerebrospinal fluid cultures may identify the infectious agent in bacteremia, urinary tract infection, pharyngitis or meningitis, in the case of LRTI, the yield of such tests is limited as the site of infection is not readily accessible (Jain et al., 2015; Woodhead et al., 2011). A large prospective, multicenter, population-based, active surveillance study recently done in the US (the EPIC study), evaluated 2320 adults with radiographic evidence of pneumonia. Although all currently available microbiological tests including bacterial cultures, real-time PCRs, serology, and urinary antigen tests, were applied on various patient specimens (e.g., blood, sputum, pleural fluid, bronchoalveolar lavage), only in 38% of the cases was a potentially pathogenic microorganism detected (Jain et al., 2015). In the day-to-day clinical settings, this number is expected to be significantly lower as fewer diagnostic tests are actually utilized. Furthermore, even when sputum cultures and nasopharyngeal PCR samples yield microbiological findings, as in the case of *S. pneumoniae*, the clinical

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* Corresponding author. Tel.: +972-4-6188452; fax: +972-4-6304955.
E-mail address: michal.stein@gmail.com (M. Stein).

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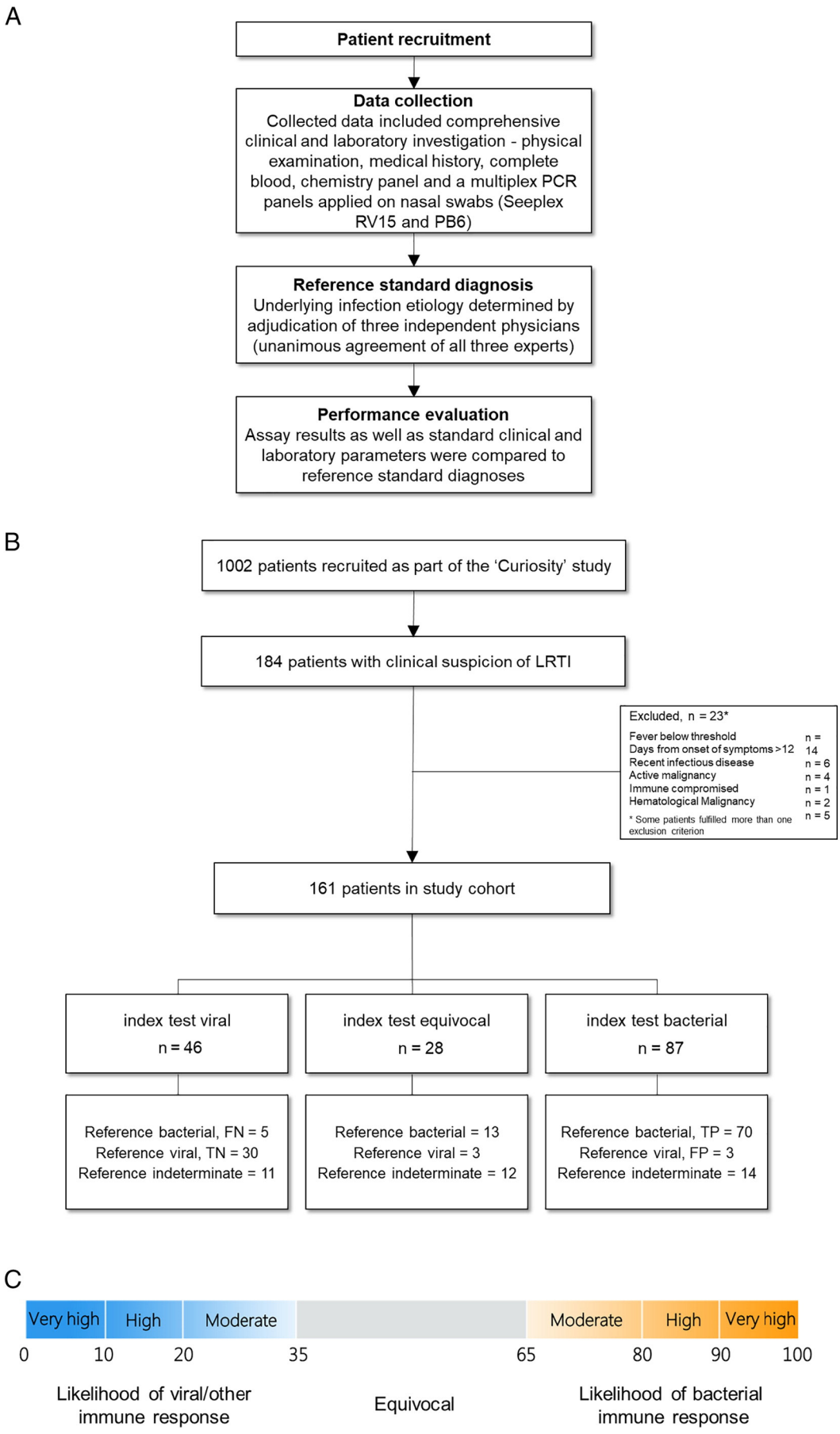

Fig. 1. (A) Study design; (B) Recruitment and flow of patients with suspicion of LRTI; (C) Index test outcomes.

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