

# A TRAIL, IP-10, CRP host-protein score distinguishes viral from viral-Bacterial co-infections in adult patients testing positive for viral detection.

Jeroen I. Stas, Ph.D.<sup>1</sup>; Cesar A. Arias M.D., Ph.D.<sup>2</sup>; Karen C. Carroll M.D.<sup>3</sup>; Richard Gordon Jr., M.D.<sup>4</sup>; Salim Halabi M.D.<sup>5</sup>; Theresa Jacob, Ph.D. M.P.H.<sup>6</sup>; Sergey M. Motov, M.D.<sup>7</sup>; Mical Paul M.D.<sup>8</sup>; Octavia M. Peck Palmer, Ph.D.<sup>9</sup>; Richard Rothman M.D., Ph.D.<sup>3</sup>; Pninit Shaked Mishan Ph.D.<sup>5</sup>; Shachaf Shiber M.D.<sup>10</sup>; Henry E. Wang, M.D.<sup>11</sup>; Alexandra Weissman, M.D., M.S., M.P.H.<sup>9</sup>

Contact: [Jeroen.stas@me-med.com](mailto:Jeroen.stas@me-med.com)

<sup>1</sup> MeMed, Tirat Carmel, Israel ; <sup>2</sup> Houston Methodist Hospital, 6560 Fannin St, Houston, TX, 77030, US ; <sup>3</sup> The Johns Hopkins University School of Medicine, 600 N Wolfe St Baltimore MD 21287, US ; <sup>4</sup> University of Texas Health Science Center at Houston (UTHealth), 6431 Fannin St, Houston, TX, 77030, US ; <sup>5</sup> Carmel Medical Center, Mikhal St 7, Haifa, 3436212, Israel ; <sup>6</sup> Maimonides Medical Center, Clinical and Translational Research Labs, 4802 Tenth Avenue, Brooklyn, NY 11219, US ; <sup>7</sup> Maimonides Medical Center, Emergency Medicine 965 48th Street, Brooklyn, NY 11219, US ; <sup>8</sup> Rambam Health Care Campus, HaAliya HaShniya St 8, Haifa, 3109601, Israel ; <sup>9</sup> University of Pittsburgh Medical Center, 3550 Terrace Street, Pittsburgh PA 15261, US ; <sup>10</sup> Rabin Medical Center, Zeev Jabotinsky St 39, Petah Tikva, 49100, Israel ; <sup>11</sup> The Ohio State University, 281 W Lane Ave, Columbus, OH 43210, US

**Background:** Determining the etiology of respiratory tract infections (RTI) is challenging and leads to antibiotic misuse. Viral testing for diagnosis of RTI has limited value as it cannot rule out a bacterial co-infection.

**Aim:** Differentiate viral from viral-bacterial co-infections in RTI within the Emergency department.

**Objective:** Evaluate the host-protein 'MeMed BV' score's ability to discriminate bacterial co-infection in patients testing positive by viral PCR and/or antigen.

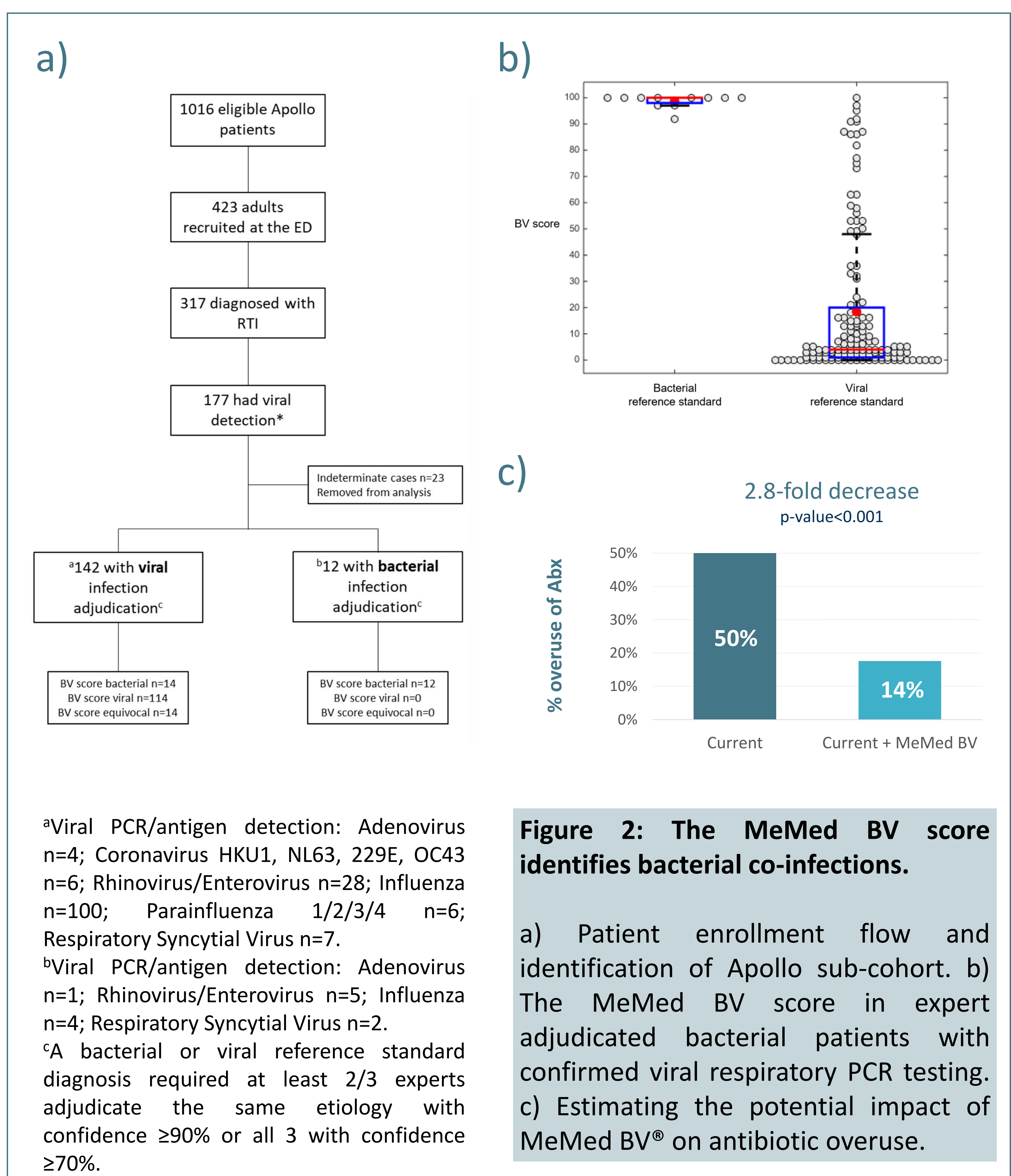
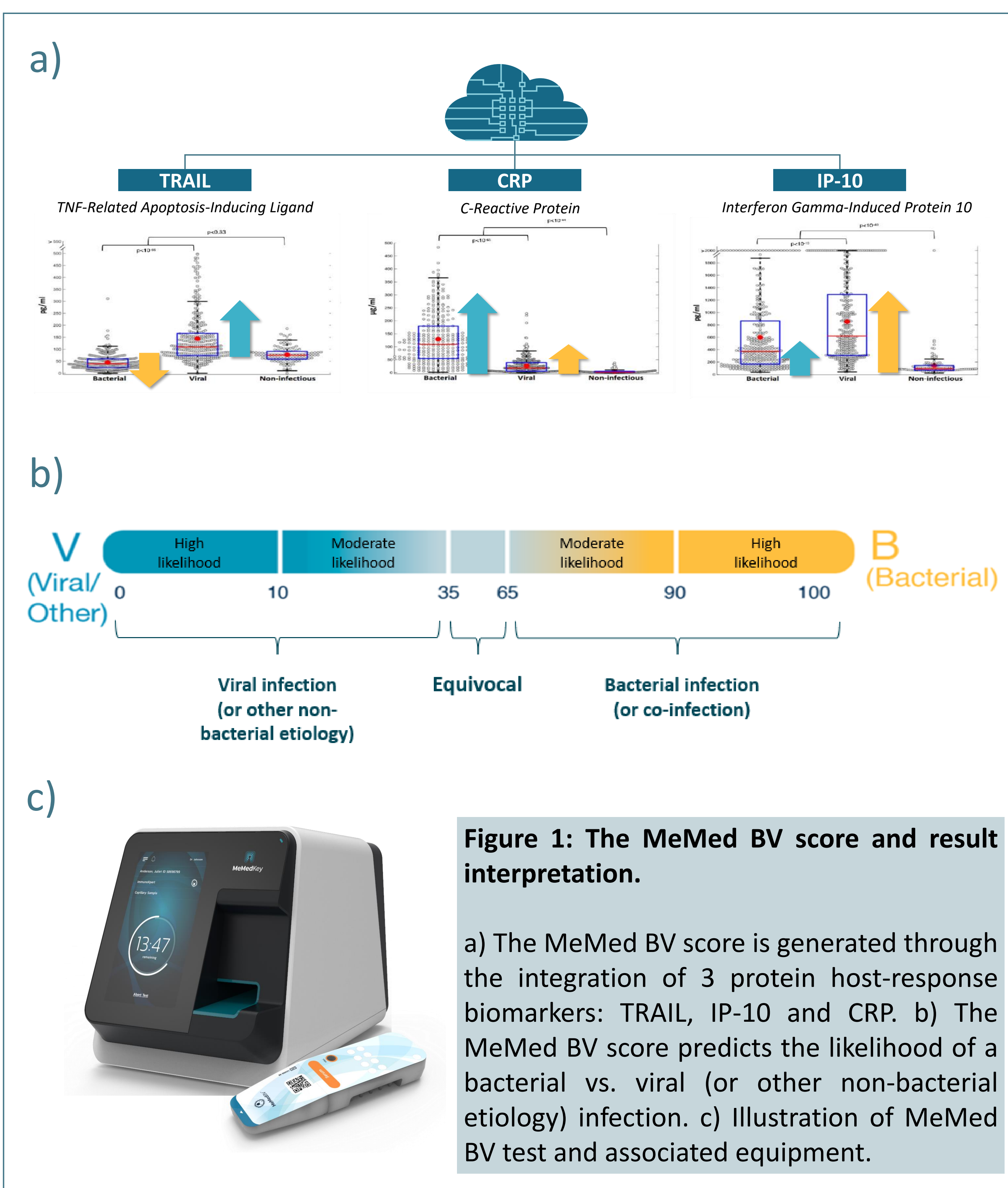


## Methods:

This was a sub-analysis of adult Emergency Department (ED) patients enrolled in the Apollo study with discharge diagnosis of RTI (NCT04690569). Reference standard diagnosis was adjudicated by independent experts based on comprehensive patient data. BV results (Figure 1) are defined as viral or other non-bacterial etiology ( $0 \leq \text{score} < 35$ ), equivocal ( $35 \leq \text{score} \leq 65$ ), and bacterial or co-infection ( $65 < \text{score} \leq 100$ ). To estimate BV's potential influence on antibiotic use, it was assumed antibiotic prescription in the medical record indicated diagnosis of a bacterial infection and that if a MeMed BV score had been available at the point-of-need, it would have influenced the physician's decision-making.

## Results:

Of 423 adults (median age, 50.7 years, interquartile range 35.8-63.9; 47% female) recruited at the ED, 154 were diagnosed with RTI (58.4% upper, 41.6% lower) and had at least one viral detection. Twelve were reference standard bacterial, all correctly receiving bacterial BV scores (Figure 2). The 12 bacterial patients were more likely to be admitted (66.7% vs. 12.7%;  $p < 0.001$ ). BV yielded sensitivity 100% (95%CI: 73.5-100.0) and specificity 89.1% (95%CI: 82.3-93.9), with 9.1% equivocal cases. BV is estimated to potentially reduce antibiotic treatment of viral infections 2.8-fold (from 50% to 17.6%;  $p < 0.001$ ), without causing antibiotic withholding from patients with bacterial infections.



**CONCLUSION:** BV discriminated bacterial co-infection in adult patients with viral PCR/antigen detection and has potential to reduce antibiotic overuse up to 3-fold.