# A TRAIL/IP-10/CRP Signature Distinguishes between Viral and Bacterial Infection in Chronic Obstructive Pulmonary Disease Patients

Meital Paz[1], Salim Halabi[2], Shachaf Shiber[3], Ami Neuberger[4], Neta Petersiel[4], Mordechai Grupper[4], Dani Kirshner[4], Noa Avni[1], Michal Stein[1], Gali Kronenfeld[1], Liran Shani[1], Tanya Gottlieb[1], Ynon Lishtzinsky[3], Yasmin Maor[5], Shirly Yanai[3], Kfir Oved[1], Eran Eden[1], Michael Drescher[3], Michal Paul[4]

[1]MeMed Diagnostics, Tirat Carmel, Israel; [2]Carmel medical center, Haifa, Israel; [3]Rabin medical center, Petach Tikva, Israel; [4]Rambam Health Care Campus, Haifa, Israel; [5]Wolfson Medical Center, Holon, Israel

Background

- Challenges in determining the etiology of suspected pneumonia in patients with a medical history of chronic obstructive pulmonary disease (COPD) lead to significant overuse of antibiotics.
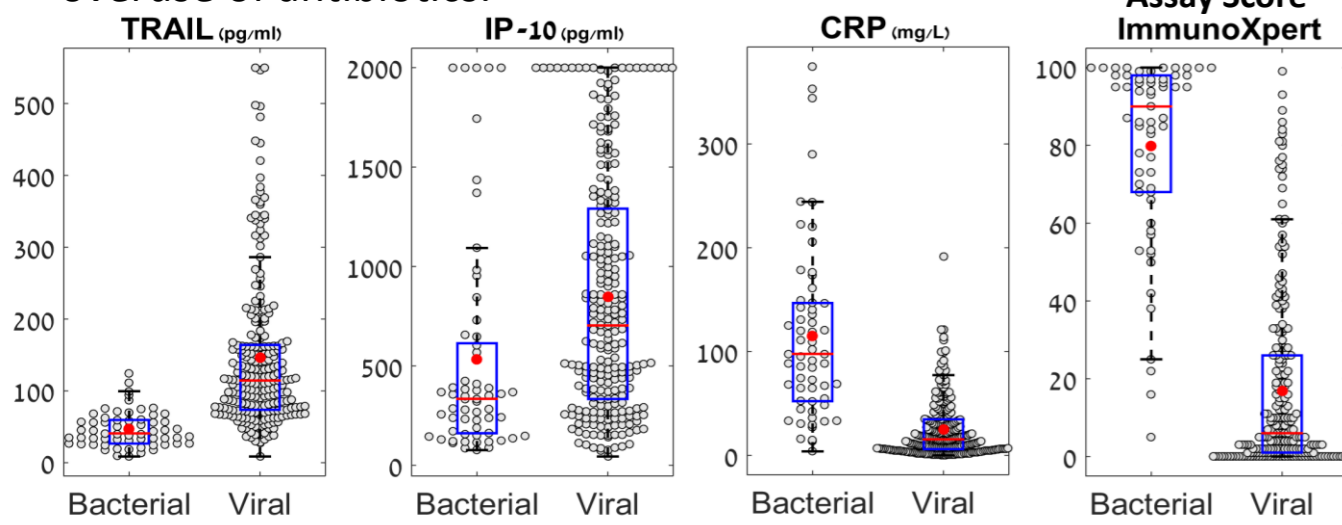
Oved et al., *PLoS ONE 2015*

- A novel host-response assay that integrates the levels of three proteins (TRAIL, IP-10, and CRP) was shown to exhibit high performance in distinguishing between bacterial and viral infection in double-blind validation studies.
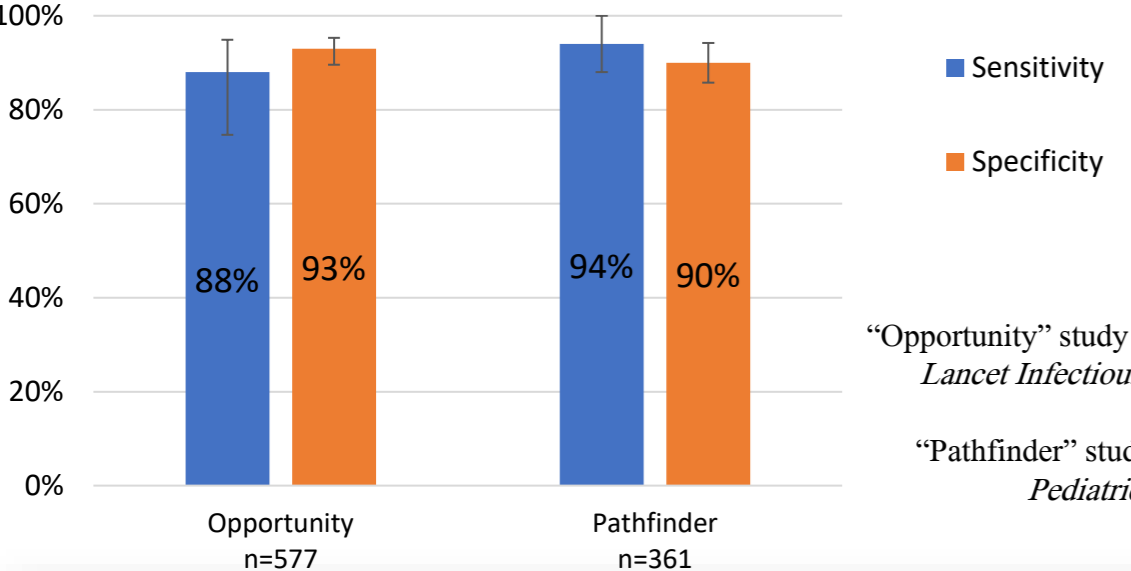
"Opportunity" study – van-Houten et al. *Lancet Infectious Diseases* 2016

"Pathfinder" study – Srugo et al. *Pediatrics* 2017

Here we sought to evaluate its potential clinical utility in reducing antibiotic overuse in adult COPD patients presenting to the ED with suspicion of lower respiratory tract infection (LRTI).

Methods

In a preliminary analysis the study population included 492 febrile adult patients prospectively recruited in "Observer", an EU Horizon 2020 funded study (grant #684589). Patient etiology was determined by majority expert panel based on clinical, laboratory, multiplex PCR, radiological and follow-up data. We compared the expert panel diagnosis with the assay that gives three possible outcomes: viral, bacterial (including viral with bacterial coinfection) or equivocal.

Results

45 out 492 adult patients prospectively recruited with suspicion of LRTI had a medical history of COPD. Of these, 20 cases were assigned by experts as viral infections and 19 as bacterial infections (Figure 1).

Antibiotics were prescribed to 19/19 bacterial infections and 16/20 viral infections. The assay correctly classified 19/19 bacterial infections and 12/20 viral infections, with 2 viral cases classified by the assay as bacterial and 6 receiving an equivocal outcome. These data support the assay's potential to reduce antibiotic overuse from 16/20=80% to 8/20=40% (P=0.01).

Conclusions

A novel TRAIL/IP-10/CRP signature has potential to significantly reduce antibiotic overuse in COPD patients with suspected LRTI without missing bacterial infection.
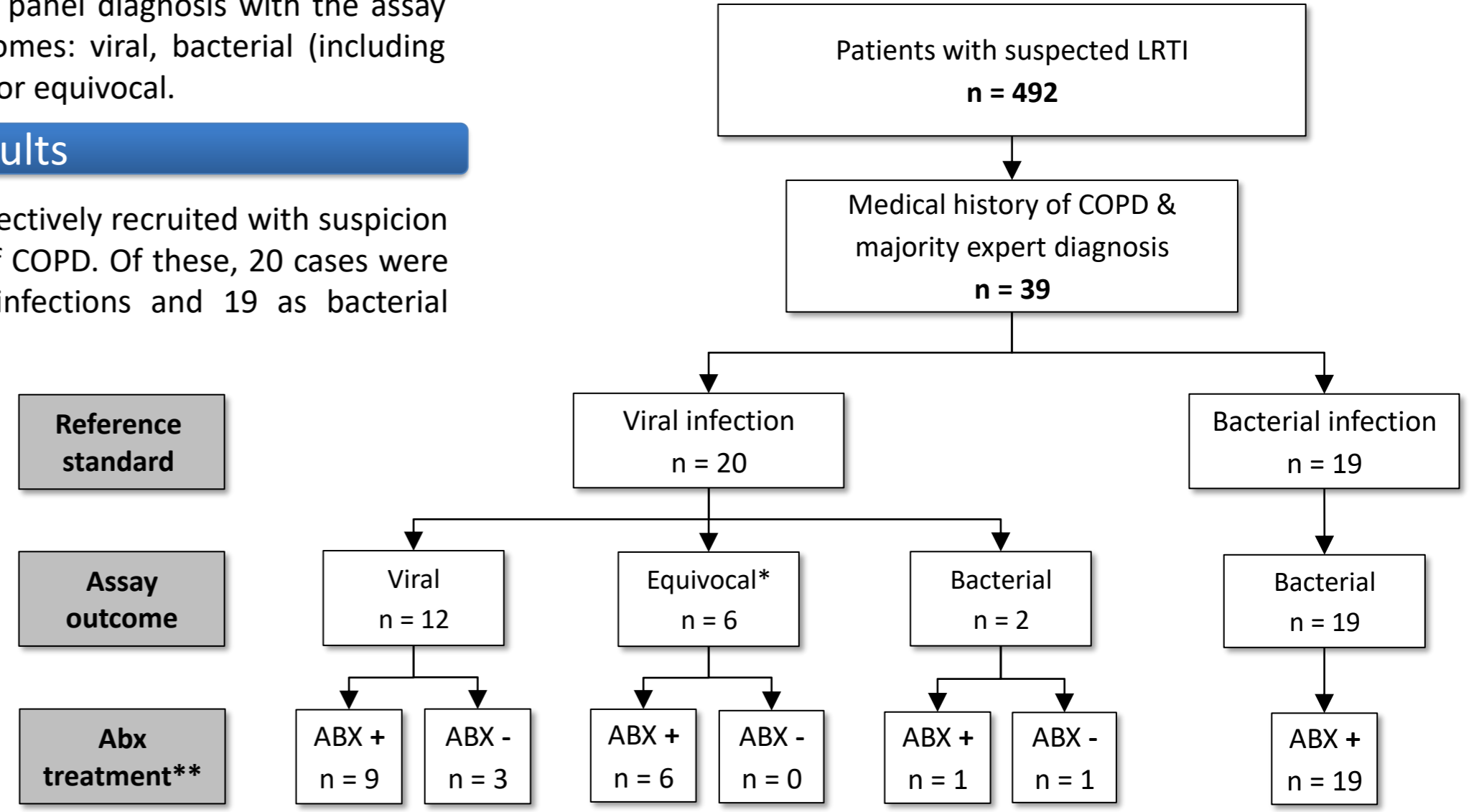

Figure 1: Flow through of COPD patients in prospective diagnostic performance validation study "Observer"
*Equivocal= an equivocal outcome dose not provide diagnostic information. **Abx treatment as reported on medical record.