Double-blind validation in febrile children of host-protein assay [TRAIL, IP-10, CRP] for distinguishing bacterial and viral infections

Isaac Srugo[a], Adi Klein[b], Michal Stein[b], Orit Golan-Shany[a], Nogah Kerem[a], Irina Chistyakov[a], Jacob Genizi[a], Oded Glazer[a], Liat Yaniv[a], Alina German[a], Dan Miron[c], Yael Shahor[d], Ellen Bamberger[a,e], Maanit Shapira[b], Sarit Freimann[b], Kfir Oved[e], Tanya Gottlieb[e], Roy Navone[e], Meital Paz[e], Liat Etshtein[e], Olga Boico[e], Gali Kronenfeld[e], Eran Eden[e], Robert Cohen[f], Helène Chappuy[g], François Angoulvant[h], Laurence Lacroix[i], and Alain Gervaix[i]

[a]Bnai-Zion Medical Center, Haifa, [b]Hillel Yaffe Medical Center, Hadera, Israel; [c]Emek Medical Center, Afula, Israel; [d]Rambam Health Care Campus, Haifa Israel; [e]MeMed Diagnostics, Tirat Carmel, Israel; [f]Centre Intercommunal de Creteil, Creteil, France; [g]Armand Trousseau Hospital, Paris, France; [h]Necker-Enfants Malades Hospital, Paris, France; [i]Geneva University Hospitals, Geneva, Switzerland
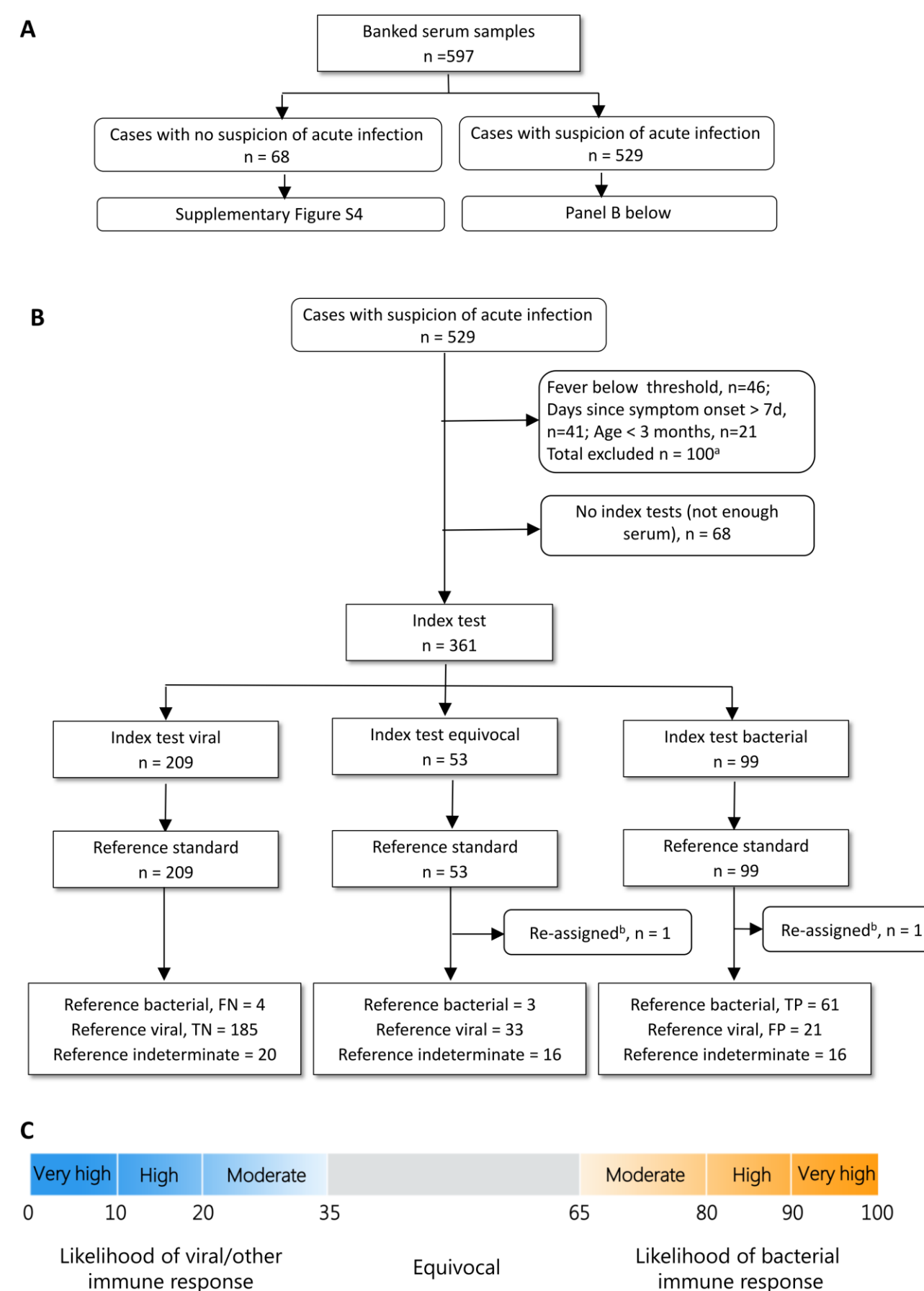
27th ECCMID
ESCMID

Background and design

Background: Reliably distinguishing between bacterial and viral infections in febrile children is often challenging, leading to antibiotic misuse. A novel assay that integrates measurements of three blood-borne host-response proteins (TRAIL: TNF-related apoptosis-inducing ligand; IP-10: Interferon gamma induced proten-10; CRP: C-reactive protein) was recently developed to assist in differentiation between bacterial and viral disease (Oved et al. 2015). We performed double-blind, multi-center assay evaluation.

Materials and methods: Infectious and non-infectious children presenting to 5 pediatric emergency departments and inpatients aged ≥3 months to ≤18 years were retrospectively enrolled. Inclusion criteria for the infectious cohort were: suspicion of acute infection, fever ≥38°C, and symptom duration ≤7 days.

Reference standard diagnosis was based on predetermined criteria plus adjudication by an expert panel blinded to assay results. Assay performers were blinded to reference standard.
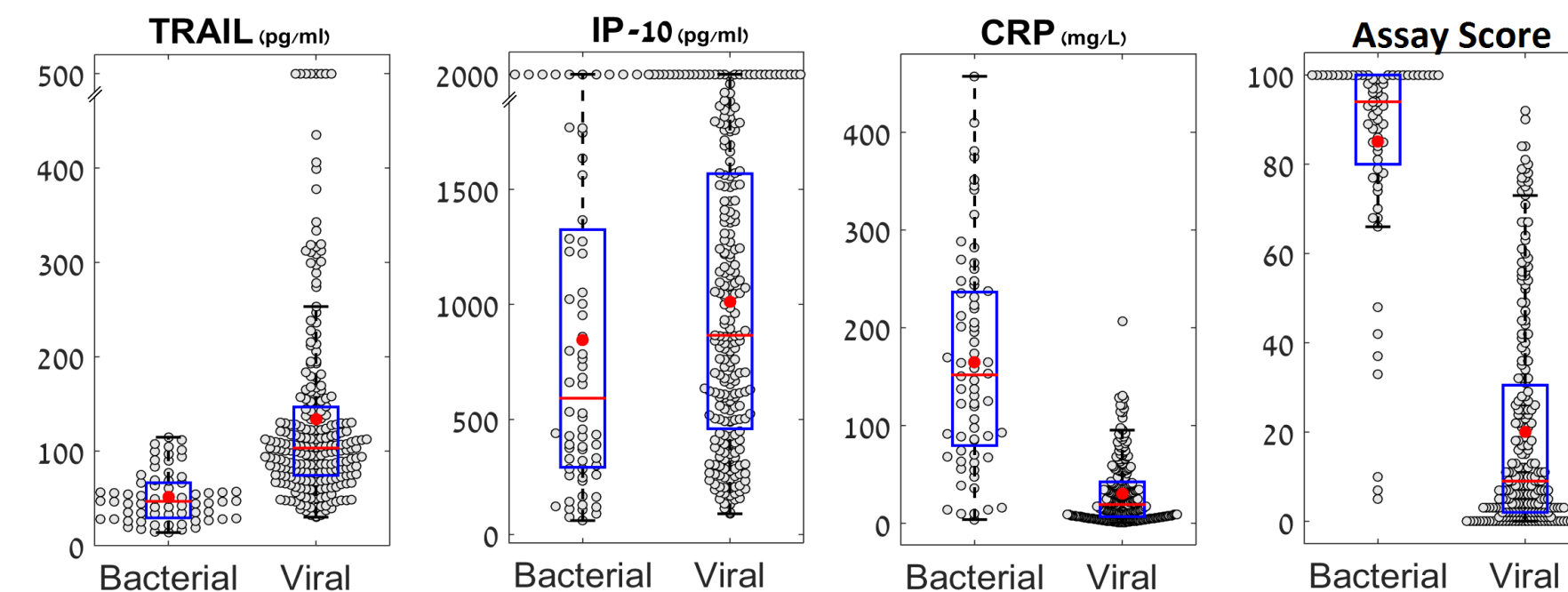
Assay and routine parameter cutoffs were pre-defined before un-blinding.

(A) Banked serum samples from potentially eligible participants were classified as without or with suspicion of acute infection. (B) Flow through of participants with suspicion of acute infection. (C) Host-signature assay outcomes.
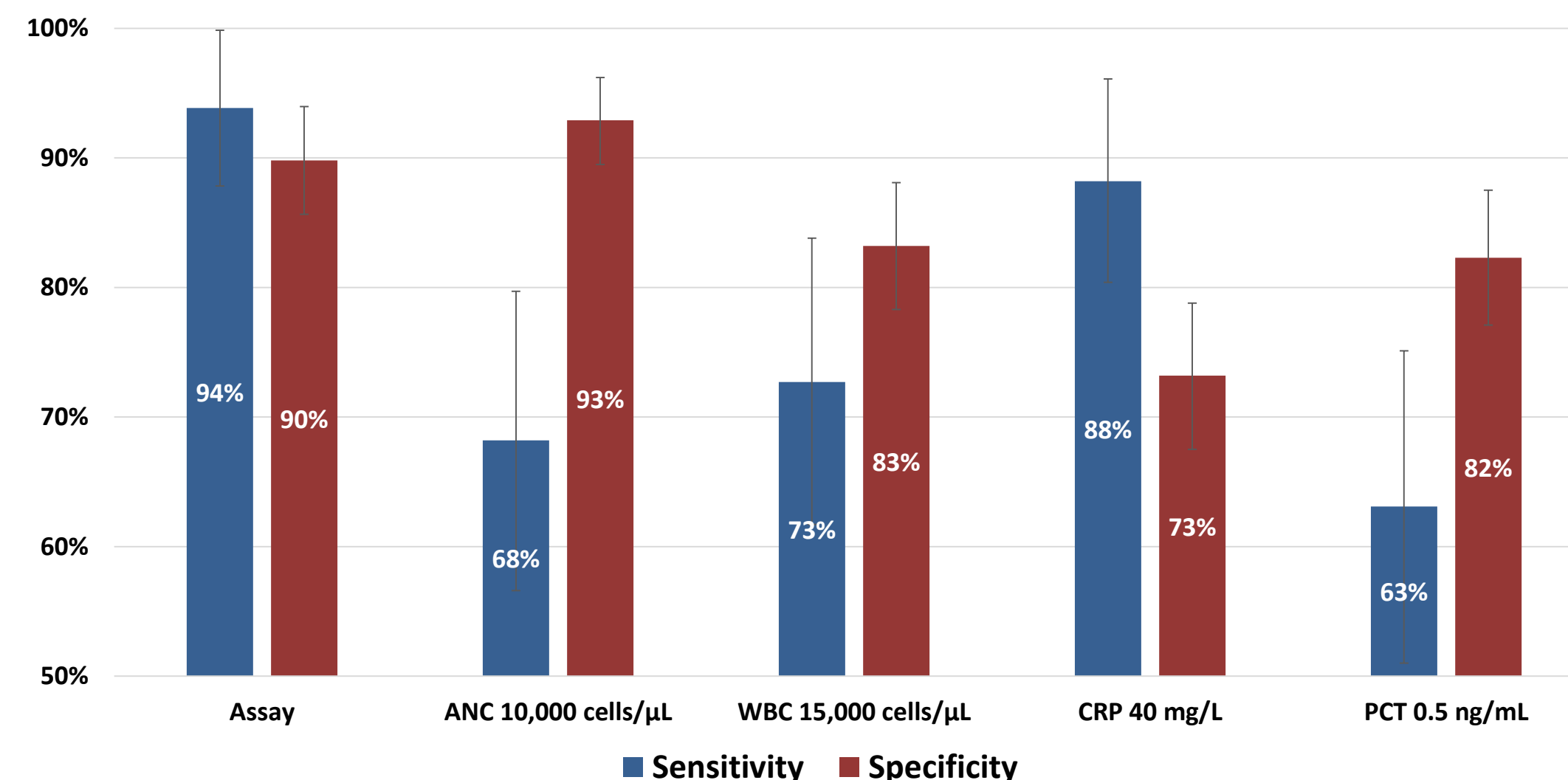
Results and conclusion

Differential expression of the host proteins TRAIL, IP-10, CRP and the host-signature assay score in children with bacterial and viral infections

Red line and circle correspond to group median and average respectively (n=307).

Host-signature assay outperforms routine laboratory parameters and other biomarkers

Conclusions: Assay performance was validated in febrile children in a double-blinded study. Assay was more accurate than CRP, PCT and routine laboratory parameters. These promising results merit evaluation in a clinical utility study, to measure the impact of the host-signature assay on actual clinical practice.

HUG Hôpitaux Universitaires Genève