MeMed

TRAIL, IP-10, CRP Host-protein Signature score distinguishes between Viral and Bacterial Infection in Sepsis Patients.

BSAC Spring Meeting, May 11th

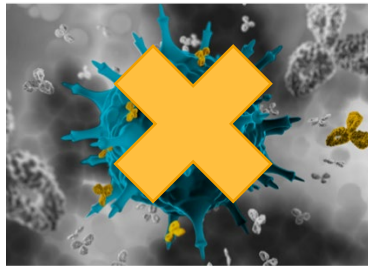
Jeroen Stas, Medical Affairs Manager, MeMed Diagnostics.

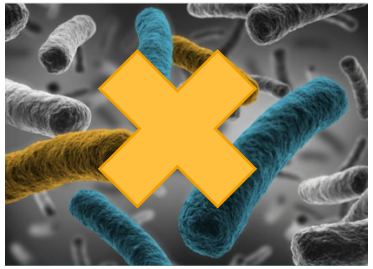
Investigators of Apollo (sub-)study

Sergey M. Motov, M.D.	Maimonides Medical Center, Emergency Medicine. Brooklyn, US.
Cesar A. Arias, M.D., Ph.D.	University of Texas Health Science Center (UTHealth). Houston, US.
Richard G. Bachur, M.D.	Boston Children's Hospital. Boston, US.
Susanna Esposito, M.D.	Pediatric Clinic, Pietro Barilla Children's Hospital. Parma, Italy.
Salim Halabi, M.D.	Carmel Medical Center. Haifa, Israel.
Sheldon L. Kaplan, M.D.	Texas Children's Hospital. Houston, US.
Adi Klein, M.D.	Hillel Yaffe Medical Center. Hadera, Israel.
Richard Rothman, M.D., Ph.D.	Johns Hopkins University. Baltimore, US.
Leticia M. Ryan, M.D., M.P.H.	Johns Hopkins University. Baltimore, US.
Shachaf Shiber, M.D.	Rabin Medical Center. Petah Tikva, Israel.
Tobias Tenenbaum, M.D.	Sana Klinikum Lichtenberg. Berlin, Germany.
Alexandra Weissman, M.D.	University of Pittsburgh Medical Center. Pittsburgh, US.

DISCLAIMER: MeMed funded the Apollo study with payments to participating institutions. I am a MeMed employee.

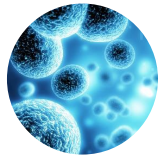
Changing Clinical Diagnostics by measuring the host-response





Wh Bug?

Inaccessible infection sites



Often, no pathogens are detected

False Alarms due to colonization

Poor performance in emerging pathogens

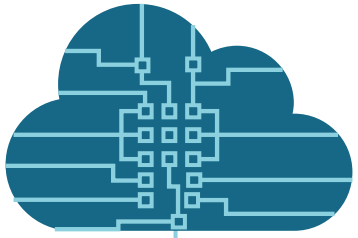
How is the patient responding?

Measure & quantify relevant immune response biomarkers.

Integration of biomarkers in a clinical score instead of using cutoffs

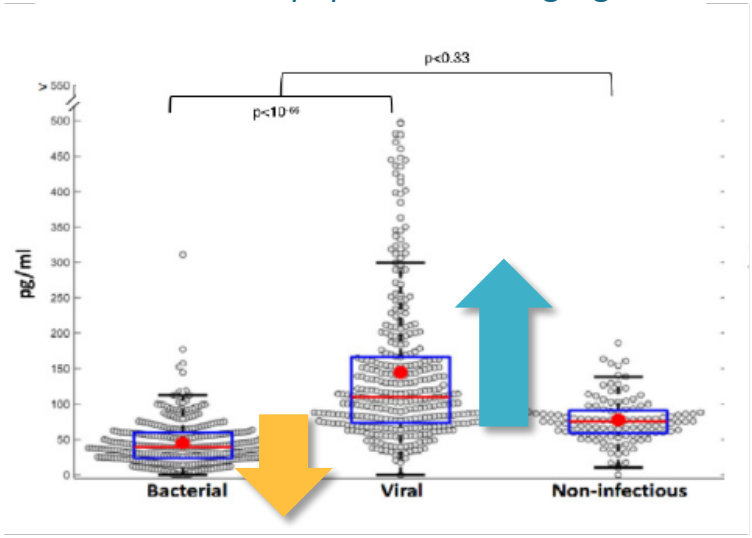
Small blood volume (100µl serum) in 15 minutes

Background: Host-protein Signature score.



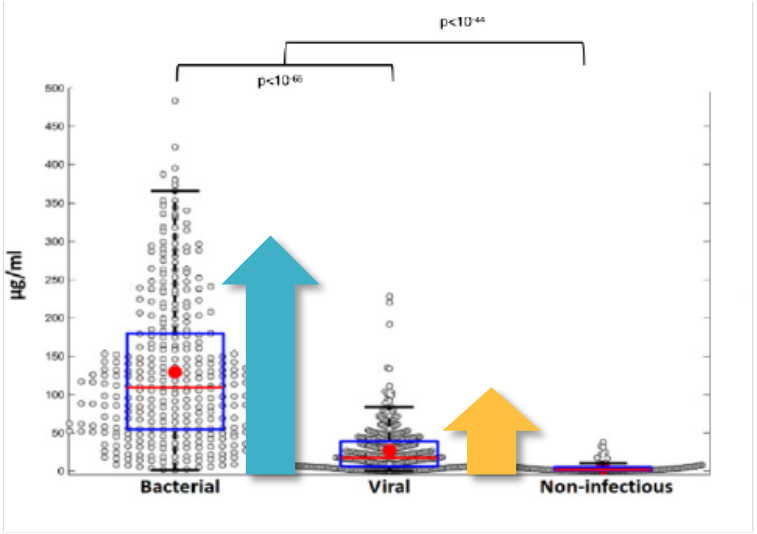
TRAIL

TNF-Related Apoptosis-Inducing Ligand



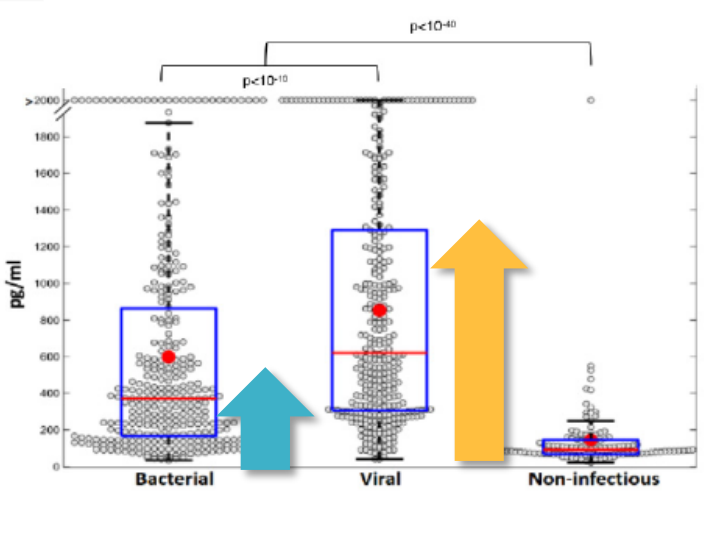
CRP

C-Reactive Protein

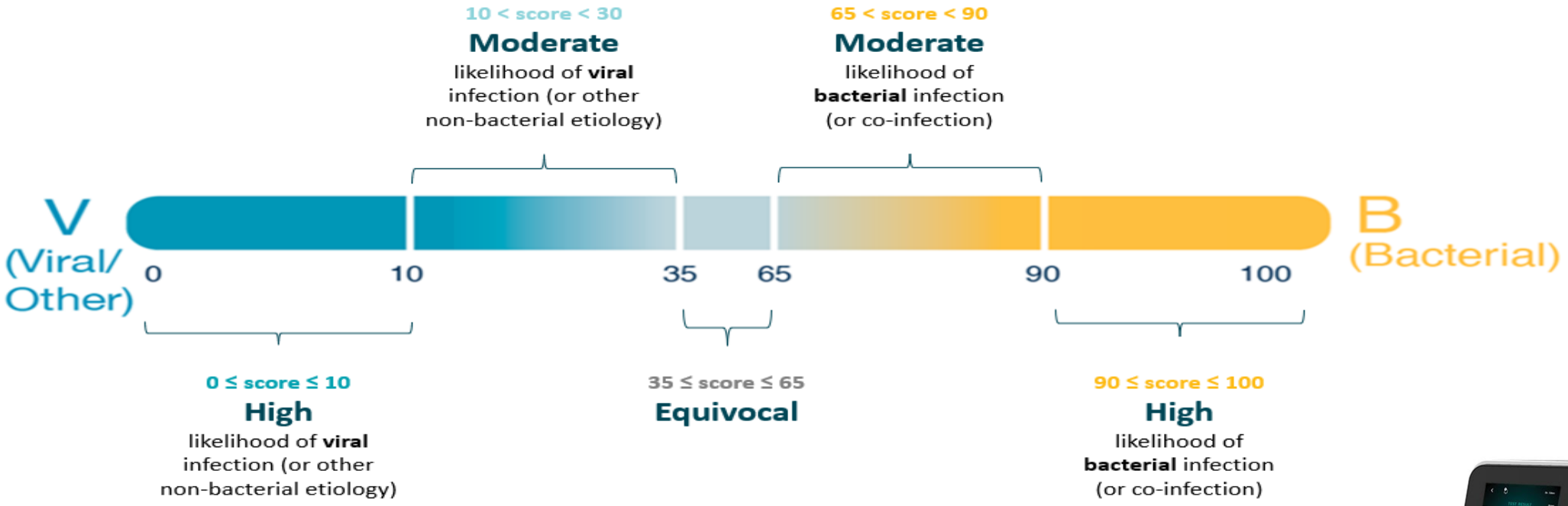


IP-10

Interferon Gamma-Induced Protein 10



Background: Host-protein Signature score.



Validation: Host-protein Signature score

Study Name	Patients #	Clinical Setting	Age	Clinical Syndrome	BV Performance
Curiosity / ISR **[PLOS One, 2015]**	1,002	ED, wards	Pediatrics and Adults, >=3mo	Suspicion of acute infection	AUC 93%
Pathfinder* / ISR, SWISS **[Pediatrics, 2017]**	597	ED, wards	Pediatrics, >=3mo, <=18yr	Pneumonia, FWS, blood drawn for serology	AUC 92%
Opportunity / ISR,NL **[The Lancet, 2016]**	777	ED, wards	Pediatrics, 2-60 months	Symptoms of LRTI or FWS	AUC 90%
Rosetta / ISR **[Data on File]**	550	ED	Pediatrics, >=3mo, <=18yr	Symptoms of RTI or FWS	AUC 91%
Autopilot / GER, ITA **[CMI, 2021]**	1,140	ED	Pediatrics, >=3mo, <=18yr	Suspicion of RTI or FWS	AUC 94%
Observer / ISR **[Data on File]**	583	ED	Adults, >18 years	Suspicion of LRTI or pneumonia	AUC 98%
Apollo / US, ISR, GER*, ITA* **[Data on File]**	1,016	ED, UCC	Pediatrics and Adults, > 3mo	Suspicion of acute bacterial or viral infection	AUC 97%

*Retrospective

The Apollo study

Regulatory
Work in US patient population and design new FDA regulatory pathway for host-response testing.

Validate
MeMed BV test together with the MeMed Key platform.

Compare
Diagnostic performance to other inflammatory biomarkers and their combinations.

Apollo study

Inclusion:
- Older than 90 days of age
- Suspected viral or bacterial infection
- Febrile within last 7 days
- Duration of illness less than 7 days

Exclusion:
- Unrelated febrile episode within 2 weeks
- Immunocompromised

90% Specificity

99% NPV

97% Sensitivity

Clinical setting
Emergency department and / or urgent care centers (no hospital-admitted inpatients).

Expert panel adjudication
Using the full patient case file + 28-day follow-up data.

The Apollo study: sub-analysis on Sepsis patients

- Sub-study objective:
  - "Evaluate the MeMed BV's ability to differentiate viral from bacterial infection in Sepsis patients"
- Sepsis definition:
  - "Two or more SIRS criteria".

  → Still commonly used in the US, despite Sepsis-3 definition.
  - Expert adjudication: Viral or bacterial classification by at least 2/3 experts to assign same etiology label with confidence ≥90% or all 3 assign with confidence ≥70%.

SIRS criteria for children:

	Pediatric SIRS Criteria (≥1 of the criteria from Column 1 AND Column 2)							
	Column 1 (≥1 of the below criteria)				Column 2 (≥1 of the below criteria)			Cardiovascular Dysfunction
	Core Temperature (°C)		Leukocyte Count (Leukocytes ×10³/mm) [3]		Heart Rate (Beats/Min) [1]			
Age Group	Hypothermia	Hyperthermia	Leukopenia	Leukocytosis	Bradycardia	Tachycardia	Respiratory Rate[2] (Breaths/Min)	Systolic Blood Pressure (mmHg)
0 days to 1 wk	<36	>38.5	NA	>34	<100	>180	>50	<65
1 wk to 1 mo	<36	>38.5	<6	>19.5	<100	>180	>40	<75
1 mo to 1 yr	<36	>38.5	<6	>17.5	<90	>180	>34	<100
2-5 yrs	<36	>38.5	<6	>15.5	NA	>140	>22	<94
6-12 yrs	<36	>38.5	<4.5	>13.5	NA	>130	>18	<104
13 to <18 yrs	<36	>38.5	<4.5	>11	NA	>110	>14	<117

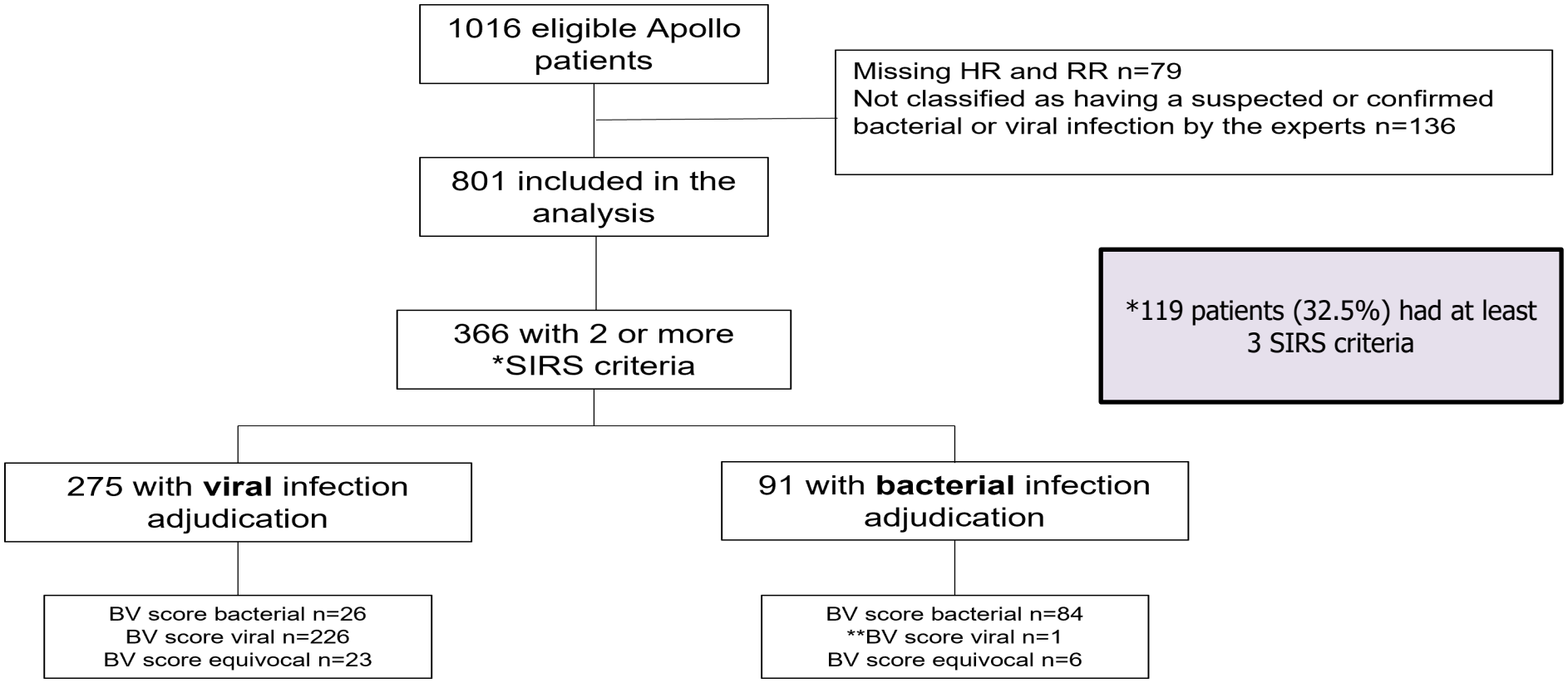
SIRS criteria for adults:

Box 1. SIRS (Systemic Inflammatory Response Syndrome)

Two or more of:
- Temperature >38°C or <36°C
- Heart rate >90/min
- Respiratory rate >20/min or $PaCO_2$ <32 mm Hg (4.3 kPa)
- White blood cell count >12 000/mm³ or <4000/mm³ or >10% immature bands

From Bone et al.[9]

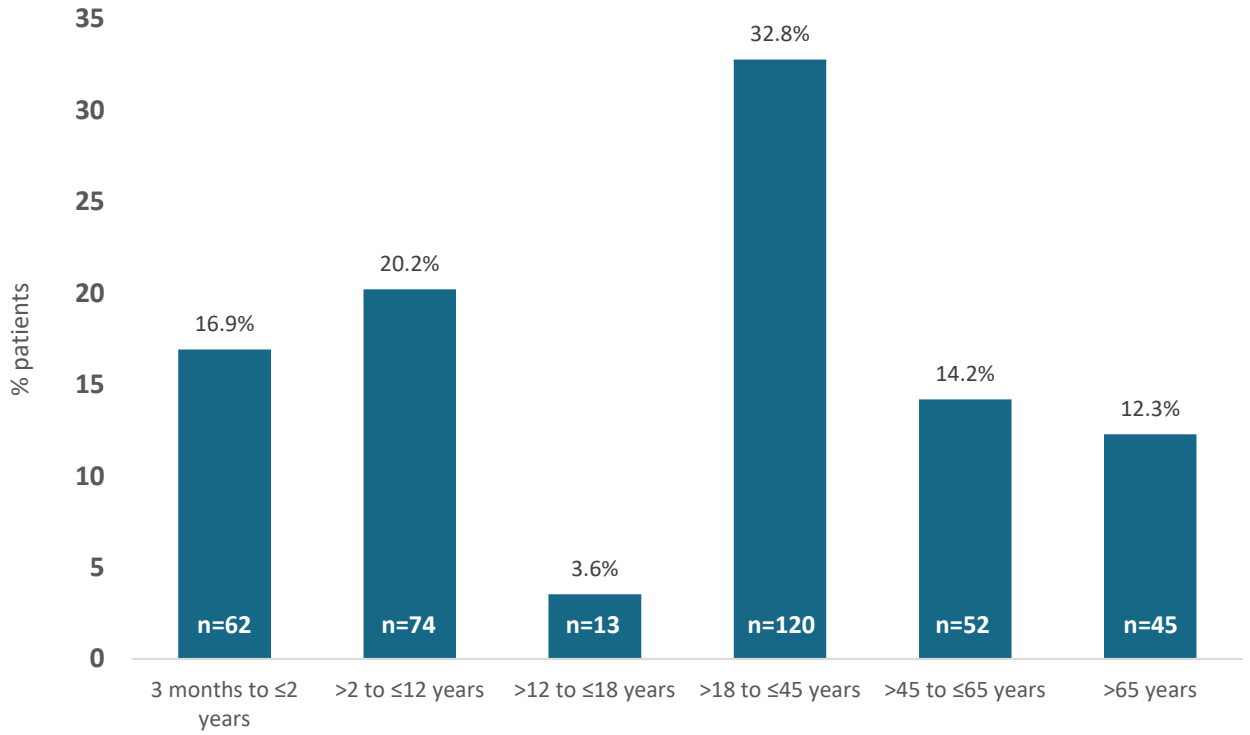
Sub-analysis: Results – Patient Flow



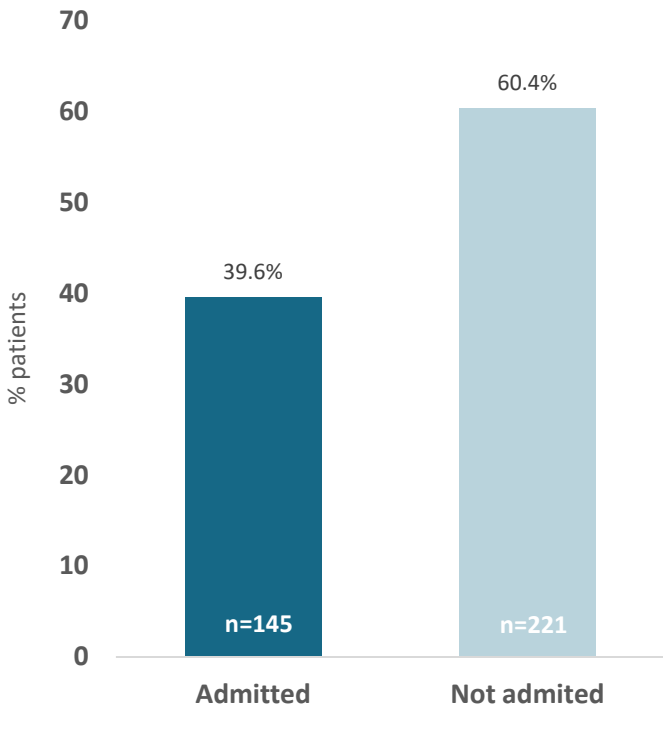
**This was a 9-year-old child presenting within 2 days of fever with a sore throat and pharyngeal erythema; rapid strep A test was negative, antibiotic was prescribed, and the child was discharged.

HR = heart rate; RR = respiratory rate

Sub-analysis: Results – Patient Characteristics



Median age of children was 2.4 years (IQR: 1.4-5.4); adults was 41.8 years (IQR: 29.2-61)



Median duration of hospitalization was 4 days (IQR: 3-6)

Sub-analysis: Results – Clinical Syndromes

URTI discharge diagnoses included:

Acute Otitis Media; Tonsillitis; Upper Respiratory Infections; Peritonsillar Abscess; Pharyngitis; Sinusitis; Aphthous Stomatitis; Coronavirus (Covid19) Infection; Scarlet Fever; Flu/Influenza; Flu Like Illness/Symptoms; Herpangina; Laryngitis; Respiratory Viral Syndrome; Tracheitis

LRTI discharge diagnoses included:

Bronchiolitis; Acute Bronchitis; Acute Respiratory Failure; Bronchopneumonia; COPD Exacerbation; Community Acquired Pneumonia; Lobar Pneumonia; Pneumonia

UTI discharge diagnoses included:

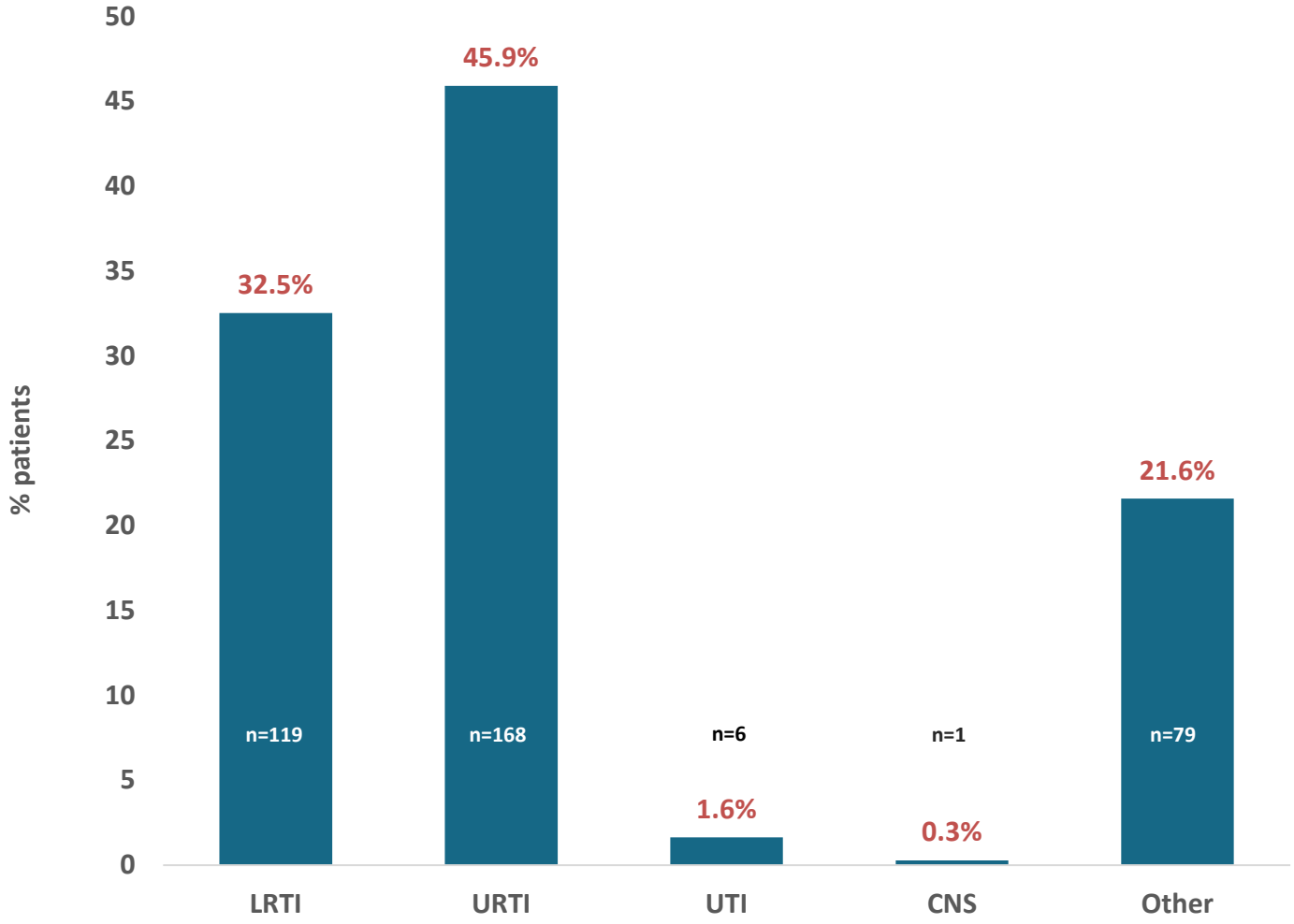
Acute Cystitis; Pyelonephritis; Urinary Tract Infection

CNS discharge diagnoses included:

Meningitis

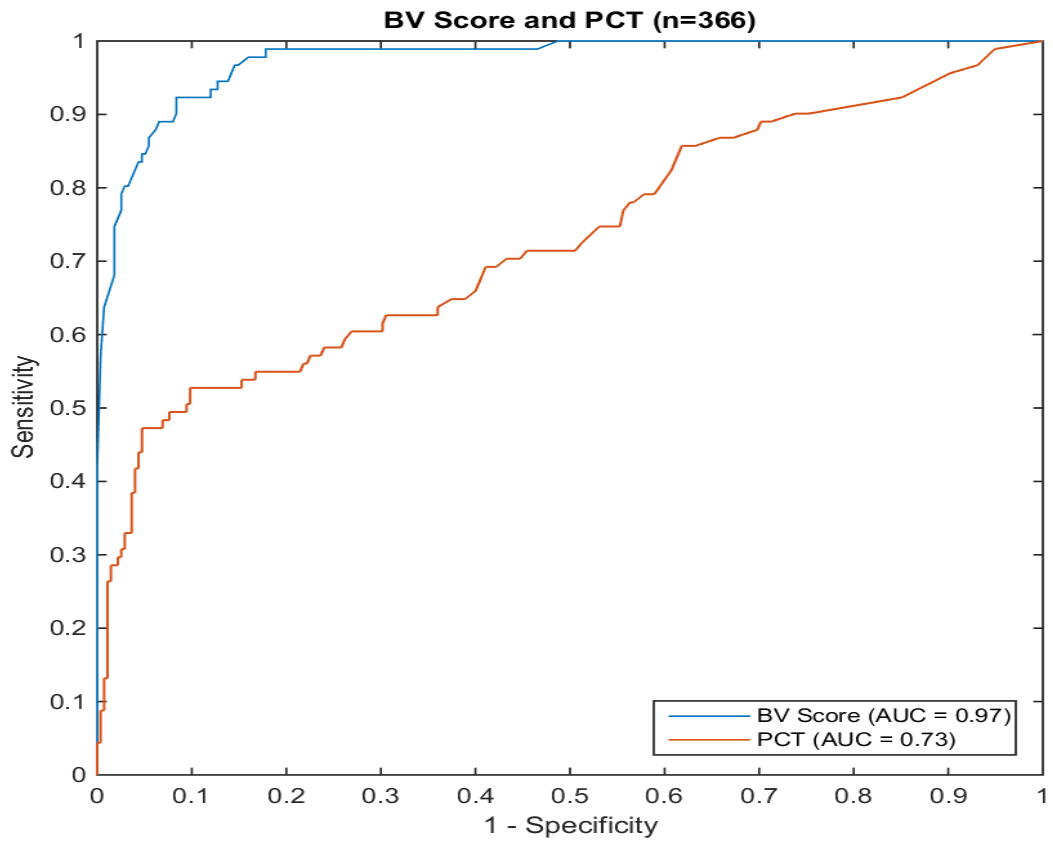
The 'Other' category included:

Abdominal Pain; Abscess; Appendicitis; Asthma; Cellulitis; Febrile Convulsions; Fever; Gastroenteritis; Headache; Unspecified viral infection



Patients could be included in more than one clinical syndrome except for Other

Sub-analysis: MeMed BV performance



hm)

-70.5)

-77.2)

-87.8)

MeMed BV Score Cut-offs:

- < 35 - viral infection
- 35 ≤ score ≤ 65 – equiv. (7.9%)
- > 65 - bacterial infection

Procalcitonin Cut-offs

Sepsis algorithm:

- ≥0.5ng/mL - bacterial infection
- <0.5ng/mL - viral infection

LRTI algorithm:

- ≥0.25ng/mL - bacterial infection
- <0.25ng/mL - viral infection

Apollo Sepsis sub-analysis - Conclusions

- MeMed BV accurately distinguished viral from bacterial infection in sepsis patients.
- This new triage tool has potential to help with timely identification of bacterial infection, enabling prompt treatment.
- MeMed BV accurately rules out bacterial infection, allowing antibiotic overuse to be minimized.

MeMed

Thank you