

MeMed BV Distinguishes between Viral and Bacterial Infection in Sepsis Patients

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Disclaimer

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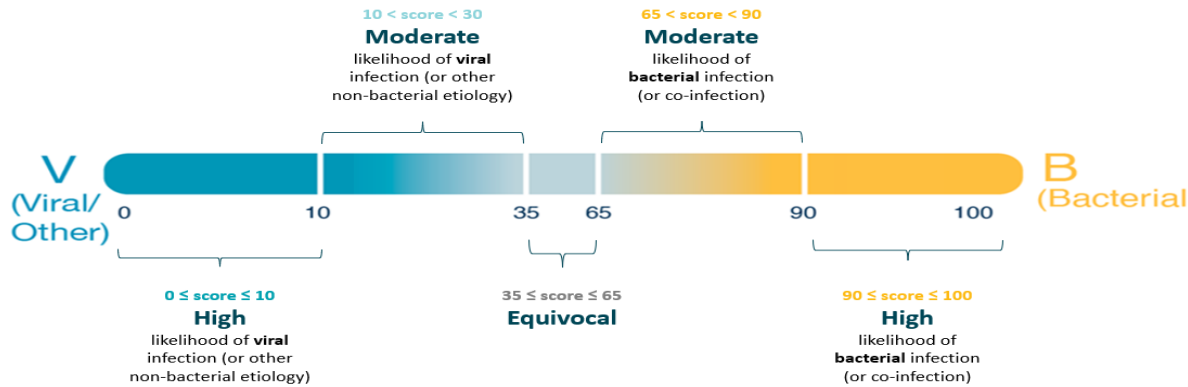
Background - Sepsis

- Sepsis is a life-threatening organ dysfunction syndrome caused by the body's response to infection
- Early identification and appropriate management improves outcomes¹
- Standard of care for sepsis is immediate use of broad-spectrum antibiotics
- In case of viral sepsis, this inevitably leads to:
 - unnecessary antimicrobial use
 - unwarranted side effects on the host microbiome
 - excess healthcare costs
 - antimicrobial resistance²

1. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive Care Med.* 2021;47(11):1181-1247. doi:10.1007/s00134-021-06506-y
2. Lin GL, McGinley JP, Drysdale SB, Pollard AJ. Epidemiology and Immune Pathogenesis of Viral Sepsis. *Front Immunol.* 2018;9:2147. Published 2018 Sep 27. doi:10.3389/fimmu.2018.02147

Background – MeMed BV

- A test for differentiating between viral and bacterial infection
- Based on computational integration of the circulating levels of three proteins:
 - TNF-related apoptosis-induced ligand (TRAIL)
 - Interferon gamma-induced protein-10 (IP-10)
 - C-reactive protein (CRP)
- Generates a score (0-100) indicative of bacterial versus viral infection:
 - Scores < 35 indicate viral (or other non-bacterial) infection
 - $35 \leq \text{scores} \leq 65$ are equivocal (valid but non-informative result)
 - Scores > 65 indicate bacterial infection (or co-infection)



The Apollo Study

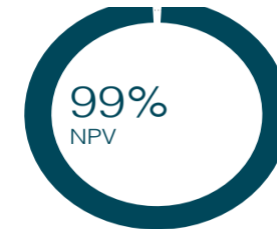
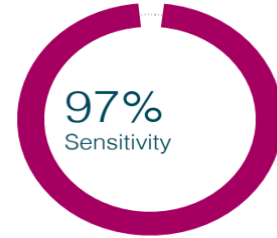
Apollo study

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



Sub-analysis of Sepsis Patients in the Apollo Study

Sub-study objective:

- To evaluate MeMed BV's ability to differentiate viral from bacterial infection in sepsis patients

Sepsis definition:

- Two or more SIRS criteria
- Suspected viral or bacterial infection classified by expert adjudication*

*Viral or bacterial classification required at least 2/3 experts to assign the same etiology label with confidence $\geq 90\%$ or all 3 assign with confidence $\geq 70\%$

SIRS Criteria

SIRS criteria for children:

Pediatric SIRS Criteria (≥1 of the criteria from Column 1 <u>AND</u> Column 2)								Cardiovascular Dysfunction
Age Group	Column 1 (≥1 of the below criteria)			Column 2 (≥1 of the below criteria)			Respiratory Rate ² (Breaths/Min)	Systolic Blood Pressure (mmHg)
	Core Temperature (°C)		Leukocyte Count (Leukocytes ×10 ³ /mm) ³	Heart Rate (Beats/Min) ¹				
	Hypothermia	Hyperthermia	Leukopenia	Leukocytosis	Bradycardia	Tachycardia		
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

*Mathias B, Mira JC, Larson SD. Pediatric sepsis. *Curr Opin Pediatr.* 2016;28(3):380-387. doi:10.1097/MOP.0000000000000337

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 PaCO₂ <32 mm Hg (4.3 kPa)

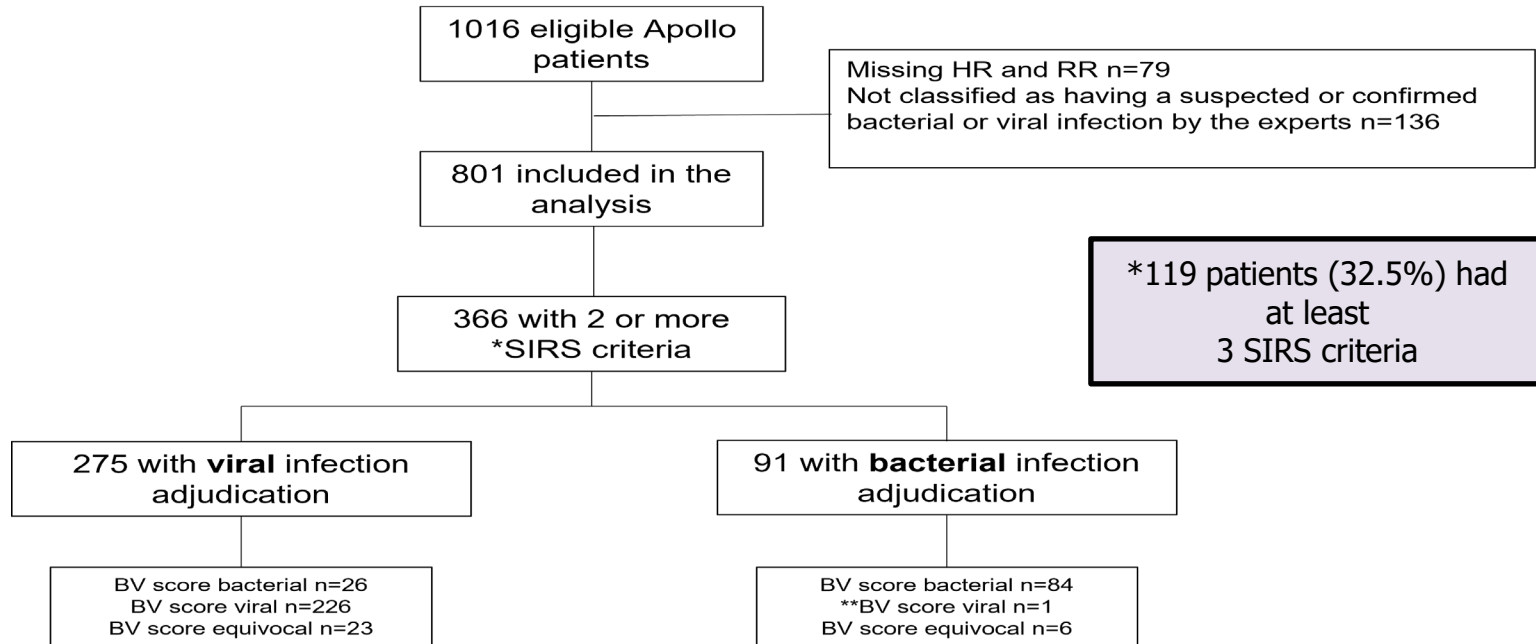
White blood cell count >12 000/mm³ or <4000/mm³
or >10% immature bands

From Bone et al.⁹

*Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA.* 2016;315(8):801-810. doi:10.1001/jama.2016.0287

RESULTS

Patient Flow

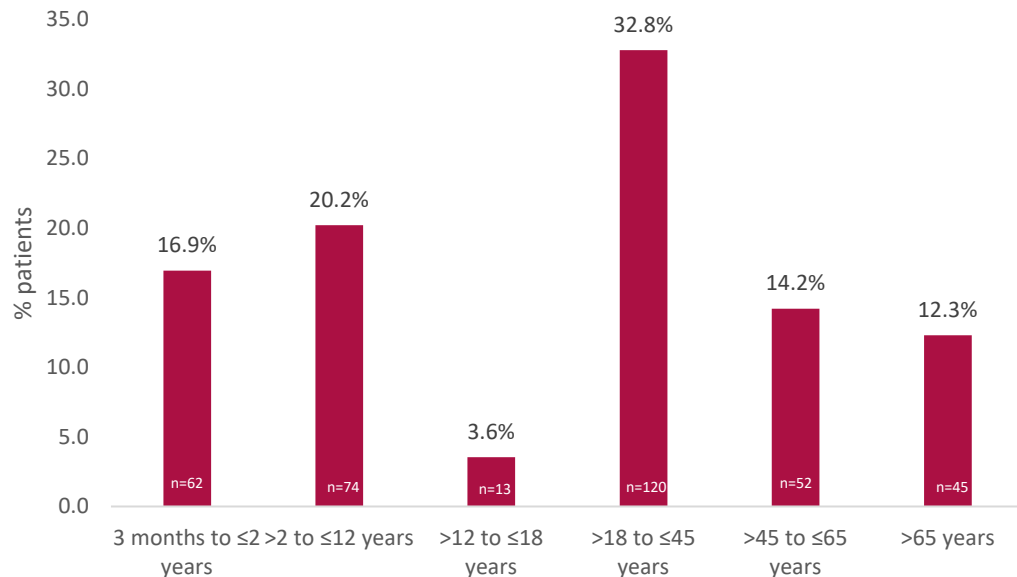


**This was a 9-year-old child presenting within 2 days of fever with a sore throat and pharyngeal erythema; rapid strep A test was negative, antibiotic was prescribed, and the child was discharged.

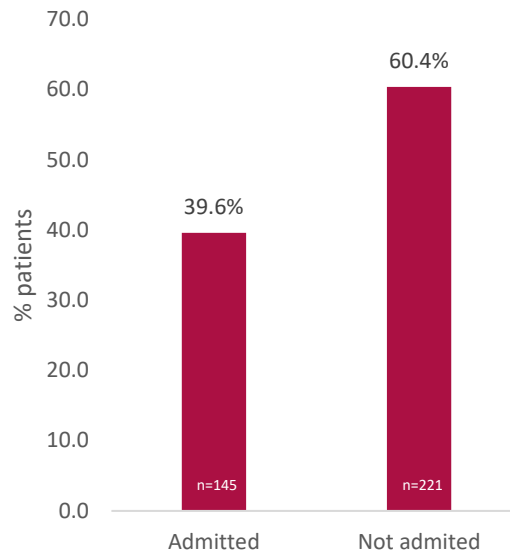
HR = heart rate; RR = respiratory rate

RESULTS

Patient Characteristics (n = 366)



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)

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:

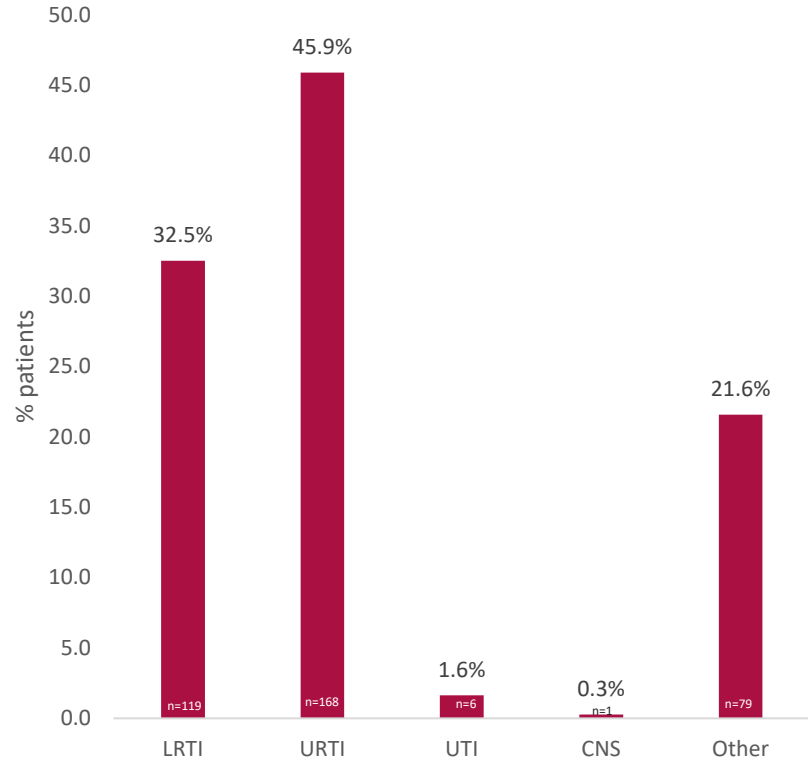
Acute Cystitis; Pyelonephritis; Urinary Tract Infection

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

RESULTS

	MeMed BV
Sensitivity	98.8% (95%CI: 93.6-100)
Specificity	89.7% (95%CI: 85.3-93.2)
Negative Predictive Value	99.6% (95%CI: 97.0-99.9)

RESULTS

BV Score Outperforms Procalcitonin

	MeMed BV	PCT (Sepsis algorithm)	PCT (LRTI algorithm)
Sensitivity	98.8% (95%CI: 93.6-100)	52.8% (95%CI: 42.0-63.3)	60.4% (95%CI: 49.6-70.5)
Specificity	89.7% (95%CI: 85.3-93.2)	86.2% (95%CI: 81.5-90.0)	72.0% (95%CI: 66.3-77.2)
Negative Predictive Value	99.6% (95%CI: 97.0-99.9)	84.6% (95%CI: 81.5-87.3)	84.6% (95%CI: 80.9-87.8)

MeMed BV Score Cut-offs

- < 35 - viral infection
- $35 \leq \text{scores} \leq 65$ – equivocal (7.9%)
- > 65 - bacterial infection

Procalcitonin Cut-offs

Sepsis algorithm:

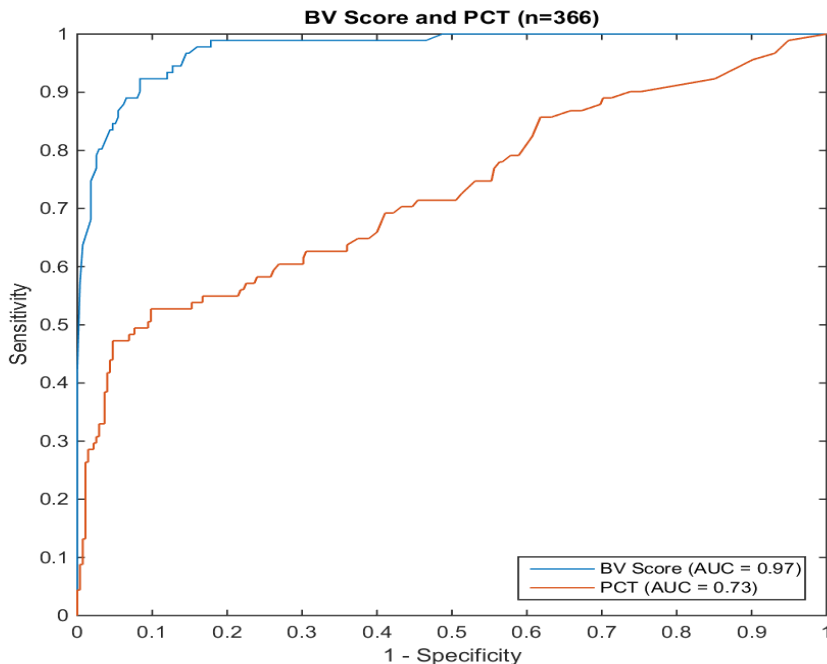
- ≥ 0.5 ng/mL - bacterial infection
- <0.5 ng/mL - viral infection

LRTI algorithm:

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

RESULTS

BV Score Outperforms Procalcitonin



Receiver operating characteristic-area under the curve (ROC-AUC)

CONCLUSION

- 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

THANK YOU