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## **Use of Clinical Criteria for Prediction of Invasive Bacterial Infection in Febrile Infants: Evaluation of the PROS Criteria**

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# Use of Clinical Criteria for Prediction of Invasive Bacterial Infection in Febrile Infants: Evaluation of the PROS Criteria

Yankova LC, Neuman MI, Wang ME, DePorre AG, Desai S, Sartori LF, Marble RD, Nigrovic LE, Leazer RC, Pruitt CM, Woll C, Rooholamini SN, Balamuth F, Aronson PL; for the Febrile Young Infant Research Collaborative



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Mentor: Paul Aronson

# Disclosure

## Lyubina Yankova

Has documented no financial relationships to disclose or Conflicts of Interest (COIs) to resolve.

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# Unapproved or Off Label

**Lyubina Yankova** has documented this presentation ***will not*** involve discussion of unapproved or off-label, experimental or investigational use.



# Background

- Should a primary care doctor obtain lab testing or refer a febrile infant to the ED?
- 2004 AAP Pediatric Research in Office Settings (PROS) network study
  - 3 clinical criteria:
    - Age <25 days
    - Maximum temperature  $\geq 38.6^{\circ}\text{C}$
    - Ill-appearance
  - Sensitivity 93.6% for invasive bacterial infection (IBI)
    - Need for external validation



# Objective

To evaluate the sensitivity of the PROS criteria for IBI in febrile infants  $\leq 60$  days old



# Methods

## Study Design:

- Secondary analysis of retrospective cohort study
- Setting: 11 EDs between 7/1/2011 – 6/30/2016





# Methods

## Study population:

- Identified by query of each site's microbiology laboratory or EHR system

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"><li>- Age <math>\leq 60</math> days</li><li>- Temp of <math>\geq 38^{\circ}\text{C}</math> at home or ED triage</li><li>- Blood or cerebrospinal fluid (CSF) pathogen</li></ul>	<ul style="list-style-type: none"><li>- Clinically apparent source of infection</li></ul>



# Methods

## Study Definitions:

- Ill-appearing: toxic, limp, unresponsive, gray, cyanotic, apneic, weak cry, poorly perfused, grunting, listless, lethargic, or irritable
- IBI: pathogen identified in blood and/or CSF AND treated as bacteremia or bacterial meningitis
- Bacterial Meningitis:
  - Pathogen in CSF culture
  - CSF pleocytosis with bacteremia if pretreated



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# Methods

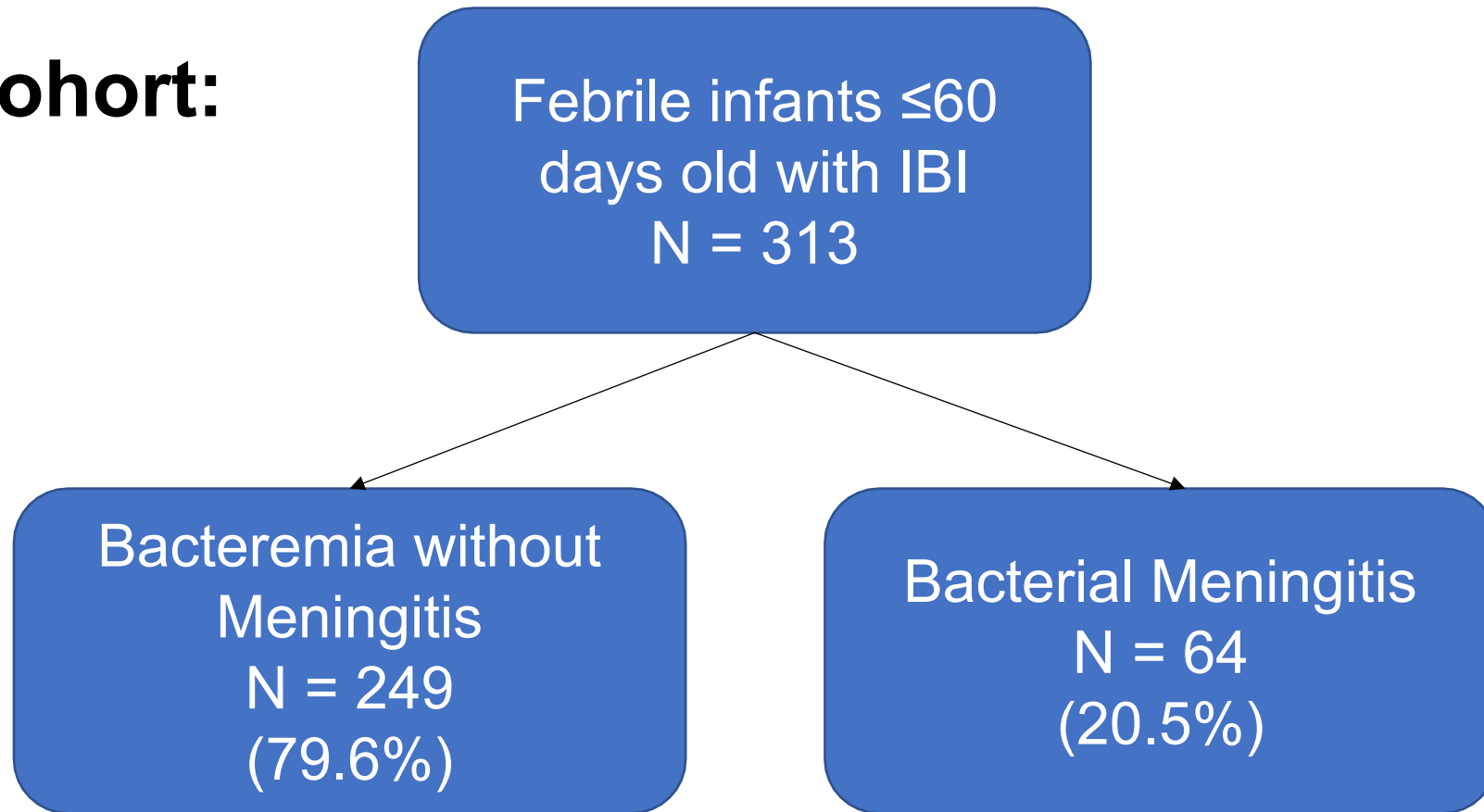
## Outcome Measure:

- Sensitivity of PROS criteria
  - Age <25 days
  - Maximum temperature  $\geq 38.6^{\circ}\text{C}$
  - Ill-appearance



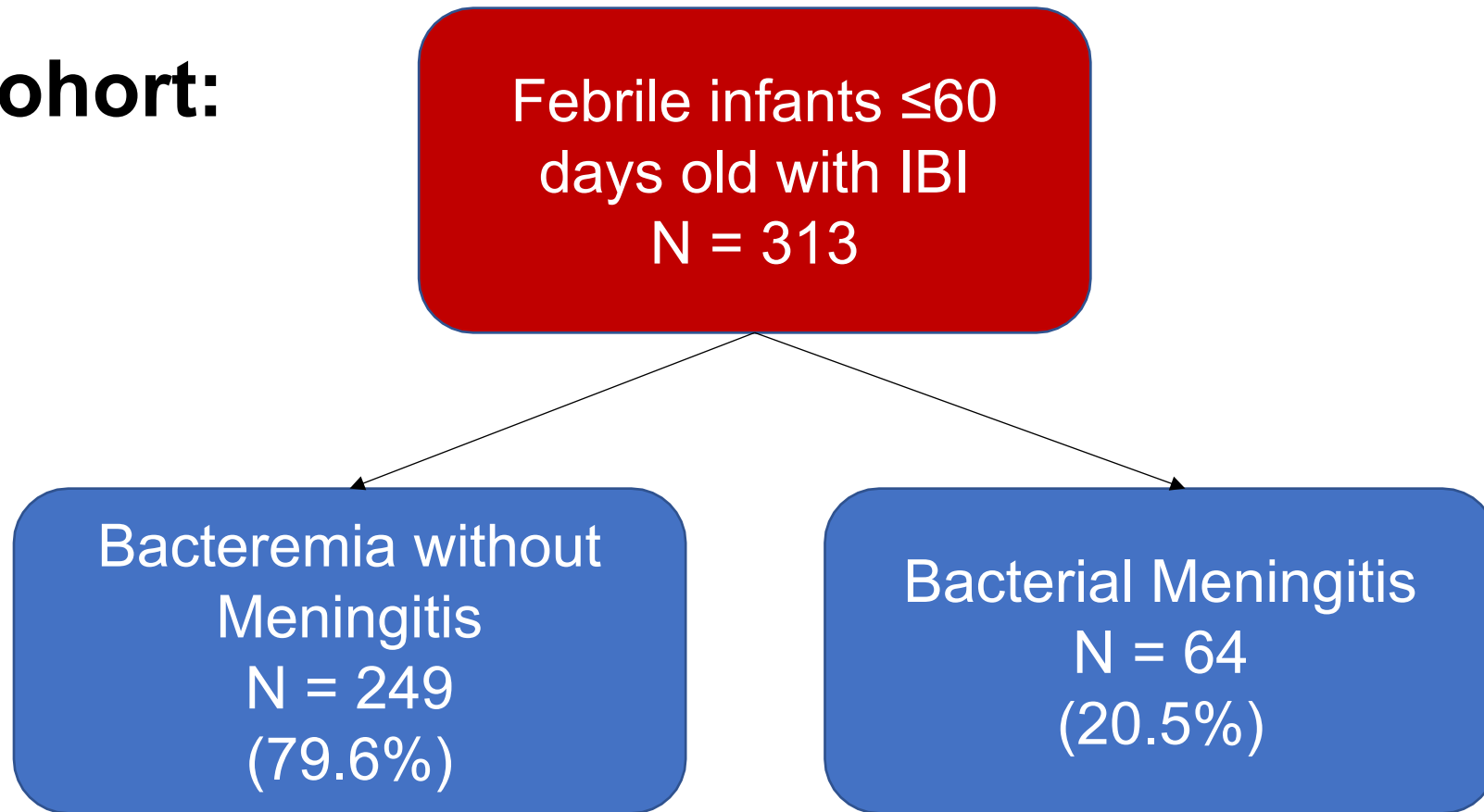
# Results

## Study Cohort:



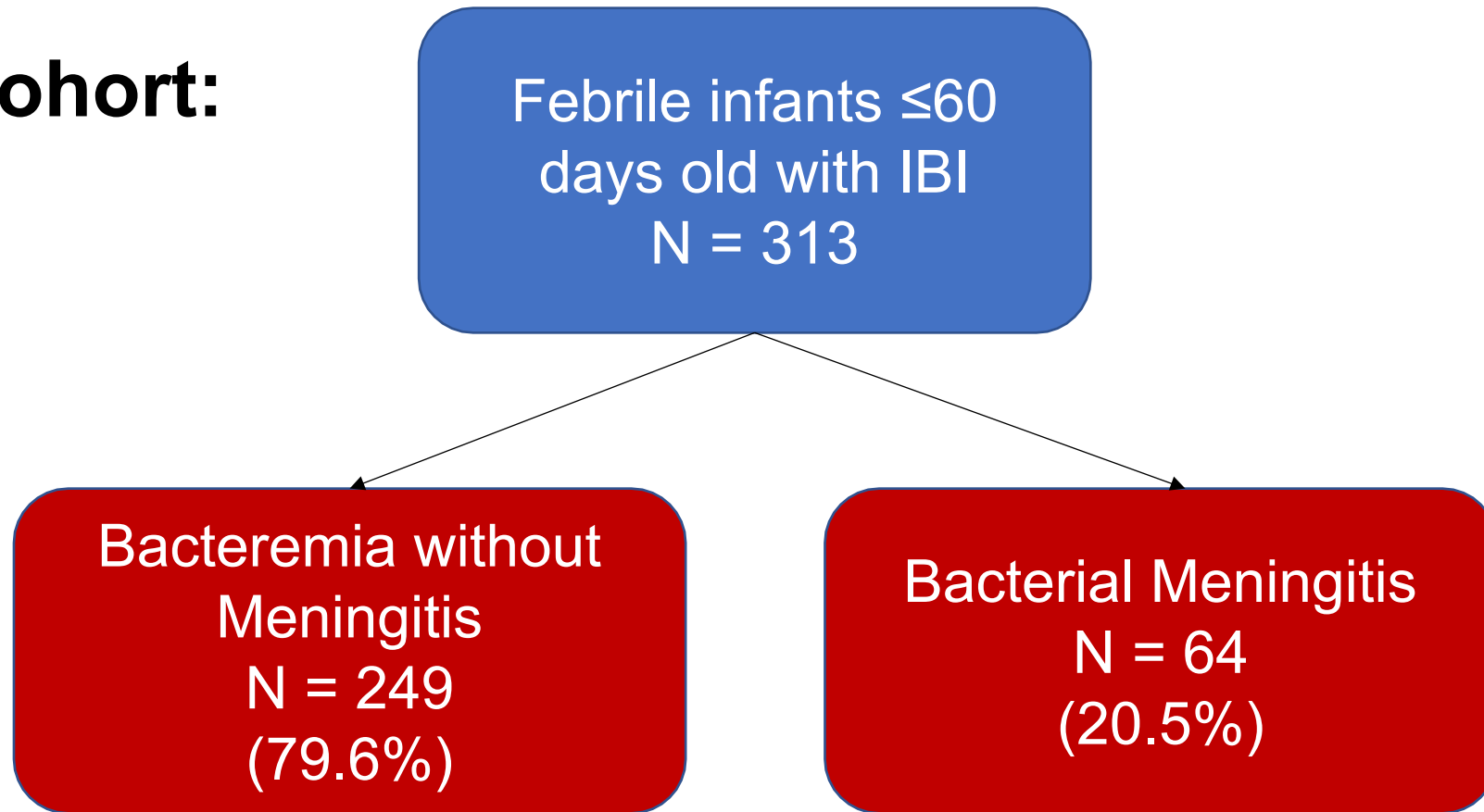
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# Results

## Study Cohort:

- Age Group:
  - <25 days: 130 (41.5%)
  - 25-60 days: 183 (58.5%)
- Clinical Appearance
  - Ill-appearing: 87 (27.8%)
  - Non-ill-appearing: 226 (72.2%)



# Results

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# Results

	<b>IBI Overall</b>	<b>Bacteremia Without Meningitis</b>	<b>Bacterial Meningitis</b>
<b>Sensitivity (95% CI)</b>	<b>87.9% (83.7-91.3)</b>	<b>87.1% (82.3-91.0)</b>	<b>90.6% (80.7-96.5)</b>



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# Results

## Missed IBI:

- 38 infants with IBI (12.1%) misclassified as low-risk
- 6 of these infants had bacterial meningitis



# Results

Age, d	Maximum temperature (°C)	Ill- Appearing Y/N	Peripheral WBC (cells/ $\mu$ L)	CSF WBC (cells/ $\mu$ L)	Blood culture	CSF culture
25	38.4	N	9,670	91	K. pneumoniae	No growth*
25	38.0	N	4,600	820	S. gallolyticus	S. gallolyticus
26	38.3	N	11,450	Not performed	No growth	E. coli
36	38.2	N	5,630	3	GBS	GBS
39	38.3	N	14,800	102	E. coli	No growth*
54	38.3	N	4,300	432	GBS	GBS





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\*CSF culture obtained >11 hours after antimicrobial administration; treated as bacterial meningitis



# Limitations

- Outpatient criteria applied to ED cohort
- Retrospective determination of “ill-appearance”
- Cannot calculate specificity or predictive values



# Conclusions

- Sensitivity of PROS criteria for identifying febrile infants at low-risk for IBI was lower in our study (87.9%) than in original study (93.6%)
- Caution in applying PROS criteria



# Future Directions

- Derive and validate clinical criteria for use when laboratory testing unavailable
- Evaluate outcomes of infants managed without laboratory tests



# Acknowledgements

Mentor: Paul Aronson

Co-Authors: Mark Neuman, Marie Wang, Adrienne DePorre, Sanyukta Desai, Lisa Sartori, Richard Marble, Lise Nigrovic, Rianna Leazer, Christopher Pruitt, Christopher Woll, Sahar Rooholamini, Frances Balamuth

The Febrile Young Infant Research Collaborative





# Questions?

