AI, ML, and Pediatric Sepsis

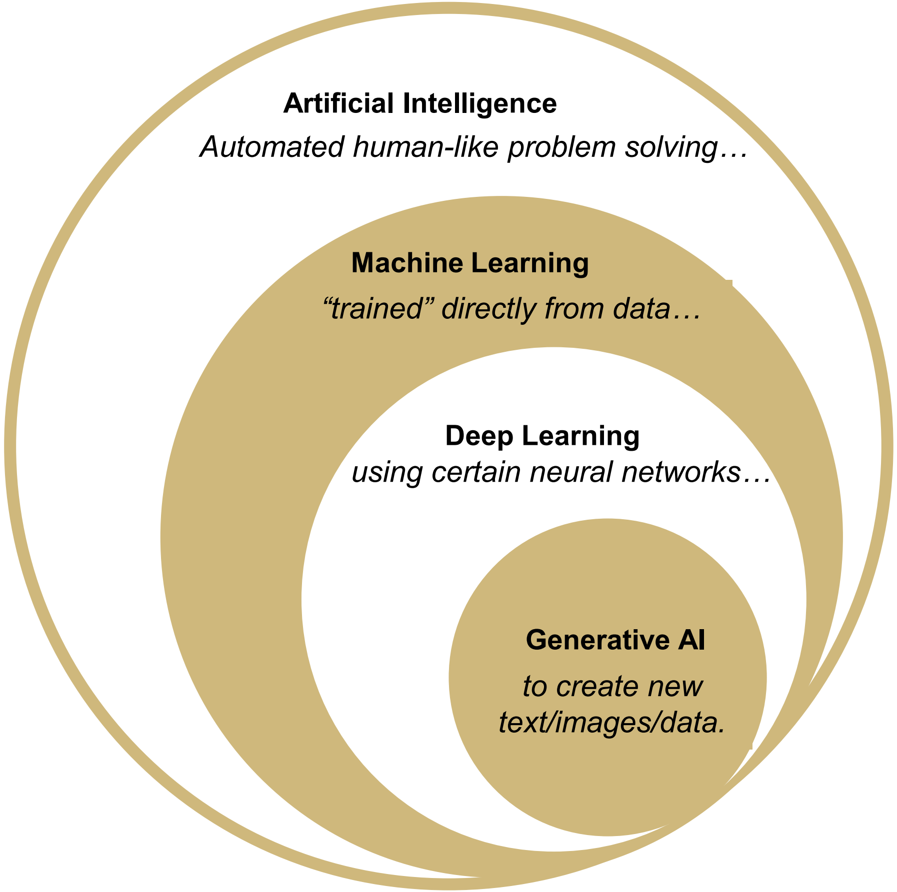
Tellen D. Bennett, MD, MS
Professor, Biomedical Informatics and Pediatrics
University of Colorado School of Medicine
PICU Attending Physician, Children's Hospital Colorado

tell.bennett@cuanschutz.edu

Department of Biomedical Informatics
SCHOOL OF MEDICINE
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

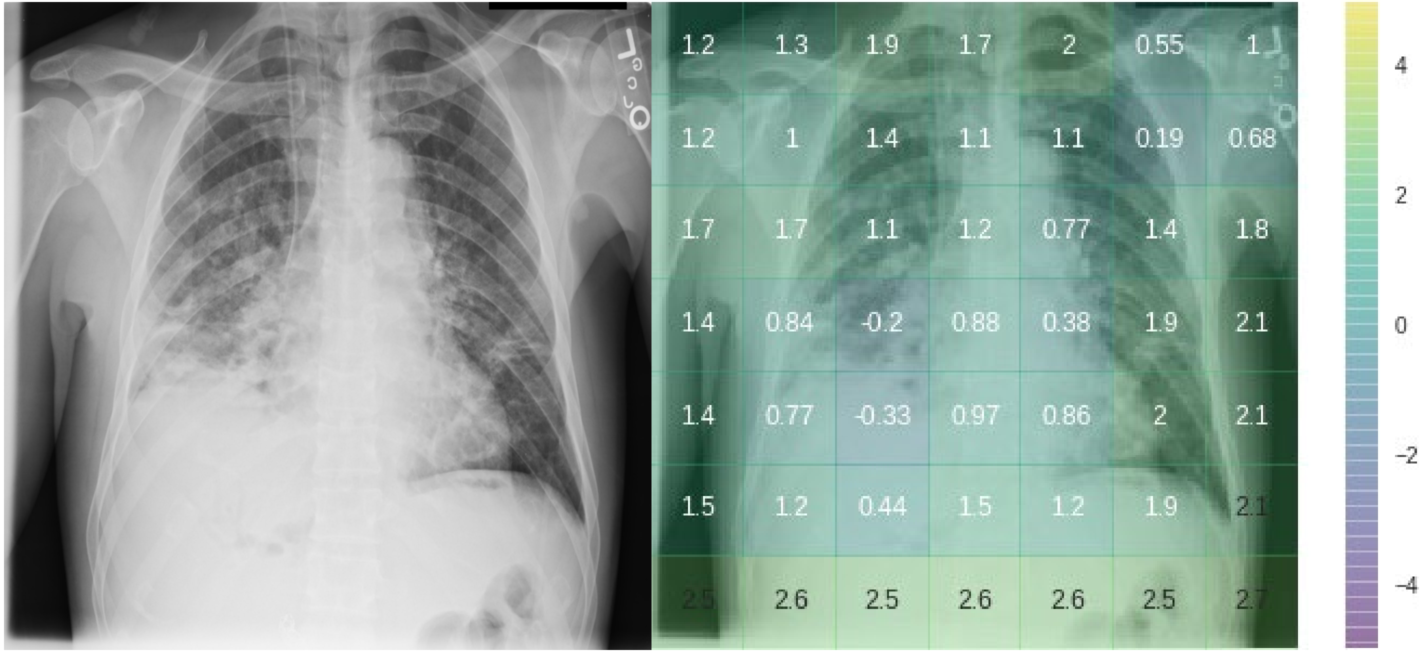
Children's Hospital Colorado

What is AI?



Artificial Intelligence
Automated human-like problem solving…
Machine Learning
"trained" directly from data…
Deep Learning
using certain neural networks…
Generative AI
to create new
text/images/data.

Sometimes, learning from data is not ideal

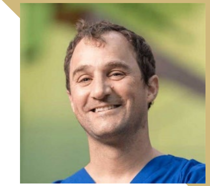


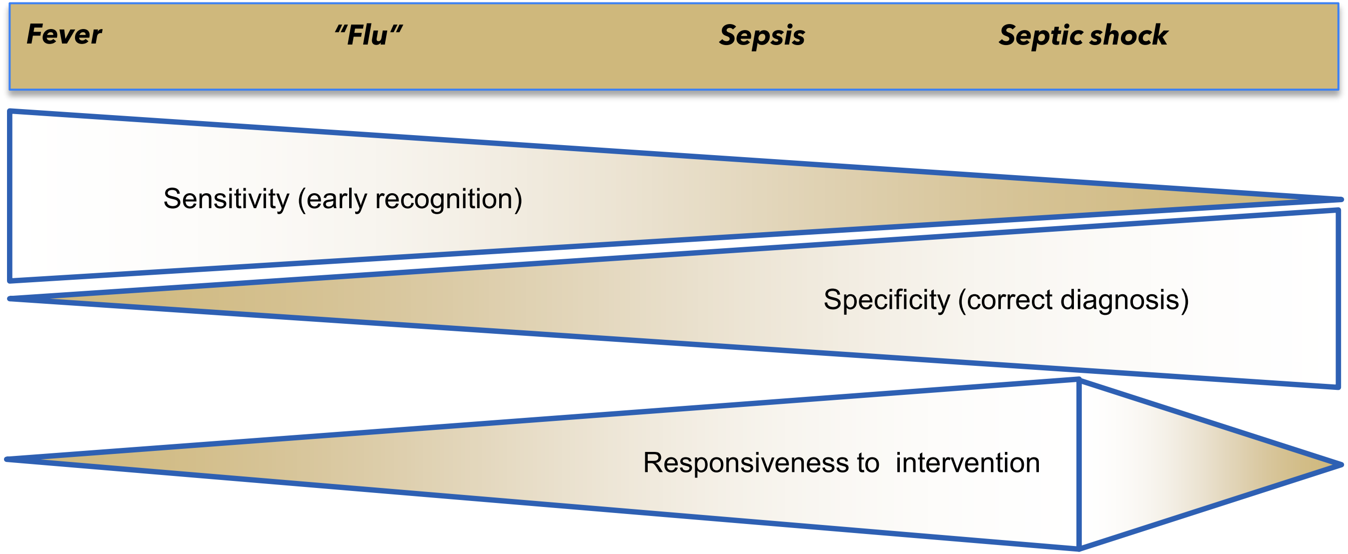
What are radiological deep learning models actually learning? John Zech (medium.com)

AI/ML: A Complete Story, Data to Patient Impact

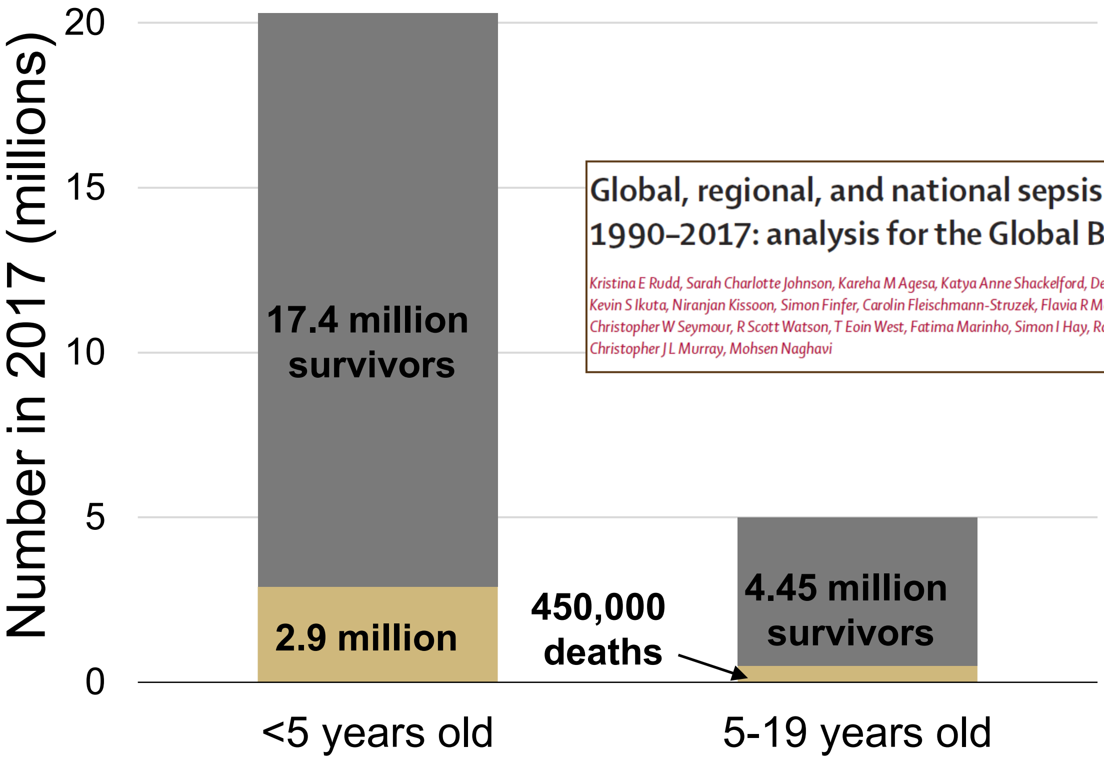
Pediatric Sepsis Definition Task Force, June 2019

Is this sepsis?





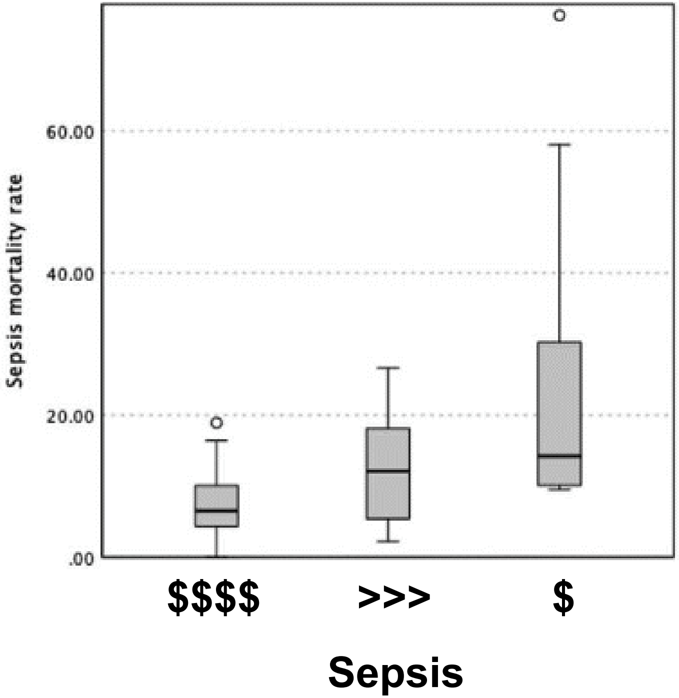
Pediatric Sepsis Burden

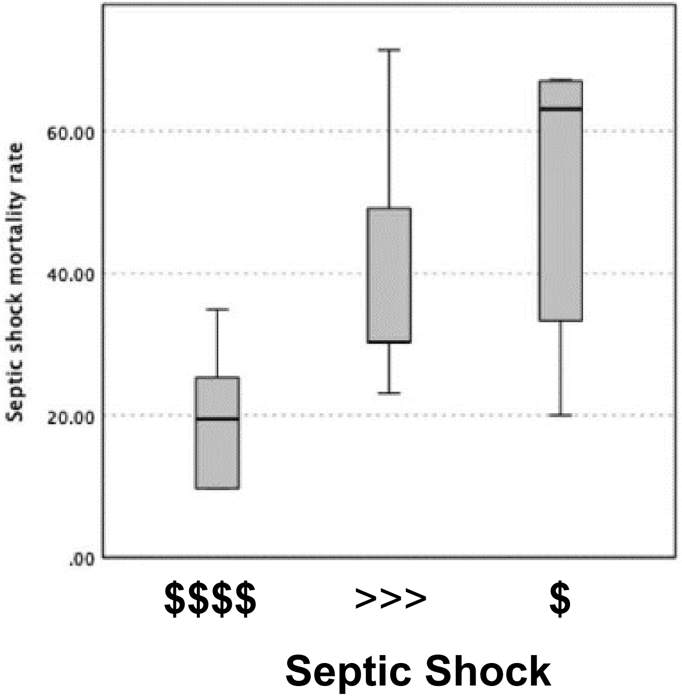


Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study

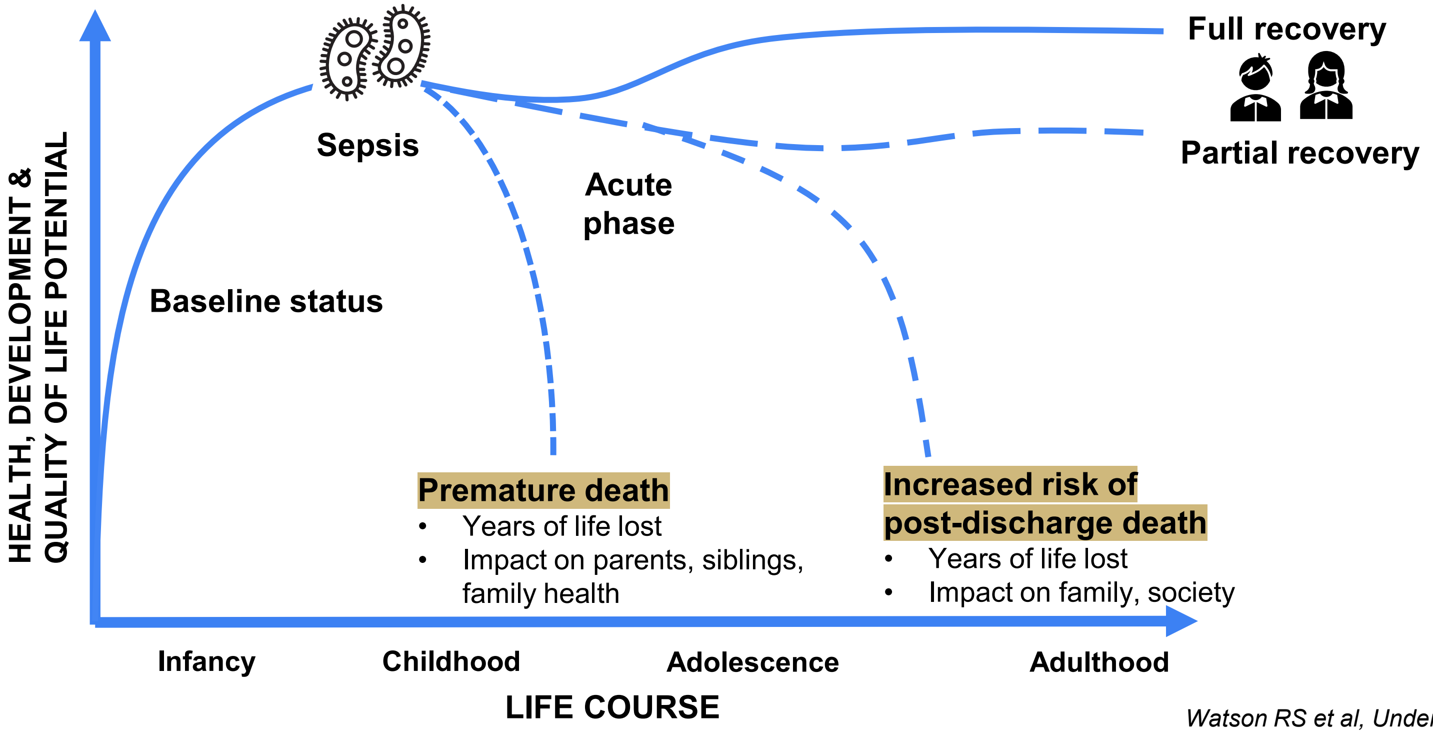
Kristina E Rudd, Sarah Charlotte Johnson, Kareha M Agesa, Katya Anne Shackelford, Derrick Tsoi, Daniel Rhodes Kievlan, Danny V Colombara, Kevin S Ikuta, Niranjan Kissoon, Simon Finfer, Carolin Fleischmann-Struzek, Flavia R Machado, Konrad K Reinhart, Kathryn Rowan, Christopher W Seymour, R Scott Watson, T Eoin West, Fatima Marinho, Simon I Hay, Rafael Lozano, Alan D Lopez, Derek C Angus, Christopher J L Murray, Mohsen Naghavi

Mortality by World Bank Income Class



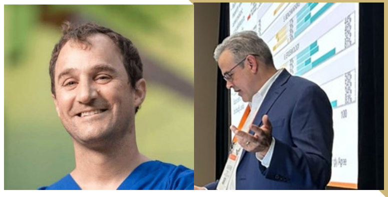


Long-term Impacts on Survivors



Watson RS et al, Under Review

Current Pediatric Criteria



International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics*

Brahm Goldstein, MD; Brett Giroir, MD; Adrienne Randolph, MD; and the Members of the International Consensus Conference on Pediatric Sepsis

- Not data-driven (“eminence-based”)
- Performed OK in some environments, poorly in others

By this definition, many patients in the ED or on the floor with non-life-threatening infection have “sepsis”

2016: New Adult Criteria

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

Box 3. New Terms and Definitions

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

- ADULTS ONLY
- Data-driven + consensus
- High resource countries only

Pediatric Sepsis Definition Task Force Timeline

2018

- SCCM support
- Panel formation

2019

- Salzburg Kick-Off

2020/21

- Systematic review
- International survey
- Successful NIH funding (Bennett, Sanchez-Pinto)

2022

- Other Manuscripts
- Data Curation

2023

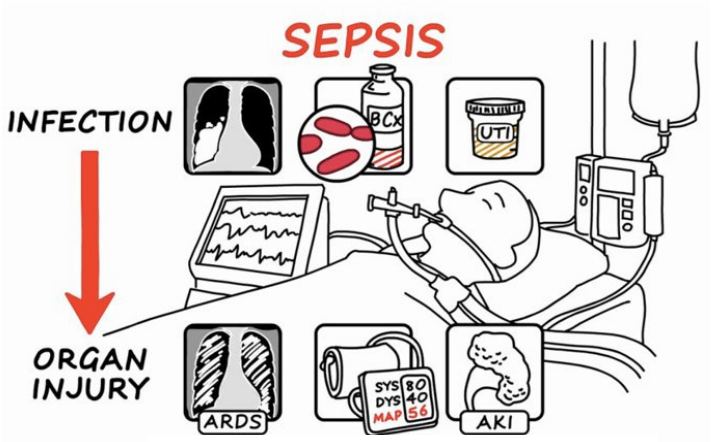
- Analyses
- Delphi process
- Consensus

2024: Dissemination

Conceptual Framework

Pediatric Sepsis =

"An infection with life-threatening organ dysfunction"



Source: JAMA Twitter feed, 2016

Conceptual Framework

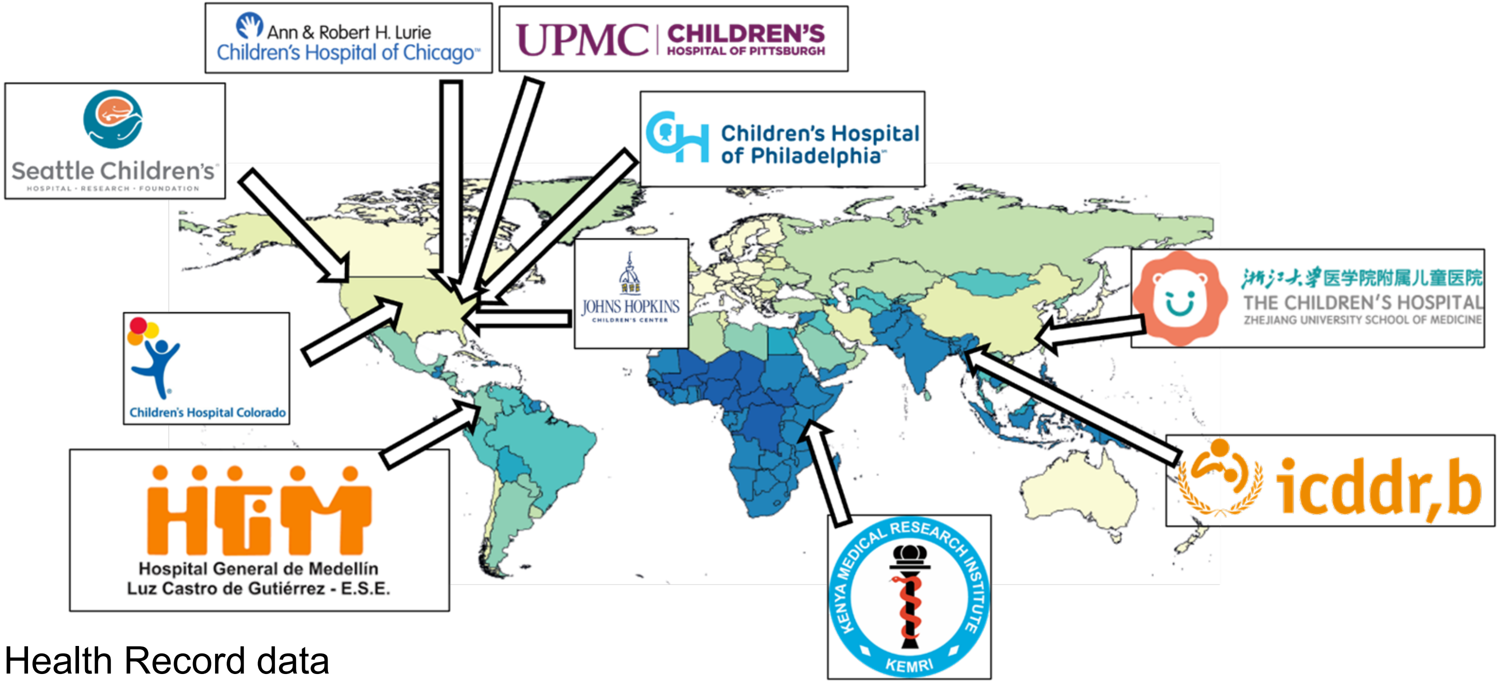
Suspected infection <=24 hours

"An infection with life-threatening organ dysfunction"

Primary outcome: in-hospital **mortality**

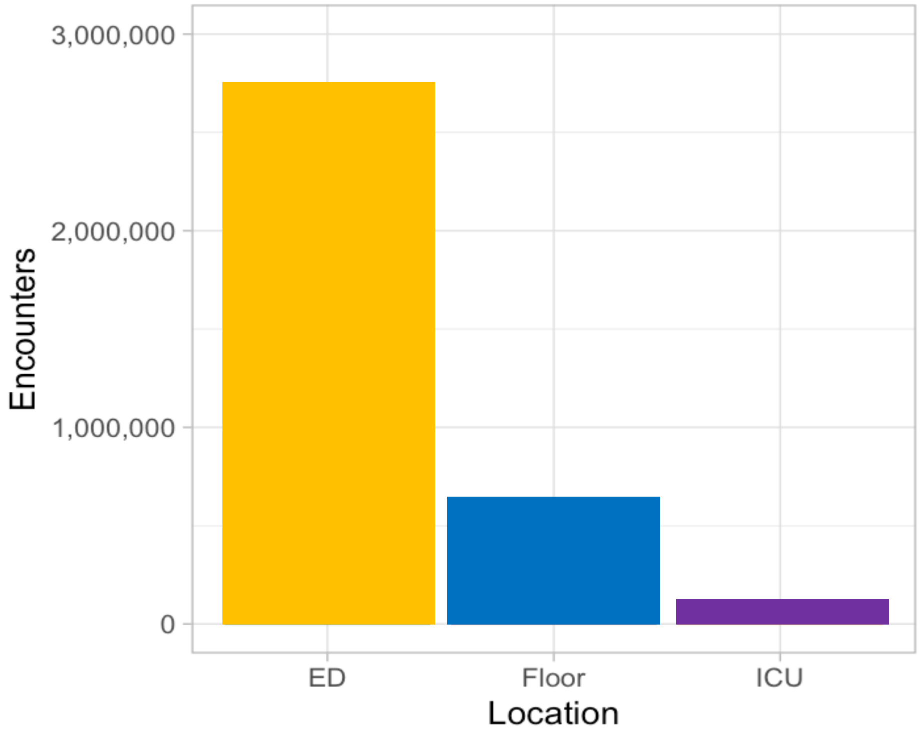
Identify the **best-performing organ dysfunction subcomponents** from existing scores, applicable to higher and lower resource settings

10 Study Sites: 6 Higher and 4 Lower Resource Settings

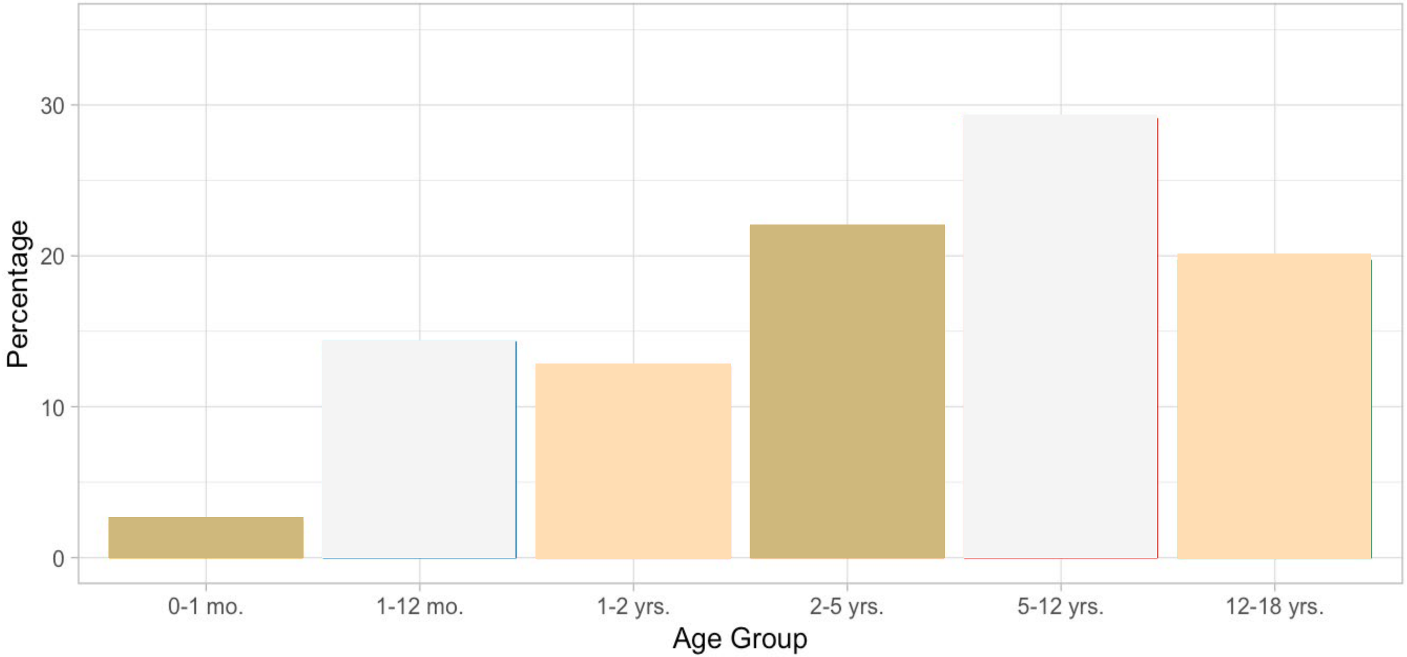


- Electronic Health Record data
- Date range 2010-2019

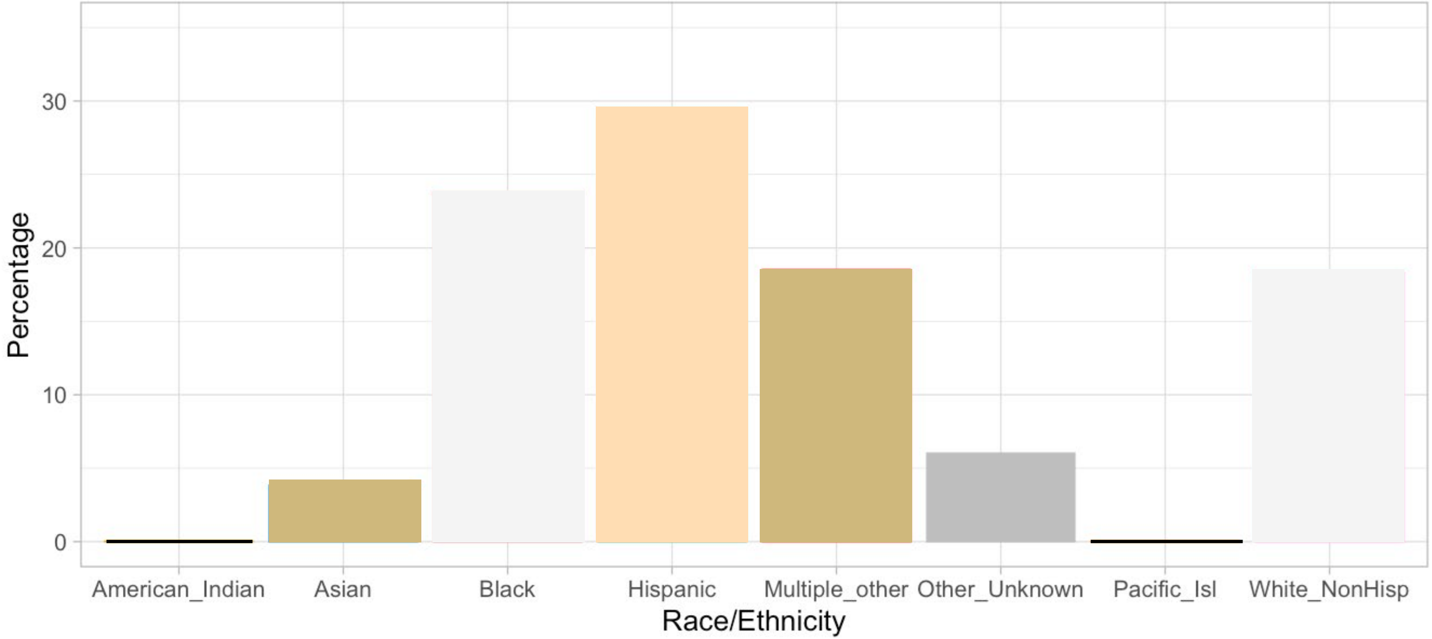
Cohort Size: >3.6 million Pediatric Hospital Encounters



Representative Population: Adequate Age Distribution

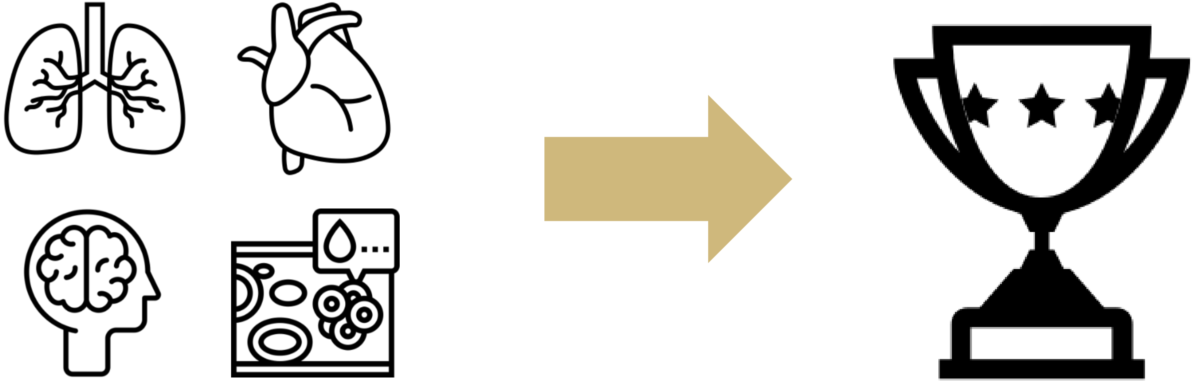


Representative Population: Diverse Race and Ethnicity



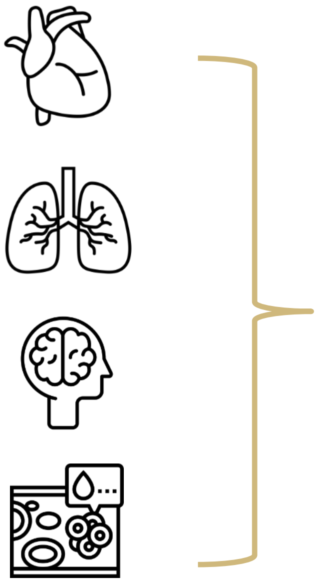
STEP 1 RESULTS:

Identify the best organ dysfunction subcomponents of existing scores

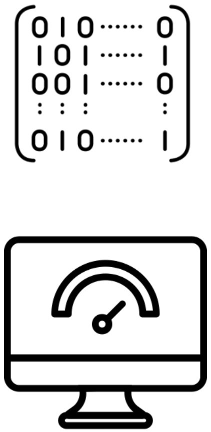


STEP 2 RESULTS: Sepsis Models Using Machine Learning

All-Stars



Machine Learning



Model 1: Eight Organs

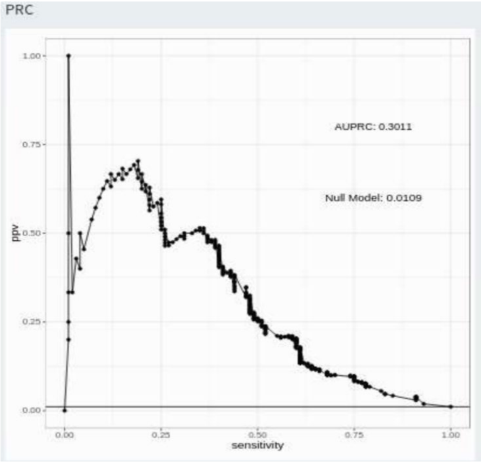
- Cardiovascular
- Respiratory
- Coagulation
- Neurologic
- Endocrine
- Renal
- Immuno
- Hepatic

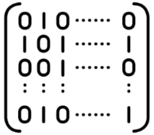
Model 2: Four Organs

- Cardiovascular
- Respiratory
- Coagulation
- Neurologic

STEP 3 RESULTS:

Translate the Best Sepsis Model to the Phoenix Sepsis Score

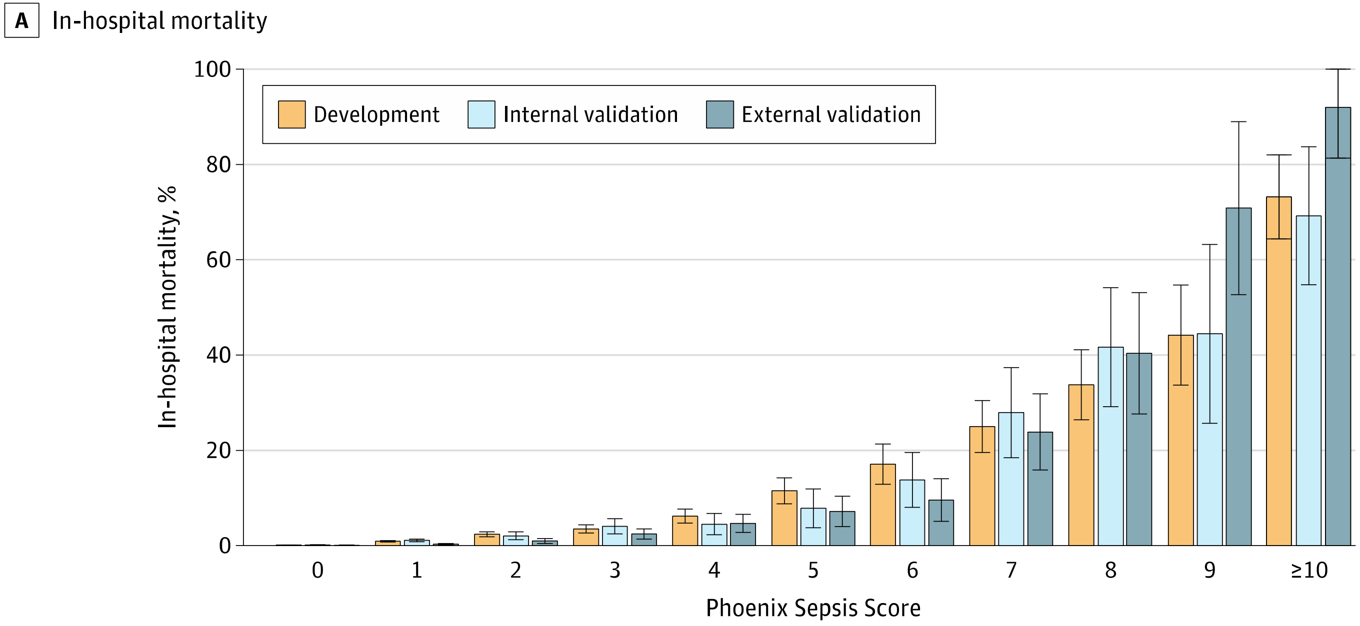




One integer, 0-13

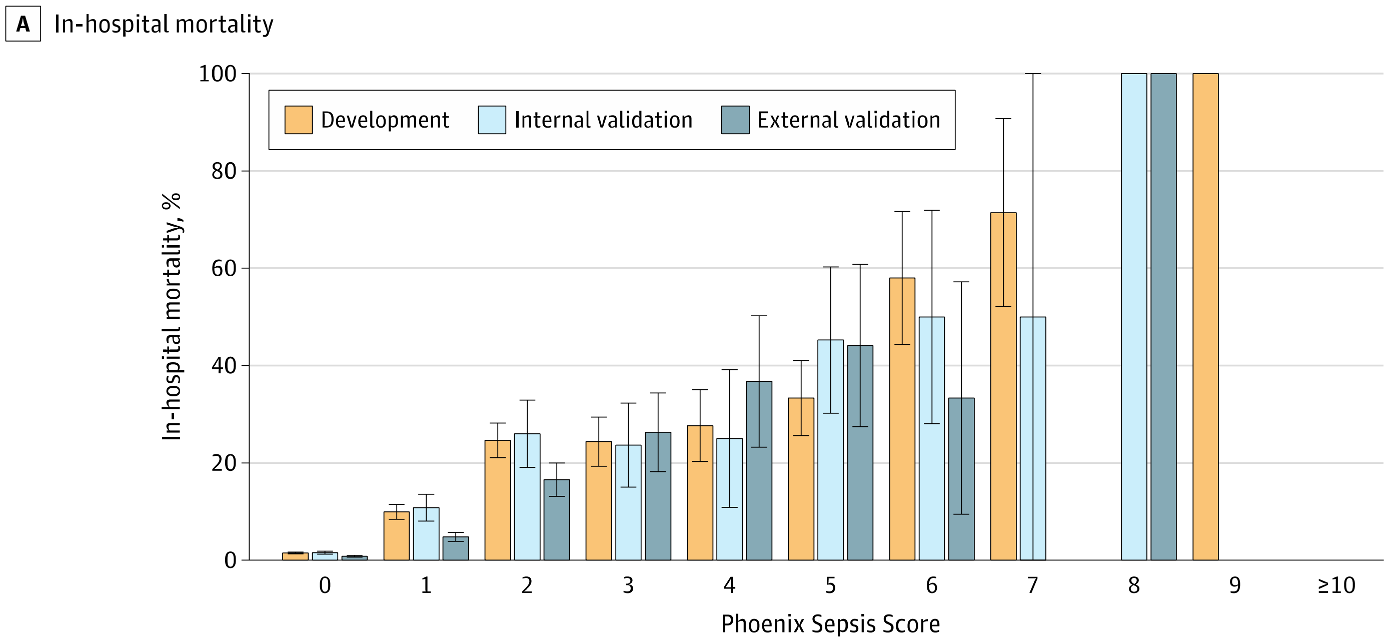
STEP 3 RESULTS:

Phoenix Sepsis Score has Good Calibration in <u>Higher</u> Resource Sites



STEP 3 RESULTS:

Phoenix Sepsis Score has Good Calibration in Lower Resource Sites



STEP 4 RESULTS:

Translation of Phoenix Sepsis Score to Phoenix Sepsis/Septic Shock Criteria Selecting Thresholds

One integer, 0-13

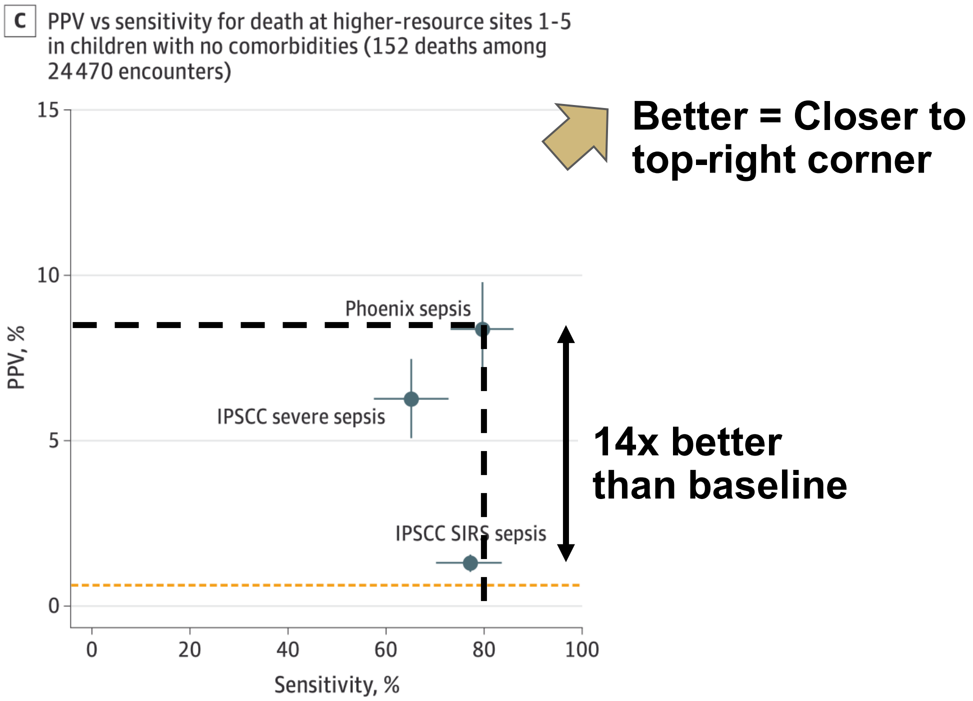
Task Force Delphi process:

- **Sepsis**: **≥ 2 points** on Phoenix Sepsis Score
- **Septic Shock**: Sepsis and **≥ 1 CV point**

STEP 4 RESULTS:

PPV and Sensitivity for Phoenix Sepsis Criteria Higher than for 2005 IPSCC Sepsis Criteria

Interpretation recap



Research

JAMA | Original Investigation

Development and Validation of the Phoenix Criteria for Pediatric Sepsis and Septic Shock

L. Nelson Sanchez-Pinto,* MD, MBI; Tellen D. Bennett,* MD, MS; Peter E. DeWitt, PhD; Seth Russell, MS;
Margaret N. Rebull, MA; Blake Martin, MD; Samuel Akech, MBChB, MMED; David J. Albers, PhD;
Elizabeth R. Alpern, MD, MSCE; Fran Balamuth, MD, PhD, MSCE; Melania Bembea, MD, MPH, PhD;
Mohammod Jobayer Chisti, MBBS, MMed, PhD; Idris Evans, MD, MSc; Christopher M. Horvat, MD, MHA;
Juan Camilo Jaramillo-Bustamante, MD; Niranjan Kissoon, MD; Kusum Menon, MD, MSc;
Halden F. Scott, MD, MSCS; Scott L. Weiss, MD; Matthew O. Wiens, PharmD, PhD; Jerry J. Zimmerman, MD, PhD;
Andrew C. Argent, MD, MBBCh, MMed; Lauren R. Sorce, PhD, RN, CPNP-AC/PC; Luregn J. Schlapbach, MD, PhD;
R. Scott Watson, MD, MPH; and the Society of Critical Care Medicine Pediatric Sepsis Definition Task Force

* Co-first auth

2024

Research

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

International Consensus Criteria for Pediatric Sepsis and Septic Shock

Luregn J. Schlapbach,* MD, PhD; R. Scott Watson,* MD, MPH; Lauren R. Sorce,* PhD, RN; Andrew C. Argent,* MD, MBBCh, MMed; Kusum Menon, MD, MSc;
Mark W. Hall, MD; Samuel Akech, MBChB, MMED, PhD; David J. Albers, PhD; Elizabeth R. Alpern, MD, MSCE; Fran Balamuth, MD, PhD, MSCE;
Melania Bembea, MD, PhD; Paolo Biban, MD; Enitan D. Carrol, MBChB, MD; Kathleen Chiotos, MD; Mohammod Jobayer Chisti, MBBS, MMed, PhD;
Peter E. DeWitt, PhD; Idris Evans, MD, MSc; Cláudio Flauzino de Oliveira, MD, PhD; Christopher M. Horvat, MD, MHA; David Inwald, MB, PhD;
Paul Ishimine, MD; Juan Camilo Jaramillo-Bustamante, MD; Michael Levin, MD, PhD; Rakesh Lodha, MD; Blake Martin, MD; Simon Nadel, MBBS;
Satoshi Nakagawa, MD; Mark J. Peters, PhD; Adrienne G. Randolph, MD, MS; Suchitra Ranjit, MD; Margaret N. Rebull, MA; Seth Russell, MS;
Halden F. Scott, MD; Daniela Carla de Souza, MD, PhD; Pierre Tissieres, MD, DSc; Scott L. Weiss, MD, MSCE; Matthew O. Wiens, PharmD, PhD;
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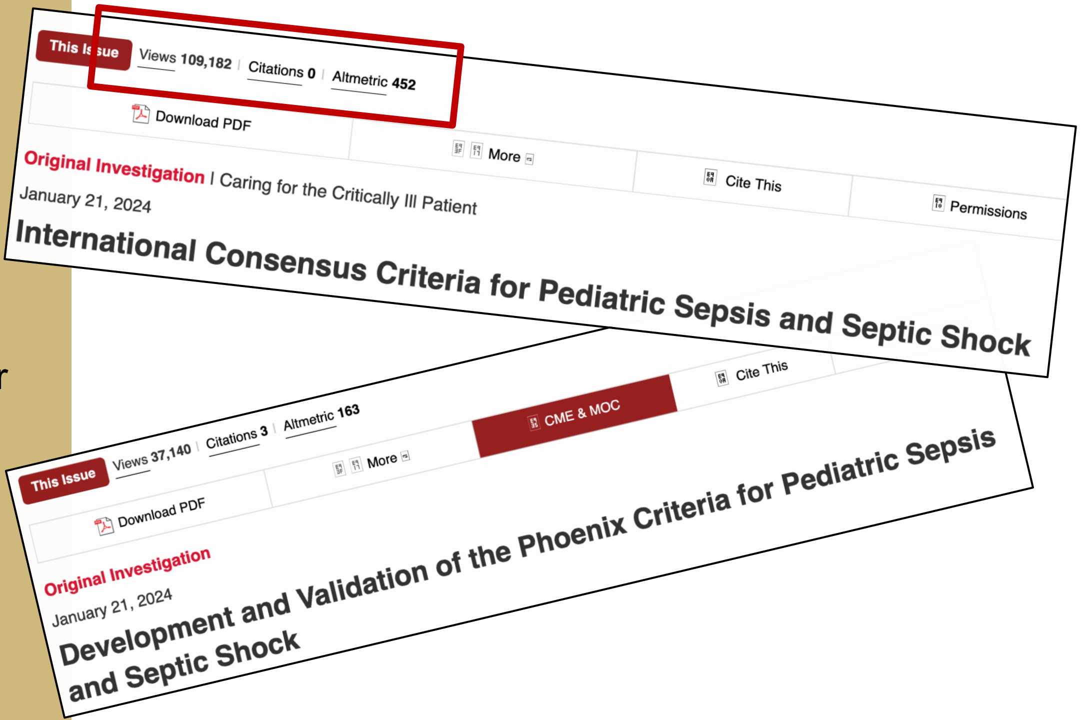
for the Society of Critical Care Medicine Pediatric Sepsis Definition Task Force

* Co-first authors

IMPACT

- **Overall goal: Decrease the number of sepsis deaths and improve long-term outcomes with more accurate diagnosis**
- Deployment started in electronic health records across the country
- We have developed a mobile application for use in low resource environments
- In clinical use already – *I used the new criteria last week in the ICU*



Locally Made (NIH Funded)

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

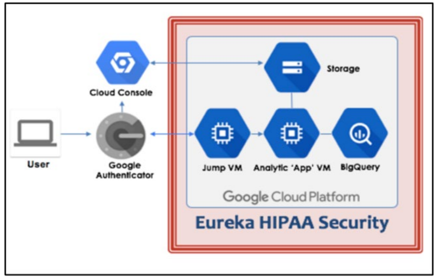
Site Data

Children's Hospital Colorado

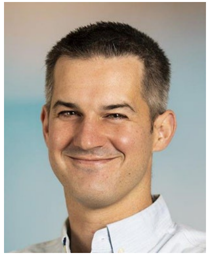
Core Data Science Team



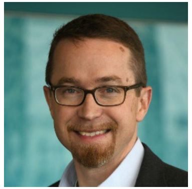
Computing Environment



Other CU Contributors

Task Force Members




Funding

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

R01 HD105939

NIH National Center for Advancing Translational Sciences

NIH National Heart, Lung, and Blood Institute

Extra Slides

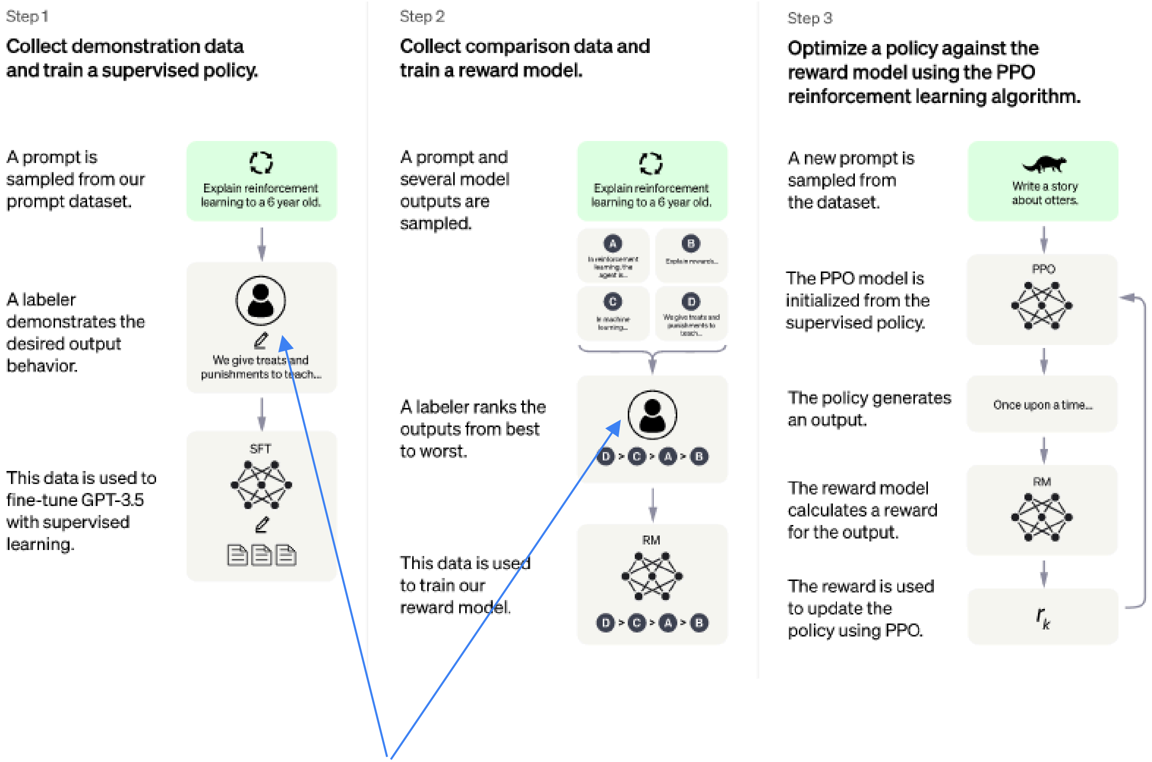
What about ChatGPT etc. (Generative AI)?

First: What is a large language model (LLM)?

- A type of deep learning model (a transformer) trained to predict sequences
  - Text is sequences of words
- Trained on enormous amounts of text
  - (generally, available on the internet)
- General LLMs are very expensive to train (computing resources)
  - Although specific LLMs have been trained affordably

Shah N et al. JAMA 2023

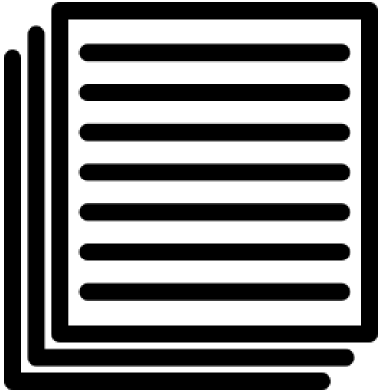
How was ChatGPT built?



Reinforcement Learning with Human Feedback

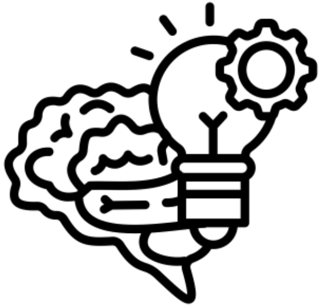
ChatGPT etc.

- **What will LLMs <u>definitely</u> be good for in medicine?**
  - Summarization
  - Documentation
  - Communications (including patient-facing chatbots)
  - Accelerating Analytics
  - Operations!



ChatGPT etc.

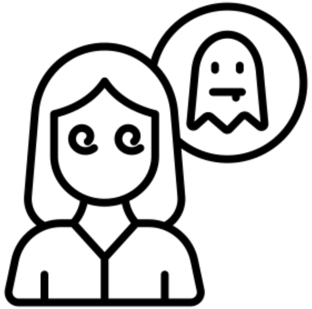
- **What <u>might</u> LLMs be good for in medicine?**
  - Diagnosis (first: adult, outpatient, conditions with a solid evidence base)
  - Interpretation of other complex data (waveforms, images, etc.) (long-term, massive compute needed)



LLMs: things to watch out for

- Hotel California for potentially sensitive data
- Has the model seen those data already (on medrxiv, pubmed, etc.)?
- "Hallucinations"

  - LLMs are like [insert very confident subspecialty]. They sound certain, even when they are wrong.



Specific Campus Expertise in LLMs

Yanjun Gao, PhD

Assistant Professor, DBMI

Start date Sept 1, 2024