AUSTERE ENVIRONMENTS
CONSORTIUM FOR ENHANCED
SEPSIS OUTCOMES

DANIELLE CLARK, PHD
DIRECTOR, ACESO
ACESO MISSION

Improve survival for patients with sepsis through development of host-based diagnostic/prognostic assays and evidence-based clinical management
**Suspected infection** + ≥ 2 SIRS criteria
Acute (hrs after enrollment): 0, 6, 12, 24, 48, 72
Follow-up: 28 days, 6 mos, 12 mos

**OBSERVATIONAL STUDY DESIGN**

**Enroll Patients**
- Cambodia
- Duke
- Ghana
- Liberia
- Uganda

**Conduct Advanced Testing**
- Transcriptomics
- Metabolomics
- Proteomics
- Phosphoproteomics
- Pathogen Identification

**Analyze Data**
- ACESO
- Duke
- Future Partners

**Discovery**

**Validation**

**ACESO Provided Cross-Program Activities**
- Protocol Development, Program Management & Partner Agreement Structure
- Data Analysis Strategy & Coordination
- Laboratory Testing Strategy & Coordination
- Data Architecture & Coordination
ANALYTIC APPROACH

• Exploratory Analysis
• Focus on identifying subgroups
• Topological Data Analysis
  • Geometric approach to pattern recognition
• Classification using machine learning algorithm
Burk Non-survivors (N=4)
All male
All burk Culture pos
1 kpneumo co-culture
75% died within 28 days

Non-survivors (N=9)
3 bacteria, 1 dengue
100% died within 28 days

Burk Non-survivors (N=3)
All female
2 burk I-stat pos
1 H. influenzae cx pos
75% died within 28 days

Non-survivors (N=5)
1 Legionella
60% died within 28 days

Burk survivors (N=4)
1 burk cx pos
All burk I-stat pos
100% survived
ACESO SITES

ACESO HQ
(NMRC-Frederick)

N Carolina
(Duke U)

Ghana, Liberia
(NAMRU-3)

Uganda
(MUWRP)

Cambodia
(NAMRU-2)
## Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Cambodia</th>
<th>Ghana</th>
<th>Duke</th>
<th>Uganda</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (median years)</strong></td>
<td>50</td>
<td>48</td>
<td>53</td>
<td>46</td>
</tr>
<tr>
<td><strong>Sex (% male)</strong></td>
<td>65%</td>
<td>45%</td>
<td>55%</td>
<td>44%</td>
</tr>
<tr>
<td><strong>Occupation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Farmer</td>
<td>55%</td>
<td>14%</td>
<td></td>
<td>50%</td>
</tr>
<tr>
<td>Trade</td>
<td>-</td>
<td>25%</td>
<td></td>
<td>17%</td>
</tr>
<tr>
<td>Home/unemployed</td>
<td>16%</td>
<td>21%</td>
<td></td>
<td>17%</td>
</tr>
<tr>
<td><strong>28 Day Mortality</strong></td>
<td>15%</td>
<td>31%</td>
<td>11%</td>
<td>21%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>377</td>
<td>204</td>
<td>181</td>
<td>36</td>
</tr>
<tr>
<td><strong>Enrollment 1 Oct 2018</strong></td>
<td>500</td>
<td>280</td>
<td>181</td>
<td>130</td>
</tr>
</tbody>
</table>
PATHOGENS IDENTIFIED

Cambodia

Duke

None

Non-infectious

E. coli

Pseudomonas

Staph. spp

Other

B. pseudomallei

O. tsutsugamushi

Dengue

Virus

Bacteria

Other
PATHOGENS IDENTIFIED

*Pathogen identification ongoing
SAMPLE COLLECTION SCHEDULE

Cambodia
- PAXgene
- PPP
- PBMC
- Serum
- WB

Ghana
- PAXgene
- PPP
- PBMC
- Serum
- WB

Duke
- PAXgene
- PPP
- PBMC
- Serum
- WB

Uganda & Liberia
- PAXgene
- PPP
- PBMC
- Serum
- WB

Time 0 6 12 24 48 72 28D
OTHER POSSIBLE COHORTS

• Peru – NAMRU-6
  • Peru, Columbia, Honduras, Paraguay, Bolivia, Brazil
  • Acute febrile illness patients ≥5 years of age
  • Whole blood and serum samples

• Darwin, Australia – Menzies University
  • Burkholderia pseudomallei

• Human Challenge Studies
  • Dengue – SUNY Upstate
  • Respiratory illness – Duke University
## ACKNOWLEDGEMENTS

**NMRC/ACESO**  
CDR Matthew Doan  
Janice Hepbum  
Kevin Schully  
Josh Chenoweth  
Michelle Rozo  
James Lawler  
Michael Gregory  
Matthew Bell  
Chris Duplessis

**Duke University**  
Geoffrey Ginsburg  
Chris Woods  
Ephraim Tsalik  
Duke study team

**NAMRU-2**  
Angela Prouty  
Daraarith Nhim  
Tin Som

**Cambodia CDC**  
Kheng Sim  
Takeo Provincial Hospital

**LIBR**  
Fatorma Bolay  
Phebe Hospital study team

**KATH**  
George Oduro  
Daniel Ansong  
KATH study team

**MUWRP**  
Hannah Kibuuka  
MUWRP study team  
Fort Portal Hospital
• This work was supported by the Chemical Biological Technologies Directorate contract from the Department of Defense Chemical and Biological Defense program through the Defense Threat Reduction Agency, the Defense Health Agency through the Joint West Africa Research Group, and the Joint Program Executive Office, Medical Countermeasures Systems.

• The study protocol was approved by the NMRC IRB in compliance with all applicable Federal regulations governing the protection of human subjects. The Uganda protocol was approved by the MRMC IRB.

• The views expressed are those of the authors and should not be construed to represent the positions of the Department of the Navy, or Department of Defense. Title 17 U.S.C. §105 provides that “Copyright protection under this title is not available for any work of the United States Government.”