Overview on sepsis in low- and middle-income countries

FLAVIA MACHADO
We don't know the numbers

Getting data
World numbers are extrapolating from HICs

- 5.3 million deaths
- 19.4 million cases of severe sepsis
- 31.5 million cases of sepsis

Incidence:
- 437 sepsis cases per 100,000 person-years
- 270 severe sepsis cases per 100,000 person-years

Mortality for severe sepsis: 26%

Fleischmann et al.  AJRCCM 2015

Mapa mundial mostrando estudo em sepse e sepse grave que permitem o cálculo de taxas de incidência no nível da população. (EUA, Alemanha, Austrália, Tailwan, Noruega, Espanha, Suécia)

N = 27 studies
7 high-income countries
Asia 2013-2014
Prospective hospital-treated sepsis
Sites = 13, patients = 815
28-d mortality = 13%

Brazil 2001-2002
Prospective ICU-treated sepsis
Sites = 5, patients = 415
Sepsis 28-d mortality = 47%
Septic shock 28-d mortality = 52%

Brazil 2003
Prospective ICU-treated sepsis
Sites = 65, patients = 521
Sepsis 28-d mortality = 34%
Septic shock 28-d mortality = 65%

Brazil 2003-2004
Prospective ICU-treated sepsis
Sites = 21, patients = 524
28-d mortality = 43%

Brazil 2005-2014
Retrospective QI hospital-treated sepsis
Sites = 63, patients = 21103
Hospital mortality
pre-intervention: 53.9%,
post-intervention 38.5%

Crit Care 2004;8(4):R251-260
RBTI 2006;18:9-17
Crit Care Med 2017
China 2003-2008
Prospective ICU-treated sepsis
Sites = 4, patients = 479
Sepsis hospital mortality = 53%

China 2009
Prospective ICU-treated sepsis
Sites = 22, patients = 484
Hospital mortality = 34%

Colombia 2007-2009
Prospective hospital-treated sepsis
Sites = 10, patients = 1658
Hospital sepsis mortality = 22%
Septic shock = 46%

Uganda 2006-2009
Before-after QI ER-treated sepsis
Sites = 2, patients = 671
30-d mortality before = 46%
After = 33%

Crit Care Med 2007;35(11):2538-2546
PLoS One 2014;9(9):e107181
Anaesthesist 2013;62(12):995-1002
Crit Care Med 2011;39(7):1675-1682
Population-Based Epidemiology of Sepsis in a Subdistrict of Beijing

Jianfang Zhou, MD¹; Hongcheng Tian, MD²; Xueping Du, MD³; Xiuming Xi, MD⁴; Youzhong An, MD⁵; Meili Duan, MD⁶; Li Weng, MD¹; Bin Du, MD¹; for China Critical Care Clinical Trials Group (CCCCTG)

Incidence:
- Sepsis: 461 cases per 100,000 population
- Severe sepsis: 68 cases per 100,000 population
- Septic shock: 52 cases per 100,000 population

Mortality rate:
- All: 20%
- Severe sepsis: 26.0%
- Septic shock: 84.5%
Incidence rate of ICU-treated sepsis (severe): 290 per 100,000 population

Mortality rate: 55%
Severe sepsis - 50%
Septic shock - 60%
Why it is not possible???

HOST
- Sex and race
- Genetic susceptibility
- Poverty and malnutrition
- Lifestyle (smoking, alcohol, physical activity)
- Chronic illnesses

PATHOGEN
- Unusual pathogens (protozoa, virus, fungus) with poor disease knowledge.
- Antimicrobial resistance
- Virulence factors
- Important co-infections (tuberculosis, HIV)
- Site of infection

HEALTH CARE
- Low vaccination rates
- Poor sanitation and hygiene
- Low awareness
- Suboptimal provision of basic resources
- Inadequate access to ICU care
- Inadequate process of care
- Shortage of skilled personnel
- Unsafe environments with high rates of AE
- High incidence of HAI

OTHERS
- Lack of generalizability of sepsis guidelines to LMICs
- Insufficient research on sepsis epidemiology in LMICs
- Failure to recognize sepsis as a global healthcare priority

Disparities
We don’t have the resources

Prioritizing the resources
Severe infrastructure limitation

Access to emergency and surgical care in sub-Saharan Africa: the infrastructure gap

Renee Y Hsia,1* Naboth A Mbembati,2 Sarah Macfarlane3 and Margaret E Kruk4

Health Policy and Planning 2012;27:234–244

Figure 4. Availability of infection control materials and disposal of infectious waste across health facilities.

Figure 6 Education (training and supervision) programmes existing across health facilities.
<table>
<thead>
<tr>
<th>Resource limitation - lactate availability</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Always</th>
<th>Some times</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>25.7%</td>
<td>24.1%</td>
<td>36.9%</td>
</tr>
</tbody>
</table>

*Baelani et al CC 2011*

<table>
<thead>
<tr>
<th>Always</th>
<th>Some times</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.2%</td>
<td>13.2%</td>
<td>60.5%</td>
</tr>
</tbody>
</table>

*Baaar et al Bull WHO 2010*

<table>
<thead>
<tr>
<th>Always</th>
<th>Some times</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>8.1%</td>
<td>88.7%</td>
</tr>
</tbody>
</table>

*Baelani et al MED Anest 2012*
Accepted Manuscript

Healthcare infrastructure capacity to respond to severe acute respiratory infection (SARI) and sepsis in Vietnam: A low-middle income country

Dat Vu Quoc, Long Nguyen Thanh, Kim Bao Giang, Pham Bich Diep, Ta Hoang Giang, Janet V. Diaz

Resource availability for the management of maternal sepsis in Malawi, other low-income countries, and lower-middle-income countries

Mohammed Abdu¹ | Amie Wilson² | Chisale Mhango³ | Fatima Taki¹ | Arri Coomarasamy¹ | David Lissauer¹,*
How about Brazil?

The epidemiology of sepsis in Brazilian intensive care units (the Sepsis PREvalence Assessment Database, SPREAD): an observational study

Lancet Infect Dis 2017

Resources scores according to type of hospital – main source of funding

Items:
- Blood gas analysis within 3 hours
- Lactate results within 3 hours
- Basic cultures
- Basic antibiotics
- Crystalloids
- Noradrenaline
- Central venous catheter
- Central venous pressure measurement
The epidemiology of sepsis in Brazilian intensive care units (the Sepsis PREvalence Assessment Database, SPREAD): an observational study

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPS 3</td>
<td>1.03 (1.02–1.04)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Resource availability*</td>
<td>..</td>
<td>..</td>
</tr>
<tr>
<td>High</td>
<td>1.00</td>
<td>..</td>
</tr>
<tr>
<td>Intermediate</td>
<td>1.20 (0.72–1.98)</td>
<td>0.484</td>
</tr>
<tr>
<td>Low</td>
<td>1.67 (1.02–2.75)</td>
<td>0.045</td>
</tr>
<tr>
<td>Health-care-associated infection</td>
<td>1.55 (1.13–2.12)</td>
<td>0.0069</td>
</tr>
<tr>
<td>Septic shock</td>
<td>1.71 (1.24–2.37)</td>
<td>0.0013</td>
</tr>
<tr>
<td>Compliance with bundles</td>
<td>..</td>
<td>..</td>
</tr>
<tr>
<td>Non-compliance with antibiotics</td>
<td>1.00</td>
<td>..</td>
</tr>
<tr>
<td>Compliance at least with antibiotics</td>
<td>0.63 (0.44–0.89)</td>
<td>0.0090</td>
</tr>
<tr>
<td>Compliance with 6-h bundle</td>
<td>0.56 (0.37–0.84)</td>
<td>0.0059</td>
</tr>
</tbody>
</table>

Table 2: Multivariate analysis of factor associated with mortality
Almost no access...

Intensive Care Unit Capacity in Low-Income Countries: A Systematic Review

Srinivas Murthy¹*, Aleksandra Leligdowicz², Neill K. J. Adhikari²,³

Nepal - 1,67 beds/100,000
Uganda - 0.1 beds/100,000

Zambia: 0.077 beds/100,000
Andrews JAMA 2017

Sri Lanka 2.5 beds
Malasia 2.4 beds
China 3.9 beds
Bangladesh 7.9 beds
Per 100,000 habs
Hanniffa JCC 2014
Most critically ill patients are managed outside of ICUs in resource-limited settings

Courtesy from Shevin Jacob, Uganda
Access to whom?

7.6 public ICU beds for 100,000 habitants

Northeast 5.0
Middle-West 7.4
South 9.4
Southest 10.4
North 3.2

25.5 private ICU beds for 100,000 habitants

Northeast 28.4
Middle-West 38.5
South 22.2
Southest 24.2
North 28.8
Low awareness among lay people = delay in searching for care

Making noise!
Low awareness among lay people

Brazil

2,126 people
134 cities
June 2014

Percentage of positive answers to the question: “Have you ever heard the word sepsis?”
VOCE JÁ PLANEJOU A CAMPAHNA DESSE ANO?

O ILAS disponibiliza materiais impressos além do KIT ILAS

ACESSE NOSSO SITE: WWW.DIAMUNDIALDASEPSE.COM.BR

#DMS2017 #PENSEPODESERSEPSE

Mais informações: secretaria@ilas.org.br

* A solicitação de materiais e kits devem ser feitas até dia 07/08
A sepse se não tratar ela mata
14 mil visualizações

Sepse - A rapidez que salva vidas
18 mil visualizações • Há 1 ano

A sepse mata de montão
14 mil visualizações • Há 4 meses

!!La rapidez que salva vidas!!
1,1 mil visualizações • Há 1 ano
Raising awareness - the World Sepsis Day

Brazil 2014
N = 2.126
134 cities
June 2014

Brazil 2017
N = 2.100
130 cities
March 2017

Have you ever heard the word sepsis?

- Yes
- No
Healthcare professionals
Limited awareness + shortage and high turnover + inadequate training

Train!
Campaign!
Motivate!
# The Knowledge of the Physicians about Sepsis Bundles is Suboptimal: A Multicenter Survey

<table>
<thead>
<tr>
<th>Bundle element</th>
<th>Residents (n=153) n, %</th>
<th>Specialists (n=70) n, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood lactate measurement (need for measurement within 3 hours)</td>
<td>113; 74%</td>
<td>54; 77%</td>
</tr>
<tr>
<td>Threshold of blood lactate level in sepsis (&gt;4mmol/L)</td>
<td>45; 30%</td>
<td>27; 39%</td>
</tr>
<tr>
<td>Blood culture, within 3 hours prior to antibiotic use</td>
<td>135; 88%</td>
<td>63; 90%</td>
</tr>
<tr>
<td>Target mean arterial blood pressure (&gt;65mmHg) (severe sepsis)</td>
<td>89; 58%</td>
<td>41; 59%</td>
</tr>
<tr>
<td>Target central venous pressure (8-12mmHg) (septic shock or lactate&gt;4mmol/L)</td>
<td>97; 63%</td>
<td>44; 63%</td>
</tr>
<tr>
<td>Target central venous oxygen saturation (&gt;70%) (severe sepsis)</td>
<td>18; 12%</td>
<td>11; 16%</td>
</tr>
<tr>
<td>Fluid resuscitation, 30ml/kg within 3 hours, (hypotension or lactate &gt;4mmol/L)</td>
<td>53; 35%</td>
<td>37; 53%</td>
</tr>
</tbody>
</table>

**Table/Fig-6:** Knowledge of sepsis bundles: residents versus specialists
A Multicenter Survey of House Staff Knowledge About Sepsis and the “Surviving Sepsis Campaign Guidelines for Management of Severe Sepsis and Septic Shock”

Richard R. Watkins, MD, MS¹,², Nairmeen Haller, PhD³, Melinda Wayde, MD⁴, and Keith B. Armitage, MD⁵

Survey on physicians' knowledge of sepsis: Do they recognize it promptly?☆☆☆

Murillo Assunção MDᵃᵇ⁺, Nelson Akamine MDᵇ, Guttemberg S. Cardoso MDᵃ, Patrícia V.C. Mello MDᶜ, José Mário M. Teles MDᵇᵈ, André Luis B. Nunes MDᵉ, Marcelo Oliveira Maia MDᶠ, Álvaro Rea-Neto MDᵇᵍ, Flavia Ribeiro Machado MDᵃᵇ for the SEPSES study group
A complex intervention to improve implementation of World Health Organization guidelines for diagnosis of severe illness in low-income settings: a quasi-experimental study from Uganda

Fort Portal Regional Referral Hospital (Fort Portal, Uganda): Medical and Nursing Officers participating in a mock patient scenario as part of the WHO IMAI QuickCheck+ training course
Training course of the National Association Of Nurse Intensivists Of Nigeria
Sepsis 3 from the perspective of clinicians and quality improvement initiatives

Flavia R. Machado\textsuperscript{a, b, *}, Emmanuel Nsutebu\textsuperscript{b}, Salman Abdulaziz\textsuperscript{b}, Ron Daniels\textsuperscript{a}, Simon Finfer\textsuperscript{a}, Niranjan Kissoon\textsuperscript{a, b}, Harvey Lander\textsuperscript{b}, Imrana Malik\textsuperscript{b}, Elizabeth Papathanassoglou\textsuperscript{b}, Konrad Reinhart\textsuperscript{a, b}, Kevin Rooney\textsuperscript{b}, Hendrik Rüddel\textsuperscript{b}, Giulio Toccafondi\textsuperscript{b}, Giorgio Tulli\textsuperscript{b}, Vida Hamilton\textsuperscript{b}

\textsuperscript{a} Global Sepsis Alliance Executive Committee, Paul-Schneider-Str. 2, 07747 Jena, Germany
\textsuperscript{b} Global Sepsis Alliance Quality Improvement Committee, Paul-Schneider-Str. 2, 07747 Jena, Germany
Low quality of care

Finding a way
QUALITY IMPROVEMENT

DOES IT WORK?
Quality Improvement Initiatives in Sepsis in an Emerging Country: Does the Institution's Main Source of Income Influence the Results? An Analysis of 21,103 Patients

Flavia R. Machado, MD, PhD; Elaine M. Ferreira, MSc, RN; Juliana Lubarino Sousa, RN; Carla Silva, RN; Pierre Schippers, MD; Adriano Pereira, MD, PhD; Ilusca M. Cardoso, MD, MSc; Reinaldo Salomão, MD, PhD; Andre Japiassu, MD, PhD; Nelson Akamine, MD, MSc; Bruno F. Mazza, MD, MSc; Murillo S. C. Assunção, MD, MSc; Haggeas S. Fernandes, MD; Aline Bossa, MSc Mariana B. Monteiro, RN; Noemi Caixeita; Luciano C. P. Azevedo, MD, PhD; Eliezer Silva, MD, PhD; on behalf of the Latin American Sepsis Institute Network

Mortality throughout the intervention according to the type of hospital
Total cost per patient:
Baseline: 29.3 (95 %CI 23.9–35.4)
Last 3 months: 17.5 (95 % CI 14.3–21.1) thousand US
(mean difference -11,815; 95 % CI -18,604 to -5,338)
Sepsis is (was?) a neglected disease

Join efforts!
The solutions: increase partnership
The Seventieth World Health Assembly,

Having considered the report on improving the prevention, diagnosis and clinical management of sepsis;