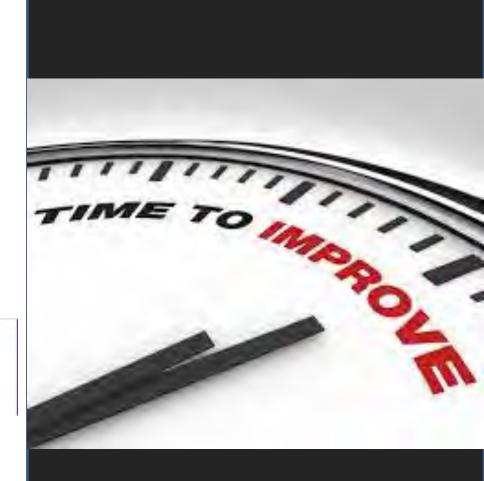
# Overview on sepsis in low- and middle-income countries

FLAVIA MACHADO





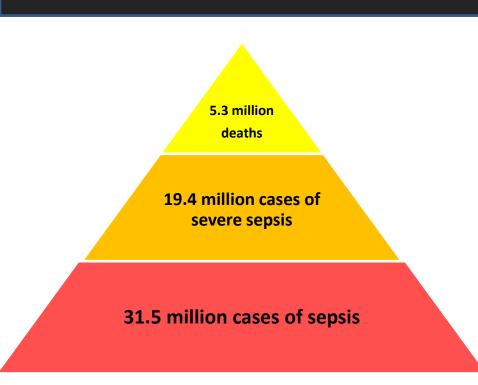


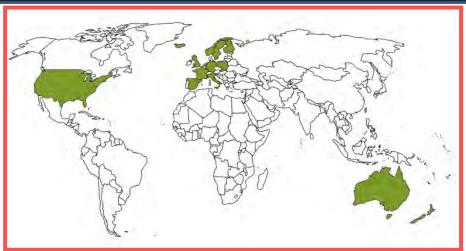




We don't know the numbers

### World numbers are extrapolating from HICs





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 studies7 high-income countries

#### Incidence:

437 sepsis cases per 100000 person-years 270 severe sepsis cases per 100000 person-years Mortality for severe sepsis : 26% Asia 2013-2014

Prospective hospital-treated sepsis

Sites = 13, patients = 815

28-d mortality = 13%

Brazil 2003
Prospective ICU-treated sepsis

Sites = 65, patients = 521

**Sepsis 28-d mortality = 34%** 

**Septic shock 28-d mortality = 65%** 

Brazil 2001-2002

Prospective ICU-treated sepsis

Sites = 5, patients = 415

Sepsis 28-d mortality = 47%

**Septic shock 28-d mortality = 52%** 

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%

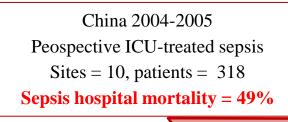
Lancet Glob Health 2017;5(2):e157-e167

Crit Care 2004;8(4):R251-260

RBTI 2006;18:9-17

Pharmacoeconomics 2008;26(5):425-434

Crit Care Med 2017



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

China 2003-2008

Prospective ICU-treated sepsis

Sites = 4, patients = 479

Sepsis hospital mortality = 53%

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. 2014 Nov;42(11):2315-24

Crit Care Med 2011;39(7):1675-1682

## High quality data from LIMCs

## Population-Based Epidemiology of Sepsis in a Subdistrict of Beijing

CCM 2017

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%

53.5%

## SPREAD study

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

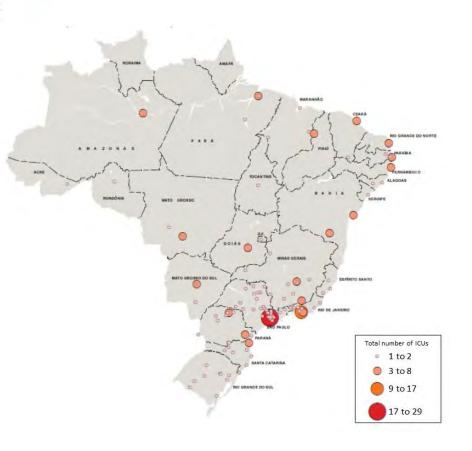
Flavia R Machado, Alexandre Biasi Coval conti, Fernando August o Bozra, Elaine M Ferretra, Fernando Soissa Angetti Carrora, Juliana Lubarino Soissa, Noemi Cabutta, Reinaldo Salomao, Derek C Angus, Luciano Cesar Pontes Azeveda, on behalf of the SPRE AD investigators and the Latin American Sepsisinat Eure Network?



Lancet Infect Dis 2017

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 PATHOGEN -Sex and race -Unusual pathogens protozoa, virus, fungi) with poor disease knowledge. - Genetic susceptibility -Antimicrobial resistance - Poverty and malnutrition -Virulence tactors - Life style (smoking, alcohol, Important co-infections (bc, HIV) physical activity) -Site of infection - Chronic illnesses High **Disparities** Incidence Poor **Outcomes HEALTH CARE** OTHERS Low vaccination rates HOSPITAL Poor sanitation and hygiene - Lack of generalizability of sepsis Low awareness auidelines to LMICs Suboptimal provision of basic resources Insufficient research on sepsis Inadequate access to ICU care epidemiology in LMICs -Inadequate process of care Failure to recognize sepsis as -Shortage of skilled personnel a global healthcare priority -Unsafe environments with high rates of AE -High incidence of HAI **Disparities** Inadequate rehabilitation and post ICU care

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 Macfarlane 3 and Margaret E Kruk 4

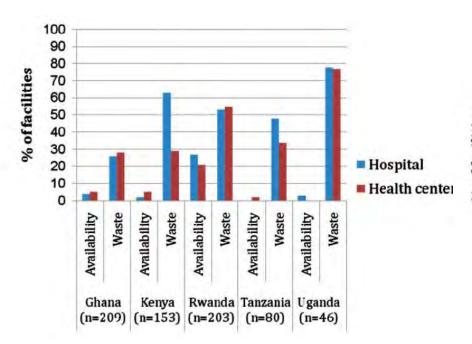
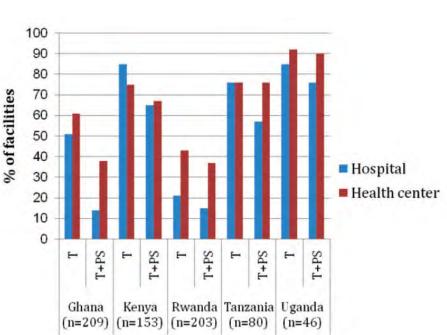


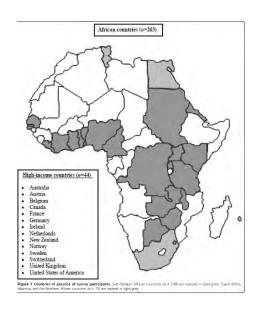
Figure 4. Availability of infection control materials and disposal of infectious waste across health facilities.



Health Policy and Planning 2012;27:234-244

Figure 6 Education (training and supervision) programmes existing across health facilities

## Resource limitation - lactate availability







Always 25.7%

Some times 24.1%

Never 36.9%

Baelani et al CC 2011

Always 13.2%

Some times 13.2%

Never 60.5%

Baaar et al Bull WHO 2010

Always 0%

Some times 8,1%

Never 88.7%

Baelani et al MED Anest 2012

### Resource limitation -

#### 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



#### CLINICAL ARTICLE Obstetrics



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

```
Mohammed Abdu<sup>1</sup> | Amie Wilson<sup>2</sup> | Chisale Mhango<sup>3</sup> | Fatima Taki<sup>1</sup> | Arri Coomarasamy<sup>1</sup> | David Lissauer<sup>1,*</sup>
```

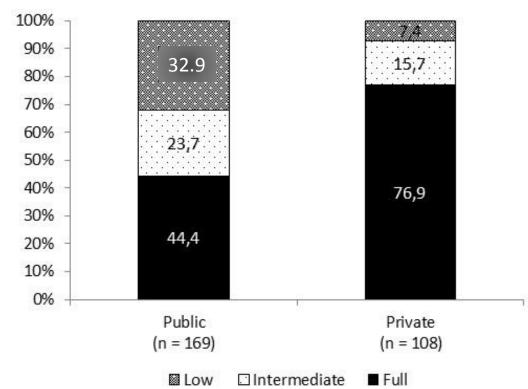
### How about Brazil?

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



Lancet Infect Dis 2017

Flavia R Machado, Alexandre Biosi Covalconti, Fernando August o Bozza, Elaine M Ferreta, Fernando Sousa Angotti Carrora, Juliana Lubarino Sousa, Noemi Cabeta, Reinaldo Salomao, Derek C Angus, Luciano Cesar Pontes Azevedo, on behalf of the SPRE AD investigators and the Latin American Sepsisinat Euro Network



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

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

## SPREAD study - risk factors for mortality

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



Flavia R.Machado, Alexandre Blasi Covalcanti, Fernando August o Bozza, Elaine M.Ferret a, Fernando Sousa Anget ti Carrara, Juliana Lubatino Sousa, Noemi Caixeta, Reinaldo Salomao, Derek C.Angus, Luciano Cesar Pontes Az eveda, on behalf of the SPRE AD investigators and the Latin American Sepsis institute Network\*

	OR (95% CI)	pvalue
SAPS 3	1.03 (1.02-1.04)	<0.0001
Resource availability*	**	**
High	1.00	341
Intermediate	1.20 (0.72-1.98)	0.484
Low	1.67 (1.02-2.75)	0-045
Health-care-associated infection	1.55 (1.13-2.12)	0-0069
Septic shock	1.71 (1.24-2.37)	0.0013
Compliance with bundles	*	
Non-compliance with antibiotics	1.00	
Compliance at least with antibiotics	0.63 (0.44-0.89)	0-0090
Compliance with 6-h bundle	0.56 (0.37-0.84)	0.0059

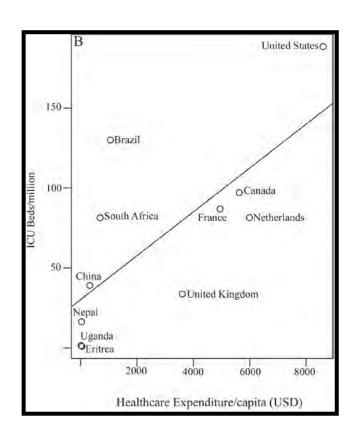


### Almost no access...

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

Srinivas Murthy<sup>1\*</sup>, Aleksandra Leligdowicz<sup>2</sup>, Neill K. J. Adhikari<sup>2,3</sup>

PLOS ONE | January 24, 2015



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



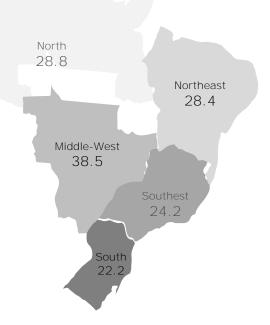


### Access to whom?

7.6 public ICU beds for 100,000 habitants



25.5 private ICU beds for 100,000 habitants







Low awareness among lay people = delay in searching for care

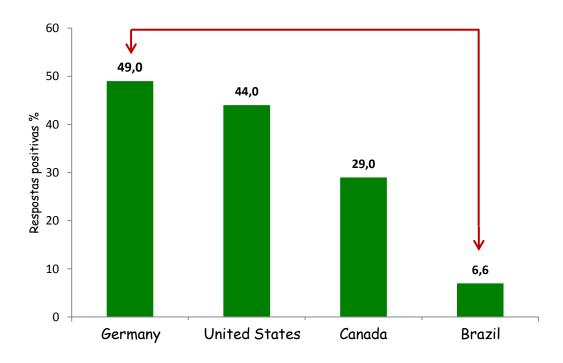
Making noise!

## Low awareness among lay people

#### **Brazil**

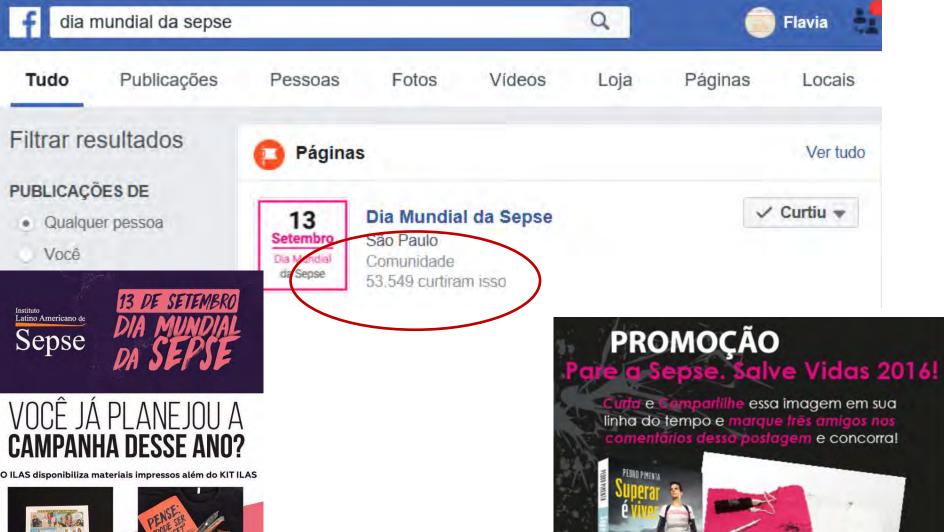
2.126 people 134 cities June 2014





Percentage of positive answers to the question: "Have you ever heard the world sepsis?"





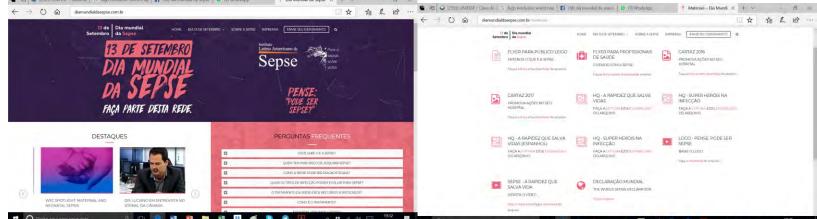




Pimenta, e o segundo e terceiro receberão um Kit Dia Mundial

da Sepse: 2 camisetas, 2 canetas, 1 carregador portátil e bótons!

Válida até 12 de agosto





#### A sepse se não tratar ela mata

14 mil visualizações ·



#### A sepse mata de montão

14 mil visualizações • Há 4 meses



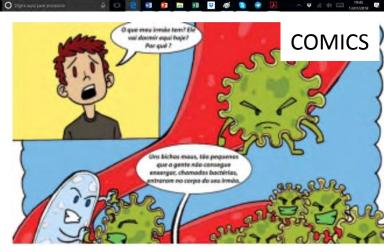
#### Sepse - A rapidez que salva vidas

18 mil visualizações • Há 1 ano



#### !!La rapidez que salva vidas!!

1,1 mil visualizações • Há 1 ano













## Raising awareness - the World Sepsis Day

Brazil 2014

N = 2.126

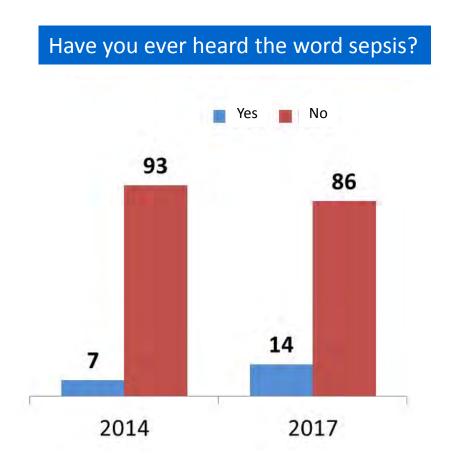
134 cities

**June 2014** 

Brazil 2017

N = 2.100 130 cities

**March 2017** 





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

Journal of Clinical and Diagnostic Research, 2015 Jul, Vol-9(7): OC13-OC16

ZELIHA KOCAK TUFAN', FATMA CIVELEK ESER", EMRE VUDALI", AYSE BATIREL', BIRCAN KAYAASLAN', ALIYE TANRICI BASTUG',
DENIZ ERAY', VEDAT TURHAN', FAZILET DUYGU', DURAN TOK'', SERIFE ALTUN'', CEMAL BULUT'', MEHMET A. TASYARAN''

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

[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, MS<sup>1,2</sup>, Nairmeen Haller, PhD<sup>3</sup>, Melinda Wayde, MD<sup>4</sup>, and Keith B. Armitage, MD<sup>5</sup>

Journal of Intensive Care Medicine

© The Author(s) 2017 Reprints and permission: sagepub.com/journalsPermissions.nav DOI: 10.1177/0885066617737304

DOI: 10.1177/088506661773730 journals.sagepub.com/home/jic



Journal of Critical Care (2010) 25, 545-552



Journal of Critical Care

Sepsis

Survey on physicians' knowledge of sepsis: Do they recognize it promptly? \*\*.\*\*\*

Murillo Assunção MD<sup>a,b,\*</sup>, Nelson Akamine MD<sup>b</sup>, Guttemberg S. Cardoso MD<sup>a</sup>, Patricia V.C. Mello MD<sup>c</sup>, José Mário M. Teles MD<sup>b,d</sup>, André Luis B. Nunes MD<sup>e</sup>, Marcelo Oliveira Maia MD<sup>f</sup>, Álvaro Rea-Neto MD<sup>b,g</sup>, Flavia Ribeiro Machado MD<sup>a,b</sup> for the SEPSES study group

#### RESEARCH

Open Access

CrossMark

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

Matthew J. Cummings <sup>1</sup> <sup>1</sup> <sup>1</sup> <sup>1</sup> Elijah Goldberg <sup>2,3†</sup>, Savio Mwaka<sup>3</sup>, Olive Kabajaasi<sup>3</sup>, Eric Vittinghoff<sup>4</sup>, Adithya Cattamanchi<sup>5</sup>, Achilles Katamba<sup>6</sup>, Nathan Kenya-Mugisha<sup>3</sup>, Shevin T. Jacob<sup>3,7†</sup> and J. Lucian Davis<sup>8,9</sup>

Courtesy from Shevin Jacob, Uganda

Fort Portal Regional Referral Hospital (Fort Portal, **Uganda):** Medical and Nursing Officers participating in a mock patient scenario as part of



#### Courtesy from Halima Salisu Kabara, Nigeria





Contents lists available at ScienceDirect

#### Journal of Critical Care

journal homepage: www.elsevier.com



#### Sepsis 3 from the perspective of clinicians and quality improvement initiatives

Flavia R. Machado<sup>a, b, \*</sup>, Emmanuel Nsutebu<sup>b</sup>, Salman AbDulaziz<sup>b</sup>, Ron Daniels<sup>a</sup>, Simon Finfer<sup>a</sup>, Niranjan Kissoon<sup>a, b</sup>, Harvey Lander<sup>b</sup>, Imrana Malik<sup>b</sup>, Elizabeth Papathanassoglou<sup>b</sup>, Konrad Reinhart<sup>a, b</sup>, Kevin Rooney<sup>b</sup>, Hendrik Rüddel<sup>b</sup>, Giulio Toccafondi<sup>b</sup>, GiOrgio Tulli<sup>b</sup>, Vida Hamilton<sup>b</sup>

\* Global Sepsis Alliance Executive Committee, Paul-Schneider-Str. 2, 07747 Jena, Germany



Global Sepsis Alliance Quality Improvement Committee, Paul-Schneider-Str. 2, 07747 Jena, Germany

Low quality of care

Finding a way



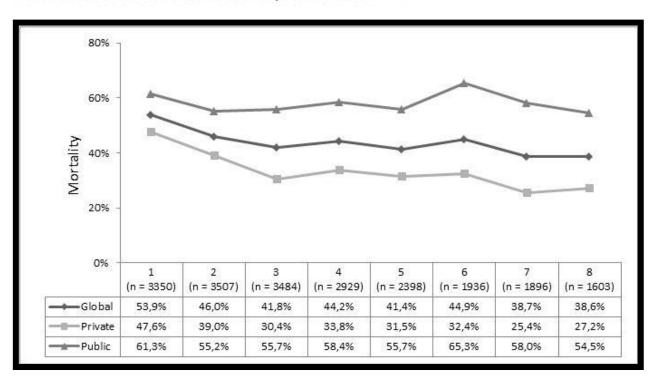




## Inadequate process of care

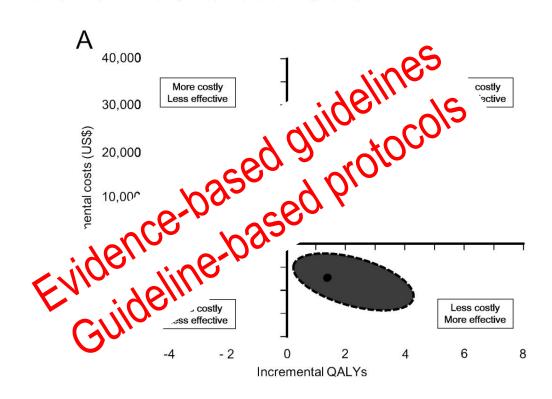
#### Quality Improvement Initiatives in Sepsis in an Emerging Country: Does the Institution's Main Source of Income Influence the Results? An Analysis of 21,103 Patients

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



Danilo Teixeira Noritomi Otavio T. Ranzani Mariana Barbosa Monteiro Elaine Maria Ferreira Sergio Ricardo Santos Fernando Leibel Flavia Ribeiro Machado

Implementation of a multifaceted sepsis education program in an emerging country setting: clinical outcomes and cost-effectiveness in a long-term follow-up study



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)

## Building research capacity

## The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JUNE 30, 2011

VOL. 364 NO. 26

#### Mortality after Fluid Bolus in African Children with Severe Infection

Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group\*

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of an Early Resuscitation Protocol on In-hospital Mortality Among Adults With Sepsis and Hypotension A Randomized Clinical Trial

Health Care for Women International, 35:758–770, 2014 Published with license by Taylor & Francis ISSN: 0739-9332 print / 1096-4665 online DOI: 10.1080/07399332.2014.915843

Routledge
Taylor & Francis Group

Ben Andrews, MD: Matthew W. Semler, MD, MSc; Levy Muchemwa, MBChB; Paul Kelly, MD, FRCP; Shabir Lakhi, MBChB; Douglas C. Heimburger, MD, MS; Chileshe Mabula, MBChB; Mwango Bwalya, MBChB; Gordon R. Bernard, MD

Women's Health in Women's Hands: A Pilot Study Assessing the Feasibility of Providing Women With Medications to Reduce Postpartum Hemorrhage and Sepsis in Rural Tanzania

GAIL C. WEBBER

Department of Family Medicine, University of Ottawa, Ottawa, Ontario, Canada

BWIRE CHIRANGI

Shirati District Hospital, Shirati, Tanzania



Sepsis is (was?) a neglected disease

Join efforts!



## Global Sepsis Alliance









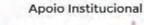




## The solutions: increase partnership



























## The biggest step forward

SEVENTIETH WORLD HEALTH ASSEMBLY

WHA70.7

Agenda item 12.2

29 May 2017

## Improving the prevention, diagnosis and clinical management of sepsis

The Seventieth World Health Assembly,

Having considered the report on improving the prevention, diagnosis and clinical management of sepsis; <sup>1</sup>



Perspective



Recognizing Sepsis as a Global Health Priority — A WHO Resolution

Konrad Reinhart, M.D., Ron Daniels, M.D., Niranjan Kissoon, M.D., Flavia R. Machado, M.D., Ph.D., Raymond D. Schachter, L.L.B., and Simon Finfer, M.D.