Epidemiology of Sepsis & Impact on Vulnerable Populations

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CLINICAL RESEARCH INVESTIGATION AND SYSTEMS MODELING OF ACUTE ILLNESS

TraCS

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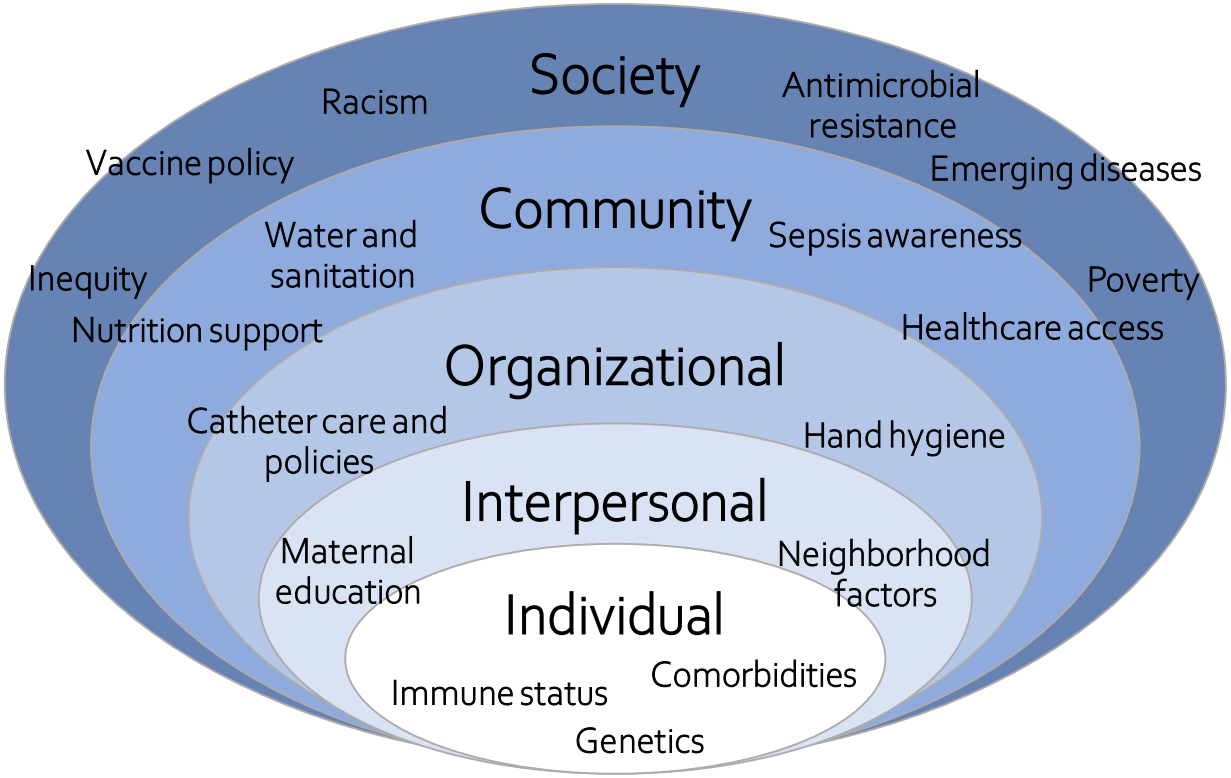
The Public Health Perspective



Articles

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

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Summary

Background Sepsis is life-threatening organ dysfunction due to a dysregulated host response to infection. It is considered a major cause of health loss, but data for the global burden of sepsis are limited. As a syndrome caused by underlying infection, sepsis is not part of standard Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) estimates. Accurate estimates are important to inform and monitor health policy interventions, allocation of resources, and clinical treatment initiatives. We estimated the global, regional, and national incidence of sepsis and mortality from this disorder using data from GBD 2017.

Methods We used multiple cause-of-death data from 109 million individual death records to calculate mortality related to sepsis among each of the 282 underlying causes of death in GBD 2017. The percentage of sepsis-related deaths by underlying GBD cause in each location worldwide was modelled using mixed-effects linear regression. Sepsis-related mortality for each age group, sex, location, GBD cause, and year (1990–2017) was estimated by applying modelled cause-specific fractions to GBD 2017 cause-of-death estimates. We used data for 8·7 million individual hospital records to calculate in-hospital sepsis-associated case-fatality, stratified by underlying GBD cause. In-hospital sepsis-associated case-fatality was modelled for each location using linear regression, and sepsis incidence was estimated by applying modelled case-fatality to sepsis-related mortality estimates.

Findings In 2017, an estimated 48·9 million (95% uncertainty interval [UI] 38·9–62·9) incident cases of sepsis were recorded worldwide and 11·0 million (10·1–12·0) sepsis-related deaths were reported, representing 19·7% (18·2–21·4) of all global deaths. Age-standardised sepsis incidence fell by 37·0% (95% UI 11·8–54·5) and mortality decreased by 52·8% (47·7–57·5) from 1990 to 2017. Sepsis incidence and mortality varied substantially across regions, with the highest burden in sub-Saharan Africa, Oceania, south Asia, east Asia, and southeast Asia.

Interpretation Despite declining age-standardised incidence and mortality, sepsis remains a major cause of health loss worldwide and has an especially high health-related burden in sub-Saharan Africa.

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Introduction

Sepsis is life-threatening organ dysfunction due to a dysregulated host response to infection[1] and is an important global health problem. In the USA, for example, sepsis is the most common cause of in-hospital deaths and costs more than US$24 billion annually.[2,3] Infection-prevention efforts, including those targeting both community-acquired and health-care-associated infections, can reduce sepsis incidence.[4,5] Sepsis is treatable, and timely implementation of targeted interventions improves outcomes.[6–8] The World Health Assembly has urged member states to strengthen efforts to identify, document, prevent, and treat sepsis.[9] Accurate quantification of sepsis incidence and mortality, while important for public health leaders, researchers, and funding agencies, remains a formidable challenge.[10–13]

Most previous estimates of sepsis incidence and mortality have relied on hospital administrative databases, excluding patients who were never admitted to hospital,[14–16] and were restricted to national or subnational locations in a selected group of middle-income or high-income countries.[17–19] A few additional studies have used electronic health record data[20] or death certificates.[21] These studies used various methods, thereby hampering comparability over time or by location.[22] Additionally, many studies were restricted to adults, with a paucity of data for children.[23,24]

The most recent global estimates for sepsis incidence and mortality were based on data for adults admitted to hospital in seven high-income countries[17] and reported 19·4 million sepsis (formerly, severe sepsis) incident cases and 5·3 million sepsis-related deaths annually. No estimates are available for the global incidence of

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Global, Regional, and National Sepsis Incidence and Mortality, 1990–2017: Analysis for the Global Burden of Disease Study

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Global Sepsis Incidence, All Ages, Both Sexes, All Causes, 2017

48.9 million
(95% UI, 38.9-62.9 million)

Incident cases

677.5
(95% UI, 535.7-876.1)

Age-standardized incidence per 100,000 population

Rudd et al., *Lancet* 2020

Global Sepsis Mortality, All Ages, Both Sexes, All Causes, 2017

11.0 million
(95% UI, 10.1-12.0 million)

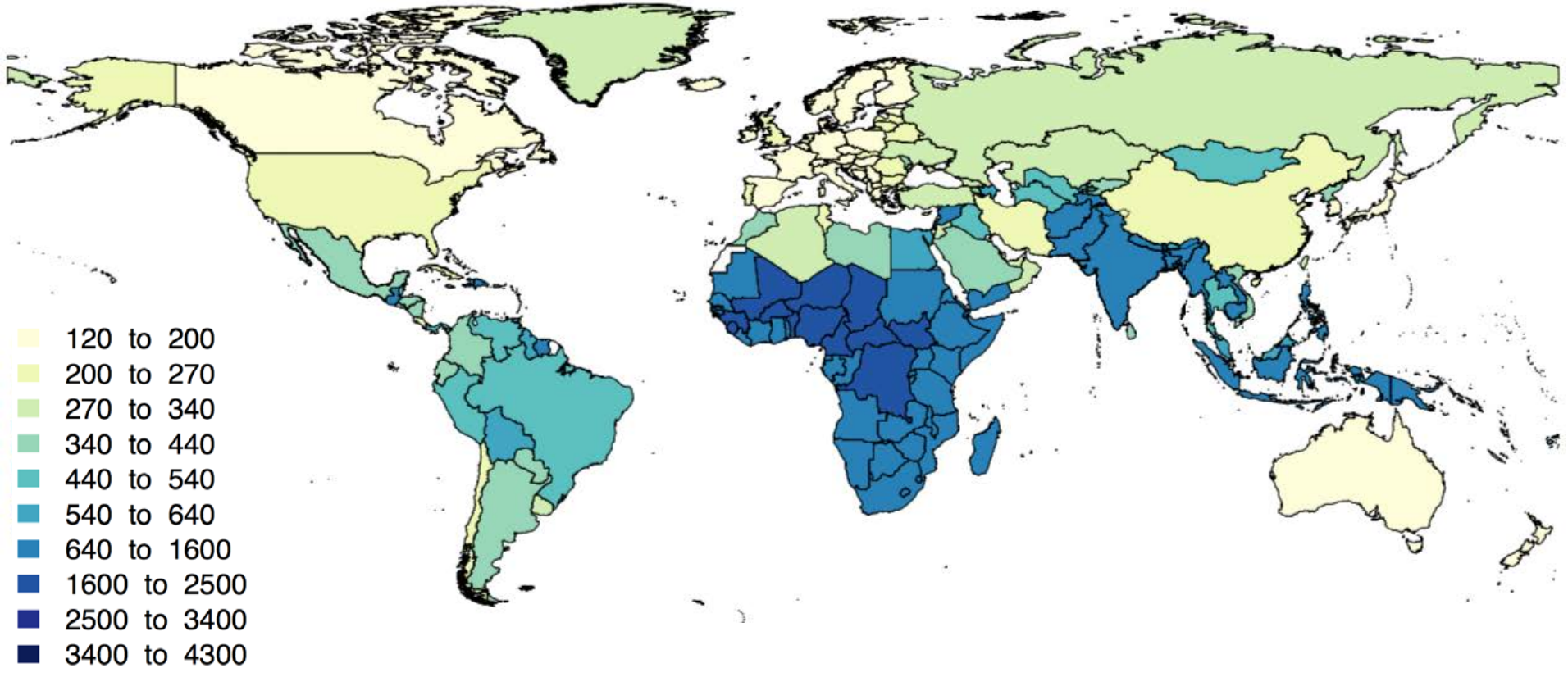
Sepsis-related deaths

148.1
(95% UI, 136.4-161.0)

Age-standardized mortality per 100,000 population

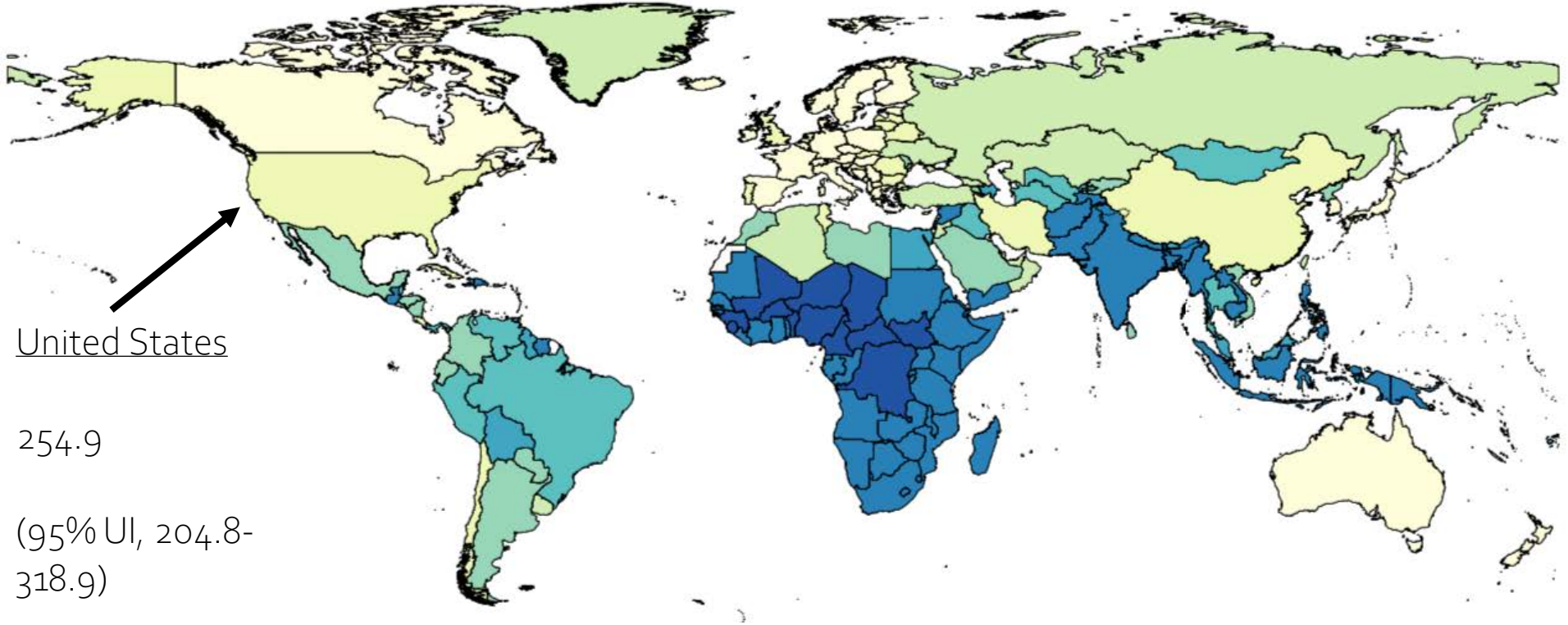
Rudd et al., *Lancet* 2020

Age-Standardized Incidence per 100,000, 2017



Rudd et al., *Lancet* 2020

Age-Standardized Incidence per 100,000, 2017



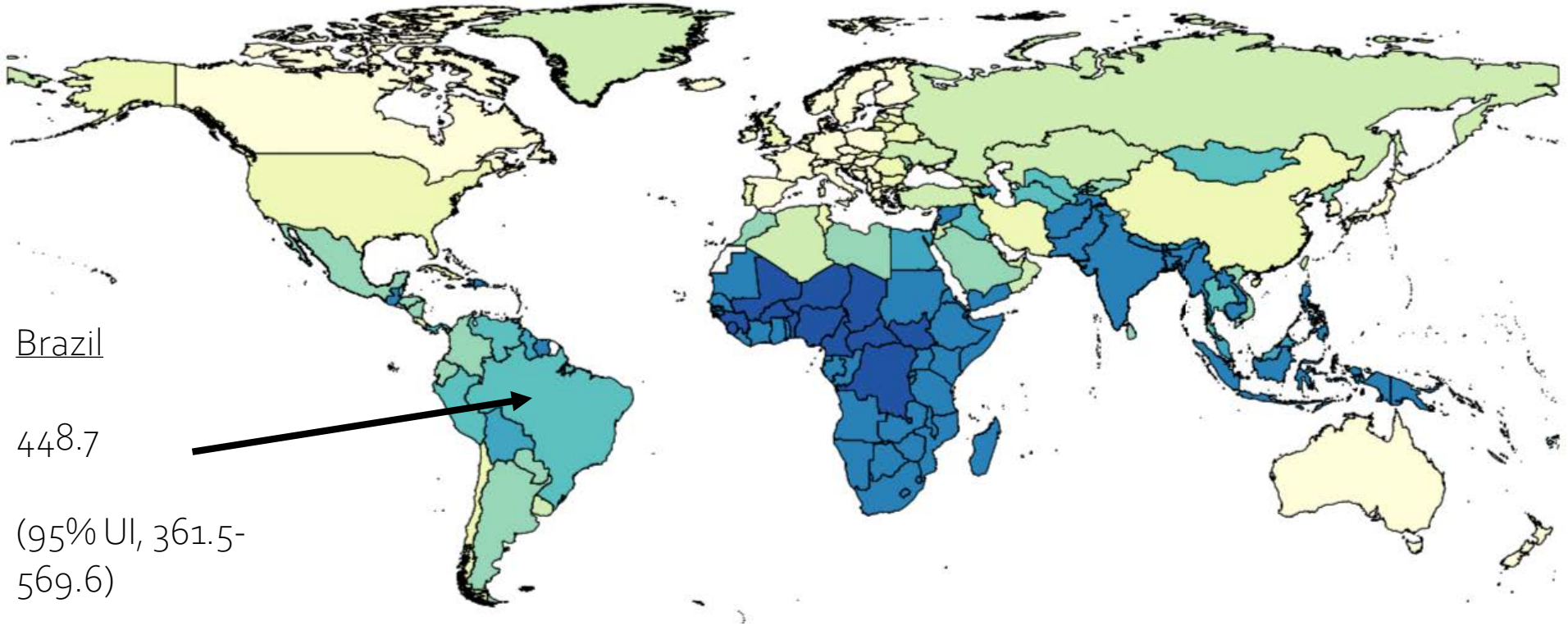
United States

254.9

(95% UI, 204.8-318.9)

Rudd et al., *Lancet* 2020

Age-Standardized Incidence per 100,000, 2017



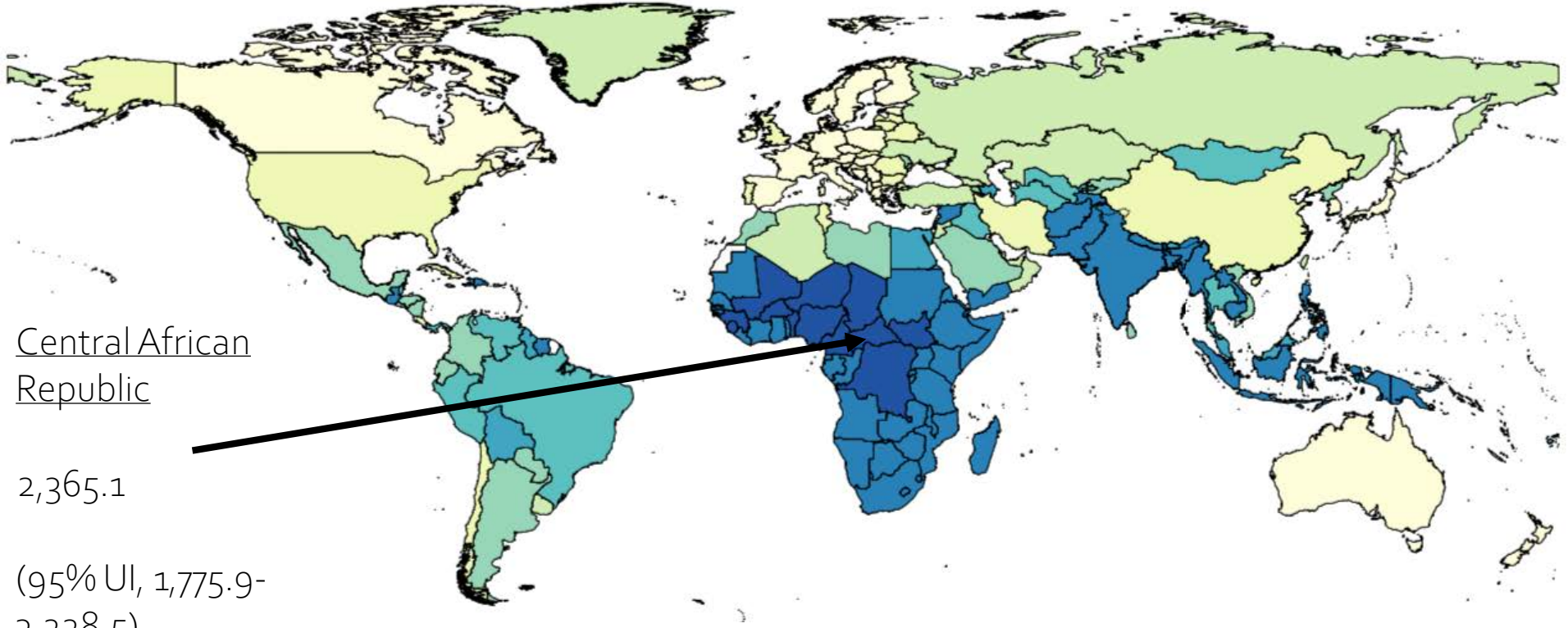
Brazil

448.7

(95% UI, 361.5-569.6)

Rudd et al., *Lancet* 2020

Age-Standardized Incidence per 100,000, 2017



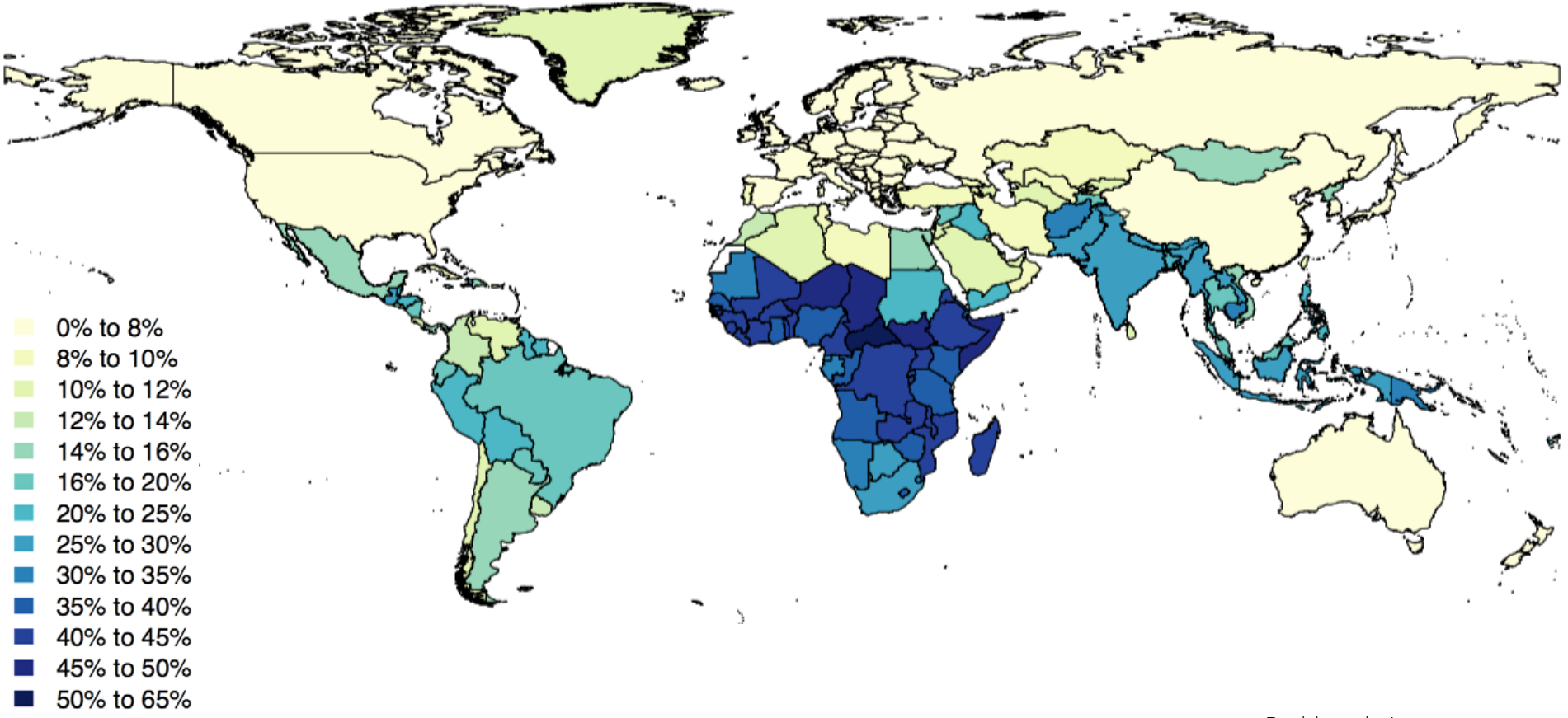
Central African Republic

2,365.1

(95% UI, 1,775.9-3,228.5)

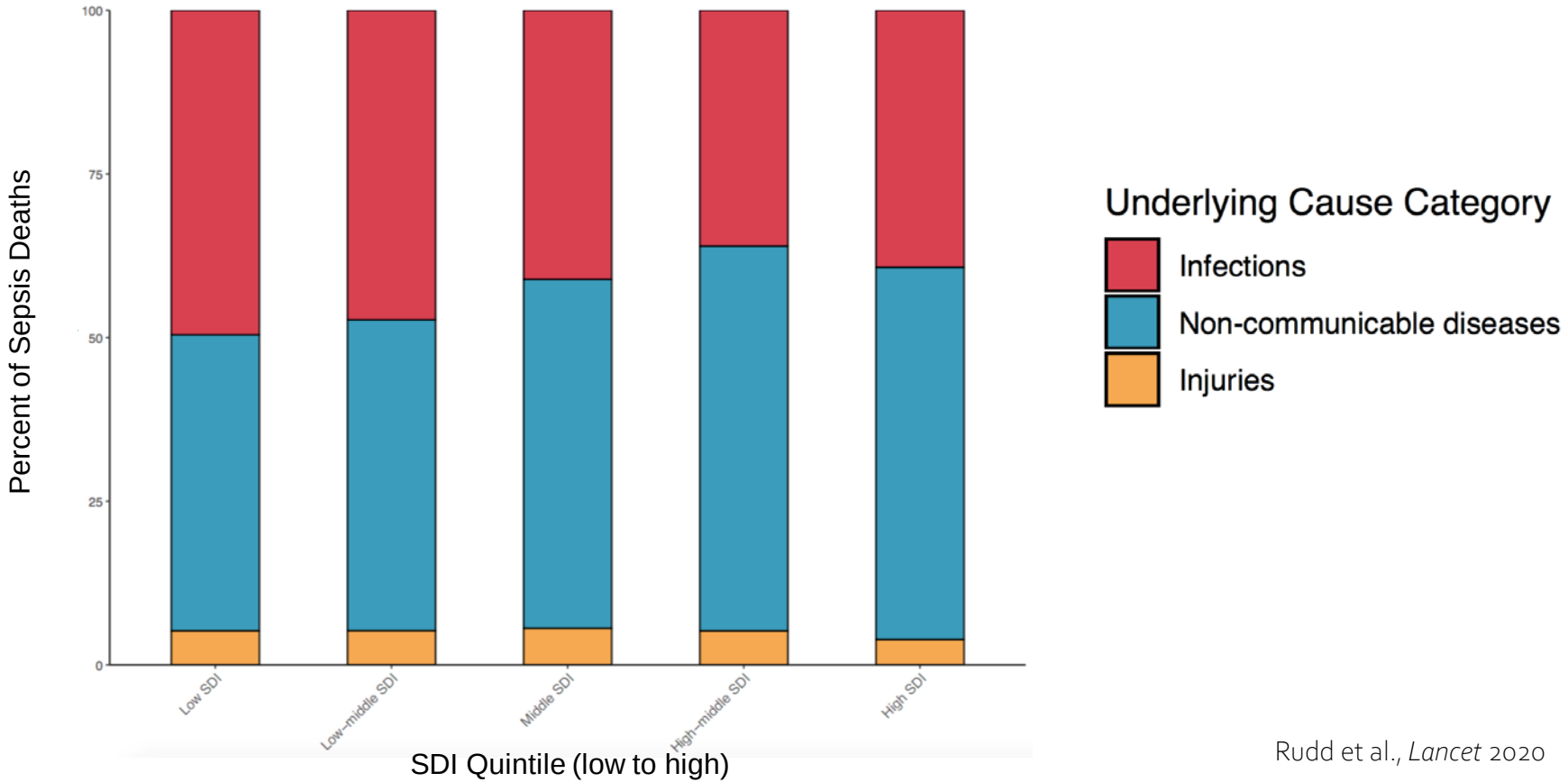
Rudd et al., *Lancet* 2020

Percentage of all Deaths Related to Sepsis, 2017



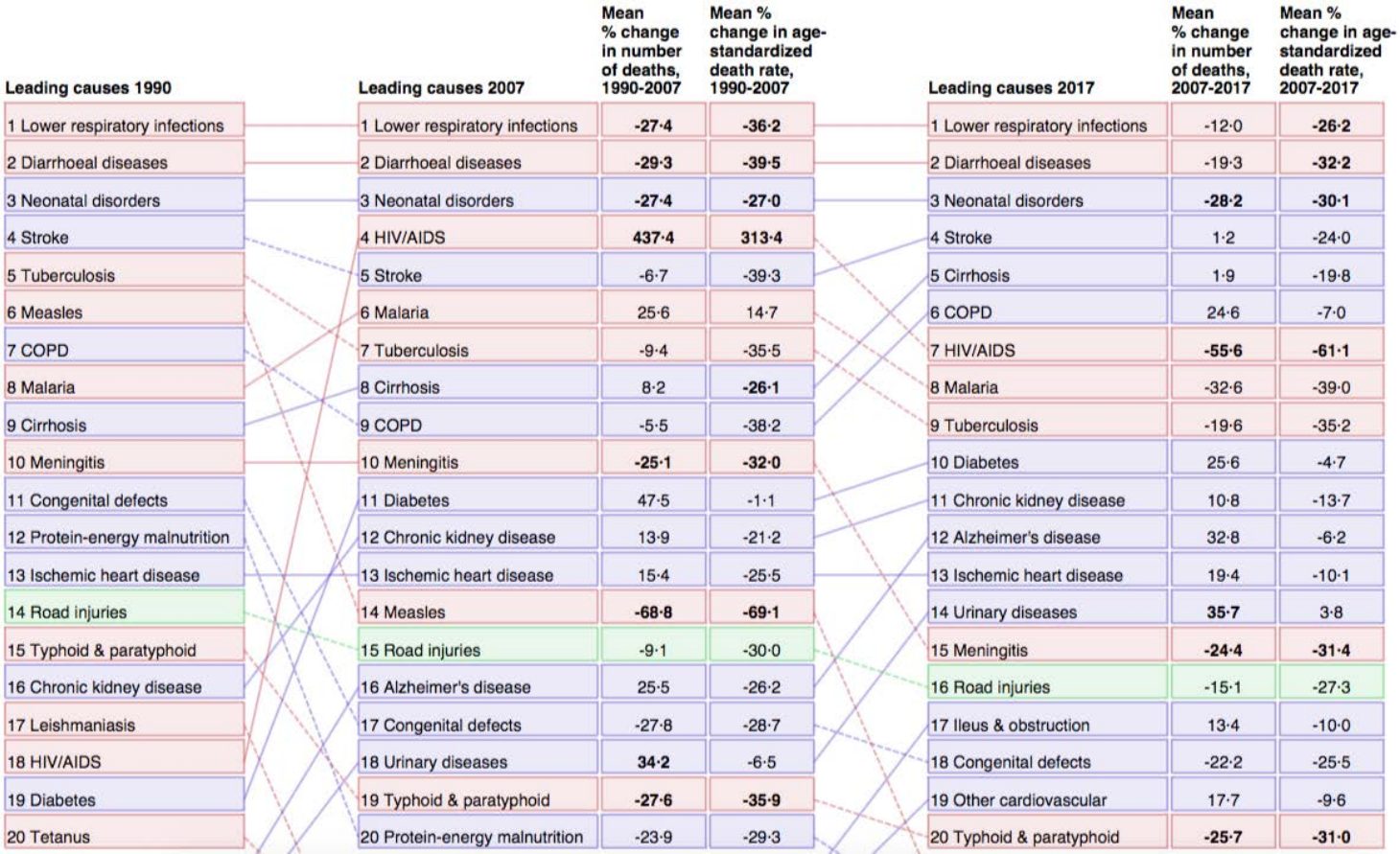
Rudd et al., *Lancet* 2020

Percentage of Sepsis Deaths by Underlying Cause Category and Socio-Demographic Index, 2017



Rudd et al., *Lancet* 2020

Leading Causes of Sepsis-Related Deaths, Both Sexes, All Ages, in 1990, 2007, and 2017



Leading causes 1990	Leading causes 2007	Mean % change in number of deaths, 1990-2007	Mean % change in age-standardized death rate, 1990-2007	Leading causes 2017	Mean % change in number of deaths, 2007-2017	Mean % change in age-standardized death rate, 2007-2017
1 Lower respiratory infections	1 Lower respiratory infections	**-27·4**	**-36·2**	1 Lower respiratory infections	-12·0	**-26·2**
2 Diarrhoeal diseases	2 Diarrhoeal diseases	**-29·3**	**-39·5**	2 Diarrhoeal diseases	-19·3	**-32·2**
3 Neonatal disorders	3 Neonatal disorders	**-27·4**	**-27·0**	3 Neonatal disorders	**-28·2**	**-30·1**
4 Stroke	4 HIV/AIDS	**437·4**	**313·4**	4 Stroke	1·2	-24·0
5 Tuberculosis	5 Stroke	-6·7	-39·3	5 Cirrhosis	1·9	-19·8
6 Measles	6 Malaria	25·6	14·7	6 COPD	24·6	-7·0
7 COPD	7 Tuberculosis	-9·4	-35·5	7 HIV/AIDS	**-55·6**	**-61·1**
8 Malaria	8 Cirrhosis	8·2	**-26·1**	8 Malaria	-32·6	-39·0
9 Cirrhosis	9 COPD	-5·5	-38·2	9 Tuberculosis	-19·6	-35·2
10 Meningitis	10 Meningitis	**-25·1**	**-32·0**	10 Diabetes	25·6	-4·7
11 Congenital defects	11 Diabetes	47·5	-1·1	11 Chronic kidney disease	10·8	-13·7
12 Protein-energy malnutrition	12 Chronic kidney disease	13·9	-21·2	12 Alzheimer's disease	32·8	-6·2
13 Ischemic heart disease	13 Ischemic heart disease	15·4	-25·5	13 Ischemic heart disease	19·4	-10·1
14 Road injuries	14 Measles	**-68·8**	**-69·1**	14 Urinary diseases	**35·7**	3·8
15 Typhoid & paratyphoid	15 Road injuries	-9·1	-30·0	15 Meningitis	**-24·4**	**-31·4**
16 Chronic kidney disease	16 Alzheimer's disease	25·5	-26·2	16 Road injuries	-15·1	-27·3
17 Leishmaniasis	17 Congenital defects	-27·8	-28·7	17 Ileus & obstruction	13·4	-10·0
18 HIV/AIDS	18 Urinary diseases	**34·2**	-6·5	18 Congenital defects	-22·2	-25·5
19 Diabetes	19 Typhoid & paratyphoid	**-27·6**	**-35·9**	19 Other cardiovascular	17·7	-9·6
20 Tetanus	20 Protein-energy malnutrition	-23·9	-29·3	20 Typhoid & paratyphoid	**-25·7**	**-31·0**

- Pneumonia (16.4%)
- Neonatal disorders (8.2%)
- Road injuries (1.3%)

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Incidence and Trends of Sepsis in US Hospitals Using Clinical vs Claims Data, 2009-2014

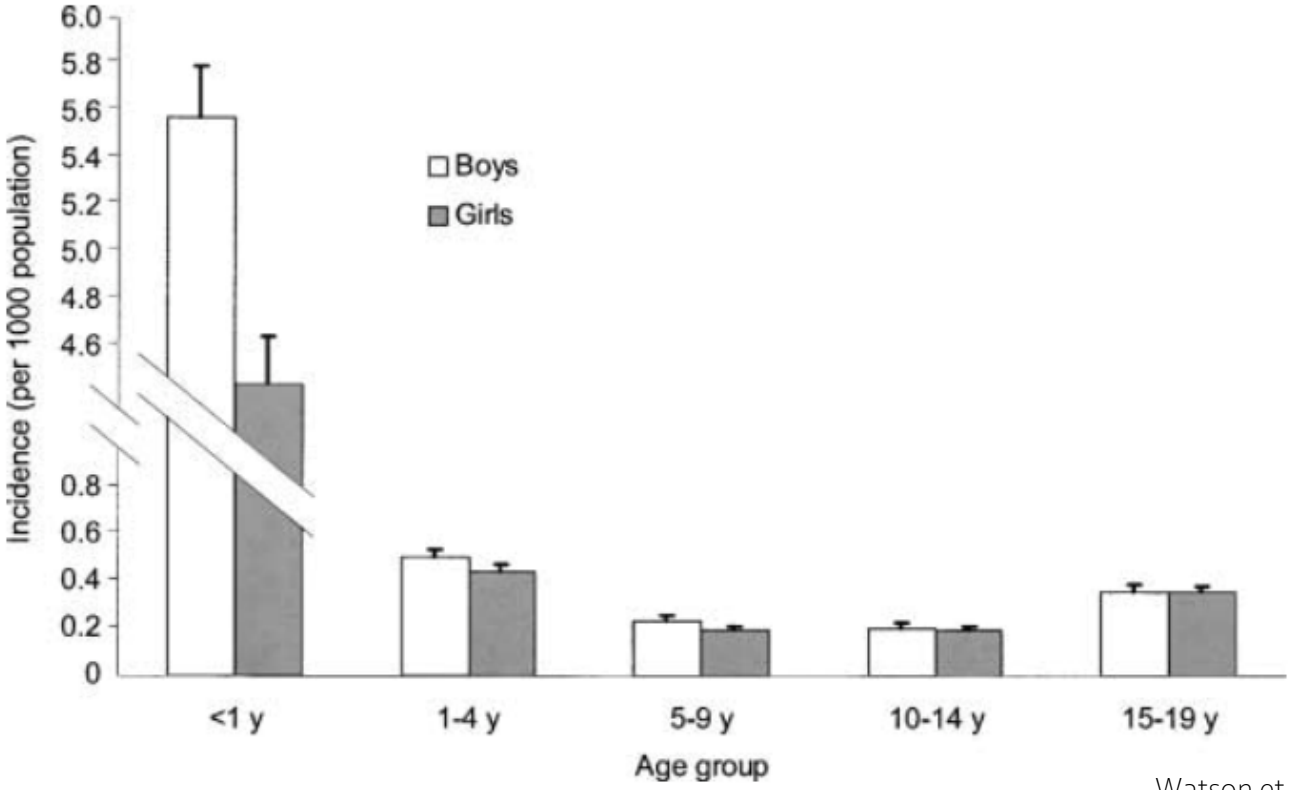
Chanu Rhee, MD, MPH; Raymund Dantes, MD, MPH; Lauren Epstein, MD, MS; David J. Murphy, MD, PhD; Christopher W. Seymour, MD, MSc; Theodore J. Iwashyna, MD, PhD; Sameer S. Kadri, MD, MS; Derek C. Angus, MD, MPH; Robert L. Danner, MD; Anthony E. Fiore, MD, MPH; John A. Jernigan, MD, MS; Greg S. Martin, MD, MSc; Edward Septimus, MD; David K. Warren, MD, MPH; Anita Karcz, MD, MBA; Christina Chan, MPH; John T. Menchaca, BA; Rui Wang, PhD; Susan Gruber, PhD; Michael Klompas, MD, MPH; for the CDC Prevention Epicenter Program

US Adult Incidence 903,000 - 1.7 million

US Adult Mortality 174,000 - 270,000

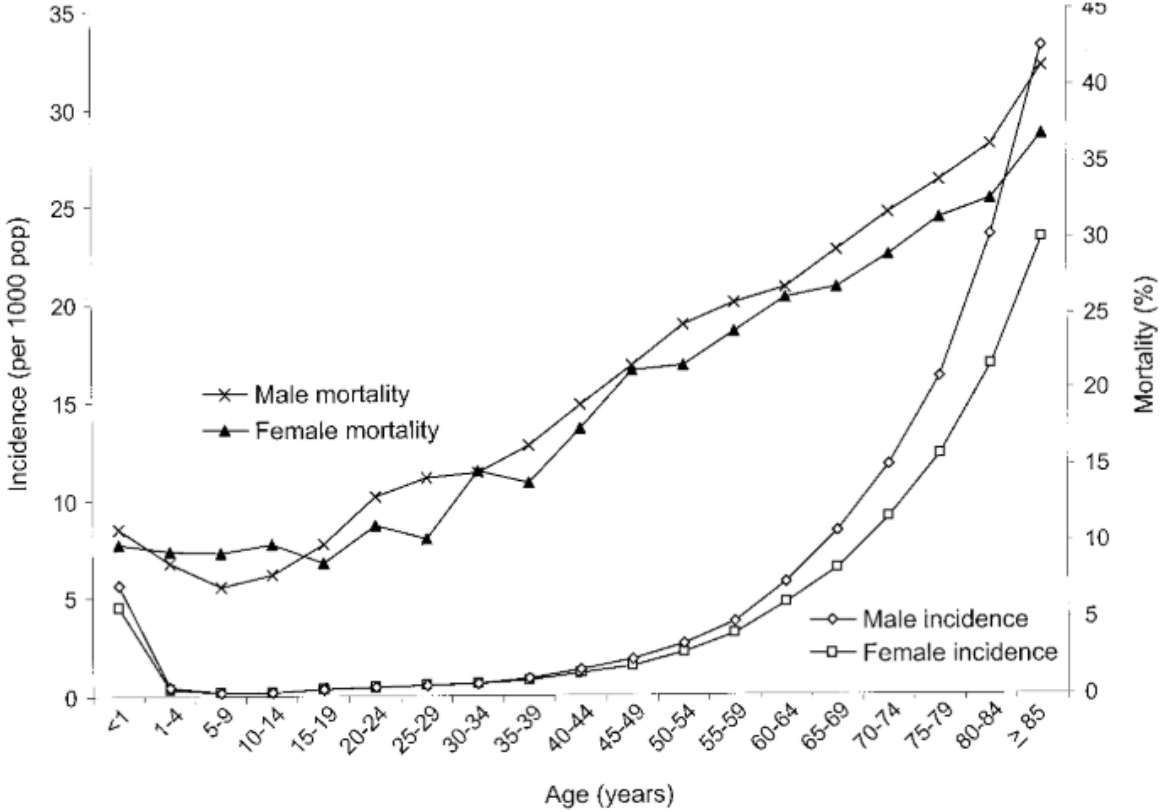
Rudd et al., *Lancet* 2020
Rhee et al., *JAMA* 2017

Incidence of Pediatric Sepsis by Age and Sex, US



Watson et al., *AJRCCM* 2003

Sepsis Incidence and Mortality by Age and Sex, US



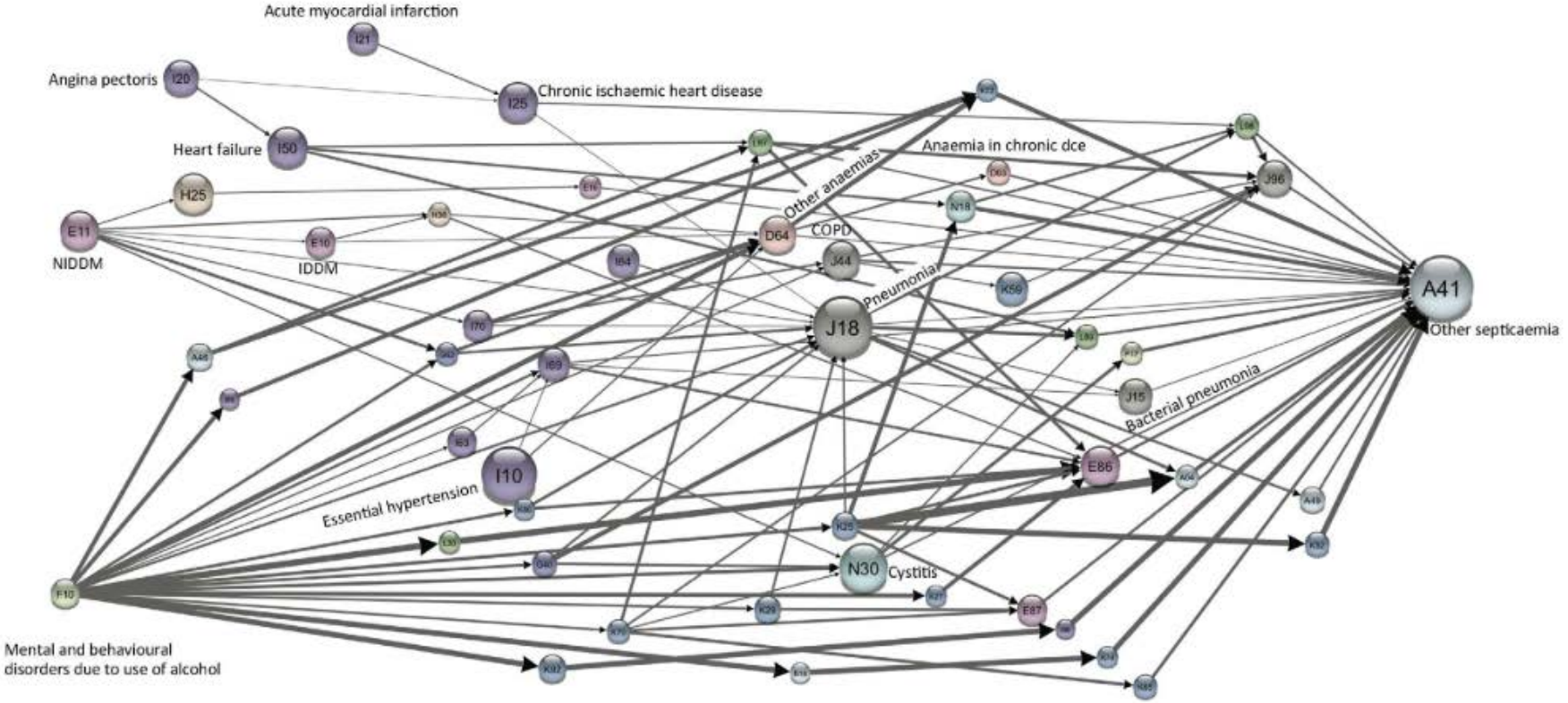
Angus et al., *CCM* 2001

Aging, Frailty, and Inflammation

Characteristic	Clinical Frailty Scale		
	No Frailty ($n = 1,003$)	Frailty ($n = 507$)	p
In-hospital mortality, *n* (%)	294 (29.3)	264 (52.1)	< 0.001
ICU length of stay, d, median (IQR)	4 (2–7)	5 (3–9)	< 0.01
Total hospital length of stay, d, median (IQR)	9 (5–13)	13 (8–17)	< 0.001
Survivors discharged to long-term care, *n* (%)[a]	145 (23.2)	59 (40.1)	< 0.001
Survivors with hospital readmission within 30 d, *n* (%)	144 (20.3)	95 (39.0)	< 0.001

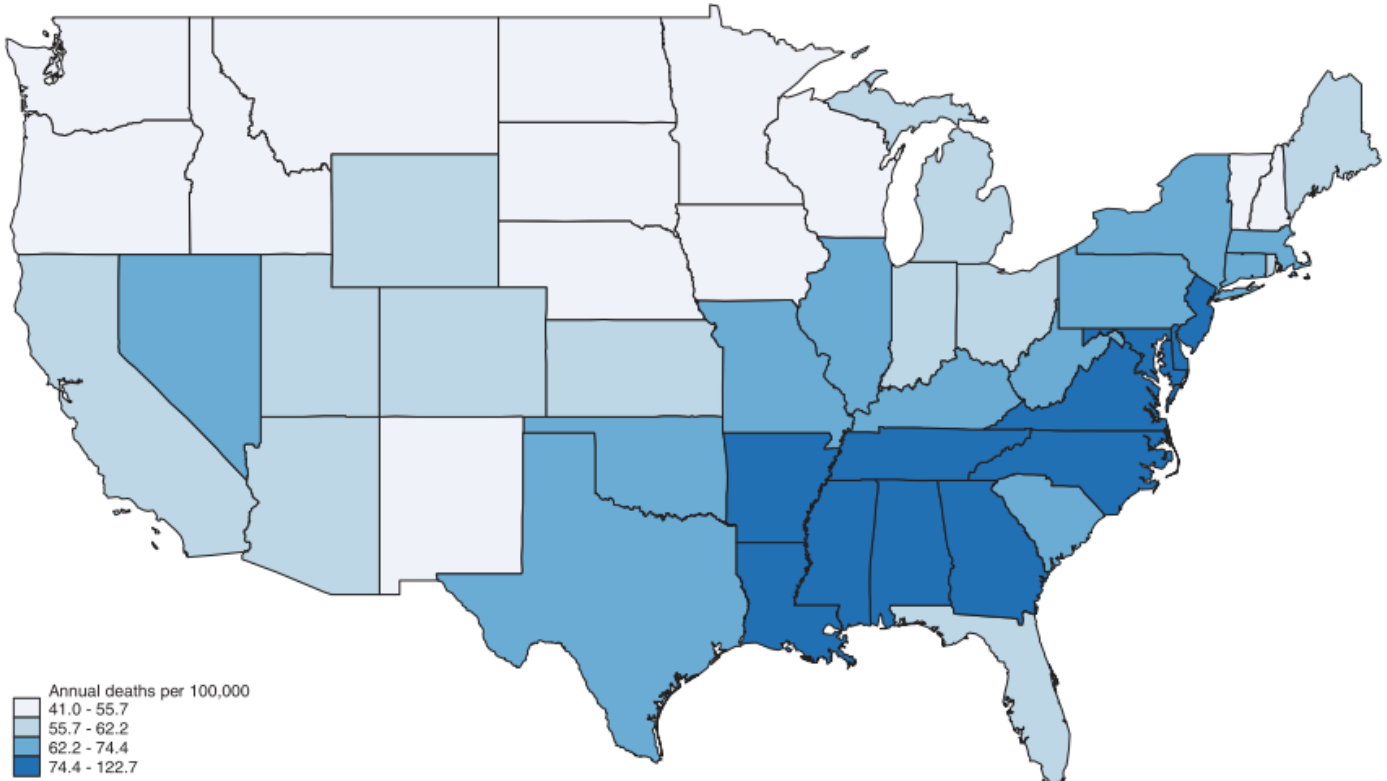
Fernando et al., *CCM* 2019

Multimorbidity is a Major Sepsis Risk Factor



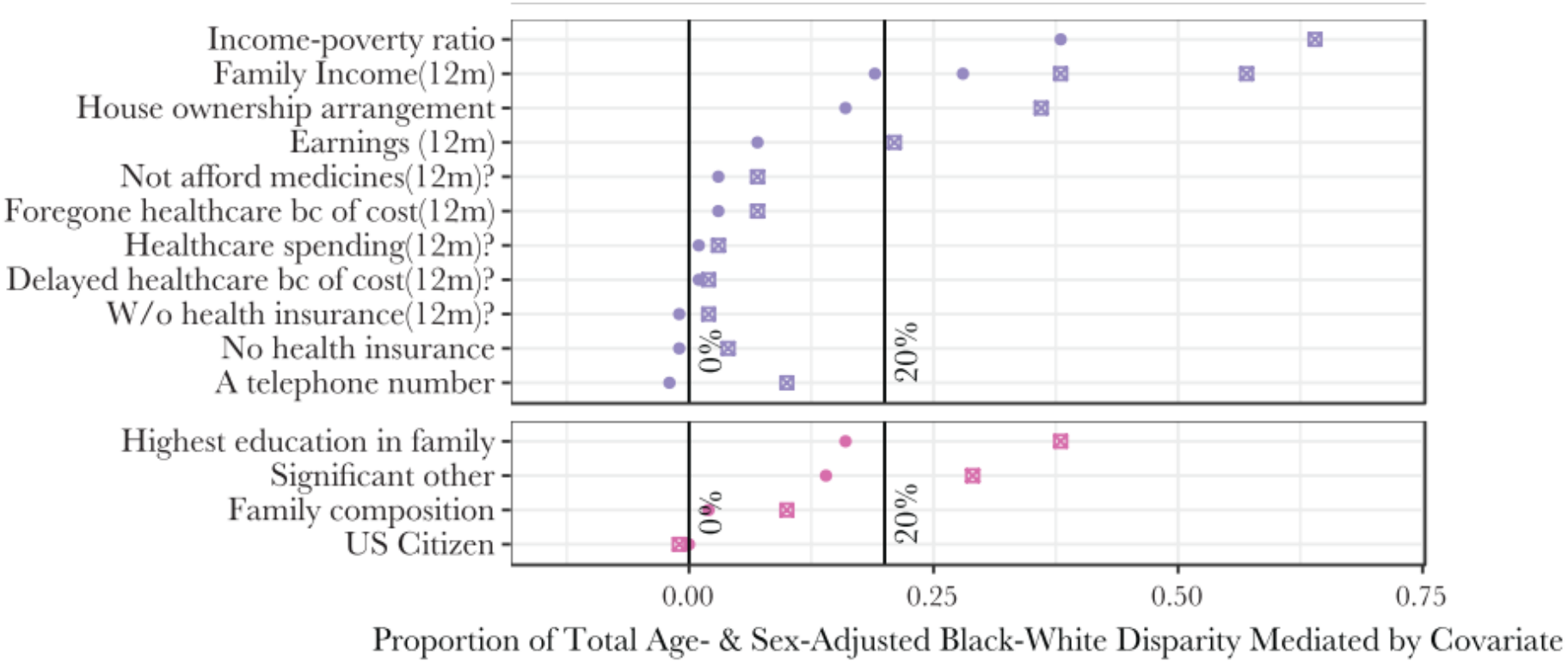
Beck et al., *Sci Rep* 2016

Sepsis Clusters Geographically in Medically Underserved Areas



Goodwin et al., *Chest* 2016
Wang et al., *Int. J Health Geogr* 2010

Social Risk Factors



Kempker et al., *Open Forum Infect Dis* 2018

Conclusions

- Significant disparities by location and healthcare access and quality
- Neonates are high-risk age group
- Among adults in the US, aging, frailty, and multimorbidity are major risk factors
- Over half of all sepsis-related deaths among patients with underlying chronic diseases or injuries
- Social disparities linked to sepsis incidence and mortality