

SEPSIS

A Public Health Challenge

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COI Disclosures

Djillali Annane

No financial disclosure

Member of the Sepsis 3 Task Force

Member of the SSC panel for 2008; 2012 and 2016 updates

Commissioned by the Ministry of Health and Prevention for national implementation of WHO recommendations about sepsis

Definition

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

Singer et al, Jama 2016

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

The Sepsis Definitions Task Force

The Definition of Sepsis

Sepsis is life-threatening *organ dysfunction* caused by a dysregulated host response to infection

The Definition of Sepsis

Sepsis is life-threatening organ dysfunction caused by a *dysregulated host response* to infection

As opposed to the
“regulated host response”
that characterizes the non-septic response to infection

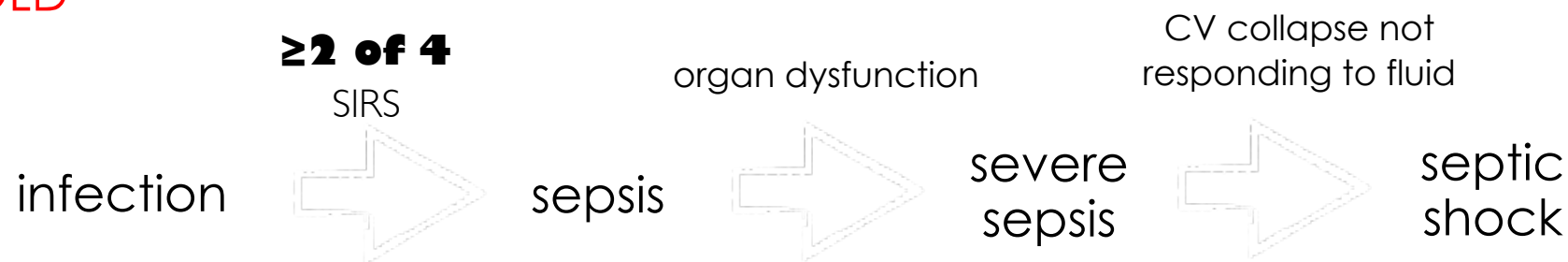
The Definition of Septic Shock

- What tangibly differentiates septic shock from sepsis ?
 - MORTALITY
 - Septic shock is “really bad” sepsis

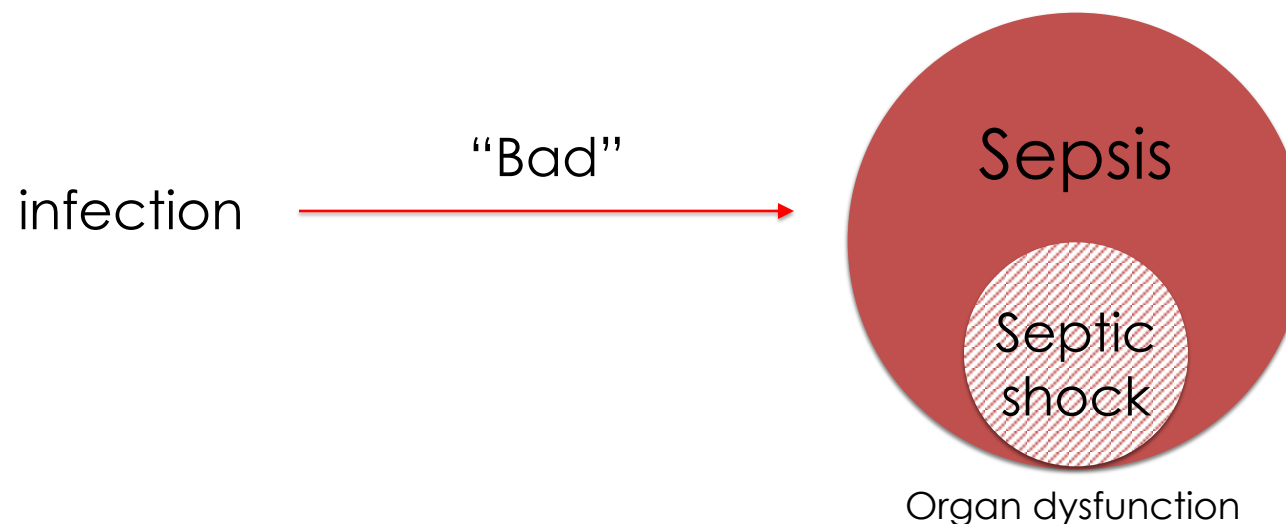
Septic shock is a subset of sepsis in which profound circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone

Conceptual changes

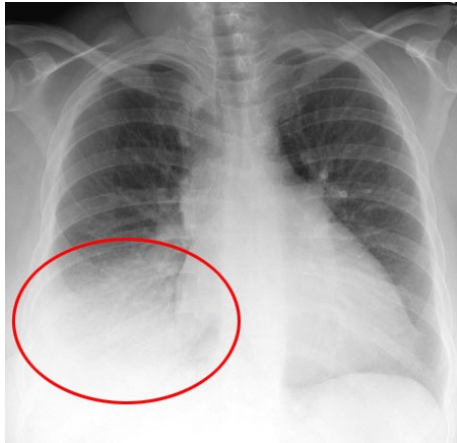
OLD



NEW



Definition



Infection

- **Sepsis:** Life-threatening organ dysfunction caused by dysregulated host response to infection
- **Septic Shock:** Subset of sepsis with circulatory and cellular/metabolic dysfunction associated with higher risk of mortality



SOFA > 2

LACTATE > 2
VASOPRESSOR

JAMA. 2016

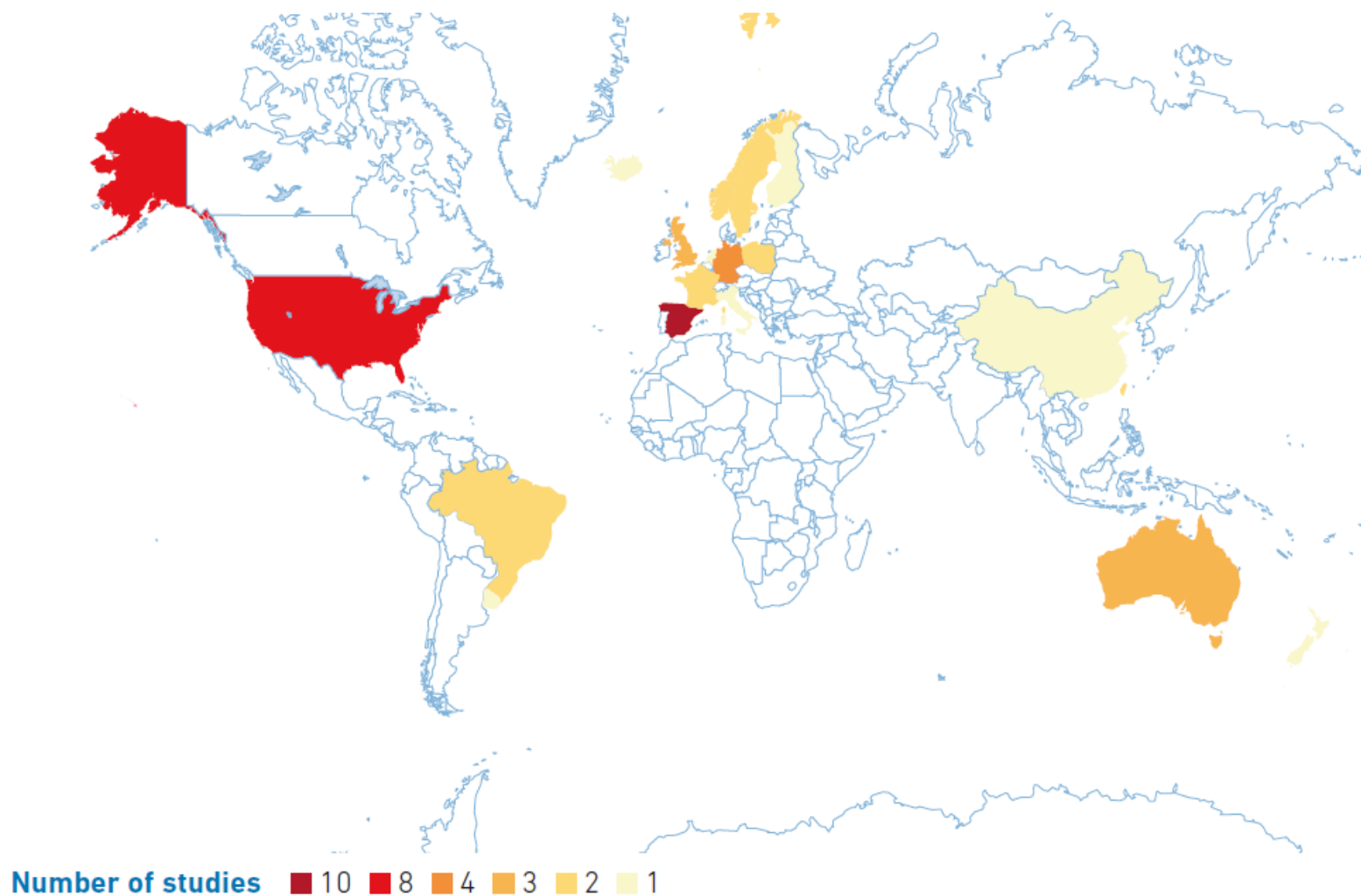
Sepsis Burden

GLOBAL REPORT ON THE EPIDEMIOLOGY AND BURDEN OF SEPSIS

World Health Organization · 2020

Sepsis is the final common pathway to death for severe infectious diseases, including bacterial bloodstream infections, diarrhoeal disease, lower respiratory tract infections, malaria, dengue, and systemic fungal infections.

Figure 2.1.1 Country-level coverage of studies on sepsis incidence.



Source: Reproduced from reference (11). Published under the CC BY 4.0 licence (<https://creativecommons.org/licenses/by/4.0/>).

Table 1 Summary findings of the systematic review and meta-analysis of the literature on the incidence of hospital-treated sepsis.

WHO regions (number of studies on sepsis incidence/mortality)	Incidence per 100.000 population [95% confidence interval]	Mortality % [95% confidence interval]
Hospital-treated sepsis		
All regions (AMR, EUR, WPR; n= 28/22)	189 [133, 267]	26.7 [22.9, 30.7]
AMR (n= 9/6)	124 [78, 197]	30.1 [25.1, 35.6]
EUR (n= 13/12)	289 [166, 504]	22.1 [16.7, 28.7]
WPR (n= 6/4)	245 [124, 485]	24.3 [17.2, 33.1]
ICU-treated sepsis		
All regions (AFR, AMR, EUR, WPR; n= 34/19)	58 [42, 81]	41.9 [36.2, 47.7]
AFR (n= 1/1)	52 [39, 71]	40.4 [34.9, 46.2]
AMR (n= 5/4)	2 [0, 6]	76.0 [58.5, 87.7]
EUR (n= 21/11)	139 [75, 256]	42.7 [33.7, 52.2]
WPR (n= 7/3)	72 [43, 120]	34.6 [25.4, 45.2]

Note: numbers in brackets represent 95% confidence intervals. This table has been produced by WHO based on data included in reference 11.

ICU: intensive care unit; AFR: African Region; AMR: Region of the Americas; EUR: European Region; WPR: Western Pacific Region.

Sepsis worldwide in 2017

48.9 million

cases of sepsis

11 million

sepsis-related deaths

20%

of all global deaths

Age specific burden

Sepsis incidence in 2017 and children

Sepsis incidence was biphasic; it peaked in early childhood and again in elderly adults.

41.5% (20.3 million)
of incident sepsis cases

26.4% (2.9 million)
deaths related to sepsis

children younger than 5 years

Mortality due to severe neonatal infections

24%

of neonatal deaths are caused by severe neonatal infections (including sepsis)

Geographical specific burden

Sepsis regional and economic disparities

85.0% of sepsis cases and 84.8% of sepsis related deaths occurred in countries with low, low-middle, or middle sociodemographic indices, particularly in sub-Saharan Africa and South-East Asia.

Sepsis and maternity

For every 1000 live births

70 women

had a suspected or confirmed maternal infection requiring hospital management

11 women

presented with severe maternal outcomes

Infection was the underlying cause or contributing cause in over one-half of the intra-hospital maternal deaths

Regional disparities in intra-hospital maternal infection

Maternal infection

UMICs:

106 per 1000 live births

HICs:

39 per 1000 live births

Infection-related SMO

LMICs:

12 to 155 per 1000 live births

HICs:

0.6 per 1000 live births

Intra-hospital case fatality rates with infection-related SMO (6.8%)

LICs:

14.8%

LMICs:

7%

UMICs:

1.1%

UMICs: upper-middle-income countries; HICs: high-income countries; LMICs: low- and middle-income countries; LICs: low-income countries; SMO: severe maternal outcome.

Hospital-acquired sepsis cases

1 in 4 cases of sepsis were acquired in the hospital

Patients with hospital-acquired sepsis had a longer length of stay and high AMR rates, which can significantly impact on patient outcomes.

Sepsis in intensive care units (ICUs)

24.4% of cases of sepsis with organ dysfunction were acquired during ICU stay

48.7% had a hospital origin

Sepsis and mortality

24.4% mortality of patients with HA-sepsis

52.3% mortality among ICU-treated patients with HA-sepsis

2x to 3x higher median length of stay of patients with HA-sepsis compared to community-acquired sepsis

Up to one third of HA-sepsis cases were caused by drug-resistant bacteria

Fig. 2.1.2 Age-standardized sepsis incidence per 100 000 population for both sexes in 2017 (A), and percentage of all deaths related to sepsis, age-standardized for both sexes, in 2017 (B).

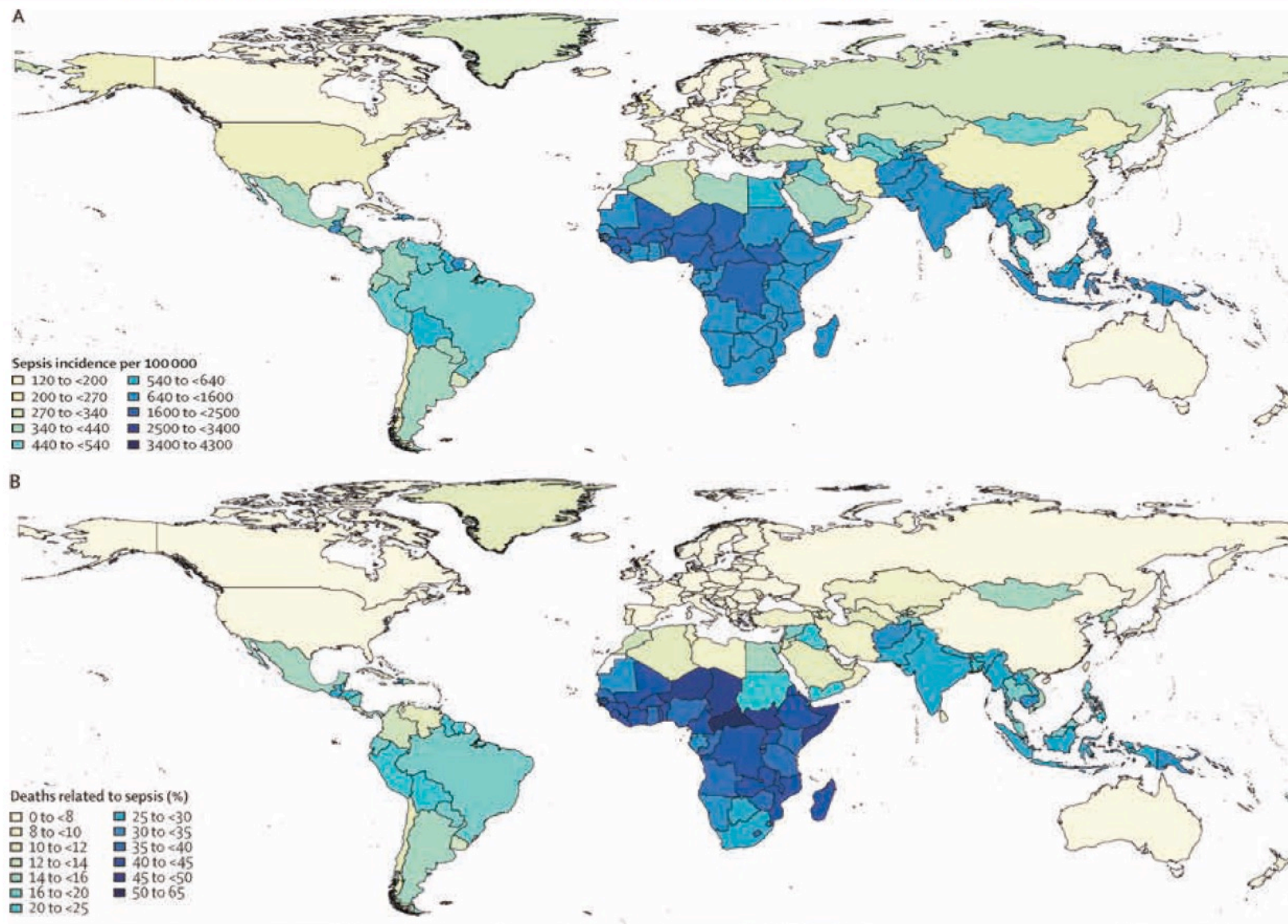
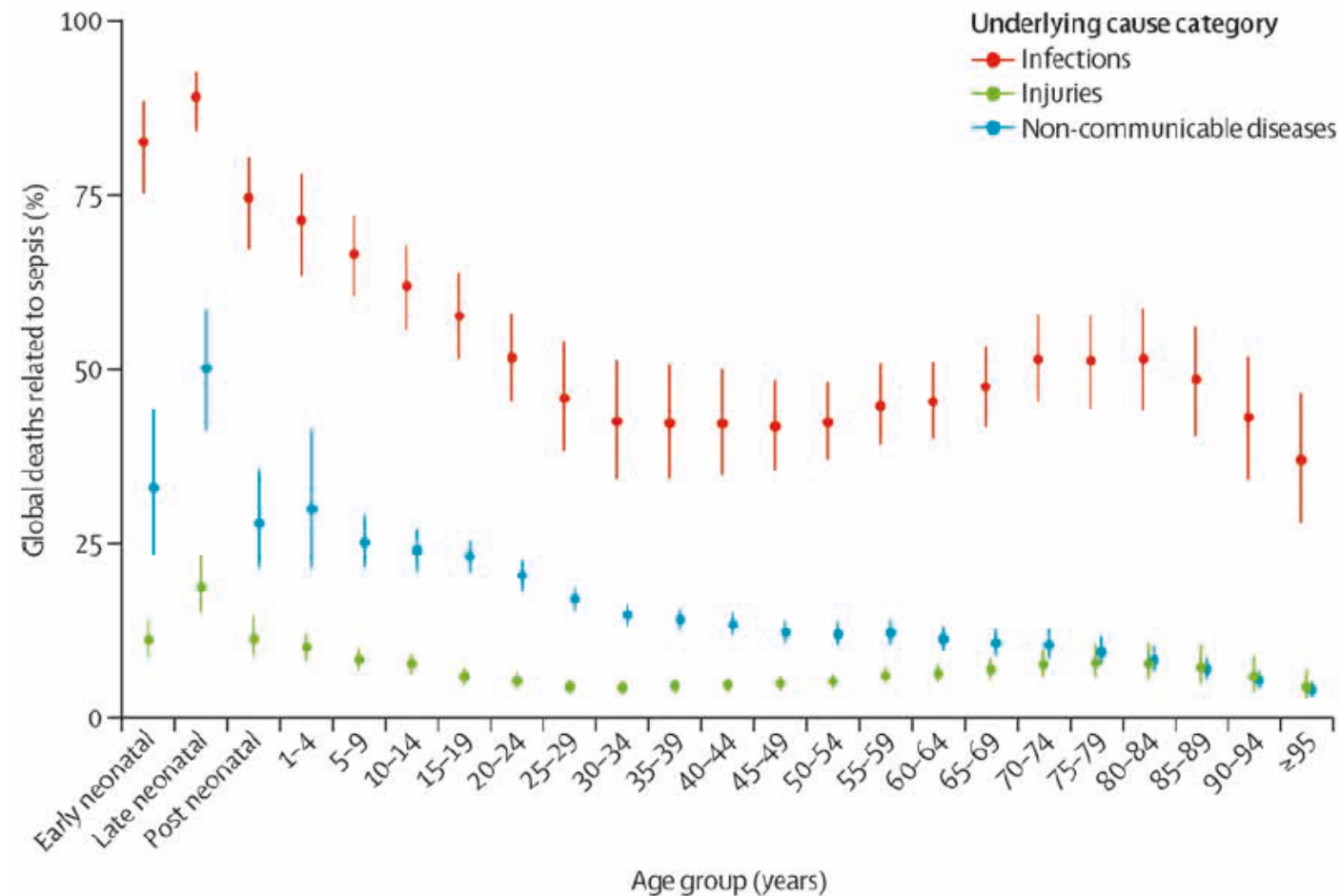


Fig. 2.1.3 The percentage of all global deaths (from any cause) related to sepsis in each underlying cause category in 2017, by age group and for both sexes.



Note: Bars represent 95% uncertainty intervals.

Source: Reproduced from reference (4). Published under the CC BY 4.0 licence (<https://creativecommons.org/licenses/by/4.0/>).

Sepsis contributors (2017)

Diarrhoeal diseases:
caused 9.2 million cases of sepsis.

Lower respiratory infections:
caused 1.8 million deaths due to sepsis.

Focus on France

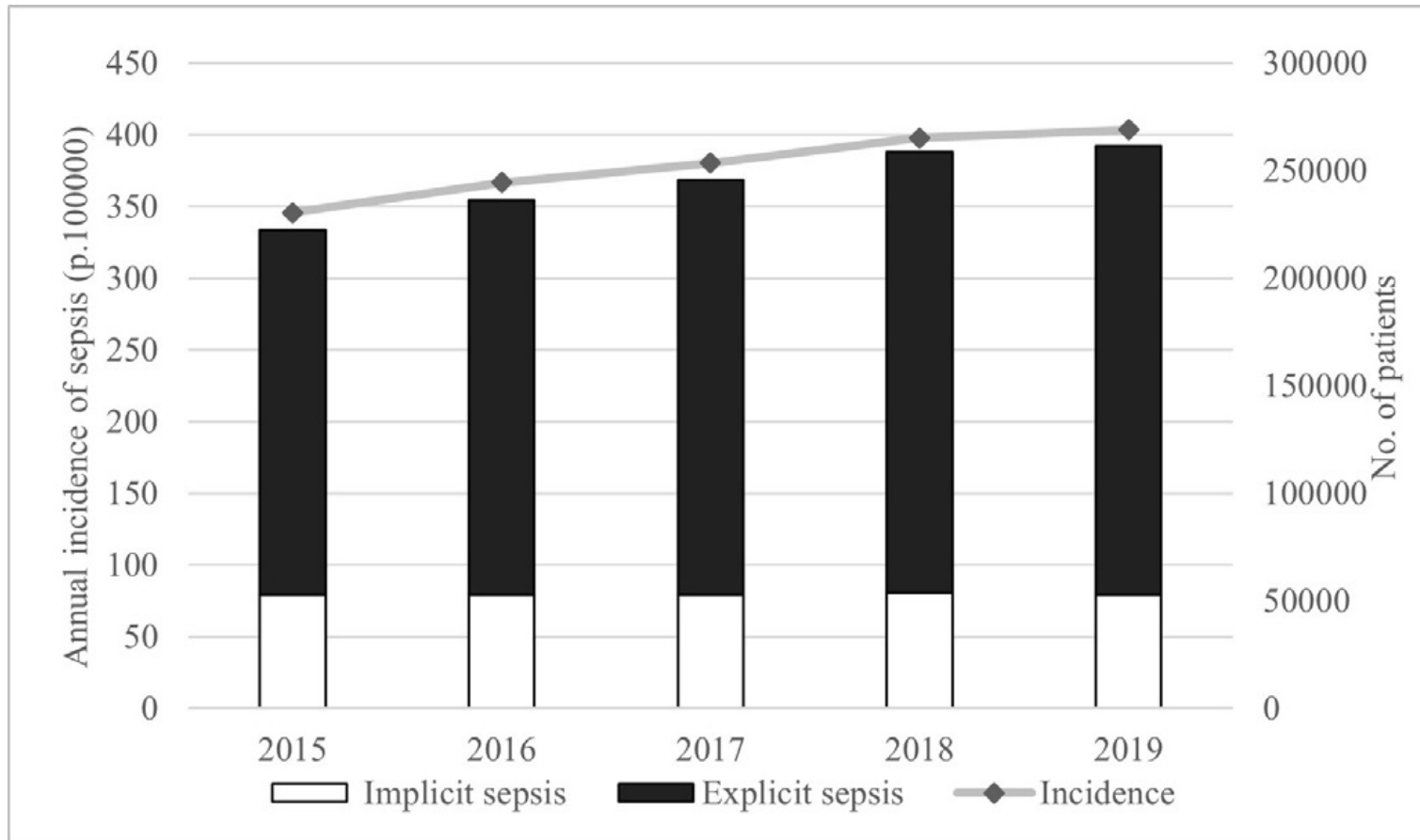


Figure 1 Sepsis incidence per 100 000 inhabitants and number of cases between 2015 and 2019 in metropolitan France.

Focus on France

Table 3 Characteristics of hospital stays with sepsis, France 2015–2019

Variables	2015 (n=222 232)	2016 (n=236 314)	2017 (n=245 780)	2018 (n=258 608)	2019 (n=261 499)
Admission source, n (%)					
Home	194 616 (87.6)	202 500 (85.7)	210 221 (85.5)	221 543 (85.7)	223 879 (85.6)
Acute care*	22 651 (10.2)	28 743 (12.2)	30 312 (12.3)	31 483 (12.2)	32 093 (12.3)
Long-term care†	4965 (2.2)	5071 (2.2)	5247 (2.1)	5582 (2.2)	5527 (2.1)
Length of stay (days), n (%)					
<7	53 135 (23.9)	58 561 (24.8)	61 192 (24.9)	68 677 (24.6)	69 367 (24.9)
7–14	65 184 (29.3)	70 842 (30.0)	75 365 (30.7)	89 195 (32.0)	89 297 (32.0)
15–30	62 373 (28.1)	65 549 (27.7)	67 988 (27.7)	78 123 (28.0)	77 442 (27.8)
>30	41 540 (18.7)	41 362 (17.5)	41 235 (16.8)	43 187 (15.4)	42 771 (15.3)
Length of stay, median (P10–P90)	13 (3–43)	13 (3–41)	13 (3–41)	13 (3–40)	12 (3–39)
Septic shock‡, n (%)					
Yes	50 145 (22.6)	49 948 (21.1)	51 964 (21.1)	53 635 (20.7)	54 145 (20.7)
No	172 087 (77.4)	186 366 (78.9)	193 816 (78.9)	204 973 (79.3)	207 354 (79.3)
ICU admission§, n (%)					
Yes	130 587 (58.8)	134 181 (56.8)	137 025 (55.8)	142 001 (54.9)	141 685 (54.2)
No	91 645 (41.2)	102 133 (43.2)	108 755 (44.3)	116 607 (45.1)	119 814 (45.8)
Hospital discharge, n (%)					
Home	106 133 (47.8)	113 812 (48.2)	119 069 (48.5)	127 894 (49.5)	130 250 (49.8)
Acute care*	25 992 (11.7)	29 436 (12.5)	30 904 (12.6)	31 329 (12.1)	30 784 (11.8)
Long-term care†	33 035 (14.9)	34 958 (14.8)	36 198 (14.7)	38 010 (14.7)	38 891 (14.9)
Death	57 072 (25.7)	58 108 (24.6)	59 609 (24.3)	61 375 (23.7)	61 574 (23.6)

*Acute care unit in medicine, surgery or obstetrics or psychiatry unit.

†Follow-up and rehabilitation care unit, long-term care unit or home care.

‡10th revision of the International Classification of Diseases (ICD-10) codes R57.2 and R57.8 as the primary diagnosis, related diagnosis or significant associated diagnosis.

§Including implicit sepsis for which ICU admission is part of the selection criteria.

ICU, intensive care unit.

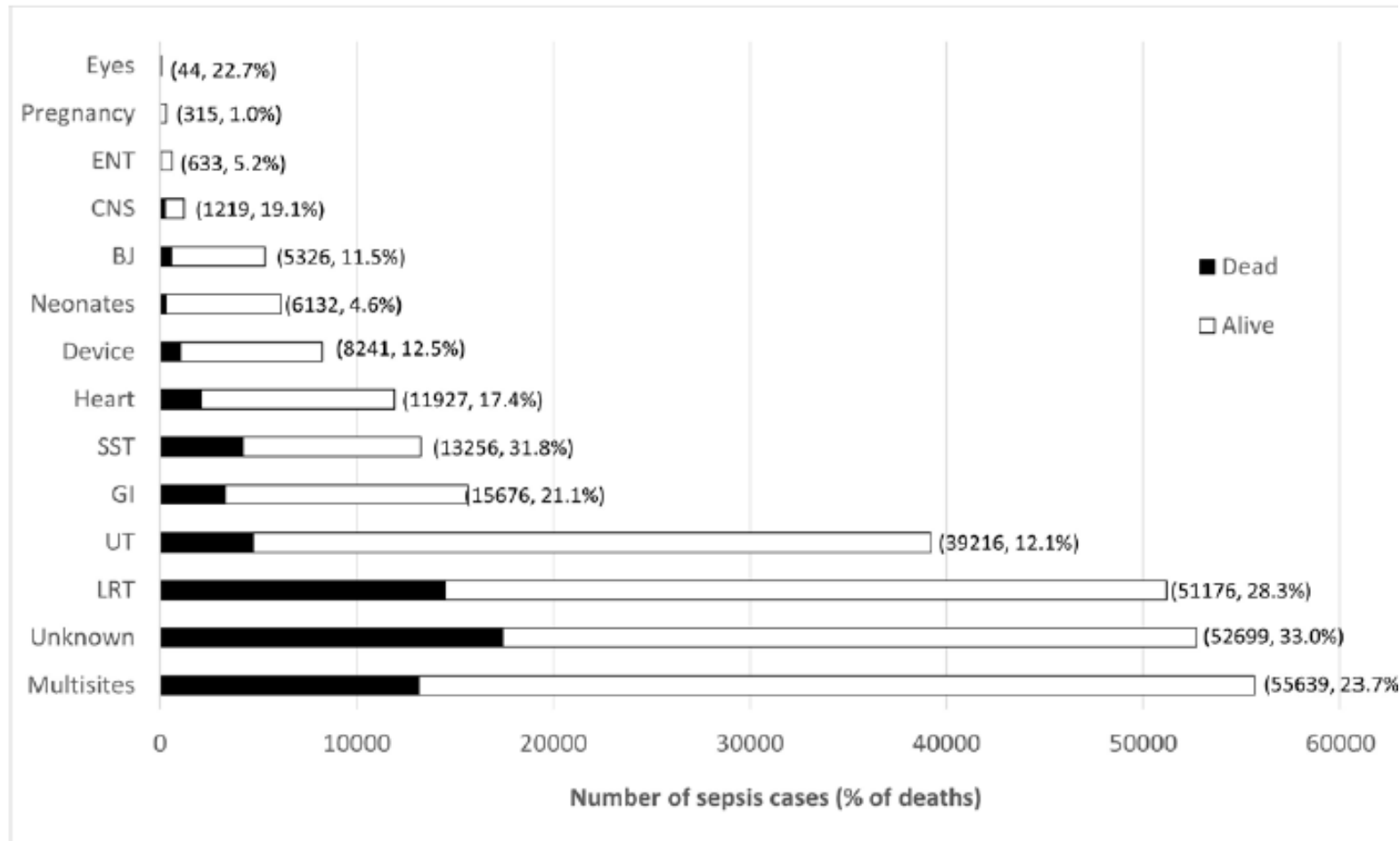
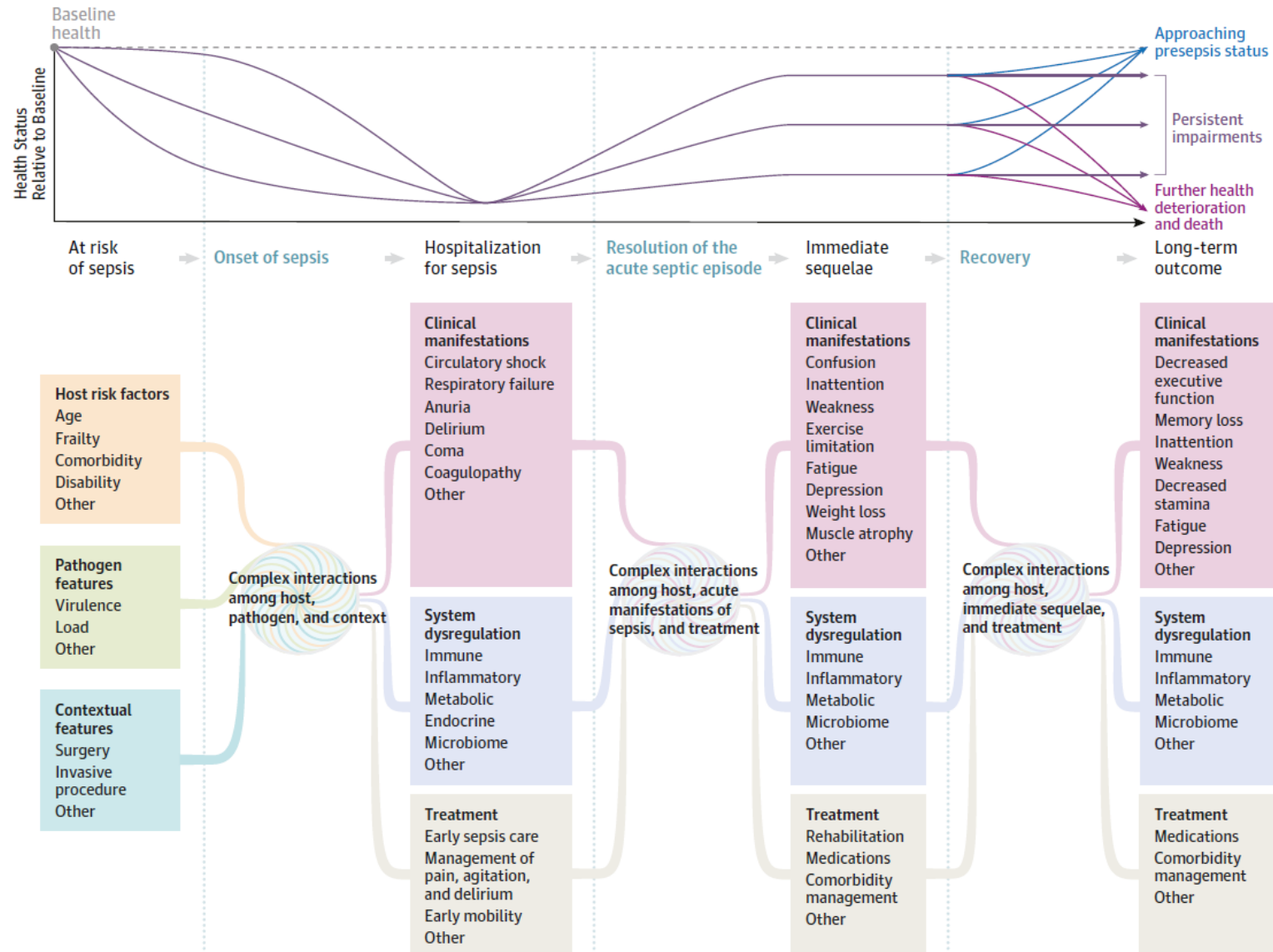


Figure 2 Number of patients with sepsis in 2019 and the associated percentage of in-hospital deaths by infection, n

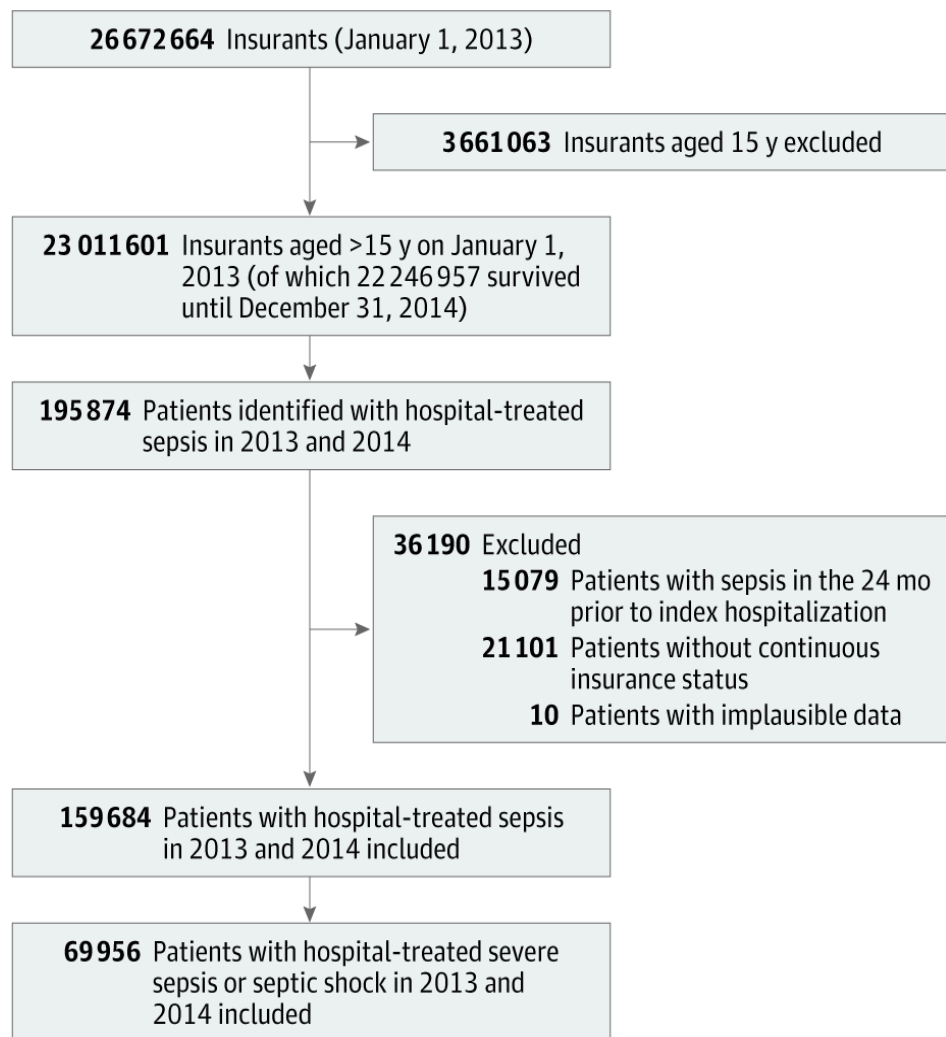
Mid and Long-term consequences

Sepsis survivors		
One third	One sixth	40%
die within one year	experience significant morbidity, such as functional limitations	are re-hospitalized within 90 days of discharge

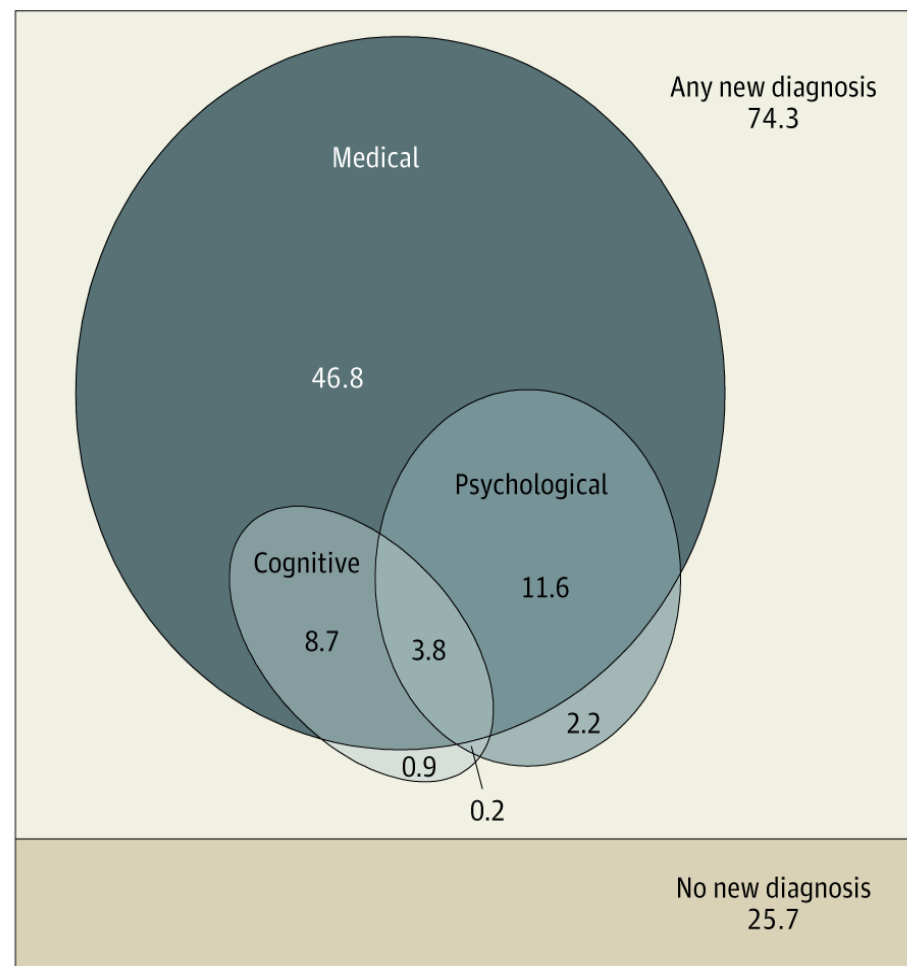
Fig. 2.1.4 A conceptual model of the potential network of factors and interactions important to determining a patient's clinical course and long-term outcome after sepsis.



A Flow of cohort

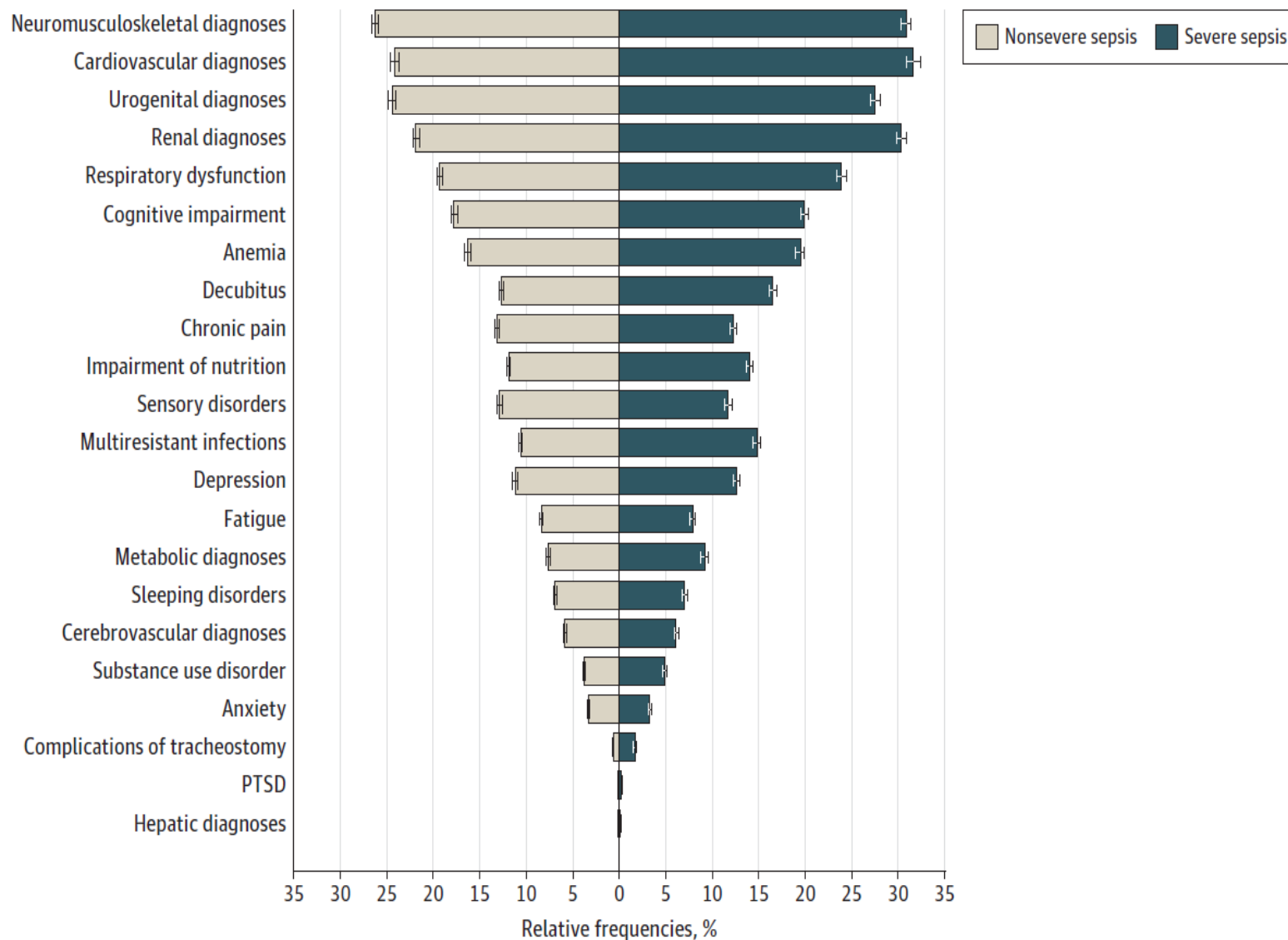


B Postsepsis morbidity by domains and co-occurrence

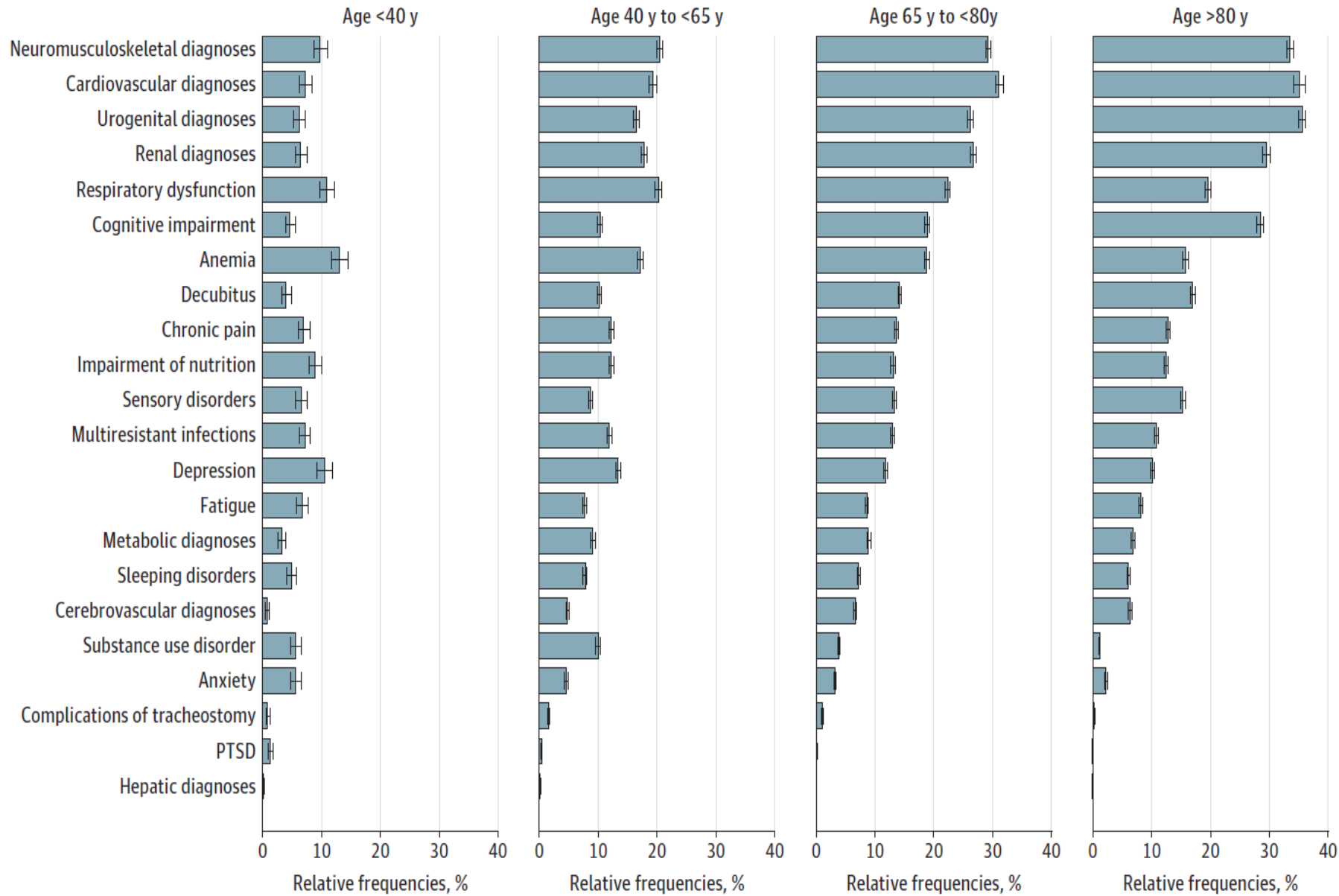


Percentage of survivors of hospital-treated sepsis in 2013 and 2014 (n = 116 507). New diagnoses 12-mo postsepsis.

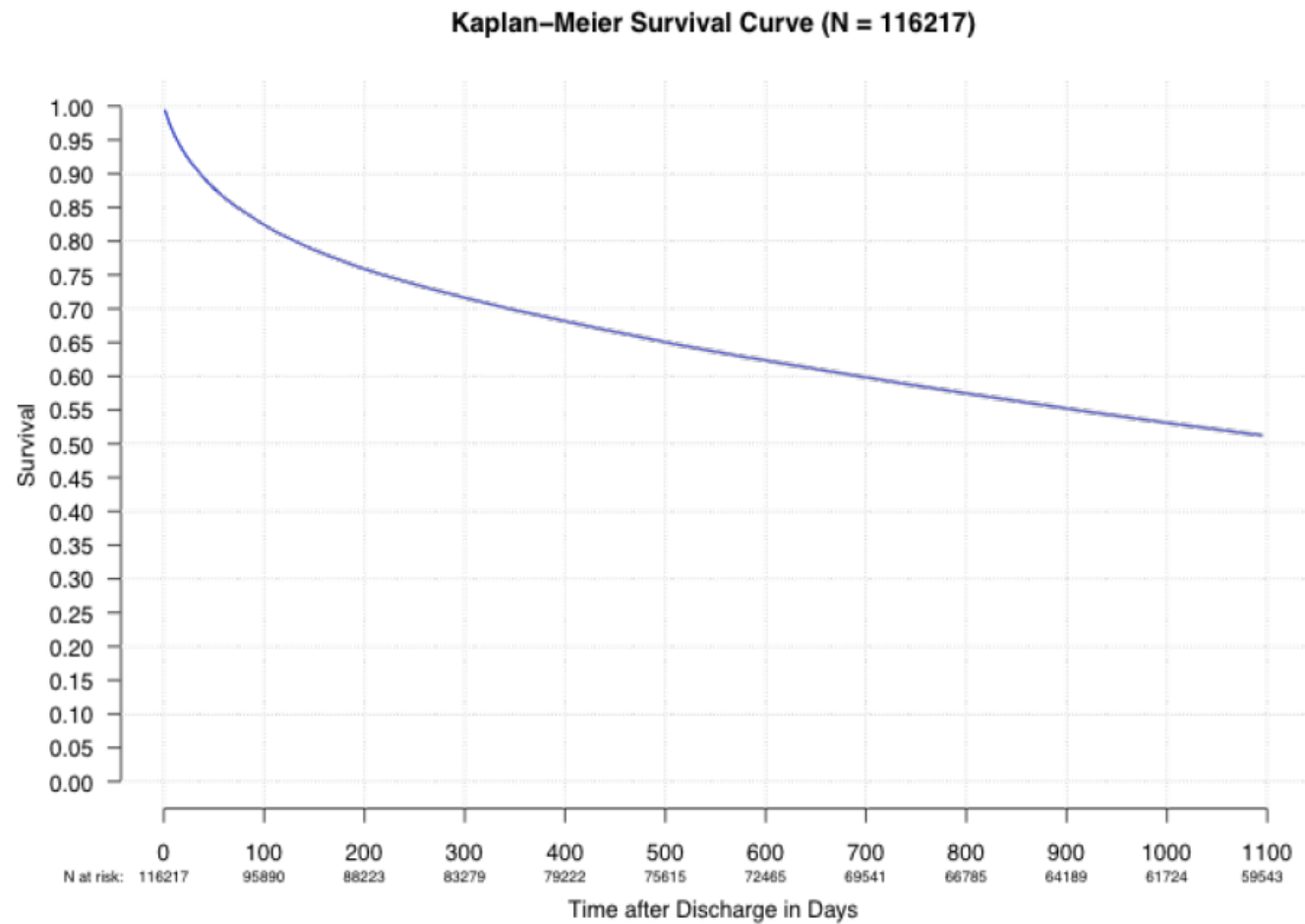
A New diagnoses among survivors of nonsevere vs severe sepsis



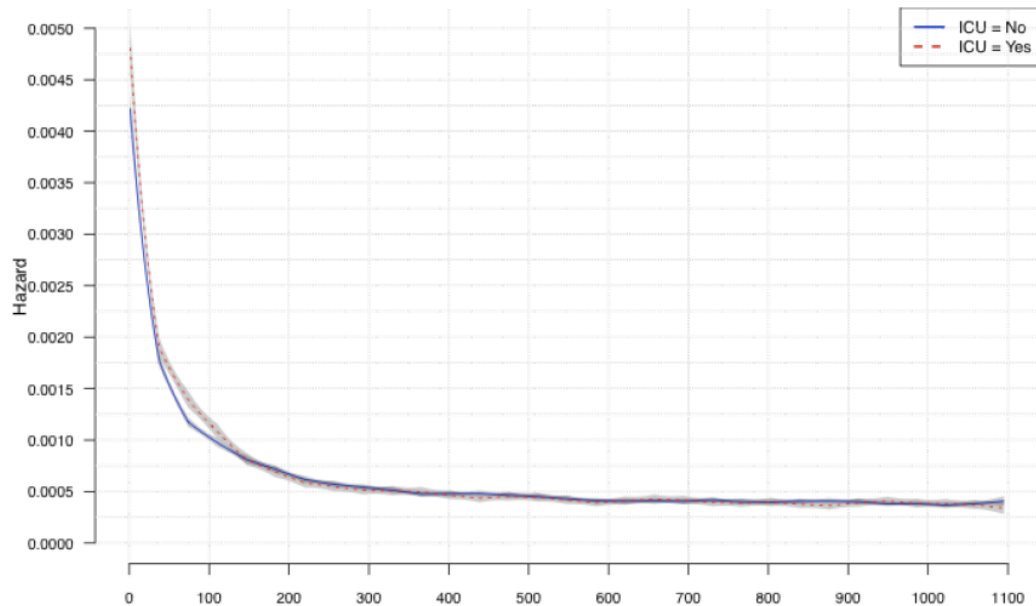
B New diagnoses by age group



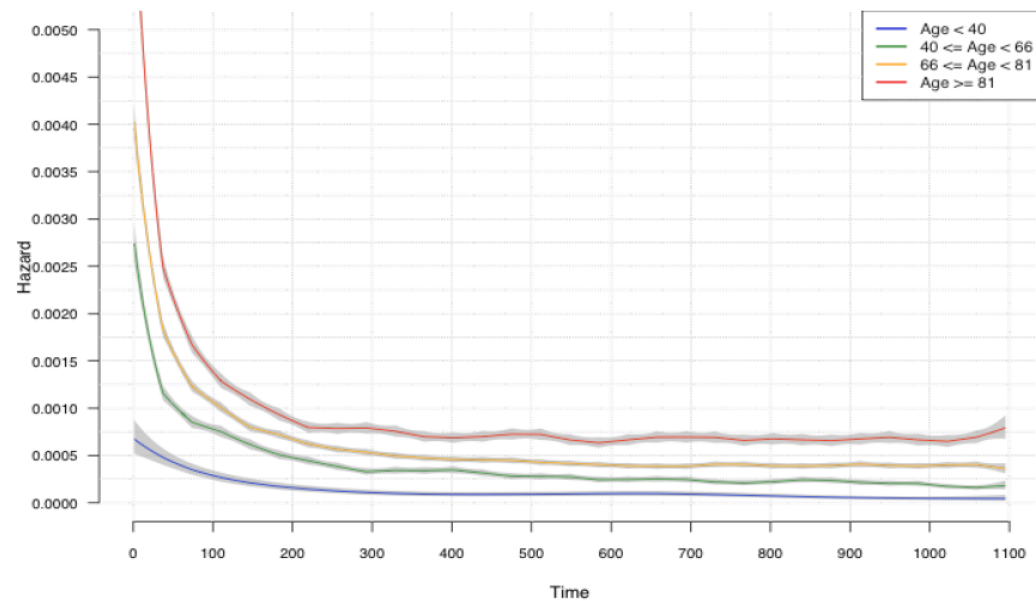
eFigure 2. Kaplan Meier Survival Curve Until 36 Months After Discharge



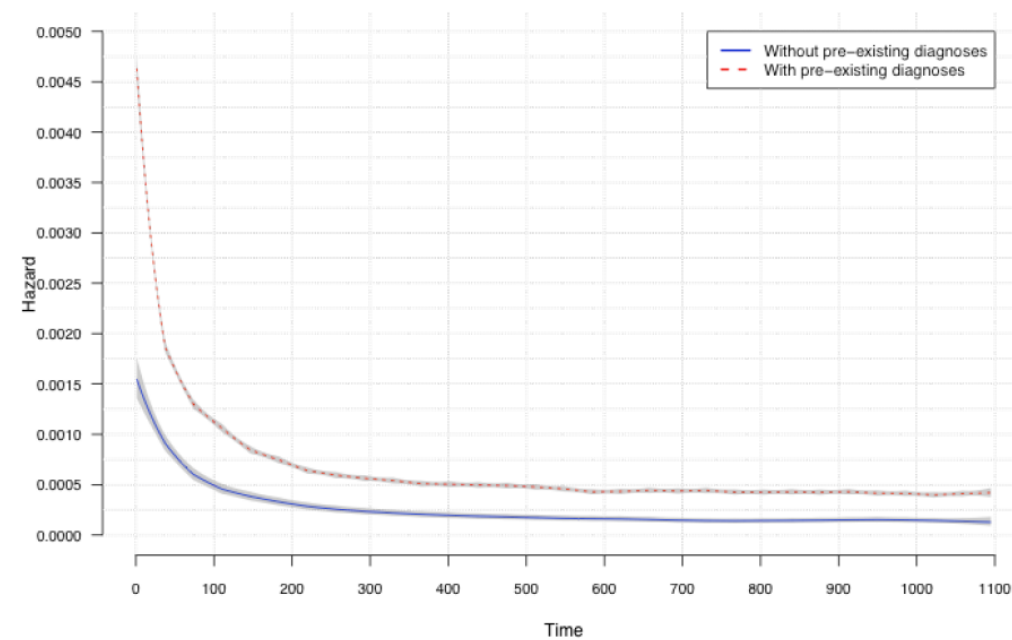
Hazard Function by ICU Treatment



Hazard Function by Age Group



Hazard Function by Pre-existing Diagnoses



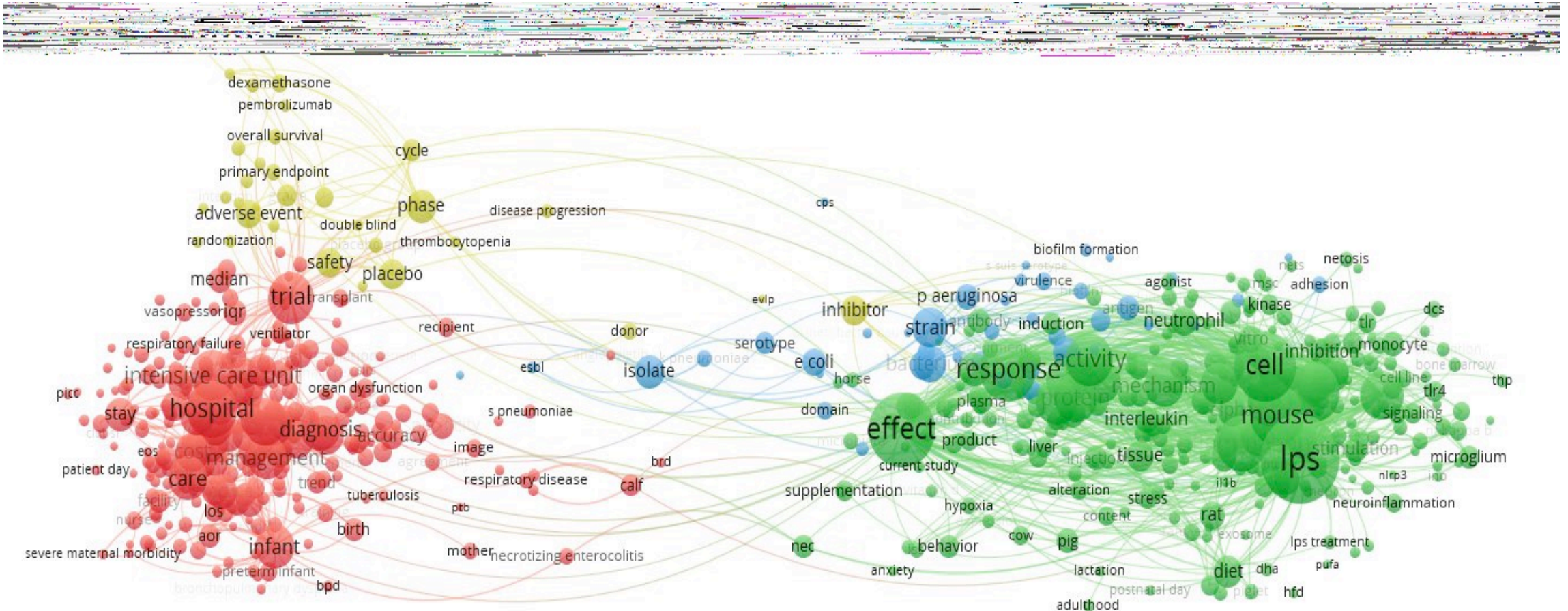
eTable 8: Total health care costs hospital survivors, 1-12, 13-24 and 25-36 months after sepsis

	Sepsis	Severe Sepsis	Non-Severe Sepsis
	n; mean (SD); median (IQR)		
12 months prior to index	116,507; 12,451 (18,767); 5,893 (1,954, 15,074)	37,840; 12,243 (18,833); 5,891 (1,954, 14,723)	78,667; 12,550 (18,734); 5,895 (1,954, 15,278)
Index hospitalization	116,507; 13,601 (26,281); 5,514 (3,471, 11,027)	37,840; 22,636 (36,943); 8,752 (4,673, 26,152)	78,667; 9,255 (17,559); 4,185 (3,362, 8,043)
12 months after index	116,507; 14,891 (24,737); 7,055 (2,422, 17,379)	37,840; 15,969 (25,610); 7,736 (2,536, 18,933)	78,667; 14,372 (24,289); 6,763 (2,368, 16,625)
24 months after index	80,742; 11,503 (20,788); 5,040 (1,909, 12,813)	25,020; 12,498 (21,213); 5,638 (2,138, 14,194)	55,722; 11,057 (20,579); 4,784 (1,823, 12,176)
36 months after index	68,940; 10,521 (19,146); 4,607 (1,771, 11,573)	21,313; 11,226 (18,687); 5,058 (1,943, 12,789)	47,627; 10,205 (19,339); 4,419 (1,706, 11,049)
Total costs 0-36 months follow up*	116,507; 29,088 (44,195); 15,903 (6,004, 34,568)	37,840; 30,555 (43,815); 16,893 (5,866, 37,452)	78,667; 28,383 (44,359); 15,505 (6,069, 33,206)
IQR = Interquartile range; SD = Standard deviation; *Total health care costs include cost for hospitalizations, outpatient consultations, medication and treatments (e.g. physical or occupational therapy) and rehabilitation.			

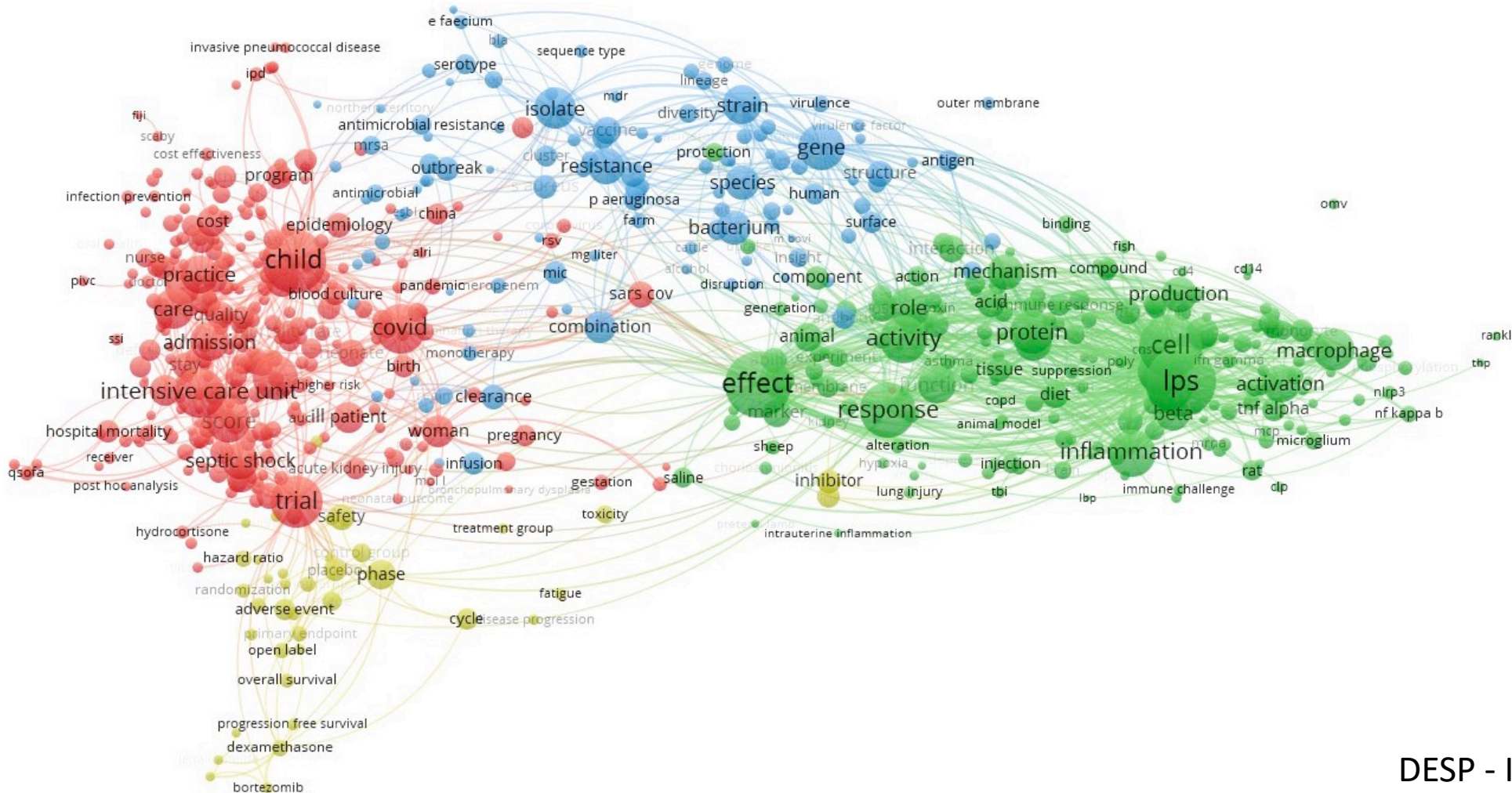
Sepsis Research Gaps

High but siloed scientific production in the field of sepsis including basic, translational and clinical research!

Same in Canada



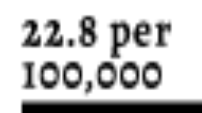
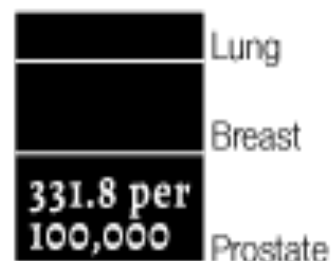
Same in Australia NZ



DESP - INSERM

Sepsis is one
of the most
common diseases¹

Cases per
100,000 population
(US / *Europe)



Sepsis

Stroke*

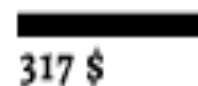
Cancer

Heart

HIV

Million US-Dollars
spent for
state-funded
research 2011

91 \$



Sepsis research
receives the
lowest funding²

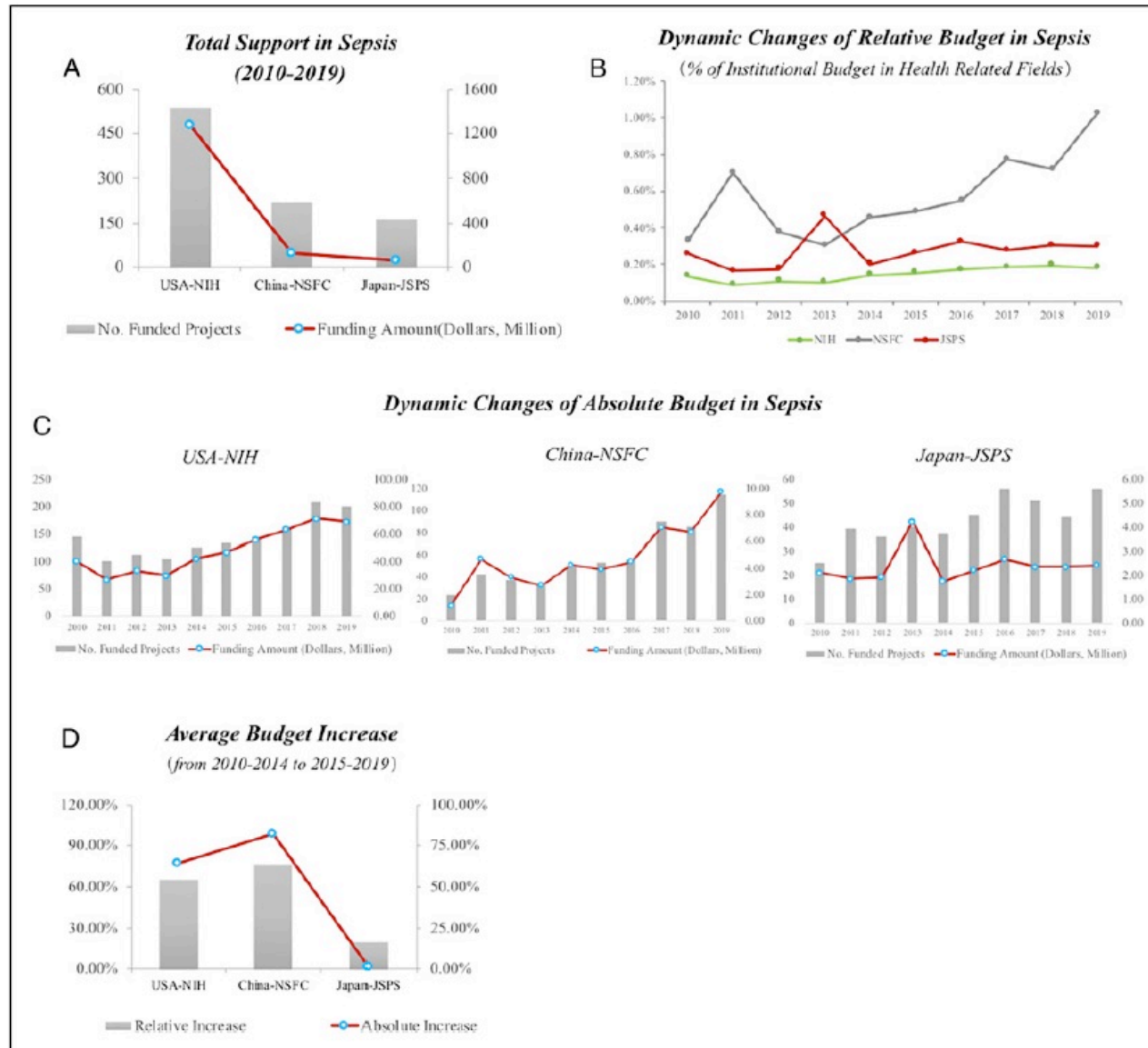


Figure I. Comparisons of national government funding support in the field of sepsis among the NSFC, NIH, and KAKENHI (2010–2019). (A)

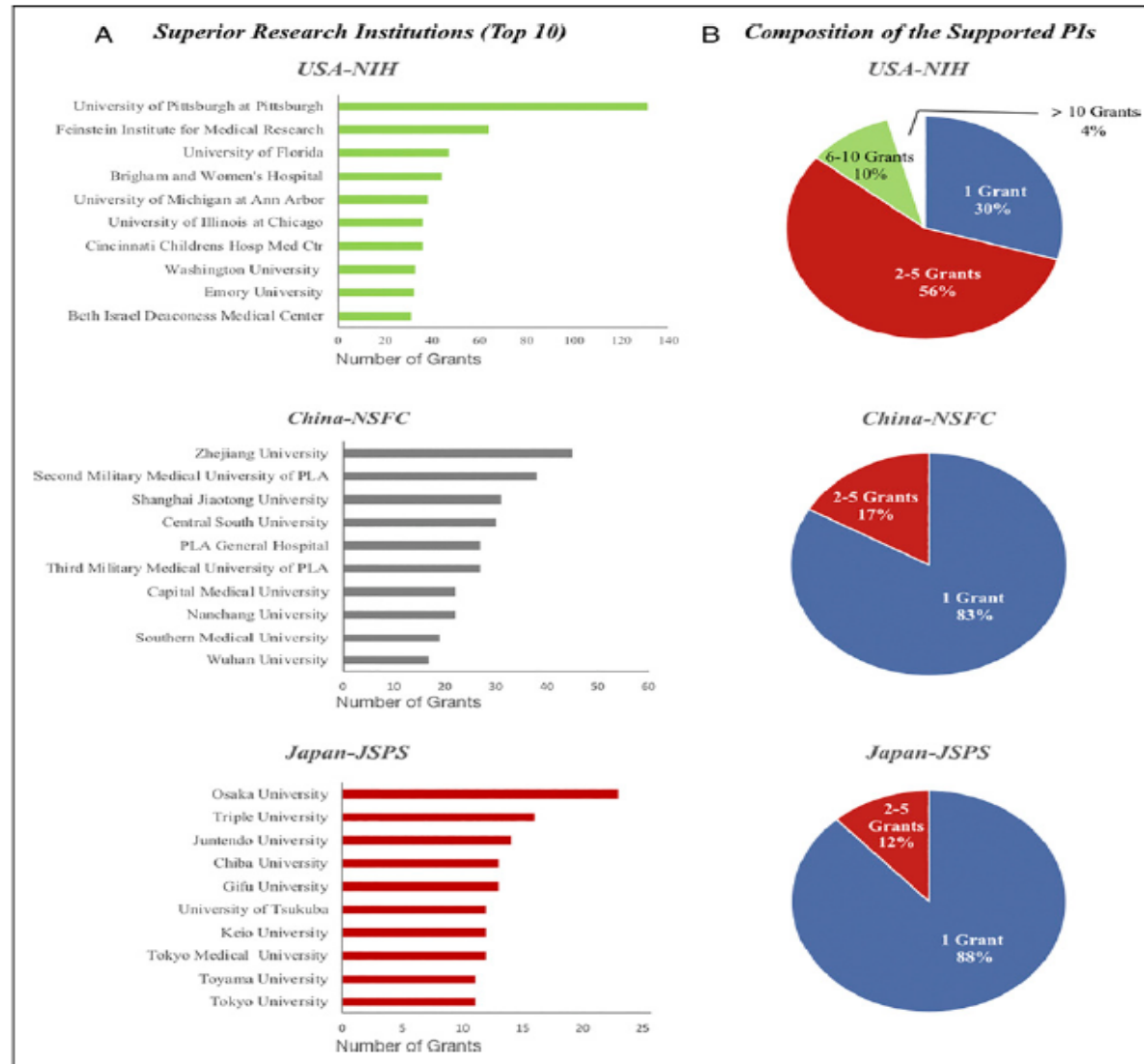


Figure 3. Superior research institutions and principal investigators (PIs) in the field of sepsis in the USA, China, and Japan from 2010 to 2019. (A) Top 10 research institutions in the field of sepsis research supported by the NIH of USA, NSFC of China, and JSPS of Japan, respectively. (B) Composition of the supported PIs in numbers of grants from the NIH, NSFC, and JSPS, respectively.

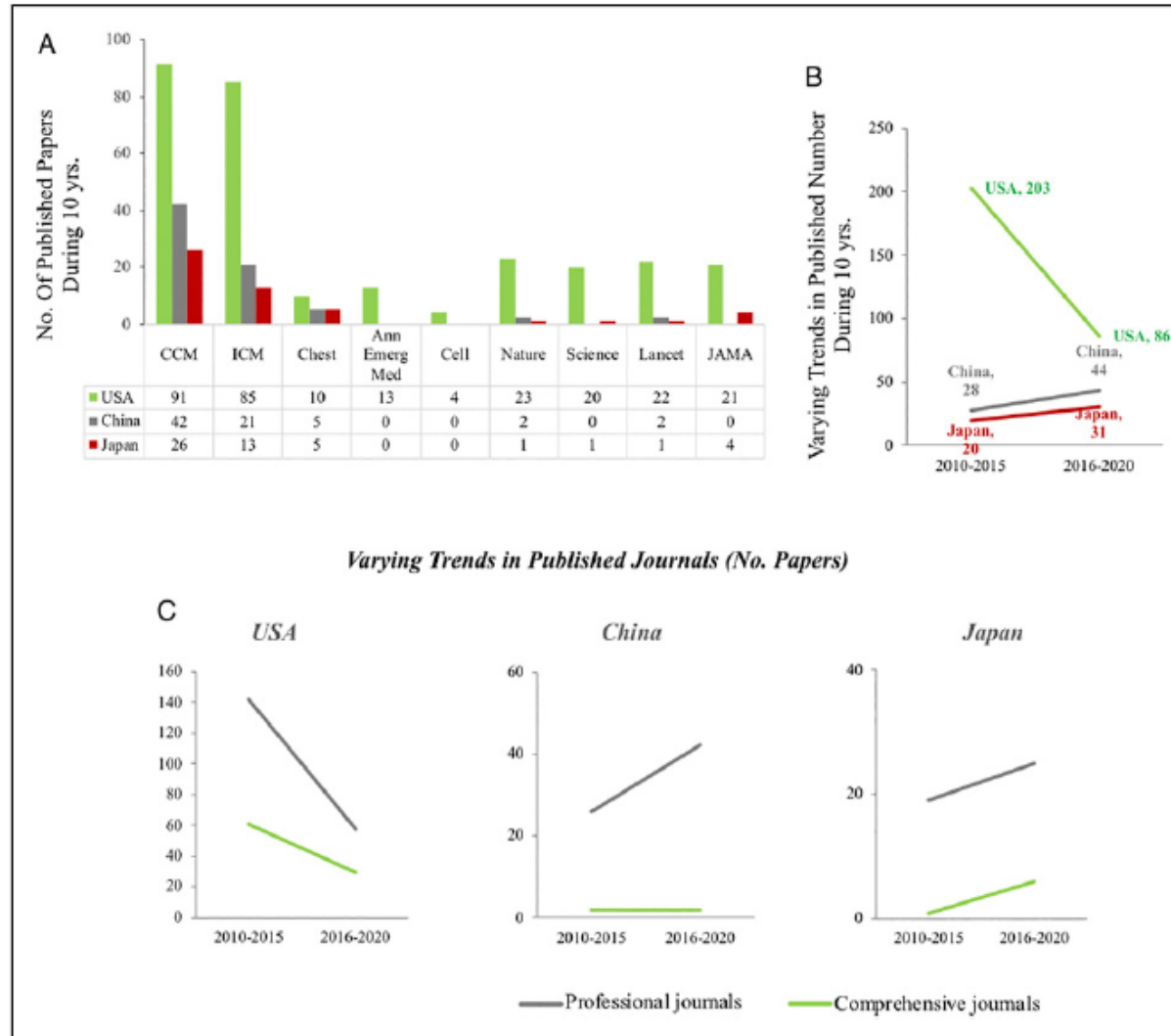


Figure 4. Comparisons of studies related to sepsis published by scholars from the USA, China, and Japan. (A) Comparisons of the numbers of published studies between 2010 and 2020 in representative journals. (B) Comparisons on five year varying trends from Jan 2010–Dec 2015 to Jan 2016–Aug 2020 in the USA, China, and Japan. (C) Comparisons of publication preferences in the USA, China, and Japan.

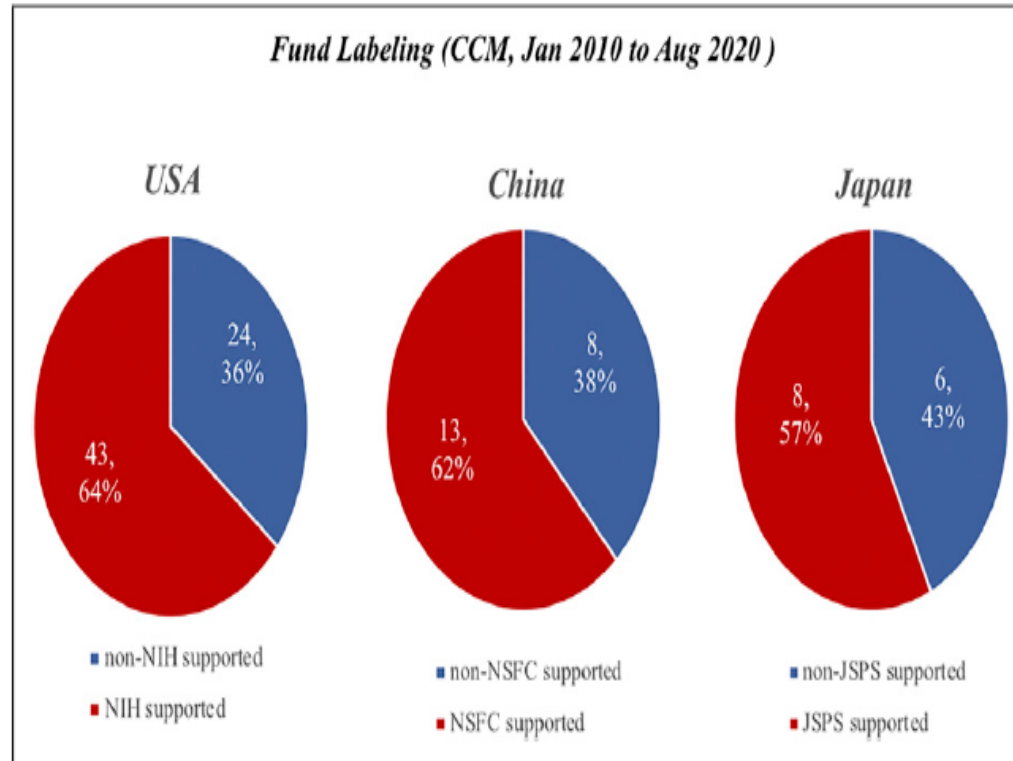


Figure 5. Fund labeling on original papers published in Critical Care Medicine by authors from the USA, China, and Japan from Jan 2010 to Aug 2020.

Sepsis France Plan



Direction générale de la Santé
Paris, 13th septembre 2019

Press Release

World sepsis day

Delivery of the report "*Sepsis - all united against a little-known scourge*":

10 measures to improve the management in France of the most serious form of infections



**To increase
knowledge**

To sensitize
to train

General Public
Health (care)
professionnels

**To provide
better care**

To prevent
to detect
to cure

Vaccine, Hygiene
Rapid point-of-care
diagnosis
Antibiotic stewardship

**To increase
surveillance
coverage**

Hospitalization
coding system
national
surveillance

Health (care) professionnels
national Health Insurance
Role of the Santé Publique
France Agency
Ministry of Health


From reporting to implementing

2018 REPORT

Recommendation n°1

- To define a standard care specific for patients with sepsis
- National Program for Diagnosis and Treatment of sepsis (protocole national de diagnostic et de soins - PNDS)

2022 CURRENT STATUS



HAUTE AUTORITÉ DE SANTÉ

**Prise en charge du sepsis
du nouveau-né, de l'enfant et de l'adulte :
recommandations pour
un parcours de soins intégré**

Note de cadrage

Recommandation de Bonne Pratique
CRPPI du 21 septembre 2021
E. NOUYRIGAT, Chef de Projet SBP/URBP

From reporting to implementing

2018 REPORT

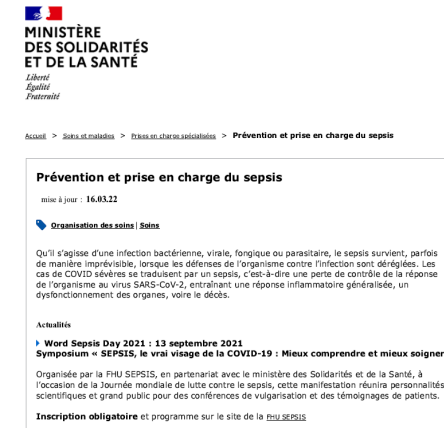
Recommendation n°2 &3

- Raising Public Awareness

2022 CURRENT STATUS

Dedicated pages at webportal of Ministry of health

[Prévention et prise en charge du sepsis -
Ministère des Solidarités et de la Santé
\(solidarites-sante.gouv.fr\)](#)



National Health Service of medical and nurse students

From reporting to implementing



2018 REPORT

Recommendation n°4&5

- **Obligatory sepsis course for all health care students and professionals**

2022 CURRENT STATUS

- **A 2 to 4 hours MOOC obligatory for all medical student during first year of resident ship**
- **Continuous medical education,**
 - Organization in collaboration with scientific societies
 - Diffusion of appropriate information about CME program specific for sepsis
 - All professionals (including GPs).

From reporting to implementing



2018 REPORT

Recommendation n°6 to 8

- Promote funding for researches on sepsis

2022 CURRENT STATUS

- National ad'hoc committee on research for sepsis
- **Chairs:** Yazdan Yazdanpanah (Dir National Institute for Immunology, Inflammation and Infection)
 - Pluri-annual funding of research programs focusing on sepsis
 - National Label for two FHU on sepsis
 - One Health approach

From reporting to implementing

2018 REPORT

Recommendation n°9

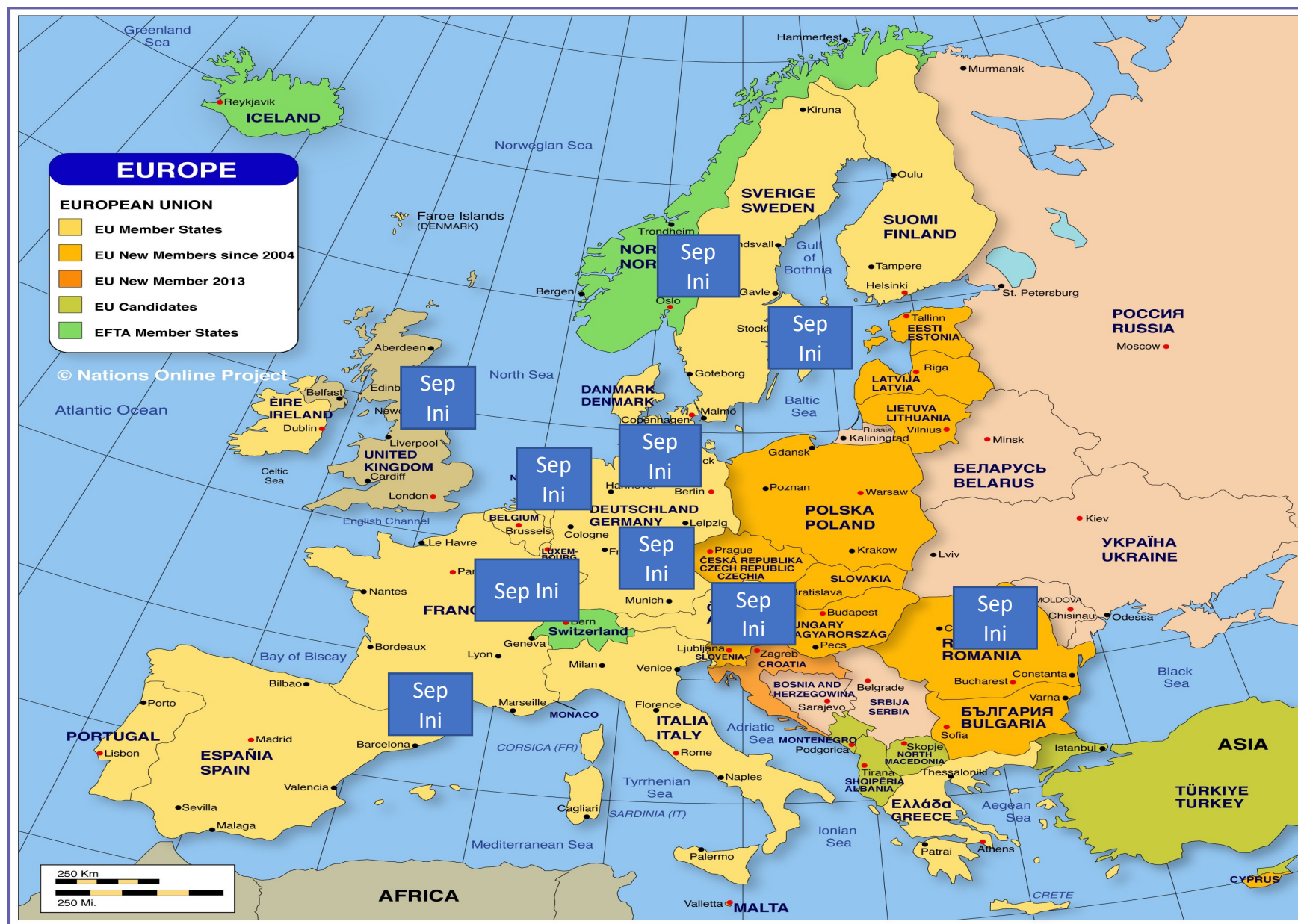
- Improve coding for sepsis via national adjustment of ICD10

2022 CURRENT STATUS

Positionnement de la restitution dans ScanSanté



The screenshot displays the ScanSanté web application interface. The header includes the logo of the Agence Technique de l'Information sur l'Hospitalisation (Atih) and the title 'Positionnement de la restitution dans ScanSanté'. The main navigation bar contains tabs for 'Indicateurs synthétiques', 'Activité', 'Coûts-finances', 'Qualité', and 'Médico Social'. The 'Activité' tab is selected. The interface is divided into several sections: 'Consommation et production de soins', 'Analyse de l'activité', 'Analyse d'activités spécifiques', and 'NOUVEAUTÉ'. The 'Sepsis' indicator is highlighted with a red dashed box under the 'Analyse d'activités spécifiques' section. The 'NOUVEAUTÉ' section on the right lists various indicators and their dates.





Ms. Norman performs at the Montreux Jazz Festival in Switzerland in 2010. (Dominic Favre/AP)

By **Mesfin Fekadu**

September 30 at 9:25 PM

Jessye Norman, the renowned international opera star whose passionate soprano voice won her numerous Grammy Awards, the National Medal of Arts and the Kennedy Center Honors, died Sept. 30 at a hospital in New York City. She was 74.

A family spokesperson, Gwendolyn Quinn, confirmed the death. A statement released to the Associated Press said Ms. Norman **died from septic shock and multi-organ failure** secondary to complications from a spinal cord injury she suffered in 2015.