Recommendations HAS pour un parcours de soins intégré du sepsis du nouveau-né, de l'enfant, de l'adulte et de la personne âgée Contexte et méthodes

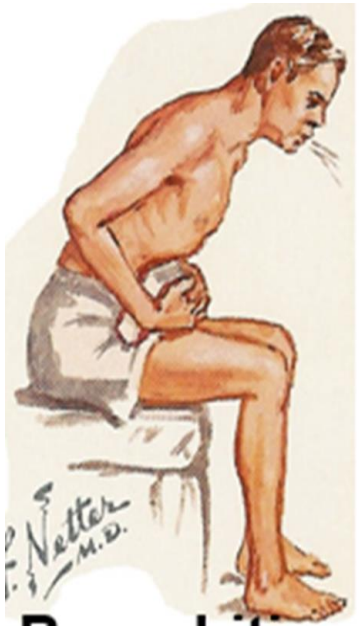
Djillali ANNANE, Raymond Poincaré Hospital,
University Paris Saclay-UVSQ, Garches, France
IHU PROMETHEUS

Conflict of Interest

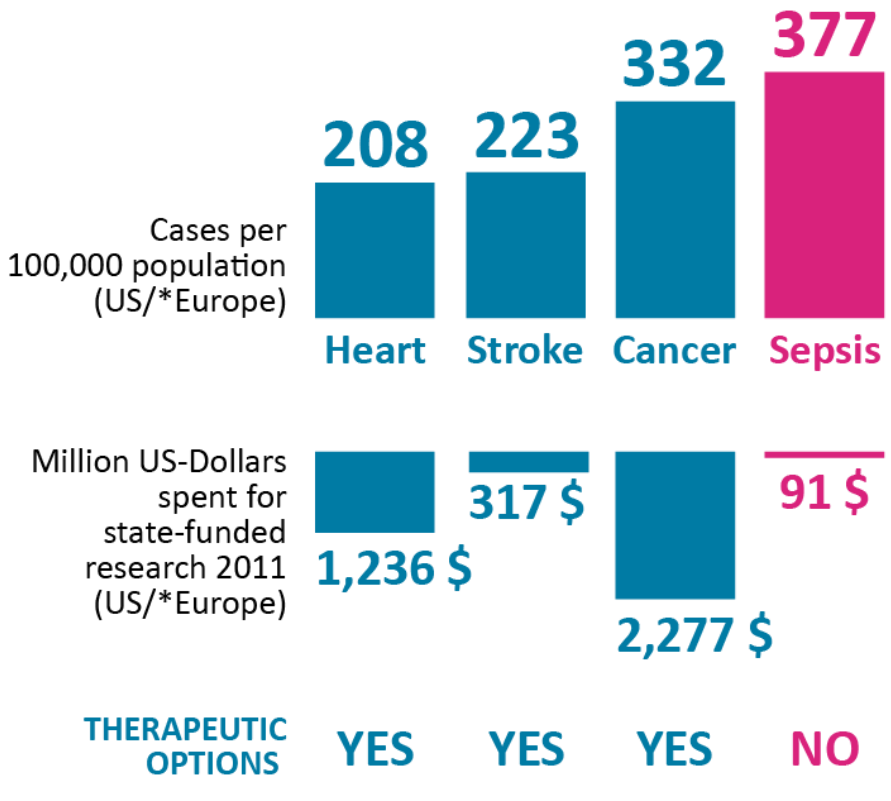
- Financial:
  - since 1995 I have received multiple grants from French ministry of health, French ministry of higher education, research and innovation, various European research programs, from charity entities - french national programme d'investissement d'avenir: ANR RHU 004; France 2030 IHU-3
  - In 2021/2022 I received honorarium to contribute to advisory board on corticosteroids for sepsis (Pfizer), biomarkers for sepsis (Baxter, Biomerieux), vaccines (Janssen)
- Academic :
  - Contributed to SSC 2008/2012/2016 updates
  - Co-chair the Task Force of CIRCI/corticosteroids in the ICU guidelines, since 2008
  - Corticosteroids for acute inflammation is the main topic of research of my group since 1991
  - Vice president of France Sepsis Association
  - Member of Steering committee of the European Sepsis Alliance
  - Contributor to Sepsis Stronger Together

Contexte

SEPSIS, The Unknown Killer



50M cases
11M deaths
42% children under 5
50% with sequelae



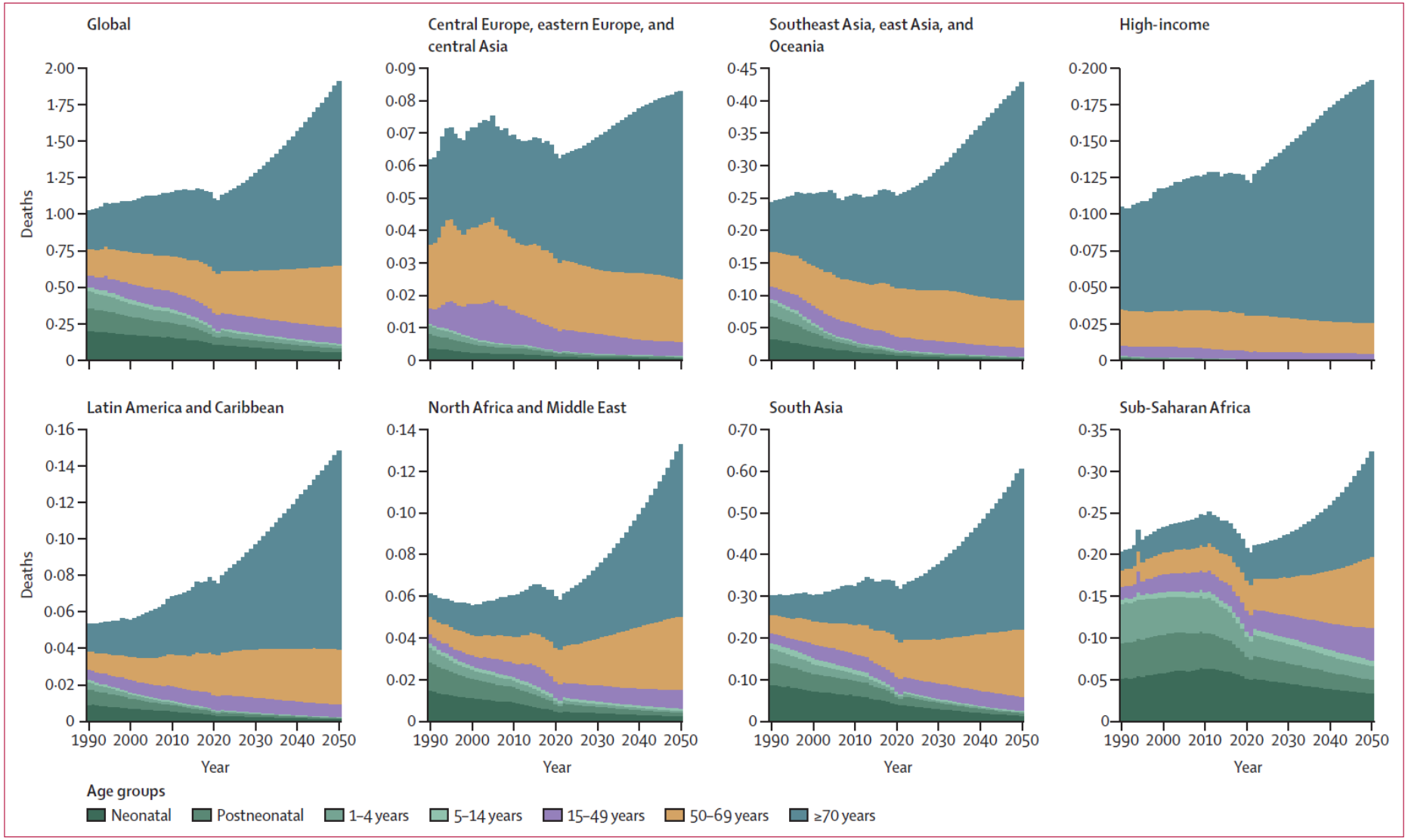
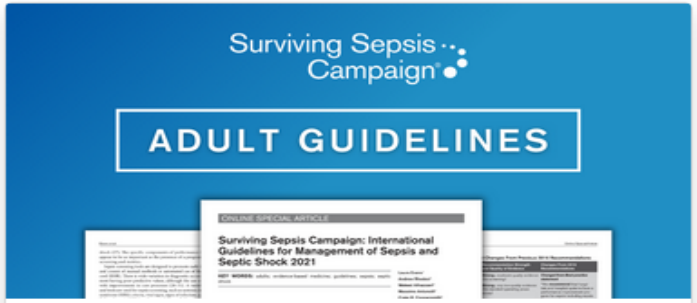


Figure 7: Deaths attributable to AMR by age group and location in the reference scenario, 2022–2050 Units are in millions.

GBD 2021 Antimicrobial Resistance Collaborators Lancet 2024

Guidelines

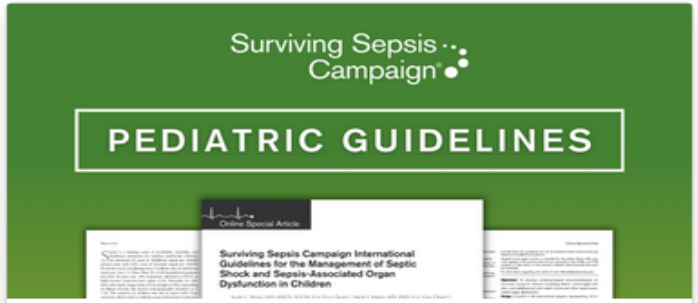


CLINICAL

Surviving Sepsis Campaign Adult Guidelines

Review guidance for clinicians caring for adult patients with sepsis or septic shock.

Access Now

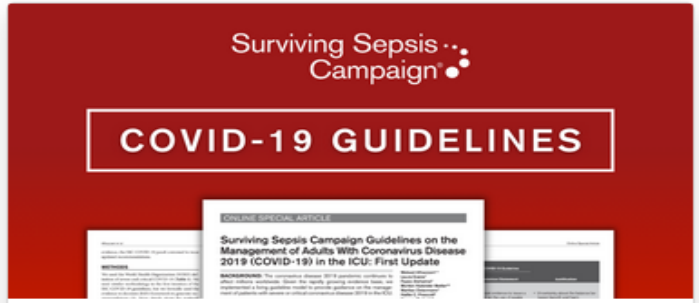


GUIDELINE

Surviving Sepsis Campaign Pediatric Guidelines

Review guidance for clinicians caring for pediatric patients with sepsis or septic shock.

Access Now



CLINICAL

Surviving Sepsis Campaign COVID-19 Guidelines

Review guidelines on the management of critically ill adults with COVID-19.

Access Now

Sepsis also places heavy health, social and economic burden, in France

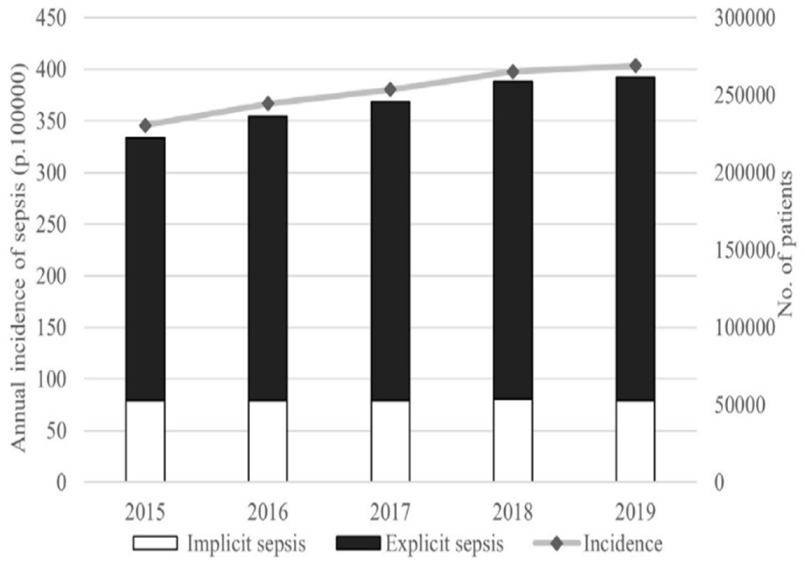


Figure 1 Sepsis incidence per 100 000 inhabitants and number of cases between 2015 and 2019 in metropolitan France.

Pandolfi BMJ Open 2022

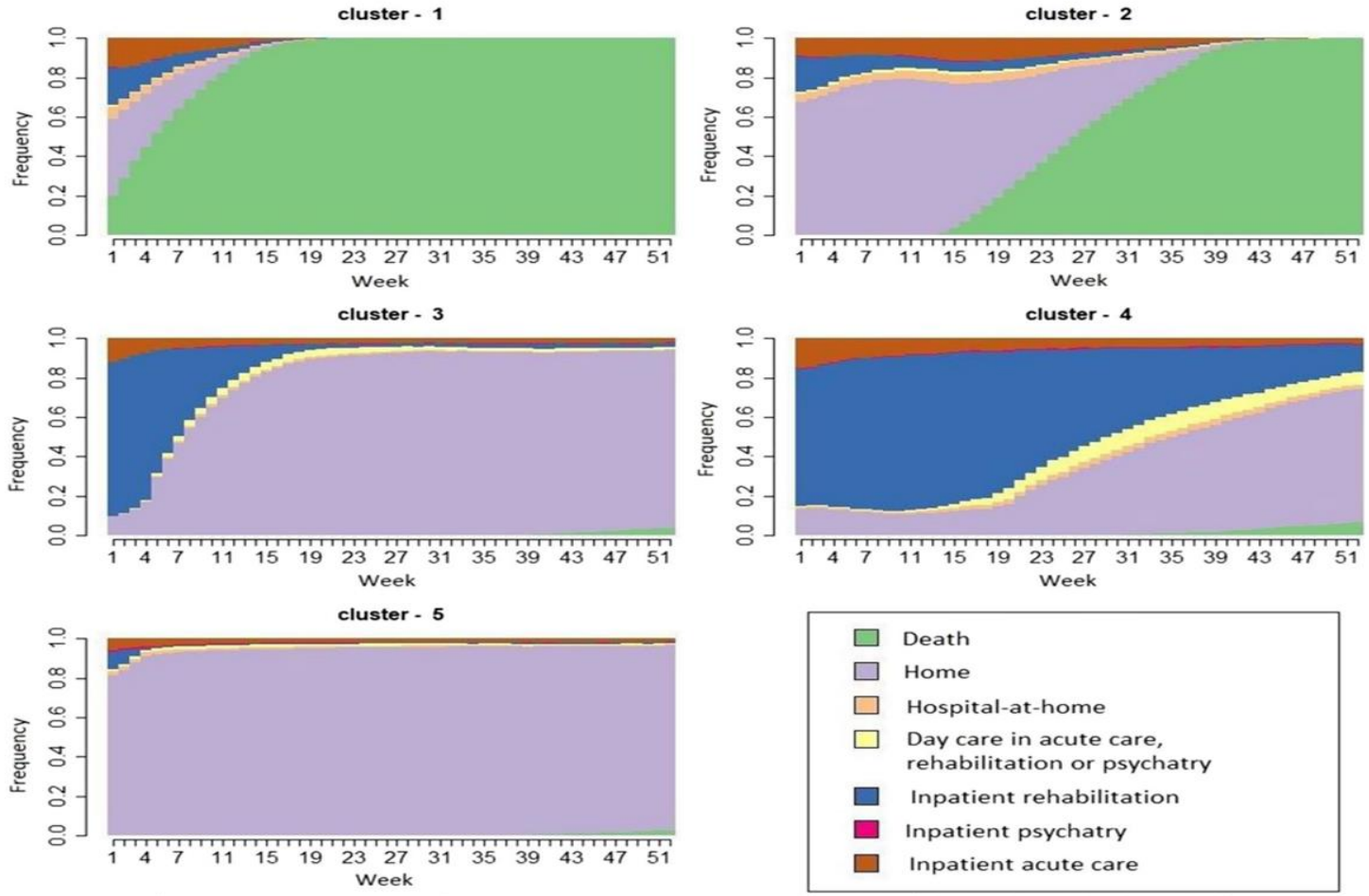


Fig. 2 Results of the state sequence analysis of the 1-year post-sepsis period: weekly distribution of the health states by cluster. This figure is composed of 5 chronograms for each of the 5 identified care trajectories (clusters). On the *x* axis, time is graduated from discharge after the index sepsis hospitalization (week 1) to 1-year post-discharge (week 52). The *y* axis corresponds to the proportion of patients (from 0 to 1) in each health state. Clusters determined by the state sequence analysis of the healthcare pathways of survivors: cluster 1 (early death), cluster 2 (late death), cluster 3 (short-term rehabilitation), cluster 4 (long-term rehabilitation), cluster 5 (home)

Pandolfi, Crit Care 2023


21 recommandations
10 recommandations (dont 1 validant la SSC) 14 recos sur réadaptation
28 recommandations
Ambulatoire
Urgences pré-hospitalières
Urgences hospitalières
Réanimation
Post-aigu
0 recommandation
73 recommandations
12 recommandations

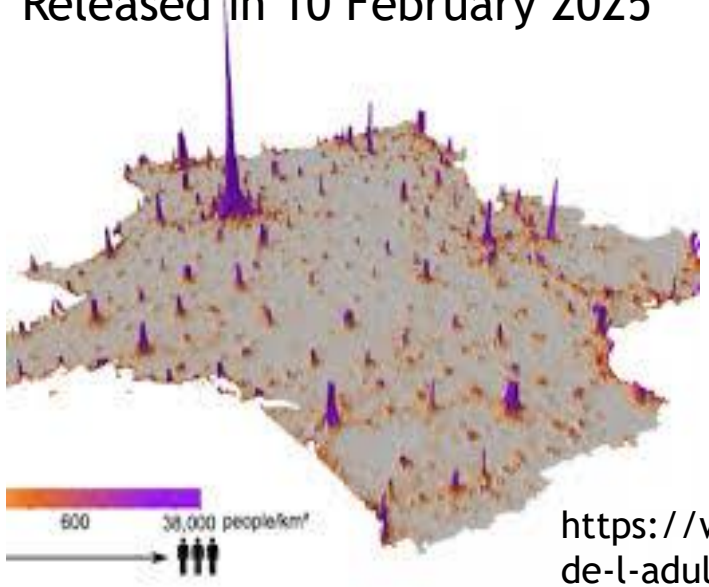
ADULTE

Méthodes

Elaboration of Integrated Care Program and Clinical Pathway

HAUTE AUTORITÉ DE SANTÉ

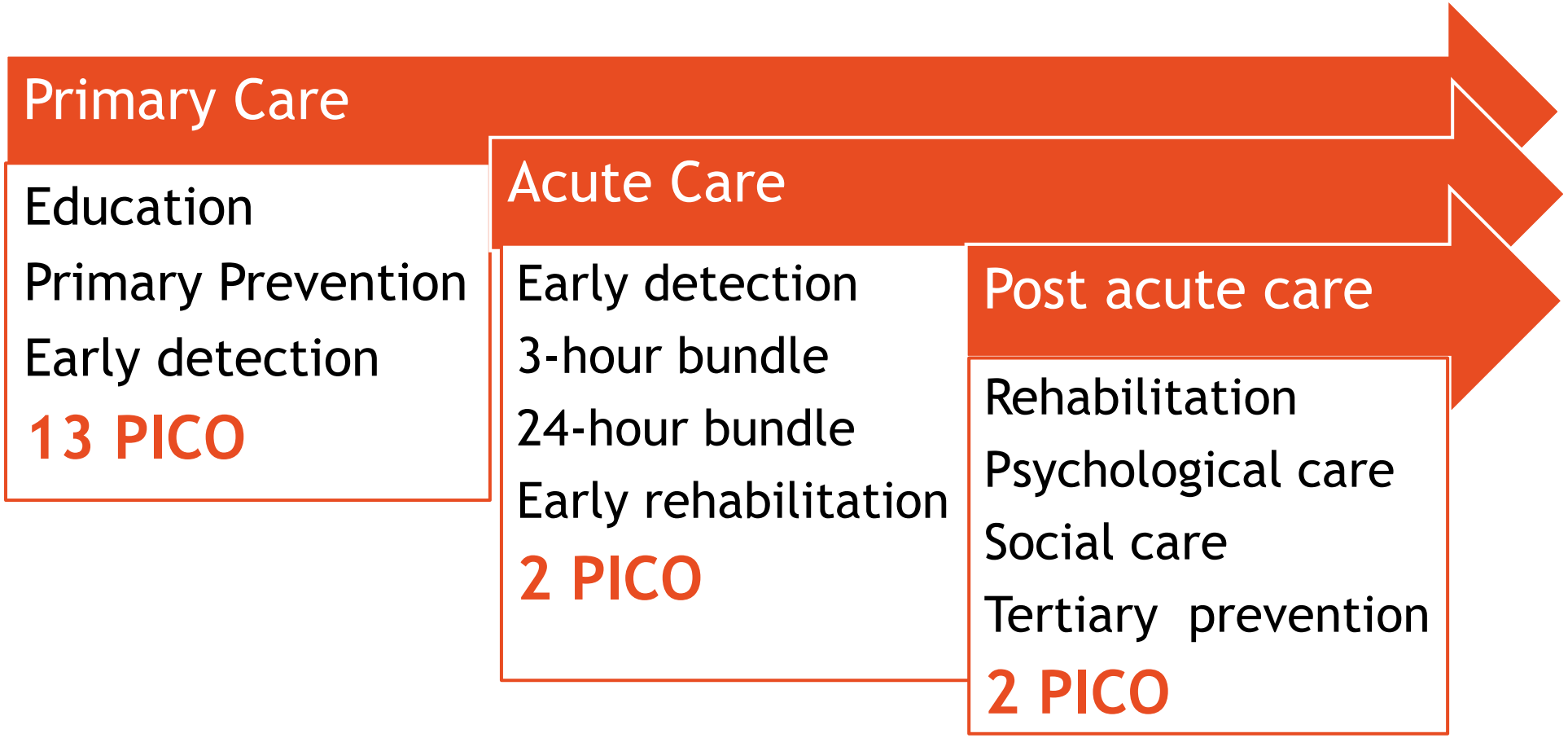
National **Multidisciplinary** Guidelines
Released in 10 February 2025

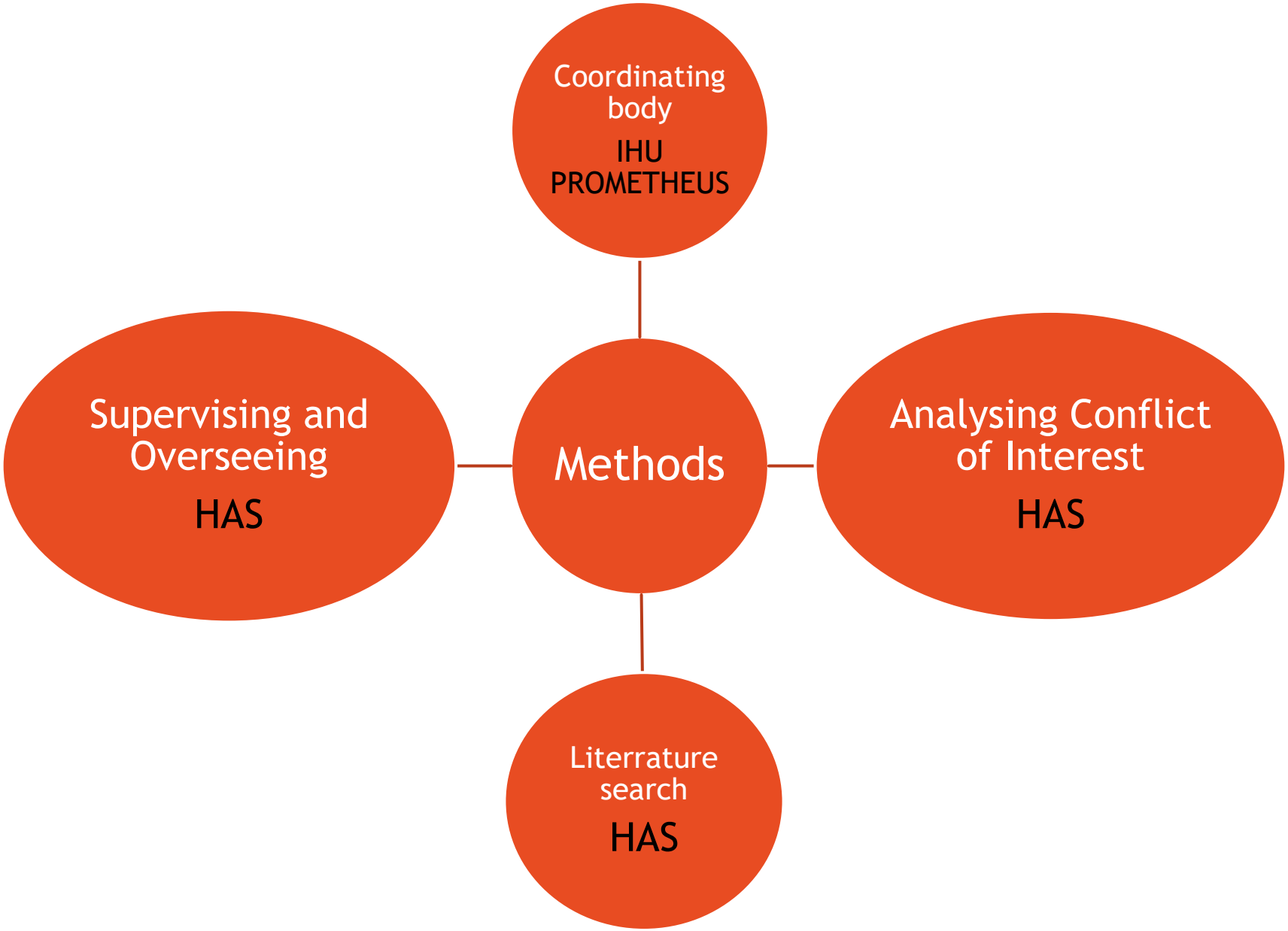


Society of Intensive Care Medicine (SRLF),
Society of Anesthesiology and CCM (SFAR),
Society of Emergency Medicine(SFMU),
Society of Infectious Diseases (SPILF),
Society of Rehabilitation (SOFMER),
Society of Pediatry (SFP),
Society of Neonatology (SFN),
Society of Pediatric Intensive Care & Emergengy Medicine (GFRUP),
Society of Pediatric Infectious Diseases (GPIP),
Society of Microbiology (SFM),
Society of Medical Mycology (SFMM),
Society of Hospital Hygiene (SF2H),
Society of Geriatry (SFGG),
Society of Public Health (SFSP),
National College of General Practitioners (CNGE),
World Alliance Against Antibiotic Resistance –(WAAR)
and
FRANCE SEPSIS ASSOCIATION

https://www.has-sante.fr/jcms/p_3587144/fr/prise-en-charge-du-sepsis-du-nouveau-ne-de-l-enfant-et-de-l-adulte-recommandations-pour-un-parcours-de-soins-integre

Elaboration of Integrated Care Program and Clinical Pathway




Coordinating body
IHU PROMETHEUS
Supervising and Overseeing
HAS
Methods
Analysing Conflict of Interest
HAS
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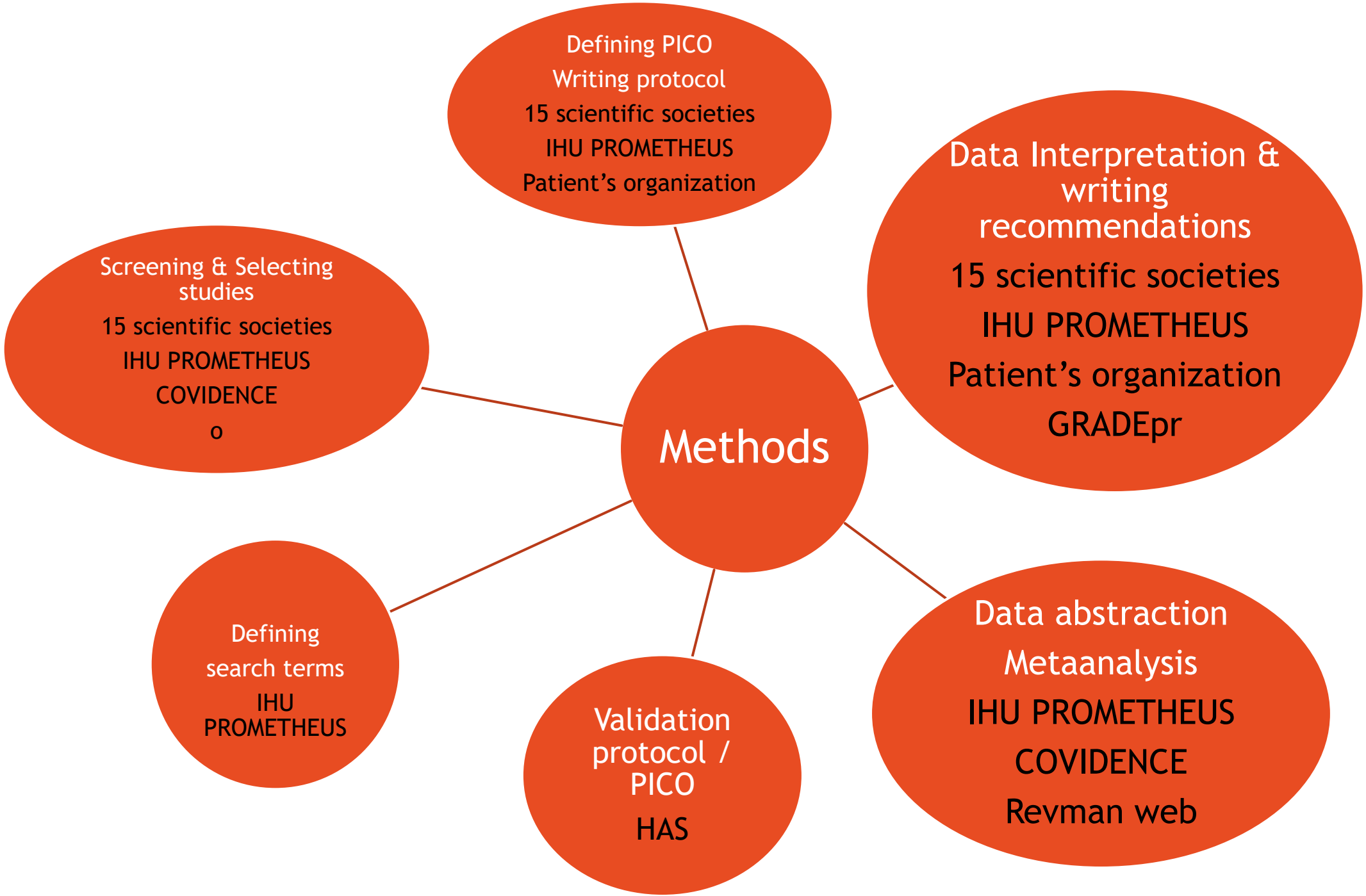
Defining PICO
Writing protocol
15 scientific societies
IHU PROMETHEUS
Patient's organization
Screening & Selecting studies
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COVIDENCE
o
Data Interpretation & writing recommendations
15 scientific societies
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Patient's organization
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Validation protocol / PICO
HAS
Data abstraction
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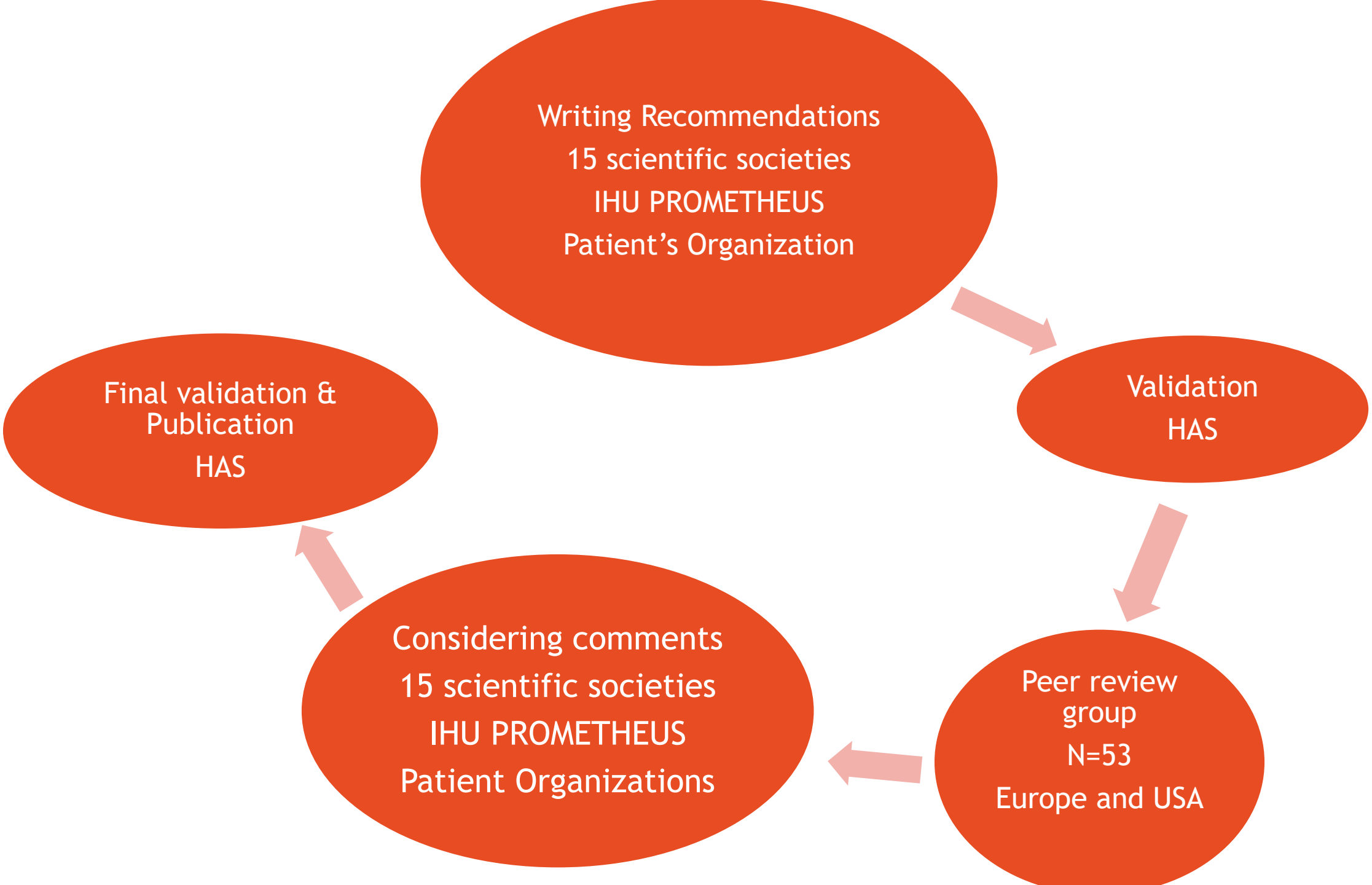

Writing Recommendations
15 scientific societies
IHU PROMETHEUS
Patient's Organization
Validation
HAS
Peer review group
N=53
Europe and USA
Considering comments
15 scientific societies
IHU PROMETHEUS
Patient Organizations
Final validation & Publication
HAS

Key Recommendations

Better prevention of sepsis means:

1. Respect the vaccination schedule, at all ages
2. Know the risk factors, in the event of infection, for progression to sepsis
3. Respect hygiene rules

Key Recommendations

Better prevention of sepsis means:

Know the risk factors, in the event of infection, for progression to sepsis

Age/ Frailty	Immune disorders	Non-immune disorders

Key Recommendations

Better detection of sepsis means:

Recommandation 3

Incidence sepsis

Nné	2202/100 000
Enfants	48/100 000

- **Nourrisson <1 mois :** Toute fièvre = suspicion de sepsis → Urgences.
- **Enfant 1-3 mois :** Fièvre → Avis médical sous 6h.
- **Tout enfant fébrile :** Recherche de purpura et évaluation des signes vitaux.

b) Signs of poor peripheral perfusion: prolonged CRT, mottling, cold extremities

c) Increased respiratory rate and tachycardia

d) Decreased blood pressure

e) Appearance and spread of ecchymotic or necrotic purpura

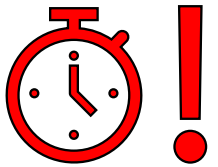
Key Recommendations

Better detection of sepsis means:

3. In an adult, look for the presence of **3** or more of the 6 clinical variables:
    a) Age >65 years
    b) Temperature >38°C
    c) Systolic blood pressure ≤110 mmHg
    d) Heart rate >110/min
    e) Peripheral O2 saturation ≤95%
    f) Confusion, disorientation

Key Recommendations

Better early management of sepsis means:



1. Act without delay

2. In community setting:
   a) Contact 15 immediately
   b) Do not carry out any additional examinations in children
   c) In adults on an outpatient basis, with a risk factor for sepsis, take a blood culture (at least 40 ml) and/or urine culture
   d) Medically transport patients, regardless of age, to a facility with critical care

Biomarkers and microbiological examinations

Recommendation 4

- C-reactive protein (CRP), procalcitonin (PCT), and lactate **should not be used** for the early diagnosis of sepsis.

Recommendations 5-7

- Microbiological samples **only for patients at risk**.
- Child suspected of sepsis = Transfer to the Emergency Department.

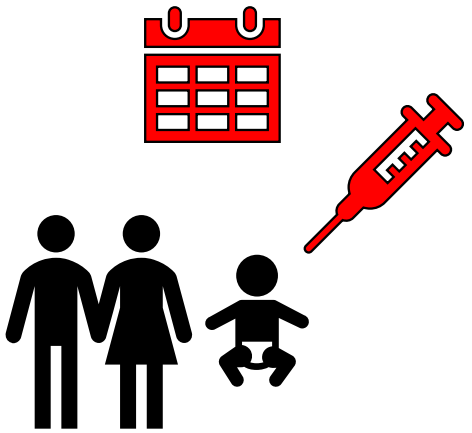
Role of connected devices and vaccination

Recommendation 8

- No recommendation regarding the use of connected devices.

Recommendation 9

- **Priority Prevention:** Adherence to the vaccination schedule.
- **At-Risk Populations: Vaccination against pneumococcus, meningococcus, influenza, and SARS-CoV-2**.



Interventions at primary care level

Recommendation 10

- Raising awareness among the **general publi**c and healthcare professionals about early recognition of sepsis.

Recommendations 11-13

- Immediate antibiotic therapy for **immunocompromised** patients with fever.
- **No systematic antibiotic** therapy for children without clinical signs.

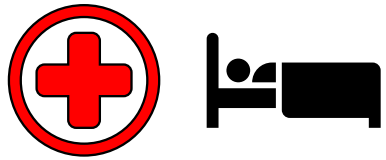
Recommendations 14-16

- The use of NSAIDs, aspirin, or corticosteroids is **not recommended** for the prevention of sepsis.

Alternatives to hospitalization

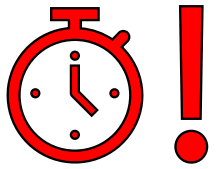
Recommendations 20-21

- Suspected sepsis → **Immediate hospitalization** (except in palliative care contexts).



- For GIR 1 and 2 patients, **home care** may be considered depending on available resources.

Key Recommendations



Better early management of sepsis means:

3. In hospital:
    a) Apply, as best as possible within **1 hour**, a group of coordinated and standardized actions including:
        i. Placement of a venous or intraosseous access line
        ii. Collection of a blood culture (**at least 40 ml**), and a lactate level
        iii. Intravenous antibiotic therapy considering the nature of the infection (site and pathogens), the community nature or not, the existence of MDR risk factors and the local microbial ecology
        iv. Restore hemodynamics by favoring **individualized management** guided by clinical and ultrasound hemodynamic assessment, and including vascular filling of 10 to 20 ml/kg in 15-20 min and the introduction of vasoinotropic agents in the event of non-response or poor tolerance to vascular filling

Antibiotic therapy and multidrug-resistant infections

In adults

Recommendation 24

- **Rapid microbiological tests** are recommended in case of suspected infection with multidrug-resistant bacteria (MDR).
- Empirical **combination antibiotic** therapy is preferred over monotherapy.

Recommendation 25

- **Dosage** optimization according to PK/PD principles and CASFM* guidelines.

* Comité de l'Antibiogramme de la Société Française de Microbiologie

Recommendation 26

- Duration **≤ 7 days** if the infectious source is controlled and there is no indication for extension.

Antibiotic therapy

In children

Recommendation 35

- **Do not** use multiple antibiotic therapy except in case of risk of multidrug-resistant organisms.

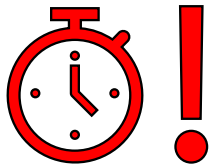
Recommendation 36

- Combination with an **antitoxin** antibiotic in case of streptococcal or staphylococcal toxic shock.

Recommendation 37

- Addition of an aminoglycoside as empirical therapy in **neonates**.

Key Recommendations



Better early management of sepsis means:

3. In hospital:
   a) Importance of rapid and personalized management.
   b) Admit to ICU if clinical variables do not resolve after initial treatment
   c) Follow the recommendations of the Surviving Sepsis Campaign
   d) Adaptation to the patient's needs and clinical context

Key Recommendations

Better prevention of sepsis complications means:

1. From the first **48 hours** of hospitalization for sepsis:
   - **a) Recommandation 57:** Start a standardized and progressive **rehabilitation program (**Schweickert program), following the evolution of the patient's condition, in **6 stages** from passive mobilization to ambulation within the perimeter of the care unit (strong recommendation, moderate level of certainty). The addition of respiratory rehabilitation must be systematic if initial pulmonary sepsis or in the event of mechanical ventilation
   - b) Then, ***adapt*** the rehabilitation management ***and prepare*** the referral if necessary to a rehabilitation structure, by a ***mobile physical medicine and rehabilitation (MPR) team*** or, failing that, by a reference team on site or nearby

Techniques to avoid

- **Recommendation 61**

Do not use surface electrical muscle stimulation alone or as an adjunct to conventional rehabilitation programs (conditional recommendation, low level of certainty).

- **Recommendation 62**

Do not use cycle ergometers or passive mobilization devices as first-line interventions (conditional recommendation, low level of certainty).

The balance between benefits and adverse effects of using surface electrical stimulation or automated passive mobilization techniques does not support their use in the acute phase.

Programs involving cycle ergometer mobilization, with or without adjunctive electrical muscle stimulation, have not demonstrated superiority over the Schweickert program.

Role of healthcare professional

- **Recommandation 65**

Rehabilitation sessions should be conducted by **physiotherapists trained** in the specific needs of critical care and/or acute care patients (strong recommendation, very low level of certainty).

- **Recommandation 66**

Ideal staffing ratio of **1** physiotherapist per **5** patients, with the presence of an occupational therapist and a speech therapist within the rehabilitation team (strong recommendation, very low level of certainty).

Composition of the mobile team

Recommendation 67

- Presence of a PM&R physician, a physiotherapist, a speech therapist, an occupational therapist, a psychologist trained in neuropsychology, a dietitian, and a social worker.

- Early targeted clinical assessment in acute care settings to guide the patient to the appropriate facility and implement a coordinated multidisciplinary rehabilitation program (strong recommendation, very low level of certainty).

Information for patients and families

Recommendation 68

- **Regularly inform the patient and their family** during formal consultations about rehabilitation care.
- **Do not involve relatives in rehabilitation sessions during the acute phase of sepsis** (strong recommendation, very low level of certainty).

The few studies reporting on family involvement and participation in rehabilitation sessions were Chinese studies, which are not applicable to the French healthcare and cultural context. None demonstrated added benefit compared to coordinated early rehabilitation care.
In the absence of impact studies, particularly regarding the occurrence of post-intensive care syndrome in families (PICS-f), it does not seem appropriate to involve family members in rehabilitation sessions during the acute phase of sepsis.

Key Recommendations

Better prevention of sepsis complications means:

2. In post-acute:
   a) Refer patients according to their rehabilitation needs as best as possible to **structures with rehabilitation** teams including: physiotherapist, occupational therapist, speech therapist, neuropsychologist, psychologist, dietician, social worker, and medical coordination by an MPR doctor
   b) Home referral must be secured by formalized and organized **outpatient** follow-up, if possible with the help of a mobile rehabilitation or geriatrics team
   c) Organize the follow-up consultation within **3** months following discharge from hospital

Patient orientation according to individual needs

In adults

Recommendation 70

- Care should be provided based on the patient's specific rehabilitation needs as determined by a PM&R assessment:
  - **PM&R unit**,
  - **General rehabilitation facility**,
  - **Home** - provided that home care is secured through a structured and pre-arranged outpatient follow-up program (e.g., Prado or equivalent)

  (Strong recommendation, very low level of certainty).

- Organization of outpatient follow-up before hospital discharge.

Assistance with transition to home

In adults

Recommendation 71

- Implementation of a **support program for returning home**, which can be coordinated by advanced practice nurses or the referring general practitioner, initiated as early as during hospitalization.
- **Written information** about sepsis and its potential consequences.

(Strong recommendation, low level of certainty)

Key messages

In adults

- Early and tailored organization of post-acute care pathway.
- Coordination between the hospital, rehabilitation facilities, and home care services.
- Active involvement of the patient and their family.

- There is no specific literature regarding specific post-sepsis rehabilitation programs.
- However, patients requiring such care (following PMR assessment) should have access to rehabilitation facilities that include physiotherapists, occupational therapists, adapted physical activity instructors, speech therapists, psychologists, dietitians, and social workers, coordinated by physicians specialized in physical medicine and rehabilitation or geriatrics in the case of geriatric rehabilitation facilities.

Post-acute care facilities

In children

Inpatient care:

- Multidisciplinary team (PM&R physician, physiotherapist, speech therapist, psychologist…).
- Assessment of functional limitations.

In rehabilitation facilities:

- Outpatient care and neuropsychological evaluation.
- Support for a gradual return home.

Pediatric-specific care

In children

Recommendation 76

- Screening of **primary immunodeficiencies** if no known predisposing cause (Strong recommendation, very low level of certainty)

Recommendation 77

- Early clinical assessment of activity and participation limitations in short-term hospital stays
- Coordination between pediatric intensivist, neurologist, and PM&R physician, in link with the child and family (strong recommendation, very low level of certainty).

Recommendation 79

- **Neuropsychological evaluation and brain MRI**, before returning home or within the first year post-sepsis, to document potential long-term impairments (strong recommendation, very low level of certainty).

There is no pediatric literature specifically assessing the impact of care provided in medical and rehabilitation facilities on post-sepsis outcomes in children.
The literature on long-term outcomes in children remains limited and heterogeneous in terms of follow-up duration and parameters.

Home return and follow-up to be organized before discharge

In children

Recommendations 83, 84, 85, 86, 87

- Support pathway.
- Coordination by advanced practice nurses, pediatricians, or general practitioners.
- Clear information about sepsis and its consequences.
- Organization of outpatient rehabilitation care.
- **Annual monitoring of growth and neuropsychological development**.

(Strong recommendations, very low level of certainty)

Key Recommendations

Better long term support means:

1. Perform a **systematic psychological assessment after returning home** and continue monitoring based on the initial assessment.

2. Use a local **social support service** in the event of precarious and/or high-risk situations, identified in advance.

3. Ensure post-sepsis clinical monitoring at least **3** months and **1** year after hospitalization.

Key stakeholders in care management

In adults

- General practitioners and specialists.
- Home care nurses.
- Home hospitalization services.
- Rehabilitation therapists (physiotherapists, occupational therapists).
- Psychologists.
- Social services and support organizations.

In children

A multidisciplinary approach:

- General practitioners & pediatricians: regular follow-up, monitoring for possible complications.
- Psychologists: management of post-traumatic stress.
- Physiotherapists & occupational therapists: physical rehabilitation.
- Social workers: assistance with administrative procedures.
- Teachers & disability support services: school adaptation in case of sequelae.

Secondary prevention

- **Vaccination** and regular medical follow-up.
- Patient and family therapeutic **education**.
- Early detection of **relapse signs**.
- **School reintegration**: coordination with the school physician and the local disability support service if needed (Recommendation 95, strong recommendation, very low level of certainty).
- Promote **physical and leisure activities** to improve quality of life (Recommendation 96, strong recommendation, very low level of certainty).

Commitments

To halve by 2030

Sepsis morbidity and mortality in France