

2030 Global Agenda for Sepsis

Making the Next Success Story in Global Health

| urgency of action | 48.9 million sepsis cases | 1 in every 5 deaths worldwide | 20.3 million under-5 children | 5.7 million maternal sepsis | 85% burden in low-resource settings | invisible global health threat | policy, investment and knowledge gaps | 5 strategic pillars | political leadership and multilateralism | health system readiness for sepsis and its sequelae | whole-of-society approach | sepsis research and innovations | sepsis in pandemics and other emergencies |



Global
Sepsis
Alliance

ACKNOWLEDGMENTS

The Global Sepsis Alliance (GSA) initiated and led the development of the 2030 Global Agenda for Sepsis through an inclusive consultation process with Regional Sepsis Alliances and over 70 member and partner organizations representing Sepsis patients and their families, public, private, academic and civil society sectors. The multi-stakeholder strategic planning dialogue started in 2023 on the margins of the 78th Session of the UN General Assembly in New York, followed by Sepsis side-events in parallel to the 2023 World Health Summit in Berlin and the 77th Session of the World Health Assembly in Geneva in 2024.

First, we would like to thank our strategic partners in co-convening the multilateral dialogue meetings, including the UNITE Parliamentarians Network for Global Health (UNITE), Virchow Foundation, Sepsis Stiftung, Clinton Health Access Initiative (CHAI), the Medical Women's International Association (MWIA), and the Global Antibiotic Research and Development Partnership (GARDP).

The GSA extends special gratitude to Prof. Dr. Andrew Ullmann, the Chair of the Global Health Sub-Committee in the German Parliament for launching the 2030 Global Agenda for Sepsis at the German Bundestag on the occasion of the 2024 World Sepsis Day.

We are honoured that Dr. Tedros Adhanom Ghebreyesus, the Director-General of the World Health Organization and Prof. Dr. Karl Lauterbach, the Federal Minister of Health of Germany have once again extended their Patronage to the World Sepsis Day in 2024.

The Global Sepsis Alliance would like to hereby acknowledge the technical input by the staff from the World Health Organization Headquarters and Regional Offices to the development of this document.

Finally, we are grateful for the review and technical contributions received from leaders and experts of the African Sepsis Alliance (ASA), Asia-Pacific Sepsis Alliance (APSA), European Sepsis Alliance (ESA), ESA Patient and Family Support Working Group, UK Sepsis Trust, END SEPSIS – Rory Staunton Foundation (US), Eastern Mediterranean Sepsis Alliance (EMSA), Sepsis Alliance (US), Japanese Sepsis Alliance (JaSA), Nepalese Society of Critical Care Medicine (NSCCM), Society of Critical Care Medicine (SCCM), the World Federation of Critical Care Nurses (WFCCN), Sepsis-en-daarna (Netherlands), Sepsisfonden (Sweden), FHU SEPSIS (France), SEPSIBEL (Belgium) and the Global Antibiotic Research and Development Partnership (GARDP). The majority of the GSA strategic partners and contributors have also officially endorsed the 2030 Global Agenda for Sepsis, along with the French Intensive Care Society - Société de Réanimation de Langue Française (SRLF – FICS), International Network Promoting Research in ICU (CRICS-TRIGGERSEP), International Fluid Academy (IFA), Sepsis Australia, Hellenic Society for Chemotherapy, Hellenic Sepsis Study Group, Hellenic Institute for the Study of Sepsis, The George Institute for Global Health, Associazione Microbiologi Clinici Italiani (AMCLI), The Synergist, Physician-Patient Alliance for Health and Safety (US), and the World Federation of Societies of Anaesthesiologists (WFSA).

We look forward to future endorsements of the document and to making Sepsis the next success story in Global Health through coherent voice and actions of national, regional and global partners. For the continuously updated list of organizations officially endorsing the 2030 Global Agenda for Sepsis, please visit: globalsepsisalliance.org/2030-global-agenda-for-sepsis

2030 Agenda Changes

Table of Contents

5	EXECUTIVE SUMMARY
9	SECTION 1 – GLOBAL BURDEN OF SEPSIS Human and Societal Burden Economic and Health Sector Burden Sepsis – A Critical Milestone for Attaining 2030 SDGs
20	SECTION 2 – TWO DECADES OF SEPSIS FIGHT AND ACHIEVEMENTS Clinical Knowledge Evolution in Sepsis Positioning Sepsis in Global Health Dialogue Success Stories Driven by Sepsis Patients and Families
30	SECTION 3 – MAJOR GAPS IN GLOBAL SEPSIS RESPONSE
37	SECTION 4. WAY FORWARD - 2030 GLOBAL AGENDA FOR SEPSIS Strategic Pillar 1. Political Leadership and Multilateral Cooperation Strategic Pillar 2. Health System Readiness for Sepsis and Its Sequelae Strategic Pillar 3. Whole-of-Society Response Strategic Pillar 4. Sepsis Research and Innovations Strategic Pillar 5. Sepsis in Pandemics and Other Emergencies
65	SECTION 5. RESULTS FRAMEWORK – 2030 GLOBAL AGENDA FOR SEPSIS
72	ACRONYMS AND ABBREVIATIONS
74	REFERENCES



“We need to urgently change the status quo. Sepsis, affecting almost 50 million children, women and men every year, remains invisible in the global health dialogue and architecture. The urgency of our action is even more critical, as proven, cost-effective interventions are available to prevent millions of Sepsis-related deaths and disabilities. Research and development priorities for novel solutions are also clear, how to improve prevention, early detection and treatment of this medical emergency, and ensure appropriate care and rehabilitation for Sepsis survivors. The 2030 Global Agenda for Sepsis presents a roadmap for these critically needed actions. We hope, political leaders, public health and clinical practitioners, donor and philanthropic institutions, innovators and Sepsis advocates join us in making Sepsis the next success story in Global Health.”

Dr. Mariam Jashi

CEO, Global Sepsis Alliance

Former Deputy Minister of Health and Member of Parliament of Georgia



“The 2030 Global Agenda for Sepsis can take our common fight to the next level and enable us to save millions of children and adults from unnecessary deaths and disabilities. Over the last two decades, the global Sepsis community has achieved significant progress. We are honoured to see the ever-increasing recognition of the role the Global Sepsis Alliance has played since its commencement in 2010. The World Sepsis Day movement, initiated by the GSA now engages more than 50,000 stakeholders. The World Sepsis Congress launched in 2016 has already reached 107,000 policymakers, healthcare workers, scholars and Sepsis advocates across 180 countries with the state-of-the-art knowledge in the field. The 2017 World Health Assembly Resolution on Sepsis was a pivotal moment, and today, the Global Sepsis Alliance is proud to present the very first multi-year global strategy for future actions.”

Prof. Dr. Konrad Reinhart

Founding President, Global Sepsis Alliance

President, Sepsis Stiftung



“We cannot achieve the 2030 Sustainable Development Goals without reinvigorated fight against Sepsis and its sequelae. We shall scale up clinical knowledge and proven interventions to protect 5.7 million mothers and 20 million children who are afflicted with Sepsis every year. Stopping Sepsis and its sequelae needs robust political commitment and investments in multi-lateral and multi-sectoral actions. We will address the inequities leading to low- and middle-income countries continuing to bear an inordinately high burden, 85% of the global Sepsis cases, and disproportionately less investment in infection prevention and control measures. We are confident that the 2030 Global Agenda for Sepsis catalyses action to decrease the inequities in knowledge and increase resources to provide quality Sepsis care for children, women, older adults and other vulnerable populations.”

Prof. Niranjana “Tex” Kissoon

President, Global Sepsis Alliance

Past President, World Federation of Paediatric Critical and Intensive Care Societies

EXECUTIVE SUMMARY

The 2030 Global Agenda for Sepsis

The **2030 Global Agenda for Sepsis** is the first multi-year strategic vision aimed at alleviating the significant human, societal, healthcare and economic burden of Sepsis and its sequelae through concerted efforts of UN Member States and multiple stakeholders at national, regional and global levels.

The Global Sepsis Alliance (GSA) initiated and coordinated the development of this document with the engagement of its 5 Regional Sepsis Alliances, and over 70 member and partner organizations from Africa, Asia-Pacific, the Caribbean, Eastern Mediterranean, Europe, Latin America and North America. The multi-stakeholder strategic dialogue started in 2023 on the margins of the 78th Session of the UN General Assembly in New York, followed by Sepsis side events in parallel to the 2023 World Health Summit in Berlin and the 77th Session of the World Health Assembly in Geneva in 2024. The strategic planning process also included focus group discussions and series of on-line consultations with Sepsis survivors and family representatives, healthcare practitioners as well as partners from public, private, academia and civil society sectors.

The ultimate goal of the 2030 Global Agenda is to avert millions of preventable deaths and disabilities among children, women, and men by stronger positioning of Sepsis in the global health and development architecture and enhancing response capacities to this medical emergency in community and healthcare settings. The strategy aims at reducing the global incidence of Sepsis by at least 25%, improving the survival rates of paediatric and adult patients by over 20%, and reducing the median cost per Sepsis patient per country by 20% from the 2017-2020 baselines.

Section 1 consolidates the latest epidemiological, clinical and economic data on Sepsis and its sequelae, reaffirming that Sepsis is a major killer of children and adults, accounting for 1 in every 5 deaths worldwide. Children, women, immunocompromised individuals and older adults are most vulnerable to this medical emergency. Sepsis is estimated to affect 48.9 million people and claim 13.7 million lives every year. The economic impact is also significant, accounting for 2.65% of healthcare budgets and a median hospital cost of €36,191 per septic patient per country. Indirect costs from productivity losses due to illness, disability, and premature death are even more substantial, constituting 70-80% of the total societal costs of Sepsis. With 5.7 million maternal Sepsis cases and 2.9 million deaths in children under five annually, the 2030 Sustainable Development Goals (SDGs) cannot be achieved without fundamental changes in the global Sepsis response. The new Sepsis agenda can help accelerate progress towards 9 out of 17 SDGs by closing inequality and knowledge gaps, and enhancing universal health coverage (UHC) and financial protection for the most vulnerable. The document also highlights the urgency of synergizing policies and actions for Sepsis and antimicrobial resistance (AMR), as the estimated 4.95 million AMR-related deaths annually are part of the 13.7 million Sepsis-related deaths. Finally, with increased risks of infections and accordingly, increased risks of Sepsis, any future pandemics, armed conflicts, humanitarian crisis and climate change will require stronger response capacities to Sepsis.

Section 2 summarizes the achievements of the past two decades in the fight against Sepsis. Important progress has been made in clinical knowledge evolution and international guidance from the Surviving Sepsis Campaign. The World Health Organization has also

advanced in the development of Sepsis-related guidelines and tools that will help bridge the critical knowledge gaps in the Global South. High-level advocacy and alliance-building efforts have led to the historic World Health Assembly Resolution on Sepsis in 2017 (WHA70.7). The G7 Health Ministers' Communique (2022) and the 2023 Berlin Declaration endorsed by 75 international health partners were two other important advocacy platforms. Sepsis Survivors and families of patients who have lost their lives to Sepsis have championed national action plans (NAPs) and evidence-based policy initiatives in a number of countries, saving thousands of children and adults. The success stories, primarily from high-income countries such as Australia, Belgium, Ireland, Sweden, the UK and the US may inspire and guide Sepsis NAPs, patient-focused policies and changes in other countries and territories.

Section 3 consolidates the remaining gaps in the global Sepsis response. Despite the documented progress, and the fact that proven and affordable interventions are feasible to scale-up in all settings, implementation gaps remain that cost lives every day. Sepsis and its sequelae are still largely invisible in the global health landscape and receive disproportionately low political and financial investments compared to their human and economic costs. Seven years after the adoption of the WHA70.7 Resolution, fewer than 10% of the UN Member States have developed NAPs and evidence-based policies. Sepsis remains underfunded in national and international agendas, with no earmarked development funding from governments, international financing institutions (IFIs), public-private partnerships (PPPs) or innovative financing platforms. Even well-resourced healthcare systems document poor clinical outcomes due to insufficiencies in pre-hospital recognition of Sepsis, and timely identification and management at primary and hospital levels. A hospitalized patient with Sepsis is more likely to die than a patient with a heart attack or stroke, yet Sepsis is still not treated with the same urgency as other critical conditions. Research and development (R&D) funding to generate knowledge and innovations, including novel vaccines, diagnostics, therapeutics or AI tools are also limited. The quantity and quality of epidemiological and clinical data remain scarce to inform policy actions, especially in LMICs. The 2020 publications on the global burden of Sepsis established foundational evidence; however, the Sepsis response needs more sustainable data reporting and analysis systems through routine administrative health statistics, Sepsis registries or specialized studies to inform relevant policies and action.

Building on the achievements in the global Sepsis fight, the WHA70.7 Resolution and the analysis of remaining gaps **Section 4** presents the 2030 Global Agenda for Sepsis and its **five strategic pillars**

Strategic Pillar 1: Political Leadership and Multilateral Cooperation

Multilateralism will be key to the success of the new Global Agenda for Sepsis. The strategic pillar calls for the establishment and operationalization of a High-Level Political Platform to mainstream the Sepsis agenda in global health and development dialogue and architecture. By 2030, at least 80% of HICs and 50% of LMICs need to complete National Action Plans or national action planning (NAP) process for Sepsis with earmarked domestic budgetary resources. The countries should ensure synergies of Sepsis NAPs with broader health sector

plans and initiatives, such as UHC, maternal, newborn and child health (MNCH), infection prevention and control (IPC), AMR, PPPR, patient safety and healthy aging. By 2030, at least 80% of HICs and 50% of LMICs should incorporate services for Sepsis into national packages of priority services for UHC. Governments, IFIs, PPPs in global health and philanthropic foundations are called to initiate grant, loan and/or innovative funding mechanisms for improving Sepsis response locally and internationally, with special considerations for LMICs. Sepsis investment cases should focus on “Saving Lives and Saving Costs”, as success stories from Australia, Canada and other countries have documented high returns on investments of relevant policies. Finally, GSA and its partners should initiate regular data collection and annual Global Sepsis Reports to map progress vis-à-vis the WHA70.7 Resolution, related World Health Assembly resolutions and the targets set by the current 2030 Global Agenda for Sepsis.

Strategic Pillar 2: Health System Readiness for Sepsis and Its Sequelae

By 2030 at least 50% of UN Member States should launch evidence-based and patient-focused Clinical Pathways for Sepsis and Sepsis Bundles for adult and paediatric patients, with special emphasis on vulnerable populations, such as pregnant women, newborns, children, older adults and patients living with chronic diseases. Increased investments in perinatal care, primary health care (PHC) and emergency, critical and operative care (ECO) services are essential. Healthcare institutions engaged in the care cascade should have essential supplies and equipment for managing Sepsis and related organ dysfunction. This includes microbiology labs or rapid diagnostic tools, ventilators with adequate oxygen supply, renal replacement therapies, patient monitoring systems, antibiotics, and IV fluids. Key clinical processes can be strengthened and lives saved even without new input of material resources, with adequate training on clinical management of Sepsis. Countries should incorporate services for Sepsis into packages of priority services for UHC and design associated curricula for all health worker groups, from community health workers to undergraduate and post graduate medical and nursing students, and for all health workers who care for the acutely ill. Curricula should focus on active and lifelong learning methodologies, telemedicine and other digital solutions, including digital clinical decision support. UN Member States should also initiate quality improvement (QI) programmes for Sepsis, including regionalization and accreditation initiatives. Finally, cross-cutting IPC initiatives should be strengthened for improved prevention of healthcare-associated infections (HAIs), high routine immunization coverage in children and adults, accessibility of WASH facilities in over 80% of healthcare institutions across LMICs and effective AMR stewardship.

Strategic Pillar 3: Whole-of-Society Response

Awareness on Sepsis and its sequelae should be improved among the general public, media representatives and policymakers through consistent advocacy, a simplified new narrative on Sepsis, and the engagement of Sepsis survivors and patient families. As over 80% of cases originate in the communities, public representatives should be able to identify Sepsis as a medical emergency requiring immediate emergency care seeking. Simplified

and contextualized messages and stronger media engagement will be essential for making “Sepsis” a household name and holding governments accountable for action. Patients-for-Patient support services and groups should be further promoted, and Sepsis Survivors should lead the patient voice in designing policy, institutional and community-level interventions, including for post-hospital rehabilitation and recovery. Community care seeking behaviours should be studied and analysed to inform education and engagement strategies.

Strategic Pillar 4: Sepsis Research and Innovations

Public and private research opportunities and funding for Sepsis should be substantially improved along with investments in novel prevention, diagnostic, treatment and AI solutions. The UN Member States, especially the OECD countries are called to allocate earmarked funds for Sepsis research and academic collaboration. By 2025, a Global Sepsis Research and Innovation Platform, an international PPP, should be launched to systematically address unmet needs in Sepsis prevention, diagnostics and treatment, as well as regulatory aspects. The platform should facilitate R&D investments for novel vaccines, fast pathogen detection tools, antimicrobial and immunomodulatory therapies, precision medicine approaches, and innovations to address Sepsis sequelae, care and rehabilitations needs of patients and their families.

Strategic Pillar 5: Sepsis in Pandemics and Other Emergencies

In line with the WHA70.7 Resolution, medical countermeasures should be strengthened for managing Sepsis in emergencies. Services for the clinical management of Sepsis should be incorporated into all packages of High-priority Health services for Humanitarian response (H3 package). UN Member States are called to integrate Sepsis-related interventions into national PPPR plans. Sepsis prevention, early detection, treatment, and post-hospital care and rehabilitation should also be integrated into health protocols for defence/military personnel and the essential care services for civilians in humanitarian settings. Humanitarian response protocols and health service packages from leading international humanitarian aid organizations should consistently address Sepsis prevention and response measures. Finally, UN Member States need to integrate Sepsis into the national laws and policies on climate change adaptation.

SECTION 1

GLOBAL BURDEN OF SEPSIS

1.1. Human and Societal Burden

Sepsis is a life-threatening medical emergency, when the body's (the host's) response to infection causes injury to its own tissues and organs. This can lead to shock, multi-organ failure, disability and death, especially if it is not recognized early and treated promptly. *Please see Annex A for the latest consensus definitions for Sepsis and septic shock.* (1)

The current section consolidates the latest epidemiological, clinical and economic data on Sepsis and its sequelae, reaffirming that Sepsis is one of the leading causes of mortality, disability and healthcare expenditures worldwide, accounting for approximately 20% of all annual deaths. (2,3) This global health threat affects 48.9 million people every year, including 20.3 million children and 5.7 million women during pregnancy, delivery, or post-partum. (4)

An estimated 11 million Sepsis-related deaths were reported in 2017. (4) However, according to the latest estimates from the Institute of Health Metrics and Evaluation (IHME), Sepsis is responsible for 13.7 million deaths annually, claiming lives of 2.9 million children under the age of five and accounting for 10.7% of all maternal deaths. (4,5)

Sepsis affects both resource-limited and economically developed nations. People living in countries with low, low-middle, or middle sociodemographic indices (SDI) bear 85% of the global burden of Sepsis, with sub-Saharan Africa and South-East Asia affected the most. (4) The sub-Saharan African region with nearly 17 million cases and 4 million Sepsis-related deaths, documents the highest Intensive Care Unit (ICU) and hospital mortality rate (47.2%) in septic patients. (6) Despite the advancements, 30-day septic shock mortality remains high even in developed regions of North America (33.7%) and Europe (32.5%). (7) In the United States, Sepsis is the leading cause of hospital mortality, taking 350,000 adult lives annually - more than the lives lost to stroke, prostate cancer, breast cancer, and opioid overdoses combined. (8,9)

Figure 1. Global Burden of Sepsis

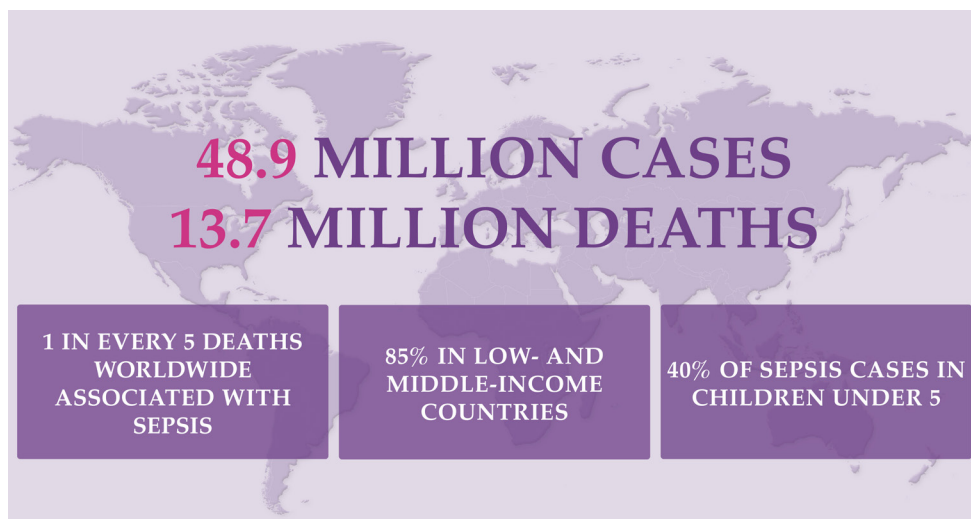
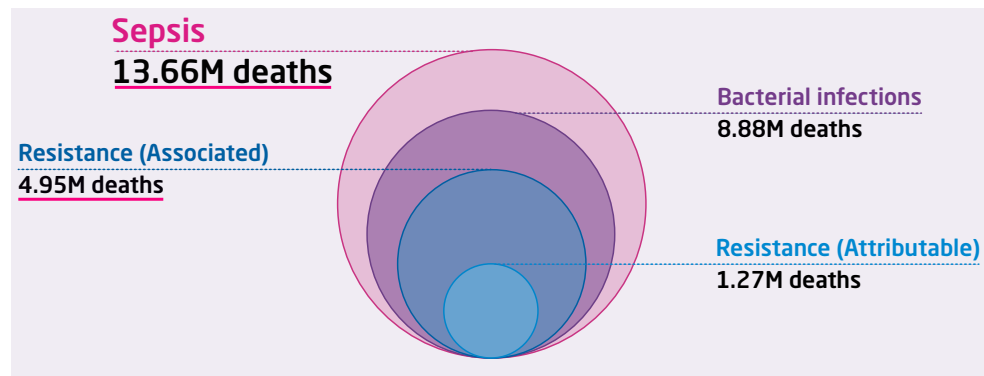


Figure 2. Composition of Global Infection-Related Deaths
Source: IHME, 2023



Sepsis is the final common pathway to death from most infectious diseases, including bacterial, viral and fungal pathogens, as well as parasites, such as those causing malaria.

Out of the 13.7 million Sepsis-related deaths annually, 8.8 million are estimated to be caused by bacterial infections (Figure 2), and this number includes 4.95 million deaths attributable to or associated with antimicrobial resistance (AMR). (5) In addition, the estimated 7.7 million infection-related or Sepsis-related deaths in 2019 were associated with 33 individual bacterial pathogens, which would rank these infections as the 2nd leading cause of mortality globally. (10) Among the leading bacterial pathogens causing Sepsis are *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Streptococcus pyogenes*, along with fungal pathogens of the *Candida* species. (11)

Most of the 14.9 million excess deaths documented during the COVID-19 pandemic were also likely to be associated with or attributable to Sepsis, as 78% and 33% of COVID-19 patients in intensive care units (ICUs) and hospital wards, respectively, met diagnostic criteria for Sepsis. (12,13) The pandemic fundamentally changed the landscape of Sepsis epidemiology, with a high burden of SARS-CoV-2-associated Sepsis and a growing consensus, that severe COVID-19 causing organ dysfunction was appropriate to label as Sepsis. (13,14)

Contrary to the common belief that only communicable diseases lead to Sepsis, 15.8 million Sepsis cases, and 5.1 million, or nearly half of all Sepsis-related deaths occur as infectious complications of underlying injuries or non-communicable diseases (NCDs). (4) From the perspective of patients consulted for this document, Sepsis is often perceived as primarily an ICU problem. In contrast, 50% of septic patients hospitalized in the US and two-thirds of those in Germany were not treated in an ICU, and post-sepsis syndrome is not limited to patients treated in an ICU. (15) Another common misconception is that Sepsis primarily occurs in hospitals, often as a result of healthcare-associated infections (HAIs). However, studies have repeatedly confirmed that over 80% of patients have community-onset Sepsis, diagnosed within 3 days of hospitalization. (16,17)

Finally, the impaired quality of life, disability, increased rehospitalization and mortality risks, are all part of the Sepsis sequelae and contribute to the significant human burden of this global health challenge. (18) Sepsis survivors often face long-term sequelae, life-changing effects of the critical illness, and need specialized care and rehabilitation. Sepsis

may also lead to post-ischaemia limb amputation and reinfection risks, such as those from prosthetic pressure injuries. Chronic pain, post-traumatic stress disorder, organ dysfunction, fatigue and Post Exertional Malaise (PEM) are common after effects of Sepsis. Post-Sepsis Syndrome (PSS) includes long-term physical, medical, cognitive, and psychological issues after recovering from Sepsis, and between 40% to 74% of septic patients receive a new medical, psychological, or cognitive diagnosis consistent with post-sepsis morbidity. (15,19) PSS often manifests in medical and mental health conditions comparable to long-term sequelae of COVID-19. (20) (21)

1.2 Economic and Health Sector Burden

Along with the immense human suffering, affecting up to 50 million children and adults every year, Sepsis has a significant economic impact. Even before the COVID-19 pandemic Sepsis-related expenditures were estimated to account for 2.65% of healthcare budgets or 0.33% of Gross National Product (GNP). (22)

Globally, the mean total hospital costs per Sepsis patient vary from €1,101 to €91,951, and the median of the total Sepsis costs per country is estimated at €36,191, equivalent to €50 per capita annually. (22) In addition to high ICU mortality rates (25.8%), septic patients require a prolonged length of stay in intensive care units (ICU-LOS) and incur higher treatment costs compared to other ICU patients. (23,24)

Figure 3. Economic and Healthcare Burden

Economic and Healthcare Burden of Sepsis	
€ 36,191 Median Cost per Sepsis Patient per Country	\$ 41,500 Average Total Hospital Costs for Paediatric Sepsis Stays (US)
2.65% Healthcare Budget Expenditures	0.33% GNP Expenditures

Most published studies address the financial and economic impact of Sepsis in High-Income Countries (HICs) and reaffirm the urgency of action even in well-resourced healthcare contexts.

- Sepsis is estimated to cost US\$ 62 billion in hospitalizations and skilled nursing care to the United States annually and account for 9.9% of all hospital costs. (9,25) The average hospital cost per adult and paediatric Sepsis stays in 2021 was US\$ 28,800

and US\$ 41,500, respectively. (26) Overall, 18% of nationwide paediatric hospitalization costs from 2012-2018 were related to Sepsis, and the median cost of Sepsis hospitalization (US\$ 26,592) was 12-times higher than that of all-cause child hospitalizations (US\$ 2,199). (27)

- Australia further documented that about half of the Sepsis patients were readmitted within 90 days of discharge, and over 70% were re-hospitalized within a year. (23) High readmission rates increase the demand for inpatient services and the overall healthcare costs for Sepsis, which could be prevented by timely and appropriate management of Sepsis and its sequelae.
- The Sepsis burden is especially challenging in the context of the aging population in high-income countries, as this medical emergency is significantly associated with age. Adults aged ≥ 65 years were 13-times more likely to be hospitalized with Sepsis, and nursing home residents had 6-times higher risks of presenting with Sepsis in emergency rooms. (28,29)

Sepsis is expected to have an even greater economic impact on patients and families living **in Low- and Middle-Income Countries (LMICs)**, with the highest disease burden and limited access to universal health coverage (UHC) and financial protection mechanisms in health.

- Over 75% of the 3.1 billion people left without effective UHC coverage in 2023 live in LMICs of South Asia, Southeast Asia, East Asia, and Sub-Saharan Africa. (30) As a result, individuals and families affected by Sepsis are expected to experience higher out-of-pocket payments, and catastrophic and impoverishing health expenditures.
- As an example, 47% of patients admitted to hospitals for the treatment of septic shock in Vietnam and families of 56% of patients who died from septic shock have incurred catastrophic expenditures. (31)
- Notwithstanding data limitations from LMICs, the annual economic burden of neonatal Sepsis only in Sub-Saharan Africa (SSA) is estimated to range from US\$ 10 to 469 billion. (32)

Finally, the significant direct healthcare costs represent only a small proportion (20-30%) of the true fiscal burden of Sepsis, as the major economic impact of this medical emergency is observed after hospital discharge. (18) (24) Indirect costs from loss of productivity, disability, and premature deaths account for 70-80% of the total societal costs of Sepsis. (16, 21)

- Australia estimates \$700 million Australian Dollars (AUD) as direct hospital costs of Sepsis annually. However, these estimates represent only 14% of the total societal cost, and indirect costs due to premature deaths and disability from Sepsis exceed AUD \$4 billion. (33)
- Within the UK, direct costs of Sepsis to the National Health Services (NHS) were estimated to be as high as £2.6 billion a year, but the estimated cost to broader society through lost productivity and premature death was £15.6 billion. (34)



- The Netherlands estimates € 3.8 to € 6.5 billion as the combined disease and indirect economic burden of Sepsis, larger than the annual burden associated with coronary heart disease or stroke.(35) Sepsis was found to account for 57,304 Quality-Adjusted Live Years (QALYs) and more than half or 30,406 QALYs were lost in quality of life of survivors.
- According to the same study, one year after ICU treatment, 47% of previously employed Sepsis survivors remained unemployed, while the remaining 53% continued to work with lower productivity. (35) Similar trends were observed in the US, with almost half, or 49% of ICU Sepsis survivors remaining newly unemployed after one year of the critical illness.(36)
- Sub-Saharan Africa, with the highest neonatal mortality from severe infections, is estimated to lose 5.29–8.73 million Disability-Adjusted Life Years (DALYs) every year only to neonatal Sepsis.(32) Finally, the high burden of Sepsis and the high burden of caring for Sepsis survivors by family members, are expected to further increase Sepsis-related productivity losses in LMICs, and the overall economic impact of Sepsis.

1.3. Sepsis – A Critical Milestone for Attaining 2030 SDGs

The 2030 Sustainable Development Goals (SDGs) and related aspirations for Maternal, Newborn, and Child Health (MNCH), UHC, AMR, and Pandemic Prevention, Preparedness and Response (PPPR) cannot be achieved without robust actions against Sepsis at national, regional and global levels.

A reinvigorated Sepsis response is essential to accelerate progress towards health-related SDG 3 (*Figure 4*) as well as 8 other Sustainable Development Goals (*Figure 5*).

Figure 4.

Sepsis and Health SDG 3		
 3 GOOD HEALTH AND WELL-BEING 	Annual Sepsis Cases	Annual Sepsis Deaths
	48.9 Million	13.7 Million
	20.3 Million Children Under -5	2.9 Million Children Under -5
	5.7 Million Pregnant Women	10.7% Maternal Deaths
	15.8 Million NCDs and Injuries	5.1 Million NCDs and Injuries

SDG 3: Good Health and Wellbeing

Maternal Sepsis

Sepsis affects 5.7 million women during pregnancy, childbirth, or postpartum every year and remains the 3rd most common cause of maternal deaths. (37) Sepsis accounts for 10.7% of maternal mortality in resource-limited countries, compared to 4.7% in developed regions, with Southern Asia and Sub-Saharan Africa bearing the highest burden. (38,39) Even though this critical condition occurs in only 0.04% of deliveries, 23% of all maternal deaths in the United States were found to be related to Sepsis. (40) Therefore, a robust response to Sepsis is essential to reduce the global maternal mortality, especially among the most vulnerable groups in LMICs (SDG 3.1. target).

Sepsis in Children

The Sepsis agenda is also central to SDG target 3.2 as children are disproportionately affected. Over 40% of the global burden of Sepsis occurs in children, with an estimated 20.3 million paediatric Sepsis cases and 2.9 million deaths in children under the age of five. These numbers include 1.3 million neonatal Sepsis cases that most commonly affect pre-term and low-weight newborns. (41) (4,10) Sepsis remains the 3rd most common cause of neonatal deaths globally, with LMICs, particularly the African region, reporting the highest incidence of severe infections and Sepsis among newborns. (4) (32,42–44)

Immunization and Sepsis

Any infection can lead to Sepsis, and immunization of children and adults against vaccine-preventable diseases is one of the most effective prevention strategies to avert Sepsis and related deaths and disability. Therefore, the global Sepsis community reiterates the need to accelerate progress towards the 2030 Immunization Agenda targets. (45) Promotion of routine, catch-up, or campaign immunization rounds against diphtheria, tetanus, measles, influenza, COVID-19 and other infections should be a central element of Sepsis prevention measures both in communities and healthcare settings.

Sepsis in Patients Living with HIV, TB and Malaria

Sepsis is always a serious condition; however, people living with other infectious diseases or immunocompromised conditions are at a higher risk. (46) The clinical course of Sepsis is more severe in patients with the human immunodeficiency virus (HIV). (47,48) HIV increases the risk of Sepsis mortality by 28% compared with people living without HIV across all time periods and geographic areas, especially among patients treated in low-income countries. (47,48)

Sepsis and septic shock are rare complications of Tuberculosis (TB) in immunocompetent patients; however, TB is the leading cause of Sepsis in regions of high HIV and TB prevalence, such as sub-Saharan Africa. (49) (50) Mycobacterium tuberculosis was found to be responsible for 25%-30% of bloodstream infections in septic patients in Africa. Furthermore, empirical treatment of TB in septic patients in Uganda was associated with improved 28-day survival. (50,51)

Finally, an estimated 7.3% of patients with severe malaria develop clinical Sepsis, 6% of children hospitalized with severe falciparum malaria in Africa were found to have bacteraemia, and common misdiagnosis complicates effective treatment of Sepsis in patients with malaria. (52) (53,54)

NCDs and Injuries

An effective Sepsis response is equally important for reducing premature deaths from NCDs (SDG target 3.4) and injuries (SDG target 3.6), as 5.1 million Sepsis-related deaths occur secondary to Sepsis complicating underlying injuries or NCDs. (4) WHO reaffirms that anyone affected by severe injury or serious NCD can progress to Sepsis, and older persons, pregnant or postnatal women, newborns, hospitalized and ICU patients, immunocompromised individuals and people with chronic medical conditions (such as diabetes) are at a higher risk. Sepsis may not be the primary cause of hospital admission, but can occur as a complication of other presenting conditions, such as NCDs and trauma.

Finally, cancer patients face 4-10 times higher risk of Sepsis, with the variation in risk attributed to the differences in cancer types. (55,56) In-hospital mortality rates for Sepsis in cancer patients range between 18-45%, (55–58) although these rates have been gradually decreasing over time, likely due to improved Sepsis management strategies and innovations in cancer therapies.(59)

Universal Health Coverage

The effectiveness of the Sepsis response is closely linked to SDG target 3.8 for adequate Universal Health Coverage. The challenge, however, remains how to achieve universal prevention, diagnosis and management of Sepsis through the integration of clinical pathways and Sepsis bundles into national UHC programmes and budgets.

The GSA and the African Sepsis Alliance recommend the clinical and epidemiological data for Sepsis be considered as tracer indicators for UHC index measurement. Comprehensive Sepsis Care Cascades across the different levels of healthcare can holistically reflect the capacities of national healthcare systems to ensure universal access to immunization, Water, Sanitation and Hygiene (WASH), emergency and critical care, and other essential UHC services.

R&D of Vaccines and Medicines

Research and development (R&D) of novel vaccines, diagnostics (e.g., point-of-care, AI solutions), antimicrobial and immunotherapies for Sepsis are closely linked to the SDG 3.b agenda. Effective prevention of Sepsis in children and adults relies on improved and sustained coverage of routine immunization, as well as the development of new vaccines against the pathogens most commonly causing Sepsis (e.g., E. coli, Klebsiella). The Sepsis response also needs more effective diagnostic solutions, as the delayed recognition remains a key barrier to timely initiation of life-saving treatment and source control measures. The delayed administration of antimicrobials after the onset of Sepsis can, in fact, increase the mortality risk from 0.42% to 7.6% per hour. (60,61)

Pandemic Prevention, Preparedness and Response

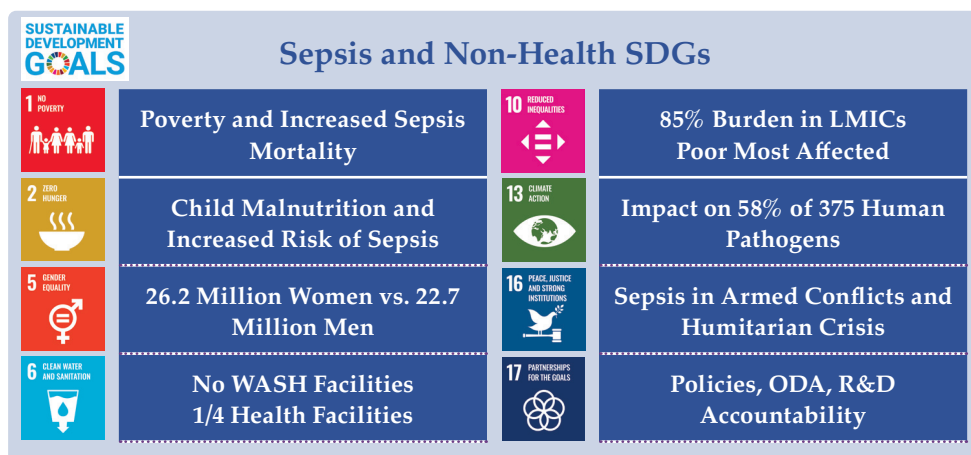
The Sepsis agenda should be central to any discussions on International Health Regulations and broader aspects of PPPR (SDG target 3.d.1). Up to 80% of COVID-19 patients in ICUs were affected by Sepsis, and any future pandemics will lead to an increased burden of Sepsis and its long-term sequelae. (12) If the next pandemics are caused by dominant strains of multi-drug resistant pathogens, the AMR impact on patient outcomes is likely to be even greater than that of the COVID-19. Any pandemic will further aggravate the 10 million shortage of health workforce, especially in LMICs, and constrain the delivery of effective Sepsis care. (62)

Antimicrobial Resistance

Stronger synergies are essential between AMR and Sepsis advocacy, policies, investments and R&D agenda, as an estimated 4.95 million out of 13.66 million Sepsis-related deaths are associated with or attributable to AMR. (5) AMR, when present, contributes to rapid evolution to Sepsis and septic shock, and septic patients with resistant pathogens have higher risks of hospital mortality. (46) As more pathogens become resistant, more people are at risk of infections that can progress to Sepsis.

AMR and Sepsis actions should also be synergized in clinical practice. Building on the WHA70.7 resolution, the current strategy acknowledges that the inappropriate and excessive use of antimicrobials contributes to the threat of antimicrobial resistance and that Sepsis represents the most vital indication for the responsible use of effective antimicrobials for human health. Starting antimicrobial therapy in septic patients within the 1st hour of recognition, and shorter time-to-antibiotics, can be life-saving, as every hour of delay increases mortality risks by 0.42%-7.6%. (60,61). India confirmed that delayed administration of antibiotics beyond 1 hour of recognition of paediatric Sepsis is also associated with higher mortality rates in children. (63) While general public and healthcare practitioners are advised to avoid unnecessary use of antibiotics, effective Antimicrobial Stewardship in Sepsis has shown no significant increase in inappropriate antibiotic use. (64) Earlier administration of antibiotics have also shown minimal adverse effects compared to the clinical outcomes and deaths averted from Sepsis. (65)

Figure 5.



In addition to health-related SDG 3, progress towards 8 other Sustainable Development Goals (1, 2, 5, 6, 10, 13, 16 and 17) will also be closely linked to the success of the global Sepsis agenda.

SDG 1: Poverty and Sepsis

The poor are affected the most, as the community poverty rate and lack of insurance are associated with higher Sepsis incidence and mortality. (66,67) Racial and ethnic minority groups, those who are unemployed or living in neighbourhoods with poverty rates greater than 10% were found to suffer from higher mortality when admitted to hospitals for septic shock.(66) Socio-economic deprivation was also linked to an increased risk of developing non-COVID-19 related Sepsis and 30-day mortality in England. (68)

SDG 2: Sepsis and Malnutrition

As of 2022, 45 million children under the age of 5 suffer from wasting, 149 million are stunted, and nearly half of deaths among children are linked to malnutrition. (69) Studies repeatedly document increased risks of Sepsis in malnourished children, as malnutrition is associated with depressed immune responses, higher susceptibility to infectious diseases, Sepsis and septic shock. (70,71) International guidance for managing Sepsis in paediatric patients also includes special therapeutic considerations for malnourished children. (70) Finally, the presence of malnutrition is associated with poor hospitalization outcomes among older adults admitted for Sepsis. (72)

SDG 5: Gender Equality

Sepsis affects 26.2 million women and girls every year, compared to 22.7 million men and boys. This gender difference may be explained by 5.7 million cases of maternal Sepsis. However, disparities are also observed in clinical care and sex-based differences in Sepsis outcomes remain even in countries with high Gender Equality Index. Sweden, as an example, demonstrated that the 1-hour Sepsis bundle was administered to 30% of female patients vs. 41.5% male patients, and 30-day mortality was higher in women with Sepsis and septic shock. (73) Furthermore, female patients are less likely to receive mechanical ventilation or renal replacement therapy. (74)

SDG 6: Clean Water and Sanitation

Practicing basic hygiene and good sanitation is essential for preventing infections that can progress to Sepsis and septic shock. The European Centre for Disease Prevention and Control (ECDC) reaffirms that proper cleaning of hands and use of antiseptic solutions are the most effective ways to prevent healthcare-associated infections that may lead to Sepsis. (75) However, LMICs bearing the highest burden of Sepsis do not have adequate WASH facilities even in health care settings. (76) WHO and UNICEF estimate, that 1 in 4 health care facilities lack basic water services and 896 million people have no water services at their health care facilities. (77)

SDG 10: Sepsis and Inequality Agenda

Equality is central to the Sepsis agenda. Sepsis widens inequality gaps, as it disproportionately affects children, women, and men living in resource-limited countries, and areas of high socio-economic deprivation. Over 4/5 of Sepsis cases occur in LMICs, where health-care systems are the least advanced and the economic burden of Sepsis will only perpetuate inter-generational poverty and disparities. Even in high income countries, disparities exist in accessing healthcare and infection-related mortality in children and young people across socio-economic and ethnicity divides.(78) Finally, studies reveal sex-based differences in timely access to life-saving treatment and Sepsis survival rates across different geographic regions. (71) (73)

SDG 13: Climate Action

Climate change has the potential to exacerbate outbreaks of 58 percent of 375 human pathogens. (79) Accordingly, the Sepsis burden will be further aggravated by the climate change impact with already concerning trends in the incidence of dengue and other infectious diseases. (80) The global Sepsis community should prioritize inter-disciplinary collaboration for human, animal and planetary health, under the Quadripartite Agreement for One Health signed by the Food and Agriculture Organization (FAO), the United Nations Environment Programme (UNEP), the World Health Organization (WHO), and the World Organization for Animal Health (WOAH). (81)

SDG 16: Sepsis in Humanitarian Crisis

The Sepsis agenda is critical in the context of over 120 armed conflicts around the world, 362 million people in need of humanitarian assistance, and more than 110 million forced to leave their homes. (82,83) Armed conflicts, humanitarian crisis and displacement pose civilians and military personnel to increased risks of infections and Sepsis. Sepsis was the most common cause of death in Iraqi patients admitted to burns units, and the Syria conflict showed increased probability of Sepsis in wounds as a result of unclean primary closures. (84) Refugees and migrants are also at an increased risk of infections that can lead to Sepsis, due to their exposure to infectious diseases, poor hygiene, limited access to clean water and sanitation, limited and interrupted healthcare, and poor living conditions. (85)

SDG 17: Partnership for Development

Multilateralism at global, regional and national levels will be key to the success of the renewed Sepsis agenda. Reinvigoration of the global Sepsis response calls for the transfer and exchange of knowledge in national policy planning, data generation, clinical management, and R&D between countries of the Global North and South, as well as South-South and Triangular Cooperation. The Sepsis response calls for domestic investments and official development assistance (ODA). Finally, multilateral collaboration can facilitate the development of national Sepsis policies and accountability mechanisms within the overarching accountability frameworks for the 2030 Sustainable Development Agenda.

SECTION 2 TWO DECADES OF SEPSIS FIGHT AND ACHIEVEMENTS

2.1. Clinical Knowledge Evolution in Sepsis

Discussions on the harmonization of clinical management approaches to Sepsis among professional associations and medical practitioners began as early as the 1970s. Over the past 50 years, the medical community has witnessed substantial evolution in international consensus on definitions, criteria, and recommendations for clinical management of Sepsis in both adult and paediatric patients. Current clinical knowledge and approaches will continue to improve in parallel with the development of new intelligence.

Some of the most significant advancements in clinical management include the introduction of the pulmonary artery catheter for the measurement of hemodynamic profiles of patients with septic shock (1970), the coining of the term “Sepsis syndrome” (1989), and the first definition of Sepsis, along with the Sequential Organ Failure Assessment (SOFA) score and the Multiple Organ Dysfunction Score (MODS) in 1992. (86) (87)

The International Sepsis Forum (ISF) was established in 1997 with the mission of improving the scientific study, clinical management, and understanding of Sepsis. Since 2001 the ISF has been convening annual forums for the advancement of clinical and research knowledge globally, fostering transfer of experience and innovations.

In 2002, the Surviving Sepsis Campaign (SSC) was formed by three leading professional organizations in the field of Sepsis: the European Society of Intensive Care Medicine (ESICM), the Society of Critical Care Medicine (SCCM), and the International Sepsis Forum. The Campaign's debut initiative was the "Barcelona Declaration". (88) After the first iteration of the Surviving Sepsis Guidelines, the collaboration on the Campaign continued between SCCM and ESICM only.

The first SSC guidelines for the management of Sepsis and septic shock and the first SSC Sepsis bundles for early detection and management of severe Sepsis were published in 2004. Later, in 2020-2021, the SSC released the first international Sepsis guidelines for children, guidelines for the care of critically ill patients with COVID-19 and an update of SSC guidelines for adult patients. In 2024 the SCCM Paediatric Sepsis Definition Task Force validated Phoenix criteria for Sepsis and septic shock in children, and the next review, or the sixth version of the SSC guidelines is estimated to be available in early 2026 (January-March). (89–91)

Finally, in response to the 2017 World Health Assembly (WHA70.7) Resolution on Sepsis, the World Health Organization (WHO) is finalizing the first set of Guidelines on the Clinical Management of Sepsis. These guidelines, expected to be released by end of 2024, will include clinical recommendations and tools for resource-limited settings, including the LMICs affected the most.

2.2. Positioning Sepsis in Global Health Dialogue

In contrast to the clinical management aspects, concerted advocacy for positioning Sepsis in the global health dialogue as the leading cause of death and disability started much later, 20 years ago.

However, the last two decades have already documented achievements in advocacy and alliance building, high-level political engagement, and generation of foundational evidence for Sepsis.

Most importantly, 15 UN Member States have championed National Action Plans and/or evidence-based policies for Sepsis, as well as success stories and lessons for knowledge sharing. *See section 2.2.3.*

2.2.1. Advocacy and Alliance Building

Systemic efforts for awareness raising and international response to Sepsis stem from national and regional level initiatives. The German Sepsis Society was the first national association founded in 2001 and the Latin American Sepsis Institute (LASI) was the first regional alliance launched as early as in 2004. The US Sepsis Alliance, the UK Sepsis Trust, END SEPSIS - Rory Staunton Foundation, the German Sepsis Foundation and the Swedish Sepsis Trust (Sepsisfonden) followed in 2007-2015 with prominent national-level initiatives.

The Global Sepsis Alliance (GSA) guided by the mission of consolidating evidence-based international response to Sepsis and the vision of a World Free of Sepsis was established in 2010. The GSA was launched by the US Sepsis Alliance and the German Sepsis Society together with 4 co-founding organizations, including the World Federation of Societies of Intensive and Critical Care Medicine, the World Federation of Paediatric Intensive and Critical Care Societies, the International Sepsis Forum, and the World Federation of Critical Care Nurses.

The Global Sepsis Alliance initiated the World Sepsis Day (WSD) on September 13 and since 2012 the WSD Movement has mobilized and engaged more than 45,000 supporters in advocacy, public awareness raising, and capacity building initiatives. A scoping review completed in 2022 documented that patient/public awareness of Sepsis has gradually improved over time with the changing Sepsis definitions and the inception of the World Sepsis Day.⁽⁹²⁾

The GSA also elaborated the World Sepsis Declaration in 2012, currently endorsed by over 14,000 supporters - representatives of international health organizations, medical and public health associations, research and academic institutions, Sepsis survivors and their families.

In 2016 the GSA launched another flagship initiative, the annual World Sepsis Congresses (WSC), that have already reached more than 107,000 delegates from 180 countries, including medical professionals, policymakers, academia, private sector, and civil society actors. WHO and other leading actors in global health have joined forces with the Global Sepsis Alliance in co-convening some of the World Sepsis Congress events and reaching multiple stakeholders with the state-of-the-art knowledge.

Since 2016 the Global Sepsis Alliance has spearheaded the establishment of 5 regional alliances, including the African Sepsis Alliance (ASA), European Sepsis Alliance (ESA), Asia-Pacific Sepsis Alliance (APSA), Eastern Mediterranean Sepsis Alliance (EMSA) and Caribbean Sepsis and AMR Alliance (CSA). Finally, over 120 Member Organizations, representing Sepsis foundations, professional associations, patient organizations, civil society, academia and international health agencies, have joined the GSA and its regional Sepsis alliances since 2010.

2.2.2. High-Level Political Engagement

“Some very important clinical issues, some of them affecting life and death, stay largely in a backwater which is inhabited by academics and professionals and enthusiasts, dealt with very well at the clinical and scientific level, but not visible to the public, political leaders, leaders of healthcare systems... The public and political space is the space in which [Sepsis] needs to be in order for things to change.”- Sir Liam Donaldson, the former Chief Medical Officer for England and WHO Envoy for Patient Safety.(3)

The first and most prominent achievement in global political advocacy for Sepsis was the adoption of the World Health Assembly Resolution (WHA 70.7) in 2017 on “Improving the prevention, diagnosis and clinical management of Sepsis”. The Resolution was the foundational document endorsed by WHO Member States for stronger positioning of Sepsis in global and national health agendas.

The WHA70.7 Sepsis Resolution was jointly initiated by five German speaking countries, including Germany, under the leadership of Hermann Gröhe, the Federal Health Minister, as well as Austria, Luxemburg, Lichtenstein, and Switzerland. The Global Sepsis Alliance and Sepsis Stiftung played an important role in the elaboration of the WHA Resolution, through the establishment of a special task force in 2014 and engagement of leading experts from Australia, Brazil, and Canada. In 2018, the WHO Sepsis Technical Experts Meeting, with experts’ consensus, defined priority actions at country and international levels for full-scale implementation of WHA70.7 Resolution. (93)

The second major achievement in global Sepsis advocacy followed in 2022, when under the Presidency of Germany, the G7 Health Ministers’ Communiqué reaffirmed high-level political commitment to Sepsis. (94) The Communiqué specifically called on G7 and G20 leaders, “to intensify efforts to strengthen early detection, diagnosis and therapy of Sepsis and ensure synergy with Antimicrobial Stewardship and IPC programmes, through national educational campaigns, and boosting the implementation of the WHA Sepsis Resolution”.

In 2023, the Central World Sepsis Day Event in Germany convened under the Patronage of Dr. Tedros Adhanom Ghebreyesus, Director-General of the World Health Organization, and Dr. Karl Lauterbach, Federal Minister of Health of Germany, adopted the Berlin Declaration on Sepsis as an “Urgent Call for the Enforcement of the World Health Assembly Resolution (WHA70.7) and Reinvigorated Global Action on Sepsis”. (95) The document has been endorsed by 75 international health organizations as a common roadmap for a robust Sepsis response globally.

Finally, the Berlin Declaration was followed by the first high-level Sepsis side events on the margins of the 78th Session of the UN General Assembly and the 2023 World Health Summit, with engagement of Parliamentarians and global health leaders. (96,97) The GSA convened the meetings in partnership with the UNITE Parliamentarians Network for Global Health (UNITE), Virchow Foundation for Global Health, Clinton Health Access Initiative (CHAI), Sepsis Stiftung, Medical Women’s International Association (MWIA) and Global Antibiotic Research & Development Partnership (GARDP).

2.2.3. Evidence Generation

The global fight against Sepsis is still challenged by the lack of reliable routine administrative health statistics and epidemiological data, especially from low- and middle-income countries.

The landmark 2020 Lancet publication on the Global Burden of Sepsis generated foundational evidence for global advocates and policymakers.⁽⁴⁾ Researchers from IHME, GSA and the University of Pittsburgh Medical Center (UPMC) for the first time estimated age-standardized Sepsis incidence and mortality across 195 countries and territories.

Despite substantial reductions in Sepsis incidence (37%) and mortality (52.8%) from 1990 to 2017, the study reaffirmed the urgency of global action, as Sepsis affected 48.9 million children and adults in 2017 alone. IHME published a renewed annual estimate of 13.66 million Sepsis-related deaths in 2023, which includes 4.95 million deaths attributable to or associated with AMR. ⁽⁵⁾

The Global Burden of Sepsis report was a major step forward in evidence-based advocacy. However, this stand-alone research initiative with its known limitations, cannot replace the need for sound epidemiological surveillance, regular data collection and analysis at national and international levels.

In 2020, the World Health Organization published its first Global Report on Epidemiology and Burden of Sepsis, where Dr. Tedros Adhanom Ghebreyesus, WHO Director-General noted, that “policy-makers must be ready to forge partnerships to stimulate funding and help place Sepsis more firmly on the list of critical health conditions to target in the pursuit of universal health coverage”. ⁽⁴¹⁾

Against the background of scarce evidence on Sepsis epidemiology in LMICs, we shall note the following two research initiatives that can help bridge the critical knowledge gap. The African Research Cooperation on Sepsis (ARCS) with a £2 million grant from the UK National Institute for Health and Care Research, was designed to better understand the burden of Sepsis and case definitions across 10 African countries. In parallel, the Sub-Saharan Consortium for the Advancement of Innovative Research and Care for Sepsis (STAIRS) supported by a €11 million grant from the German Federal Ministry of Education and Research (BMBF) is generating evidence from community and health care settings across 7 countries of Africa. STAIRS will also support capacity building and sequelae engagement of policymakers, and facilitate better integration of Sepsis into national HSS initiatives.

2.3 Success Stories Driven by Sepsis Patients and Their Families

Success stories in the fight against Sepsis that have already saved thousands of lives, have been primarily inspired and led by Sepsis survivors and family members, who have lived through the life-changing and tragic experiences.

Below, we present a select number of success stories from Australia, Belgium, Ireland, Sweden, the UK and the US to inform policymakers, healthcare practitioners and Sepsis advocates in other countries and regions. The best practices and examples presented in the current section and throughout the document stem primarily from high-income countries, as policy initiatives and implementation evidence remain scarce in LMICs.

Overall, since the historic 2017 WHA Resolution, 15 countries, or less than 10% of the UN Member States, have developed National Action Plans (NAPs) for Sepsis and/or evidence-based policies for Sepsis (e.g., Sepsis clinical pathways, Sepsis bundles). Some of these countries have also generated evidence and investment cases from implementation research, on how targeted policy interventions have led to reduced incidence and mortality of Sepsis, and significant cost-savings. (see table 2.3.a). The current data has been consolidated by the Global Sepsis Alliance based on the European Sepsis Report and consultations with Regional Sepsis Alliances across 6 geographic regions. (98)

Australia	Sudan
Belgium	Sweden
Canada	Switzerland
France	Qatar
Ireland	Thailand
Netherlands	UK
Saudi Arabia	USA
Spain	

Table 2.3.b lists the UN Member States that have made significant progress in raising Sepsis awareness among policymakers and implementing capacity-building initiatives at national and/or sub-national levels.

Table 2.3.b. Countries with National and/or Sub-national Initiatives for Sepsis Awareness Raising and Capacity Building	
Austria	Italy
Brazil	Japan
Germany	Turkey

Australia

Australia was one of the first countries to develop a National Action Plan (NAP) for Sepsis following the 2017 WHA Resolution. The country has also developed and enforced a national Sepsis Clinical Care Standard for all primary and acute care health services, which is a requirement of the National Health Services Accreditation programme. This initiative led to the broad implementation of clinical pathways and quality improvement (QI) in Sepsis, along with revised coding for Sepsis data reporting and analysis through the International Classification of Diseases (ICD), or the routine health statistics system.

The state-wide implementation of the Sepsis Pathway ‘Think Sepsis. Act Fast.’ in the state of Victoria generated ground-breaking evidence.⁽⁹⁹⁾ The initiative was implemented across 10 public health services providing healthcare to 62% of the state’s population. The Sepsis Pathway was based on a nurse-led model with early warning, severity criteria, and actions to be initiated within 60 minutes of Sepsis recognition. The Sepsis bundle included oxygen administration, blood cultures, venous blood lactate, fluid resuscitation, intravenous antibiotics, and increased monitoring.

Data from 2,942 patients revealed significant improvements in patient outcomes, with a 50% reduction in Sepsis mortality, a 34% reduction in ICU admissions and a 2.9-day reduction in mean ICU LOS. Furthermore, increased adherence to Sepsis pathways from 4.9% to 78% and reduced total hospital LOS (3,781 bed days) resulted in US\$ 11.7 million savings and 6-fold return on investment (ROI).

Finally, the role of The George Institute for Global Health and Sepsis Australia has been critical in advocacy, policy development and technical expertise in Australia. The Institute has been providing in kind infrastructure and operational support to the Asia-Pacific Sepsis Alliance, and its working groups for Sepsis Research and Advocacy and Guidelines and Quality Improvement. APSA assists the development of Sepsis NAPs in countries within its network, including New Zealand, and this effort has recently extended to assisting the development of an NAP in Switzerland.

Belgium

The national Sepsis response in Belgium was initially driven by Sepsis Survivors, Michael Clarke and Carine Nelissen, who in 2020, in collaboration with the European Sepsis Alliance, established a patient organization “Sepsibel”. (98) The Sepsis survivors consistently advocated for legislative and executive government policies for implementing the WHA70.7 Sepsis Resolution. Despite substantial support in the Federal Parliament for the development of the Belgian Sepsis Action Plan, the adoption of the resolution was halted.

However, 2023-2024 marked a new phase of national-wide Sepsis advocacy following the publication of the book “Every Hour Counts” and a national TV documentary featuring the story of Ilse Malfait, a septic shock survivor.

As a result of consistent efforts from Sepsibel, Frank Vandenbroucke, the Minister of Health of Belgium commissioned a multidisciplinary team in December 2023 and the first National Sepsis Report was completed in a record time of 5 months, in May 2024. (100)

Ireland

Following a significant Sepsis-related patient safety incident in Ireland, the Health Service Executive (HSE) established a National Sepsis Steering Group (NSSG) in 2013. The NSSG first quantified the burden of Sepsis and documented that 60% of all in-hospital deaths and 42% of all in-hospital bed occupancy were related to Sepsis or infection codes.(98)

Accordingly, the Department of Health prioritized the development of a National Clinical Guideline on Sepsis Management, released in 2014, and training of Emergency Departments, acute medical assessment units (AMAU), acute surgical assessment units (ASAU), and medical and surgical wards in early recognition and management of Sepsis. The national Sepsis programme provides clinical decision support tools, including Sepsis Forms and Algorithms, that prompt clinicians to complete the ‘Sepsis-6’ bundle within the first hour of recognizing the signs and symptoms of Sepsis. The ‘Sepsis-6’ bundle includes Take 3: Blood cultures, Blood tests, and Urinary output assessment and Give 3: Antimicrobials, Fluids and Supplementary oxygen, if required.

In 2023 Ireland published its 8th National Sepsis Report, documenting a substantial increase in the identification and reporting of Sepsis cases and 26.7% reduction in Sepsis-related mortality, from 26.8% in 2011 to 19.4% in 2019. Despite the deteriorated epidemiological context and increased Sepsis incidence during the COVID-19 pandemic, in-hospital Sepsis-related mortality in 2022 was 22.2%, still 17% lower compared to the 2011 baseline. (101)

Sweden

In Sweden, Sepsis has been selected as one of the ten first diagnoses to be addressed, and in 2019 the Swedish government allocated funds for the development of a national patient-centred and evidence-based clinical pathway in healthcare. (102) The Sepsis clinical pathway was elaborated by a national multidisciplinary working group that included a patient representative along with technical experts.

The tool is currently implemented across the Swedish healthcare system and focuses on four areas: (1) Sepsis alert systems for early detection and management optimization for the most severely ill Sepsis patients in the Emergency Departments (ED); (2) accurate Sepsis diagnosis coding; (3) structured information to patients at discharge after Sepsis care, and (4) structured telephone follow-up after Sepsis care.(102)

United Kingdom

The United Kingdom developed its first Cross-System Action Plan for “Improving outcomes for patients with Sepsis” in 2015, followed by the second Action Plan in 2017. The UK National Institute for Health and Care Excellence (NICE) released the first Sepsis Guidelines in 2016 and the updated edition in 2024, in close collaboration with the UK Sepsis Trust. (103) Sepsis is included in the National Early Warning Score (NEWS2) system to detect and respond to acute deterioration of adult patients.

From 2016 until 2019 the NHS in England provided incentivization for hospitals to improve the reliability of their recognition and management of Sepsis. This resulted in the rate of delivery of first-hour antimicrobials across English hospitals rising from 32% in 2016 to 80% in 2019 (unpublished data, NHS England).

According to the UK National Health Service (NHS) the “Sepsis Six” bundle developed by the UK Sepsis Trust defines six tasks to be instituted within 1 hour of Sepsis detection by non-specialist practitioners at the front line. The 6 elements of the bundle include oxygen, cultures, antibiotics, fluids, lactate measurement and urine output monitoring. The “Sepsis Six” bundle has been adopted by hospitals in England and Wales, and the compliance with the tool has demonstrated a 46.6% reduction in the relative risk of patients’ deaths from Sepsis. (104)

The nation’s attention to Sepsis was once again heightened after the tragic death of Martha Mills, when Martha’s family’s concerns about her deteriorating condition were not responded to, and a coroner ruled that Martha would probably have survived had she been moved to intensive care earlier. The Secretary of State for Health and Social Care and NHS England mandated the first phase introduction of ‘Martha’s Rule’ from April 2024 which will ensure that the vitally important concerns of the patient and those who know the patient best are listened to and acted upon. (105)

United States

The first Sepsis patient advocacy organization in the United States, Sepsis Alliance, was started by Dr. Carl Flatley who tragically lost his daughter Erin to Sepsis in 2002. Sepsis Alliance hosts the Sepsis.org website which educates and supports more than 2 million users each year and has helped drive Sepsis awareness in the U.S. from 19% (2003) to 69% (2024). In 2019, Sepsis Alliance started the world's first Sepsis professional education and training site, Sepsis Alliance Institute, which has trained more than 54,000 healthcare professionals to date. More recently, Sepsis Alliance formed Sepsis Alliance Connect, which supports the needs of Sepsis survivors and family members. This work has positioned Sepsis Alliance to lead national public awareness raising and capacity building. Sepsis Alliance successfully fought for the reauthorization of the CMS SEP-1 Sepsis care measure and its adoption into the payer's Value-Based Purchasing Program (VBP), and successfully supported the passage of Lochlin's Law in the state of Maryland which requires Sepsis protocols and training in all hospitals and urgent care settings. Most recently, Sepsis Alliance worked with partners to secure the creation of an ICD-10 diagnosis code for post-hospital Sepsis care. Sepsis Alliance also hosts the Sepsis Innovation Collaborative, an FDA-facing Collaborative Community, that drives the acceleration of Sepsis innovation to meet unmet needs in Sepsis prevention, diagnosis, treatment, and support for Sepsis survivors. (106)

Systemic changes in hospital management of Sepsis began in 2014 with the New York State (NYS) Sepsis Care Improvement Initiative. This initiative, which supports hospitals and partner organization in improving early detection and timely treatment of Sepsis and septic shock, is estimated to have saved 16,000 lives between 2015 and 2019. (107) These changes were driven by consistent advocacy led by END SEPSIS - Rory Staunton Foundation, established by Ciaran and Orlaith Staunton after the tragic loss of their son. The Rory Staunton Foundation through dedicated leadership of Senator Charles Schumer (D-NY), catalysed systemic changes not only in the NY State, but the strategic funding deployment for Sepsis from the 2024 Congressional Budget. (108) The largest ever allocation of 3 million USD for Sepsis will support the US CDC in integrating essential Sepsis data into the National Healthcare Safety Network (NHSN) and evaluating Sepsis care standards, known as the Sepsis Core Elements, across healthcare facilities. The latest remarkable achievement of the END SEPSIS advocacy is the Sepsis Bill planned to be introduced in the US Senate in September 2024. The new legislation can substantially strengthen capacities of the US CDC and healthcare providers in quality of Sepsis care in general, and for paediatric patients in particular. Considering the prominent role of the United States in global health diplomacy and cooperation, the Sepsis Bill, may catalyse historic changes for children, women and other vulnerable groups both in Global South and Global North.

Furthermore, the US CDC documented that 73% of hospitals had dedicated Sepsis teams, though only half (55%) of the team leaders were provided with a dedicated time to manage Sepsis programmes. (9) As the follow-up, in 2023, CDC launched the Hospital Sepsis Program Core Elements and will measure implementation of the standards through annual hospital surveys funded by Congress. (109) Earlier initiatives included a national educational programme for patients and health care providers "Get Ahead of Sepsis (GAOS)". Finally, it is noteworthy, that before the COVID-19 pandemic, the US documented a 17% decline in in-hospital Sepsis mortality from 14.4 per 100 Sepsis stays in 2016 to 11.9 in 2019. (26)

SECTION 3

MAJOR GAPS IN GLOBAL SEPSIS RESPONSE

Despite the documented progress, and the fact that proven and affordable interventions are feasible to scale-up in all settings, implementation gaps remain that cost lives every day. Sepsis and its sequelae are still largely invisible in the global health landscape and receive disproportionately low political and financial investments compared to their human and economic costs. The gaps in the global Sepsis response will be also analysed primarily based on the evidence and data from high-income countries, as the policy initiatives and operational research are rather limited in LMICs.

Concerted efforts of multiple stakeholders are essential to change the status quo and overcome the following challenges at policy, institutional and community levels, especially in resource-limited settings.

- Policy and investment gaps
- Awareness gaps on Sepsis as a medical emergency
- Health system capacity gaps
- Limited investments in Sepsis science
- Monitoring and evaluation (M&E) gaps

3.1. Policy and Investment Gaps

For a global health threat affecting up to 50 million people and claiming 13.7 million lives every year, including 4.95 million AMR-related deaths, Sepsis receives disproportionately low political attention and financial investments at national, regional and global levels. (4,5)

- Even after the 2017 World Health Assembly Resolution, Sepsis remains invisible in national and global health agendas. While being responsible for 1 in every 5 deaths and 2.65% of health sector expenditures, Sepsis has not been prioritized in high-level discussions of G7/G20, World Health Assemblies, UN General Assemblies, or World Economic Forums. We do not see “Sepsis Ambassadors” or “Special Envoys” of national governments, parliaments, ministries or global health authorities as in the case of AMR, Climate Change, or other health priorities.
- While policy-makers rightly prioritize AMR, they continue to pay disproportionately low attention to Sepsis, and rarely acknowledge that the estimated 4.95 million AMR-related deaths globally are part of the 13.7 million Sepsis related deaths. The fact that over 170 UN Member States have National Action Plans for AMR, while only 15 countries have developed Sepsis NAPs or national policies, reaffirms the urgency for synergizing Sepsis and AMR advocacy and policies.

- While LMICs bear 85% of the Sepsis burden, policy interventions are primarily concentrated in high income countries. Even in Sub-Saharan Africa, with the highest death toll of maternal and neonatal Sepsis, none of the countries have developed a Sepsis NAP as of 2024.
- Decision-makers continue to underestimate that, similar to COVID-19, every future pandemic will increase the risk of Sepsis and its sequelae. As an example, while it is encouraging to see targeted policy and programme interventions for long-term sequelae of COVID-19 in Germany, post-sepsis care and rehabilitation for long-term sequelae of Sepsis has not been equally prioritized.
- National health authorities and centres for disease control (CDCs) continue to address Sepsis primarily from the prism of healthcare associated infections, when more than 80% of Sepsis cases have community-onset.
- Few countries have earmarked resources for Sepsis policies and interventions. The US Federal funding for CDC, Australia's investments in Sepsis national clinical quality standard, and the UK's funding for the Red Flag Sepsis alert systems and Sepsis 6 treatment pathways, are exceptions, rather than standard practices observed around the world.
- UN Member States need sound political and technical guidance in designing and monitoring implementation of evidence-based NAPs and policies. In addition, LMICs, which are the most affected, need international aid to catalyse policy changes and implementation. However, even the global health and international development agencies, including WHO, other UN entities and CDCs, have limited institutional and financial capacities to ensure appropriate action and guidance to countries.
- The World Health Organization, the leading global health authority, coordinates the Sepsis-related work through the Integrated Health Services (IHS) Department and a multi-sectoral Sepsis Coordination Group. Global, regional and country offices of WHO have no human or financial resources earmarked to address the critical burden of Sepsis and guide national health authorities in the development and enactment of evidence-based NAPs and policies. Though, despite the resource limitations, the World Health Organization is leading the development of critically needed guidelines and tools for the clinical management of Sepsis. The resources, expected to be published in 2025, will bridge an important knowledge gap, especially for LMICs.
- The Global Sepsis Alliance and its member organizations commend the Pan-American Health Organization (PAHO) for the development of the first Regional Strategy and Action Plan for Sepsis, expected to be approved by the Directing Council in September 2024. WHO South East Asia Regional Office (SEARO) is collaborating with the Asia-Pacific Sepsis Alliance to improve Sepsis surveillance in the region, and the African Sepsis Alliance is building initial collaborative steps with Africa CDC and WHO Regional Office.

- The EU rightly prioritizing AMR due to its association with 35,000 annual deaths, continues to underestimate the Sepsis burden. Sepsis is estimated to affect more than 3 million people and cause 680,000 deaths in the European region, including the 35,000 AMR-associated deaths. (110,111) ECDC, in contrast to US CDC initiatives, still needs to develop guidance and tools for Sepsis surveillance or capacity building.
- WHO has also identified Sepsis as one of the common sources of patient harm and Sepsis is integrated into the Global Patient Safety Action Plan for 2021-2030.(112,113) However, in practice, Sepsis remains invisible in national or international Patient Safety initiatives.
- Finally, the Official Development Assistance (ODA) from bi- or multi-lateral donors has not prioritized Sepsis, even after the adoption of the WHA70.7 Resolution.
- Similarly, International Financial Institutions (IFI) have yet to explore grant and loan portfolios to incentivize national and regional responses to this medical emergency.

3.2. Awareness Gaps on Sepsis as a Medical Emergency

In contrast to myocardial infarction, stroke, or other life-threatening conditions, public awareness on Sepsis as a medical emergency remains low. As more than 80% of Sepsis cases start outside the hospital sector, seeking care on time can be life-saving and the UN member states should prioritize societal and clinical pathways for early recognition, referral and treatment.

- Significant knowledge gaps remain on Sepsis and its signs among policymakers, healthcare professionals, and the general public. A 2022 scoping review identified that the proportion of patients/public who had heard of the term “Sepsis” varied widely from 2% in Japan to 88.6% in Germany, while the proportions of patients/public who “correctly” identified the definition of Sepsis varied from 4.2% in Singapore to 92% in Sweden. (92)
- Families continue to underestimate the double-edge role of the immune system and that vaccines are imperative to prevent common causes of Sepsis in children and adults (e.g., meningitis, pneumonia, cholera, typhoid). Globally 3 doses of diphtheria-tetanus-pertussis, or DTP-containing vaccine reach 84% of children, and human papillomavirus (HPV) and rotavirus vaccine coverage is only 17% and 51%, respectively. (114) (115) Evidence-based information and communication campaigns should be further strengthened for scaling up immunization coverage, including measures to respond to anti-vaccination sentiments.

- Further advocacy is needed for scaling up vaccine coverage even in HICs, as attitudes towards vaccination and low immunization rates have significantly affected clinical outcomes of COVID-19 patients in the US. (116)
- Media engagement in awareness raising on Sepsis and its devastating impact on the lives of millions and their families is still low. GSA acknowledges the critical role that media representatives have played in demanding and driving changes in specific countries. However, media engagements were primarily triggered by personal tragedies of patients and their families, too late to save the lives of the affected children and adults, or to prevent the life-changing disabilities among the Sepsis survivors.

3.3. Health System Capacity Gaps

Health system capacities to adequately respond to Sepsis are insufficient both in LMICs and countries with stronger economies. Over 90% of countries still have no NAPs or evidence-based clinical pathways to ensure patient-focused management of Sepsis across different levels of healthcare.

- **Sepsis prevention** calls for improved enforcement of infection prevention and control (IPC) measures, including prevention of healthcare-associated infection (HAIs) and AMR, immunization and WASH. A report from WHO and other organizations have clearly identified the increasing endemic burden of HAIs and AMR infections, which often lead to Sepsis for many patients across health care systems in all countries, regardless of the income status. According to the WHO estimates, 1 in 6 cases of Sepsis treated in hospitals are healthcare-associated and the mortality estimates for health care-associated Sepsis in hospitalized adult patients range from 20% to 30%. Any Sepsis prevention strategy should include the reliable implementation of effective IPC measures with potential cost and life-saving benefits that these could bring. (117) Immunization coverage remains low even in high-risk groups of children and adults. For example, Spain documents 54.4% uptake of influenza vaccines among ≥ 65 years groups and 26.53% among healthcare workers. Furthermore, 1 in 4 health care facilities in LMICs lack basic water services, and 70% of health care workers and 50% of surgical teams do not routinely practice hand hygiene. (77)
- The **first medical contact** with Sepsis usually starts outside the hospital and is critical for timely identification and timely initiation of life-saving treatment. Sepsis suspicion by Emergency Medical Services (EMS) is associated with improved patient outcomes. (118) However, out of 20,172 Sepsis patients transported by EMS

in the US, only 18% of Sepsis cases were recognized before hospitalization. (119) In Germany, paramedics have never and emergency physicians rarely (0.1%) documented a Sepsis suspicion in EMS records. (118)

- **Primary Health Care (PHC)** capacities need to be enhanced for early recognition and referral to time-critical treatment. Delays in seeking medical care (20%), under-evaluation of severity by the physician (20%), and delayed antibiotic therapy (24%) were the primary causes behind sub-optimal care for severe bacterial infections in children. (120)
- **Emergency, critical and operative care (ECO) for Sepsis** continues to be a challenge. Countries, especially in resource-limited settings, have limited institutional capacities of EDs and ICUs to deliver quality ECO services for Sepsis. EMS studies have shown that incidence of Sepsis (1.6%) was similar to myocardial infarction (2.6%) and stroke (2.7%). However, the 30-day case fatality rate for Sepsis was three-fold higher (31.7% vs. 13.4% and 11.8%) and only 8.2% of septic patients had complete vital sign documentation. (118) Sepsis protocols or Sepsis bundles were found to be applied only in 70.7% of ICUs, 57.6% of emergency departments and 45.5% of general wards. (121). Experts engaged in the current strategy development have raised concerns on the limited availability of 24/7 laboratory capacities and resources in LMICs, and applicability of the Sepsis 3 definition in resource-limited settings due to barriers in quantifying organ dysfunction and calculating SOFA score.
- Sepsis management requires a multidisciplinary approach, and availability of 24/7 **Rapid Response Teams (RRT)** in hospitals have shown to improve clinical outcomes for Sepsis patients. (122) While global data on RRTs are not available, 1,087 hospitals in 73 countries reported having measures for early recognition of Sepsis in 61.9% of ICUs, 54.5% of emergency departments, and 47.8% of general wards. (121)
- Theoretical knowledge and practical skills in prevention, diagnosis and treatment of Sepsis varies among **health care providers (HCPs)**. A multi-country review documented, that 71% of Emergency Medical Technicians (EMTs) and 98% of nurses have heard of the term “Sepsis”, while only 17% in EMTs and 91% of nurses could correctly identify the Sepsis definition. (92)
- Robust response to Sepsis, especially in LMICs is substantially challenged by the **shortage of health workforce**. The shortage of critical care physicians and critical care nurses in general, and the shortage of paediatricians and neonatologists to respond to Sepsis in perinatal care settings are important barriers to ensuring the continuum of quality care.
- Health care institutions, especially in LMICs, have limited access to **equipment and supplies** for effective management of Sepsis and related organ dysfunction. This includes access to microbiology labs or rapid diagnostics, ventilators with adequate oxygen supply, renal replacement therapies, and antibiotics. Only 10.1% of 1,087 hospitals across 73 countries in Europe and worldwide were found to have access to 24/7 blood culture incubation, pathogen identification, and communication of results. (121)

- Sepsis survivors facing long-term consequences, including cognitive, psychological, and physical disabilities, need appropriate and affordable **rehabilitation and care** services. However, access to quality post-sepsis care and rehabilitation remains limited both in LMICs and high-income countries.
- Finally, we must consider the anachronistic cultures in healthcare systems that complicate the adoption and application of standard, evidence-based healthcare **QI initiatives**, such as clinical pathways, bundles, checklists and data reporting and analysis. A 2022 study among 74 German hospitals demonstrated, that voluntary initiatives and collaborations to improve the quality of Sepsis care are effective only when hospital-leadership prioritizes Sepsis-related QI efforts, allocates adequate resources and involves all relevant stakeholders. (123) Across 73 countries in Europe and worldwide, antibiotic stewardship programmes were in place in 2/3 of the hospitals, though only 31.3% had QI or Sepsis training programmes. (121)

3.4. Limited Investments in Sepsis Science

With already sub-optimal resource investments in global health research, earmarked investments for Sepsis-related science remain even more limited.

- OECD countries rarely invest in the generation of new knowledge around Sepsis through public programmes or clinical trials, though promising exceptions exist. The US Biomedical Advanced Research and Development Authority (BARDA) through its Division of Research, Innovations and Ventures (DRIVE) started the “Solving Sepsis Strategy” initiative in 2018. (124) In 2024 BARDA announced the expansion of its host-directed therapeutics research for immunomodulatory innovations that can lead to improved clinical outcomes of Sepsis. (125) Horizon Europa has allocated 6.9 million Euro for the “BEATSep” consortium to understand the long-lasting consequences of Sepsis. (126)
- While LMICs bear the highest global burden of Sepsis, knowledge generation from fundamental and operational research is still primarily driven by high-income countries.
- Research initiatives and funding should be fostered to catalyse the development of new and more effective diagnostics and therapeutics to address Sepsis and its long-term sequelae. The priority R&D agenda for Sepsis includes novel vaccines, point-of-care diagnostics, antimicrobials, immunotherapies, alternative medicine and combined approaches such as those offered by theragnostics.
- The private sector, including the manufacturing industry, remains an important source of funding for Sepsis innovations. However, the current investments are

insufficient and bear limitations, in view of specific business development goals or market failure risks for new therapies.

- Finally, artificial intelligence can substantially improve the early detection of Sepsis for time-critical initiation of treatment. AI-based diagnostic technologies solutions are especially promising to address healthcare challenges in developing countries (such as India) with significant shortage of the health workforce. (127) However, the existing AI-enabled solutions for Sepsis still demonstrate sub-optimal sensitivity and specificity, and high false positive results limit the wide-scale application of these tools.

3.5. Monitoring and Evaluation Gaps

- Timely and accurate data on the epidemiology of Sepsis is essential to inform evidence-based public policies, clinical practice, and research priorities. Yet, both the quantity and quality of Sepsis-related data remain scarce, especially in low- and middle-income countries with the highest burden of Sepsis.
- The 2020 Global Burden of Sepsis and WHO Global Report were two major achievement in evidence-based advocacy and accountability. (4,41) However, the global Sepsis community cannot continue relying on periodic epidemiological studies, systemic reviews or modelling to inform policy and decision-makers. With the exception of Ireland, Spain (Catalonia) and a few other countries, routine administrative health statistics do not cover regular reporting, real-time monitoring or analysis of Sepsis data.
- A reinvigorated Sepsis response calls for sustainable integration and regular data collection, reporting and analysis of epidemiological, clinical and economic data through ICD systems, Sepsis registries, Global Burden of Disease (GBD) and/or implementation research. As an example, due to the under-coding of Sepsis in in-patient administrative health data (IAHD), previous epidemiological studies have underestimated the burden of Sepsis in Germany. With a large variability between hospitals in the accuracy of diagnosing and coding for Sepsis, IAHD alone was not considered sufficient to assess the quality of Sepsis care. (128)
- The new global agenda for Sepsis also calls for regular implementation monitoring and accountability for the WHA70.7 Sepsis Resolution, to track progress with the enactment of recommended NAPs, evidence-based policies and protocols, clinical practices, and capacity building initiatives.

SECTION 4

2030 GLOBAL AGENDA FOR SEPSIS

The 2030 Global Agenda for Sepsis is the first multi-year strategic vision, how to alleviate the significant human, societal, healthcare and economic burden of Sepsis through concerted actions of UN Member States and multiple stakeholders at national, regional and global levels.

The GSA led the development of this document with the engagement of 5 Regional Sepsis Alliances, and over 70 member and partner organizations from Africa, Asia-Pacific, Caribbean, Eastern Mediterranean, Europe, Latin America and North America. The strategic planning process included focus group discussions and consultations with Sepsis survivors and family representatives, policymakers, healthcare practitioners and partners from public, private, academia and civil society.

The goals, strategic objectives and key performance indicators (KPIs) presented in the document are based on the World Sepsis Declaration, endorsed by over 14,000 stakeholders globally; the 2030 Sustainable Development Goals and health-related targets; global strategies and goals for Immunization Agenda 2030, IPC, WASH, and experts' consultations as part of the GSA-led strategic planning process. Building on the suggested results framework (Section 5), the GSA calls the global and regional health authorities to initiate an inter-agency and multilateral consensus-building process to agree on the core M&E methodology and standardized indicators for epidemiological surveillance and clinical management aspects of Sepsis.

The ultimate goal of the 2030 Global Agenda for Sepsis is to reduce the global incidence of Sepsis by at least 25% from the 2017 baselines, to improve the survival rates of paediatric and adult patients by 20%, and to reduce the median costs per Sepsis patient by at least 20%. Specifically, the impact-level indicators of the multi-year strategy are to:

- a. Reduce the incidence of Sepsis from 677 episodes per 100,000 population in 2017 to fewer than 500 episodes per 100,000 by 2030.
- b. Improve the survival rates from Sepsis among children under 5 and adults by 20% from the 2017 baseline, and
- c. Reduce the median cost per Sepsis patient per country from the estimated baseline of € 36,191 by at least 20% by 2030.

Building on the progress and achievements in the global fight against Sepsis, the WHA70.7 Resolution, as well as the analysis of the remaining gaps at policy, institutional and community level, the 2030 Global Agenda for Sepsis is built around five strategic pillars:

Strategic Pillar 1. Political Leadership and Multilateral Cooperation

Strategic Pillar 2. Health System Readiness for Sepsis and Its Sequelae

Strategic Pillar 3. Whole-of-Society Response

Strategic Pillar 4. Sepsis Research and Innovations

Strategic Pillar 5. Sepsis in Pandemics and Other Emergencies

Table 4.
Strategic Pillars and Priority Directions
2030 Global Agenda for Sepsis

1. Political Leadership and Multilateral Cooperation	2. Health System Readiness for Sepsis and Its Sequelae	3. Whole-of-Society Response	4. Sepsis Research and Innovations	5. Sepsis in Pandemics and Other Emergencies
<p>1.1. Prioritizing Sepsis in Global Health Architecture</p> <p>1.2. National Sepsis Alliances and Action Plans</p> <p>1.3. Synergizing Sepsis with SDG 3 Agenda</p> <ul style="list-style-type: none"> • UHC • MNCH • IPC • AMR • PPPR • Patient Safety • Healthy Aging <p>1.4. Multi-lateral Cooperation and Funding</p> <p>1.5. Global Monitoring and Accountability</p>	<p>2.1. Patient-focused Sepsis Clinical Pathways</p> <ul style="list-style-type: none"> • PHC • ECO <p>2.2. Sepsis Response in MNCH Services</p> <p>2.3. Equipment and Supplies for Sepsis Bundles</p> <p>2.4. Medical Education and Training</p> <ul style="list-style-type: none"> • Physicians • Nurses • Midwives • Dentists • Lab • Students <p>2.5. QI of Sepsis Care Cascade</p> <ul style="list-style-type: none"> • MDT based problem-solving • Regionalization • Accreditation <p>2.6. Cross-cutting IPC</p> <ul style="list-style-type: none"> • HAIs prevention • WASH • Immunization • Antimicrobial Stewardship 	<p>3.1. Community-level IPC</p> <ul style="list-style-type: none"> • Vaccines • WASH <p>3.2. “Sepsis” Literacy as Medical Emergency</p> <p>3.3. Media and Public Leaders for Sepsis</p> <p>3.4. Patients Care and Support Cascades</p>	<p>4.1. Investing in Sepsis Research and Academic Cooperation</p> <p>4.2. Innovations for Preven- tion, Diagnostics and Treatment</p> <ul style="list-style-type: none"> • Vaccines • Diagnostics • Therapies • AI Tools • Care and Rehabilitation 	<p>5.1. Sepsis in Pandemics</p> <p>5.2. Sepsis in Armed Conflicts</p> <p>5.3. Sepsis in Humanitarian Crisis and Displacement</p> <p>5.4. Climate Change and Sepsis</p>

STRATEGIC PILLAR 1.

POLITICAL LEADERSHIP AND MULTI-LATERAL COOPERATION

Overarching Goal(s) of the Strategic Pillar

The ultimate goal of the 1st strategic pillar is to ensure that Sepsis is positioned in the mainstream of the global and national health priorities with relevant funding streams and stronger synergies with health-related SDGs and aspirations for UHC, MNCH, IPC, AMR, PPPR and Patient Safety.

At the same time, the strategic pillar aims at strengthening the global, regional and national responses to Sepsis through multilateralism, including multilateral cooperation, allocation of domestic, public-private and international aid funding, as well as policy and accountability mechanisms.

Building on the WHA70.7 Resolution, the current pillar aims at including prevention, diagnosis and treatment of Sepsis in national health systems strengthening initiatives and reinforcing synergies with IPC programmes, clean childbirth practices, infection prevention practices in surgery, improvements in sanitation, nutrition and delivery of clean water and access to vaccination programmes.

Specific Objectives of the strategic pillar include the following:

- 1.1 Establishment and operationalization of a High-Level Political Platform for Sepsis before the end of 2025 to lead cohesive integration of the Sepsis agenda into the mainstream of global health and development dialogue and architecture.
- 1.2 By 2030, at least 80% of HICs and at least 50% of LMICs have developed and started implementation of National Action Plans (NAPs) on Sepsis, with earmarked domestic budgetary resources, as stand-alone NAPs or part of broader health sector policies and programmes.
- 1.3 By 2030, at least 80% of HICs and at least 50% of LMICs have incorporated Sepsis into national packages of priority UHC services. (129)
- 1.4 By 2026, governments, international financial institutions (IFIs), public-private partnerships (PPPs) in global health and philanthropic foundations initiate grant, loan and/or innovative funding mechanisms for improving Sepsis response capacities in LMICs.
- 1.5 By end of 2025, international health partners initiate regular data collection on the implementation of the WHA70.7 Resolution, and publication of annual Global Sepsis Reports on the status of the Sepsis-related action at national, regional, and global levels.

Priority Directions and Interventions

Attainment of the declared goals and objectives of the 1st Strategic Pillar calls for the implementation of the following 5 priority directions and interventions.

Priority Direction 1.1. Prioritizing Sepsis in Global Health Architecture

- Sepsis should be positioned in the mainstream of **global health dialogue and architecture**. With the current evidence and knowledge, we have a historic opportunity to make Sepsis the next success story in global health if political leaders and decision-makers adequately prioritize and fund relevant policies and actions.
- Sepsis should be consistently integrated in the programmes and agendas of **major global health forums**, including G7 and G20, UN General Assemblies (UNGA), World Health Assemblies (WHA), World Economic Forums, World Health Summits, IPU and UNITE Summits for Parliamentarians, High-Level Meetings and Ministerial Summits on Patient Safety, UHC, AMR, PPPR and other priority themes.
- The global health community should support the establishment of a **High-level Political Platform** for Sepsis that will lead concerted advocacy efforts for positioning Sepsis in the mainstream of the global health and development architecture. The platform, represented by senior-level politicians, including heads of state, parliamentarians, ministries (health, finance, defence, etc.) and designated “Sepsis Envoys” and/or “Sepsis Ambassadors” should ensure consistent advocacy and awareness-raising among policymakers that Sepsis, as a hidden global threat, requires immediate action if 2030 SDGs are to be attained.
- The High-level Political Platform for Sepsis along with WHO, other UN agencies, Global Health PPPs, regional and national CDCs, and other stakeholders, should consistently promote and hold national governments accountable for the **enforcement of the World Health Assembly WHA70.7 Resolution on Sepsis**. As noted, less than 10% of the UN Member State have developed National Action Plans for Sepsis since the endorsement of the WHA Resolution in 2017, and the status quo should be urgently changed.
- Apart from the WHA70.7 Resolution on Sepsis, the global community engaged in the Sepsis response, should prioritize the enforcement of **Sepsis-related policies and recommendations in WHA resolutions**, such as the Global IPC Strategy (WHA76.11), Global Action Plan on AMR (WHA68.7), Global Action Plan on Patient Safety (WHA72.6), emergency, critical and operative care and health emergencies (WHA72.16, WHA76.2), water, sanitation and hygiene in health care facilities (WHA72.7), increasing access to medical oxygen (WHA76.3) and clinical trials to provide high-quality evidence on health interventions (WHA75.8).
- Finally, the global Sepsis community should start advocacy with UN Member States for the development and sponsoring of the **2nd World Health Assembly Resolution on Sepsis** that will include more specific and measurable targets for M&E and accountability at all levels.

Priority Direction 1.2. National Sepsis Alliances and Action Plans

- National governments should be held accountable for the development and implementation of **National Action Plans** for Sepsis with relevant domestic budgetary resources. Sepsis NAPs can be stand-alone documents or part of broader national health policies and programmes based on the local context and decision of respective governments, but should be resourced and their implementation measured.
- The UN Member States, with no organized advocacy and care improvement groups for Sepsis, should consider the establishment of **National Sepsis Alliances (NSAs)** or equivalent coordination mechanisms. GSA recommends the NSAs to be established under the leadership of national health authorities and led by designated National Sepsis Coordinators. NSAs should ensure national ownership of Sepsis-related policies and action with participation of multiple in-country stakeholders from public and private sectors, patient and family support groups, academia, civil society, UN and international development partners.
- The new 2030 Global Agenda for Sepsis calls for stronger **engagement of Parliamentarians** as direct representatives of local constituencies with the mandate to approve and supervise implementation of national laws and budgets. Parliamentarians can play a critically important role in holding governments accountable for international commitments and closing unmet needs of individual patients and communities in prevention and management of Sepsis.
- The Sepsis community should prioritize national, regional and global **Sepsis Investment Cases** as opportunities of saving millions of lives with high ROIs. Joint advocacy with national health and finance authorities should ensure earmarked domestic budgetary resources for Sepsis NAPs as stand-alone initiatives or part of UHC, MNCH, IPC, AMR, PPPR and broader sectoral programmes. Adequate resources should be allocated for comprehensive Sepsis prevention and clinical management policies and programmes as part of NAPs. Domestic resources should be allocated for adequate Sepsis response in high-risk populations (e.g., pregnant and postpartum women, newborns, elderly and immunocompromised individuals) as well as public awareness campaigns, QI initiatives, clinical training and research.
- Multiple stakeholders engaged in the Sepsis fight should advocate with global health authorities, national governments, PPPs, IFIs and other funding institutions for **Sepsis Cost Benefit Investment Cases as the opportunity for “Saving Lives and Saving Costs”**.

Example(s): Australian scholars and policymakers documented not only a 50% reduction in Sepsis mortality as a result of the state-wide implementation of Sepsis Pathways, but a significant return on investment (ROI). The investment of \$1.8 million AUD resulted in a return of \$11.7 Million AUD, or a 6-fold ROI over a 5-month period. (99) Similarly, the British Columbia Sepsis Network documented that every dollar spent on the Sepsis programme resulted in a \$112 return of investment over the 2014-2018 period. Specifically, up to \$450,000 were spent for the development and implementation of the BC Sepsis Network and net savings due to the number of cases and deaths averted were \$50.6 million as of 2018. (130)

Priority Direction 1.3. Synergizing Sepsis with SDG 3 Agenda

- Global and national health authorities should ensure **synergies of action** between Sepsis-specific policies and interventions with the broader SDG agenda and national health sector priorities, including UHC, MNCH, IPC, AMR, PPPR, Patient Safety and healthy aging.
- Universal access to Sepsis prevention, diagnostics, treatment and rehabilitation can only be attained through integration of **Sepsis-related interventions into Universal Health Coverage** initiatives and packages at global and national levels. In this respect, the Global Sepsis Alliance encourages national health authorities and partners to explore the UHC Service Planning, Delivery and Implementation (SPDI) Platform offered by WHO to integrate Sepsis-related interventions in respective UHC packages. (129)
- Policymakers should also explore and build consensus on using Sepsis epidemiological and clinical data as potential **proxy or tracer indicators** for health system strengthening initiatives and UHC index measurement. In parallel, availability and quality of the clinical and epidemiological data on Sepsis should be substantially improved, especially in low-income settings.
- In view of the high morbidity and mortality burden of Sepsis in maternal, neonatal and child health indicators, special attention should be given to synergizing Sepsis interventions in **perinatal care** policies, and related regionalization and QI initiatives.
- National, regional and global **IPC policies and strategies** should consistently integrate Sepsis related messages and interventions across HAIs prevention, immunization, WASH, Antimicrobial Stewardship and other IPC initiatives.
- Stronger synergies are especially critical between **Sepsis and AMR** at policy, advocacy, awareness-raising and institutional levels, as called by the 2022 G7 Health Ministers' Communique. AMR and Sepsis actions should also be synergized in clinical practice. Building on the WHA70.7 resolution, the current strategy reaffirms that the inappropriate and excessive use of antimicrobials contributes to the threat of antimicrobial resistance, and that Sepsis represents the most vital indication for the responsible use of effective antimicrobials for human health.
- As noted, every future pandemic will increase the risk of infectious diseases and Sepsis. Accordingly, national, regional, and global policies for the Pandemic Prevention, Preparedness and Response should consistently integrate Sepsis, and Sepsis NAPs should have clear reference to the **Pandemic Accord** and related country-level PPPR instruments.
- In line with the Global Patient Safety Action Plan for 2021-2030, Sepsis should be consistently integrated into national **Patient Safety** frameworks, policies and action plans, as well as relevant QI initiatives in healthcare, including accreditation processes.

Priority Direction 1.4. Multi-lateral Cooperation and Funding

- Official Development Assistance, including bi- and multi-lateral development funding from **donor governments and IFIs** (The World Bank, IMF, Regional Development Banks, etc.) should increasingly integrate funding for Sepsis interventions at policy, institutional, and community-levels, in respective grant and development loan portfolios. Development of Sepsis NAPs or protocols could be considered as performance-linked indicators for conditional fundings of IFI budget support programmes.
- Low-income countries that are especially affected by Sepsis may face financial debt burden, and have even more limited fiscal space to invest in public health measures that can reduce Sepsis-related morbidity and mortality. Therefore, in parallel to advocating for the national action planning for Sepsis and domestic budgetary investments, the global Sepsis community can explore advocacy measures to reduce the **debt burden** of resource-limited countries, and thereby facilitate political and financial investments in Sepsis NAPs.
- **Global Health PPPs** (e.g., GAVI, Global Fund, GFF, UNITAID) and **philanthropic foundations** should offer to eligible countries and partners financial resources for the national and international response to Sepsis through respective grant applications for disease-specific interventions, health systems strengthening and/or innovative funding portfolios.
- The global community should also explore the establishment of new **innovative funding** streams for accelerating progress towards the Sepsis response, including for novel vaccines, diagnostics, antimicrobial, other therapies, and AI solutions.
- In parallel, the global Sepsis community should advocate for substantially increased **funding for Sepsis** policies, awareness-raising and training of the healthcare workforce through philanthropic foundations, private sector's corporate social responsibility (CSR) mechanisms, research and development, as well as crowd-funding mechanisms.

Example(s): Building on the WHA resolutions for emergency, critical and operative care (ECO) and increased access to medical oxygen, the ECO infrastructure, life-saving equipment and oxygen for the Sepsis response at primary health care and hospital levels in LMICs, could be supported by the World Bank or regional development bank performance-based, conditional funding as well as innovative financing mechanisms, such as UNITAID.

- Finally, increased international advocacy should ensure that AMR is included in PPPR instruments, both to improve attention to Sepsis, and to ensure that new and existing resources dedicated to the pandemic preparedness and response (such as the World Bank Pandemic Fund) also is allocated to AMR. Engagement with relevant international instruments, including a newly established Independent Panel for Evidence for action against AMR could be also explored, to have a specific focus on Sepsis, and ensure increased focus on Sepsis in the next UN High Level Meeting on AMR in 2029.

Priority Direction 1.5. Global Monitoring and Accountability

- The strategic direction aims at improving the **quantity and quality of data** on Sepsis for generating robust evidence for decision making. This includes systematic data collection and analysis through epidemiological surveillance, modification of ICD-10 coding, dedicated Sepsis registries, operational research initiatives and/or global monitoring reports.

Example(s): In 2017, based on the Septic shock registry, Korea revealed areas for improving the quality of initial resuscitation and outcomes of septic shock patients in EDs. (131) Later, in 2020, the country designed a web-based Sepsis registry system “Korean Registry for Improving Sepsis Survival”, and the multi-centre hospital-based Sepsis registry. (132)

- **Sepsis surveillance** in general should be urgently improved with focus on resource-limited settings and high-risk groups, such as pregnant and postpartum women, newborns and under-5 children, older adults and immunocompromised patients. As noted, Sepsis epidemiology is practically unknown in LMICs that are most affected, and blind spots remain in gender-disaggregated statistics, community practices, and clinical outcomes among the most vulnerable population groups.
- Efforts in improving Sepsis surveillance capacities should **build interlinkages** with other technical programmes on IPC and Safe Surgery, to ensure tracking healthcare associated infections, including surgical site infections. Stronger synergies are also needed for between AMR and Sepsis data reporting and analysis systems.
- The WHA70.7 Resolution urges the Member States to apply and improve the use of the ICD system for establishing **Sepsis epidemiological profiles**, and the international community shall work towards the establishment of an international Sepsis interoperable data set.
- Finally, the Global Sepsis Alliance and Regional Sepsis Alliances, in coordination with WHO, CDCs and other global and regional authorities, should catalyse regular data collection and publication of annual **Global Sepsis Reports** on the status of the Sepsis response at national, regional and global levels. The global reports could be translated into global and regional dashboards for tracking progress towards WHA70.7 Sepsis Resolution, related World Health Assembly resolutions on ECO, IPC and medical oxygen, the current 2030 Global Agenda for Sepsis, and consolidating evidence-informed advocacy efforts.

STRATEGIC PILLAR 2.

HEALTH SYSTEM READINESS FOR SEPSIS AND ITS SEQUELAE

Overarching Goal(s) of the Strategic Pillar

The ultimate goal of the 2nd strategic pillar is to improve prevention, early detection, timely and effective treatment of Sepsis, and management of Sepsis sequelae through strengthening the core operational capacities and emergency readiness of national health systems.

As noted, Sepsis could be considered a tracer indicator for HSS and UHC initiatives, as the complexity of Sepsis prevention, diagnosis, treatment and care calls for a multi-dimensional, multi-faceted response and resilient health systems at all levels of healthcare delivery.

Building on the WHA70.7 Resolution, the current pillar aims at including prevention, diagnosis and treatment of Sepsis in national health systems strengthening initiatives, strengthening efforts to promote the appropriate use of antimicrobials, including the development and implementation of comprehensive antimicrobial stewardship activities; developing training for all health professionals on infection prevention and patient safety, and on the importance of recognizing Sepsis as a preventable and time-critical condition with urgent therapeutic need.

In view of the limited resources and data in low- and middle-income settings, the health system strengthening initiatives for Sepsis management should prioritize local-context adaptation of the evidence-based knowledge and successful clinical practices, that still primarily originate from high-income countries.

Specific Objectives of the strategic pillar:

- 2.1 By 2030, at least 50% of UN Member States have developed and started implementation of evidence-based and patient-focused Clinical Pathways for Sepsis, and Sepsis Bundles for adult and paediatric patients, including protocols for Rapid Response Systems (RRSs), Sepsis Care Cascades (SCCs) and management of Sepsis sequelae.
- 2.2 By 2030, maternal and neonatal Sepsis-related deaths are reduced by 20% from 261,000 and 203,000 annual cases, respectively, through increased investments in prevention, early identification and effective management of Sepsis in community and ante-, peri- and post-natal care settings
- 2.3 By 2030, at least 50% of health care institutions engaged in SCCs have essential supplies and equipment for the management of Sepsis and related organ dysfunction, including access to microbiology labs or rapid diagnostic tools, ventilators with adequate oxygen supply, renal replacement therapies, patient monitoring systems, antibiotics and IV fluids.
- 2.4 By 2030, at least 20% of UN Member States have initiated QI and/or accreditation programmes for Sepsis, including regionalization of the care cascade.
- 2.5 By 2030, at least 50% of UN Member States have integrated Sepsis as a medical emergency in undergraduate curricula and postgraduate CME training for the health workforce.
- 2.6 Cross cutting HSS targets for Sepsis prevention and management:

- 2.6.1 By 2030, at least 90% global routine immunization (DTPcv3) coverage.
- 2.6.2 By 2030, at least 80% of health care institutions in LMICs have access to WASH facilities.
- 2.6.3 By 2030, at least 50% of health care institutions in HICs and LMICs monitor the time taken for patients with Sepsis to receive life-saving antimicrobials.

Priority Directions and Interventions

The 2nd Strategic Pillar calls for specific policy and institutional changes and actions in the following five priority directions and cross-cutting HSS interventions.

Priority Direction 2.1. Patient-Focused Sepsis Clinical Pathways

- Building on the 2017 WHA resolution, Ministries of Health and relevant national health authorities (e.g., national CDCs) should ensure development, application and monitoring of **evidence-based and patient-focused clinical pathways for Sepsis and Sepsis Bundles for adult and paediatric patients**. Special attention should be granted to vulnerable populations, including pregnant women, newborns, children, older adults and patients living with chronic diseases. Adherence to these protocols have proved to be life-saving with substantial reduction in hospital fatality from Sepsis. Health authorities and health service providers can develop Sepsis clinical pathways and bundles based on international guidance (e.g., SSC), and good practices and blueprints from the UK, US, Sweden, Australia, France, and other countries with relevant adaptation to local health system contexts.

Example(s): Implementation of mandatory Sepsis protocols at all hospitals in New York State is estimated to have saved more than 16,000 lives between 2015 and 2019, while compliance with the “Sepsis Six” bundle across the hospitals in England and Wales led to a 46.6% reduction in the relative risk of patients’ deaths from Sepsis. (107)

- WHO and its regional offices, European Commission for Health and Food Safety, Surviving Sepsis Campaign, regional and national CDCs and other international health actors should strengthen **collaboration, synergies and regular updates of evidence-based guidelines** for the clinical management of Sepsis. The guidance should be available for adaptation and application in different economic and

health sector contexts across HICs and LMICs. Furthermore, the guidelines and tools should target different audiences among health sector stakeholders, including physicians, nurses, midwives, paramedical personnel and public health professionals. The upcoming WHO Guidelines for Clinical Management of Sepsis and the continuously updated SSC guidance are important references for national and regional health authorities, and healthcare providers.

- Sepsis care is multidisciplinary, complex and fragmented, and a coordination model based on tools and allocated human resources is essential. Along with Sepsis clinical pathways, healthcare institutions should prioritize establishment of all-day multidisciplinary **Rapid Response Systems**. Mortality among patients with hospital-onset Sepsis is lower (35.4%) in hospitals with all-day rapid response teams (RRTs) compared to 42.7% in clinics with non-all-day RRTs services. (122) RRTs need support from the hospital leadership to ensure the allocation of essential time and resources for the implementation of Sepsis protocols.
- In addition, as part of Sepsis clinical pathways, countries should develop comprehensive **Sepsis Care Cascades** across the community, Primary Health Care (PHC), Emergency Medical Services (EMS), and secondary and tertiary Hospital Levels, including EDs, general wards, and ICUs. SCCs should include prevention, early recognition, severity assessment, prehospital EMS activation, early therapy, and referral to adequate treatment facilities in-hospital treatment with organ failure resuscitation and source control (where relevant). The 2024 study suggests that application and optimization of such integrated networks can significantly improve Sepsis clinical outcomes. (133) The cascade should also cover care and rehabilitation for long-term sequelae of Sepsis, including for cognitive, psychological, and physical disability.

Example(s): In response to the increasing Sepsis incidence in 2008-2012, Catalonia (Spain) declared Sepsis a public health problem and initiated a strategic planning exercise for early detection and treatment of this medical emergency. In 2015, a multidisciplinary advisory committee developed an Interhospital Sepsis Code (CSI) based on regionalization principles of Sepsis care across primary, secondary and tertiary healthcare facilities. CSI facilitates awareness-raising, early detection, initial care and interhospital coordination in the management of septic patients throughout the region. The process led to the development of “Radar Sepsis” system, which provides continuous screening of cases, analysis, and feedback to hospitals.

- Special attention should be given to the improvement of **Pre-hospital Sepsis recognition** both in communities and EMS, as even in the US only 18% of Sepsis cases have been diagnosed by EMS. In this respect, countries may refer to the WHO Prehospital Toolkits for ambulance providers and other resources for strengthening the capacity of community health workers, primary health care providers and EMS personnel.
- Sepsis prevention, early detection and referral capacities should be augmented at the **Primary Health Care** settings, including among PHC and community health workers. Sepsis, with its critical linkages to immunization, WASH, and rational use of antimicrobials and prevention measures, offers a unique entry point for renewing

investments and capacities of PHC systems as the inclusive platforms for UHC. Social media may serve as important tools for early Sepsis alerts at community level and immediate decision support for the primary care practitioners.

Example(s): A recent story of a Sepsis Survivor confirms that primary health care plays an important role in Sepsis clinical pathways and outcomes in China. A general practitioner saved the patient's life by activating "We Chat" communication channel, calling a multidisciplinary team to discuss the suspected Sepsis case, and ensuring timely referral and treatment at the tertiary hospital.

- **Person-centred care** for Sepsis patients should be the central element of all health-system intervention described above. As an example, Sepsis survivors engaged in the development of the 2030 Global Agenda for Sepsis, raised the concern that often the intensive care involves isolating the patient from visitors due to infection control considerations or visitor interference with care. Family presence and engagement during intensive care is better for patient safety and reduces risk of delirium, and person-centred care including flexible visitation needs to be part of patient pathways and protocols for Sepsis care, for both paediatric and adult patients.

Priority Direction 2.2. Sepsis Response in Maternal, Neonatal and Child Health

- In view of the Sepsis burden among pregnant women and newborns, especially in LMICs, global Sepsis community should prioritize the integration of cost-effective prevention, IPC, diagnostic, and treatment interventions into **ante-, peri-, and post-natal care services**.
- Sepsis management capacities should be enhanced in the **healthcare workforce** providing pregnancy, childbirth and post-delivery care to mothers and newborns, including obstetrician-gynaecologists (Ob/Gyns), midwives, nurses, neonatologists, paediatricians and community health workers.
- **Quality Improvement of Perinatal Care**, including regionalization processes, should consistently include prevention, early detection and early and effective treatment for maternal and neonatal Sepsis, as well as immunization, WASH, and hand hygiene related policies, infrastructure and practices.
- MNCH-related interventions for Sepsis should be **synergized with the Global Maternal and Neonatal Sepsis Initiative** launched by WHO and Jhpiego in 2017 and relevant international guidance from WHO, UNICEF and SSC both for HICs and LMICs. (134)

Priority Direction 2.3. Essential Equipment and Supplies for Sepsis Bundles

- The availability of ‘Sepsis Bundles’ for adult and paediatric patients as standard protocols is critical for the timely recognition of Sepsis and adequate treatment with antibiotics, IV fluids and hemodynamic monitoring.
- Healthcare institutions should have **essential supplies and equipment** for the management of Sepsis and Sepsis-related organ dysfunction, such as ventilators with adequate oxygen supply, renal replacement therapies, patient monitoring systems, antibiotics, and IV fluids. The list of essential supplies and equipment for the clinical management of Sepsis should be developed through experts’ consensus as a common reference for multiple stakeholders.
- Furthermore, healthcare providers should have 24-hour access to microbiology **laboratories for blood cultures and/or rapid diagnostic tools** for the early identification of Sepsis.
- Accordingly, national health authorities and international development partners should prioritize financial **investments in health infrastructure**, including ambulance systems, laboratory and ICU capacities for the provision of quality emergency, critical and operative care (ECO) services. Basic infrastructure investments for adequate supply of water and electricity should be also prioritized, especially in LMIC settings, as well as special consideration for Sepsis management (e.g., adequate spatial distance between hospital beds).

Priority Direction 2.4. Medical Education and Training

- This strategic direction prioritizes **capacity building** of the Health Workforce on the importance of recognizing Sepsis as a preventable and time-critical condition with urgent therapeutic need, as almost 80% of Septic shock deaths could be prevented if treated in time.⁽⁶⁷⁾ Key competencies for Sepsis management should be defined both for undergraduate medical students and healthcare professionals across different levels of healthcare, including general practitioners, surgeons, intensivists, Ob/Gyns, Infectious Diseases (ID) specialists, EMS personnel, dentists, nurses and midwives.
- In the context of significant **health workforce shortage**, especially in LMICs, special consideration should be given to building capacity of nurses, midwives and community health workers at the frontline of health service provision, in early identification, referral and management of suspected Sepsis cases.
- Sepsis prevention and management as a medical emergency should be integrated into **undergraduate** medical curricula and cooperation strengthened with medical universities and medical students’ associations for curricular reforms and extra-curricular initiatives

Example(s): France has implemented education programmes for students on the prevention of infections and Sepsis, and mandatory training on Sepsis as part of the undergraduate curricula for medical students and nurses. (135)

- Sepsis prevention, early detection, and management should be consistently integrated into **post-graduate and continuous medical education (CME) systems for healthcare professionals**. Starting from primary health care to EMS, EDs, ICUs and geriatric care facilities, physicians, nurses, paramedical personnel, and clinical managers should be trained according to the national Clinical Pathways and relevant international guidelines for adult and paediatric patients.

Example(s): Australia has proven to reduce the incidence of Sepsis and septic shock and related deaths in healthcare institutions through education of frontline workers and adherence to standard protocols. (99) The UK Sepsis Trust has CPD accredited Sepsis e-learning modules on Sepsis management completed 100,000 times annually (136), and the Latin American Sepsis Institute (LASI) offers training modules for healthcare workforce in the management of paediatric and adult patients.

- Partners should prioritize **active learning methodologies**, as systemic review of 32 studies revealed, that incorporating active learning strategies into Sepsis education interventions (such as simulation and game-based learning) can improve learners' long-term outcomes. Sepsis education and a protocol-based Sepsis care bundle at the hospital levels act in synergy to augment greater improvements in care processes and patient's clinical outcomes. (137)
- Based on the experience of the COVID-19 pandemic, **Telemedicine** has also emerged as an effective tool for closing existing knowledge gaps, and as a peer support opportunity for intensive care professionals. **Digital training** approach could be feasible for sub-Saharan Africa and other regions, to build sustainable capacities in managing medical emergencies, such as Sepsis, in resource-limited settings. (138) However, the telemedicine and digital training opportunities for rural and remote areas of LMICs should also consider additional investments in communication infrastructure. .

Example(s): Charité based Tele-ICU hub has supported countries in the management of critical care patients, including Sepsis, through a multidisciplinary team. Uzbekistan, Ukraine, Uganda and South Africa have benefited from the initiative through the financial support from Charité Foundation and the German Agency for International Cooperation (GIZ). In the Andean region of Argentina, with large rural/mountain areas, transferring patients in need can take a while, sometimes walking, using horses or mules. Therefore proper (i.e., satellite) communication infrastructure for managing medical emergencies through telemedicine opportunities could be critical.

Priority Direction 2.5. Quality Improvement in Sepsis Care Cascade

- National health authorities should establish comprehensive **Quality Improvement** initiatives for Sepsis along the SCCs, including regionalization. In collaboration with national and international accreditation bodies in healthcare UN member States should develop a set of standard QI indicators for Sepsis management, and scale up voluntary or mandatory **accreditation** initiatives for Sepsis as stand-alone modules or part of broader IPC packages.

Example(s): The Australian Commission on the Safety and Quality in Healthcare published a Sepsis Clinical Care Standard in 2022 as part of the national health services accreditation programme.(139) The standard contains 7 quality statements and indicators on early recognition and coordinated, best-practice care for septic patients. (140) Catalonia, Spain initiated the Sepsis Training Audit and Feedback (STAF) project with a specialized portal at the Health Department for Sepsis and septic shock to register key performance indicators (KPIs) on antibiotic administration, resuscitation, infection source control, and time of ICU admission.

- National QI initiatives for Sepsis should also include the establishment of **Comprehensive Sepsis Centres**, to ensure guidance for the continuum of care for SCCs and excellence in clinical research.

Example(s): France was the first country to establish the Comprehensive Sepsis Centre through government funding and Qatar is also working on the concept with a potential support from the Ministry of Health.

- Multidisciplinary **hospital programmes for Sepsis QI** are critical for monitoring and improving the quality of care, and have been associated with reduced hospital mortality, length of stay, and healthcare costs.(109) The structure of hospital Sepsis programmes may be specific to a single institution or general for healthcare systems at national and sub-national levels. The QI initiatives may focus on Sepsis specifically or be part of broader IPC and Patient Safety modules.

Example(s): Northeast Brazil through a participatory and multifaceted QI initiative documented major improvements in 8 out of 10 quality of care indicators for Sepsis in EMS and the possibility of scaling up the model countrywide.

- In countries and regions where provision of healthcare is centrally funded, **commissioning** for excellence in infections management may include rapid diagnosis and treatment of Sepsis, infection prevention, and antimicrobial stewardship. The commissioned care pathways similar to those existing for stroke, heart attack and cancer (e.g., UK NHS) would have the potential to transform not only immediate clinical outcomes of septic patients, but also the control over the rate of progression of AMR

Priority Direction 2.6. Cross-cutting IPC

- Sepsis response strengthens national health systems as it is closely inter-linked with HAIs prevention, immunization, WASH, AMR, Infection prevention and care bundles, and related QI interventions. Based on the WHA70.7 Resolution and the recent Global Action Plan and Monitoring Framework on IPC (141) national governments should strengthen HAIs prevention, immunization, WASH programmes and infrastructure, hand hygiene practices, and other IPC measures in health care facilities and communities.
- Global Sepsis stakeholders should assist national health authorities and communities in attaining at least 90% vaccination coverage rates for paediatric vaccines included in national **immunization** schedules, and aim for high vaccine coverage in adults and elderly people.⁽⁴⁵⁾ Awareness-raising and capacity-building initiatives for Sepsis among the health workforce and policymakers should clearly address the need for high immunization uptake as an essential element in Sepsis prevention.
- Due to the strong link between Sepsis and infection, sanitation and hygiene needs to be urgently improved, as 1 in 4 health care facilities in LMICs lack basic water services and 50%-70% of surgical teams and health care workers do not routinely practice hand hygiene. ⁽¹⁵⁷⁾ The Global Agenda for Sepsis calls for the improvement of **WASH** infrastructure and hand hygiene practices in at least 90% of healthcare institutions in the Global South. This improvement should prioritize cost-effective interventions, such as access to clean drinking water, increased compliance with hand washing, sanitary food preparation, and sterilisation of medical tools and equipment.
- National health authorities and health care providers should ensure synergies between Sepsis and AMR policies for reducing inappropriate and excessive use of antimicrobials as well as time-critical therapeutic interventions for septic patients, when critically needed. **Effective Antimicrobial Stewardship** means that life-saving antimicrobials are not withheld when mostly needed, as every hour of delayed treatment increases the risk of death. Special attention should be given to sub-Saharan Africa, with the highest burden of deaths associated with drug-resistant bacterial infections, where AMR-associated deaths represent 27% of lives lost to Sepsis.

Example(s): The UK NHS has published special guidance for companies wishing to apply for a contract through the Antimicrobial Products Subscription Model. The guidance builds on a joint pilot project between NICE and NHS England which is the first in the world to pay companies a fixed annual fee for antimicrobials based on their value to the NHS, as opposed to the volumes used.

STRATEGIC PILLAR 3

WHOLE-OF-SOCIETY RESPONSE TO SEPSIS

Overarching Goal(s) of the Strategic Pillar

The overarching goal of the strategic pillar is to substantially improve Sepsis literacy (awareness on Sepsis and its sequelae) among the general public, media representatives, and public policy-makers through consistent advocacy, a simplified new narrative on Sepsis, and engagement of Sepsis survivors and their families in the campaigns. This pillar links empowered communities as users and providers of care to the cross-sectoral approaches outlined in Pillars 1 and 5.

At the same time, the strategic pillar aims at improving prevention, prehospital recognition of Sepsis and emergency care-seeking behaviour, as over 80% of Sepsis cases originate in communities and early recognition is critical for timely referral, and effective treatment of this medical emergency.

The pillar reinforces the WHA70.7 resolution calling for increased public awareness of the risk of progression to Sepsis from infectious diseases, through health education, including on patient safety and to engage further in advocacy efforts to raise awareness of Sepsis, in particular through supporting World Sepsis Day activities on 13 September in Member States.

Specific Objectives of the strategic pillar:

- 3.1 Cross cutting targets for Sepsis prevention in communities:
 - 3.1.1 By 2030, at least 50% of public/community representatives incorporate immunization as a tool in a Sepsis prevention strategy.
 - 3.1.2 By 2030, at least 80% of communities living in LMICs have access to WASH facilities as a Sepsis prevention measure.
- 3.2 By 2030, at least 80% of household/community representatives in HICs and LMICs identify Sepsis as a medical emergency requiring immediate emergency care seeking.
- 3.3 By 2030, at least 80% or 155 UN Member States participate in the World Sepsis Day campaigns and ensure engagement of public leaders and media through national and international WSD events
- 3.4 By 2030, at least 20% of UN Member States have developed and started implementation of evidence-based and patient-focused Community Care Cascades for Sepsis, including prevention, early alert, treatment referral, and post-hospital care and rehabilitation for Sepsis survivors.

Priority Directions and Interventions

The goals and objectives of the Strategic Pillar, call for the implementation of the following 4 priority directions and cross-cutting interventions.

Priority Direction 3.1. Community Level IPC

- Preventing infectious at the community level is the most effective measure against Sepsis. Therefore, the 2030 Global Agenda for Sepsis calls for strengthening **community-level IPC interventions**, such as vaccination, WASH infrastructure, and health education on hand hygiene, nutrition and rational use of antibiotics.
- The global Sepsis community should assist national and local health authorities, community workers and societies in attaining at least **90% vaccination coverage** rates against basic pathogens included in respective national immunization schedules for children and adults. Public awareness raising and engagement of public opinion leaders should clearly address the need for high immunization uptake as a core element in Sepsis prevention. Recognizing that many vaccine-preventable diseases are major contributors to Sepsis, cost-effective and affordable new vaccines should be consistently integrated into national immunization programmes, where feasible.
- The 2030 Global Agenda for Sepsis reiterates the critical importance of stronger **WASH infrastructure and hand hygiene practices** for preventing infectious diseases, especially in the Global South. Hand hygiene is one of the most effective measures to prevent infections that lead to Sepsis, but awareness raising and training initiatives for improving hand hygiene practices require access to clean and safe water and sanitation facilities.

Priority Direction 3.2. Sepsis Literacy as Medical Emergency

- The international community should enforce collaboration for re-framing the Sepsis narrative and ensuring that the term “Sepsis” is recognized as a **medical emergency** requiring immediate care, similar to a heart attack, stroke or other acute life-threatening conditions. Community care seeking behaviours should be studied and analysed to inform relevant and effective education and engagement strategies.
- Substantial efforts should be invested in **Sepsis Literacy and Community-Level Early Alert Systems** for improved understanding of the term “Sepsis”, signs and symptoms of this medical emergency, and ensuring prompt and timely initial contact of the affected children and adults with EMS or the nearest healthcare provider. Education efforts should target the general public as well as policy-makers, opinion leaders and health care professionals. Simplified and contextualized messages should be developed for each country setting in local languages and communication channels accessible to different populations, including minority and other vulnerable groups.

Example(s): Canadian scholars recommend that Sepsis education initiatives prioritize prevention approaches, employ broad media strategies, and use primary healthcare providers to disseminate the evidence-based information. (142)

- Engaging **Sepsis Survivors and family members** of patients as champions of change at local and international levels is critical. The new Sepsis narrative and simplification of Sepsis communication toolkits for general public and political leaders can only be successful through active collaboration with individuals and families with lived experiences, and community-based organizations.

Example(s): The Patients and Family Support Working Group of the European Sepsis Alliance ensures active engagement of Sepsis Survivors and family members in the development of GSA and ESA communication materials, such as the “Life After Sepsis Guide”. (143)

- The **World Sepsis Day (WSD)** commemorated on September 13 since 2012 should be more consistently promoted at national, regional and global levels with the ultimate goal of recognizing WSD among the official world health days of WHO. The WSD movement and campaigns should increasingly engage policymakers, public opinion leaders, health sector experts, civil society, faith-based organizations and media for greater outreach and improved Sepsis literacy among different audiences.
- The GSA and the World Sepsis Day Movement leaders should ensure that the core information and communication materials (Sepsis toolkits, infographics, checklist, etc.) are continuously updated and available in **multiple languages** for reaching audience across different geographic regions and communities. The communication resources should be available in at least six UN languages, including Arabic, Chinese, English, French, Russian and Spanish.
- The Sepsis literacy campaigns and initiatives should engage multiple **stakeholders beyond health sectors**. As an example, the **education sector** from pre-school and school, to professional and higher education institutions, can integrate measures for Sepsis awareness, prevention and early detection into health education programmes and medical services.

Example: The “Schools-against-Sepsis” campaign initiated by the UK Sepsis Trust intends to protect students and their families against this life-threatening condition. The initiative has already engaged 2,000 schools with regular Sepsis training for children aged 5-18 and their families.

- Similarly, the **Private Sector** beyond health industries can play an important role in disseminating Sepsis literacy through CSR initiatives. The latter may include support for the World Sepsis Day movement, designating “Sepsis Ambassadors” within the corporations for knowledge dissemination, or supporting patient organizations in their advocacy efforts.
- Finally, the question remains on how we can improve literacy through innovations and entertaining. There has been some promising research into **artificial**

intelligence (AI) models.(144) AI tools can flag possible Sepsis cases for immediate response from communities and ensure time-critical initial contact with healthcare providers. More investments are needed in learning innovations and AI-enabled solutions to avert Sepsis-related deaths and disability.

Priority Direction 3.3. Media and Public Leaders for Sepsis

- Media can play an important pro-active role in increasing awareness and **making “Sepsis” a household name** as a medical emergency requiring immediate attention and medical care. Media can also be a game-changer in holding governments, decision-makers and healthcare institutions accountable for necessary policies and actions against Sepsis.
- **Media Engagement Strategies** may include training for journalists at local and international levels, provision of continuously updated media and communication toolkits, stronger engagement in annual World Sepsis Days campaigns and event (TV, Radio, Printed and Internet Press), and recognizing media champions through Global Sepsis Awards and other initiatives.
- At the same time, Media, in turn, can ensure active participation of **Sepsis Survivors and families** affected by this medical emergency, featuring human stories through traditional and social media, and engaging multiple stakeholders, including health-care experts, public opinion leaders and politicians as relevant.

Example(s): Media coverage of human stories from Sepsis Survivors and families affected by personal tragedies have not only improved public awareness, but catalysed historic changes at the policy levels in the United States, UK, Belgium and other countries.

Priority Direction 3.4. Patients Care and Support Cascades

- Sepsis Care Cascades at the community level starts with **Early Alert Systems** for timely identification and referral of newborns, children and adults with suspected Sepsis cases to the relevant emergency and healthcare institutions.
- Post-discharge, community-level support is even more important for Sepsis Survivors as the long-term consequences of Sepsis call for increased **support, care and rehabilitation** needs. Sepsis survivors who suffer life-changing consequence, physical, cognitive or psychological, should have access to relevant care and support services at community and health-care settings, along with financial protection from public programmes or insurance plans.
- **Early access to rehabilitation and continuum-of care** as part of the “chain of survival and rehabilitation for Sepsis” is essential for Sepsis survivors to recover

acceptable quality of life. ⁽¹³³⁾ Availability and quality of rehabilitation services should be improved both in LMICs and HICs. Sepsis survivors and experts engaged in the current strategy development from Argentina and Belgium emphasize the fragmentation of post-Sepsis care from hospitals to communities. Sepsis survivors and their families receive no practical guidance after hospital discharge on post-Sepsis care and rehabilitation, there is no hand-over process to a practitioner who may follow-up the patients discharged to home. Post-Sepsis care and rehabilitation services are either not available or not covered through public or private health programme or insurance plans. From the personal experience, the high readmission rates of Sepsis survivors could be explained by the lack of proper coordination and post-hospital continuum of care.

Example(s): From the perspective of Sepsis survivors in Germany, therapies should begin in the hospital setting, be more appropriate for specific ailments (including pain, weaning from mechanical ventilation and cognitive deficits of fatigue), and include better education for patients and caregivers. ⁽¹⁴⁵⁾ Existing data from sub-Saharan Africa suggest that patients after discharge commonly experience medium- and long-term sequelae, yet resources for effective follow-up and care of these patients are lacking. ⁽¹⁴⁶⁾

- **Patients-for-Patient** support services and groups, including online consultation services, should be promoted, based on the experiences of Sepsibel (Belgium), Sepsisfonden (Sweden), UK Sepsis Trust, Sepsis Stiftung (Germany) and other organizations.
- **Sepsis Survivors** should lead the patient voices in designing and advising on the needed policy, institutional, and community-level interventions, including the post-hospital management, rehabilitation, and Sepsis recovery approaches. Sepsis patients recommend stronger collaboration on a national level between Sepsis experts and Sepsis patients, as well as with experts and patients engaged in the work on the long COVID-19 for exchanging knowledge on pathophysiological and rehabilitation aspects.

Example: In 2017 Sepsis survivors in Netherlands started 'SOS for Sepsis' petition which led to negotiations with government on a national Sepsis plan and one-time financial support for launching the website SepsisNet for awareness raising. Sepsis survivors were engaged in the developing of a national guideline on clinical management of Sepsis in paediatric and adult patients, completed in 2021-2022. In 2023 SepsisNet and Sepsis en daarna jointly with other patient organizations developed the Patient Alliance of Post-Acute Infectious Syndromes (PAIS), including Sepsis.

STRATEGIC PILLAR 4.

RESEARCH AND INNOVATIONS FOR SEPSIS

Overarching Goal(s) of the Strategic Pillar

The ultimate goal of the strategic pillar is to substantially improve public and private research opportunities and funding for Sepsis both in HICs and LMICs, and to promote investments into novel prevention, diagnostic, treatment, and AI solutions for both paediatric and adult patients.

Building on the WHA70.7 resolution the current pillar will promote research aimed at innovative means of diagnosing and treating Sepsis across the lifespan, including research for new antimicrobial and alternative medicines, rapid diagnostic tests, vaccines and other important technologies, interventions and therapies.

The strategic pillar will also reinforce the WHA Resolution on clinical trials to provide high-quality evidence on health interventions and to improve research quality and coordination.

Specific Objectives of the strategic pillar:

- 4.1 By 2028, at least 50% (19 out of 38) OECD countries allocate earmarked public/government funds for Sepsis research and academic collaboration.
- 4.2 By 2025, a Global Sepsis Research and Innovation Platform, an international public-private partnership is launched to discuss unmet needs in Sepsis prevention, diagnostic and treatment, including through novel vaccines, fast pathogen detection tools, immunomodulatory therapeutics and precision medicine.

Priority Directions and Interventions

The attainment of the declared goals and objectives of the 4th Strategic Pillar calls for the implementation of the following 2 priority directions and interventions.

Priority Direction 4.1. Investing in Sepsis Research and Academic Collaboration

- **Sepsis Science** investments in HICs and LMICs, including in fundamental and operational research, remain low and should be fostered. Similarly, Sepsis related clinical research trials should be more representative of high, middle-, and low-income settings and geographic regions affected the most. Further to limited research investments from public and private sectors, research focus should be strengthened on the needs of priority population groups, such as newborns and children.

- Large continental research programmes, including the US National Institutes of Health (NIH) or EU Horizon, should catalyse increased **public funding for Sepsis research**. Building on examples from the US BARDA, Germany and the UK, individual OECD countries, should also allocate earmarked research funding for Sepsis and ensure proportional financial allocations to address the medical emergency that causes 1 in every 5 deaths globally.
- Increased research fundings should catalyse stronger **academic collaboration** for the exchange of the intelligence, best practices and innovations in the prevention, diagnostics, treatment and care of Sepsis, and closing knowledge gaps, especially across the LMICs. Academic collaboration across countries and institutions may be built on the existing academic representation and collaboration of the GSA, SSC and other key players in the global Sepsis response with *Charité* Universitätsmedizin Berlin (Germany), University of British Columbia (Canada), George Institute for Global Health (Australia) and others.
- Stronger collaboration between **professional associations and the scientific community** shall enhance research opportunities to better understand Sepsis pathophysiology, diagnostics and therapeutics. Additional studies are critical for assessing cost-effectiveness and impact of Sepsis prevention and management interventions on the human, societal or economic burden of Sepsis in specific countries and globally. Dissemination of state-of-the-art knowledge among health care professionals and scholars should be further enhanced by global knowledge sharing platforms, such as the World Sepsis Congresses and International Sepsis Forum.
- The Sepsis community should support the establishment and/or expansion of global, regional and national **Knowledge Hubs** that consolidate the latest scientific and implementation research evidence, and policy and clinical recommendations. The resources should be available in at least 6 official UN languages to facilitate global distribution and application of the state of art knowledge.

Example(s): Sepsis Stiftung in Germany operates the “Sepsis Science Info Centre” that is updated weekly with relevant scientific literature for different audiences. (147) The George Institute for Global Health based in Australia provides a repository of digital books and communication toolkits for Sepsis, while the Sepsis Alliance in the United States manages the Sepsis Alliance Institute which has more than 50,000 professional members.

Priority Direction 4.2. Innovations for Sepsis Prevention, Diagnosis and Treatment

- Public-private partnerships for Sepsis innovations should be fostered for understanding unmet needs and increased investments in **Research and Development** (R&D) for novel prevention vaccines, diagnostic, treatment (including antibiotic) and AI tools for early detection and timely and effective management of Sepsis. Such investments should focus on the needs of all populations and countries. The advocacy efforts should include incentives and push funding mechanisms provided

by governments and foundations to PPPs and private sector for the development and registration of new therapies (e.g., antibiotics) for wider accessibility to newborns, children and other priority groups.

- Building on the example of the US Sepsis Alliance, which has been managing the FDA-supported Coalition for Sepsis Innovations, GSA will lead the **establishment of a Global Sepsis Research and Innovation Platform**. The platform will bring together multiple stakeholders from academic and research institutions, the public and private sector, patient organizations and civil society to promote dialogue and novel solutions for Sepsis prevention, diagnostics and treatment. The platform will also provide recommendations and consistent approaches for facilitating licensing and registration of strengthening access to new medical tools for the most vulnerable, such as newborns and children affected by Sepsis in LMICs. The Sepsis innovation platform should coordinate its dialogue and work with other partnership mechanisms for vaccines, diagnostics and medicines, such as those led by GAVI, FIND and Medicines Patent Pool.
- R&D in innovations focusing on **Sepsis prevention** is essential, such as the development of anti-Sepsis vaccines that will have the potential to reduce the incidence of infections that most commonly lead to Sepsis, especially among women, newborns, children and older adults (e.g., methicillin-resistant *S. aureus*, *E. coli*, *Klebsiella* spp.). (11)
- As early detection largely defines clinical outcomes of septic patients, diagnostic novelities should continue to be a key priority. Further investments are needed in **innovative diagnostics** for Sepsis, including point-of-care and rapid diagnostic tools. These tools include increased availability and application of biomarkers, molecular fingerprints and other solutions for improving pathogen detection, differentiation between bacterial and other infections, or differentiation between infection-induced and non-infection-induced systemic inflammatory response syndromes. The novel and rapid diagnostics should be effectively integrated into clinical systems to provide timely and life-saving information to the prescribing clinicians at the patient's bedside.
- The strategic pillar also prioritizes R&D for **Sepsis therapies**, including new and more effective antimicrobials and immune-modulatory therapeutics. The Sepsis R&D agenda should be synergized with AMR-related discussions as the limited number of new regimens in the antimicrobial pipeline equally impacts clinical perspectives of septic patients. Discussions on market failures and other barriers should address not only antibiotics, but antiviral, antifungal and antiparasitic medications for managing septic patients with different pathogenesis.
- Strengthening research, innovation, and access on behalf of **newborns and children** would be a key priority through active dialogue with the WHO Paediatric Drug Optimization Standardization Procedure (PADO), GARDP and other core players.
- Sepsis related R&D initiatives should prioritize **immunomodulatory therapies**, similar to the recent initiative launched by BARDA. Finally, Sepsis-induced and Sepsis-related coagulopathies is critical to address due to the high frequency of disseminated intravascular coagulation (DIC) among septic patients, as an example, and high, up to 60% mortality rates. (149,150)

- Furthermore, the heterogeneous characteristics of Sepsis with varying demographics, pathogenesis or clinical manifestations make the **precision medicine** approaches even more challenging. However, additional research is equally important in the advancement of personalized therapies, including theragnostics, for the Sepsis management.
- From the patients' perspective, more attention should be paid to research and innovations in **care and rehabilitation** commodities for Sepsis survivors and **therapies for Post Sepsis sequelae**. The latter also applies to collaboration with Covid-19 researchers for exchanging the knowledge in view the documented similarities between Post-Sepsis Syndrome and long-term sequelae of COVID-19.
- Stakeholders should incentivize innovations in early identification of Sepsis through **AI tools**, including mobile applications. However, most of the AI solutions for early Sepsis alerts continue to demonstrate low sensitivity and specificity, with especially high false positive results. AI-enabled solutions should be further optimized, as the artificial intelligence tools have the potential to improve early detection of Sepsis for time-critical and life-saving treatment, especially in contexts with a significant shortage of health workforce.
- Industry partners should prioritize R&D for LMICs and emerging markets, to address market failures and ensure that new knowledge and life-saving innovations reach the most vulnerable population groups, thus **leaving no one behind**.
- The R&D agenda for **new antimicrobials**, including the initiatives how to address the market failure, should be harmonized with the Quadripartite Agreement for One Health and its AMR strategies agreed by FAO, UNEP, WHO and WOA. H.
- **The impact of antimicrobial resistance** on Sepsis outcomes may vary between countries and availability of adequate clinical data should also be prioritized to guide effective therapies and recommendations. (110)
- Evidence generation on human, societal and economic burden of Sepsis as well as **implementation research** on Sepsis policies and QI initiatives, especially in LMICs, is another important priority. The latter should also include systematic reviews on the status of implementation of the WHA70.7 Sepsis Resolution and related resolutions on integrated emergency, critical and operative care (ECO) or health emergencies, such as WHA72.16, WHA75.8 and WHA76.2. (151–153). In particular, countries should leverage the mandate of WHA 77.8 which calls for a global strategy and action plan for integrated ECO 2026–2035 to strengthen Sepsis care.(154)

Examples: Good evidence base IPC research in prevention Sepsis and AMR and spread of pathogens in a facility/community and in different settings (including fragile, conflict and violence situations) is equally important. Investments in a global network of laboratories and clinical research sites that can both support the collection of data from diverse populations, settings, and countries, as well as to improve the efficiency of research and development and reduce costs borne by pharmaceutical companies.

STRATEGIC PILLAR 5

SEPSIS IN PANDEMICS AND OTHER EMERGENCIES

Overarching Goal(s) of the Strategic Pillar

In line with the WHA70.7 resolution, the 5th strategic pillar of the 2030 Global Agenda for Sepsis aims to develop and implement standard and optimal care, and strengthen medical countermeasures for diagnosing and managing Sepsis in emergencies with health consequences, including infectious disease outbreaks, armed conflicts, and natural and other man-made disasters.

The strategic pillar calls for stronger multi-lateral and multi-sectoral cooperation for integrating Sepsis-related interventions in global frameworks and guidelines for emergency and humanitarian responses as well as national emergency preparedness and response plans.

Specific Objectives of the strategic pillar include the following:

- 5.1 By 2030, at least 50% of UN Member States have integrated Sepsis-related interventions into national PPPR frameworks and action plans.
- 5.2 By 2030, more than 80% of UN Member States have integrated Sepsis prevention, early detection, treatment and post-hospital care and rehabilitation in health protocols for defence/military personnel and relevant services for civilians under humanitarian crisis.
- 5.3 By 2026, humanitarian response protocols from at least 10 leading international humanitarian aid organizations², integrate Sepsis prevention and response.
- 5.4 By 2028, at least 50% of UN Member States have integrated Sepsis into the national laws and policies on climate change adaptation.

Priority Directions and Interventions

The goals and objective of the 5th Strategic Pillar calls for the following 5 priority directions and interventions.

² In view of the geographic and humanitarian work coverage, the organizations include: WHO, WFP, UNICEF, OCHA, UNHCR, IFRC, Save the Children, Catholic Relief Services, CARE, World Vision, Direct Relief, MSF, Actions Against Hunger, IRC, International Medical Corps, BRAC, Danish Refugee Council, Oxfam, Action Aid International, ALIMA, and Plan International.

Priority Direction 5.1. Sepsis in Pandemics

- Building on the experience from the latest COVID-19 pandemic, any future pandemics or disease outbreaks will increase the risk of infectious diseases and accordingly the risk of Sepsis morbidity and mortality. Sepsis is the final common pathway from all pathogens that may cause pandemics. Therefore, the global Sepsis community should advocate at the level of the Intergovernmental Negotiation Body to integrate the Sepsis response into the final or amended versions of the international PPPR instrument, the **Pandemic Accord**.
- In parallel, UN Member States should ensure that Sepsis-related communication and preparedness interventions are integrated into **national PPPR plans** and synergized with relevant advocacy, health system strengthening, and multi-sectoral initiatives.

Priority Direction 5.2. Sepsis in Armed Conflicts

- During armed conflicts, wound infections affect from 4.9% to 78% of **civilians and military personnel** and subject them to an increased risk of Sepsis. ⁽⁸⁴⁾Therefore, in parallel to the national health system strengthening initiatives, the 2030 Global Agenda for Sepsis calls for augmenting Sepsis prevention and management capacities (including through WASH and other IPC solutions) in **healthcare systems of defence and military sectors** and international peacekeeping forces.

Example(s): In 2011-2019, the incidence of hospitalization due to Sepsis increased by 64% in active service members of the U.S. Army, Air Force, Navy, and Marine Corps and relevant recommendations were applied by the defence authorities. (155)

- Sepsis prevention, early detection, treatment, and post-hospital care and rehabilitation should also be integrated into **health protocols** for defence/military personnel and the essential care services for civilians in humanitarian settings. This calls for multisectoral cooperation between Health, Defence and Military sectors for strengthening awareness and Sepsis management capacities, and reducing morbidity and mortality risks among military and defence personnel.
- As part of the emergency health response during armed conflicts, **civic education** should cover awareness raising and first aid training opportunities for improved prevention, early alert systems for Sepsis, as well as pre-hospital wound management techniques, as necessary.

Priority Direction 5.3. Sepsis in Humanitarian Crisis and Displacement

- During **humanitarian crises**, children, women and men, including refugees and migrants are at increased risk of infections that can lead to Sepsis.⁽⁸⁵⁾ Disruption of routine immunization programmes during the crisis and displacement further increases the risk of Sepsis. Accordingly international humanitarian agencies should prioritize Sepsis prevention and management as part of their core humanitarian response operations.
- **Sepsis awareness and prevention** measures through WASH and other IPC approaches should be strengthened during humanitarian crisis and displacement, such as the wound care and hand hygiene. **Clinical management** of Sepsis should be integrated into all packages of High-priority Health services for Humanitarian response (H3 package), including for migrant and displaced populations. Humanitarian personnel and community representatives should be equipped with relevant knowledge and resources to alert suspected Sepsis cases and ensure time-critical medical care.
- The following **UN agencies and international humanitarian organizations** will be prioritized for collaboration within the framework of the 2030 Global Agenda for Sepsis. In view of their geographic coverage and impact, the priority organizations include WHO, WFP, UNICEF, OCHA, UNHCR, IFRC, Save the Children, Catholic Relief Services, CARE International, World Vision, Direct Relief, MSF, Actions Against Hunger, IRC, International Medical Corps, Bangladesh Rehabilitation Assistance Committee (BRAC), Danish Refugee Council, Oxfam International, Action Aid International, ALIMA and Plan International.

Priority Direction 5.4. Climate Change and Sepsis

- More than 120 countries have **national laws and policies for climate change adaptation**.⁽¹⁵⁶⁾ and in view of the direct risk correlation with climate-induced emergencies, Sepsis should be consistently integrated into national climate change policies and preparedness plans.
- Global, regional and national stakeholders should integrate Sepsis into the agenda of the leading **Health and Climate Change forums**, such as the Conference of Parties (COP), UN High Level Meetings and the World Economic Forums.
- At the same time, in line with the **Quadripartite Agreement** for One Health, the global Sepsis community should prioritize promotion of carbon-free practices and technologies in community- and healthcare settings, more effective Antimicrobial Stewardship for human and animal health, and better Sepsis response preparedness to potential environmental disasters.⁽⁸¹⁾

SECTION 5

RESULTS FRAMEWORK

2030 GLOBAL AGENDA FOR SEPSIS

Impact Statement

Expected Impact	Key Performance Indicators (KPIs)	Means of Verification	Comments
Reducing the incidence of Sepsis from 677 episodes per 100,000 population in 2017 to < 500 episodes per 100,000 by 2030	Sepsis incidence per 100,000 population globally Baseline (2017): 677 episodes per 100,000 population Target (2030): < 500 episodes per 100,000	Global Burden of Sepsis (2020) and subsequent periodic reports	World Sepsis Declaration target
Survival rates from Sepsis among under-5 children and adults improved by 20% from the 2020 baseline	Sepsis-related deaths in adults and under-5 children annually Baseline (2017): 8.1 million and 2.9 million Target (2030): 6.5 million and 2.3 million	Global Burden of Sepsis (2020) and subsequent periodic reports	World Sepsis Declaration target
Reducing median cost per Sepsis patient per country and per capita by 20% by 2030	Median cost per Sepsis patient per country and per capita Baselines (2020): € 36,191 Target (2030): < € 29,000	Systemic Analysis of economic and health sector impact of Sepsis	

Strategic Pillar 1.

Political Leadership and Multilateral Cooperation

Goal(s) of the Strategic Pillar:

- Positioning Sepsis in the mainstream of global and national health policy dialogue and architecture with relevant funding streams and stronger synergies with health-related SDGs and related targets for UHC, MNCH, IPC, AMR, PPR and Patient Safety
- Strengthening global, regional and national responses to Sepsis through multilateralism, including multi-lateral cooperation, allocation of domestic, public-private and international aid funding, and accountability mechanisms for the 2030 SDG agenda

Strategic Objectives and Targets	KPIs	Means of Verification	Comments
1.1 A High-level Political Platform for Sepsis becomes operational by the end of 2025 and leads systematic integration of the Sepsis agenda into the mainstream of global health and development dialogue and architecture.	KPI (Output): A High-Level Political Platform for Sepsis Operational (Yes/No) Baseline (2024): No Target (2025): Yes	Terms of Reference (ToR), meeting minutes and composition of the Political Platform; Agenda of high-level health forums	Priority high-level forums include G7/G20, UNGAs and HLMs, WHAs, Davos WEF, WHS, IPU, UNITE and Ministerial Summits
1.2 By 2030, at least 80% of HICs and at least 50% of LMICs have developed and started implementation of National Action Plans (NAPs) on Sepsis, with earmarked domestic budgetary resources, as stand-alone NAPs or part of broader health sector policies and programmes.	KPI (Coverage): % of HICs and % of LMICs with Sepsis NAPs and earmarked budgetary resources Baseline (2024): < 30% HICs < 5% LMICs Targets (2030): > 80% HICs > 50% LMICs	Global Sepsis Reports (Country Reports on Implementation of WHA 70.7) to be initiated by GSA in 2025	Baseline estimated from GSA and RSAs reports and experts' opinions.
1.3 By 2030, at least 80% of HICs and at least 50% of LMICs have incorporated Sepsis into national packages of priority UHC services. (129)	KPI (Coverage): % of HICs and % of LMICs synergizing Sepsis NAPs with relevant policies and programmes Baseline (2024): < 30% HICs < 5% LMICs Targets (2030): > 80% HICs > 50% LMICs	Global Sepsis Reports to be initiated by GSA in 2025	Baseline estimated from GSA and RSAs reports and experts' opinions.
1.4 By 2026, donor governments, IFIs and PPPs in global health initiate grant, loan and/or innovative funding mechanisms for improving Sepsis response in LMICs	KPI (Process): Donor Governments, IFIs and PPPs integrate Sepsis in grant and loan portfolios (Yes/No) Baseline (2024): No Target (2026): Yes	Publications and call for applications by donor agencies, IFIs and PPPs. Global Sepsis Report(s)	Priority IFIs and PPPs: GAVI, The Global Fund, UNITAID, The World Bank and Regional Development Banks
1.5 By end of 2025, international health partners initiate regular data collection on the implementation of the WHA70.7 Resolution and publication of annual Global Sepsis Reports on the status of the Sepsis-related action at national, regional and global levels.	KPI (Output): Regular Data Collection and Global Sepsis Reports on Implementation of WHA70.7 Resolution (Yes/No) Baseline (2024): No Target (2025): Yes	Annual Global Sepsis Reports to be initiated by GSA in 2025	Annual Global Sepsis Reports to be initiated by GSA in 2025

Strategic Pillar 2.
Health System Readiness for Sepsis and Its Sequelae

Goal(s) of the Strategic Pillar:

- Improving prevention, early detection, timely and effective treatment of Sepsis, and management of Sepsis sequelae through strengthening the core capacities and emergency readiness of national health systems.

Strategic Objectives and Targets	KPIs	Means of Verification	Comments
2.1 By 2030, at least 50% of UN Member States have developed and started implementation of evidence-based and patient-focused clinical pathways for Sepsis and Sepsis Bundles for adult and paediatric patients, including RRS, SCC and management of Sepsis sequelae.	KPI (Coverage): % of UN Member States with operational Clinical Pathways and Sepsis Bundles Baseline (2024): < 10% Target (2030): > 50%	Annual Global Sepsis Reports to be initiated by GSA in 2025	Baseline estimated from GSA and RSAs reports and experts' opinions. Utilization data from WHO's Core clinical care readiness (C3R) tool.
2.2 By 2030, maternal and neonatal Sepsis-related deaths are reduced by 20% from 261,000 and 203,000 annual cases respectively, through increased investments in prevention, early identification and effective management of Sepsis in community and ante-, peri- and post-natal care settings	KPI (Impact): Maternal and Neonatal Deaths related to Sepsis worldwide Baseline (2017): 261,000 and 203,000 Targets (2030): < 208,000 and < 162,000	WHO and UNICEF Databases and Fact Sheets	Baseline estimated from GSA and RSAs reports and experts' opinions.
2.3 By 2030, at least 50% of health care institutions engaged in SCCs have essential supplies and equipment for the management of Sepsis and related organ dysfunction (microbiology labs or rapid diagnostic tools, ventilators with oxygen supply, renal replacement therapies, patient monitoring systems, antibiotics, IV fluids)	KPI (Coverage): % of health-care institutions at national level with essential supplies and equipment Baseline (2024): N/A Targets (2030): 50%	As part of national health sector surveys or Global Sepsis	Baseline estimated from GSA and RSAs reports and experts' opinions.
2.4 By 2030, at least 20% of UN Member States have initiated QI and/or accreditation programmes for Sepsis, including regionalization of the care cascade.	KPI (Coverage): % of UN Member States with KPI (Coverage): % of UN Member States with Regionalization, QI and Accreditation Programmes Baseline (2024): < 2% Targets (2030): > 20%	Annual Global Sepsis Reports to be initiated by GSA in 2025	Baseline estimated from GSA and RSAs reports and experts' opinions.
2.5 By 2030, at least 50% of UN Member States have integrated Sepsis as a medical emergency in undergraduate curricula and CME training for the health workforce.	KPI (Coverage): % of UN Member States with undergraduate and CME programmes on Sepsis Baseline (2024): < 10% Targets (2030): > 50%	Annual Global Sepsis Reports to be initiated by GSA in 2025	Annual Global Sepsis Reports to be initiated by GSA in 2025

2.6.1	By 2030, at least 90% global routine immunization (DTPcv3) coverage	KPI (Coverage): % of children vaccinated with 3 doses of DTP-containing vaccine (DTPcv3) Baseline (2024): 84% Targets (2030): > 90%	Global Immunization Reports – UNICEF and WHO	
2.6.2	By 2030, at least 80% of healthcare institutions in LMICs have access to WASH facilities	KPI (Coverage): % of healthcare institutions in LMICs with access to WASH facilities Baseline (2024): 57%-75% (157) Targets (2030): at least 80%	UNICEF and WHO Reports on WASH	
2.6.3	By 2030, ensure at least 50% of healthcare institutions in HICs and LMICs monitor the time taken for patients with Sepsis to receive life-saving antimicrobials.	KPI (Coverage): % of health care institutions in monitoring time taken for patients with Sepsis to receive life-saving antimicrobials Baseline (2024): N/A Targets (2030): > 50%	TBD and discussed with GSA Board/RSAs	

**Strategic Pillar 3.
Whole-of-Society Response**

Goal(s) of the Strategic Pillar:

- Improving Sepsis literacy among general public, media representatives and public policy-makers through consistent advocacy, simplified new narrative on Sepsis and engagement of Sepsis survivors and their families in the campaigns.
- Improving prehospital recognition of Sepsis and emergency care seeking behaviour in community- and pre-hospital care settings

Strategic Objectives and Targets	KPIs	Means of Verification	Comments
3.1.1 By 2030, at least 50% of public/community representatives incorporate immunization as a tool in a Sepsis prevention strategy.	KPI (Coverage): % of public/community representatives that identify immunization as a Sepsis prevention strategy Baseline (2024): 25% Targets (2030): > 50%	Community-based surveys	Baseline data from Canada
3.1.2 By 2030, at least 80% of communities living in LMICs have access to WASH facilities as a Sepsis prevention measure	KPI (Coverage): % of HHs in LMICs with access to WASH facilities Baseline (2024): 57%-75% Targets (2030): > 80%	UNICEF and WHO Reports on WASH	

<p>3.2 By 2030, at least 80% of household/ community representatives in HICs and LMICs identify Sepsis as a medical emergency requiring immediate emergency care seeking dilators with oxygen supply, renal replacement therapies, patient monitoring systems, antibiotics, IV fluids)</p>	<p>KPI (Coverage): % of the public/ community representatives who identify Sepsis as a medical emergency requiring immediate emergency care Baseline (2024): NA Targets (2030): > 80%</p>	<p>KAP and Household Surveys</p>	
<p>3.3 By 2030, at least 80% or 155 UN Member States participate in WSD campaigns and ensure engagement of public leaders and media</p>	<p>KPI (Process): % and number of UN Member States participating in the WSD campaign and ensuring media coverage of WSD movement Baseline (2024): > 51% or 100 Targets (2030): > 80% or 155</p>	<p>WSD Movement Database, GSA</p>	
<p>3.4 By 2030, at least 20% of UN Member States have developed and started implementation of evidence-based and patient-focused Community Care Cascades for Sepsis</p>	<p>KPI (Coverage): % of UN Member States with operational Patient focused Community Care Cascades for Sepsis Baseline (2024): < 10% Target (2030): > 20%</p>	<p>Annual Global Sepsis Reports to be initiated by GSA in 2025</p>	<p>The baseline data refer to estimates from GSA and RSAs reports and experts' opinions.</p>

**Strategic Pillar 4.
Sepsis Research and Innovations**

Goal(s) of the Strategic Pillar:

- Improving public and private research opportunities and funding for Sepsis both in HICs and LMICs
- Promoting investments in novel prevention, diagnostic, treatment and AI solutions for Sepsis for paediatric and adult groups

Strategic Objectives and Targets	KPIs	Means of Verification	Comments
<p>4.1 By 2028, at least 50% (19/38) OECD countries allocate earmarked public funds for Sepsis research and academic collaboration</p>	<p>KPI (Coverage): % of OECD countries allocating public funds for Sepsis research and academic collaboration Baseline (2024): < 10% Target (2030): > 50%</p>	<p>Annual Global Sepsis Reports to be initiated by GSA in 2025</p>	<p>Baseline estimated from GSA and RSAs reports and experts' opinions</p>
<p>4.2 By 2025, a Global Sepsis Research and Innovation Platform, an international public-private partnership is launched to address unmet needs in Sepsis prevention, detection and treatment (including novel vaccines, fast pathogen detection tools, immunomodulatory therapeutics and precision medicine)</p>	<p>KPI (Output): Global Sepsis Research and Innovation Platform Operational (Yes/No) Baseline (2024): No Target (2025): Yes</p>	<p>ToR and Composition of the Platform; Minutes of Inaugural and Regular Meetings;</p>	<p>The Platform to be (co)hosted by the Global Sepsis Alliance</p>

**Strategic Pillar 5.
Sepsis Research and Innovations**

Goal(s) of the Strategic Pillar:

- In line with WHA70.7, developing and implementing standard and optimal care, and strengthening medical countermeasures for diagnosing and managing Sepsis in emergencies, including outbreaks, armed conflicts, natural and other man-made disasters.
- Strengthening multi-lateral and multi-sectoral cooperation for integrating Sepsis in global frameworks and guidelines for emergency and humanitarian response, and national emergency preparedness and response plans.

Strategic Objectives and Targets	KPIs	Means of Verification	Comments
5.1 By 2030, at least 50% of UN Member States have integrated Sepsis-related interventions into national PPPR frameworks and action plans.	KPI (Coverage): % of UN Member States integrating Sepsis in national PPPR frameworks and action plans Baseline (2024): < 10% Target (2030): > 50%	Global Sepsis Reports to be initiated by GSA in 2025.	Baseline estimated from GSA and RSAs reports and experts' opinions
5.2 By 2030, at least 80% of UN Member States have integrated Sepsis prevention, early detection, treatment and post-hospital care and rehabilitation in health protocols for defence/military personnel and relevant services for civilians under humanitarian crisis.	KPI (Coverage): % of UN Member States integrating Sepsis in defence/military healthcare protocols Baseline (2024): < 10% Target (2030): > 80%	Global Sepsis Reports to be initiated by GSA in 2025.	Baseline estimated from GSA and RSAs reports and experts' opinions
5.3 By 2026, humanitarian response protocols from at least 10 leading international humanitarian aid organizations ² , integrate Sepsis prevention and response.	KPI (Output): Number of international humanitarian aid organizations integrating Sepsis in humanitarian response protocols. Baseline (2024): N/A Target (2030): > 10	Guidelines and toolkits from priority UN agencies and international humanitarian organizations.	Please see Strategic Direction 5.3 for the list of priority UN agencies and international aid organizations.
5.4 By 2028, at least 50% of UN Member States have integrated Sepsis into national laws and policies on climate change adaptation.	KPI (Coverage): % of UN Member States with laws/policies on climate change adaptation integrating Sepsis Baseline (2024): < 10% Target (2030): > 50%	Global Sepsis Reports to be initiated by GSA in 2025.	Baseline estimated from GSA and RSAs reports and experts' opinions.

² In view of the geographic and humanitarian work coverage, the organizations include: WHO, WFP, UNICEF, OCHA, UNHCR, IFRC, Save the Children, Catholic Relief Services, CARE, World Vision, Direct Relief, MSF, Actions Against Hunger, IRC, International Medical Corps, BRAC, Danish Refugee Council, Oxfam, Action Aid International, ALIMA, and Plan International.

Annex A

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

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

Organ dysfunction can be identified as an acute change in total Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score ≥ 2 points consequent to the infection.

- The baseline SOFA score can be assumed to be zero in patients not known to have pre-existing organ dysfunction.
- A SOFA score ≥ 2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection. Even patients presenting with modest dysfunction can deteriorate further, emphasizing the seriousness of this condition and the need for prompt and appropriate intervention, if not already being instituted.

In lay terms, Sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs.

Patients with suspected infection who are likely to have a prolonged ICU stay or to die in the hospital can be promptly identified at the bedside with quick SOFA (qSOFA), i.e., alteration in mental status, systolic blood pressure ≤ 100 mm Hg, or respiratory rate ≥ 22 /min.

Septic shock is a subset of Sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.

Patients with septic shock can be identified with a clinical construct of Sepsis with persisting hypotension requiring vasopressors to maintain Mean arterial pressure (MAP) ≥ 65 mm Hg and having a serum lactate level > 2 mmol/L (18mg/dL) despite adequate volume resuscitation. With these criteria, hospital mortality is in excess of 40%.

Source: Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC. *The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)*. JAMA. 2016 Feb 23;315(8):801-10. doi: 10.1001/jama.2016.0287. PMID: 26903338; PMCID: PMC4968574.

Acronyms and Abbreviations

<u>AI</u>	Artificial Intelligence
<u>AMR</u>	Anti-microbial Resistance
<u>APSA</u>	Asia-Pacific Sepsis Alliance
<u>ASA</u>	African Sepsis Alliance
<u>BMBF</u>	Federal Ministry of Education and Research in Germany
<u>CDCs</u>	Centers for Disease Control
<u>CHAI</u>	Clinton Health Access Initiative
<u>CME</u>	Continuous Medical Education
<u>CSA</u>	Caribbean Sepsis and AMR Alliance
<u>DALYs</u>	Disability-Adjusted Life Years
<u>ECDC</u>	European Centre for Disease Control
<u>ECO</u>	Emergency, Critical and Operative Care
<u>EDs</u>	Emergency Departments
<u>EMS</u>	Emergency Medical Services
<u>EMTs</u>	Emergency Medical Technicians
<u>EMSA</u>	Eastern Mediterranean Sepsis Alliance
<u>ESA</u>	European Sepsis Alliance
<u>EU</u>	European Union
<u>FAO</u>	Food and Agriculture Organization
<u>GARDP</u>	Global Antibiotic Research & Development Partnership
<u>GAVI</u>	Global Alliance for Vaccines and Immunization
<u>GBD</u>	Global Burden of Disease
<u>GF</u>	The Global Fund to Fight AIDS, Tuberculosis and Malaria
<u>GFF</u>	Global Funding Facility
<u>GIZ</u>	German International Development Agency
<u>GNP</u>	Gross National Product
<u>GSA</u>	Global Sepsis Alliance
<u>HCP(s)</u>	Health Care Provider(s)
<u>HIA(s)</u>	Healthcare-Associated Infection(s)
<u>HICs</u>	High-Income Countries
<u>ICD</u>	International Classification of Diseases
<u>ICU(s)</u>	Intensive Care Unit(s)
<u>ICU-LOS</u>	Length Of Stay in Intensive Care
<u>IFI(s)</u>	International Financial Institution(s)
<u>IHME</u>	Institute of Health Metrics and Evaluation
<u>IPC</u>	Infection Prevention and Control
<u>ISF</u>	International Sepsis Forum
<u>LASI</u>	Latin American Sepsis Institute
<u>LMICs</u>	Low- and Middle-Income Countries
<u>MAP</u>	Mean Arterial Pressure
<u>M&E</u>	Monitoring and Evaluation
<u>MNCH</u>	Maternal, Newborn and Child Health
<u>MODS</u>	Multiple Organ Dysfunction Score

<u>NAP(s)</u>	National Action Plan(s) or National Action Planning for Sepsis
<u>NCD(s)</u>	Non-Communicable Disease(s)
<u>NHS</u>	National Health Service - UK
<u>NICE</u>	National Institute for Health and Care Excellence – UK
<u>NSA(s)</u>	National Sepsis Alliance(s)
<u>NSSG</u>	National Sepsis Steering Group - Ireland
<u>ODA</u>	Official Development Assistance
<u>PAHO</u>	Pan-American Health Organization
<u>PASC</u>	Post-Acute Sequelae of COVID-19
<u>PSS</u>	Post-Sepsis Syndrome
<u>PPPR</u>	Pandemic Prevention, Preparedness and Response
<u>PPPs</u>	Public Private Partnerships
<u>PTSD</u>	Post-Traumatic Stress Disorder
<u>QALYs</u>	Quality-Adjusted Live Years
<u>QI</u>	Quality-Improvement
<u>qSOFA</u>	Quick SOFA
<u>R&D</u>	Research & Development
<u>RRS</u>	Rapid Response System
<u>RRTs</u>	Rapid Response Team(s) to Sepsis
<u>SCC(s)</u>	Sepsis Care Cascade(s)
<u>SOFA</u>	Sequential [Sepsis-related] Organ Failure Assessment
<u>SSA</u>	Sub-Saharan Africa
<u>SSC</u>	Surviving Sepsis Campaign
<u>SDGs</u>	Sustainable Development Goals
<u>UN</u>	United Nations
<u>UNEP</u>	United Nations Environmental Programme
<u>UNICEF</u>	United Nations Children’s Fund
<u>UNGA</u>	United Nations General Assembly
<u>UNITE</u>	UNITE Parliamentarians Network for Global Health
<u>UHC</u>	Universal Health Coverage
<u>US CDC</u>	US Centres for Disease Control and Prevention
<u>WASH</u>	Water, Sanitation and Hygiene
<u>WHA</u>	World Health Assembly
<u>WHO</u>	World Health Organization
<u>WOAH</u>	World Organization for Animal Health
<u>WSC</u>	World Sepsis Congress
<u>WSD</u>	World Sepsis Day

References

1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016 Feb 23;315(8):801–10.
2. Sepsis [Internet]. [cited 2024 Jul 13]. Available from: <https://www.who.int/news-room/fact-sheets/detail/Sepsis>
3. Reinhart K, Daniels R, Kissoon N, Machado FR, Schachter RD, Finfer S. Recognizing Sepsis as a Global Health Priority — A WHO Resolution. *N Engl J Med*. 2017 Aug 3;377(5):414–7.
4. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national Sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. *Lancet Lond Engl*. 2020 Jan 18;395(10219):200–11.
5. Antimicrobial resistance (AMR) [Internet]. [cited 2024 Jul 13]. Available from: <https://www.healthdata.org/research-analysis/health-risks-issues/antimicrobial-resistance-amr>
6. Sakr Y, Jaschinski U, Wittebole X, Szakmany T, Lipman J, Namendys-Silva SA, et al. Sepsis in Intensive Care Unit Patients: Worldwide Data From the Intensive Care over Nations Audit. *Open Forum Infect Dis*. 2018 Nov 19;5(12):ofy313.
7. Bauer M, Gerlach H, Vogelmann T, Preissing F, Stiefel J, Adam D. Mortality in Sepsis and septic shock in Europe, North America and Australia between 2009 and 2019—results from a systematic review and meta-analysis. *Crit Care*. 2020 May 19;24(1):239.
8. The Evolution of Sepsis Care During COVID-19 and Other Key Lessons for Sepsis Awareness Month - Penn Medicine [Internet]. [cited 2024 Jul 13]. Available from: <https://www.pennmedicine.org/news/news-blog/2021/september/the-evolution-of-sepsis-care-during-covid19-and-other-key-lessons-for-sepsis-awareness-month>
9. CDC [Internet]. 2016 [cited 2024 Jul 13]. CDC Newsroom. Available from: <https://www.cdc.gov/media/releases/2023/s0824-sepsis-patients.html>
10. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Lond Engl*. 2018 Nov 10;392(10159):1789–858.
11. S G, B F, E RA, P RC, J SA, Ea C, et al. Novel evidence on Sepsis-inducing pathogens: from laboratory to bedside. *Front Microbiol* [Internet]. 2023 Jun 23 [cited 2024 Sep 4];14. Available from: <https://pubmed.ncbi.nlm.nih.gov/37426029/>
12. Karakike E, Giamarellos-Bourboulis EJ, Kyprianou M, Fleischmann-Struzek C, Pletz MW, Netea MG, et al. Coronavirus Disease 2019 as Cause of Viral Sepsis: A Systematic Review and Meta-Analysis. *Crit Care Med*. 2021 Dec 1;49(12):2042–57.

13. Shappell C, Rhee C, Klompas M. Update on Sepsis Epidemiology in the Era of COVID-19. *Semin Respir Crit Care Med*. 2023 Feb;44(1):173–84.
14. Shappell CN, Klompas M, Chan C, Chen T, Kanjilal S, McKenna C, et al. Use of Electronic Clinical Data to Track Incidence and Mortality for SARS-CoV-2–Associated Sepsis. *JAMA Netw Open*. 2023 Sep 29;6(9):e2335728.
15. Fleischmann-Struzek C, Rose N, Freytag A, Spoden M, Prescott HC, Schettler A, et al. Epidemiology and Costs of Postsepsis Morbidity, Nursing Care Dependency, and Mortality in Germany, 2013 to 2017. *JAMA Netw Open*. 2021 Nov 12;4(11):e2134290.
16. Rhee C, Dantes R, Epstein L, Murphy DJ, Seymour CW, Iwashyna TJ, et al. Incidence and Trends of Sepsis in US Hospitals Using Clinical vs Claims Data, 2009–2014. *JAMA*. 2017 Oct 3;318(13):1241–9.
17. Fay K, Sapiano MRP, Gokhale R, Dantes R, Thompson N, Katz DE, et al. Assessment of Health Care Exposures and Outcomes in Adult Patients With Sepsis and Septic Shock. *JAMA Netw Open*. 2020 Jul 7;3(7):e206004.
18. Tiru B, DiNino EK, Orenstein A, Mailloux PT, Pesaturo A, Gupta A, et al. The Economic and Humanistic Burden of Severe Sepsis. *Pharmacoeconomics*. 2015 Sep;33(9):925–37.
19. Recovery after Sepsis & Post Sepsis Syndrome [Internet]. The UK Sepsis Trust. [cited 2024 Jul 16]. Available from: <https://sepsistrust.org/get-support/support/support-for-survivors/post-sepsis-syndrome/>
20. Comparison of Medical and Mental Health Sequelae Following Hospitalization for COVID-19, Influenza, and Sepsis | Psychiatry and Behavioral Health | JAMA Internal Medicine | JAMA Network [Internet]. [cited 2024 Jul 13]. Available from: <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2806192>
21. Slikke EC van der, Beumeler LFE, Holmqvist M, Linder A, Mankowski RT, Bouma HR. Understanding Post-Sepsis Syndrome: How Can Clinicians Help? *Infect Drug Resist*. 2023;16:6493.
22. van den Berg M, van Beuningen FE, Ter Maaten JC, Bouma HR. Hospital-related costs of sepsis around the world: A systematic review exploring the economic burden of sepsis. *J Crit Care*. 2022 Oct;71:154096.
23. Vincent JL, Marshall JC, Namendys-Silva SA, François B, Martin-Loeches I, Lipman J, et al. Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. *Lancet Respir Med*. 2014 May;2(5):380–6.
24. Burchardi H, Schneider H. Economic aspects of severe sepsis: a review of intensive care unit costs, cost of illness and cost effectiveness of therapy. *Pharmacoeconomics*. 2004;22(12):793–813.

25. Buchman TG, Simpson SQ, Sciarretta KL, Finne KP, Sowers N, Collier M, et al. Sepsis Among Medicare Beneficiaries: 3. The Methods, Models, and Forecasts of Sepsis, 2012-2018. *Crit Care Med*. 2020 Mar;48(3):302–18.
26. Owens PL. Overview of Outcomes for Inpatient Stays Involving Sepsis, 2016–2021.
27. Carlton EF, Barbaro RP, Iwashyna T “Jack”, Prescott HC. Cost of Pediatric Severe Sepsis Hospitalizations. *JAMA Pediatr*. 2019 Oct 1;173(10):986–7.
28. Rowe T, Araujo KLB, Van Ness PH, Pisani MA, Juthani-Mehta M. Outcomes of Older Adults With Sepsis at Admission to an Intensive Care Unit. *Open Forum Infect Dis*. 2016 Jan;3(1):ofw010.
29. Wang HE, Shah MN, Allman RM, Kilgore M. Emergency department visits by nursing home residents in the United States. *J Am Geriatr Soc*. 2011 Oct;59(10):1864–72.
30. Kodali PB. Achieving Universal Health Coverage in Low- and Middle-Income Countries: Challenges for Policy Post-Pandemic and Beyond. *Risk Manag Healthc Policy*. 2023 Apr 6;16:607–21.
31. McBride A, Thuy Duong B, Chau Nguyen VV, Thwaites CL, Turner HC, Hao Nguyen V. Catastrophic health care expenditure due to septic shock and dengue shock in Vietnam. *Trans R Soc Trop Med Hyg*. 2019 Oct 11;113(10):649–51.
32. Ranjeva SL, Warf BC, Schiff SJ. Economic burden of neonatal sepsis in sub-Saharan Africa. *BMJ Glob Health*. 2018;3(1):e000347.
33. cost-of-sepsis-in-australian-report.pdf [Internet]. [cited 2024 Jul 13]. Available from: <https://www.georgeinstitute.org/sites/default/files/cost-of-sepsis-in-australian-report.pdf>
34. University of York [Internet]. [cited 2024 Jul 14]. Sepsis could cost UK economy up to £15.6 billion each year, new study suggests. Available from: <https://www.york.ac.uk/news-and-events/news/2017/research/sepsis-economy-report/>
35. Luijckx ECN, van der Slikke EC, van Zanten ARH, ter Maaten JC, Postma MJ, Hilderink HBM, et al. Societal costs of sepsis in the Netherlands. *Crit Care*. 2024 Jan 22;28(1):29.
36. Norman BC, Jackson JC, Graves JA, Girard TD, Pandharipande PP, Brummel NE, et al. Employment Outcomes After Critical Illness: An Analysis of the Bringing to Light the Risk Factors and Incidence of Neuropsychological Dysfunction in ICU Survivors Cohort. *Crit Care Med*. 2016 Nov;44(11):2003–9.
37. Maternal sepsis [Internet]. [cited 2024 Jul 13]. Available from: [https://www.who.int/teams/sexual-and-reproductive-health-and-research-\(srh\)/areas-of-work/maternal-and-perinatal-health/maternal-sepsis](https://www.who.int/teams/sexual-and-reproductive-health-and-research-(srh)/areas-of-work/maternal-and-perinatal-health/maternal-sepsis)

38. Bonet M, Souza JP, Abalos E, Fawole B, Knight M, Kouanda S, et al. The global maternal sepsis study and awareness campaign (GLOSS): study protocol. *Reprod Health*. 2018 Jan 30;15(1):16.
39. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health*. 2014 Jun;2(6):e323-333.
40. Hensley MK, Bauer ME, Admon LK, Prescott HC. Incidence of Maternal Sepsis and Sepsis-Related Maternal Deaths in the United States. *JAMA*. 2019 Sep 3;322(9):890–2.
41. Global report on the epidemiology and burden of sepsis [Internet]. [cited 2024 Jul 13]. Available from: <https://www.who.int/publications/i/item/9789240010789>
42. Lawn JE, Cousens S, Zupan J, Lancet Neonatal Survival Steering Team. 4 million neonatal deaths: when? Where? Why? *Lancet Lond Engl*. 2005 Mar 5;365(9462):891–900.
43. Milton R, Gillespie D, Dyer C, Taiyari K, Carvalho MJ, Thomson K, et al. Neonatal sepsis and mortality in low-income and middle-income countries from a facility-based birth cohort: an international multisite prospective observational study. *Lancet Glob Health*. 2022 May 1;10(5):e661–72.
44. Attia Hussein Mahmoud H, Parekh R, Dhandibhotla S, Sai T, Pradhan A, Alugula S, et al. Insight Into Neonatal Sepsis: An Overview. *Cureus*. 2023 Sep;15(9):e45530.
45. ia2030-draft-4-wha_b8850379-1fce-4847-bfd1-5d2c9d9e32f8.pdf [Internet]. [cited 2024 Jul 13]. Available from: https://cdn.who.int/media/docs/default-source/immunization/strategy/ia2030/ia2030-draft-4-wha_b8850379-1fce-4847-bfd1-5d2c9d9e32f8.pdf?sfvrsn=5389656e_69&download=true
46. Snapshot [Internet]. [cited 2024 Jul 13]. Available from: <https://www.who.int/news-room/fact-sheets/detail/sepsis>
47. Pyrali FF, Iordanov R, Palacio A, Tamariz L. Excess mortality risk from sepsis in patients with HIV - A meta-analysis. *J Crit Care*. 2020 Oct;59:101–7.
48. Silva JM, dos Santos SDS. Sepsis in AIDS patients: clinical, etiological and inflammatory characteristics. *J Int AIDS Soc*. 2013 Jan 30;16(1):17344.
49. Kethireddy S, Light RB, Mirzanejad Y, Maki D, Arabi Y, Lapinsky S, et al. Mycobacterium tuberculosis septic shock. *Chest*. 2013 Aug;144(2):474–82.
50. Early empiric anti-Mycobacterium tuberculosis therapy for sepsis in sub-Saharan Africa: a protocol of a randomised clinical trial | Cochrane Library [Internet]. [cited 2024 Jul 13]. Available from: <https://www.cochranelibrary.com/es/central/doi/10.1002/central/CN-02402692/full>

51. Hazard RH, Kagina P, Kitayimbwa R, Male K, McShane M, Mubiru D, et al. Effect of Empiric Anti-Mycobacterium tuberculosis Therapy on Survival Among Human Immunodeficiency Virus-Infected Adults Admitted With Sepsis to a Regional Referral Hospital in Uganda. *Open Forum Infect Dis*. 2019 Mar 14;6(4):ofz140.
52. Njim T, Dondorp A, Mukaka M, Ohuma EO. Identifying risk factors for the development of sepsis during adult severe malaria. *Malar J*. 2018 Jul 31;17(1):278.
53. White NJ, Watson JA, Uyoga S, Williams TN, Maitland KM. Substantial misdiagnosis of severe malaria in African children. *Lancet Lond Engl*. 2022 Sep 10;400(10355):807.
54. Phu NH, Day NPJ, Tuan PQ, Mai NTH, Chau TTH, Van Chuong L, et al. Concomitant Bacteremia in Adults With Severe Falciparum Malaria. *Clin Infect Dis*. 2020 Nov 1;71(9):e465–70.
55. Taccone FS, Artigas AA, Sprung CL, Moreno R, Sakr Y, Vincent JL. Characteristics and outcomes of cancer patients in European ICUs. *Crit Care Lond Engl*. 2009;13(1):R15.
56. Danai PA, Moss M, Mannino DM, Martin GS. The epidemiology of sepsis in patients with malignancy. *Chest*. 2006 Jun;129(6):1432–40.
57. Williams MD, Braun LA, Cooper LM, Johnston J, Weiss RV, Qualy RL, et al. Hospitalized cancer patients with severe sepsis: analysis of incidence, mortality, and associated costs of care. *Crit Care Lond Engl*. 2004 Oct;8(5):R291-298.
58. The Epidemiology of Sepsis in the United States from 1979 through 2000 | *New England Journal of Medicine* [Internet]. [cited 2024 Jul 19]. Available from: <https://www.nejm.org/doi/full/10.1056/NEJMoa022139>
59. Gudiol C, Albasanz-Puig A, Cuervo G, Carratalà J. Understanding and Managing Sepsis in Patients With Cancer in the Era of Antimicrobial Resistance. *Front Med*. 2021;8:636547.
60. Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med*. 2006 Jun;34(6):1589–96.
61. Rüdell H, Thomas-Rüdell DO, Reinhart K, Bach F, Gerlach H, Lindner M, et al. Adverse effects of delayed antimicrobial treatment and surgical source control in adults with sepsis: results of a planned secondary analysis of a cluster-randomized controlled trial. *Crit Care Lond Engl*. 2022 Feb 28;26(1):51.
62. Health workforce [Internet]. [cited 2024 Jul 13]. Available from: https://www.who.int/health-topics/health-workforce#tab=tab_1
63. Sankar J, Garg M, Ghimire JJ, Sankar MJ, Lodha R, Kabra SK. Delayed Administration of Antibiotics Beyond the First Hour of Recognition Is Associated with Increased Mortality Rates in Children with Sepsis/Severe Sepsis and Septic Shock. *J Pediatr*. 2021 Jun;233:183-190.e3.

64. Fitzpatrick F, Tarrant C, Hamilton V, Kiernan FM, Jenkins D, Krockow EM. Sepsis and antimicrobial stewardship: two sides of the same coin. *BMJ Qual Saf.* 2019 Sep;28(9):758–61.
65. Donnelly JP, Seelye SM, Kipnis P, McGrath BM, Iwashyna TJ, Pogue J, et al. Impact of Reducing Time-to-Antibiotics on Sepsis Mortality, Antibiotic Use, and Adverse Events. *Ann Am Thorac Soc.* 2024 Jan;21(1):94–101.
66. Colon Hidalgo D, Tapaskar N, Rao S, Masic D, Su A, Portillo J, et al. Lower socio-economic factors are associated with higher mortality in patients with septic shock. *Heart Lung J Crit Care.* 2021;50(4):477–80.
67. Kumar G, Taneja A, Majumdar T, Jacobs ER, Whittle J, Nanchal R. The Association of Lacking Insurance With Outcomes of Severe Sepsis: Retrospective Analysis of an Administrative Database. *Crit Care Med.* 2014 Mar;42(3):583–91.
68. Zhong X, Ashiru-Oredope D, Pate A, Martin GP, Sharma A, Dark P, et al. Clinical and health inequality risk factors for non-COVID-related sepsis during the global COVID-19 pandemic: a national case-control and cohort study. *EClinicalMedicine.* 2023 Dec;66:102321.
69. Fact sheets - Malnutrition [Internet]. [cited 2024 Jul 13]. Available from: <https://www.who.int/news-room/fact-sheets/detail/malnutrition>
70. Musa N, Murthy S, Kissoon N, Lodha R, Ranjit S. Pediatric Sepsis and Septic Shock Management in Resource-Limited Settings. In: Dondorp AM, Dünser MW, Schultz MJ, editors. *Sepsis Management in Resource-limited Settings* [Internet]. Cham (CH): Springer; 2019 [cited 2024 Jul 13]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK553811/>
71. Chisti MJ, Salam MA, Bardhan PK, Faruque ASG, Shahid ASMSB, Shahunja KM, et al. Severe Sepsis in Severely Malnourished Young Bangladeshi Children with Pneumonia: A Retrospective Case Control Study. *PLoS ONE.* 2015 Oct 6;10(10):e0139966.
72. Abugroun A, Nayyar A, Abdel-Rahman M, Patel P. Impact of Malnutrition on Hospitalization Outcomes for Older Adults Admitted for Sepsis. *Am J Med.* 2021 Feb 1;134(2):221-226.e1.
73. Sunden-Cullberg J, Nilsson A, Inghammar M. Sex-based differences in ED management of critically ill patients with sepsis: a nationwide cohort study. *Intensive Care Med.* 2020 Apr;46(4):727–36.
74. Modra LJ, Higgins AM, Abeygunawardana VS, Vithanage RN, Bailey MJ, Bellomo R. Sex Differences in Treatment of Adult Intensive Care Patients: A Systematic Review and Meta-Analysis. *Crit Care Med.* 2022 Jun 1;50(6):913–23.
75. Proper hand hygiene can prevent sepsis [Internet]. [cited 2024 Jul 13]. Available from: <https://www.ecdc.europa.eu/en/news-events/proper-hand-hygiene-can-prevent-sepsis>

76. Key facts and figures [Internet]. [cited 2024 Jul 13]. Available from: <https://www.who.int/campaigns/world-hand-hygiene-day/2023/key-facts-and-figures>
77. World Health Organization, United Nations Children's Fund (UNICEF). WASH in health care facilities: global baseline report 2019 [Internet]. Geneva: World Health Organization; 2019 [cited 2024 Jul 13]. Available from: <https://iris.who.int/handle/10665/311620>
78. Infection-related-deaths-of-children-and-young-people-in-England.pdf [Internet]. [cited 2024 Jul 17]. Available from: <https://www.ncmd.info/wp-content/uploads/2023/12/Infection-related-deaths-of-children-and-young-people-in-England.pdf>
79. Mora C, McKenzie T, Gaw IM, Dean JM, Von Hammerstein H, Knudson TA, et al. Over half of known human pathogenic diseases can be aggravated by climate change. *Nat Clim Change*. 2022 Sep;12(9):869–75.
80. Ryan SJ, Carlson CJ, Mordecai EA, Johnson LR. Global expansion and redistribution of Aedes-borne virus transmission risk with climate change. *PLoS Negl Trop Dis*. 2019 Mar 28;13(3):e0007213.
81. Quadripartite call to action for One Health for a safer world [Internet]. [cited 2024 Jul 13]. Available from: <https://www.who.int/news/item/27-03-2023-quadripartite-call-to-action-for-one-health-for-a-safer-world>
82. United Nations : Information Service Vienna [Internet]. [cited 2024 Jul 13]. Record numbers of people need humanitarian assistance. Available from: <https://unis.unvienna.org/unis/en/topics/related/2023/humanitarian-need.html>
83. Defining armed conflict: some clarity in the fog of war [Internet]. [cited 2024 Jul 13]. Available from: <https://blogs.icrc.org/law-and-policy/2024/05/02/defining-armed-conflict-some-clarity-in-the-fog-of-war/>
84. Sahli ZT, Bizri AR, Abu-Sittah GS. Microbiology and risk factors associated with war-related wound infections in the Middle East. *Epidemiol Infect*. 2016 Oct;144(13):2848–57.
85. Migrants and refugees at higher risk of developing ill health than host populations, reveals first-ever WHO report on the health of displaced people in Europe [Internet]. [cited 2024 Jul 13]. Available from: <https://www.who.int/azerbaijan/news/item/21-01-2019-migrants-and-refugees-at-higher-risk-of-developing-ill-health-than-host-populations-reveals-first-ever-who-report-on-the-health-of-displaced-people-in-europe>
86. Swan HJ, Ganz W, Forrester J, Marcus H, Diamond G, Chonette D. Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. *N Engl J Med*. 1970 Aug 27;283(9):447–51.

87. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine - PubMed [Internet]. [cited 2024 Jul 13]. Available from: <https://pubmed.ncbi.nlm.nih.gov/1303622/>
88. Society of Critical Care Medicine (SCCM) [Internet]. [cited 2024 Jul 13]. SCCM | Surviving Sepsis Campaign Declarations. Available from: <https://sccm.org/SurvivingSepsisCampaign/About-SSC/History/Barcelona-Declaration>
89. Society of Critical Care Medicine (SCCM) [Internet]. [cited 2024 Jul 13]. SCCM | Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Di. Available from: <https://sccm.org/Clinical-Resources/Guidelines/Guidelines/Surviving-Sepsis-Campaign-Guidelines-on-the-Manag>
90. Guidelines | SCCM [Internet]. [cited 2024 Jul 13]. Available from: <https://www.sccm.org/Clinical-Resources/Guidelines/Guidelines/Surviving-Sepsis-Campaign-Guidelines-on-the-Manag>
91. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. *Crit Care Med*. 2021 Nov;49(11):e1063.
92. Fiest KM, Krewulak KD, Brundin-Mather R, Leia MP, Fox-Robichaud A, Lamontagne F, et al. Patient, Public, and Healthcare Professionals' Sepsis Awareness, Knowledge, and Information Seeking Behaviors: A Scoping Review. *Crit Care Med*. 2022 Aug 1;50(8):1187–97.
93. WHO Sepsis Technical Expert Meeting [Internet]. [cited 2024 Sep 4]. Available from: <https://www.who.int/news-room/events/detail/2018/01/16/default-calendar/who-sepsis-technical-expert-meeting>
94. G7 Health Ministers' Communiqué 20 May 2022, Berlin.
95. Global Sepsis Alliance [Internet]. 2023 [cited 2024 Jul 13]. The Berlin Declaration on Sepsis – An Urgent Call for the Enforcement of the WHA Resolution 70.7 and Reinvigorated Global Action on Sepsis. Available from: <https://globalsepsisalliance.org/news/2023/9/7/the-berlin-declaration-on-sepsis-an-urgent-call-for-the-enforcement-of-the-wha-resolution-707-and-reinvigorated-global-action-on-sepsis>
96. Global Sepsis Alliance [Internet]. 2023 [cited 2024 Jul 13]. High-Level Luncheon on Sepsis on the Margins of 2023 World Health Summit. Available from: <https://globalsepsisalliance.org/news/2023/10/19/high-level-luncheon-on-sepsis-on-the-margins-of-2023-world-health-summit>
97. UNGA Guide 2024 [Internet]. [cited 2024 Jul 13]. Synergizing Global Actions for Sepsis, AMR and PPPR for Attaining Health Related SDGs. Available from: <https://ungaguide.com/event/synergizing-global-actions-for-sepsis-amr-and-pppr-for-attaining-health-related-sdgs/>

98. European Sepsis Alliance [Internet]. [cited 2024 Jul 13]. European Sepsis Report. Available from: <https://www.europeansepsisalliance.org/europeansepsisreport>
99. Brusco NK, Sykes K, Cheng AC, Radia-George C, Travis D, Sullivan N, et al. A state-wide implementation of a whole of hospital sepsis pathway with a mortality based cost-effectiveness analysis from a healthcare sector perspective. *PLOS Glob Public Health*. 2023;3(5):e0000687.
100. World Sepsis Day - September 13 [Internet]. 2024 [cited 2024 Jul 13]. GSA Salutes First Report on Sepsis in Belgium, Leading to a National Plan. Available from: <https://www.worldsepsisday.org/news/2024/6/3/gsa-salutes-first-report-on-sepsis-in-belgium-leading-to-a-national-plan>
101. National Sepsis Report 2022.
102. Strålin K, Linder A, Brink M, Benjaminsson-Nyberg P, Svefors J, Bengtsson-Toni M, et al. Design of a national patient-centred clinical pathway for sepsis in Sweden. *Infect Dis*. 2023 Oct 3;55(10):716–24.
103. Stevenson-Rose L. UKST welcomes NICE sepsis guideline updates which herald end of confusing period for health professionals [Internet]. The UK Sepsis Trust. 2024 [cited 2024 Jul 13]. Available from: <https://sepsistrust.org/ukst-welcomes-nice-sepsis-guideline-updates-which-herald-end-of-confusing-period-for-health-professionals/>
104. rm-fs-10-1.pdf [Internet]. [cited 2024 Jul 13]. Available from: <https://www.england.nhs.uk/wp-content/uploads/2014/02/rm-fs-10-1.pdf>
105. NHS England » Martha's Rule [Internet]. [cited 2024 Jul 13]. Available from: <https://www.england.nhs.uk/patient-safety/marthas-rule/>
106. Sepsis Innovation Collaborative [Internet]. [cited 2024 Jul 13]. Sepsis Innovation Collaborative (Homepage). Available from: <https://www.sepsisinnovation.org/>
107. NYS Sepsis Care Improvement Initiative and NYS Regulations [Internet]. [cited 2024 Jul 13]. Available from: https://www.health.ny.gov/diseases/conditions/sepsis/care_improvement_initiative.htm
108. Horner S. \$3 Million in Sepsis Funding Announced in the Federal Budget [Internet]. End Sepsis. 2024 [cited 2024 Jul 13]. Available from: <https://www.endsepsis.org/2024/03/26/3-million-in-sepsis-funding-announced-in-the-federal-budget/>
109. CDC. Sepsis. 2024 [cited 2024 Jul 13]. Hospital Sepsis Program Core Elements. Available from: <https://www.cdc.gov/sepsis/hcp/core-elements/index.html>
110. Mellhammar L, Wollter E, Dahlberg J, Donovan B, Olséen CJ, Wiking PO, et al. Estimating Sepsis Incidence Using Administrative Data and Clinical Medical Record Review. *JAMA Netw Open*. 2023 Aug 1;6(8):e2331168.

111. Giamarellos-Bourboulis EJ, Zinkernagel AS, De Robertis E, Azoulay É, De Luca D, Artigas A, et al. Sepsis, a call for inclusion in the work plan of the European Center for Disease Prevention and Control. *Intensive Care Med.* 2023 Sep 1;49(9):1138–42.
112. Global action on patient safety. https://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_R6-en.pdf Global Action on Patient Safety, WHA72.6
113. Patient safety [Internet]. [cited 2024 Jul 13]. Available from: <https://www.who.int/news-room/fact-sheets/detail/patient-safety>
114. Immunization Data [Internet]. [cited 2024 Jul 13]. WHO Immunization Data portal - Global. Available from: <http://immunizationdata.who.int>
115. Immunization Data [Internet]. [cited 2024 Jul 13]. WHO Immunization Data portal - Detail Page. Available from: <https://immunizationdata.who.int/global/wiise-detail-page>
116. Wallace J, Goldsmith-Pinkham P, Schwartz JL. Excess Death Rates for Republican and Democratic Registered Voters in Florida and Ohio During the COVID-19 Pandemic. *JAMA Intern Med.* 2023;183(9):916–923. doi:10.1001/jamainternmed.2023.1154.
117. Global report on infection prevention and control [Internet]. [cited 2024 Sep 4]. Available from: <https://www.who.int/publications/i/item/9789240051164>
118. Piedmont S, Goldhahn L, Swart E, Robra BP, Fleischmann-Struzek C, Somasundaram R, et al. Sepsis incidence, suspicion, prediction and mortality in emergency medical services: a cohort study related to the current international sepsis guideline. *Infection* [Internet]. 2024 Feb 19 [cited 2024 Jul 14]; Available from: <https://doi.org/10.1007/s15010-024-02181-5>
119. MacAllister SA, Fernandez AR, Smith MJ, Myers JB, Crowe RP. Prehospital Sepsis Recognition and Outcomes for Patients with Sepsis by Race and Ethnicity. *Prehosp Emerg Care.* 2023 Dec 14;1–7.
120. Launay E, Gras-Le Guen C, Martinot A, Assathiany R, Martin E, Blanchais T, et al. Why children with severe bacterial infection die: a population-based study of determinants and consequences of suboptimal care with a special emphasis on methodological issues. *PloS One.* 2014;9(9):e107286.
121. Scheer CS, Giamarellos-Bourboulis E, Ferrer R, Idelevich EA, Annane D, Artigas A, et al. Sepsis Care, Diagnostics and Quality Management: A Multidisciplinary Cross-Sectional Survey in 73 Countries [Internet]. Rochester, NY; 2023 [cited 2024 Jul 14]. Available from: <https://papers.ssrn.com/abstract=4538229>
122. Hyun D gon, Lee SY, Ahn JH, Huh JW, Hong SB, Koh Y, et al. Mortality of patients with hospital-onset sepsis in hospitals with all-day and non-all-day rapid response teams: a prospective nationwide multicenter cohort study. *Crit Care.* 2022 Sep 16;26(1):280.
123. Schwarzkopf D, Rüdell H, Brinkmann A, Fleischmann-Struzek C, Friedrich ME,

Glas M, et al. The German Quality Network Sepsis: Evaluation of a Quality Collaborative on Decreasing Sepsis-Related Mortality in a Controlled Interrupted Time Series Analysis. *Front Med.* 2022 Apr 27;9:882340.

124. DRIVE [Internet]. [cited 2024 Jul 13]. Available from: <https://drive.hhs.gov/solvingsepsis.html>

125. BARDA announces new partnerships to treat serious outcomes of infectious disease [Internet]. [cited 2024 Jul 20]. Available from: <https://medicalcountermeasures.gov/newsroom/2024/hdt/>

126. Universität Bonn [Internet]. [cited 2024 Jul 13]. Funding of €6.9 Million for Sepsis Research. Available from: <https://www.uni-bonn.de/en/news/155-2023>

127. Zuhair V, Babar A, Ali R, Oduoye MO, Noor Z, Chris K, et al. Exploring the Impact of Artificial Intelligence on Global Health and Enhancing Healthcare in Developing Nations. *J Prim Care Community Health* [Internet]. 2024 Dec [cited 2024 Sep 4];15. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11010755/>

128. Understanding the biases to sepsis surveillance and quality assurance caused by inaccurate coding in administrative health data | *Infection* [Internet]. [cited 2024 Jul 14]. Available from: <https://link.springer.com/article/10.1007/s15010-023-02091-y>

129. UHCC [Internet]. [cited 2024 Jul 13]. Available from: <https://uhcc.who.int/uhcpackages/>

130. Khowaja AR, Willms AJ, Krause C, Carriere S, Ridout B, Kennedy C, et al. The Return on Investment of a Province-Wide Quality Improvement Initiative for Reducing In-Hospital Sepsis Rates and Mortality in British Columbia, Canada. *Crit Care Med.* 2022 Apr 1;50(4):e340–50.

131. Shin TG, Hwang SY, Kang GH, Kim WY, Ryoo SM, Kim K, et al. Korean Shock Society septic shock registry: a preliminary report. *Clin Exp Emerg Med.* 2017 Sep 30;4(3):146–53.

132. Kim JH, Ku NS, Kim YJ, Kim HB, Seok H, Lee DG, et al. Korean Registry for Improving Sepsis Survival (KISS): Protocol for a Multicenter Cohort of Adult Patients with Sepsis or Septic Shock. *Infect Chemother.* 2020 Mar;52(1):31–8.

133. Jouffroy R, Djossou F, Nevriere R, Jaber S, Vivien B, Heming N, et al. The chain of survival and rehabilitation for sepsis: concepts and proposals for healthcare trajectory optimization. *Ann Intensive Care.* 2024 Apr 16;14(1):58.

134. The Global Maternal and Neonatal Sepsis Initiative: a call for collaboration and action by 2030. *Lancet Glob Health.* 2017 Apr 1;5(4):e390–1.

135. France – European Sepsis Report — European Sepsis Alliance [Internet]. [cited 2024 Jul 13]. Available from: <https://www.europeansepsisalliance.org/europeansepsisreport/france>

136. Sepsis E-learning | The UK Sepsis Trust [Internet]. [cited 2024 Jul 13]. Available from: <https://sepsistrust.org/professional-resources/sepsis-e-learning/>
137. Choy CL, Liaw SY, Goh EL, See KC, Chua WL. Impact of sepsis education for healthcare professionals and students on learning and patient outcomes: a systematic review. *J Hosp Infect.* 2022 Apr;122:84–95.
138. Otu A, Onwusaka O, Otokpa DE, Edadi U, Udoh U, Yougha P, et al. Upscaling health worker training on sepsis in South Eastern Nigeria using innovative digital strategies: an interventional study [Internet]. medRxiv; 2022 [cited 2024 Jul 13]. p. 2022.06.22.22276742. Available from: <https://www.medrxiv.org/content/10.1101/2022.06.22.22276742v1>
139. Information for clinicians - Sepsis Clinical Care Standard | Australian Commission on Safety and Quality in Health Care [Internet]. [cited 2024 Jul 19]. Available from: <https://www.safetyandquality.gov.au/standards/clinical-care-standards/sepsis-clinical-care-standard/information-clinicians>
140. Souza DRX de, Araújo IDT de, Nobre TTX, Gama ZA da S, Graboís V, Nunes VM de A. Improving the quality of care for patients with sepsis in the context of an emergency service. *Enferm Glob.* 2022 Jul 2;21(3):1–49.
141. Draft global action plan and monitoring framework on IPC [Internet]. [cited 2024 Sep 4]. Available from: <https://www.who.int/teams/integrated-health-services/infection-prevention-control/draft-global-action-plan-and-monitoring-framework-on-ipc>
142. Parsons Leigh J, Brundin-Mather R, Moss SJ, Nickel A, Parolini A, Walsh D, et al. Public awareness and knowledge of sepsis: a cross-sectional survey of adults in Canada. *Crit Care.* 2022 Nov 3;26:337.
143. European Sepsis Alliance [Internet]. [cited 2024 Jul 21]. Life After Sepsis Guide. Available from: <https://www.europeansepsisalliance.org/guide>
144. Yang J, Hao S, Huang J, Chen T, Liu R, Zhang P, et al. The application of artificial intelligence in the management of sepsis. *Med Rev.* 3(5):369–80.
145. Born S, Matthäus-Krämer C, Bichmann A, Boltz HS, Esch M, Heydt L, et al. Sepsis survivors and caregivers perspectives on post-acute rehabilitation and aftercare in the first year after sepsis in Germany. *Front Med.* 2023;10:1137027.
146. Heneine E, Nsutebu E, Rylance J, Jacob S. A Call To Action: Sepsis is Africa's Neglected Silent Killer | Policy Commons. [cited 2024 Jul 19]; Available from: <https://policy-commons.net/artifacts/1449886/a-call-to-action/2081679/>
147. Sepsis - an overview | ScienceDirect Topics [Internet]. [cited 2024 Jul 14]. Available from: <https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/sepsis>

148. Dolin HH, Papadimos TJ, Chen X, Pan ZK. Characterization of Pathogenic Sepsis Etiologies and Patient Profiles: A Novel Approach to Triage and Treatment. *Microbiol Insights*. 2019;12:1178636118825081.
149. Stiel L, Delabranche X, Galois AC, Severac F, Toti F, Mauvieux L, et al. Neutrophil Fluorescence: A New Indicator of Cell Activation During Septic Shock-Induced Disseminated Intravascular Coagulation. *Crit Care Med*. 2016 Nov;44(11):e1132–6.
150. X D, J BH, P A, A B, Y M, T L, et al. Microparticles are new biomarkers of septic shock-induced disseminated intravascular coagulopathy. *Intensive Care Med* [Internet]. 2013 Oct [cited 2024 Sep 4];39(10). Available from: <https://pubmed.ncbi.nlm.nih.gov/23793890/>
151. Reynolds TA, Guisset AL, Dalil S, Relan P, Barkley S, Kelley E. Emergency, critical and operative care services for effective primary care. *Bull World Health Organ*. 2020 Nov 1;98(11):728-728A.
152. Emergency care systems for universal health coverage: ensuring timely care for the acutely ill and injured.
153. Strengthening clinical trials to provide high-quality evidence on health interventions and to improve research quality and coordination.
154. Development of a global strategy and action plan for integrated emergency, critical and operative care, 2026–2035.
155. Sepsis Hospitalizations Among Active Component Service Members, U.S. Armed Forces, 2011–2020 | *Health.mil* [Internet]. [cited 2024 Jul 13]. Available from: <https://health.mil/News/Articles/2021/11/01/Sepsis-Hosp-MSMR>
156. Policy brief National laws and policies on climate change adaptation: a global review [Internet]. [cited 2024 Jul 13]. Available from: <https://primarysources.brillonline.com/browse/climate-change-and-law-collection/policy-brief-national-laws-and-policies-on-climate-change-adaptation-a-global-review;cccc014820190148510>
157. Progress on household drinking water, sanitation and hygiene 2000-2022: Special focus on gender - UNICEF DATA [Internet]. [cited 2024 Jul 13]. Available from: <https://data.unicef.org/resources/jmp-report-2023/>

