

REVIEW ARTICLE

Sepsis in Global Health: Current global strategies to fight against sepsis

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Email: hiroki.saito@mail.utoronto.ca**Abstract**

Sepsis is prevalent globally, causing a significant disease burden in global health. Sepsis is a complex disease condition, and therefore, the effective strategies to overcome sepsis need to be set up in layers across different sectors and populations. Over the years, the global society has been making progress in addressing sepsis as a public health threat. This review aims to examine and describe the current sepsis strategies globally and to sustain the fight against sepsis in the context of global health.

KEYWORDS

antimicrobial resistance, global burden of disease, global health, health policy, sepsis

INTRODUCTION

Sepsis, defined as an infection associated with organ dysfunction, causes significant morbidity and mortality worldwide.¹ It is estimated that 11 million died of sepsis in 2017, accounting for 20% of all deaths globally.² Because sepsis impacts the entire population across the globe, whether it is children, pregnant women, or the elderly, or whether it is high-income countries or low- and middle-income countries (LMICs), a systematic approach is required to fully address sepsis as a global public health threat, and every individual in health care can play a significant role in improving sepsis care. Therefore, this narrative review aims to examine and describe the overview of the global sepsis strategies in the context of global health.

WHO RESOLUTION ON SEPSIS

In 2017, based on the initiative of Germany, the World Health Organization (WHO) adopted a resolution on sepsis.³ Key stakeholders already working on sepsis, such as healthcare providers, researchers, and patient advocacy groups, welcomed this as a milestone to further advance the sepsis agenda. Once a WHO resolution is adopted, WHO is to follow up on the progress, and WHO Member States, that

is, countries and regions, are supposed to commit to it. The main action points are shown in Table 1, according to the 2017 WHO resolution.^{3,4}

Following these action points, WHO convened an expert meeting on sepsis in 2018. More than 30 experts from all 6 WHO regions participated in the meeting, reviewed the work done by WHO and other experts, and identified the gaps in their work strategies and future research agenda. They agreed that the data on disease burden posed by sepsis was critically missing and discussed how they could contribute collectively to a better understanding of the sepsis epidemiology. Later, key articles, including the one from the Global Burden of Disease (GBD) group, were published,^{2,5} which subsequently led WHO to publish the first Global Sepsis Report in 2020 in line with the WHO sepsis resolution.⁶ Currently, the WHO guidelines on the clinical management of sepsis are under development, focusing on early recognition, initial resuscitation, and the early treatment of sepsis.⁷

SURVIVING SEPSIS CAMPAIGN

Prior to the WHO resolution on sepsis, academic societies had already made a major global effort, that is, the Surviving Sepsis Campaign (SSC). SSC is a joint initiative

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TABLE 1 The action points based on the sepsis resolution adopted by the World Health Assembly in 2017 (WHA70.7).

Action points
1. Adopt prevention, diagnosis, and treatment of sepsis in national health systems strengthening
2. Improve infection prevention and control programs
3. Continue efforts to combat antimicrobial resistance and promote antimicrobial stewardship
4. Develop and implement standard and optimal care for sepsis diagnosis and management
5. Increase public awareness
6. Train all health professionals on infection prevention, patient safety, early sepsis recognition, and communication strategy with the use of the term “sepsis”
7. Promote research on sepsis
8. Improve the use of the International Classification of Diseases to better understand the burden of sepsis, and progress toward improving outcomes of sepsis
9. Engage in advocacy efforts, including the support of World Sepsis Day

of the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM), originally initiated in 2002.⁸ SSC aims to reduce mortality and morbidity from sepsis through providing guidelines, educating health care providers, and raising awareness for sepsis. With its first sepsis management guidelines published in 2004, SSC updates the guidelines every 4 years, most recently updated in 2021.⁹ Now, their recommendations, such as “sepsis bundles,” have been relatively well adopted and embedded into health care delivery, though compliance with the guideline recommendations and bundles may vary across facilities and countries. The overall consensus is that there is an association between improved compliance and reduced mortality from sepsis.^{10,11}

Antimicrobial resistance

Sepsis is not a health condition owned by emergency physicians or intensive care unit (ICU) physicians. A substantial proportion of sepsis occurs in communities and is taken care of on wards in a hospital; therefore, advocacy and awareness should reach outside traditional boundaries such as emergency rooms and ICUs. Sepsis is caused by an infection, which is often complicated by antimicrobial resistance (AMR). AMR has been recognized as a public health threat by global society, and the political commitment has mounted globally over a decade. For example, WHO published a global action plan on AMR in 2016,¹² and more and more countries and regions are creating their own national action plans (NAPs), resulting in 178 countries and regions with their NAPs on AMR in place as of November 2023.¹³ In September 2024, the United Nations (UN) General Assembly set a goal to reduce the bacterial AMR-associated deaths (currently estimated

as about 5 million/year) annually by 10% by 2030.^{14,15} The interplay between sepsis and AMR cannot be overlooked. Sepsis management is heavily compromised if sepsis is caused by infectious pathogens with multi-drug resistance.¹⁶ At the global scale, the disease burden from sepsis is higher in LMICs, and so is the AMR burden.^{2,14} Acknowledging the interplay has led to more collaborative efforts between sepsis and AMR, engaging more diverse stakeholders, experts, and researchers in sepsis-related research at the health policy and academia level.

COVID-19

Another relevant health agenda is COVID-19. The pandemic has revealed how fragile our society is to infectious disease threats and how widely an infectious disease can manifest the disease spectrum from asymptomatic to sepsis and septic shock requiring extensive organ support. On the other hand, appropriate measures of COVID-19 mirror those of sepsis, such as early detection in communities and timely treatment, highlighting that continuous effort to combat sepsis can contribute to pandemic preparedness and response.¹⁷ In addition, a vast resource allocation to COVID-19 research led to a better understanding of the pathophysiology of sepsis and optimal management of sepsis.^{18,19} Probably, one of the important lessons learned to improve COVID-19 and sepsis care is that clinicians and researchers should pay more attention to sub-phenotypes or heterogeneity of treatment effect (HTE).^{20,21} Sub-phenotypes and HTE of sepsis had already been studied, but the COVID-19 pandemic highlighted the importance. While clinicians on the front line need to individualize care and researchers consider precision medicine in their research, it is also important to deliver unified messages for simpler disease entities such as “COVID-19” and “sepsis” at the policy level so that all the efforts are not diluted. Thus, global solidarity to tackle common infectious disease threats such as AMR and COVID-19 has provided a significant opportunity for a synergetic impact to fight against sepsis.

Various populations: Neonatal, pediatric, and maternal sepsis

It is important to note that sepsis can not only be seen across disease conditions such as AMR and COVID-19, but also recognized across the entire population globally with the highest rates in LMICs, where 85% of deaths caused by sepsis are concentrated.² Furthermore, a GBD study estimated that 20 million cases of sepsis per year occurred in children under 5 years of age globally, in addition to 5.7 million women with maternal disorders complicated with sepsis. A global study on maternal sepsis by WHO confirmed that maternal sepsis caused significant maternal mortality and morbidity.²² While the definition

of maternal sepsis was updated by WHO in 2017,²³ that of pediatric sepsis was also recently updated in 2024 using the Phoenix Sepsis Score, in consistency with the current sepsis definition of infection and organ failure.²⁴ The unified definitions of sepsis across different populations will help better understand the epidemiology of sepsis and assess the progress in sepsis prevention, diagnosis, and care at the global level.

NATIONAL ACTION PLAN ON SEPSIS

One of the lessons learned from AMR is that a NAP can be a powerful tool to politically leverage important health issues. Some countries have spearheaded steps toward the creation of their NAPs on sepsis so that they approach sepsis at the national level. For example, in Australia, the George Institute for Global Health and the Australian Sepsis Network published a document “Stopping Sepsis: A National Action Plan” in 2018.²⁵ The key recommendations were as follows:

1. Establish a nationally coordinated sepsis body to facilitate the action plan.
2. Invest in prevention and awareness campaigns to spur action within the community.
3. Establish and implement a nationally recognized clinical standard for sepsis detection and treatment.
4. Invest in community and peer support services for sepsis survivors and their families.

This was followed by the formal engagement of the Australian Commission on Safety and Quality in Health Care, a governmental body to coordinate the national sepsis program in 2019, which included multiple projects such as a report on sepsis epidemiology, quality improvement in sepsis care, and a public awareness campaign. With its successful implementation, the program has now been extended with

further emphasis on awareness campaigns, sepsis education resources, and support for sepsis survivors.²⁶ Lessons from AMR where NAPs are more commonly available at the national level, suggest the importance of the operationalization of NAPs, requiring each stakeholder to better understand their defined roles in the strategy.²⁷ As more NAPs on sepsis are expected in the future, the interplay between the health policy and the utilization of the existing resources and its expansion can never be overlooked. In addition, the impact of NAPs on sepsis morbidity and mortality needs to be appropriately measured to reflect on and revise NAPs accordingly.

BERLIN DECLARATION AND 2030 GLOBAL AGENDA FOR SEPSIS

While a NAP is created and implemented by the government, civil societies can also play a significant role in advancing the sepsis agenda. Global Sepsis Alliance (GSA), founded in 2012, and its regional alliances have been strong advocates for sepsis. GSA, with its regional alliances according to the WHO regional offices, closely works with WHO and advances the global sepsis agenda. In September 2023, the Berlin Declaration on sepsis was announced.²⁸ The declaration was co-led by GSA and supported by multiple organizations, recognizing that less than 10% of the UN member states (i.e., countries and regions) have prioritized sepsis in their national policies and strategies, and calling for the urgent enforcement of the 2017 WHO resolution on sepsis. Furthermore, the ‘2030 Global Agenda for Sepsis’ was officially launched in September 2024. The document, initiated by GSA in collaboration with multiple stakeholders including WHO, aims to reduce the global incidence of sepsis by 25% and to improve the survival rates by 20% by 2030 through the multi-year strategies. The proposed five strategic pillars are presented in Table 2. The pillars include “Whole-of-Society Response” and emphasize the continued

TABLE 2 Five strategic pillars of the 2030 Global Agenda for Sepsis.

Pillar	Key points
1. Political Leadership and Multilateral Cooperation	<ul style="list-style-type: none"> Place the sepsis agenda in global health architecture 80% of high income countries and 50% of low- and middle-income countries to complete national action plans by 2030 Synergy with other initiatives such as universal health coverage, antimicrobial resistance, and infection prevention and control (IPC)
2. Health System Readiness for Sepsis and Its Sequelae	<ul style="list-style-type: none"> 50% of countries to launch evidence-based and patient-centered clinical pathways for Sepsis and sepsis bundles by 2030 Training of clinical management of sepsis and incorporation of sepsis services into priority health care delivery Quality improvement programs for sepsis Improve IPC and achieve high immunization coverage for sepsis prevention
3. Whole-of-Society Response	<ul style="list-style-type: none"> Improve awareness of sepsis and its sequelae among the general public, media representatives, and policymakers Improve health literacy of sepsis as a medical emergency in communities
4. Sepsis Research and Innovations	<ul style="list-style-type: none"> Countries to allocate earmarked funds to sepsis-related research Improve public and private research funding Establish Global Sepsis Research and Innovation Platform to be launched by 2025
5. Sepsis in Pandemics and Other Emergencies	<ul style="list-style-type: none"> Strengthen medical countermeasures in the context of pandemics Incorporate sepsis care into humanitarian response Sepsis in the climate change agenda

effort to improve sepsis awareness among the general public, on which the following two sections particularly focus.

WORLD SEPSIS DAY

World Sepsis Day (WSD) was originally started by GSA in 2012. The aim is to raise public awareness for sepsis through campaign activities. Every year on September 13, relevant events take place across the globe. As an example, Japan is part of the campaign: The GSA committee was originally established under the Japanese Society of Intensive Care Medicine (JSICM) in 2013, which further evolved into Japan Sepsis Alliance (JaSA) in 2019, co-organized by JSICM, the Japanese Association for Acute Medicine, and the Japanese Association for Infectious Diseases. They have been joining the campaign since 2013 to promote the importance of sepsis as a health issue.²⁹ JaSA is not only a central body of the campaign but also plays an important role in the knowledge dissemination of sepsis through its website and seminars.³⁰ In addition, JaSA has expanded its role in sepsis research, attracting researchers in Japan and informing health care providers and policymakers of the important sepsis data in Japan.³¹ These local activities have been shared with the Asia Pacific Sepsis Alliance, one of the GSA regional alliances. WSD, as a global campaign, provides opportunities to facilitate mutual communications across different levels.

PATIENT, FAMILY AND THE PUBLIC

Patient-centered care is one of the major goals of today's health care, and it should be the case with sepsis care. For example, during the early phase of the COVID-19 pandemic, the patients were isolated from their family, or the family was restricted from visiting the patients, as a result of prioritizing public health measures.³² Therefore, the importance of patient and public involvement and engagement (PPIE) was emphasized in some countries, including health research during the pandemic.³³ Another example is about sepsis survivors: sepsis is not only an acute illness but also causes long-term sequelae, whether it is physical or cognitive/mental, and it is called post-intensive care syndrome (PICS).³⁴ Sepsis influences the family of a sepsis survivor (PICS-F), as they may experience emotional and/or physical stress.^{35,36} The care for PICS and PICS-F needs to be tailored individually and should take a multidisciplinary approach. On the other hand, the question arises as to whether we measure their issues properly in alignment with patients' views or values. A study showed that commonly used measures such as health-related quality of life (HRQoL) may not necessarily reflect "how (sepsis) survivors feel about their health" all the time.^{37,38} While healthcare providers and/or researchers are often trained to be objective, patient values can never be overlooked. Traditionally, clinical research has been led by clinician-scientists, but ensuring PPIE in research will become more important in the upcoming era of

patient-centered medicine. In addition, some countries are successful in engaging sepsis survivors and their families to raise sepsis awareness among the public: the real voices and stories can play a significant role in society.³⁹

CONCLUSIONS

Sepsis has been and will remain the major global burden of disease. The attention to fight against sepsis has been mounting over the last several years globally. Sepsis is so common among acute illnesses, affecting all the various populations and causing a significant impact on mortality and morbidity, including long-term sequelae, that a holistic and sustained approach is of paramount importance. It is important to note that individual clinicians, scientists/researchers, or health care providers take an important role in the "global strategies": it is not only owned by a UN agency such as WHO or a global body such as GSA. PPIE must be central in the strategies, and the lessons and the success stories on PPIE should be shared among the stakeholders. In addition, in the global health policy agendas, it is essential to advance the sepsis strategies in alignment with other interlinked global health initiatives/issues such as AMR, health emergencies, and universal health coverage. As we make more strides in patient-centeredness in future healthcare, engagement of patients and the public in all the strategies can never be underestimated. With all the stakeholders hand in hand, further implementation of the strategies should be ensured to mitigate the global impact posed by sepsis in the future.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable – no new data generated.

ETHICS STATEMENT

Approval of the research protocol: This is a narrative review. Therefore, the protocol approval was not required.

Informed consent: Not applicable.

Registry: This is a narrative review. Therefore, the registration was not required.

Animal studies: Not applicable.

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