

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Recognizing Sepsis as a Global Health Priority — A WHO Resolution

Konrad Reinhart, M.D., Ron Daniels, M.D., Niranjan Kissoon, M.D., Flavia R. Machado, M.D., Ph.D., Raymond D. Schachter, L.L.B., and Simon Finfer, M.D.

S ome 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."

So said Sir Liam Donaldson, the former chief medical officer for England and the current World Health Organization (WHO) envoy for patient safety, on May 24, 2017.¹ Two days later, the World Health Assembly (WHA), the WHO's decision-making body, adopted a resolution on improving the prevention, diagnosis, and management of sepsis.²

The term "sepsis" dates back to at least the time of Hippocrates,

who considered it the process by which flesh rots and wounds fester. More recently, it has been defined as life-threatening organ dysfunction resulting from infection. Despite this long history, sepsis has existed in the backwater described by Donaldson, and as a result innumerable patients around the world have died prematurely or faced long-term disability. This toll of unnecessary suffering drove Germany, with the unanimous support of the WHO executive board and at the urging of the Global Sepsis Alliance (GSA), to propose the resolution adopted by the WHA. The resolution urges member states and the WHO director general to take specific actions to reduce the burden of sepsis through improved prevention, diagnosis, and management (see table).

The true burden of disease arising from sepsis remains unknown. The current estimates of 30 million episodes and 6 million deaths per year come from a systematic review that extrapolated from published national or local population estimates to the global population.3 The likelihood that the result was a significant underestimate was recognized by the authors, who could find no data from the low- and middle-income countries (LMICs) where 87% of the world's population lives. Thus, their estimate is based on data on hospital-treated sepsis in highincome countries. This lack of data is compounded by the fact that sepsis is treated as a "garbage code" in the Global Burden of Disease statistics, where most

N ENGLJ MED NEJM.ORG

The New England Journal of Medicine

Downloaded from nejm.org by K REINHART on June 28, 2017. For personal use only. No other uses without permission.

Copyright © 2017 Massachusetts Medical Society. All rights reserved.

Recommended Actions for Reducing the Global Burden of Sepsis.	
Recommendations	Suggested Actions
The World Health Assembly urges member states to:	
Develop national policy and processes to improve the preven- tion, diagnosis, and treatment of sepsis.	Governments should develop national action plans in collaboration with the professions and patient-advocacy groups.
Improve infection prevention and control strategies: access to clean water, sanitation, and hygiene (WASH); vaccina- tions; clean childbirth; surgical site infection prevention; and protective equipment for health workers.	Policymakers should evaluate public access to WASH; professional bodies should develop strategy for prevention and control of health facility– acquired infection, monitor practice, and support improvement.
Continue efforts to combat antimicrobial resistance (AMR) by promoting judicious use of antimicrobials.	WHO AMR team in partnership with governments and professions should implement comprehensive antimicrobial stewardship activities.
Develop and implement measures to recognize and manage sepsis as a core part of national and international health emergency response plans (e.g., during epidemics, pan- demics, and natural disasters).	Multisector approach should incorporate specific guidelines for sepsis awareness and management in emergency-response plans.
Increase public awareness of sepsis, particularly among high- risk groups, to ensure prompt recognition and presenta- tion for treatment.	Member states should design nationally relevant, specific messaging for educating the public and health care providers.
Promote public awareness by training health care workers to use the term "sepsis" in communication with patients, relatives, and other parties.	Professional bodies should develop educational materials for health pro- fessionals at all levels; health care provider organizations should dis- seminate them and reinforce their message.
Train health care workers about the importance of sepsis as a time-critical medical emergency and as a key element of averting deterioration and ensuring patient safety.	Professional bodies and health authorities should develop education for health professionals at all levels; provider organizations should dissem- inate and reinforce education.
Promote research to develop innovative means to prevent, diagnose, and treat sepsis.	Include sepsis as a priority research area for funding bodies and commis- sioned research.
Improve the International Classification of Diseases (ICD) cod- ing to allow for better assessment of the burden of both sepsis and AMR.	Where feasible, governments should monitor incidence and outcomes from sepsis; WHO should work with agencies to improve ICD coding.
Monitor progress toward improving outcomes for patients and survivors.	Governments and health care provider and professional organizations should develop and implement monitoring and evaluation tools, epide- miologic surveillance systems, and national registries.
Develop evidence-based strategies for policy change related to prevention, diagnosis, and treatment of sepsis and survi- vors' access to rehabilitation.	Governments should change health policy where high-quality evidence supports change.
Engage in advocacy efforts to raise sepsis awareness by sup- porting activities promoting such awareness including but not restricted to World Sepsis Day (September 13 each year).	Governments, professional and community groups should plan and support awareness activities centered on World Sepsis Day.
The World Health Assembly requests that the director general:	
Develop WHO guidance including guidelines, as appropriate, on sepsis prevention and management.	Director general or delegates should develop context and country-specific guidance or guidelines in collaboration with national and international experts, patient advocates, and patient-safety representatives.
Draw attention to public health impact of sepsis through a WHO report by the end of 2018.	WHO should publish, independently or in collaboration with others, a re- port on global epidemiology of sepsis and impact on burden of disease.
Identify successful approaches for integrating timely diagno- sis and management of sepsis into health systems and provide guidance on adoption.	Director general or delegates in conjunction with others should identify ini- tiatives whose success is supported by reliable data and provide advice to member states on adapting such approaches to local conditions and resources.
Support member states in defining standards and improving infrastructure and developing and implementing strate- gies for reducing incidence, mortality, and long-term bur- den.	WHO in partnership with governments should promote national standards and guidelines related to recognition, treatment, laboratory support, and follow-up and support learning, including in low- and middle-in- come countries.
Collaborate globally to improve access to safe, affordable, ef- fective prevention including immunization, particularly in developing countries.	WHO should work with member states to improve public access to WASH, vaccination programs, and professional health care providers.

deaths due to sepsis are classified as being caused by the underlying infection. Improving the coding of sepsis and establishing a proper accounting in those statistics are essential steps envisaged by the WHA.

The resolution also calls for health care workers to increase awareness of sepsis by using the term "sepsis" in communication with patients, relatives, and other parties.4 National surveys consistently report low community awareness of sepsis, its signs and symptoms, its causes, and its toll of death and disability. In Australia, only 40% of surveyed people had heard of sepsis and only 14% could name one of its signs. In Brazil, the figures are even lower, with 7% of surveyed people aware in 2014 and 14% in 2017. In the United States, the United Kingdom, and Germany, high-profile campaigns have proven effective and increased awareness to 55%, 62%, and 69%, respectively.

Ensuring greater awareness on the part of both the public and health care workers is a crucial step in reducing the global burden of sepsis. Approximately 70% of sepsis cases are community-acquired, and since treatment with appropriate antibiotics must begin early to be effective, educating people about seeking treatment without delay is key to preventing unnecessary deaths and disability. The progression from infection to sepsis can be insidious and is unpredictable. Although populations such as the very young, the very old, and the immunosuppressed are known to be at high risk and should be targeted for education, sepsis can affect anyone at any time, which means that national public awareness programs are needed.

Awareness programs should

also teach health care workers both to recognize sepsis and to understand it as a true time-critical medical emergency. Government reports and individual patient stories consistently identify delayed treatment as a major cause of preventable death and disability.⁵ Encouraging patients, relatives, and health care workers to ask "Could this be sepsis?" saves lives.

Clear treatment guidelines and performance targets tailored to local environments and available resources are also essential. Effective examples of this approach that have reduced mortality can serve as templates to be adapted for local conditions and use; these include "Rory's Regulations" in New York State, the "Sepsis Kills" program in New South Wales, Australia, the National Health Services' commissioning levers in England, and a multifaceted education program in Brazil.

Promulgation of comprehensive treatment guidelines such as those developed by the Surviving Sepsis Campaign has been associated with reduced mortality in high-income countries, but guidelines written for and by clinicians in these countries may not be applicable in the LMICs that bear most of the sepsis burden. Context-specific guidelines or modification of current guidelines for individual LMICs will be most effective if the guideline process is led by local clinicians and policymakers; the resolution envisages the WHO, in collaboration with others, playing a role in the development and promulgation of such guidelines. In addition, attention to bolstering public health initiatives to prevent sepsis, surveillance systems for detecting outbreaks early, and provision of simple early treatment can help to counterbalance the effects of a

lack of critical care facilities in many LMICs.

The WHO resolution recognizes the perceived conflict between rapid administration of antibiotics to treat sepsis and efforts to combat antimicrobial resistance. Global efforts to reduce the burden of sepsis must go hand in hand with measures to minimize antimicrobial resistance and be consistent with the WHO-approved Global Action Plan on Antimicrobial Resistance. However, sepsis is the condition that is most appropriate to treat empirically with broadspectrum antibiotics, with rapid deescalation based on identification of the causative organisms.

Progress toward the GSA's vision of "a world free of sepsis" also requires recognition of the key role of prevention. Prevention of infection and resultant sepsis through vaccination; access to clean water, sanitation, and hygiene (WASH) in homes, schools, and health care facilities; clean childbirth and surgical practices; and hand hygiene in health care facilities is already the focus of WHO programs. The new resolution on sepsis supports and reinforces these programs.

Increased awareness, early presentation to a health care facility or early recognition of health care-associated sepsis, rapid administration of appropriate antibiotics, and urgent treatment according to locally developed guidelines can significantly reduce deaths from sepsis. Since such measures have reduced case fatality rates in high-income countries, however, the substantial burden carried by survivors of sepsis has become clearer. The sequelae of sepsis can include clinically significant physical, cognitive, and psychological disability that often goes unrecognized and untreat-

N ENGLJ MED NEJM.ORG

The New England Journal of Medicine

Downloaded from nejm.org by K REINHART on June 28, 2017. For personal use only. No other uses without permission.

Copyright © 2017 Massachusetts Medical Society. All rights reserved.

ed. In LMICs, postdischarge mortality after sepsis is about the same as sepsis-related mortality in the hospital, and perinatal sepsis poses great and ongoing risks for both mother and infant. Yet around the world, coordinated services for sepsis survivors are virtually nonexistent.

The WHA resolution, with its implicit recognition of sepsis as a major threat to patient safety and global health, has the potential to save millions of lives. To realize this potential, the actions proposed in the resolution need to be taken. These actions require coordinated efforts by politicians, policymakers, health care administrators, researchers, and clinicians working with people of all ages in all health care settings and in the community. Actions will vary by region and country and must acknowledge the unique challenges faced by LMICs.

Disclosure forms provided by the authors are available at NEJM.org.

From Jena University Hospital, Jena, Germany (K.R.); the Heart of England NHS Foundation Trust, Birmingham, United Kingdom (R.D.); the Department of Pediatrics, Emergency Medicine and Critical Care, University of British Columbia (N.K.), and Synergy Business Lawyers (R.D.S.) — both in Vancouver, Canada; the Department of Anesthesiology, Pain and Intensive Care Medicine, Federal University of São Paulo, São Paulo (F.R.M.); and the George Institute for Global Health, University of New South Wales, Sydney (S.F.). The authors constitute the Executive Board of the Global Sepsis Alliance.

This article was published on June 28, 2017, at NEJM.org.

 "WHA Side Event on Sepsis" in Geneva. YouTube. May 24, 2017 (https://www.youtube .com/watch?v=k-dEPnBzuMc&feature=youtu .be).

2. WHA adopts resolution on sepsis. Jena, Germany: Global Sepsis Alliance, May 26,2017 (https://www.global-sepsis-alliance.org/news/ 2017/5/26/wha-adopts-resolution-on-sepsis).

3. Fleischmann C, Scherag A, Adhikari NKJ, et al. Assessment of global incidence and mortality of hospital-treated sepsis: current estimates and limitations. Am J Respir Crit Care Med 2016;193:259-72.

 Just say sepsis! A review of the process of care received by patients with sepsis. London: National Confidential Enquiry into Patient Outcome and Death, November 2015 (http://www.ncepod.org.uk/2015report2/ downloads/JustSaySepsis_FullReport.pdf).
Time to act: severe sepsis — rapid diagnosis and treatment saves lives. London: Parliamentary and Health Service Ombuds: man, 2013 (https://www.ombudsman.org.uk/ publications/time-act-severe-sepsis-rapid -diagnosis-and-treatment-saves-lives-0).

DOI: 10.1056/NEJMp1707170 Copyright © 2017 Massachusetts Medical Society.