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New Study Shows Deadly Sepsis Rates are Double Prior Estimates – *Global Burden of Sepsis* Says Poor Countries and Children Hit Hardest

A new study, the most comprehensive to date on the staggering incidence of sepsis and sepsis deaths, was released today in The Lancet, confirming that the actual rates are double than previously estimated, and that 20 per cent of global deaths are due to this under-reported but deadly medical condition.

The <u>Global Burden of Sepsis study</u>, led by Dr. Kristina Rudd and Mohsen Naghavi PhD of the University of Washington and the Institute of Health Metrics and Evaluation (IHME), is the first to produce data according to age, sex, location, and the underlying cause of sepsis.

The study found that there were 48.9 million cases of sepsis in 2017 resulting in 11 million deaths worldwide. Prior to this analysis, the most recent global estimate of 19.4 million sepsis cases and 5.3 million sepsis-related deaths, was based on data from hospitalized adults in seven high-income countries.

"These estimates are at least double the figures we had previously assumed, likely because this study included data from low- and middle-income countries," said Prof. Dr. Konrad Reinhart, co-author of the paper, and president of the <u>Global Sepsis Alliance</u> and Professor at the Center for Sepsis Control and Care at Jena University Hospital and Charité Berlin, Germany. "The highest burden of sepsis is in Sub-Saharan Africa, Oceania including Polynesia, Melanesia and Micronesia, and the southern, eastern and southeastern parts of Asia – in locations the least equipped to prevent, identify, treat or care for sepsis survivors, many of whom have long-term health consequences."

The most notable difference between prior estimates and the *Global Burden of Sepsis* study, he noted, is that half of all cases worldwide in 2017 occurred among children, many of whom were newborns.

"These findings highlight the urgent need for action by health policy makers, clinicians and researchers, particularly in the regions hardest hit, and among the most vulnerable populations, such as newborns, children President Konrad Reinhart

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and the elderly," said co-author Dr. Niranjan "Tex" Kissoon, vice-president of the Global Sepsis Alliance, and Executive Medical Director, Children's and Women's Global Health, UBC & BC Children's Hospital Professor in Critical Care. "There are a number of cost-effective measures that can be implemented such as adequate hand-washing practices, proper sanitation of hospital devices, and vigilant administration of antimicrobial therapy such as shorter courses of treatment, and development of new antibiotic remedies."

The study looked at 109 million death records, related to 282 underlying causes of sepsis, between the years 1990 to 2017. The study included 195 countries and territories, applying estimates for age, sex, location, cause of illness, and the year.

Among all age groups, both sexes, and all locations, in every year from 1990-2017, the most common underlying cause of sepsis was diarrheal diseases, such as shigella, e coli or other bacterial form of infection. More common underlying causes of sepsis in 2017 were infection related to road traffic injury and complications of pregnancy for mothers and newborns. Data for 2017 showed that the incidence of sepsis was slightly higher in females than males, and peaked overall in early childhood, and again, among older adults. Among all ages, both sexes, and all underlying causes of deaths -- an estimated 87 per cent, and 85 per cent of the sepsis cases worldwide in 1990 and 2017, respectively, occurred in low or low middle-income countries.

Sepsis, sometimes referred to as 'blood poisoning', is the life-threatening condition that arises when the body's response to infection results in organ dysfunction or failure. Sepsis is often confused with other conditions in its early stages, with delayed recognition of the signs and symptoms quickly leading to multi-system organ failure, and, ultimately, death. Sepsis needs to be treated as an emergency because every delay in administration of antimicrobials and other measures increases mortality rate on an hourly basis.

In partnership with the Global Sepsis Alliance, sepsis was designated an urgent global priority by the World Health Organization in May 2017 which adopted a <u>resolution to improve</u>, <u>prevent</u>, <u>diagnose</u>, <u>and manage sepsis</u> through a series of actions directed at developed and developing countries around the world. In the resolution, the WHO recognizes that most of sepsis cases are preventable, also through education and professional training on patient safety.



Public figures such as Muhammad Ali, Christopher Reeve, Patty Duke, Robert Palmer, Nathalie Cole, Roy Scheider, Mother Theresa, Christian Brando, Jeff Conaway, Jim Henson, Brittany Murphy, Prince Rainier of Monaco, Leslie Nielson, Lawrence Welk, Rita McNeil, Anna Nicole Smith, and Pope John Paul II, to name but a few -- all died from sepsis.

Funding for the Global Burden of Sepsis study was provided by the Bill & Melinda Gates Foundation, the National Institute of Health, the University of Pittsburgh, and the University of British Columbia.

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Q&A on the Global Burden of Disease Sepsis Study

What Is Sepsis?

Sepsis is a life-threatening, systemic, inflammatory reaction to an infection that affects the entire body and damages its organs. Sepsis can be caused by most microorganisms – bacteria, fungi, viruses, and parasites. Twenty to thirty per cent of sepsis cases occur in the hospital from healthcare-associated infections. Sepsis can be fatal without swift and effective treatment with antimicrobial substances, fluids, and other appropriate clinical measures. For survivors, sepsis may cause long term consequences such as disabilities or cognitive impairment, beside lasting symptoms such as, among others, poor memory, difficulty in concentrating, constant sense of fatigue. Sepsis survivors are subject to high risk of readmission. For further information about sepsis, please consult the <u>World Sepsis Day website</u>.

Is Sepsis Preventable?

Sepsis is the most preventable cause of death. The World Health Organization (WHO) assumes that the majority of deaths caused by sepsis, which are worldwide at least 11 million, could be preventable through vaccinations, infection prevention and control programs at health institutions, and through early detection and management of sepsis.

What Is the Impact of Sepsis?

The *Global Burden of Sepsis* study, published in 2020, found that there were 48.9 million cases of sepsis in 2017 resulting in 11 million deaths worldwide, approximatively. Prior to this analysis, the most recent global estimate of 19.4 million sepsis cases and 5.3 million sepsis-related deaths was based on data from hospitalized adults in seven high-income countries. The 2019 study also clearly shows that medium and low-income countries are the most affected, as well as children (especially newborns) and the elderly, for whom the immune system's response to infections is generally altered. The data for the 2017 period also showed that the incidence of sepsis was slightly higher in females than males. An estimated 85 per cent of the sepsis cases worldwide in 2017 occurred in low or low middle-income countries. The highest burden of sepsis is in Sub-Saharan Africa, Oceania including Polynesia, Melanesia and Micronesia, and the southern, eastern and southeastern parts of Asia.

According to the Centers for Disease Control and Prevention, sepsis accounts for more than \$24 billion in total annual hospital costs in the US.



In 2017 the York Health Economics Consortium 2017 suggested cost to UK economy as high as £15.6 billion annually.

Although not in the scope of the study, the impact for the 38 million sepsis survivors is less quantifiable, albeit not negligible. In most cases they suffer from disabilities and cognitive impairment, with long lasting effects on them and their families.

Why Is This Study Important?

The Global Burden of Sepsis study is the first to produce sepsis data from countries of varying socio-demographic index (SDI) levels and for both hospital and community settings, with relation to age, sex, and the underlying cause of sepsis. Previously the Lancet Global Burden of Disease study had limited the scope of sepsis reporting to neonatal sepsis only. This study takes a much broader approach and looks at the whole spectrum of sepsis worldwide. The Global Burden of Sepsis study reveals that the number of sepsis cases and deaths caused by sepsis is double that of the previously available figures, and estimates that 20 per cent of global deaths are due to sepsis.

Why Have Sepsis Cases and Deaths Increased?

There a number of factors that could explain the significant difference compared to previous findings, and the ongoing difficulties in gathering accurate data. Most importantly, the scope of the Global Burden of Sepsis study is broader than previous studies. The study looked at 109 million death records, related to 282 underlying causes of sepsis, between the years 1990 to 2017. The study included 195 countries and territories, applying estimates for age, sex, location, cause of illness, and the year. Often diseases are classified with the ICD codes¹ related to the underlying diagnosis, rather than with the sepsis code itself. This has altered data accuracy, especially in previous studies. Probably the burden of sepsis has remained proportionally similar through the years, but today physicians and healthcare personnel are more aware and medical records are more accurate.

Among the many threats that can cause infections (and therefore sepsis) are included environmental and public health aspects. The direct and indirect consequences of the climate crisis, which have spiked in the last few years, have particularly hit low- and middle-income countries (LMIC). Precarious

¹ The International Classification of Diseases (ICD) is the international "standard" diagnostic tool for epidemiology, health management, and clinical purposes.



sanitary conditions following environmental catastrophes, limited access to clean water, and massive urbanization often in insalubrious areas, are examples of preconditions for the spreading of communicable diseases and the development of infections that can lead to sepsis. Therefore, the impact of sepsis is higher in areas less equipped to tackle it.

All the above puts sepsis on the map of the global public health and environmental priorities identified by the UN Sustainable Development Goals. Considering the links with maternal and neonatal mortality, combating sepsis will clearly contribute to the achievement of UN Sustainable Development Goals (SDGs) targets 3.1 and 3.2. Sepsis can also lead to death in patients affected by HIV, tuberculosis, malaria and other infectious diseases that are included in target 3.3, although sepsis is not one of the indicators.

Even if less directly, sepsis is also relevant to other health targets in SDG 3 (i.e. adequate vaccine coverage, quality universal health coverage, capacity to comply with the International Health Regulations, preparedness, and water and sanitation services).

What Does the GSA Expect from the Publication of the Study?

The Global Sepsis Alliance's vision is a world free of sepsis and we can reach this through prevention², recognition, appropriate treatment, and research. The Global Burden of Sepsis study creates a momentum to raise awareness about sepsis amongst professionals, stakeholders, the public, and more importantly, among policy makers. We have made some fantastic progress over the past few years but much still remains to be done. We ask policy makers and governing bodies around the world to acknowledge the great burden that sepsis represents for public health, allocate resources, and act accordingly in order to implement national sepsis prevention and treatment plans. We also need better data collection and continued awareness raising campaigns to fight sepsis.

What Has Already Been Done?

Through the years the Global Sepsis Alliance and many other organizations and individuals have contributed to raising awareness and implementing effective treatment for sepsis. In 2012, the GSA established World Sepsis Day. On September 13th every year, hundreds of initiatives organized by

² Through awareness raising and implementation of few cost-effective measures such as adequate hand-washing practices, proper sanitation of hospital devices, and vigilant administration of antimicrobial therapy such as shorter courses of treatment, and development of new antibiotic remedies.



World Sepsis Congress and the Sepsis Symposium, that gather renowned experts and key stakeholders engaged in the fight against sepsis. Additionally, we are also working to engage policy makers to implement the recommendations of the WHO. In fact, in 2017 the World Health Assembly, the executive body of the WHO, adopted a resolution on sepsis. The Sepsis Resolution urges the 194 United Nation Member States to implement appropriate measures to reduce the human health and economic burden of sepsis. However, to date, only 16 countries³ have implemented or proposed national plans.

What Needs to Be Done?

Governments and international organizations must allocate funds and resources to research, awareness raising campaigns, implementation of procedures in hospitals and support to survivors and families. In this regard, WHO members states have the obligation to tackle sepsis more comprehensively. Regional governing bodies, such as the European Union, can facilitate this process through setting up specific programs (i.e. infection management programs) and exchange of best practices. Further, the WHO, including its regional offices, should focus more on sepsis by allocating more resources and dedicated personnel.