

What can we do to reduce mortality from sepsis?



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Overview

What is sepsis and its consequences?

High on research agenda at NIHR

- Antimicrobial stewardship
- Precision adjuvant immune modulating therapies
- Sepsis as a global challenge

Sepsis definition

“**Life-threatening** organ dysfunction caused by a dysregulated **host response** to **infection**”

Sepsis V3.0 definition

Clinical Review & Education



Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

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

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

Sepsis burden

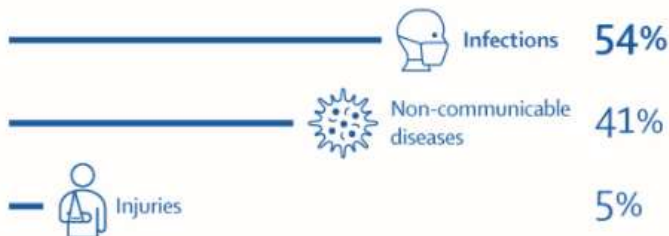
Global Burden of Disease

Global Sepsis Mortality Rates from 1990–2017

Sepsis-related mortality

11 million estimated no. of sepsis-related deaths in 2017 / **19.7%** of total deaths globally in 2017

Underlying causes



Global disparities

The burden is especially high in sub-Saharan Africa



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Sepsis burden

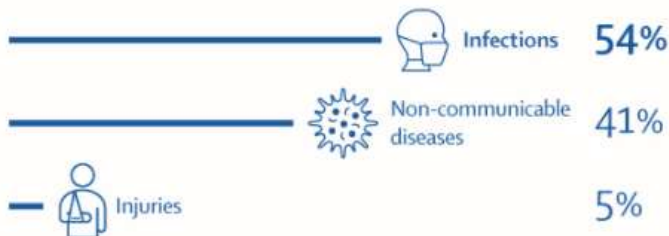
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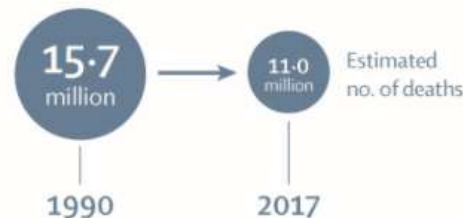
Sepsis-related mortality



Underlying causes



Trends over time



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Sepsis burden

- Impact of sepsis on longer term mortality (years)
- Considerable long term physical and psychological burden for survivors
- Fiscal impacts for patients, their families and health services

Understanding and Enhancing Sepsis Survivorship: Priorities for Research and Practice
American Journal of Respiratory and Critical Care Medicine 2019-06-04

Challenge of recognition/diagnosis

**“COULD
IT BE
SEPSIS?”**

**IT'S A SIMPLE QUESTION,
BUT IT COULD SAVE LIVES.**

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Unintended consequences (individual)

JAMA Internal Medicine | [Original Investigation](#)

Association of Adverse Events With Antibiotic Use in Hospitalized Patients

Unintended consequences (populations)



The evolving threat of antimicrobial resistance
Options for action



World Health
Organization

- Surveillance systems
- **Better use of available antibiotics** (humans and animals)
- Hygiene
- Innovation (**rapid diagnostics** and drugs)
- Political commitment to enable

Innovation in antimicrobial stewardship

Key diagnostic decision problems to deliver precision

Within an hour:

Is it infection?

Which, if any, empiric antimicrobial treatments?

Within the day:

What's the causative pathogen and its phenotype?

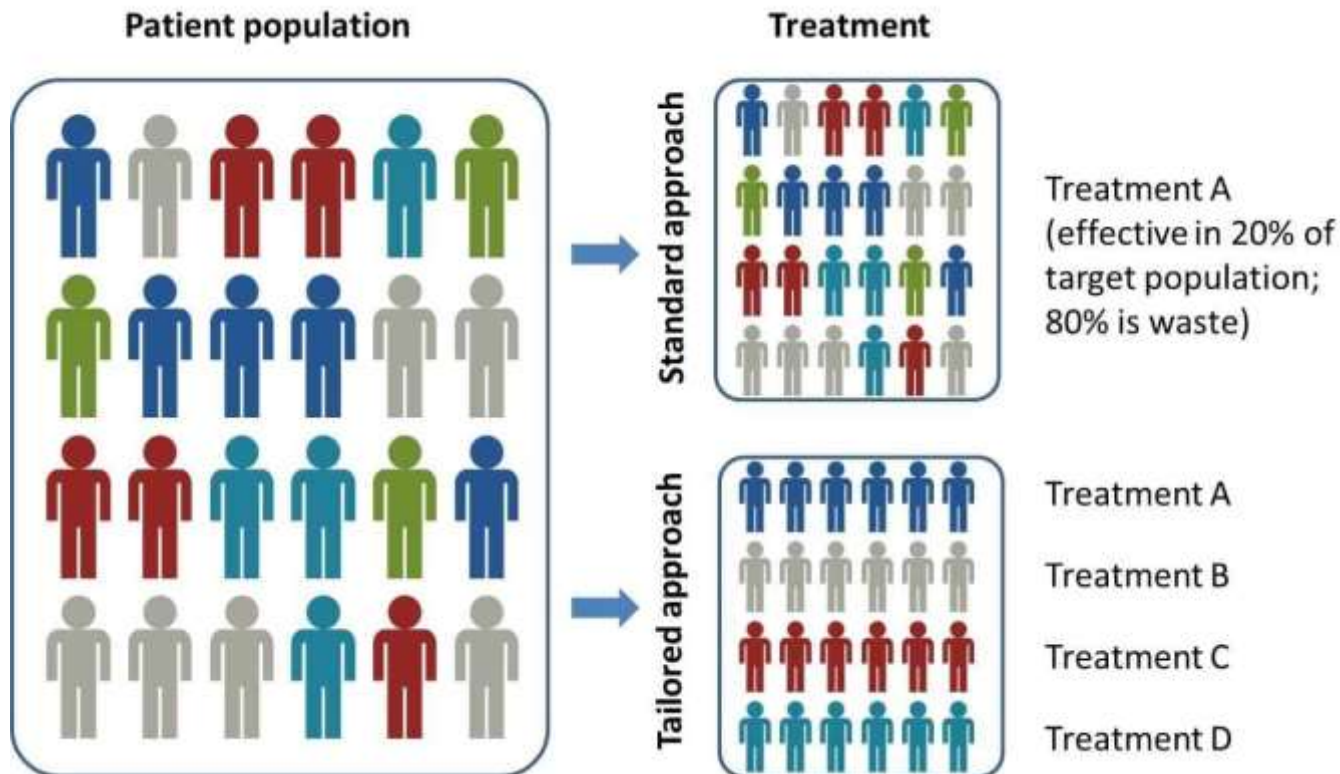
Can antimicrobial treatments be refined safely?

Within days:

What is optimal dose and duration of antimicrobial treatment?

Determining impact on antimicrobial resistance

Innovation in precision adjuvant therapy: modulating host responses



Sepsis as a global challenge



World Health
Organization

Populations at risk

- Poor access to health care (including preventive)
- Unidentified and inadequately controlled comorbidities (e.g. HIV)
- Malnutrition
- Genes

Infecting microorganisms

- Parasitic, viral, and mycobacterial infections
- Antimicrobial resistance

Clinical circumstances

- Inadequate resources (knowledge, human and equipment)
- Limited laboratory diagnostic and acute/critical care capacity



NIHR cross-cutting priority (forward view)

- Antimicrobial stewardship/antimicrobial resistance
- Precision adjuvant immune modulating therapies
- Sepsis as a global challenge (focus on multi-morbidity)

Emerging infectious diseases