WHO work on sepsis

Ed Kelley
Director, Service Delivery and Safety

on behalf of the Sepsis Coordination Group

WHO-HQ, Geneva
Improving the prevention, diagnosis and clinical management of sepsis

The Seventieth World Health Assembly.

Having considered the report on improving the prevention, diagnosis and clinical management of sepsis;

- Concerned that sepsis continues to cause approximately six million deaths worldwide every year, most of which are preventable;
- Recognizing that sepsis as a syndromic response to infection is the final common pathway to death from most infectious diseases worldwide;
- Considering that sepsis follows a unique and time-critical clinical course, which in the early stages is highly amenable to treatment through early diagnosis and timely and appropriate clinical management;
- Considering also that infections which may lead to sepsis can often be prevented through appropriate hand hygiene, access to vaccination programmes, improved sanitation and water quality and availability, and other infection prevention and control best practices; and that forms of sepsismies associated with nosocomial infections are severe, hard to control and have high fatality rates;
- Recognizing that while sepsis itself cannot always be predicted, its ill effects in terms of mortality and long-term morbidity can be mitigated through early diagnosis and appropriate and timely clinical management;
- Recognizing also the need to improve measures for the prevention of infections and control of the consequences of sepsis, due to inadequate infection prevention and control programmes, insufficient health education and recognition in respect of early sepsis, inadequate access to affordable, timely and appropriate treatment and care, and insufficient laboratory services, as well as the lack of integrated approaches to the prevention and clinical management of sepsis;
- Noting that health care-associated infections represent a common pathway through which sepsis can place an increased burden on health care resources;
HEALTH IN THE SDG ERA

3 GOOD HEALTH AND WELL-BEING

ENSURE HEALTHY LIVES AND PROMOTE WELL-BEING FOR ALL AT ALL AGES

17 PARTNERSHIPS FOR THE GOALS

16 PEACE AND JUSTICE

15 LIFE ON LAND

14 LIFE BELOW WATERS

13 CLIMATE ACTION

12 RESPONSIBLE CONSUMPTION AND PRODUCTION

11 SUSTAINABLE CITIES AND COMMUNITIES

10 REDUCED INEQUALITIES

9 INDUSTRY, INNOVATION AND INFRASTRUCTURE

8 DECENT WORK AND ECONOMIC GROWTH

7 AFFORDABLE AND CLEAN ENERGY

6 CLEAN WATER AND SANITATION

5 GENDER EQUALITY

4 QUALITY EDUCATION

3 FIGHTING GENDER INEQUALITIES, INCLUDING VIOLENCE AGAINST WOMEN

2 ZERO HUNGER

1 NO POVERTY

17 EMPOWERING STRONG LOCAL INSTITUTIONS TO DEVELOP, IMPLEMENT, MONITOR AND ACCOUNT FOR AMBITIOUS NATIONAL SDG RESPONSES

16 MOBILIZING PARTNERS TO MONITOR AND ATTEMPT THE HEALTH-RELATED SDGs

15 PROMOTING HEALTH AND PREVENTING DISEASE THROUGH HEALTHY NATURAL ENVIRONMENTS

14 SUPPORTING THE RESTORATION OF FISH STOCKS TO IMPROVE SAFE AND DIVERSIFIED HEALTHY DIETS

13 PROTECTING HEALTH FROM CLIMATE RISKS, AND PROMOTING HEALTH THROUGH LOW-CARBON DEVELOPMENT

12 PROMOTING RESPONSIBLE CONSUMPTION OF MEDICINES TO COMBAT ANTIBIOTIC RESISTANCE

11 FOSTERING HEALTHIER CITIES THROUGH URBAN PLANNING FOR CLEANER AIR AND SAFER AND MORE ACTIVE LIVING

10 ENSURING EQUITABLE ACCESS TO HEALTH SERVICES THROUGH UNIVERSAL HEALTH COVERAGE BASED ON STRONGER PRIMARY CARE

9 PROMOTING NATIONAL R&D CAPACITY AND MANUFACTURING OF AFFORDABLE ESSENTIAL MEDICAL PRODUCTS

8 PROMOTING HEALTH EMPLOYMENT AS A DRIVER OF INCLUSIVE ECONOMIC GROWTH

7 PROMOTING SUSTAINABLE ENERGY FOR HEALTHY HOMES AND LIVES

6 PREVENTING DISEASE THROUGH SAFE WATER AND SANITATION FOR ALL

5 PROMOTING GENDER EQUALITY

4 SUPPORTING HIGH-QUALITY EDUCATION FOR ALL TO IMPROVE HEALTH AND HEALTH EQUITY

3 ADDRESSING THE CAUSES AND CONSEQUENCES OF ALL FORMS OF MALNUTRITION

2 SUPPORTING THE RESTORATION OF FISH STOCKS TO IMPROVE SAFE AND DIVERSIFIED HEALTHY DIETS

1 NO POVERTY

World Health Organization
WWW.WHO.INT/SDGS
SDG 3: health targets & linkages with sepsis

3.1 By 2030, reduce the global maternal mortality ratio to less than 70 per 100,000 live births

3.2 By 2030, end preventable deaths of newborns and children under five years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-five mortality to at least as low as 25 per 1,000 live births

3.3 By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, waterborne diseases and othercommunicable diseases

3.4 By 2030, reduce by one third premature mortality from noncommunicable diseases through prevention and treatment and promote mental health and well-being

3.5 Strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol

3.6 By 2020, halve the number of global deaths and injuries from road traffic accidents

3.7 By 2030, ensure universal access to sexual and reproductive health-care services, including for family planning, information and education, and the integration of reproductive health into national strategies and programmes

3.8 Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all

3.9 By 2030, substantially reduce the number of deaths and illnesses from hazardous chemicals and air, water and soil pollution and contamination

3.10 Strengthen the implementation of the World Health Organization Framework Convention on Tobacco Control in all countries, as appropriate

3.b Support the research and development of vaccines and medicines for the communicable and noncommunicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration on the TRIPS Agreement and Public Health, which affirms the right of developing countries to use the full the provisions in the Agreement on Trade-Related Aspects of Intellectual Property Rights regarding flexibilities to protect public health, and, in particular, provide access to medicines for all

3.c Substantially increase health financing and the recruitment, development, training and retention of the health workforce in developing countries, especially in least-developed countries and small island developing States

3.d Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks

- Maternal, neonatal and <5y mortality
- UHC coverage index
- Mortality due to unsafe WASH services
- Vaccine coverage
- IHR capacity and emergency preparedness
WHO Activities and Sepsis

**WHO PROGRAMMES focusing on Sepsis**
- Antimicrobial Resistance
- Essential Medicines and Health Products
- Immunization, Vaccines and Biologicals
- Infectious Hazard Management
- Information, Evidence and Research
- Innovation Access and Use
- Maternal, Newborn, Child and Adolescent Health
- Public Health, Environmental and Social Determinants of Health
- Reproductive Health and Research
- Service Delivery and Safety & Infection Prevention and Control

**WHO ACTIVITIES supporting Sepsis management and prevention**
- Networking, coordinating partners’ actions
- Evidence-based guidelines
- Policies and standards
- Implementation strategies, with special focus on low-resources settings
- Research
Main aspects of sepsis according to the resolution

1. Epidemiology and global burden of sepsis
2. Prevention
3. Diagnosis
4. Clinical management, including AMR
Main actions for tackling sepsis according to the resolution

- Awareness raising activities
- Reports
- Policies
- Evidence-based guidelines
- Implementation strategies
- Education and training activities
- Research
- Networking, coordinating partners’ actions
Main areas for tackling sepsis according to the resolution

1. Epidemiology and global burden of sepsis

2. Prevention

3. Diagnosis

4. Clinical management, including AMR
Improving the prevention, diagnosis and clinical management of sepsis

Report by the Secretariat

1. The Executive Board at its 141st session considered an earlier version of this report. 1 The Board then adopted resolution EB141.R7.

2. Sepsis arises when the body’s response to infection injures its own tissues and organs. It can lead to septic shock, multiple organ failure and death, if not recognised early and managed promptly. It is a major cause of maternal and neonatal morbidity and mortality in low- and middle-income countries and affects millions of hospitalised patients in high-income countries, where rates of sepsis are climbing rapidly. The present report summarises the problem of sepsis as a key issue for global health, describes the Secretariat’s actions to address it and broadly outlines priority actions for the future.

3. An international consensus has recently recommended that sepsis should be defined as: “Life-threatening organ dysfunction caused by a dysregulated host response to infection” and septic shock as “a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone.”1 Such definitions are accompanied by clinical criteria to translate them into practice to support diagnosis and clinical management during patient care.

4. The occurrence and frequency of sepsis are determined by a complex interplay of many host, pathogen and health system response factors. Several chronic diseases, such as chronic obstructive pulmonary disease, cancer, diabetes, AIDs and other immunocompromised disorders, are associated with an increased risk of sepsis. Demographic and social factors, such as diet and lifestyle (for example, use of tobacco and alcohol), poverty and stress, also influence the occurrence of sepsis. Access to health care systems, in particular intensive care, as well as the timeliness and quality of care, are also associated with the occurrence of sepsis and its fatality rate.

5. Most types of microorganisms can cause sepsis, including bacteria, fungi, viruses and parasites, such as those that cause malaria. Bacteria such as Staphylococcus pneumoniae, Haemophilus influenzae, Streptococcus aureus, Escherichia coli, Salmonella spp and Neisseria meningitidis are the most common etiological pathogens. Manifestations of sepsis and septic shock can be the final frequent pathway of infections with seasonal influenza viruses, dengue viruses and highly transmissible...

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1 See document EB140/12 and the summary records of the Executive Board at its 141st session, fourth meeting and seventh meeting, session 2.

Interagency reports on maternal and child mortality
A. Global distribution of deaths among children under age 5, by cause, 2016

Deaths among children aged 1–59 months (54%)

- Pneumonia, 13%
- Other, 12%
- Congenital, 4%
- Intrapartum-related events, 1%
- Preterm birth complications, 2%
- Meningitis, 2%
- AIDS, 1%
- Malaria, 5%
- Injury, 6%
- Measles, 1%
- Diarrhoea, 8%

Neonatal deaths (46%)

- Preterm birth complications, 16%
- Intrapartum-related events, 11%
- Sepsis or meningitis, 7%
- Other, 3%
- Injury, 1%
- Congenital, 5%
- Tetanus, 1%
- Diarrhoea, 0.3%
Global distribution of deaths among newborns

B. Global distribution of deaths among newborns, by cause, 2016

- Preterm birth complications: 35%
- Intrapartum-related events: 24%
- Sepsis or meningitis: 15%
- Congenital abnormalities: 11%
- Other: 7%
- Tetanus: 1%
- Pneumonia: 6%
- Diarrhoea: 1%
WHO efforts to better understand epidemiology of sepsis

- Morbidity and Mortality data
  - ICD 11 currently under development

- Maternal sepsis
  - Periodic prevalence study on maternal and early newborn sepsis in the context of the Global Maternal and Neonatal Sepsis Initiative
  - 53 countries, over 2770 women in LMIC (47 countries) and 350 women in HIC

- Neonatal sepsis
  - WHO Global Health Observatory data portal on the Global Strategy for Women’s, Children’s and Adolescents’ Health
  - Every Newborn Action Plan
  - Global Technical Working Group on maternal and perinatal death audit and response
New WHO definition for Maternal Sepsis (2016)

“Maternal sepsis is a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, child-birth, post-abortion, or post-partum period”

Global burden of Health Care-Associated Infections (HAIs)

- Globally, hundreds of millions of people every year are affected by HAIs = 1 in 10 patients

- **Intensive care:** In high-income countries, up to 30% of patients may be affected by at least one HAI in intensive care units; in developing countries the frequency is at least 2–3 times higher.

- **Neonatal care:**
  - Among hospital-born babies, infections are responsible for 4% to 56% of all causes of death in the neonatal period (3/4 in South-East Asia and sub-Saharan Africa).
  - Neonatal sepsis: 6·5-38/1000 live hospital-born babies

- **Maternal care:**
  - In Africa, up to 20% of women who have delivered through caesarian section get a wound infection affecting their health and ability to take care of their newborn child.

Allegranzi B et al. Lancet 2011;377:228-41
Global AMR Surveillance System (GLASS)

- GLASS early implementation (2015-19):
  - Data on the status of national AMR surveillance
  - Aggregated national AMR data for priority pathogen-antibacterial combinations
    - Antibiotic susceptibility test (AST) data from blood and other priority specimens sent routinely to labs for clinical purposes
  - GLASS promotes a shift from surveillance based solely on lab data to a system that includes epidemiological, clinical, and population-level data

First GLASS report January 2018!
GLASS – Incidence of Blood Stream Infection by pathogen under surveillance
Preliminary results

Blood – Community infection origin (n tested = 26998)

Blood – Hospital infection origin

Embargoed!
2014 WHO survey of AMR in health care

- Prevalence of multidrug resistance from inpatient clinical blood and urine specimens

- Most important resistant pathogens (MRSA, ESBL, CRE and MRAB) from blood cultures significantly higher in LMICs
Main areas for tackling sepsis according to the resolution

1. Epidemiology and global burden of sepsis
2. Prevention
3. Diagnosis
4. Clinical management, including AMR
Group B streptococcus (GBS) Vaccination

- Leading etiologic agent of neonatal sepsis and of neonatal meningitis with substantial maternal morbidity/mortality during pregnancy and postpartum.

- During 2015 and 2016, the WHO Product Development for Vaccines Advisory Committee (PDVAC) identified as a priority the development of GBS vaccines suitable for maternal immunization in pregnancy and use in LMIC.

- WHO subsequently developed a preferred product characteristic document:
  "To develop and license safe, effective, and affordable GBS vaccines for maternal immunization during pregnancy to prevent GBS-related stillbirth and invasive GBS disease in neonates and young infants, appropriate for use in high-, middle- and low-income countries."
Understanding the public health value of GBS vaccination

- GBS vaccine development for use in low resource settings however requires more data to better understand the public health and economic value of this intervention, as well as its feasibility.

- **WHO Initiative for Vaccine Research** in collaboration with LSHTM is developing a comprehensive value proposition for GBS vaccination for pregnant women (2017-2020), based on
  - Assessment of the medical need for maternal immunization against GBS at global level
  - Economic analysis of economic burden of disease, vaccine cost effectiveness, and anticipated vaccine introduction costs in different settings
  - Identification of potential impact of operationalizing GBS vaccination programmes

- The analysis will aim to provide an overview over major data gaps to the creation of a favourable environment for future vaccine introduction

Liu L, et al., Lancet 2015
WHO Infection Prevention and Control (IPC) Global Unit

Based at WHO HQ and providing support to Member States through the 3 levels of WHO

**Functions**

1. Leadership, connecting and coordinating
2. Campaigns and advocacy
3. Technical guidance and implementation
4. Capacity building
5. Measuring and learning

**Technical areas of work**

- IPC programmes
- IPC to combat AMR
- Hand hygiene in health care
- Injection safety
- Surveillance & burden of HAIs
- Prevention of infections associated with invasive procedures (e.g. surgery and catheters) - sepsis

http://www.who.int/infection-prevention/en/
Why IPC is important for patient outcomes (incl. sepsis)

- Effective **IPC programmes** lead to more than a **30% reduction in overall Health Care-Associated Infections (HAIs) rates**
- **HAI surveillance** contributes to a **25-57% reduction in HAIs**
- Improving **hand hygiene** practices may **reduce pathogen transmission in health care by 50%**
- With strong **IPC national plans**, the **USA** succeeded in reducing central line-associated bloodstream infections by 50%, surgical site infections (SSI) by 17% and MRSA bacteraemia by 13%, between 2008 and 2014
- A **56% decline in MRSA** was achieved over a four-year period in **England** in line with a national target
- A safety culture and IPC programme **reduced SSI risk by 41% in African hospitals**

http://www.who.int/infection-prevention/en/
Global infection prevention and control priorities 2018-22: a call for action

Panel: Call for action

Priorities for IPC at country level

Countries where IPC has just started
- Decisive and visible political commitment, including IPC policy development and enforcement
- Availability of resources (both human and infrastructure)
- Establishment and execution of IPC programmes at the national and acute health facility levels to ensure advocacy, training and data for future improvement and sustainability
- Action to increase availability of in-country IPC knowledge and expertise

Countries with advanced IPC programmes
- Increased accountability with IPC as a quality indicator
- Development of advanced information technology tools to support IPC monitoring and implementation
- Translation of information through enhanced communications to sustain awareness and engagement
- Credible incentives considering the local context to increase compliance rates
- Enhanced education and training to embed IPC knowledge across all disciplines

www.thelancet.com/lancetgh  Vol 5 December 2017
WHO SAVE LIVES: Clean Your Hands campaign

It takes just 5 Moments to change the world

Clean your hands, stop the spread of drug-resistant germs!

Surgical patients are IN your hands. See what's ON your hands. Practice hand hygiene for surgical patients from admission to discharge.

See your hands: Hand hygiene supports safe surgical care

Fight antibiotic resistance: It's in your hands

Links to broader global health issues

http://www.who.int/infection-prevention/en/
Main areas for tackling sepsis according to the resolution

1. Epidemiology and global burden of sepsis
2. Prevention
3. Diagnosis
4. Clinical management, including AMR
Several WHO projects on improving access to essential medicines, in vitro diagnostics (IVDs) and other medical devices/equipment that contribute to prevent, diagnose and treat sepsis, including:

- WHO list of essential medicines with categorization of antibiotics
- Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics
- Antibiotic R&D pipeline report
- Global Antibiotic and Development Partnership (GARDP)
- WHO list of essential in vitro diagnostics
- Mapping of IVDs for AMR, identification of gaps, prioritization and development of target product profiles for priority IVDs
- Semi-open multiplex multi-analyte diagnostic platform for levels 1-2 in collaboration with FIND and MSF that could be used with a sepsis panel
- Priority medical devices and equipment
20th EML: 433 medicines

6th EMLc (children): 314 medicines
EML 25 syndromes guidances/ recommendations

Infectious syndromes included in EML/EMLc

- Community acquired pneumonia*
  - mild to moderate
  - severe
- Pharyngitis
- Sinusitis
- Otitis media
- Hospital-acquired pneumonia
- Sepsis in neonates and children*
- Lower urinary tract infections
- Pyelonephritis and prostatitis
  - mild to moderate
  - severe
- Acute bacterial meningitis
- Complicated intra-abdominal infections
  - mild to moderate
  - severe
- Skin and soft-tissue infections
- Acute invasive bacterial diarrhoea/dysentery*
- Cholera*
- Clostridium Difficile
- Sexually transmitted infections
  - Neisseria gonorrhoeae
  - Chlamydia trachomatis
  - Syphilis
  - Trichomonas vaginalis
- Exacerbations of chronic obstructive pulmonary disease
- Bone and joint infections
- Febrile neutropenia
  - low-risk
  - high-risk
- Severe acute malnutrition*
  - uncomplicated
  - complicated

Antibiotic recommendations by syndrome

*Unless specified, all recommendations are for both EML and EMLc
*All medicines are considered ACCESS antibiotics. Medicines in italics are also included in the WATCH group

Community acquired pneumonia (CAP)

<table>
<thead>
<tr>
<th>Indication</th>
<th>First choice</th>
<th>Second choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild to moderate CAP</td>
<td>Amoxicillin</td>
<td>Amoxicillin + clavulanic acid</td>
</tr>
<tr>
<td></td>
<td>Phenoxymethylpenicillin</td>
<td>Doxycycline</td>
</tr>
<tr>
<td>Severe CAP (EML)</td>
<td>Ceftriaxone or cefotaxime in</td>
<td>Amoxicillin + clavulanic acid in combination with clarithromycin</td>
</tr>
<tr>
<td></td>
<td>combination with clarithromycin</td>
<td></td>
</tr>
<tr>
<td>Severe CAP (EMLc)</td>
<td>Amoxicillin + clavulanic acid</td>
<td>Ceftriaxone or cefotaxime</td>
</tr>
<tr>
<td></td>
<td>Gentamicin in combination with</td>
<td>benzylpenicillin, ampicillin or amoxicillin</td>
</tr>
<tr>
<td></td>
<td>clindamycin</td>
<td></td>
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</tbody>
</table>

Pharyngitis

NOTE: Watchful waiting, symptom relief and no antibiotic treatment should be considered as the first line treatment option.

<table>
<thead>
<tr>
<th>Indication</th>
<th>First choice</th>
<th>Second choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharyngitis</td>
<td>Phenoxymethylpenicillin</td>
<td>Clarithromycin (erythromycin as an alternative)</td>
</tr>
<tr>
<td></td>
<td>Amoxicillin</td>
<td>Cephalexin</td>
</tr>
</tbody>
</table>
**WHO EML 2017: Sepsis**  
**(neonatal and paediatric)**

**EML listings**  
Antibiotics proposed for both EML and EMLc unless specified  
*Endorsement* indicates those antibiotics currently included on EML/EMLc  
*Addition* indicates new antibiotics not currently on EML/EMLc

<table>
<thead>
<tr>
<th></th>
<th><strong>First choice</strong></th>
<th><strong>Second choice</strong></th>
</tr>
</thead>
</table>
| **Endorsement** | benzylpenicillin, ampicillin or amoxicillin  
gentamicin | ceftriaxone or cefotaxime  
cloxacillin in combination with amikacin |
| **Addition** | N/A | amikacin |

**Committee recommendations**

The Expert Committee endorsed the inclusion on the EMLc of gentamicin, in combination with benzylpenicillin or ampicillin or amoxicillin, as the first-choice treatment for sepsis in neonates and children, and of ceftriaxone or cefotaxime as a second-choice treatment.

The Committee recommended the addition of amikacin in combination with cloxacillin as a second-choice option for use in sepsis in neonates and children.
Critically Important Antimicrobials (WHO CIA list)

WHO supports optimization of the non-human use of antimicrobial medicines to preserve their effectiveness by taking a One Health approach.

<table>
<thead>
<tr>
<th>Antimicrobial class</th>
<th>Example of drug(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CRITICALLY IMPORTANT ANTIMICROBIALS</strong></td>
<td></td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>gentamicin</td>
</tr>
<tr>
<td>Ansamycins</td>
<td>rifampicin</td>
</tr>
<tr>
<td>Carbapenems and other penems</td>
<td>meropenem</td>
</tr>
<tr>
<td>Cephalosporins (3rd, 4th, and 5th generation)</td>
<td>ceftriaxone, cefepime, ceftaroline</td>
</tr>
<tr>
<td>Glycopeptides</td>
<td>vancomycin</td>
</tr>
<tr>
<td>Glycylcyclines</td>
<td>tigecycline</td>
</tr>
<tr>
<td>Lipopeptides</td>
<td>daptomycin</td>
</tr>
<tr>
<td>Macrolides and ketolides</td>
<td>erythromycin, telithromycin</td>
</tr>
<tr>
<td>Monobactams</td>
<td>aztreonam</td>
</tr>
<tr>
<td>Oxazolidinones</td>
<td>linezolid</td>
</tr>
<tr>
<td>Penicillins (natural, aminopenicillins, and antipseudomonal)</td>
<td>ampicillin</td>
</tr>
<tr>
<td>Phosphonic acid derivatives</td>
<td>fosfomycin</td>
</tr>
<tr>
<td>Polymyxins</td>
<td>colistin</td>
</tr>
<tr>
<td>Quinolones</td>
<td>ciprofloxacin</td>
</tr>
<tr>
<td>Drugs used solely to treat tuberculosis or other mycobacterial diseases</td>
<td>isoniazid</td>
</tr>
</tbody>
</table>

Prioritize by Prioritization Criterion 1, 2, 3

- Critically Important
- Highly Important
- Important
- Highest Priority
- High Priority
Priority Pathogens List (PPL)

The list is to guide and promote research and development (R&D) of new antibiotics, as part of WHO’s efforts to address AMR.

Priority 1: CRITICAL

- Acinetobacter baumannii, carbapenem-resistant
- Pseudomonas aeruginosa, carbapenem-resistant
- Enterobacteriaceae*, carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

- Enterococcus faecium, vancomycin-resistant
- Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant
- Helicobacter pylori, clarithromycin-resistant
- Campylobacter, fluoroquinolone-resistant
- Salmonella spp., fluoroquinolone-resistant
- Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

- Streptococcus pneumoniae, penicillin-non-susceptible
- Haemophilus influenzae, ampicillin-resistant
- Shigella spp., fluoroquinolone-resistant
Global efforts to tackle AMR

World Health Assembly 2015

UNGA (September 2016)

Global Action Plan (GAP) on AMR

National Action Plans

Global Monitoring Questionnaire

Guidelines on Antimicrobial Use

And more...
### Global strategic objectives

<table>
<thead>
<tr>
<th>Objective</th>
<th>Examples of key actions for national action plans</th>
</tr>
</thead>
</table>
| 1. Improve awareness and understanding of AMR | • Risk communication  
• Education |
| 2. Strengthen knowledge through surveillance and research | • National AMR surveillance system  
• Laboratory capacities  
• Research and development |
| 3. Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures | • IPC in health care (incl. liaison with WASH)  
• Community level prevention (incl. liaison with WASH)  
• Animal health |
| 4. Optimize the use of antimicrobial medicines | • Access to qualified antimicrobial medicines  
• Animal health |
| 5. Ensure sustainable investment in countering antimicrobial resistance | • Measuring the burden of AMR  
• Assessing investment needs  
• Establishing procedures for participation |

Awareness raising activities

Objective 1: “Improve awareness and understanding of AMR through effective communication, education and training.”

A) World Antibiotic Awareness Week

B) Behaviour Change Group

C) Health Workforce Education
Global Momentum in addressing AMR
Progress in Developing multisectoral National Action Plans (Nov
2017)

Country progress of National Action Plan on AMR

<table>
<thead>
<tr>
<th>Date</th>
<th>No information</th>
<th>Not started</th>
<th>In progress</th>
<th>Completed</th>
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<tr>
<td>5 January 2017</td>
<td>44</td>
<td>54</td>
<td>23</td>
<td>61</td>
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<tr>
<td>19 June 2017 (Country self-assessment survey)</td>
<td>43</td>
<td>49</td>
<td>79</td>
<td>61</td>
</tr>
<tr>
<td>27 October 2017</td>
<td>33</td>
<td>61</td>
<td>86</td>
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<tr>
<td>8 November 2017</td>
<td>15</td>
<td>15</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

Data source: Country self-assessment questionnaire (2016) and other updated information received by WHO; some of which are not validated
Maternal and Newborn Health packages delivered along the continuum of care

Focus of the Every Newborn Action Plan:

- Reproductive health, including family planning
- Management of pregnancy complications
- Skilled care at birth: Comprehensive emergency obstetric and newborn care
- Essential newborn care: Emergency care of small and ill newborn babies
- Hospital care of childhood illness

First and secondary level facility:

- Reproductive health, including family planning
- Pregnancy care
- Skilled care at birth: Comprehensive emergency obstetric and newborn care
- Essential newborn care: Emergency care of small and ill newborn babies
- Prevention and management of childhood illness

Community:

- Adolescent and preconception health care and nutrition
- Counselling and birth preparedness
- Home birth with skilled care and clean practices
- Essential newborn care: Postnatal home visits for mothers and newborn babies
- Ongoing care for the child at home

Intersectoral: Improved living and working conditions, including housing, water and sanitation, and food security; education and empowerment, especially of girls; folic acid fortification; safe and healthy work environments for women and pregnant women

Care at birth, triple return:

- Highest impact,
- Highly cost effective,
- Benefits women, stillbirths, newborns
WHO’s technical guidance on neonatal sepsis
WHO guidance on neonatal sepsis

- Integrated practice guide for care of mother and newborn at first level
- Includes preventive measures: WASH, safe and clean delivery and cord care, preventive antibiotic treatment
- Use of syndromic approach to identify neonatal infections, classify, and decide treatment and referral

- In 2014, a guidance document on management of neonatal sepsis, based on clinical experience and expert opinion

- Careful approach
  - Referral to hospital
  - Injectable therapy for 7-10 days (i.e., injectable ampicillin/benzyl penicillin x 4 times plus gentamicin once daily)
  - Single regimen irrespective of severity
WHO Guideline for Management of Possible Serious Bacterial Infection (PSBI) in neonates and young infants when referral is not possible

- For low resource settings in the context of primary health care only where referral is not possible
- Rationalize the use of antibiotics for young infants with suspected infection
- For use by professionally trained health workers, and not for lay community health workers
- The health workers should be appropriately trained, supplied with necessary equipment and medicines and supervised for the identification of signs of illness, referral, treatment if referral is not accepted and close follow up
- Monitoring is essential for ensuring high quality of identification, treatment and follow up activities
- Surveillance for antimicrobial resistance should be strengthened

http://apps.who.int/iris/bitstream/10665/181426/1/9789241509268_eng.pdf?ua=1
The Global Maternal and Neonatal Sepsis Initiative

A global initiative to accelerate the reduction of preventable maternal and newborn deaths due to sepsis

Objectives

- Raise awareness about maternal and newborn sepsis among health care providers, policy makers and the public;
- Assess the burden and the management of maternal and newborn sepsis at global scale;
- Develop and test effective strategies to prevent, detect and successfully manage maternal and newborn sepsis.
2017 Global Maternal Sepsis Study and Awareness Campaign

- WHO launched awareness campaign in the week of 13 Sep, 2017 (the 2017 World Sepsis Day), starting with World Sepsis Congress Spotlight to raise provider awareness on maternal and neonatal sepsis
- STOP SEPSIS campaign was implemented in over 500 facilities around the world
- During one week in November, a massive and coordinated data collection effort took place to assess the burden and the current management of maternal and early newborn sepsis
  - 53 countries, over 2770 women in LMIC (47 countries) and 350 women in HIC
- For more information visit: http://srhr.org/sepsis/
WHO’s Health Emergencies Programme
Infectious Hazards Management (IHM)

- **Timely and appropriate clinical management** is crucial to reduce the fatality rate, e.g.:
  - Viral hemorrhagic Fever: from 80~90% to 40% (West Africa), 18% (Europe and USA, Ebola 2014-15)
  - H5N1: from 60% to 30% (WHO pooled analysis)

- **The WHO Clinical Management team aims** to save lives from emerging infectious diseases by optimal clinical management
  - Rapid deployment of clinicians to field to ensure quality care and field adaptation of guidance
  - Production of rapid guidance and normative guidelines
  - Production and implementation of training programs
  - Clinical research
WHO’s Health Emergencies Programme
Infectious Hazards Management (IHM)

- **Focus on dangerous pathogens infection**
  - Emerging or re-emerging infectious diseases (i.e. Ebola, MERS-CoV, influenza, yellow fever, plague, diphtheria, etc.)

- **Focus on care of critically ill patients**
  - Management of complications such as ARDS, sepsis, septic shock, multi-organ failure

- **Coordination of clinical network** (Emerging Disease Clinical Assessment and Response Network – EDCARN)
  - Prepare and respond to outbreaks
Clinical Management Team (IHM) products

Pandemic & Epidemic Diseases

Critical care training

Learning sequence 5

Sepsis and septic shock
Deliver targeted resuscitation

evidence-based guidelines for supportive care of patients with Ebolavirus disease

https://openwho.org/courses/diphtheria-clinical-management
Conclusions

- WHO leads several programmes focusing on sepsis based on the resolution
- WHO’s role supporting sepsis management and prevention spans from:
  - Networking, coordinating partners’ actions and supporting ID emergency response, to
  - Developing evidence-based guidelines, policies and standards
  - Developing and rolling out implementation strategies, with special focus on resource-limited settings
  - Promoting and leading research
- Mechanisms for better coordination and synergy among the different programmes established and will lead to a more structured corporate approach
- WHO is eager to work with partners to raise awareness on the importance of sepsis and to develop resolutions and actions to tackle this problem
Improving the prevention, diagnosis and clinical management of sepsis

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. If not recognized early and managed promptly, it can lead to septic shock, multiple organ failure and death. It is a serious complication of infection, particularly in low- and middle-income countries where it represents a major cause of maternal and neonatal morbidity and mortality.

Although a precise estimate of the global epidemiological burden of sepsis is difficult to ascertain, some scientific publications reported that it affects more than 30 million people worldwide every year, potentially leading to 6 million deaths. The burden of sepsis is most likely highest in low- and middle-income countries.
SURPRISE! New web page launch: TODAY!

In collaboration and coordination with WHO Regional Offices, Member States and other stakeholders, several WHO programmes listed below are currently working on the public health impact of sepsis, and provide guidance and country support on sepsis prevention, early and appropriate diagnosis, and timely and appropriate clinical management, in order to address sepsis comprehensively.

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