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HOTEL NHOW MILAN

One Health priority research agenda for antimicrobial resistance

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Outline

Overview & AMR burden

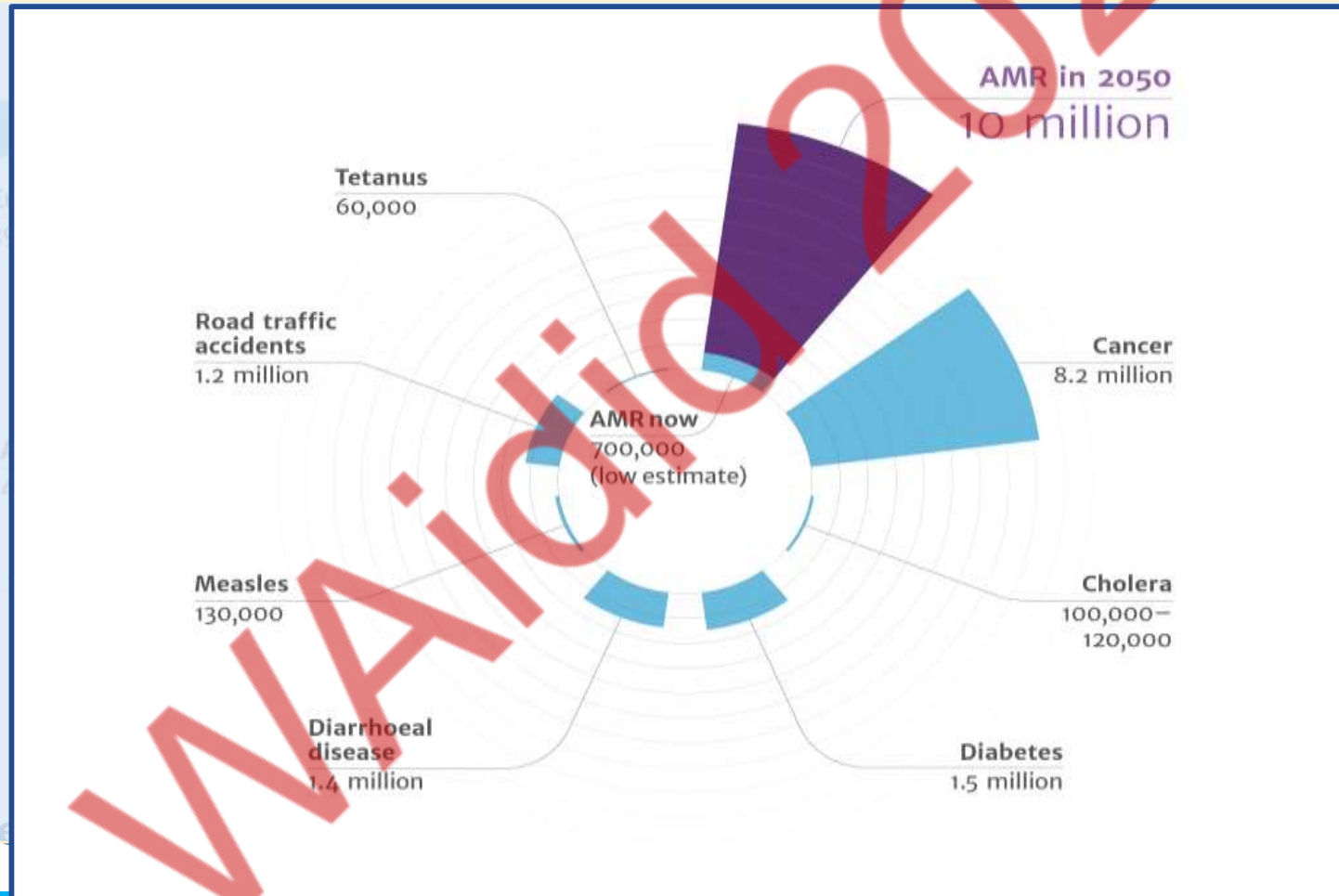
Drivers of AMR

Milestone/Progress in AMR containment

One Health Research Agenda

Conclusion

Antimicrobial resistance (AMR) is one of the top 10 global public health threats facing humanity



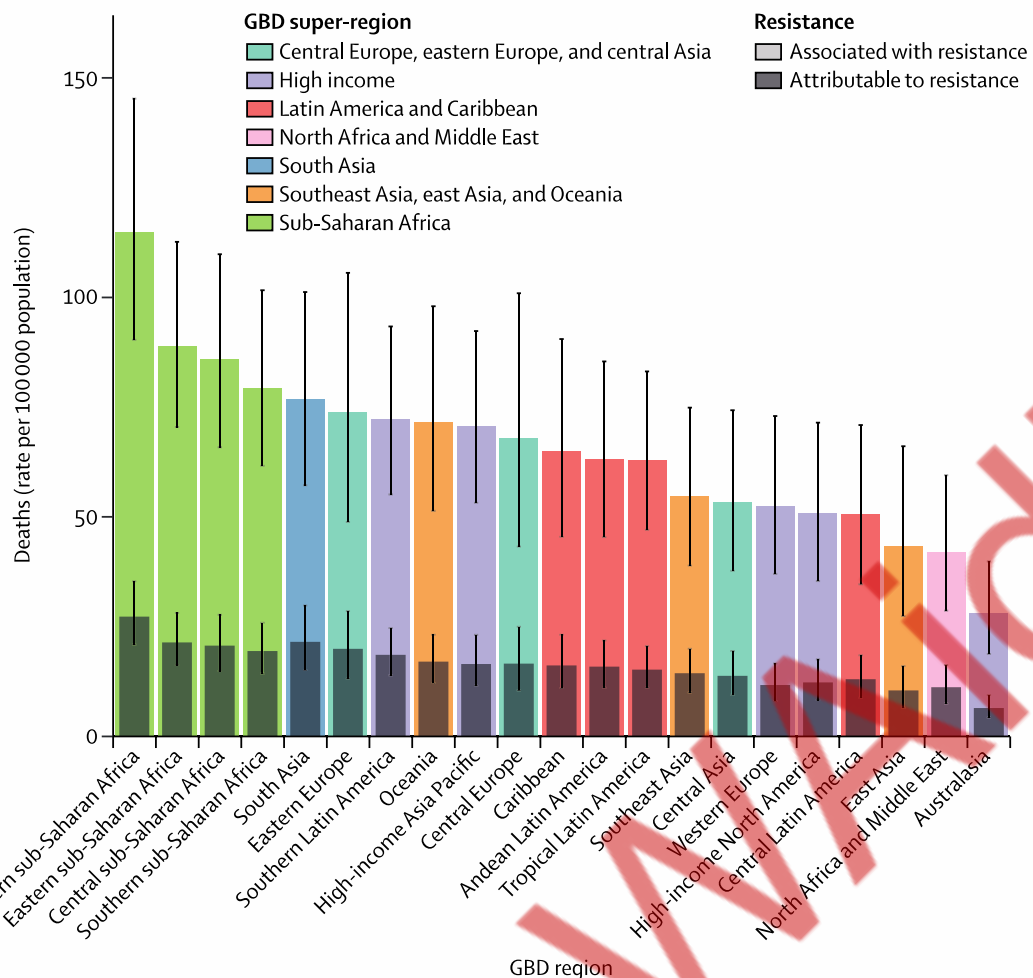
...sive to treat

Mortality rate
24%

35,000
...t drug-resistant
infection (MRSA)

AMR - Not a future problem..

Global death attributable to and associated with AMR, 2019



- 4.95 million deaths **associated** with bacterial AMR
- 1.27 million deaths **attributable** to bacterial AMR

All-age death rate attributable to resistance:

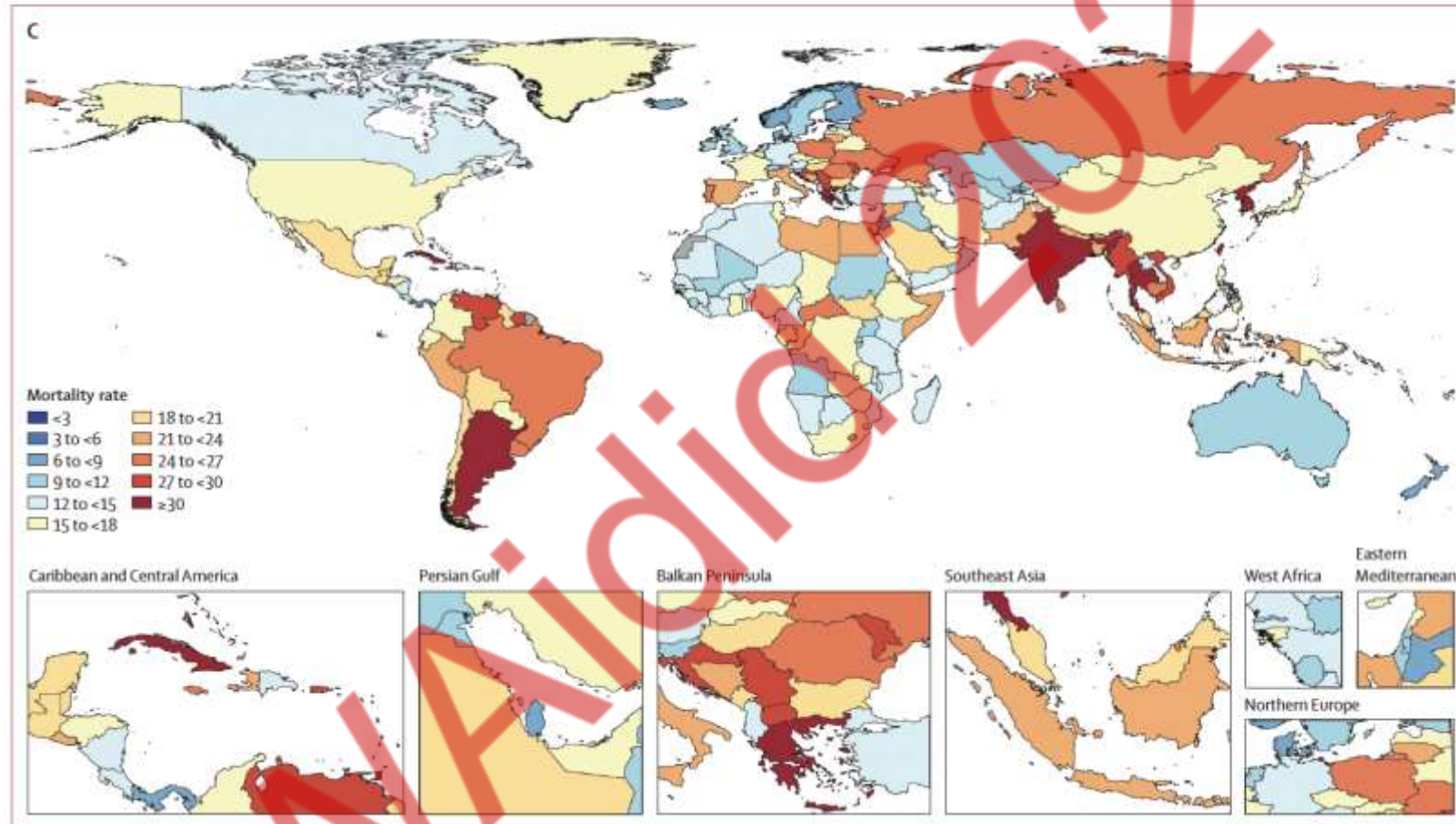
- **highest in western sub-Saharan Africa** (27.3 deaths per 100 000)
- **lowest in Australasia** (6.5 deaths per 100 000).

**Lower respiratory
Bloodstream infections
intra-abdominal infections**

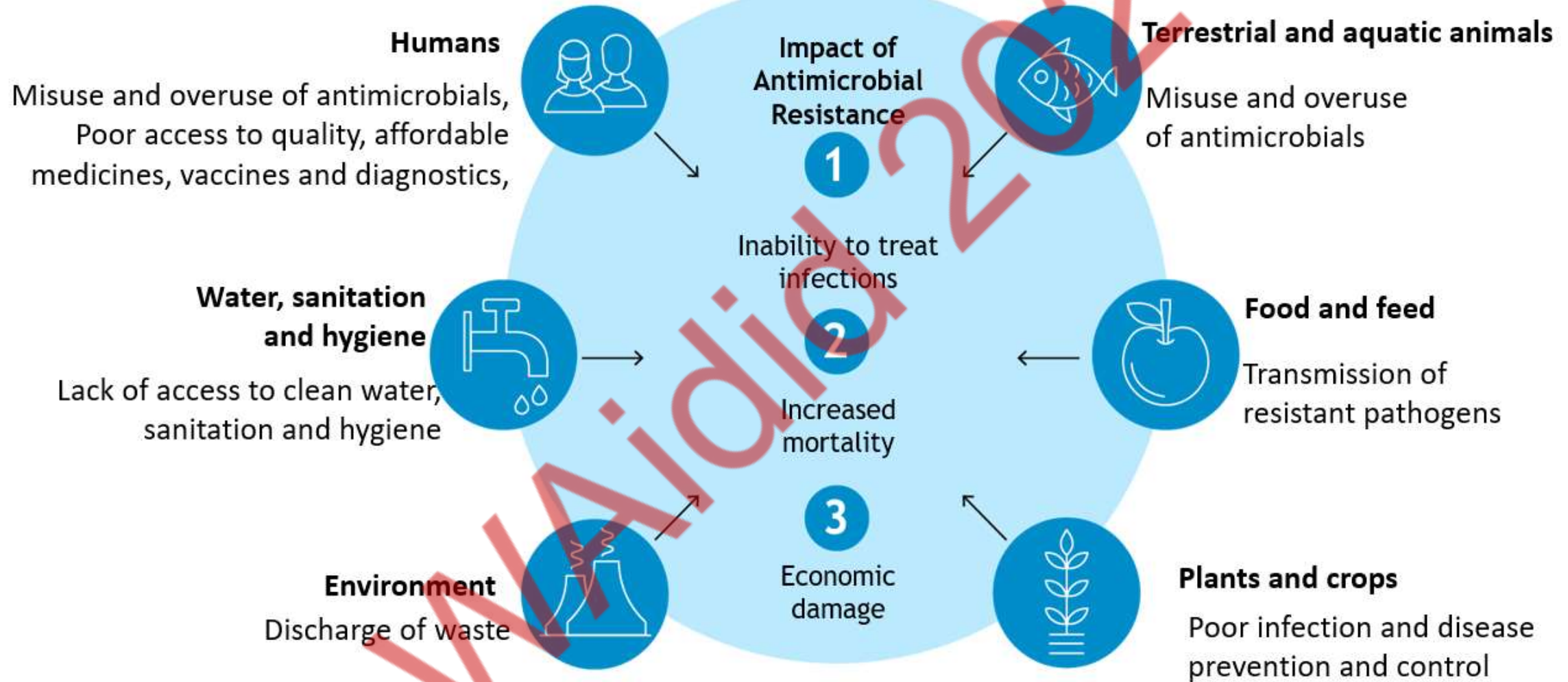


78.8%
of deaths

Death rates per 100 000 attributable to AMR 1990 -> 2021 -> 2050



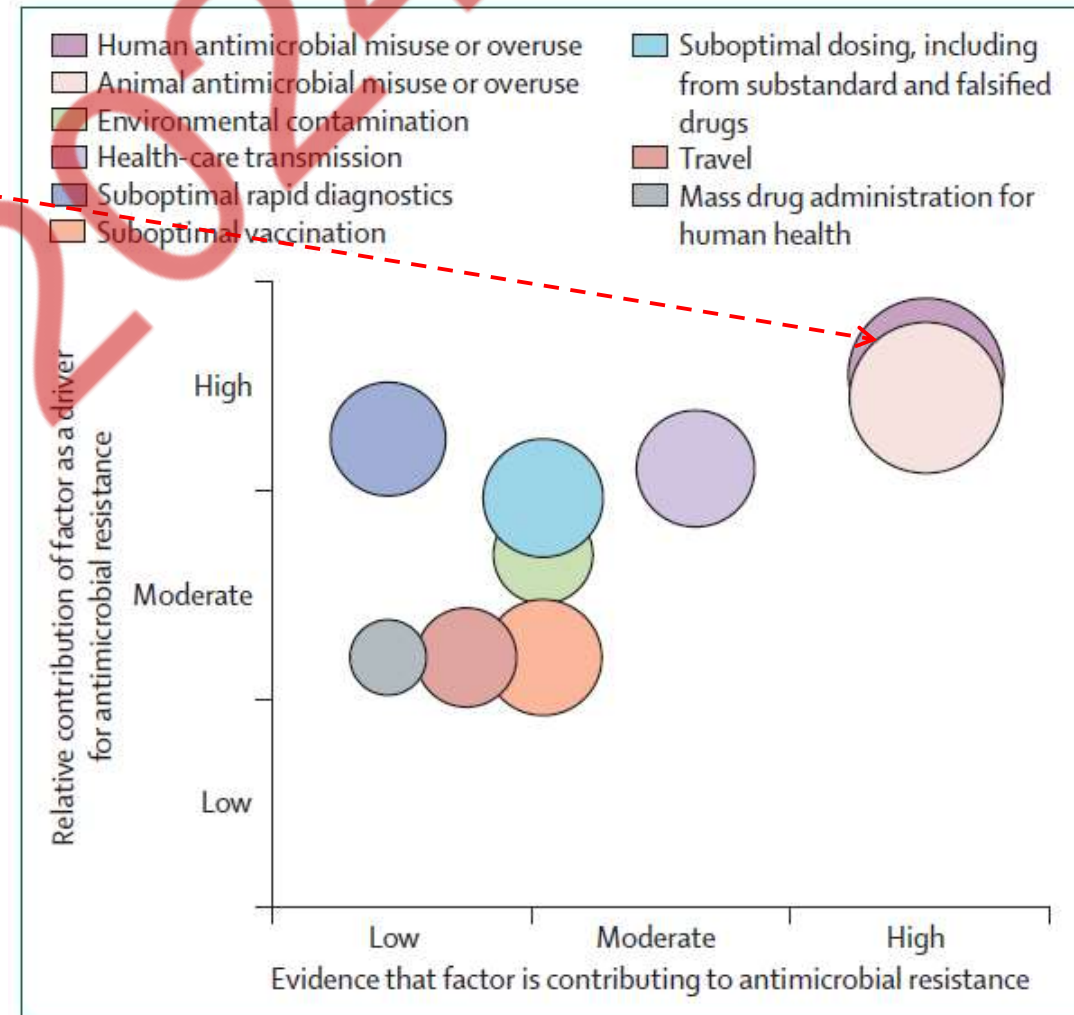
Complex and interlinking drivers are increasing the prevalence of AMR



Drivers of AMR: antimicrobials exacerbates the selection of resistant organisms

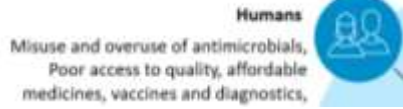
AMR drivers² can either impact directly or indirectly

- **Overuse and misuse of antimicrobials**
- Poor Infection Prevention and control (IPC)
- Agricultural practices
- Globalization and trade
- Lack of new antibiotics
- Lack of clean water, sanitation and hygiene
- Poor public awareness
- Poor access to quality medicines, vaccines and diagnostics



2. Holmes, A. H., Moore, L. S., Sundsfjord, A., Steinbakk, M., Regmi, S., Karkey, A., Guerin, P. J., & Piddock, L. J. (2016). Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet (London, England)*, 387(10014), 176–187. [https://doi.org/10.1016/S0140-6736\(15\)00473-0](https://doi.org/10.1016/S0140-6736(15)00473-0)

Drivers of AMR: Lack of diagnostic tools contributes to antibiotic misuse.



- **Blood cultures** remain the gold standard for diagnosing infections -> still **not widely used** as a standard of care in many **countries**, particularly in LMICs.
- **Diagnostic Gap:** Expanding access to rapid point-of-care tests is critical for better antimicrobial stewardship and combating AMR.

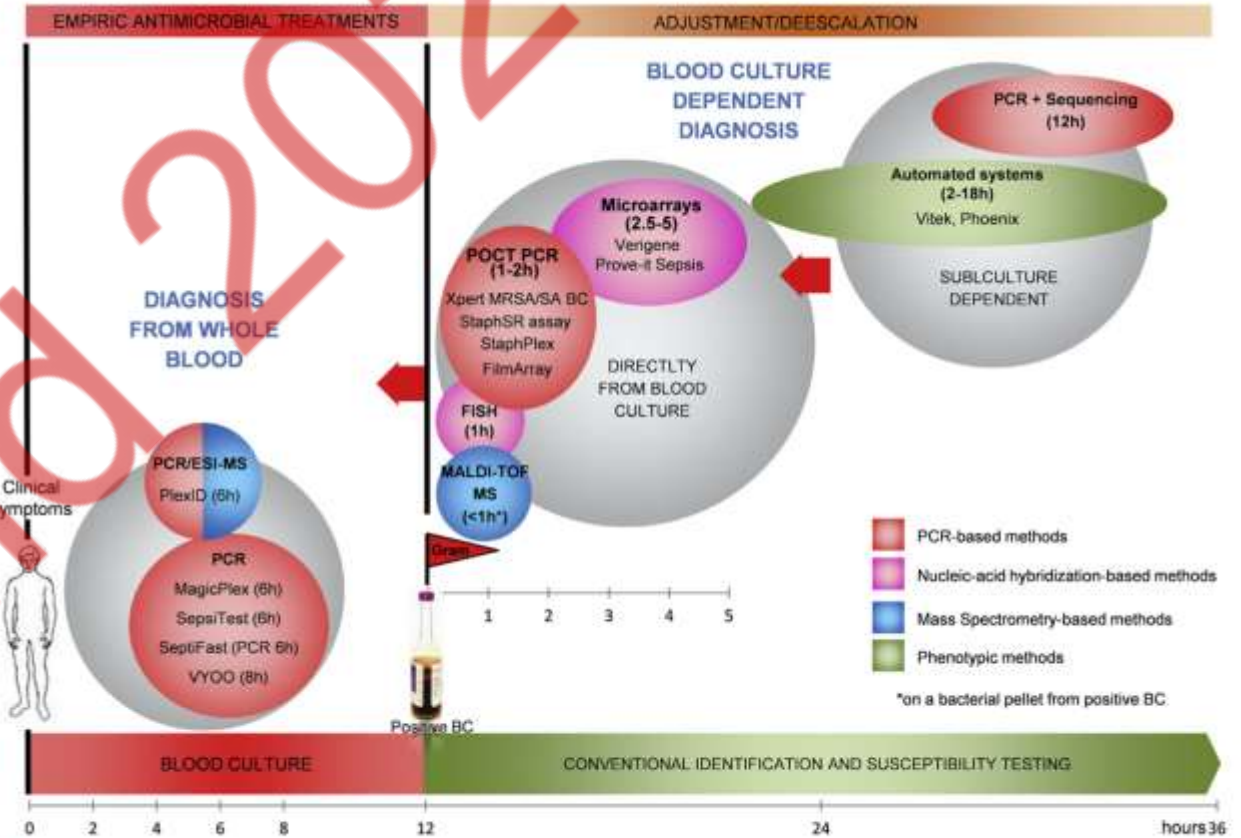


FIG. 2. Nucleic acid methods for the microbial diagnosis of BSI, BC-independent and BC-dependent methods. Nucleic acid-based methods have shortened the time to result BSI diagnosis. In the absence of microbial documentation of the etiologic agent of the BSI, anti-infectious treatments are initiated on the basis of clinical and epidemiologic information. Diagnosis directly from blood samples could shorten the length of empiric treatment.

REVIEW

Microbial diagnosis of bloodstream infection: towards molecular diagnosis directly from blood

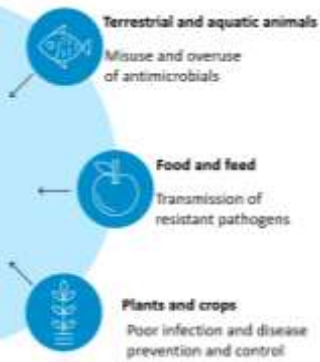
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SL
 PARTNER TO REALITY
 DONNA E RAIMONDO



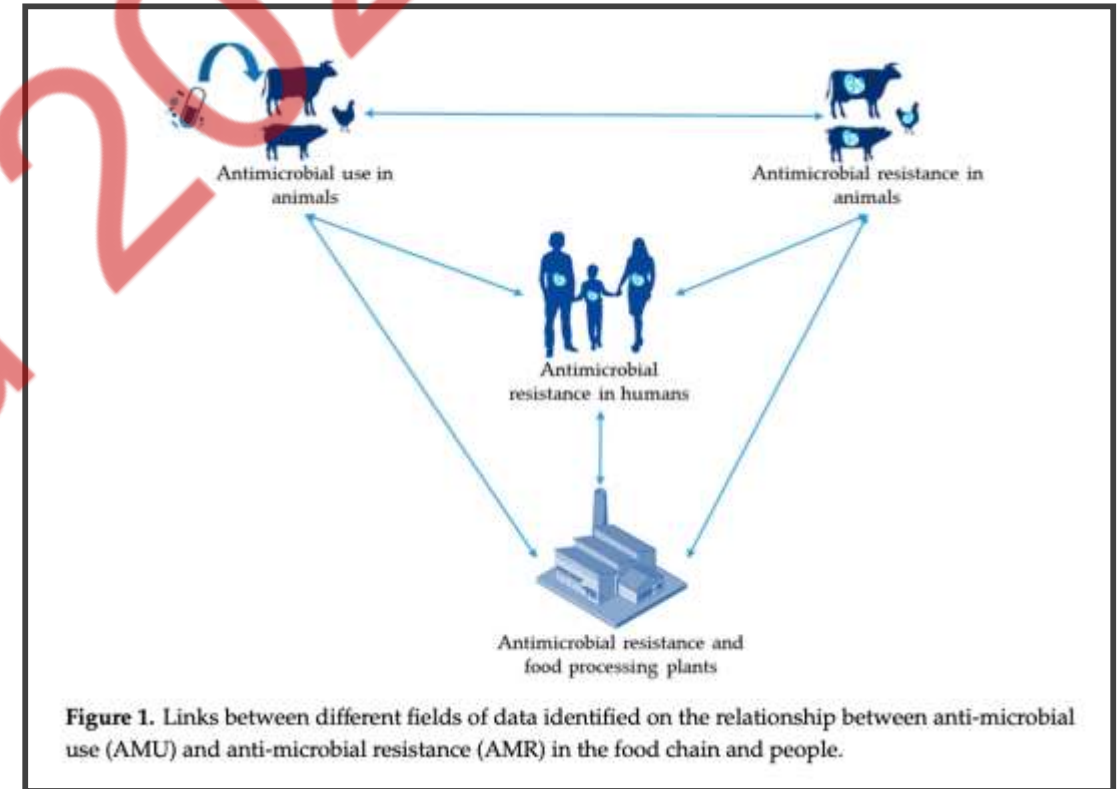
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Drivers of AMR: Overuse of antibiotics in livestock and fishfarming significantly contributes to AMR



•Therapeutic and Non-Therapeutic Use:

- **Prophylaxis:** Administered to entire herds or flocks at risk of disease.
- **Metaphylaxis:** Given to healthy animals in groups where some show infection signs.
- **Growth Promotion:** Used in sub-therapeutic doses to enhance productivity (banned in the EU since 2006).



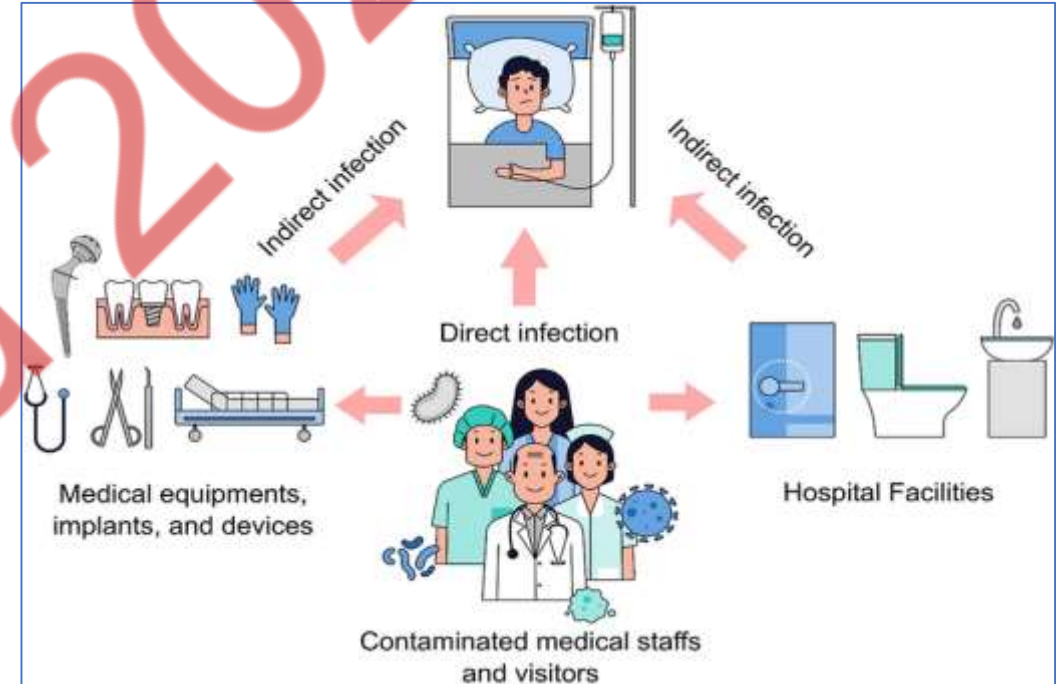
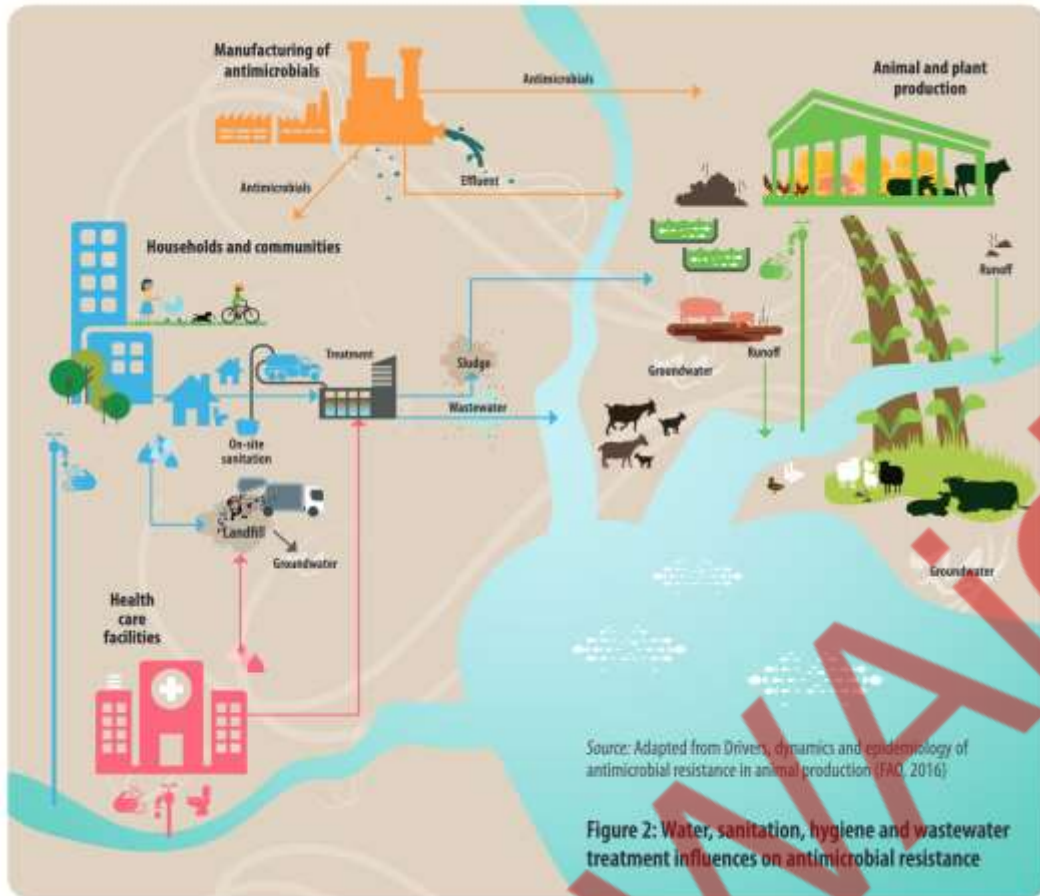
Adapted from «Overview of Evidence of Antimicrobial Use and Antimicrobial Resistance in the Food Chain», Bennani et al

Inadequate hand hygiene, poor sanitation and hygiene, and lack of infection control measures contribute to the spread of resistant infections.

Water, sanitation and hygiene

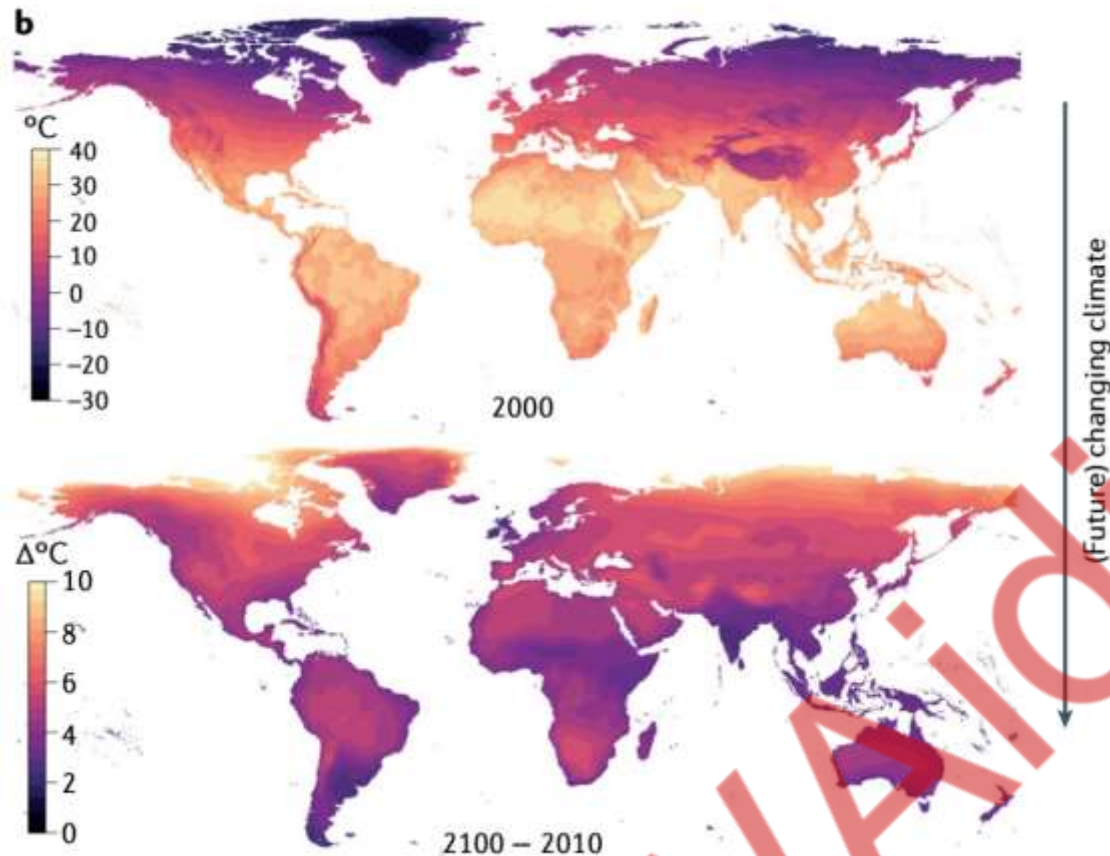


Lack of access to clean water, sanitation and hygiene



Patients who are hospitalized or receive medical treatment are particularly vulnerable to resistant infections.

AMR: The Role of Climate Change



Average monthly maximum temperature in 1970–2000 and difference between 2070–2100 and 1970–2000 averages (data from WorldClim, Shared Socioeconomic Pathway 3 (SSP3))

- Accelerate the spread of resistant bacteria and pathogens.
- Extreme weather events compromise sanitation and water systems
- Climate-induced agricultural shifts may increase antibiotic usage in new regions.

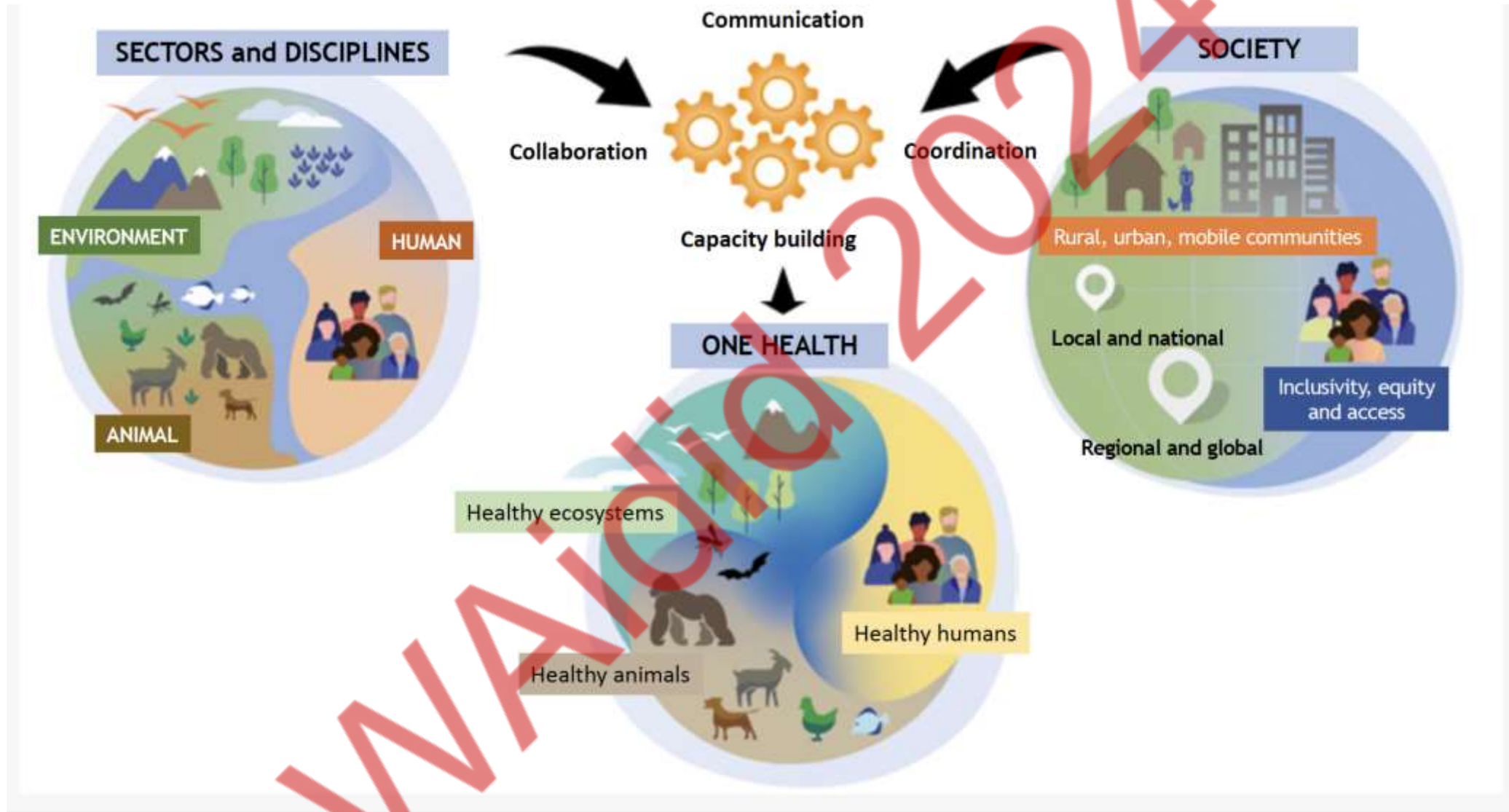
NATURE REVIEWS | MICROBIOLOGY

REVIEWS

Infectious disease in an era of global change

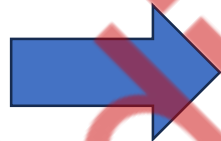
Rachel E. Baker^{1,2,3*}, Ayesha S. Mahmud⁵, Ian F. Miller^{1,4}, Malavika Rajeev¹, Fitsoa Rasambolnarivo^{2,5}, Benjamin L. Rice^{1,6}, Saki Takahashi⁷, Andrew J. Tatem⁸, Caroline E. Wagner⁹, Lin-Fa Wang^{10,11}, Amy Wesolowski¹² and C. Jessica E. Metcalfe^{1,12,13}

...One Health Approach



Milestone/Progress in AMR containment

The Global Action Plan serves as a framework to combat AMR at the global level



MAIN OBJECTIVES:

- Improve **AWARENESS** and **UNDERSTANDING** of AMR.
- **STRENGTHEN SURVEILLANCE** and research.
- **OPTIMIZE THE USE OF ANTIMICROBIALS** in human and animal health.
- **SUPPORT INVESTMENTS IN NEW TECHNOLOGIES AND DRUGS.**

This plan had already recognized the importance of the **One Health** approach, but it primarily focused on human health

Milestone/Progress in AMR containment

Global Collaboration and Partnerships

Strengthening partnerships with governments, NGOs, academia, and the private sector

Facilitating knowledge-sharing and developing global standards for AMR prevention and control.

Supporting low- and middle-income countries in implementing AMR strategies

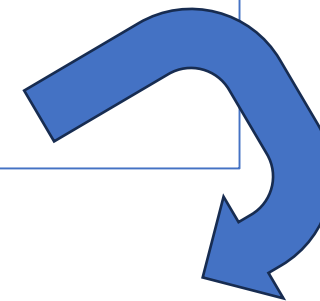
Milestone/Progress in AMR containment

National Action Plans



WHO Implementation Handbook for National Action Plans on AMR:

- **step-by-step guidance**
- Focuses on priority setting, monitoring, and evaluation.
- Promotes a **One Health approach with multisectoral collaboration.**
- Includes **best practices, capacity-building tools,**
- Aligns national efforts with global standards and WHO recommendations.



TrACSS (Tracking Antimicrobial Resistance Country Self-Assessment Survey)

A crucial tool to:

- Track progress
- Identify gaps
- Facilitate reporting in a standardized format
- Multi-Agency Collaboration

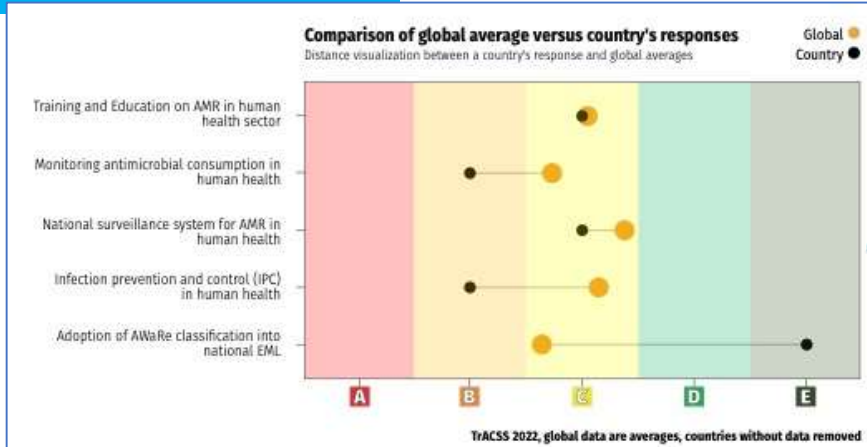
Milestone/Progress in AMR containment

TrACSS (Tracking Antimicrobial Resistance Country Self-Assessment Survey)

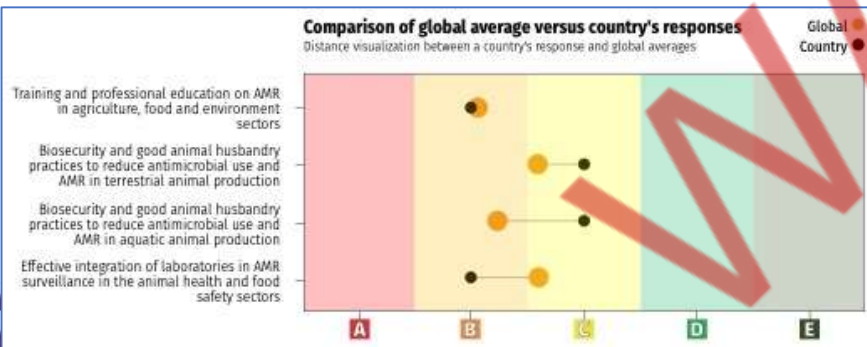
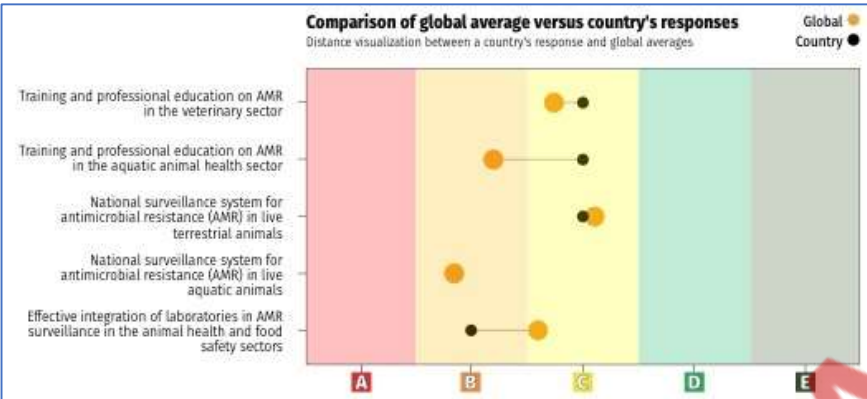
- **Annual Monitoring:** Tracks the implementation of AMR national action plans through yearly surveys.

- **Regional Reporting:** Produces individual country reports for each WHO region based on responses to the 2022 survey.

- **Data Visualization:** Includes tools that compare each country's responses to global averages, highlighting progress, gaps, and areas for improvement.



capacity
none A
limited B
developed C
demonstrated D
sustained E



 170 countries have NAP; 166 reported their progress on TrACSS 2022; Out of 166, 109 NAPs implementation is underway



Milestone/Progress in AMR containment

UNIFIED APPROACH FOR COLLECTING, ANALYZING, INTERPRETING, AND SHARING
AMR DATA GLOBALLY

GLASS (Global Antimicrobial Resistance and Use Surveillance System)

Global Antimicrobial Resistance and Use Surveillance System (GLASS)

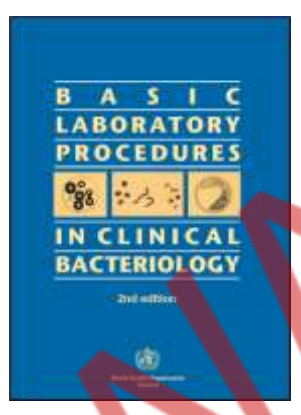
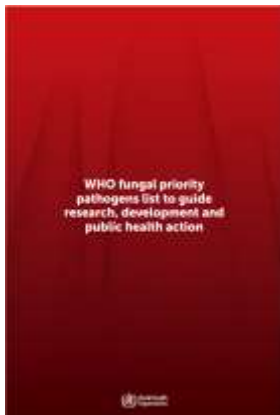
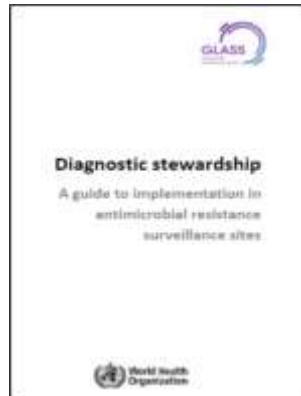
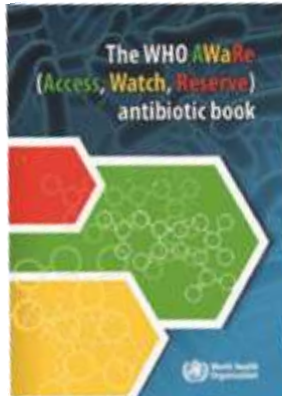
- ❑ **Capacity Building:** collecting data with a unified approach
- ❑ **Expanded Membership-** activation of new sites
- ❑ **Comprehensive Data Inclusion:** development of national surveillance
- ❑ **Data Transparency**
- ❑ **One Health Integration**



- **127** countries **enrolled** in GLASS; **87** countries **provided** data on **AMR** in 2022; **57** countries provided data on **AMC**.

Milestone/Progress in AMR containment

WHO Initiatives on Antimicrobial Resistance and Stewardship in humans



•Clinical Guidance (AWaRe Antibiotics Handbook):

- Provides practical guidelines for the appropriate and safe use of antibiotics, categorized into Access, Watch, and Reserve groups to minimize resistance.

•Diagnostic Stewardship:

•Antimicrobial Stewardship:

- Promotes policies and practices to optimize antimicrobial use in healthcare settings, ensuring effective treatment and preserving antibiotic efficacy.

•Infection Prevention and Control (IPC):

- Implements measures to prevent healthcare-associated infections, reducing the need for antibiotics and limiting resistance spread.

•WHO Bacteria Priority List:

•WHO Fungal Priority List:

THE GLOBAL RESEARCH AGENDA FOR ANTIMICROBIAL RESISTANCE IN HUMAN HEALTH

..even more has been done to **identify** and **prioritize** 40 research topics to produce evidence-based policies to combat AMR globally by 2030.

Goals:

- Improve prevention and diagnostics.
- Develop new treatments
- Promote antibiotic stewardship and public health measures.

Antimicrobial resistance research priorities

Prevention

- Investigate the impact and contribution of community WASH and waste management interventions on the burden and drivers of antimicrobial resistance
- Investigate implementation strategies and the impact of WASH-related interventions in health-care settings on the burden of health care-associated infections and antimicrobial medicine prescribing
- Identify (cost-) effective, acceptable and feasible multimodal infection prevention and control strategies and the relative effect of their components on reducing health care-associated infections
- Assess the impact of vaccines on colonization and infection by resistant pathogens, and on reducing the use of antimicrobial medicines, health-care encounters and health system costs

Diagnosis

- Investigate and evaluate rapid point-of-care tests to discriminate bacterial versus non-bacterial infections
- Investigate and evaluate rapid antimicrobial susceptibility testing methods from blood cultures
- Investigate and evaluate diagnostic tests for detecting pathogens and antimicrobial susceptibility testing
- Investigate and evaluate diagnostic tests for detecting fungal pathogens
- Investigate the clinical and diagnostic value of phenotypic antifungal susceptibility testing
- Investigate, assess and evaluate the implementation of novel rapid point-of-care assays and optimal testing approaches for (resistant) *Neisseria gonorrhoeae*

Treatment and Care

- Investigate antimicrobial stewardship interventions that are context specific, feasible, sustainable, effective and cost-effective in outpatient and inpatient settings
- Identify feasible, effective and scalable pharmacist antimicrobial medicines dispensing practices and related regulatory frameworks to improve antimicrobial stewardship in the community, especially in low- and middle-income countries
- Investigate criteria and strategies to optimize empirical antimicrobial therapy for main infectious syndromes, especially in settings with limited medicine availability, diagnostic capacity and access to health care services
- Determine optimal methods, metrics and targets to monitor antimicrobial use and consumption
- Determine the patterns and drivers of appropriate and inappropriate prescribing, use and consumption of antibiotics
- Investigate approaches to effectively use antimicrobial consumption and antimicrobial resistance surveillance data to inform stewardship and guidelines
- Investigate antibiotic treatment regimens for infections, especially for extended-spectrum beta-lactamase-producing and carbapenem-resistant Enterobacteriales
- Investigate antibiotic treatment regimens for infections by drug-resistant typhoid and non-typhoidal salmonellae
- Investigate empirical antibiotic treatments for gram-negative bacteria causing bloodstream infections among neonates and young children in settings with high antimicrobial resistance prevalence
- Investigate antifungal regimens for infections caused by WHO fungal priority pathogens with critical importance for antimicrobial resistance
- Investigate regimens for urogenital and extragenital sexually transmitted infections in the context of increasing antimicrobial resistance levels

Cross-cutting

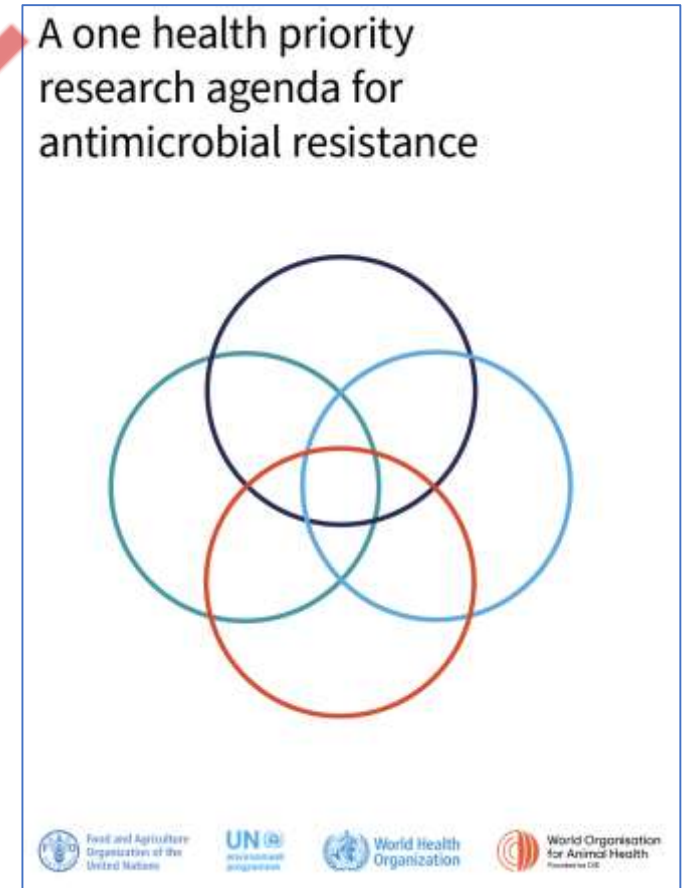
- Investigate the epidemiology, mortality, morbidity and impact of infections by resistant WHO bacterial priority pathogens
- Investigate the epidemiology, morbidity, mortality and impact of infections by resistant WHO fungal priority pathogens with critical importance for antimicrobial resistance
- Investigate factors driving colonization and infection by resistant WHO bacterial priority and fungal pathogens
- Identify optimal surveillance methods to generate accurate and reliable data on the epidemiology and burden of antimicrobial resistance
- Assess the impact of mass administration of antimicrobial medicines on antimicrobial resistance
- Evaluate how currently recommended syndromic sexually transmitted infection management and treatment of people with asymptomatic sexually transmitted infections affect antibiotic prescribing and antimicrobial resistance
- Determine the most (cost-) effective behavioural change interventions to mitigate antimicrobial resistance emergence and spread
- Evaluate the implementation of antimicrobial resistance-related policies and regulations and their effectiveness in mitigating antimicrobial resistance and improving health outcomes
- Investigate implementation strategies for national policies, legislation and regulations to improve infection prevention, patient care and the use of antimicrobial medicines
- Identify the most (cost-) effective interventions and an investment case to mitigate antimicrobial resistance globally and across countries
- Investigate strategies to integrate antimicrobial resistance interventions into broader health, health financing, development and welfare structures and evaluate their impact
- Investigate how regulatory frameworks, marketing incentives and financing models affect the sustainable development, availability, equitable access and use of new antimicrobial medicines

Antimicrobial-resistant bacterial and fungal infections

- Investigate effective preventive TB vaccines that meet WHO preferred product characteristics criteria and demonstrate impact on prevention of infection, disease and recurrence
- Investigate how the diagnostic performance of molecular assays can be improved to detect drug resistance among people with extrapulmonary and pulmonary TB
- Determine optimal diagnostic and treatment delivery models to improve the access, effectiveness, cost-effectiveness, feasibility and acceptability of drug-resistant TB treatment
- Investigate better tolerated, optimally dosed, more effective and shorter combination regimens for treating all forms of drug-resistant TB
- Determine the optimal (cost-) effective, shortest duration and safest TB preventive treatment for the contacts of people with drug-resistant TB
- Investigate strategies for improving treatment outcomes among people with drug-resistant TB who have known risk factors and conditions and among populations experiencing vulnerability
- Investigate the programmatic effectiveness, safety and tolerability of currently used WHO-recommended treatment regimens for drug-resistant TB

Drug-resistant TB

Following Global Action Plan, the international community increasingly recognized the roles of animals, the environment and agricultural practices in the development and spread of AMR.



The **Global Action Plan** remains the primary framework for combating AMR, while the **One Health** approach is an operational strategy adopted to address the issue in a more integrated and holistic manner.

5 Pillars

Top 10 Research Priorities

One Health Research Agenda



- ✓ **TO STRENGTHEN RESEARCH CAPACITY**
- ✓ **ACTIONABLE AND IMPACTFUL IN 4–8 YEARS** (short to medium term).

Transmission

Transmission

Focus → Generating evidence of **DYNAMICS AND DRIVERS** of AMR in shared environmental settings

- ❑ **WHERE** transmission happens
- ❑ **WHAT** drives this transmission
- ❑ **WHY** transmission happens
- ❑ **HOW** human practices affects the interface between humans, plants, animals

Integrated Surveillance

Integrated surveillance

Focus → CROSS-SECTOR SURVEILLANCE to improve common **technical understanding** and **generate and exchange** information about AMR/AMU between One Health sectors

- questions about **HARMONIZATION** and **IMPLEMENTATION** of One Health **INTEGRATED SURVEILLANCE** and applicability to **LMICs**;
- considerations for innovative surveillance approaches to AMR

Interventions

Interventions

Focus → PROGRAMMES, PRACTICES, TOOLS and activities designed to
PREVENT, CONTAIN OR REDUCE
the incidence, prevalence and circulation of AMR

Interventions commonly implemented

- water, sanitation and hygiene (WASH) measures;
- biosecurity and infection prevention and control (IPC) on farms and in health care facilities

significant gaps persist in understanding the availability of potential technical interventions and the reality of implementing these in LMIC contexts

Behavioural insights and change

Behavioural
insights
and change

Focus → **UNDERSTANDING BEHAVIOUR** across **DIVERSE GROUPS** and **ACTORS** that are implicated in the development and circulation of AMR

- ways to change behaviours that increase AMR risk

- ❑ understanding **macrostructural** and policy factors as well as **microcommunity** and individual behaviours
- ❑ understanding **influences on human behaviour in different contexts** (social influences and support, livelihoods, financial resources, etc.).
- ❑ It operates at multiple levels of **complex** systems, including organizational structures that enable or disable AMR mitigation, as well as individual and interpersonal sociocultural practices.

Focus → INVESTMENT AND ACTION in AMR prevention and control

- ❑ policy, governance, legislative and regulatory instruments, cross-sector processes and strategies affecting AMR (e.g. regulation of antimicrobial manufacturing, use, disposal, monitoring), joint planning and policy goals among ministries
- ❑ **cost-effectiveness considerations to support development of the AMR investment**
- ❑ **financial sustainability and long-term financial impact**

Conclusions

- Most AMR drivers stem from a common origin—**inappropriate antimicrobial use across human, animal, and environmental sectors**, emphasizing the interconnectedness of One Health.
- There is **no 'one size fits all' solution**; success requires **synergizing strategies across human, veterinary, and environmental health** to protect antimicrobials effectively.
- Researching the mechanisms of AMR and its long-term persistence across ecosystems is vital for developing **innovative strategies, diagnostic tests and therapeutic agents**.
- Deeper insights into the **bacterial evolution, and AMR mechanisms** in humans, animals, and the environment **are critical** for sustainable solutions.

Thank YOU!

WHAT DOES ANTIMICROBIAL RESISTANCE MEAN FOR EVERYONE?

IT MEANS THAT MOST MEDICINES WE RELY ON TO SAVE LIVES MAY STOP WORKING.

HANDLE ANTIMICROBIALS WITH CARE

EDUCATE. ADVOCATE. ACT NOW.

ANTIMICROBIAL RESISTANCE IS NOT A SMALL-SCALE ISSUE, WE'RE DEALING WITH A GLOBAL HEALTH CRISIS.

HANDLE ANTIMICROBIALS WITH CARE

EDUCATE. ADVOCATE. ACT NOW.

THE THREAT OF ANTIMICROBIAL RESISTANCE IS A PROBLEM FOR PEOPLE AND THE PLANET.

HANDLE ANTIMICROBIALS WITH CARE

EDUCATE. ADVOCATE. ACT NOW.

ANTIBIOTICS ARE LOSING THEIR POWER.

OVERUSING AND MISUSING ANTIBIOTICS IS ASKING FOR TROUBLE. IT CAN LEAD TO ANTIMICROBIAL RESISTANCE WHICH MEANS LIFE-SAVING TREATMENTS STOP WORKING FOR PEOPLE AND ANIMALS.

HANDLE ANTIMICROBIALS WITH CARE

EDUCATE. ADVOCATE. ACT NOW.

WHY IS ANTIMICROBIAL RESISTANCE A BIG DEAL?

BACTERIA, VIRUS, FUNGI AND PARASITES WILL NO LONGER RESPOND TO MEDICINES, MAKING DISEASES MORE DANGEROUS AND UNTREATABLE.

HANDLE ANTIMICROBIALS WITH CARE

EDUCATE. ADVOCATE. ACT NOW.

NOT TAKING ANTIMICROBIALS LIKE ANTIBIOTICS AS PRESCRIBED, CAN LEAD TO ANTIMICROBIAL RESISTANCE.

THIS CAN MAKE INFECTIONS HARDER TO TREAT, LEADING TO:

- MORE COSTS
- LONGER HOSPITAL STAYS
- AND EVEN DEATH

HANDLE ANTIMICROBIALS WITH CARE

EDUCATE. ADVOCATE. ACT NOW.

OVERUSING AND MISUSING ANTIBIOTICS CAN LEAD TO THE EMERGENCE AND SPREAD OF ANTIMICROBIAL-RESISTANT BACTERIA IN PEOPLE, PLANTS, ANIMALS AND THE ENVIRONMENT.

HANDLE ANTIMICROBIALS WITH CARE

EDUCATE. ADVOCATE. ACT NOW.

PROTECT OUR ENVIRONMENT, PREVENT ANTIMICROBIAL RESISTANCE.

WATER POLLUTION CAN CAUSE ANTIMICROBIAL RESISTANCE AND WASH AWAY THE EFFECTIVENESS OF OUR BEST MEDICINES.

HANDLE ANTIMICROBIALS WITH CARE

EDUCATE. ADVOCATE. ACT NOW.

WE'RE IN THIS TOGETHER.

OUR HEALTH GOES HAND IN HAND WITH THE HEALTH OF ANIMALS AND OUR SHARED ENVIRONMENT.

HANDLE ANTIMICROBIALS WITH CARE

EDUCATE. ADVOCATE. ACT NOW.

ANTIMICROBIAL RESISTANCE CAN AFFECT US ALL:

1. WHEN ANTIBIOTICS ARE OVERUSED AND MISUSED IN ANIMAL AND FOOD PRODUCTION, IT CAN LEAD TO DRUG-RESISTANT BACTERIA
2. THE BACTERIA REACHES HUMANS THROUGH HUMAN-ANIMAL CONTACT, OR THROUGH THE ENVIRONMENT (FOOD, SOIL, WATER, AIR)
3. THE DRUG-RESISTANT BACTERIA SPREADS FROM PERSON TO PERSON

HANDLE ANTIMICROBIALS WITH CARE

EDUCATE. ADVOCATE. ACT NOW.

