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WHITEPAPER ON THE
INDO – FRENCH SYMPOSIUM ON

ANTIMICROBIAL STEWARDSHIP & IMPROVED DIAGNOSTICS FOR BETTER MANAGEMENT

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FOREWORD

The Importance of the Indo-French Symposium entitled "Antimicrobial Stewardship to Improve Diagnosis for Better Management" June 2023

The World Health Organization considers Antimicrobial Resistance (AMR) to be one of the ten greatest threats to public health on a global scale. Knowing no borders, crossing countries as it flows, the burden caused by AMR is at least as great as the one of malaria and HIV combined. Such a scourge must be and remain at the center of international discussions and negotiations on global health, aiming at providing health security to everyone.

Beyond its harmful impact on human health, Antimicrobial Resistance also threatens animals, plants and the environment. This is why the efforts to tackle AMR must be pursued and reinforced, through sustained mobilization and coordinated action. It must be done by systematically integrating the "One Health" approach, which fully articulates human health, animal health and ecosystem health.

The link between antimicrobial use in animals and resistance in humans - and vice versa - has been scientifically demonstrated. By taking into account the "unity" of the living world, the "One Health" approach provides a methodological response to optimize the way in which we all work together to combat AMR, not only at international level but also at national and local scales.

France's global health strategy (2023-2027) – published on October 12, 2023 – establishes the "One Health" approach as one of its guiding principles. It focuses on transdisciplinary and multi-sectoral management of major public health issues, to better anticipate, prevent, prepare for and respond to future health crises and emergencies, and to meet the challenges of climate change. Like France, India has made the fight against AMR one of its main priorities for the coming years, through the effective implementation of the "One Health" approach.

The joint Indo-French commitment was showcased at the symposium on Antimicrobial Stewardship and Improved Diagnosis for Better Management, organized in New Delhi at the French Embassy on June 20 this year. It shows the mutual determination of both countries to collaborate, by encouraging research networking .

Dr. Anne-Claire Amprou
French Ambassador for Global Health.

FOREWORD

Prof. Y K Gupta
President AIIMS Bhopal and President AIIMS Jammu
Principal Advisor India, Global Antibiotic Research and Development Partnership (GARDP)
Vice Chairman, Standing National Committee on Medicines (SNCM), GOI Former Dean & HOD Pharmacology, AIIMS New Delhi

Antimicrobial Resistance is a pressing issue globally with dire consequences for public health and the economy. It is rightly being said that if we do not act now, we will soon be hitting the post antibiotic era. Addressing AMR requires a multifaceted approach involving government regulations, healthcare professionals, pharmaceutical companies, and the public. With concerted efforts and global cooperation, it is possible to mitigate the threat of AMR and ensure the continued effectiveness of antibiotics for future generations. The One Health approach will be pivotal in the implementation, sustainability, and success of the mitigation strategies.

The First Indo-French AMR symposium was curated on this premise, and it gives me immense pleasure and pride to be a part of this pioneering endeavour. The sessions were engaging, and the event had all the relevant stakeholders with in- depth insights on the problem at hand and plenty of key takeaways and actionable.

I would like to congratulate biomerieux, French embassy, CEFIPRA and IFI for this ground-breaking initiative, that has a huge potential of bringing about collaboration and global concerted efforts, hence proving as a deterrent in the AMR rise. We sincerely hope that this shall translate into a better healthcare ecosystem for all.

FOREWORD

Antimicrobial resistance (AMR) poses both health and economic burden for patients and healthcare systems, globally. India has a large burden of infectious diseases and is one of the largest consumers of antibiotics in the world. The efficacy of several antibiotics is jeopardized by the emergence of resistant microorganisms. As per an ICMR study, many patients in India may no longer benefit from carbapenem, a group of antibiotics, administered typically in ICU settings to treat pneumonia and septicemia, as bugs have developed resistance to it. Multiple interlinked factors are at play including high burden of infections, a resource-limited public health infrastructure, lack of a robust diagnostic framework, poor infection control practices and the behavioural trend of clinicians to continue empirical treatment practices, have contributed to the crisis of AMR in India. There is a large unmet need to address AMR with a more holistic approach. The ICMR-AMR Surveillance Network fulfils an important gap by providing evidence for trends of AMR in tertiary care hospitals in India. There is need to expand the footprint of this network to secondary level hospitals. A better understanding on how these bugs evolve and are transmitted can be immensely helpful in containment of AMR. Global partnerships and multidisciplinary collaborations have a huge potential of addressing this mammoth task.

The First Indo-French AMR symposium was a commendable step in this direction. As the world continues to grapple with this challenge, it is crucial to prioritize and sustain efforts to mitigate the impact of AMR and ensure the continued efficacy of antimicrobial drugs.

Dr. Kamini Walia
Scientist F, Indian Council of Medical Research, ICMR

FOREWORD

Air Cmde, Dr. Ranjan Kumar Choudhury
VSM Advisor, Healthcare Technologies,
National Health Systems Resource Centre

1. Unregulated and inappropriate use of antibiotics globally has raised serious concerns on combating Antimicrobial Resistance (AMR) worldwide. Rising trends in purchase power, easy availability of antibiotics over the counter without prescription, self-medication, use of antibiotics indiscriminately in agriculture, livestock animal sector etc has contributed to the epidemic of AMR.
2. Government of India has given due cognizance to the problem of Antimicrobial Resistance (AMR). Ministry of Health and Family Welfare (MoHFW) has initiated various activities for containment of AMR as under:

(A) National Action Plan for containment of Antimicrobial Resistance (NAP-AMR) was launched on 19th April, 2017, involving stakeholders from various ministries / sectors.

(B) National Programme on Containment of AMR was initiated during the 12th Five Year Plan. National Centre for Disease Control (NCDC) coordinates this programme. Under the programme National AMR surveillance network of state medical colleges, labs (NARS-Net) have been established in order to generate quality data on AMR for seven priority bacterial pathogens of public health importance using WHONET software.

(C) National Guidelines on Infection, Prevention and Control in Healthcare facilities were released in Jan, 2020. These guidelines have been shared with various stakeholders across the country to be used in training modules for country-wide trainings in a systematic manner.

(D) Under the programme, NCDC conducts AMR surveillance through a network of 30 state medical college laboratories in 25 states. The network is expanded across the country in a phased manner.

(E) Indian Council of Medical Research (ICMR) coordinates another AMR surveillance network of 20 laboratories located in tertiary care centres (both public and private) in the country.

(F) Antimicrobial stewardship (AMSP) activities: In order to promote rational use of antibiotics among the healthcare providers, a series of sensitization and training workshops have been organized in different healthcare facilities in the country for the benefit of the practicing clinicians.

(G) Standard treatment guidelines developed by NCDC for rational use of antibiotics have been made available to clinicians across the country.

(H) To create awareness among the public about AMR, various IEC activities like quiz competition in schools, participation in Perfect Health Mela, poster & quiz competition for healthcare workers at NCDC and the sites included in the NARS-Net during World Antibiotic awareness each year have been conducted to raise awareness about AMR.

(I) IEC material (audio /video /Print OD Media) to raise awareness about AMR and to prevent misuse of antibiotics has been made available on the website of NCDC for use by the States-UT governments and other stakeholders.

3. There is an urgent need for developing rapid highly sensitive, affordable and cost-effective detection platforms for AMR diagnostics. Rapid diagnostic tests (RDTs) are considered as an essential weapon in any strategy against AMR. RDTs have known to reduce mortality, reduce the hospital stay, and lower health costs.

4. The conventional methods & technologies addressing AMR diagnostics & antibiotic sensitivity testing (AST) employed in clinical microbiology are tedious, with high turn around time and usually expensive. Non-conventional technologies like whole genome sequencing, MALDI-TOF/FTIR spectrophotometry, and microfluidics technologies are the emerging technologies capable for addressing the gap.

5. It is important to develop point of care diagnostic tests for early decision making and initiation of the appropriate treatment. Government of India has always supported and encouraged such innovative technologies in the country. National Health Innovation Platform (NHInP) is an IT platform for submission of such novel technologies which is appraised by a Technical Appraisal Committee at the MoHFW. Such innovative rapid Point of Care tests/ devices which can detect and analyse the sensitivity pattern of the microbes will be the answer to the growing menace of AMR in the country.

FOREWORD

Dr. Shirshendu Mukherjee
Mission Director - Grand Challenges India Mission In charge - Mission COVID Suraksha Head,
Specialized Services Group Head, Communication Head, India-CEPI

Antimicrobial resistance is a challenge which the global community is facing. It is the next pandemic which be a challenge for both human and animal health. The emergence of resistant pathogen and irrational use of frontline antibiotics is root cause of the challenge. The global scientific community has the responsibility to address the challenge by creating pipeline of new anti-microbials to be part of our drug portfolio also create awareness to prevent irrational use of antibiotics. We at DBT-BIRAC through it various programs are addressing the challenge, by supporting initiatives to develop diagnostic platforms, new vaccine development initiatives to reduce disease burden and also supporting programs for new antimicrobial development. We need a mission mode approach, multidisciplinary team of researchers, clinicians industry partner's and global partnership to address the AMR challenge.

FOREWORD

The Indo-French Symposium on Antimicrobial Stewardship and Improved Diagnosis for Better Management highlights the urgent need for a mission-mode approach to combat antimicrobial resistance. I am delighted to write the foreword for this white paper encapsulating the essence of the symposium's discussions, insights, and collective wisdom.

At the core of this symposium was a crucial lens through which to view AMR – the One Health concept. This interdisciplinary perspective acknowledges the interconnectedness of human, animal, and environmental health, recognizing that

effective solutions to AMR demand collaborative efforts that transcend traditional boundaries.

The white paper distils the invaluable contributions of experts, encapsulating their expertise, insights, and recommendations. As the symposium concluded, it was evident that our collective journey had only just begun. This white paper is a testament to our commitment to combating AMR through innovative thinking, cross-disciplinary collaboration, and proactive action.

The panellists, who generously shared their knowledge and insights, guided us through a range of pivotal questions like defining OneHealth, global ecosystem dynamics, stakeholder engagement, stewardship programs, the collateral impact of AMR on every walk of life, shared and sector-specific challenges in the containment of AMR, alternative therapeutics, diagnostics and other innovative approaches.

Considering the current sub-optimal status of GAP and NAPs implementation, it is evident that we need alternative approaches to contain the AMR scourge. Annihilating "nightmare bacteria" solely with newer antibiotics is an inadequate prescription for the AMR pandemic. Targeting Universal Health Coverage and AMR containment without sustainable access to affordable and effective antimicrobials and diagnostics would be a myth. As Seamus O Brien of GARDP says, AMR "is a public health failure, and it needs to be addressed urgently."

Moving ahead, we can not do the same and expect a different result. Acknowledging the critical role of diagnostic and antimicrobial stewardship in combating AMR is essential. The significant advancement in digital technologies is a blessing that we should harness to enhance the efficiency of surveillance, diagnosis, and the optimal utilization of antimicrobials.

May the thoughts and recommendations captured within these pages catalyze continued dialogue, exploration, and, most importantly, impactful change.

Dr. Ranga Reddy Burri
President – Infection Control Academy of India

FOREWORD

Dr. Benjamin Roche
Institut de Recherche pour le Développement, - France

The "One Health" approach, which acknowledges the interconnection between environmental, animal and human health, stands as a pivotal approach in preventing and combating antimicrobial resistance (AMR). Indeed, this approach acknowledges that the overuse or misuse of antibiotics in humans, animals, or agriculture contributes to the emergence and spread of drug-resistant pathogens in the other compartments. By considering this interdependency, the "One Health" approach facilitates a comprehensive understanding of the dynamics behind AMR, enabling the development of holistic strategies to mitigate its spread.

The "One Health" approach also highlights the necessity to foster collaboration among diverse sectors-human medicine, veterinary medicine, agriculture, environmental science—to collectively address AMR. This collaboration encourages the sharing of knowledge, data, and resources, leading to more informed decisions in managing antimicrobials. Additionally, it promotes the judicious use of antimicrobials across sectors, reducing selective pressure on microbes to develop resistance.

This is also crucial to not oppose the approaches. Adopting a "One Health" perspective amplifies the effectiveness of interventions against antimicrobial resistance that relies on human and veterinary medicine, including diagnostic and therapies development. But, the integration of surveillance systems across human and animal health enables early detection and response to emerging resistance patterns. Furthermore, it facilitates the development of novel antimicrobial alternatives and vaccines while emphasizing the importance of infection prevention and control measures. This comprehensive strategy ensures a more resilient defense against AMR, safeguarding the efficacy of antimicrobials for current and future generations.

This is why embracing the "One Health" approach is not merely a choice but a necessity in the battle against antimicrobial resistance. Its holistic nature acknowledges the intricate connections between humans, animals, and the environment, advocating for a collaborative, informed, and proactive approach to preserve the effectiveness of antimicrobials and protect global health.

FOREWORD

The Importance of the Indo-French Symposium entitled "Antimicrobial Stewardship to Improve Diagnosis for Better Management" June 2023

The importance and global threat of Antimicrobial Resistance (AMR) cannot be overstated. No geographic region or country has been spared, and the proportion of infections which are resistant to currently available antimicrobials is growing at an alarming rate. It has been called "The Silent Pandemic" but it can equally be called "The Pandemic without an End" since no slowing is in sight.

In 2014, public health officials and economists predicted that by the year 2050 there would be 10 million AMR-related deaths globally (more than cancer deaths predicted for that year), but this did not include all types of infections and was acknowledged to be an under-estimate. Indeed, a recent comprehensive global analysis showed that in 2019, it is estimated that 1.27 million people died directly from bacterial AMR infections, with another 4.95 million deaths associated with bacterial AMR. These frightening numbers give us a glimpse of what will happen each and every year if we do not control or slow global AMR, with numbers likely to increase as AMR continues to spread world-wide. Additionally, the prospect of uncontrolled AMR will have a disastrous impact on "usual medical care" as we know it, making even routine procedures like elective surgery and cancer chemotherapy exceedingly dangerous or deadly due to the AMR-related infection risk.

We continue to see a disproportionate burden of AMR in low- and middle-income countries (LMIC), making the AMR saga even more worrisome with respect to its impact on them - the countries and populations who are inadequately prepared or insufficiently funded to control its effects and its spread.

The key actions to "winning the war" against AMR cannot be shouldered by any single entity, whether it is an international organization, a government, a private industrial, a non-governmental organization (NGO), an academic research group, or even a patient advocacy group. The vital and complementary roles of each of these bodies have shown that partnerships are key in fighting the global AMR menace: significant and meaningful collaborations involving multiple public and private players have demonstrated synergy and improved ability to fight AMR.

The crucial role of partnerships in our ongoing struggle to control and slow the growth and impact of AMR is highlighted by the Indo-French symposium which transpired in June 2023. This collaboration between the Indian and French governments, private industry and academic researchers has highlighted the strength of such mutually beneficial and complementary relationships.

In the ongoing struggle against AMR, we must all use our respective skills, influence and collaborative spirit if we hope to secure a safe and healthy environment for future generations, where AMR will not become the menace which threatens our personal health and leaves our healthcare systems and economies in shambles.

Dr. Mark Miller
MD, Executive VP, & Chief Medical Officer,
bioMerieux SA

FOREWORD

Dr. Marc Bonneville
Vice President
Medical and Scientific Affairs, Institut Mérieux

Antimicrobial resistance (AMR) is among the top 10 public health threats, estimated to be responsible for nearly 5 million deaths in 2019. This is a global problem, but particularly so in countries with limited resources. The socio-economical impact of AMR is huge as it is associated with increased healthcare costs, higher hospitalization rates and longer stays, long term disabilities and loss of productivity.

Many factors contribute to the acceleration of AMR, like the overuse or misuse of antimicrobials in humans, in animals and in agriculture, the massive release of antibiotics in the environment by the pharmaceutical sector, the dissemination of antimicrobial resistance genes through horizontal gene transfer, and the transmission of AMR genes or bugs between the human, animal and environmental sectors, which is further worsened by poor sanitation and hygiene.

Under the impetus of the WHO, national action plans have been launched worldwide that aim to tackle AMR through a multi-pronged approach combining enhanced communication, education and training, strengthened surveillance and research, effective sanitation, hygiene and infection prevention measures, as well as optimized antimicrobial use in humans and animals. Despite this, there's still a long way to go to solve the AMR problem, and any initiative such as the Indo-French meeting that has addressed many of the above issues fleshed out in the present report can only be encouraged to move forward together on this path.

As highlighted in the following pages, an effective fight against AMR must be global, holistic and cross-sectoral, and both public and private actors have a major role to play. The challenges are still immense, but the increased global awareness of the importance of fighting AMR across sectors and disciplines, of the central role played by microbiology diagnostics to curb AMR, and of the increased willingness of national and global players to mobilize sufficient funds to ensure the sustainability of the actions initiated to tackle AMR, should encourage us to pursue them relentlessly.

FOREWORD

The growing global and societal concern about the Rise of Antimicrobial Resistance (AMR) underscores the fact despite the progress we have seen in improving healthcare since the invention of antibiotics, we as a society were perhaps a bit hasty in assuming that we had achieved a victory over microbes. This was evident in the ill-informed claim made in the 1960's - "It is time to close the book on infectious diseases". As a recent pandemic and increasing public health challenge of AMR shows, it was too early and a little presumptuous to make such a claim. A lot more needs to be done and understood to combat future widespread diseases and public health crises like AMR.

A future without effective antibiotics presents a future with significant challenges. This calls attention to the urgency with which we must act to address antimicrobial resistance (AMR), to ensure we have the right tools necessary to save lives and protect the health of our communities. Currently, infections caused by antimicrobial-resistant microorganisms are difficult to treat because antimicrobials are increasingly becoming ineffective against these infections resulting in higher mortality rates.

Medical and environmental bodies and institutions in all the countries (most definitely in countries with high burdens) need to collectively work together to find definitive and implementable solutions. It is in this context that the First Indo-French AMR Symposium on Antimicrobial Stewardship: Improved Diagnosis for Better Management was conceptualized to bring under one roof all the subject matter experts and relevant stakeholders to collectively work towards effective solutions under the overarching One Health Approach.

bioMérieux, as a pioneer in Infectious Diseases Diagnostics, was honoured to work on this event in collaboration with The French Embassy, Institute France, Indo-French Centre for the Promotion of Advanced Research. It gives us immense pleasure to see the overwhelming response that we received from various stakeholders and attendees.

Key to the success of an endeavour of this scale is the sustained ability of mitigation strategies across all sectors. bioMerieux in its unwavering commitment to the cause, looks forward to all possible collaborations and public engagements, and brings about a transformation in healthcare.

Mr. Saurabh Rajadhyax
Senior Vice President, Clinical Operations,
bioMerieux ASPAC

FOREWORD

Mr. Rajan Nagar
Vice President & General Manager,
bioMerieux South Asia

I on behalf of bioMérieux India, would like to extend my deepest gratitude to His Excellency, Ambassador of France to India, Mr. Emmanuel Lenain for hosting the first **"Indo French Symposium on Antimicrobial Stewardship - Improved Diagnosis for Better Management"** held at the French Embassy on 20th June 2023! I would also like to thank all the experts from India and abroad, who came together under one roof to share their rich experience and expertise on "AMR and The One Health" approach. I would also like to take this opportunity to extend my sincerest gratitude to Institut français India & CEFIPRA, ICMR, NHSRC, NCDC & WHO India office for their Scientific inputs and deliberations in the event. We owe each delegate a special vote of thanks for being a part of this event and making it memorable with their presence.

This White Paper is an effort to capture the rich scientific discussions during the proceedings of the Pre-Conference Workshop as well as various Panel discussions & Fireside Chats, in the pioneering Indo-French AMR Symposium. First, this is a collaborative endeavour that marked a significant milestone in the ongoing global effort to address one of the most unprecedented challenges of our times – the emergence of antimicrobial resistance and its far-reaching consequences for public health, agriculture, and the environment. The apocalyptic predictions of a backsliding of modern medicine are translating into reality with drugs not being able to keep pace with the evasive bugs due to AMR. In an increasingly interconnected world, the spread of antimicrobial resistance transcends geographical, disciplinary, and societal boundaries, demanding a unified comprehensive approach. Interdisciplinary collaboration is at the heart of the One Health concept and will be a cornerstone in the implementation of AMR mitigation strategies.

The Indo-French Symposium on AMR is a testament to the unwavering commitment of both nations to foster global cooperation, and knowledge exchange, and create consensus for resolute solutions to combat this multifaceted threat. This symposium provided a unique platform for experts, researchers, policymakers, healthcare professionals, and relevant stakeholders from India and France to come together and engage in constructive dialogues. The insightful exchange, research findings, best practices, and experiences will go a long way toward a deeper understanding of the intricacies of antimicrobial resistance. By combining multiple perspectives, expertise, and resources from both countries, we hope to create a strong scaffolding of new strategies, interventions, and policies that can address AMR on a global scale.

We truly believe that the Indo-French Symposium on AMR will catalyze transformative change, fostering sustainable partnerships and pathbreaking initiatives under the overarching One Health umbrella for a safer and healthier world.

AMR BACKGROUND

Virtually addressing the G20 Health Ministers' meet in Gandhinagar, Gujarat, in August 2023, Prime Minister Modi said AMR is a grave risk to global public health and all pharmaceutical advancements so far. He expressed happiness that the G20 Health Working Group has prioritized ''One Health''. Our vision of ''One Earth, One Health'' that envisages good health for the entire ecosystem - for humans, animals, plants, and the environment.

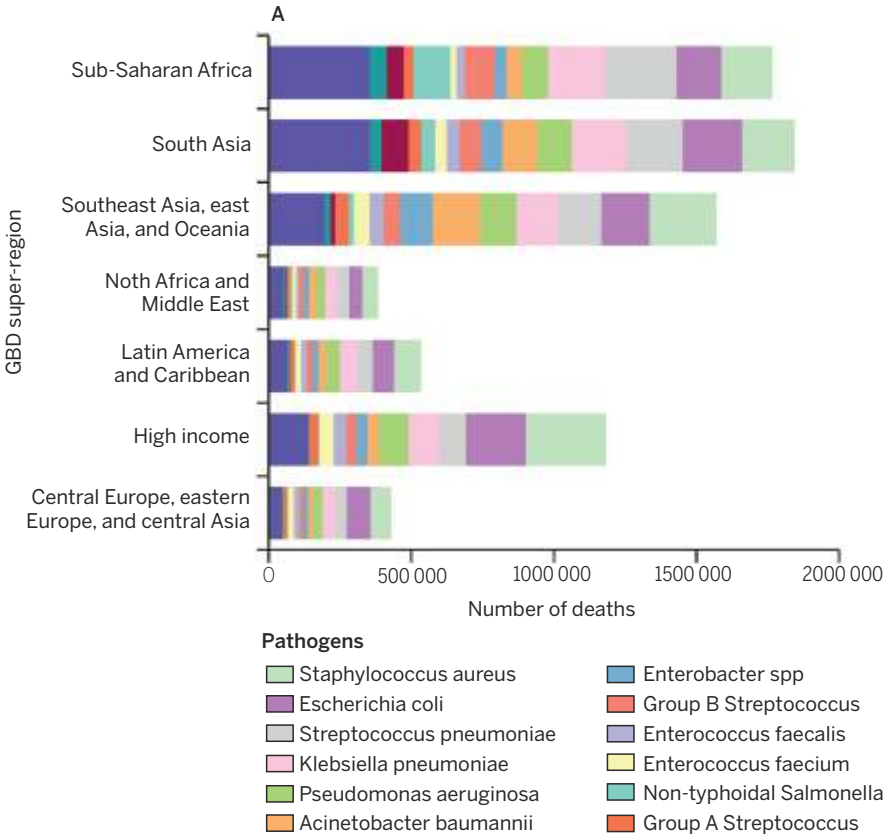
In G20 New Delhi Leaders Declaration One of the interesting development is inclusion of "One Health Approach " including AMR / AMS adoption by each country National Action Plan through AMR as quoted below

"Implement and prioritise tackling Antimicrobial Resistance (AMR) following the One Health approach, including through research and development, infection prevention and control, as well as antimicrobial stewardship efforts within respective national action plans through AMR and antimicrobial consumption surveillance."

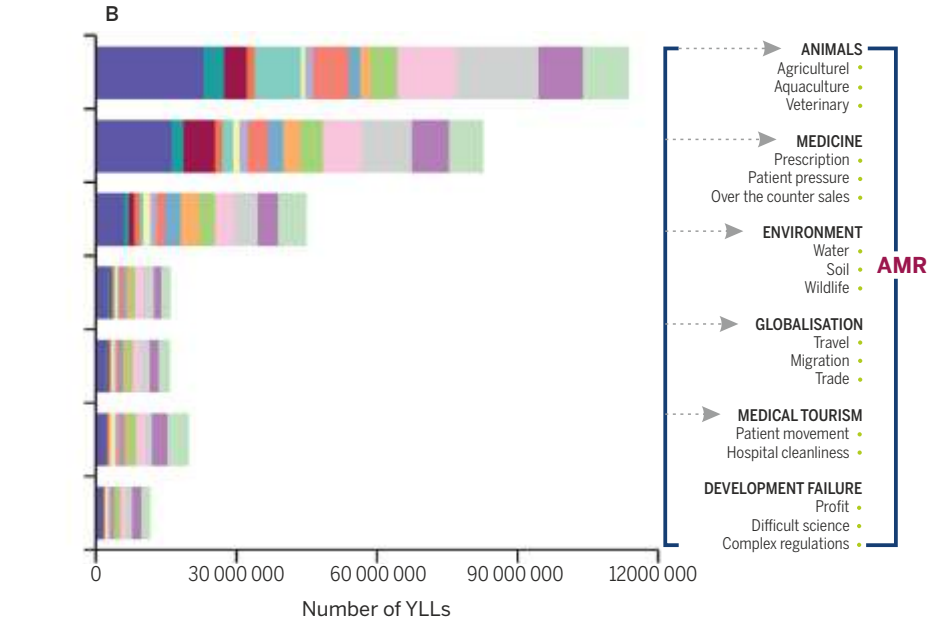
AMR: a global problem

1.2 million deaths were due to resistant bacterial infections and 4.95 million deaths associated with resistant bacterial infections in 2019

Antimicrobial Resistance



(AMR): A Global Problem



10.1016/S0140-6736(21)02724-0 | 10.1016/S0140-6736(22)02185-7

Antimicrobial Resistance Research and Surveillance Data: India

Jan-Dec 2021: 95,728 isolates

Escherichia coli was the most commonly isolated pathogen followed by Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Staphylococcus aureus.

- Imipenem susceptibility in E. coli dropped from 86% in 2016 to 64% in 2021
- Imipenem susceptibility of Klebsiella pneumonia dropped from 65% in 2016 to 45% in 2021
- Acinetobacter baumannii resistant to carbapenems were 87.5%, limiting treatment options
- In Pseudomonas aeruginosa, only 67.2% isolates were susceptible to meropenem
- In Staphylococcus aureus, MRSA rates increased from 28.4% in 2016 to 42.6% in 2021
- 37.5% of Enterococcus faecium causing blood stream infections (BSIs) were vancomycin resistant (VRE).

Journal Article

The Mortality Burden of Multidrug-resistant Pathogens in India: A retrospective, observational study

Sumanth Gandra, Katie K Tseng, Anita Arora, Bhaskar Bhowmik, Matthew L Robinson, Bishnu Panigrahi, Ramanan Laxminarayan, Eili Y Klein

Author Notes

Clinical Infection Diseases, Volume 69, Issue 4, 15 August 2019, Page 563-570, https://doi.org/10.1093/cid/ciy955

Published: 08 November 2018 Article history

The overall mortality rate of patients was 13.1% (n=581). Infections with MDR and extensively drug resistant E Coli, K. pneumoniae and MDRA. baumanniiwere associated with 2-3 times higher mortality. https://doi.org/10.1093/cid/ciy955

Ref: ICMR Antimicrobial Resistance Research and Surveillance Network, Annual Report 2021

Pathogen priority list : ICMR

CRITICAL PRIORITY	
Enterobacteriaceae (Klebsiella pneumonia and Escherichia coli)	**Carbapenem - R , Tigecyclin - R , Colistin - R**
Non-fermenting bacteria (Acinetobacter baumannii and Pseudomonas aeruginosa)	**Carbapenem - R, Colistin - R**

HIGH PRIORITY	
Staphylococcus aureus	MRSA, hVISA , Daptomycin - NS , Linezolid - R
Enterococcus species	Vancomycin - R , Linezolid - R , Daptomycin - NS
Salmonella species (Typhoidal and Non-typhoidal)	Azithromycin - NS , Third generation cephalosporins - NS , Carbapenem - NS

MEDIUM PRIORITY	
Steptococcus pneumoniae	Cephalosporin - R , Fluoroquinolones - R , Linezolid - R
Staphylococcus, coagulase-negative	Vancomycin - R , Linezolid - R
Shigella species	Third generation cephalosporins - R, Azithromycin - R
Haemophilus influenzae	Third generation cephalosporins - NS , Carbapenem - NS
Neisseria meningitidis	Fluoroquinolones - NS , Third generation cephalosporins - NS

R: resistant; NS: non-susceptible; MRSA: methicillin-resistant Staphylococcus aureus; hVISA: heterogous vancomycin - intermediate Staphylococcus aureus; Mycobacteria (including Mycobacterium tuberculosis) were not included in this prioritization exercise as it is a well-established global and national priority for which innovative new treatments are urgently needed and being developed.

Similar to WHO priority list

Value of Diagnostic Information in Antimicrobial Resistance

Background

Antimicrobial resistance (AMR) is one of the major threats to global health, food security and development as it threatens the effective prevention and treatment of infections caused by bacteria, parasites, viruses and fungi. About 700,000 people die each year from bacterial infections, according to the World Health Organization (WHO). It is a silent pandemic which needs urgent attention from every sector.

Factors such as over-prescription and over-the counter availability of antibiotics, lack of awareness amongst patients to complete the dosages, overuse of antibiotics in livestock, fish farming and agriculture, poor hygiene and infection control measures in the society, contributes majorly towards this cause. Another area of concern is the absence of new antibiotics development, which makes it more difficult to overcome this issue.

As per WHO data, it has been estimated that every 45 seconds someone dies from an infection caused by resistant bacteria. Also, it has been attributed that around 1·27 million deaths are cause due to bacterial AMR. The number is equivalent to the deaths caused due to HIV/AIDS and Malaria together. There is also an estimate of 10 million deaths by 2050 due to AMR. The impact of AMR goes well beyond health as it can have serious implications on poverty reduction and inequality, animal welfare, the environment, food safety and security. As per an estimate by The World Bank, 28 million people could be pushed into extreme poverty every year by 2050 and overall cost to the global economy of US$1 trillion per year.

Patient-centered care requires a focus on prevention, early detection, and monitoring treatment efficacy. By promoting better health and preventing serious illness, we not only alleviate the burden on the healthcare system, but also save lives.

In-vitro diagnostics play a crucial role in enhancing health outcomes and informing the majority of healthcare decisions for patients. Despite their importance, their value is often underappreciated and not fully reflected in reimbursement and funding policies within the healthcare system. It is crucial to recognize the value of diagnostic information and integrate it into healthcare decision-making and funding processes.

How does AMR occurs ?

AMR occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines/antibiotics making infections harder to treat and increasing the risk of disease spread, severe illness and death. As a result, the medicines become ineffective and infections persist in the human body, increasing the risk of spread to others. Microorganisms that develop antimicrobial resistance are sometimes referred to as "superbugs".

Antibiotics are supposed to save millions of life, but today its pervasive use is leading to increase in resistance of these lifesaving drugs. Factors such as over-prescription of antibiotics, lack of awareness amongst patients to complete the dosages, overuse of antibiotics in livestock and fish farming, poor hygiene and infection control measures in the society, contributes majorly towards this cause. Another area of concern is the absence of new antibiotics development, which makes it more difficult to overcome this issue.

Introduction to VODI concept

The "Value of Diagnostic Information" (VODI) assessment framework considers the complete range of benefits that diagnostic testing can bring, providing a starting point for enhancing informed decision-making in healthcare and ensuring that the value of diagnostic information is properly recognized. By maximizing the full potential of diagnostic information, both societal and individual health outcomes can be improved in a sustainable manner. To achieve this, it is essential to establish relevant and practical assessment methods that support the recognition of the VODI. These assessments should encompass multiple dimensions of value and multiple outcome measures relevant to medical decision-making, rather than just focusing on technological criteria.

Antimicrobial Stewardship (AMS) is critical to fight the AMR crisis. AMS programs help fight antimicrobial resistance by providing a framework for responsible antibiotics prescribing and use, optimizing individual therapy, helping reduce the spread of resistance and raising awareness & education. Successful antimicrobial stewardship programs require a continued and diligent interaction between all levels of healthcare providers and policy makers, including physicians, infectious disease specialists, infection control practitioners, nursing staff, pharmacists, microbiologists, pathologists, lab directors and healthcare administrators.

The core elements of antimicrobial stewardship programs include:

- Implementation of national and international guidelines and clinical pathways for the diagnosis and treatment of infectious diseases
- Limiting the use of antibiotics where not needed or not indicated
- Delivering the most appropriate antibiotic, with the correct dose established according to the type and site of infection, patient's age, weight and clinical situation. Switching antibiotics from parenteral to oral form as soon as possible
- Timely conversion to the most narrow antibiotic spectrum according to the organism susceptibility
- Use of the shortest effective antibiotic course and discontinuation of antibiotic courses as soon as possible

"Diagnostics are the single biggest potential game changer in the fight against AMR"

Lord Jim O'Neill

Need for VODI

Value assessment frameworks are not tailored for in-vitro diagnostics (IVDs), leading to a need to fully capture the value of diagnostic information. This requires considering factors that matter to patients, society, and all other stakeholders involved in healthcare delivery.

Decision-makers and assessors responsible for funding and reimbursement should consider the full extent of the value that diagnostic information can provide, including:

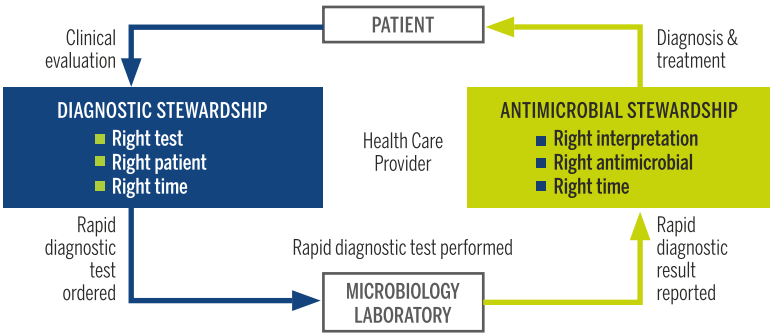
- From a patient's perspective: the direct and indirect impact on relevant outcomes
- From a healthcare system perspective: the impact on resource utilization by different stakeholders in various healthcare settings and pathways over time
- The challenges posed by missed or late diagnoses, re-hospitalizations, inefficient use of healthcare resources, and poor patient engagement highlight the need for timely diagnoses, treatments, and effective monitoring through diagnostic information

Role of Diagnostics (Diagnostics Stewardship)

Quick and timely actions in understanding the causes of serious infections such as sepsis, pneumonia and meningitis and starting the right antibiotic therapy is a matter of life or death of the patient. Hence, it is important to identify the etiological pathogen and to differentiate between viral and bacterial infections, to identify the antimicrobial resistances in microbes, and to find out which antimicrobial agent should be used for the cure. Thereby the unnecessary use of antibiotics could be minimized and the spread of antibiotic resistance better controlled.

The microbiology laboratory therefore plays a crucial role in identifying the infectious agent, as well as any potential resistance to antibiotics, in order to help clinicians prescribe the most appropriate treatment with the shortest time delay.

Adapted from Messacar et al. *J Clin Microbiol.* 2017;55:715-723



Therefore, the need of the hour is to bring diagnostics closer to the general practitioners and hence to the patient would cause a paradigm shift from empirical to evidence-based treatments of infectious diseases in outpatient clinics. Rapid diagnostics are needed for both pathogen identification and resistance testing. The prevalence of AMR may be very high for some species in certain geographic locations. According to the current recommendations on AST (antimicrobial susceptibility testing), pure culture isolates are used to test the effect of antimicrobial drugs.

These diagnostic tools help to identify patients who have a bacterial infection which would require antibiotic treatment, identify the organism causing the infection in order to determine the appropriate patient management, determine whether the pathogen is resistant to one or more antibiotics as a critical step to help the clinician prescribe the most appropriate antibiotics as early as possible.

Importance of such a concept in APAC

In the Asia-Pacific region, the need for VODI is particularly pressing as the region has a high burden of infectious diseases and a rapidly growing resistance problem. In addition, many countries in the region have limited resources and capacities for diagnostic testing, making it even more important to ensure that the information obtained is used effectively. By highlighting the VODI, decision-makers can understand the impact of diagnostics on patient outcomes and make informed decisions about investments in diagnostic testing and AMR Stewardship programs.

Act now: It's the only way we will reduce the threat of resistance

Antimicrobial Stewardship (AMS) is critical to fight the AMR crisis. AMS programs help fight antimicrobial resistance by providing a framework for responsible antibiotics prescribing and use, optimizing individual therapy, helping reduce the spread of resistance and raising awareness & education. Successful antimicrobial stewardship programs require a continued and diligent interaction between all levels of healthcare providers, including physicians, infectious disease specialists, infection control practitioners, nursing staff, pharmacists, microbiologists, pathologists, lab directors and healthcare administrators.

The core elements of antimicrobial stewardship programs include:

- Implementation of national and international guidelines and clinical pathways for the diagnosis and treatment of infectious diseases
- Limiting the use of antibiotics where not needed or not indicated
- Delivering the most appropriate antibiotic, with the correct dose established according to the type and site of infection, patient's age, weight and clinical situation
- Switching antibiotics from parenteral to oral form as soon as possible
- Timely conversion to the most narrow antibiotic spectrum according to the organism susceptibility
- Use of the shortest effective antibiotic course and discontinuation of antibiotic courses as soon as possible

Antimicrobial resistance as a high priority health area

Antimicrobial resistance (AMR) is a growing global public health threat that is exacerbated by the overuse and misuse of antibiotics. AMR occurs when bacteria, viruses, fungi, and parasites evolve to resist the effects of antibiotics, making infections more difficult to treat and leading to increased morbidity and mortality.

The magnitude of the health problem posed by AMR is undeniable. In 2017, AMR was estimated to cause 700,000 deaths globally . This number is projected to rise to 10 million by 2050 if the trend continues . AMR is having significant impact on human health in APAC:

- In India, it has been estimated that over 58,000 newborn deaths each year are due to sepsis caused by antimicrobial-resistant infections.
- In China, it has been reported that AMR is responsible for approximately 33,000 deaths annually.
- In Indonesia, the annual number of deaths caused by AMR is estimated to be over 11,000.
- In Thailand, AMR has been estimated to cause over 9,000 deaths per year.
- It is a pressing public health challenge that must be addressed through effective measures, such as promoting responsible use of antibiotics and enhancing infection prevention and control practices.

https://www.worldbank.org/en/topic/health/brief/antimicrobial-resistance amr#:~:text=Each%20year%2C%20700%2C000%20people%20die, Threat%20to%20Our%20Economic%20Future'.
https://www.ncid.sg/News-Events/News/Pages/Antimicrobial-resistance-remains-a-public-health threat.aspx#:~:text=WHY%20IS%20AMR%20A%20SERIOUS, were%20associated%20with%20bacterial%20AMR.
Antimicrobial resistance testing, multidrug resistant organism infection | bioMérieux (biomerieux-diagnostics.com)
Publication - GLOBAL BURDEN OF BACTERIAL ANTIMICROBIAL RESISTANCE IN 2019: A SYSTEMATIC ANALYSIS
Antimicrobial resistance; an emerging crisis | United Nations Development Programme (undp.org)

Timely diagnosis: it can help to reduce the time between symptom onset and proper treatment,

reducing the risk of disease progression, and improving patient outcomes.

Resource optimization: it can help to optimize the use of resources and reducing waste.

Improved patient engagement: it can help to improve patient engagement and increasing their adherence to treatment plans.

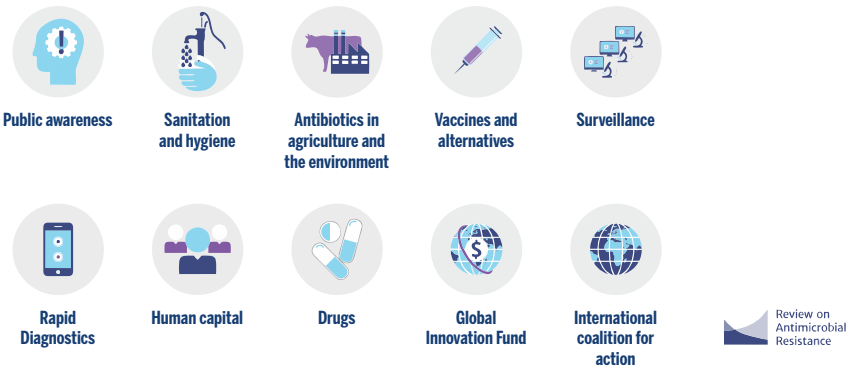
Better informed decision-making: it can help make better informed decisions by providing crucial information about the causative agent of an infection and determining the most appropriate treatment.

Since it is well known now that AMR is a major concern now, there is a need for global coordination, especially in developing relevant guidelines for the management of infectious diseases, using diagnostics, novel antimicrobials & implementation of antibiotics policy and surveillance. In addition, creating awareness and increasing education amongst all stakeholders (healthcare workers, the general public and politicians) about the dangers associated with inappropriate use of antimicrobials should be made mandatory.

Conclusion:

Since it is well known now that AMR is a major concern for the human kind and could be the next pandemic in making, there is a need for global coordination, especially in developing relevant guidelines for the management of infectious diseases, using diagnostics, novel antimicrobials & implementation of National Antibiotics Policy. In addition, creating awareness and increasing education amongst all stakeholders (healthcare workers, the general public and politicians) about the dangers associated with inappropriate use of antimicrobials should be made mandatory

TACKLING ANTIMICROBIAL RESISTANCE ON TEN FRONTS



WHY IMPLEMENT ANTIMICROBIAL STEWARDSHIP IN HOSPITALS?

Antimicrobial use

Misuse and over-use of antibiotics

The last 50 years have witnessed the golden age of antibiotic discovery and their widespread use in hospital and community settings. Regarded as very effective, safe and relatively inexpensive, antibiotics have saved millions of lives. However, this has led to their overuse and misuse in the human, animal and other sectors (Figure 1).

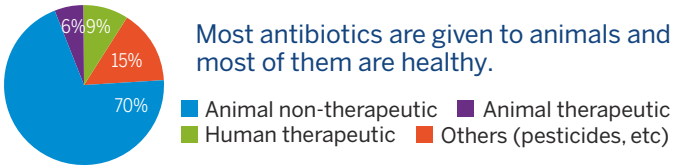
Globally, between 2000 and 2010 there has been a massive rise in overall antimicrobial consumption (Figure 2), largely as a consequence of uncontrolled prescription or over-the-counter sales.

> At global level, 70% of antibiotics are used for animals *[O'Neill report, 2016]*. In the US, this is 85% (Figure 1). In hospitals, up to 50% of antimicrobial use is inappropriate *[Dellit et al., 2007]*.

More recent global data on the quality of antimicrobial prescribing in hospitals, undertaken using a global point prevalence survey method [Global PPShttp://www.global-pps.com] reveals significant variation in practice against commonly used metrics of the quality of prescriptions (Figure 3). Such real world data is beginning to provide much needed intelligence of what the problem is, the scale of the problem and ways of measuring the effectiveness of our interventions.

Figure 1: Current use of antibiotics in the United States

Adapted from www.pewhealth.org



WHY IMPLEMENT ANTIMICROBIAL STEWARDSHIP IN HOSPITALS?

Figure 2: Percentage change in antibiotic consumption per capita 2000-2010* by country

Adapted from Van Boekel TP et al. 2015. Lancet Infect Dis. 2014;14:742-750

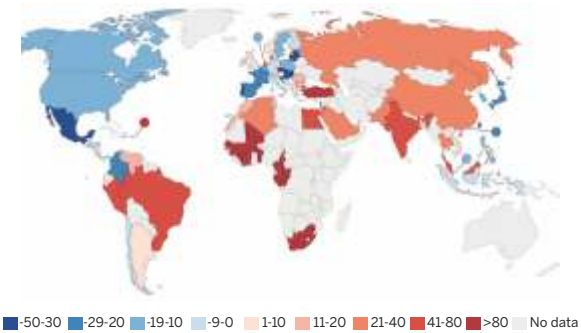
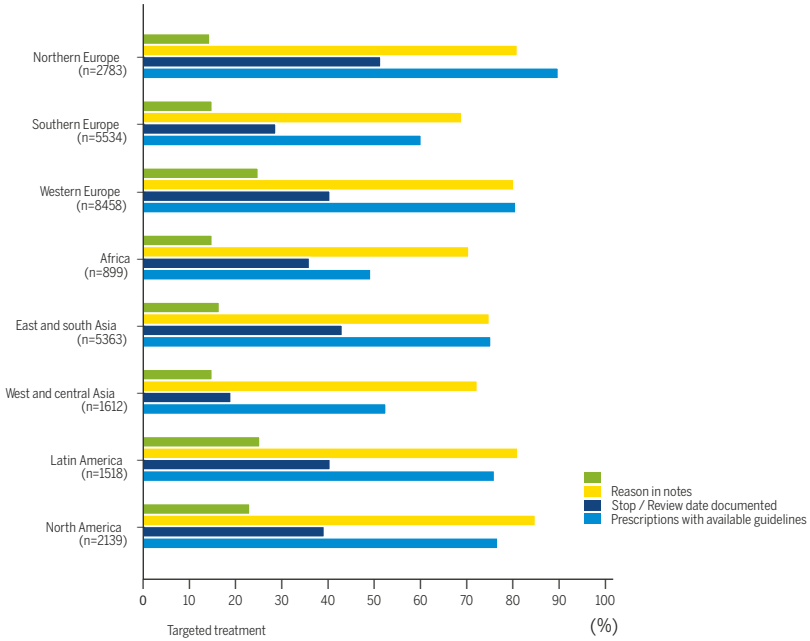


Figure 3: Overview of antimicrobial/antibiotic quality indicators for adult inpatients by region, 2015 Global Point Prevalence Survey

Adapted from Versporten A et al. Lancet Global Health. 2018; 6: 619-629



The 30% Rule

- ~ 30% of all hospitalized inpatients at any given time receive antibiotics
- ~ over 30% of antibiotics are prescribed inappropriately in the community
- ~ up to 30% of all surgical prophylaxis is inappropriate
- ~ 30% of hospital pharmacy costs are due to antimicrobial use
- ~ 10-30% of pharmacy costs can be saved by antimicrobial stewardship programs

(Hoffman et al., 2007; Wise et al., 1999; John et al., 1997)

The rising threat of antimicrobial resistance

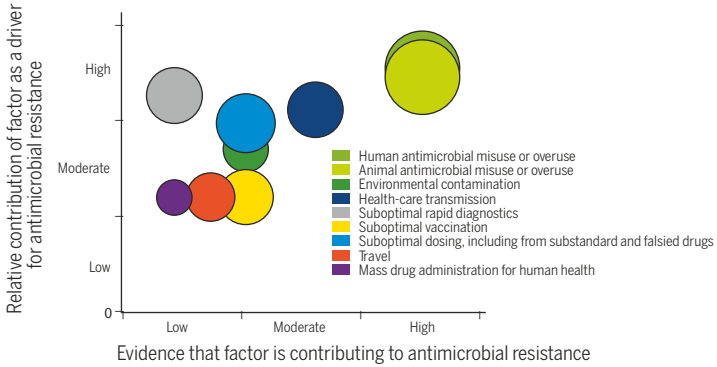
Antimicrobial resistance has been identified as a major threat by the World Health Organization [WHO, 2012] due to the lack of new antibiotics in the development pipeline and infections caused by multi-drug resistant pathogens becoming untreatable [Goossens et al., 2011; Carlet et al., 2011]. In 2015, the WHO set out the global action plan for AMR [WHO, 2015] and a subsequent broader stewardship framework.

Combating Antimicrobial Resistance

There are numerous drivers for AMR (Figure 4). Human antimicrobial misuse and overuse is a key driver factor, as are suboptimal dosing, lack of availability and/or under-use of rapid diagnostics or point of care tests and insufficient infection prevention and control.

Figure 4: Mechanisms and drivers of antimicrobial resistance

Adapted from Holmes AH et al. The Lancet 2016;387:176-187



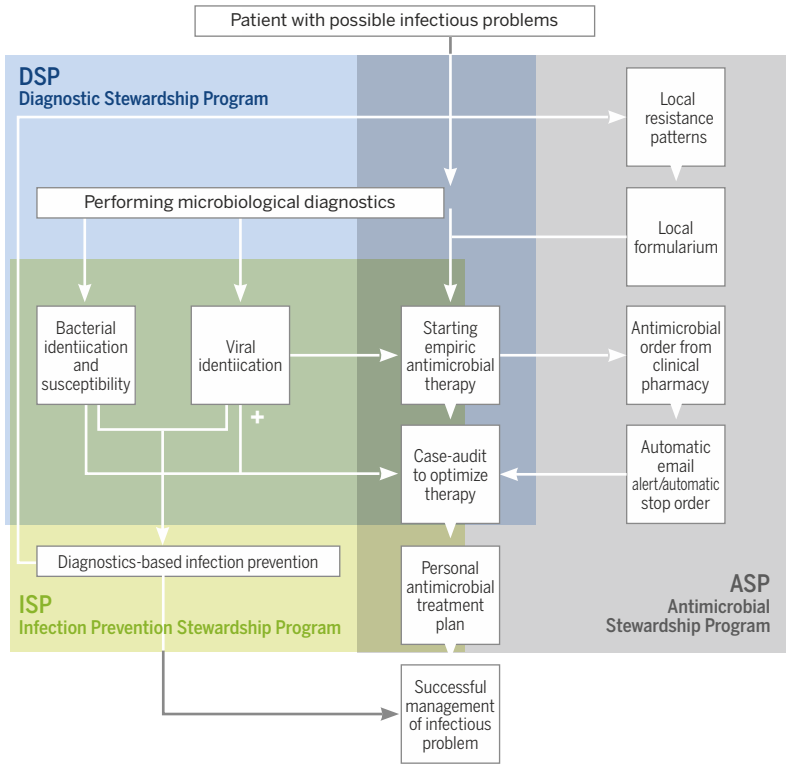
WHY IMPLEMENT ANTIMICROBIAL STEWARDSHIP IN HOSPITALS?

To combat AMR, a "three-pillar" approach is recommended:
1. Optimize the use of antimicrobials,
2. Prevent the transmission of drug-resistant organisms,
3. Improve environmental decontamination.

To achieve this approach, an integrated stewardship approach has been advocated, encompassing antimicrobial stewardship, diagnostic stewardship and infection control (Figure 5).

Figure 5: An integrated stewardship model: antimicrobial, infection prevention and diagnostic (AID)

Adapted from Dik JH et al. Future Microbiol. 2015; 11: 93-102



Defining antimicrobial stewardship

Antimicrobial stewardship (AMS) is a key strategy to overcome resistance. It involves the careful and responsible management of antimicrobial use.

Two definitions help to understand the objectives of AMS

Adapted from Nathwani D et al. 2012 Hosp Epidemiol Infect Control

Systems level

"Antimicrobial stewardship is an organisational or healthcare system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness"

Individual/team level

"Antimicrobial stewardship:

- is an inter-professional effort, across the continuum of care,
- involves timely and optimal selection, dose and duration of an antimicrobial,
- for the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient,
- and minimal impact on resistance and other ecological adverse events such as C. difficile."

AMS can also simply be put as achieving:

> **"The right antibiotic for the right patient, at the right time, with the right dose, the right route and cause the least harm to the patient and future patients."**

www/cdc.gov/getsmart/healthcare/inpatient-stewardship

Goals of antimicrobial stewardship and evidence for success

The four main goals of antimicrobial stewardship are illustrated in Figure 6 with examples of evidence that stewardship programs can help achieve these goals. The importance of additional balancing measures or measurement of unintended consequences is also emphasized [Toma et al., 2017].

Figure 6: The goals of antimicrobial stewardship programs for patient and public health

Adapted from D. Nathwani, personal communication

IMPROVE PATIENT OUTCOMES	OPTIMIZE PATIENT SAFETY	REDUCE RESISTANCE	CONTROL HEALTHCARE COSTS

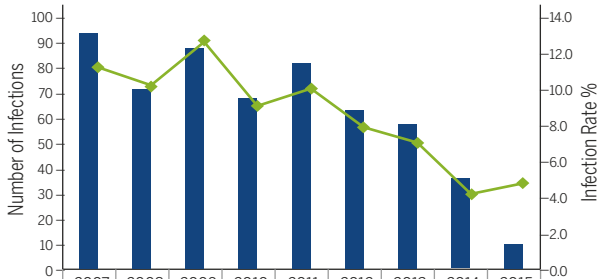
Goal 1: Improve patient outcomes

- Improve infection cure rates
- Reduce surgical infection rates
- Reduce mortality and morbidity

The prevention of surgical site infections (SSIs) remains one of the mostaccessible and "doable" areas of antimicrobial stewardship programs (ASPs) usually in combination with infection prevention measures. The effect of ASPs on reducing surgical site infections can be dramatic and of high impact, making SSIs a very visible "quick win" that can encourage buy-in into stewardship programs (Figure 7).

Figure 7: Impact of ASP on surgical site infection rates

Adapted from Frenette C et al. Am J Inf Control. 2016;44:977-82



	2007	2008	2009	2010	2011	2012	2013	2014	2015
# OF INFECTIONS	94	72	88	68	81	63	58	36	9
# OF PROCEDURES	838	695	703	751	819	802	831	887	192
INFECTION RATE	11.2%	10.4%	12.5%	9.1%	9.9%	7.9%	7.0%	4.1%	4.7%

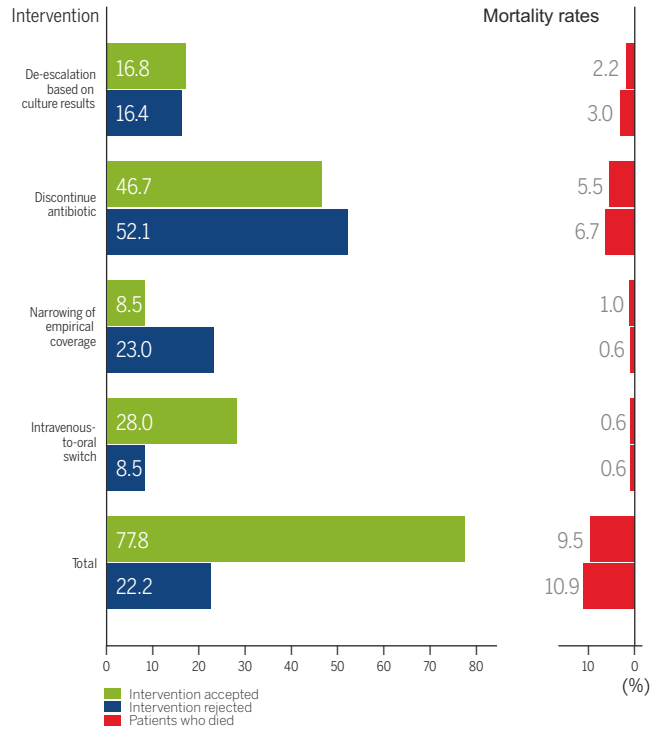
Goal 2: Optimize patient safety

(Minimize unintended consequences of antimicrobials)

Studies have shown that ASPs can effectively reduce antibiotic utilization, cost of care and even antimicrobial resistance rates, without increasing mortality.However, ASPs should avoid the perception that the goal of the program is primarily to reduce antibiotic purchases and costs, instead of focusing on improving the quality of care. To address the patient safety concern, data showing no adverse impact on morbidity or mortality is important for reassurance and engagement (Figure 8).

Figure 8: Types of ASP interventions that may impact morbidity and mortality

Adapted from Liew YX et al.Int J Antimicrob Agents 2012;40:55-60



Reduce duration of hospital stay, without increasing mortality or infection-related readmissions (Figure 8).

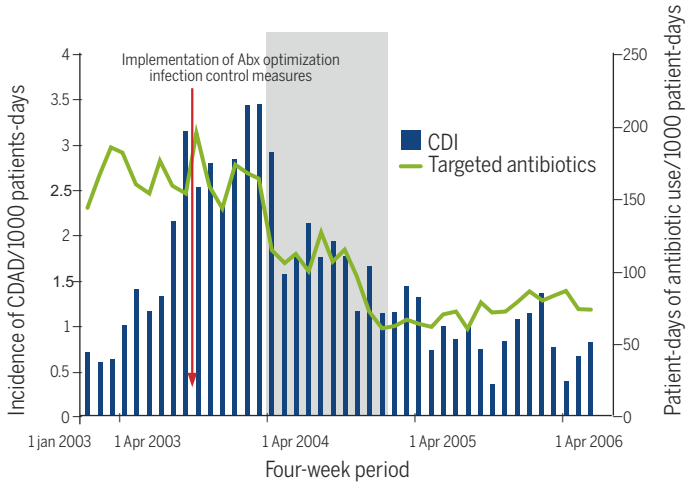
This Singapore-based study showed that in patients whose physicians accepted suggested ASP interventions, there was:

- shorter average length of stay (mean 19.4 days vs. 24.2 days),
- significantly shorter hospital stay between ASP intervention and discharge (mean 10.2 days vs 16.6 days),
- significant reduction in 14-day re-infection rates between accepted (0%) and rejected (10%) groups,
- no difference in all-cause mortality (P = 0.191).

Reduce C.difficile colonization or infection by controlling the use of "high-risk" antibiotics (Figure 9).

Figure 9: Example of a robust stewardship program with strict implementation of infection control measures leading to sustained reduction in C. difficile infection (CDI) cases during an epidemic

Adapted from Valiquette L et al. Clin Infect Dis.2007;45:S112-121



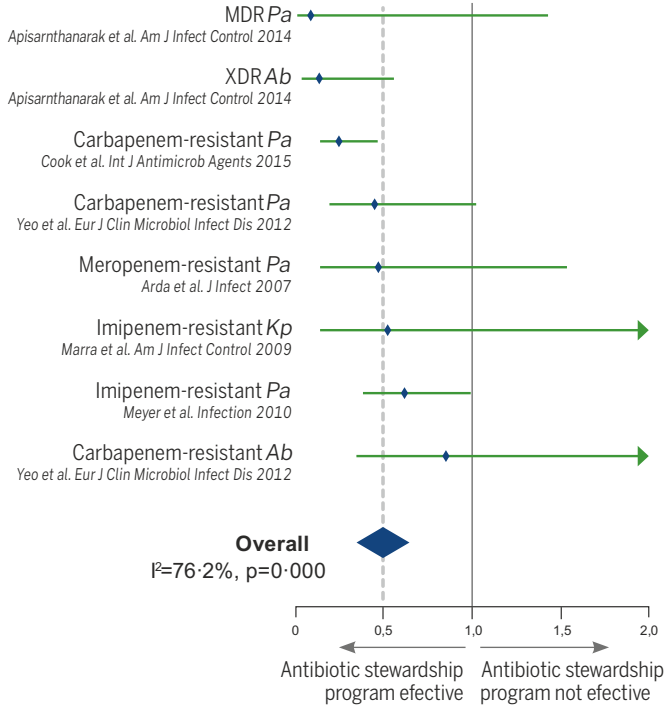
A more recent example in Scotland showed a reduction in C. difficile infection (CDI) applicable at a national level following restriction of high risk antibiotics that included cephalosporins, co-amoxiclav, quinolones and clindamycin [Lawes et al, 2017]. This illustrates the potential for massive impact of stewardship programs at nationwide levels.

Goal 3: Reduce resistance

Restricting relevant agents can reduce colonization or infection with Gram-positive or Gram-negative resistant bacteria (Figure 10). Numerous other examples of the effect of ASPs on multi-drug resistant Gram-negative bacteria are given in this meta-analysis [Baur et al., 2017]

Figure 10: Efect of ASPs on the incidence of MDR GNB

Adapted from Baur D et al. Lancet Infect Dis. 2017;17:990–1001 / Systematic review and meta-analysis
(Refer to source article for full references of reviewed articles)



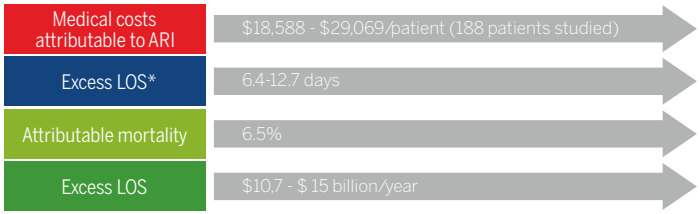
ABBREVIATIONS
GNB: Gram-negative bacteria - MDR: Multidrug-resistant - XDR: Extremely drug-resistant
Ab: Acinetobacter baumannii - Kp: Klebsiella pneumoniae - Pa: Pseudomonas aeruginosa

Goal 4: Control healthcare costs (without adversely impacting quality of care)

Antibiotic-resistant infections are associated with high costs (Figure 11).

Figure 11: The costs of antibiotic-resistant infections (ARI)

Adapted from Roberts RR et al. Clin Infect Dis. 2009;49:1175–1184



* LOS: length of stay

Figures 12a and 12b are examples of how stewardship programs in hospitals can deliver signiicant cost savings through improved antimicrobial prescribing practices.

Figure 12a: Changes in antibiotic prescribing rates

Adapted from Bao L et al. PLoS ONE 2015;10:e0118868

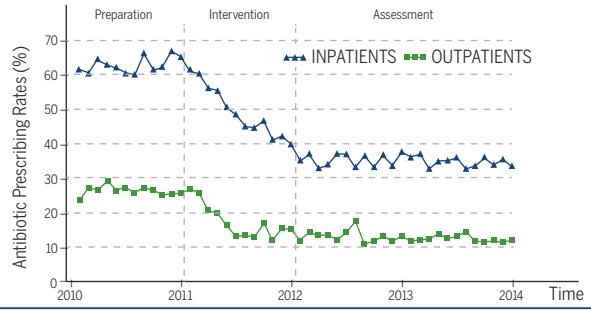
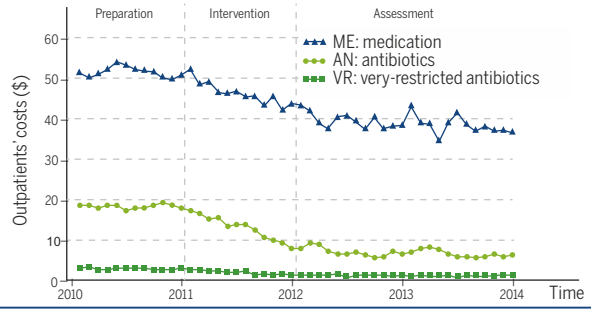


Figure 12b: Changes in outpatients' costs

Adapted from Bao L et al. PLoS ONE 2015;10:e0118868

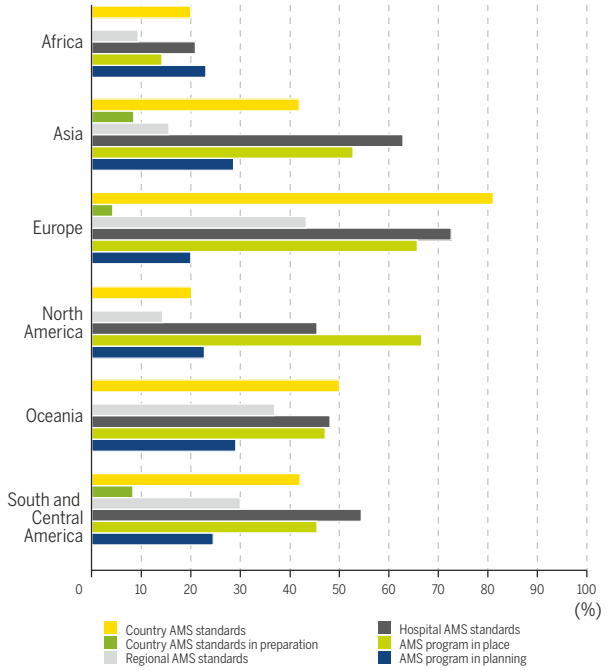


Implementation of Antimicrobial Stewardship Programs

A global survey has outlined the availability of stewardship programs across the continents (Figure 13).

Figure 13: Summary of AMS standards and programs

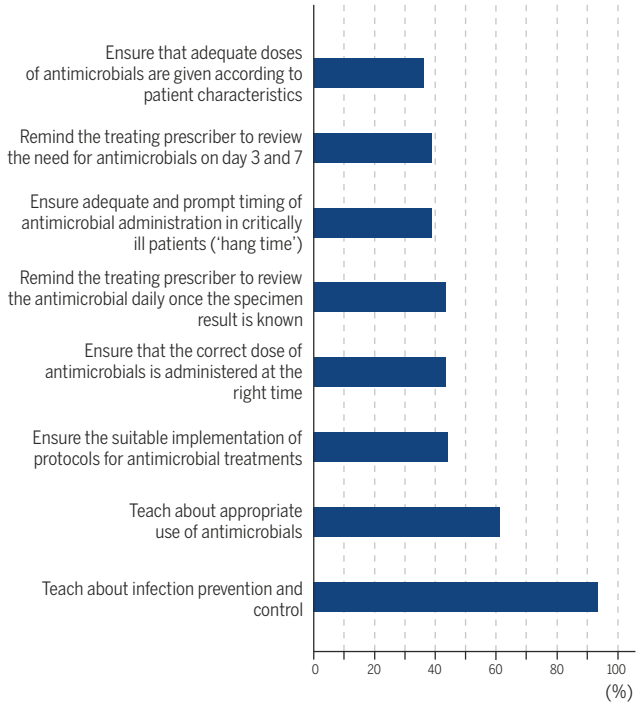
Adapted from Howard P et al. J Antimicrobial Chemother. 2015; 70: 1245-1255



This remains a unique global survey, although more recent continental data is emerging showing that in Africa, for example, nurses are a key part of hospital stewardship programs (Figure 14) [Bulabula et al. 2018].

Figure 14: AMS tasks undertaken by nurses

Adapted from Bulabula ANH et al. J Antimicrobial Chemother 2018;73:1408–1415



A recent systematic review of antimicrobial stewardship programs in Asia illustrates emerging experience of their impact on a range of outcomes [Lee et al. 2018]. This meta-analysis, which reviewed 77 studies, showed that among those studies:

- 91% reported reduced antibiotic usage,
- 100% reported cost savings,
- duration of antibiotic therapy was reduced in 6 of 7 studies,
- rates of all-cause mortality and HAI were not significantly different between the intervention and control groups,
- mortality rates were significantly improved by ASPs using drug monitoring,
- HAI rates were also improved by ASPs that included infection control or hand hygiene programs.

HOW TO IMPLEMENT AN ANTIMICROBIAL STEWARDSHIP PROGRAM?

Antimicrobial stewardship (AMS) strategies can use different methods or techniques to support the adoption, implementation, and sustainability of a clinical program or practice.

The strategies include 'top down/bottom up,' 'push/pull,' and 'carrot/stick' tactics, and typically involve 'package' approaches. They also include methods for provider training and decision support; intervention-specific tool kits, checklists, and algorithms; formal practice protocols and guidelines; learning collaboratives, business strategies and organizational interventions (such as "plan-do-study-act" cycles) and economic, fiscal, and regulatory methods.

> Although strategies depend on local needs and issues, and available expertise and other resources, there are a number of core elements that make up the basis of a good stewardship program.

In 2014, the CDC released The Core Elements of Hospital Antibiotic Stewardship Programs *[https://www.cdc.gov/antibiotic-use/healthcare/pdfs/core-elements.pdf]* that identifies key structural and functional aspects of effective programs.

In 2018, these core elements were adapted for a global audience and supplemented by a check list descri bing essential and minimum standards for AMS programs in hospitals worldwide (Figure 15).

Figure 15: Core elements and checklist items for global hospital AMS programs

Adapted from Pulcini C et al., Clin Microbiol Infect. 2019;25:20-25

CORE ELEMENT 1

Senior hospital management leadership towards antimicrobial stewardship

This section relates to governance of the programme by hospital executives, and specifies how senior hospital management supports the antimicrobial stewardship programme

CORE ELEMENT 2

Accountability and responsibilities

CORE ELEMENT 3

Available expertise on infection management

CORE ELEMENT 4

Education and practical training

CORE ELEMENT 5

Other actions aiming at responsible antimicrobial use

CORE ELEMENT 6

Monitoring and surveillance (on a continuous basis)

Does your hospital monitor the quality of antimicrobial use at the unit and/or hospital wide level?

This can be done for example by undertaking point prevalence surveys or audits, assessing appropriateness of infection management and antimicrobial prescription (e.g. indication, choice and duration of antibiotic therapy in pneumonia or surgical prophylaxis according to policy/guidance)

CORE ELEMENT 7

Reporting and feedback (on a continuous basis)

All these reports should also be shared with the hospital management leadership

Once these core elements have been identified, an 8-step process of implementation described on page 16 is one pragmatic way of implementingthe stewardship program.

A program devised for hospitals in the Netherlands is also worthy of review *[http://esgap.escmid.org/wp-content/uploads/2015/ 11/SWAB_guideline_ABS_hospitals.pdf]*.

EIGHT KEY STEPS

for implementing an Antimicrobial Stewardship Program (ASP)

1. Assess the motivations
2. Ensure accountability and leadership
3. Set up structure and organization
4. Deine priorities and how to measure progress and success
5. Identify efective interventions for your setting
6. Identify key measurements for improvement
7. Educate and Train
8. Communicate

1. Assess the motivations

Analyze your situation and what problems you want to address. There are many international guidelines available, but you will need to adapt them to your local situation.

Define where you are and where you want to go, with quantitative figures. One of the ways of obtaining these data is to measure the quantity and quality of antibiotic use, for example, using a Point Prevalence Survey, such as the Global-PPS (see Section 6.1.1).

What can be implemented will depend on local needs/issues, geography, available skills/expertise and other resources.

For example, easier or less costly approaches can include:

- simple clinical algorithms,
- prescribing guidance for treatment, surgical prophylaxis,
- IV to oral conversion,
- provision of microbiological support,
- restricting availability of certain antibiotics (formulary restriction),
- automatic therapeutic substitution,
- IV antimicrobial batching,
- promoting education.

[Goff et al., 2012]

2 . Ensure accountability and leadership

To ensure a successful Antimicrobial Stewardship Program:

- the program should be supported by the senior hospital management,who are accountable for the outcomes,
- a team of people and resources should be allocated by the head of the organization to implement and evaluate the program,
- the ASP team members must possess power, expertise, credibility and leadership. These individuals need to convince managers and healthcare staff of the added value of the program.

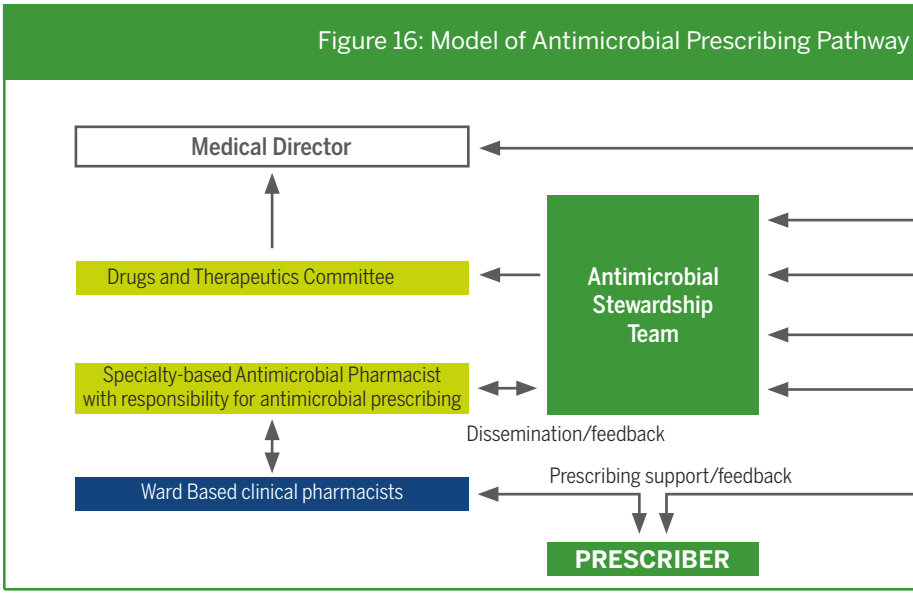
A key component of a stewardship program is leadership and culture. This can be set out as a driver diagram (see Table 1 on page 18 for more details).

Table 1: Driver Diagram - Overarching Driver: Leadership and Culture

https://www.cdc.gov/getsmart/healthcare/pdfs/Antibiotic_Stewardship_Driver_Diagram_10_30_12.pdf

SECONDARY DRIVER	KEY CHANGE CONCEPTS	SPECIFIC CHANGE IDEAS
Promote a culture of optimal antibiotic use within the facility	Engage administrative and clinical leadership to champion stewardship effort	1. Identify clinical providers as champions to be thought leaders about antibiotic stewardship. 2. Work with administrators to ensure that they understand the rationale and goals for stewardship programs and interventions and provide support (financial and non-financial). 3. Engage a physician champion and core team to enhance the focus of antimicrobial stewardship into the current process of care. 4. Bring disciplines together to improve communication and collaboration about improving antibiotic use, including: - Infection preventionists; - Hospitalists; - Intensivists; - Emergency department physicians; - Microbiologists; - Pharmacists; - Nurses; and - Infectious disease experts. 5. Consider having the multi-disciplinary group perform a gap analysis of antimicrobial use at the facility to identify priority areas for improvement.

Figure 16: Model of Antimicrobial Prescribing Pathway



3. Set up structure and organization

The key components of the structure and governance of the ASP are:

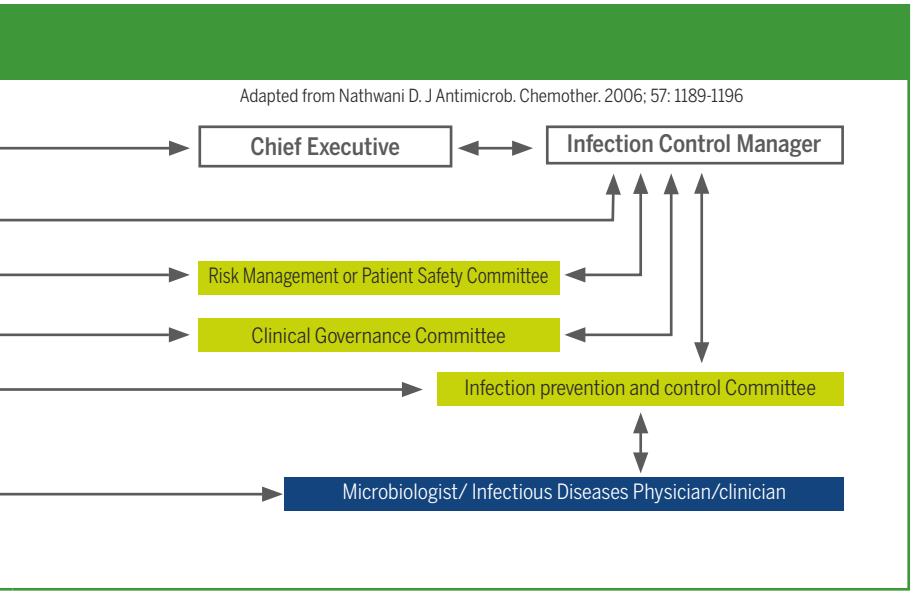
Dedicated resources, including dedicated personnel time for stewardship activities, education, and measuring/monitoring antimicrobial use.

A multidisciplinary AS team with core membership of:

- an infectious diseases physician (or lead doctor or physician champion),
- a clinical microbiologist,
- a clinical pharmacist with expertise in infection.

Other members could be specialist nurses, for example infection prevention or stewardship nurses, quality improvement /risk management/patient safety managers and clinicians with an interest in infection.

- Governance within the hospital's quality improvement and patient safety governance structure
- Clear lines of accountability between the chief executive, clinical governance, drug and therapeutics committee, and infection prevention and control committees, and the AST. Figure 16 illustrates such an organization structure. This structure would need to be adapted to local context and available resources.



4. Define priorities and how to measure progress and success

> The objectives of the ASP and how they are going to be achieved and measured need to be agreed by all the key stakeholders and communicated clearly.

One way of doing this is to produce a Driver Diagram (see Figure 17 as an example). A Driver Diagram is a logic chart with three or more levels, including:

- a goal or vision,
- the high-level factors needed to achieve this goal (called 'primary drivers'),
- specific projects and activities that would act upon these factors.

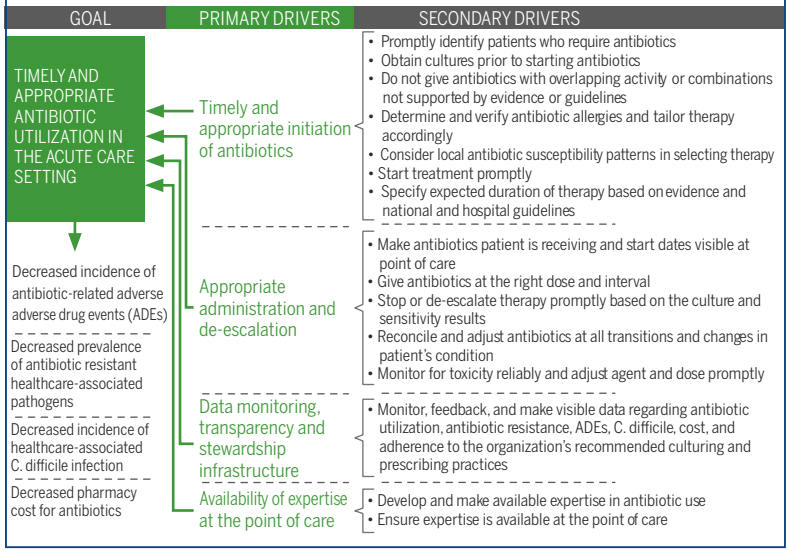
For more complex goals, each primary driver could have its own set of 'secondary drivers' (or lower level drivers).

Driver diagrams can help an ASP team to:

- explore the factors that need to be addressed to achieve a specific overall goal,
- show how the factors are connected,
- act as a communication tool for explaining a change strategy,
- provide the basis for a measurement framework.

Figure 17: Example of a Driver Diagram for Antimicrobial Stewardship

Adapted from www.cdc.gov/getsmart/healthcareimprove-eforts/



5. Identify effective interventions for your setting

A range of stewardship interventions has been reviewed in the IDSA guidelines [Barlam et al.2016].

> When establishing a new stewardship program, it is best to start with the core strategies and focus on achieving and maintaining them before adding some of the supplemental strategies (Table 2).

Table 2: Antimicrobial Stewardship Toolkit: Quality of Evidence to support interventions

Adapted from Dellit TH et al. Clin Infect Dis. 2007; 44:159-77; Barlam TF et al. Clin Infect Dis. 2016; 62:51 -77

CORE STRATEGIES	SUPPLEMENTAL STRATEGIES
Formulary restrictions and preauthorization*	Streamlining / timely de-escalation of therapy*
Prospective audit with intervention and feedback*	Dose optimisation*
Multidisciplinary stewardship team*	Parenteral to oral conversion*
	Guidelines and clinical pathways*
	Antimicrobial order forms
	Education
	Computerized decision support, surveillance
	Laboratory surveillance and feedback
	Combination therapies
	Antimicrobial cycling

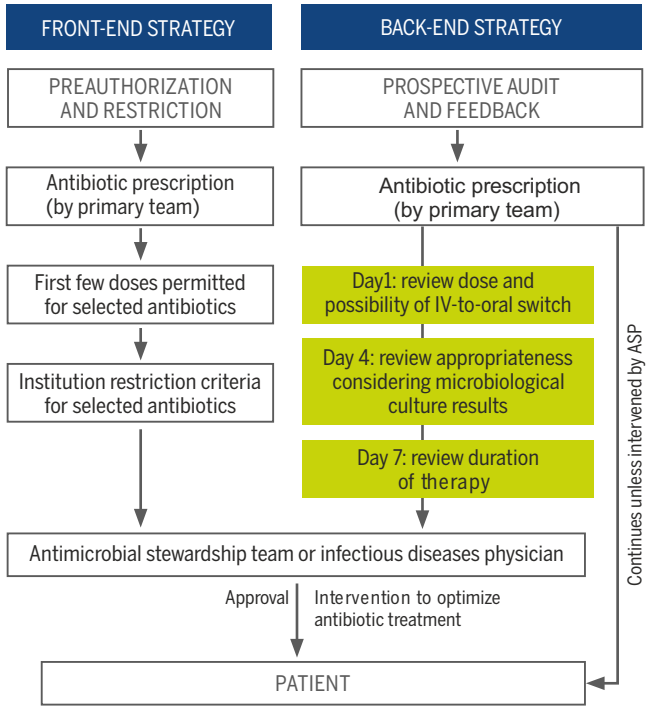
*Strategies with strongest evidence and support by IDSA

Two core ASP strategies have evolved (Figure 18):

FRONT–END STRATEGIES	Antimicrobials made available through an approval process (formulary restrictions and preauthorization)
BACK-END STRATEGIES	Antimicrobials reviewed after antimicrobial therapy has been initiated (prospective audit with intervention and feedback)

Figure 18: Front- and Back-end Antimicrobial Stewardship Strategies

Adapted from Chung GW et al. Virulence 2013;4:151-157



Some of the advantages and disadvantages of these two strategies are given in Figure 19.

Although more labour-intensive, **back-end strategies are**:

- **more widely practiced,**
- **more easily accepted** by clinicians as they reflect the daily decision-making process,
- provide a **higher opportunity for educational opportunities,**
- ultimately provide a **more sustained impact** of improving the overall quality of antimicrobial prescribing.

[Chung et al., 2013].

In the UK, this approach has been innovatively adapted to create a simple pragmatic approach that is aligned with the clinical teams' daily decision-making process (Figure 20).

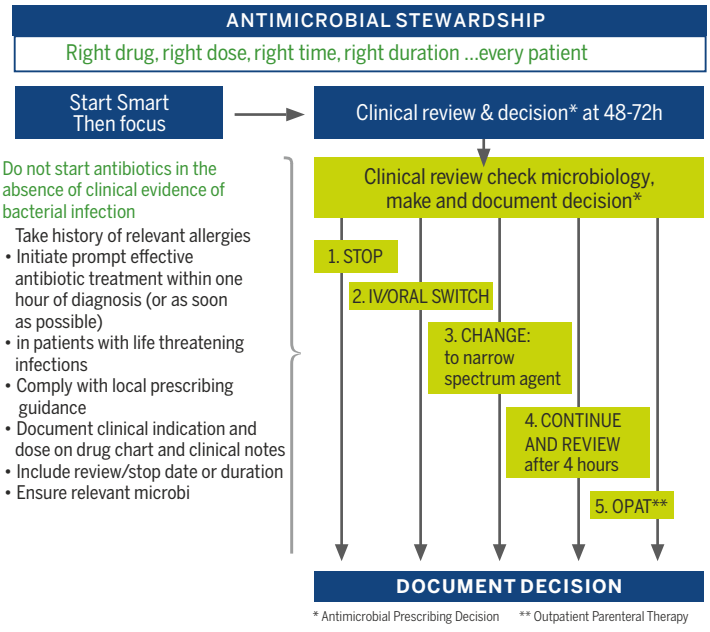
Figure 19: Advantages and Disadvantages of Pre-Authorization and Prospective Audit and Feedback

Adapted from Dellit TH et al. Clin Infect Dis. 2007;44:159–77; Barlam TF et al. Clin Infect Dis. 2016;62:51-77

PRE-AUTHORIZATION	PROSPECTIVE AUDIT AND FEEDBACK
EXAMPLES OF ADVANTAGES	
Prevents unnecessary/ inappropriate initiation of antibiotics	Increases visibility of ASP and helps to form professional relationships
Ensures optimal empirical therapy	Maintains autonomy of prescribers
Prompts review of clinical parameters, patient history and prior cultures before initiating antimicrobial therapy	Frequency can be tailored based on resources available to the ASP
EXAMPLES OF DISADVANTAGES	
Has little efect post empirical therapy	Compliance voluntary
Loss of prescriber autonomy	Labour intensive
May delay initiation of therapy	Success is dependent on how feedback is communicated to prescribers

Figure 20: Antimicrobial Stewardship Treatment Algorithm

Adapted from Start Smart Then Focus Guidance for Antimicrobial Stewardship in hospitals (PHE, UK)



5.1 Front-end strategies

5.1.1. Antimicrobial Prescribing Policy

Hospital ASPs should include an Antimicrobial Prescribing Policy that is regularly reviewed and updated.

The important messages that need to be incorporated into the policy (MINDME) from Australian Stewardship Guidelines [Duguid et al., 2010] are illustrated in Table 3.

Table 3: The Golden Rules of Antimicrobial Prescribing "MINDME"

Adapted from Antibiotic Expert Group. Therapeutic guidelines: antibiotic. Version 14. Melbourne: Therapeutic Guidelines Limited; 2010

M	microbiology guides therapy wherever possible
I	indications should be evidence based
N	narrowest spectrum required
D	dosage appropriate to the site and type of infection
M	minimise duration of therapy
E	ensure monotherapy in most cases

5.1.2. Clinical guidelines or care pathways

Clinical guidelines or care pathways should take into account local microbiology and antimicrobial susceptibility patterns, as well as local resources and priorities, clinician preference/views and potential risk or unintended consequences. For guidelines to be relevant to daily practice, it is important they are updated on a regular basis and that older or outdated recommendations are removed.

The publication of national guidelines for South Africa and India for the antimicrobial treatment of infectious disease are recent examples of good practice. Furthermore, India has just published specific guidelines for Antimicrobial Stewardship Programs [ICMR, 2018].

5.1.3. Formulary restrictions / approval systems

This involves determining the list of restricted antimicrobial agents (broad spectrum and later generation antimicrobials) and criteria for their use combined with an approval system which is subject to regular audit and feedback to the prescribers. It is essential that all aspects of prescribing are supported by expert advice 24 hours a day where possible.

5.2 Back-end strategies

5.2.1. Antimicrobial review methods

Antimicrobial review methods are employed post-prescription and outlined in Table 4. The most appropriate interventions for your institution should be chosen, according to local resources.

Table 4: Antimicrobial Review Methods

Adapted from Johannsson B et al. Inf Control Hosp Epidemiol. 2011;32: 367-374

TYPE OF INTERVENTION
COMMONLY USED
■ Review of indication for antibiotic and compliance with policy/guideline/formulary; note any recording of exception
■ Review of appropriateness of antibiotic choice, dose, route and planned duration; review of drug allergy, review of agents that may provide duplicative therapy (potential overlapping spectra)
■ Review of directed therapy based on culture and susceptibility test results
■ Potential for conversion from IV to oral route
■ Review requirement for therapeutic drug monitoring
■ Review any antibiotic related adverse events
LESS COMMONLY USED AND DEPENDENT ON LOCAL RESOURCES
■ Unsolicited review of speciic resistant pathogens (e.g MRSA) or site of infection (e.g blood stream infections)
■ Speciic review of high cost/high use/novel agents
■ Review of optimal dose (PK/PD) in relation to dose and frequency; renal adjustment, need for extended infusion, review of any potential drug interactions
■ Review of directed therapy based on microscopy or PCR or other rapid tests**
■ Review of empiric or directed therapy based on biomarkers**

**The lack of diagnosis and delay in microbiology remains a significant hurdle to good stewardship and source of high cost.

5.2.2. Audit and direct feedback to prescribers

The audit and feedback process can be managed by either the medical infection specialist or specialist pharmacist. However, depending on the intervention, specialist nurses or clinical pharmacists can also be trained to support this process.

During clinical review, a range of point-of-care stewardship interventions are useful to provide direct and timely feedback to the prescriber at the time of prescription or laboratory diagnosis, and provide an opportunity to educate clinical staff on appropriate prescribing.

POINT-OF-CARE INTERVENTIONS CAN INCLUDE:

- appropriate use of guidance,
- indication for antibiotic,
- choice of agent,
- route [IV vs. oral] of administration of treatment,
- timeliness of treatment,
- likelihood of on-going infection or not,
- use of diagnostic tests for investigation,
- interpretation of microbiology with a view to de-escalation,
- duration of therapy.

The types of interventions selected, how they are delivered and by whom, will be determined by local resources, need and available expertise.

Feedback on antimicrobial prescribing should be provided regularly to prescribers in the **critical care setting**, and **areas of high and/or poor quality antimicrobial use.**

One way of evaluating prescribing within a unit or hospital is through regular point prevalence surveys (PPS) [Ansari et al., 2009, Seaton et al., 2007].

These data can be used in an audit process to provide structured feedback to prescribing teams and to define areas for improvement. Such point prevalence surveys can be used to establish baseline prescribing information and identify priorities for quality improvement.

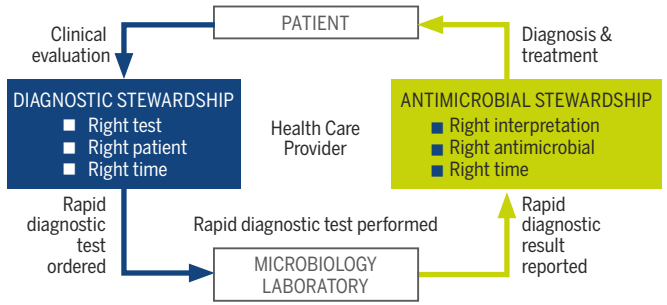
See section 6.1.1 for more details on Point Prevalence Surveys.

5.3 Role of Diagnostics in Stewardship

Diagnostic stewardship refers to the appropriate use of laboratory testing to guide patient management, including treatment, in order to optimize clinical outcomes and limit the spread of antimicrobial resistance. This requires a seamless partnership between clinical laboratories, pharmacists, and infectious diseases clinicians, so that appropriate tests are ordered and diagnostic information is translated into appropriate management in real time.

Figure 21: Example of diagnostic and antimicrobial stewardship in the implementation of rapid molecular disease diagnostics

Adapted from Messacar et al. J Clin Microbiol. 2017;55:715-723



Laboratories play a key role in antimicrobial stewardship (Figure 21). However, they are often not used optimally or, in many parts of the world, they do not exist or have poor capacity and capability to deal with the problem. An example of an antimicrobial stewardship program for the microbiology laboratory and how it could be achieved is described in Figure 22.

Figure 22: Examples of essential, achievable, and aspirational antimicrobial stewardship activities for the microbiology laboratory

Adapted from Morency-Potvin et al. Clin Microbiol Rev. 2017;30:381-407

ESSENTIAL	ACHIEVABLE	ASPIRATIONAL
■ Collaborate in educating local healthcare workers on microbiology issues that impact treatment and AMR ■ Optimize communication of critical results and alert systems ■ Provide annual Cumulative Antimicrobial Susceptibility Report	Provide comments, in collaboration with ASP team, to guide therapy on microbiology reports ■ Use rapid diagnostics, multiplex PCR and AST* for targeted critical specimen types and respiratory pathogens ■ Collaborate in audit and feedback of antimicrobial therapies when lab tests are critical (eg: C.difficile, bloodstream infections)	Participate in national/ regional surveillance systems ■ Promote appropriate use of point-of-care microbiological tests

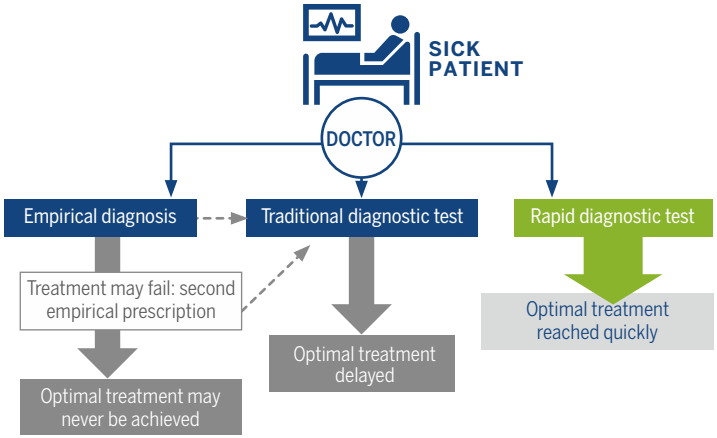
5.3 Role of Diagnostics in Stewardship

> The O'Neill report on AMR highlights the critical importance of the laboratory in reducing antimicrobial resistance and supporting prudent prescribing, as well as the role of new diagnostics and point-of-care tests [O'Neill et al. 2015].

The role that rapid diagnostic tests can play in optimizing the prescription of the most appropriate antibiotic therapy is illustrated in Figure 23.

Figure 23: How rapid diagnostic tests help optimize treatment

Adapted from O'Neill et al. The Review On Antimicrobial Resistance. 2015



The case study in Figure 24 illustrates the real world impact of a rapid respiratory panel (RP) on antibiotic and resource use.

Figure 24: Efect of rapid diagnostics on duration of antimicrobial therapy (ABX) and hospital length of stay (LOS)

Adapted from File et al. Open Forum Infect Dis. 2017;4(Suppl 1): S628–S629

RP result for virus	Mean Duration ABX after test result	LOS after test result
Virus + (n=30)	1.6 days	3.6 days
Virus - (n=51)	4 days	4.9 days
Virus +; PCT<0.25 (n=17)	1.2 days	2.9 days
Virus +; PCT<0.25; AST* (n=10)	0.6 days	2.7 d ys a

* Antimicrobial Stewardship Team recommendation. There was no difference in 30-day readmission rates. Of the patients with pneumonia; 11 had + RP for virus (7-HMV), 4 had co-infection with + bacteria with mean PCT of 0.62 and mean duration of ABX 6 days after test result; of the 7 with no bacterial co-infection the mean PCT was 0.12 with mean duration of ABX 0.28 days after the test result. RP: Respiratory Panel

Integration of diagnostics with other AS interventions, to provide fast **accurate identification and susceptibility testing, will achieve better clinical outcomes and timely streamlining/de-escalating of empiric broad-spectrum antibiotics** in seriously ill patients.

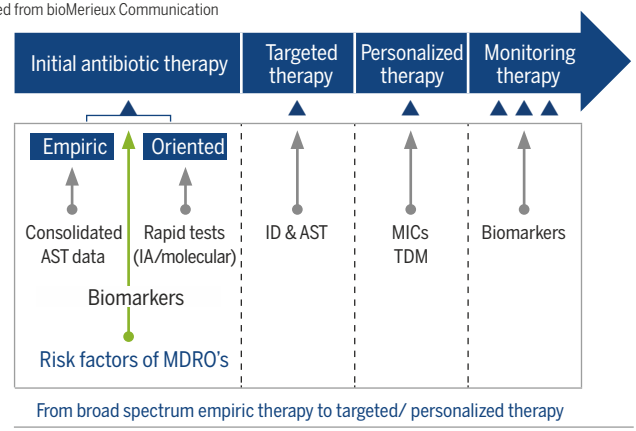
Many studies have assessed algorithms based on procalcitonin (PCT) as a rapid-reacting biomarker of bacterial infection for antibiotic stewardship. Recent systematic reviews showed benefits of PCT among patients with respiratory tract infection and sepsis by significantly reducing antibiotic exposure as well as a trend towards reduced costs and reduced length of ICU stay [Schuetz et al., 2011, Agarwal et al., 2011, Heyland et al., 2011, Mann et al., 2011, Matthaiou et al., 2012].

Near-patient rapid tests, e.g. influenza, Strep A, can be useful to identify patients with bacterial versus viral infections.

Molecular diagnostics or screening tests providing a faster result play an important role in pathogen detection in critically ill patients which will improve antibiotic stewardship and clinical outcomes [Afshari et al., 2012].

Figure 25: Role of diagnostics in supporting ASPs and appropriate antibiotic therapy

Adapted from bioMerieux Communication



ABBREVIATIONS
AST: Antimicrobial Susceptibility Testing - IA: Immuno Assay - ID: Identiication - MDRO: Multi Drug Resistant Organism - MIC: Minimum Inhibitory Concentration - TDM: Therapeutic Drug Monitoring

Diagnostic tests are key components of Antimicrobial Stewardship Programs, enabling the adjustment of treatment from broad spectrum antibiotic therapy to targeted and personalized treatments (Figure 25).

6. Identify key measurements for improvement

> "If you cannot measure it, you cannot improve it"
> Lord Kelvin 1824-1907

Measurement of prescribing performance is essential to evaluate the impact of stewardship interventions on clinical practice and demonstrate benefits for patients.

Establishing what to measure, the frequency of measurement and how the data will be communicated and acted upon are also key.

In addition to the audit and feedback described in section 5.2.2, three other types of measurement are commonly used within stewardship programs:

- surveillance of antimicrobial use and resistance,
- data collection for quality improvement,
- analysis of hospital datasets to evaluate positive and negative consequences of interventions.

6.1 Surveillance of antimicrobial use and resistance

Monitoring trends in antimicrobial use and resistance within a hospital over several years and also identifying small changes in a single ward over a one-month period are essential to:

- adapt empiric treatment according to local resistance trends,
- demonstrate changes in practice over time,
- identify wards with high antimicrobial usage or use of non-policy antimicrobials and define targeted interventions required.

> Measure improvement after implemented interventions

Surveillance of antimicrobial use and resistance is important:

- at hospital, local, regional, national levels (i.e.: Strama [http://en.strama.se], Wales [Heginbothom M and Howe R, 2012], Australia [www.health.sa.gov.au/INFECTIONCONTROL]),
- at global level (i.e.: ECDC: consolidation of resistance data at the European level [EARSS.net] with consolidation of antibiotic use [ESAC.net]), CDC National Antimicrobial Resistance Monitoring System [cdc.gov/NARMS] or Global PPS [www.global-pps.com].

6.1.1. Prescription surveillance through Point Prevalence Surveys

Regular point prevalence surveys (PPS) can be used to evaluate prescribing within a unit or hospital [Ansari et al., 2009, Seaton et al., 2007]. A new e-learning module is also now available to provide training for those undertaking these surveys [https://www.futurelearn.com/courses/point-prevalence-surveys].

These data can be used in an audit process to provide structured feedback to prescribing teams and to define areas for improvement. At a national level, as illustrated in an example for Scotland (Table 5), such point prevalence surveys can be used to establish baseline prescribing information and identify priorities for quality improvement. This information has led to the development of national prescribing indicators [Malcolm et al., 2012].

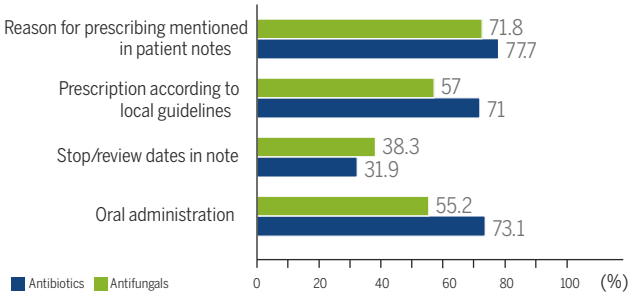
Table 5: Overview of prescribing from baseline PPS (May 2009) and follow up PPS (September 2011) in acute hospitals in Scotland

Measure	Baseline PPS (May 2009)	Follow up PPS (Sept 2011)
Number of patients surveyed	7,573	11,604
Number of patients (%) prescribed antimicrobials	2,289 (30.2%)	3,728 (32.3%)
Number of patients (%) prescribed single antimicrobial	1,432 (62.6%)	2,268 (60.8%) ↓ ☺
Number of prescriptions (%) for parenteral antimicrobials	1,731 (51.8%)	2,147 (47.8%) ↓ ☺
Number of prescriptions (%) with indication recorded in notes	2,538 (75.9%)	3,811 (86.8%) ↑ ☺
Number of prescriptions (%) compliant with local policy	1939 (81.0%)	2,245 (82.8%) ↑ ☺
Number of surgical prophylaxis prescriptions (%) with duration single dose	146 (49.3%)	287 (59.5%) ↑ ☺
Number of surgical prophylaxis prescriptions (%) with duration = 1 day	57 (19.3%)	81 (16.8%) ↓ ☺
Number of surgical prophylaxis prescriptions (%) with duration >1 day	93 (31.4%)	114 (23.7%) ↓ ☺

The value of these metrics has recently been illustrated at a global level. The GLOBAL PPS mentioned previously (see Figure 3) can provide not only metrics in relation to the prescribing quality process, but the ability to compare variations in practice between classes of agents. For example, in Figure 26, the quality of antibacterial and antifungal prescribing is compared, the latter being an important and rapidly emerging area for stewardship.

Figure 26: Global-PPS: Diference in quality of prescribing between antibacterials and antifungals

Adapted from Yusuf E et al. J Antimicrob Chemother. 2017;72:2906-2909



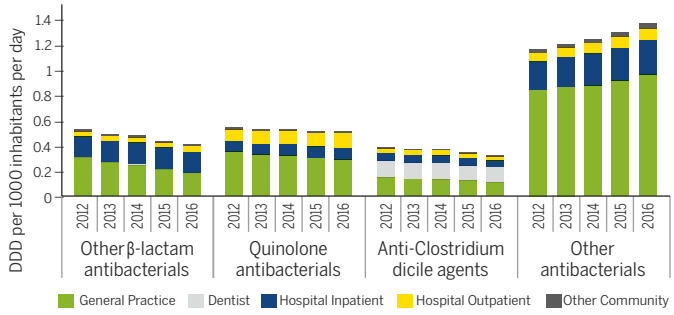
6.1.2. How is antimicrobial use data collected and analyzed?

- Antimicrobial use at individual patient level, using an electronic prescribing system through the Hospital Information System.
- Data from hospital pharmacy computer systems, showing antimicrobials delivered to each ward and used as a proxy measure for antimicrobials administered to patients.
- The measure used is Defined Daily Dose (DDD) which represents the average daily maintenance dose of an antimicrobial for its main indication in adults (Figure 27). For instance, the DDD of oral amoxicillin is 1000 mg, so a patient receiving 500 mg every 8 hours for 5 days consumes 7.5 DDDs.
- Usage data may then be divided by a measure of hospital activity such as number of admissions or in-patient bed days to provide more meaningful trend analysis. In-patient bed days is more commonly used as this data can usually be obtained earlier than admissions data.
- Other denominators are also used and their strengths and limitations have been described [Monnet D et al., 2007; Berrington A, et al., 2010]

Hospital level data may be transferred to a national database for further analysis.

Figure 27: Total antibiotic consumption by key antibiotic groups, expressed as DDD per 1000 inhabitants per day, England, 2012-2016

Adapted from Public Health England. English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Report 2017



ABC Calc is a simple computer tool to measure antibiotic consumption in hospitals. It transforms aggregated data provided by hospital pharmacies into meaningful antibiotic utilisation rates.

[http://www.escmid.org/research_projects/study_groups/esgap/abc_calc/]

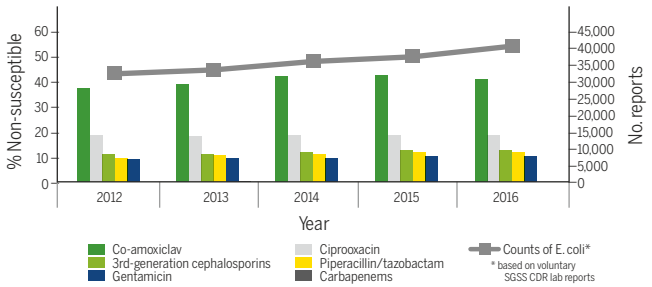
Pareto charts are another useful tool to provide an overview of antimicrobial usage at ward level and identify wards that have high total usage or high use of restricted antimicrobials.

6.1.3. How is antimicrobial resistance data collected and analyzed?

Resistance data is obtained from the Microbiology laboratory through computer systems. Hospital level data may then be transferred to national databases. This is illustrated by an example from England (Figure 28).

Figure 28: Number of bloodstream isolates of E. coli reported to the mandatory surveillance scheme and the proportions non-susceptible to indicated antibiotics

Adapted from Public Health England. English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Report 2017



6.2 Data collection for quality improvement

Antimicrobial stewardship is part of many patient safety programs. To measure the performance of these programs, data is primarily used for 3 purposes [Solberg et al., 1997]:

- accountability (e.g. targets),
- improvement,
- research.

A range of such measures for antimicrobial stewardship programs have been proposed. They can be summarized as four types (Table 6): structural, process, outcomes and balancing (are the changes causing new problems?) [www.abs-international.eu; Dumartin et al., 2011].

Table 6: AMS program measures for quality improvement

Adapted from Dumartin C et al. J Antimicrob Chemother. 2011;66:1631-7; Morris AM et al. Inf Control Hosp Epidemiol. 2012;33:500-506

STRUCTURAL INDICATORS

- Availability of multi-disciplinary antimicrobial stewardship team
- Availability of guidelines for empiric treatment and surgical prophylaxis
- Provision of education in the last 2 years

PROCESS MEASURES

- Amount of antibiotic in DDD/100 bed days
  - Promoted antibiotics
  - Restricted antibiotics
- Compliance with acute empiric guidance (documented notes and policy compliance)
- % appropriate de-escalation; % appropriate switch from IV to oral
- Compliance with surgical prophylaxis (<60 min from incision, <24 hours and compliance with local policy
- Compliance with care "bundles" – all or nothing (3-day antibiotic review bundle, ventilator-associated pneumonia, community-acquired pneumonia, sepsis)

OUTCOME MEASURES

- C. diffcile infection rates
- Surgical Site Infection (SSI) rates
- Surveillance of resistance
- Mortality: Standardized Mortality Rates (SMRs)

BALANCING MEASURES

- Mortality
- SSI rates
- Readmission within 30 days of discharge
- Admission to ICU
- Rate of complications
- Treatment-related toxicity (e.g. aminoglycoside-related toxicity)

A focus on outcomes data must be the key to convincing leadership, budget holders and decision makers of the value of stewardship programs. Such measures are outlined in Table 7.

Table 7: Examples of diferent outcome measures and some general remarks general

Adapted from Dik J et al. Expert Review of Anti-infective Therapy, 2016. 14:6, 569-575

OUTCOME MEASURES	REMARKS
CLINICAL	
Mortality	Important, but less suitable for mild infections (e.g. uncomplicated UTI)
Length of Stay	General or ward-speciic (e.g. ICU stay); easy to obtain, but highly sensitive to biases
Complications	Eg: IV catheter-related problems and phlebitis
Clostridium diffcile	Indirect measure for antimicrobial use
Readmission rates	Due to relapse. Also consider efect of neighboring institutions
Toxicity (systemic)	Most frequently in renal function and liver
MICROBIOLOGICAL	
Resistance levels	Diffcult to measure due to generally long time frame (months to years) (months to years)
ANTIMICROBIAL CONSUMPTION	
Total use	Often measured in DDDs
IV/PO ratio	Of interest with an active IV-to-PO switch program
Broad/narrow ratio	Potentially relevant with regard to resistance development
FINANCIAL	**Preferably done as cost-efectiveness study**

UTI: urinary tract infection; ICU: intensive care unit; PO: per os; LOS: Length of stay; DDDs: deined daily doses; IV: intravenous.

Checklists are increasingly used to measure quality of care. A study of the use of an antibiotic checklist implemented in nine Dutch hospitals showed that use of the checklist resulted in more appropriate antibiotic use (Table 8).

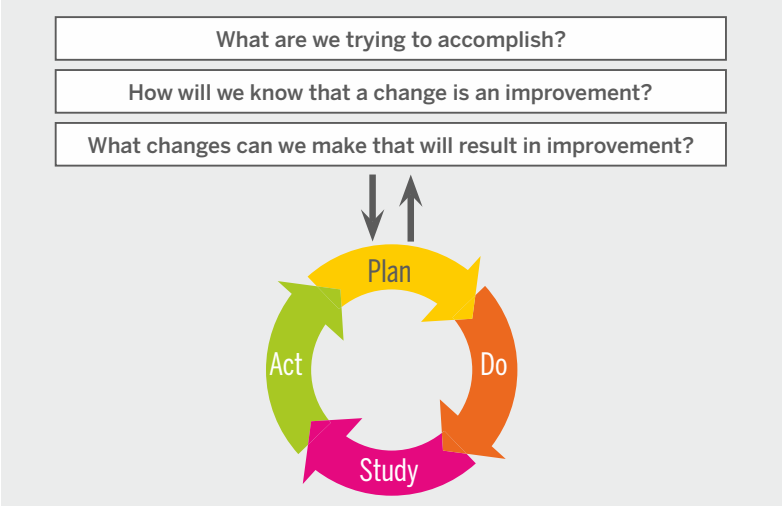
Table 8: Examples of checklist items

Adapted from van Daalen F et al., BMC Infect Dis. 2018;18:16

- Blood cultures
- Culture from suspected site of infection
- Guideline adherence
- Adapt dose to renal function
- Documentation of indication
- Adapt therapy when cultures become available
- IV-oral switch

6.2.1. Examples of measures for improvement

A common quality improvement methodology is the "Plan- Do- Study- Act" model.

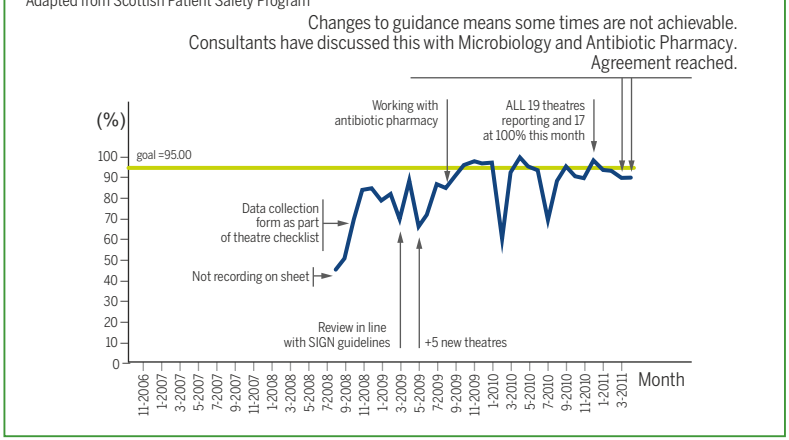


www.ihi.org/knowledge/Pages/HowtoImprove/ScienceofImprovementHowtoImprove

Quality improvement programs often use annotated run charts to display data and show the effects of changes. Figure 29 shows an example of a run chart used to measure improvement of administration of surgical antibiotic prophylaxis on time.

Figure 29: Percent on-time administration of prophylactic antibiotics

Adapted from Scottish Patient Safety Program

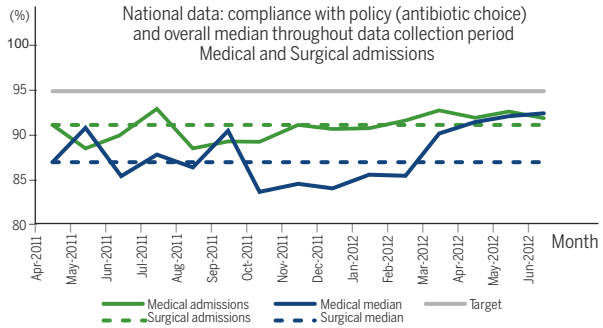


6.2.2. Example of measures used for accountability

Compliance with policy is a process measure (Figure 30).

Figure 30: Antibiotic choice compliant with policy

Adapted from Empirical Prescribing Indicator Report April 2011 – June 2012. Scottish Antimicrobial Prescribing Group August 2012



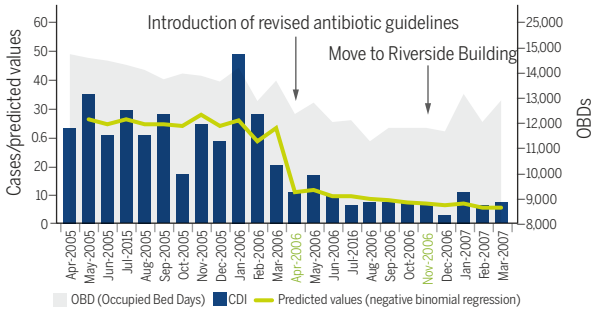
6.3. Analysis of hospital datasets

Linkage of hospital datasets such as hospital admissions, laboratory data and patient outcomes allows measurement of the impact of stewardshipinterventions on patient morbidity and mortality.

This provides information about effects of antimicrobial interventions onclinical outcome. Figure 31 shows how restriction of cephalosporins and fluoroquinolones has resulted in reduced Clostridium difficile rates by linking antimicrobial usage data and microbiology data [Talpaert et al., 2011, Vernaz et al.,2009, Mamoon et al., 2012].

Figure 31: New cases of CDI and the number of OBDs before and after the introduction of revised antibiotic guidelines

Adapted from Talpaert MJ et al. J Antimicrobial Chemother. 2011; 66: 2168-2174



7. Educate and Train

Education is a key component of any Antimicrobial Stewardship Program. It should include healthcare professionals from all care settings, as well as patients and the public.

By increasing people's knowledge and understanding of how antimicrobials should be used to treat common infections and why inappropriate use may lead to resistance and loss of effective treatments, we can protect this valuable resource for future generations.

7.1 Who should receive education?

Prescribers and other healthcare staff with modules adapted to their background including:

- undergraduate curriculum,
- internship,
- professional training for new staff,
- continuing professional development for all prescribers,
- postgraduate education.

The content of education should be adapted to each profession and include:

- basic knowledge of infection management,
- basic microbiology,
- importance of prudent prescribing in tackling antimicrobial resistance,
- best practices for prescribing to support safe and effective prescribing, administration and monitoring of antimicrobial therapy.

The training is usually delivered by the antimicrobial management team and should include competency assessment. In 2014, the first national antimicrobial prescribing and stewardship competences were developed in the UK, and their implementation was an important contribution to the delivery of the UK 5 year Antimicrobial Resistance Strategy [Ashiru-Oredope et al., 2014]. The Stewardship Competency Framework for all healthcare professionals has also been developed by WHO [https://www.who.int/hrh/resources/ WHO-HISHWF-AMR-2018.1/en/] and advocates the principles shown in Table 9 [Ashiru-Oredope et al., 2014].

Table 9: The Stewardship Competency Framework

Table 9: The Stewardship Competency Framework

This consists of five dimensions, each of which includes statements that describe the activity and outcomes that prescribers should be able to demonstrate:

- Infection prevention and control
- Antimicrobial resistance and antimicrobials
- The prescribing of antimicrobials
- Antimicrobial stewardship
- Monitoring and learning

Educating patients and the general public about hygiene and antibiotic use is also important, and may indirectly support hospital education efforts. National and regional public health campaigns, including education aimed at parents and children, have had a variable level of success [Huttner et al., 2010].

Some examples of public awareness campaigns:

www.e-bug.eu www.ecdc.europa.eu/en/eaad www.cdc.gov/getsmart

7.2 How to design an education program?

Programs should take into account local recommendations for antimicrobial stewardship, if available. If not, they could be inspired by international policies (see section on "Additional Resources", page 48) but adapted as required. Table 10 shows educational measures to improve antibiotic use in hospitals.

Table 10: Main antimicrobial stewardship strategies recommended to improve antibiotic use at the hospital level

Adapted from Pulcini C and Gyssens IC. Virulence 2013;4:192–202

PASSIVE EDUCATIONAL MEASURES

Developing/updating local antibiotic guidelines, clinical pathways or algorithms

Face to face educational sessions, workshops, local conferences

ACTIVE INTERVENTIONS

- Clinical rounds discussing clinical cases, morbidity & mortality meetings, significant event analysis/reviews
- Prospective audit with intervention and feedback
- Reassessment of antibiotic prescriptions, with streamlining and de-escalation
- Academic detailing, educational outreach visits
- E-learning resources used as individual or group activities can compliment traditional learning methods, as a "blended learning" approach (see page 49).

An evaluation process should be included in the education program to measure attendance, understanding and assimilation, using regular training assessment tools such as attendance forms, completion certificates, questionnaires, tests etc.

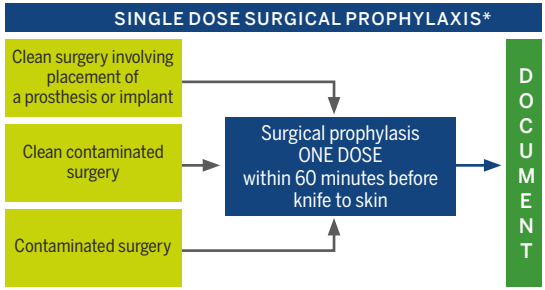
8. Communicate

Communication is a key component of the success of an ASP.

> Clear, simple communication should show the vision and the benefits of the program, with core clinical messages.

Communicating to prescribers what the program recommends them to do is one of the essential implementation steps to successful stewardship. This requires a simple messaging approach that has identified key processes where stewardship interventions are required to be considered and actioned, such as the "Start Smart-Then Focus" approach developed in the UK. Figure 32 identifies the process for delivering effective surgical prophylaxis.

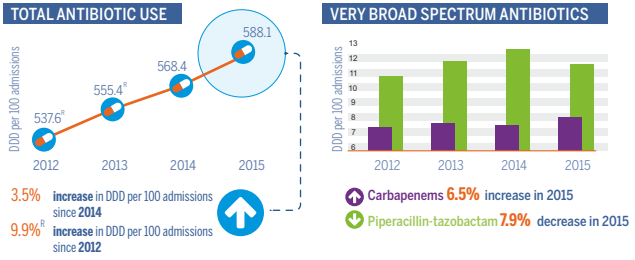
Figure 32: Start Smart ... Then Focus approach



*A repeat dose dose of prophylaxis may be required for prolonged procedures or where there is significant blood loss. A treatment course of antibiotics may also need to be given (in addition to appropriate prophylaxis) in cases of dirty surgery or infected wounds. The appropriate use and choice of antibiotics should be discussed with infection specialists for each case.

Another key communication tool that improves the effectiveness of conveying key messages is data visualization. Using infographic or other visual aids can be a compelling means of communicating data (Figure 33).

Figure 33: Examples of infographics on Antibiotic Use



Finally, it is important to keep messages for clinical practice simple. For example, the 10 point principles approach below is easy to assimilate into practice and is relevant to the whole team looking after a patient with infection on antibiotics (Table 11).

Table 11: Ten key points for the appropriate use of antibiotics in hospitalized patients

Adapted from Levy et al. Int J Antimicrob Agents. 2016; 48: 239-46

1. Get microbiological samples before antibiotic administration and carefully interpret results: if no clinical signs of infection, colonization rarely requires antimicrobial treatment.
2. Only treat significant bacterial infections.
3. When indicated, start empirical antibiotic treatment, according to site of infection, risk factors for MDR bacteria, and local microbiology/susceptibility patterns.
4. Prescribe drugs at optimal dose, administration mode and length of time.
5. Use antibiotic combinations only when current evidence suggests some benefit.
6. Avoid antibiotics with a higher likelihood of promoting drug resistance or hospital-acquired infections.
7. Remove all infected devices.
8. Always try to de-escalate antibiotic treatment according to clinical situation and microbiological results; switch to oral route as soon as possible.
9. Stop antibiotics as soon as a significant bacterial infection is unlikely.
10. Set up local teams with an infectious diseases specialist, clinical microbiologist, hospital pharmacist, infection control practitioner or hospital epidemiologist; comply with antibiotic policies/guidelines.

Another approach is to identify and communicate to prescribers specific situations where antibiotics should be withheld (Table 12) and guidance in relation to the duration of antibiotic use, which is often an area of misuse (Table 13).

Communicating, sharing and learning from data is also important.

Face-to-face meetings with prescribers, where there is an opportunity for reflection about their prescribing practices, or attending multi-disciplinary team web-ex conferences, etc. are all important in promoting learning about prudent prescribing.

HOW TO IMPLEMENT AN ANTIMICROBIAL STEWARDSHIP PROGRAM

Table 12: Specific Situations where Antibiotics should be withheld

Adapted from Wlodaver CG et al., Infect Dis Clin Pract. 2012;20:12-17

RESPIRATORY TRACT INFECTIONS

- Viral pharyngitis
- Viral rhinosinusitis
- Viral bronchitis
- Noninfectious cardiopulmonary disorders misdiagnosed as pneumonia

ACUTE OTITIS MEDIA (AOM) (for selected cases, refer to article)

- Skin and Soft Tissue Infections (SSTI)

- Subcutaneous abscesses (for selected cases, refer to article)

- Lower extremity stasis dermatitis

ASYMPTOMATIC BACTERIURIA AND PYURIA, INCLUDING CATHETERIZED PATIENTS

MICROBIAL COLONIZATION AND CULTURE CONTAMINATION

LOW-GRADE FEVER

Recently, as shown in Table 13, the move towards safely and effectively reducing duration of treatment, an important antimicrobial stewardship goal, is gaining pace [Spellberg, 2016], as is the whole concept of completing courses of therapy [Llewelyn, 2017]. The use of diagnostic tests, including biomarkers, will further support the move towards a more precise approach to duration of antimicrobial therapy.

Table 13: Infections for Which Short-Course Therapy Has Been Shown to be Equivalent in Efficacy to Longer Therapy

Adapted from Spellberg B. JAMA Intern Med. 2016;176:1254-1255

TREATMENT DURATION IN DAYS	SHORT	LONG
Community-acquired pneumonia	**3-5**	7-10
Nosocomial pneumonia	**≤8**	10-15
Pyelonephritis	**5-7**	10-14
Intraabdominal infection	**4**	10
Acute exacerbation of chronic bronchitis and COPD*	**≤5**	≥7
Acute bacterial sinusitis	**5**	10
Cellulitis	**5-6**	10
Chronic osteomyelitis	**42**	84

THE KEYS TO SUCCESS

A number of interventions are key to the success of a hospital-based Antimicrobial Stewardship Program.

- Establish clear aims/vision that is shared by all the stakeholders and that conveys a sense of urgency.
- Stewardship should be a patient safety priority. Seek management support, accountability and secure funding.
- Assemble a strong coalition including a multi-professional antimicrobial stewardship team with a strong influential clinical leader.
- Establish effective communication structures within your hospital.
- Start with core evidence-based stewardship interventions depending on local needs, geography and resources and plan measurement to demonstrate their impact.
- Ensure all healthcare staff are aware of the importance of stewardship. Empower them to act and support with education using a range of effective strategies.
- Ensure early or short term wins and then consolidate success/gains while progressing with more change or innovation.

KEY EVIDENCE-BASED PUBLICATIONS ON ANTIMICROBIAL STEWARDSHIP

- Baur D, et al. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and Clostridium difficile infection: a systematic review and meta-analysis. Lancet Infectious Diseases 2017; 17:990-1001
- Davey P, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database of Systematic Reviews 2017;(2): CD003543
- Davey P, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database of Systematic Reviews 2013;(4): CD003543
- Dellit TH, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clinical Infectious Diseases 2007;44:159-77
- Dik J-WH, et al. Financial evaluations of antibiotic stewardship programs— a systematic review. Frontiers in microbiology 2015:6:317
- Feazel LM, et al. Effect of antibiotic stewardship programmes on Clostridium difficile incidence: a systematic review and meta-analysis. Journal of Antimicrobial Chemotherapy 2014;69:1748–1754
- Feazel, LM, Malhotra, A, Perencevich, EN, Kaboli, P, Diekema, DJ, and Schweizer, ML. Effect of antibiotic stewardship programs on Clostridium difficile incidence: a systematic review and meta-analysis. J Antimicrob Chemother. 2014; 69: 1748–1754
- Karanika S, et al. Systematic review and meta-analysis of clinical and economic outcomes from the implementation of hospital-based antimicrobial stewardship programs. Antimicrobial Agents and Chemotherapy 2016;60:4840–4852
- Schuts EC, et al. Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis. Lancet InfectiousDiseases 2016;16:847-56
- Van Dijck C, et al. Antibiotic stewardship interventions in hospitals in low-and middle-income countries: a systematic review. Bulletin WorldHealth Organization 2018; 6(4):266–280

USEFUL RESOURCES FOR EDUCATION AND TRAINING IN ANTIMICROBIAL STEWARDSHIP

- WHO on-line course - Antimicrobial stewardship: a competency- based approach.
  Access: https://openwho.org/courses/AMR-competency
  CDC on-line course: Antibiotic Stewardship
  Access: https://www.train.org/cdctrain/course/1075730/compilation

- Ebook- Antimicrobial Stewardship: From Principles to Practice. British Society for Antimicrobial Chemotherapy [BSAC]
  Access: http://bsac.org.uk/antimicrobialstewardship-from-principles- to-practice-e-book/

- Massive Open Online Course on Antimicrobial Stewardship. Available in English, Mandarin, Spanish, and Russian.
  BSAC with University of Dundee and FutureLearn
  Access: https://www.futurelearn.com /courses/antimicrobial-stewardship
  New on-line Stewardship module for Africa
  Access: https://www.futurelearn.com/courses /antimicrobial-stewardshipfor- africa

- Antimicrobial Stewardship (AMS), Volume 2, 1st Edition.
  Access: https://www.elsevier.com/books/antimicrobial-stewardship/pulcini/978-0-12-810477-4

- CIDRAP web-based resource: Antimicrobial stewardship project with emphasis on news, commentary, webinars, podcasts
  Access: http://www.cidrap.umn.edu/asp

- Global Point Prevalence Survey led by the University of Antwerp
  Access: http://www.global-pps.com

Photographs of the First Indo-French AMR Symposium 2023


DE FRANCE
EN INDE
INDO-FRENCH SYMPOSIUM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EN INDE
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FRANÇAIS


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Liberté Créativité Diversité


AMBASSADE
DE FRANCE
EN INDE
BIOMÉRIEUX

OVERVIEW

The 1st "Indo-French symposium on antimicrobial stewardship: Improved diagnosis for better patient management" was held on 20 June 2023. The bilateral collaboration in healthcare between France and India: bioMérieux, the French Embassy in India / Ambassade de France en Inde and Indo-French Centre for the Promotion of Advanced Research (IFCPAR/CEFIPRA) was organized in the Embassy of France in New Delhi.

Antimicrobial resistant microbes are difficult to treat because antimicrobials are increasingly becoming ineffective against these infections resulting in higher mortality rates. Antimicrobial resistance poses a considerable threat to human health, with an estimated 4.95 million deaths associated with bacterial antimicrobial resistance in 2019. Because AMR is a complex issue, it is necessary to look at it from different disciplines to frame it within the One Health approach, which is fully integrated into global efforts to address the problem of AMR. Interdisciplinary collaboration is at the heart of the One Health Concept and forefront countries, medical and environmental bodies and institutions need to collectively work together to find resolute solutions.

The symposium attracted a diverse range of participants, including over 40 key dignitaries and featured over 20 distinguished speakers representing key government institutes such as the Indian Council of Medical Research (ICMR), the National Centre for Disease Control (NCDC), the National Health Systems Resource Centre (NHSRC), the Biotechnology Industry Research Assistance Council (BIRAC), as well as international experts from prominent organizations like the World Health Organization (WHO), the French Agency for Food, Environmental, and Occupational Health & Safety (ANSES), the Mérieux Institute, and the French Research Institute for Development (IRD).

Gathering around the same table, the event brought together key stakeholders of Indian and French public health. In a first, this event marks the starting point of a strengthened collaboration between France and India on the global acute challenge of resistance to antimicrobials, one of the greatest threats of the 21st century, faced by mankind and the shared ecosystem we live in.

OVERVIEW

The event was well attended and received with many essential actionable takeaways. During the panel discussions, experts from ICMR and NCDC reiterated the indispensable role of laboratory expertise and therefore training at the elementary level in optimal utilization of diagnostic tests to curb AMR. Skill building of the users was also viewed as one of the major responsibilities of the diagnostic companies. The role of diagnostics in AMR mitigation is advocated in the Global research agenda for antimicrobial resistance in human health, WHO Policy Brief (June 2023). Right test at the right time on the right patient is essential for diagnostic stewardship that translates to right antimicrobial selection and informed prescription on a timely basis.

bioMérieux, being a global leader in Infectious Diseases diagnostic solutions, is proud to be part of this dialogue, as fast, accurate and accessible diagnostics are a key solution to this challenge.

Take home messages.

The event that gathered approximately 70 scientists and medical professionals, highlighted the **diverse landscape of diagnostic practices for appropriate antibiotic usage in India,** along with the associated needs. Thereafter are the take home messages:

- The **AMR topic has garnered significant attention within the French and Indian scientific and medical community.** A consensus emerged regarding the paramount significance of this matter in the Indian context, encompassing medical, economic, and societal dimensions. Bilateral cooperation in this sector may support mutual benefits.
- The **requirements for antimicrobial susceptibility diagnostics of pathogens, in order to select the appropriate antibiotics, are both extensive and heterogeneous,** thereby necessitating tailored technical solutions that are:

• Suited to the context (ranging from vast centralized hospitals to fragmented and under-equipped urban medical settings, as well as access to care in rural areas).

• Accessible at an affordable cost.

- The **demand for technical personnel training is substantial, and the enhancement of analytical laboratory capabilities must align with strategic choices based on the laboratory's environment, including optimizing the nature of equipment.**

KEY QUOTES

Dr. YK Gupta
"Antimicrobial resistance is a public health emergency; each one of us is a victim of inappropriate antibiotic use."

Dr. Ranga Reddy
"Real-time diagnostics has a crucial role. A quick diagnosis of infectious disease can buy time and optimize antimicrobial treatment. For diagnostic stewardship, all stakeholders have a role."

Dr. Sindhura Ganapati
"One Health is like world peace. Look into the root cause of inappropriate antibiotic use in different sectors. The onus is on each one of us to change the situation."

Dr. Kamini Walia
"Our studies show that up to 75% of antibiotic prescriptions in India are from the WATCH and reserve group. The main reason is the lack of a rapid definitive diagnostic facility. For every 1 USD spent on infection control, hospitals can earn 250 USD. "

Dr. Shirshendu Mukherjee
"Antimicrobial resistance needs a mission-mode approach like COVID. The ideal diagnostic tool should be fast, accurate, affordable, accessible, and of the highest quality. It should be available at the point of care."

Dr. Marc Bonneville
"IT solutions can be integrated into diagnostic tools for infectious diseases for better patient access."

Dr. Sankar Sengupta
"Antibiotic anarchy in India is due to wrong prescriptions, absence of evidence-based practice, OTC medication sale, irrational combinations of antibiotics, community-acquired resistance, and lack of training in the majority of hospitals in tier 2 and 3 cities."

Dr. Lata Kapoor
"One session in every medical conference should be dedicated to antimicrobial resistance. Medical education should focus on AMR."

Perspectives for the Indo-French academic and scientific cooperation

The collaboration between France and India in the realm of antimicrobial resistance holds significant potential for further advancement and could be further structured around various initiatives.

- In terms of communication, awareness and collective reflection on the subject, BIOMÉRIEUX India aims to sustain the initiative via regular symposia in Delhi and in various cities in India. Additionally, a Franco-Indian committee focussed on antimicrobial resistance is envisaged, bring together key stakeholders from the June 20 symposium and contributing to the Franco-Indian bilateral health dialogue.
- Joint training initiatives could be established to continuously raise awareness among healthcare professionals and researchers about the challenges of antimicrobial resistance (AMR) and to promote responsible practices in antimicrobial usage. These training programs and workshops could cover medical and paramedical training, strengthening local capacities and involving relevant mobility schemes (grants, summer schools, etc.), in conjunction with or independently of BIOMÉRIEUX. The possibilities of concrete actions associating BIOMÉRIEUX and the Indo-French Centre for the Promotion of Advanced Research (CEFIPRA) or BIOMÉRIEUX and the Franco-Indian Trust for Education are currently being studied.

- Several promising avenues of scientific collaboration would be pursued:

1- Special attention would be given to the structuring of data related to antimicrobial usage records. Standardization of data is a key point and limiting factor for further cooperation.

2- Collaborative efforts would be underway to model usage patterns and predict the emergence of antimicrobial resistance risk based on different usage scenarios

3- Another significant aspect of cooperation would pertain to the epidemiology of antimicrobial resistance profiles across various ecosystems, whether rural or urban. This approach would encompass human, environmental, and animal components within the framework of One Health. This holistic approach would enhance the understanding of mechanisms behind antimicrobial resistance propagation and identify effective prevention strategies.

- 4 Both countries would closely collaborate to decipher the determinants of behaviors among stakeholders involved in antimicrobial usage, and to establish incentives that would encourage the adoption of best practices. These efforts would be informed by experimental economics, aiming to better comprehend the economic and behavioural incentives that influence decisions related to antimicrobial usage.

- 5 A shared initiative could cover the efforts in creating cutting-edge diagnostic methods in the realm of antimicrobial resistance (AMR). This initiative would aim to devise advanced and precise diagnostic techniques, enabling rapid and reliable detection of antimicrobial resistance. Such an advancement would represent a significant step forward in addressing the AMR challenge.

KEY POINTS DISCUSSED

1. Antimicrobial resistance (AMR) is a significant global health problem that occurs when microorganisms, such as bacteria, viruses, fungi, and parasites, develop resistance to the drugs used to treat infections. This means that the medicines that were once effective in treating various infectious diseases become less or entirely ineffective, leading to prolonged illnesses, increased healthcare costs, and even death. In 70% of cases, antibiotics are not needed; in 30% of the cases where antibiotics are needed, 70% are inappropriate ones that are used.
2. The prevalence of AMR varies by region, type of antimicrobial agent, and specific pathogens. Here are some key points about the prevalence of antimicrobial resistance globally:

- **Bacterial Infections:** AMR is most commonly associated with bacterial infections. Some bacterial pathogens have developed resistance to multiple antibiotics, making them difficult to treat. This includes well-known pathogens such as methicillin-resistant Staphylococcus aureus (MRSA) and multidrug-resistant tuberculosis (MDR-TB).
- **Regional Variation:** The prevalence of AMR varies significantly by region and country. High rates of resistance are often found in low- and middle-income countries where antibiotics might be used more liberally, and where healthcare infrastructure and infection control measures might be limited.
- **Common Resistant Pathogens:** Certain bacteria have gained attention due to their high levels of resistance. These include, but are not limited to, Escherichia coli (E. coli), Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Staphylococcus aureus and Enterococcus fecium.
- **Resistance in Healthcare Settings:** Hospitals and other healthcare facilities can be hotspots for the development and spread of AMR due to factors such as high antibiotic usage, close patient contact, and compromised immune systems.
- **Community-Acquired Infections:** AMR is not limited to healthcare settings. Resistant infections can also be acquired in community settings, and certain strains of bacteria have become increasingly resistant in these environments.
- **Animal Agriculture:** The use of antibiotics in animal agriculture contributes to the development of AMR. Resistant bacteria can be transmitted to humans through consumption of contaminated food products.
- **Data Challenges:** In some regions, comprehensive and standardized data on AMR prevalence might be lacking. This can hinder accurate assessments of the extent of the problem.
- **Data Challenges:** In some regions, comprehensive and standardized data on AMR prevalence might be lacking. This can hinder accurate assessments of the extent of the problem.

- **Global Surveillance:** Various international organizations, including the World Health Organization (WHO) and the World Organisation for Animal Health (OIE), conduct surveillance and monitor AMR trends globally. Surveillance networks help track the spread of resistant pathogens and inform strategies for containment.
- **One Health Approach:** The "One Health" approach recognizes the interconnectedness of human, animal, and environmental health. It emphasizes collaborative efforts among human health, veterinary, and environmental sectors to address AMR comprehensively.
- **Preventive Measures:** Countries and international organizations are implementing measures to reduce the prevalence of AMR. These include promoting responsible antibiotic use, implementing infection prevention and control measures, encouraging vaccination, and supporting research and development of new antimicrobial agents.

3. **There are several key aspects and consequences associated with AMR:**

- **Increased infections:** As more microorganisms become resistant to antimicrobial drugs, infections can spread more easily and cause outbreaks that are challenging to control.
- **Limited treatment options:** As the effectiveness of existing antimicrobial drugs diminishes, healthcare providers have fewer treatment options available for common infections, making it difficult to manage diseases effectively.
- **Complicated medical procedures:** AMR can complicate medical procedures such as surgeries, chemotherapy, and organ transplants, as the risk of infection becomes higher due to limited options for preventing or treating infections.
- **Economic Burden:** The economic impact of AMR is substantial. It results in longer hospital stays, increased medical costs, and reduced productivity due to prolonged illnesses.
- **Agricultural and environmental concerns:** The misuse and overuse of antimicrobial drugs in agriculture contribute to the development of AMR in livestock and agriculture-related pathogens. Additionally, wastewater discharge from hospitals and pharmaceutical industries can also spread resistant microbes into the environment.
- **Global spread:** AMR is trans-boundary and resistant strains of microorganisms can spread globally, creating a challenge for international health organizations and governments.
- **Lack of new antibiotics:** There has been a decline in the development of new antibiotics in recent years. The pharmaceutical industry faces challenges in investing in the research and development of new antimicrobial drugs due to financial concerns and the difficulty of finding profitable markets.

- **Misuse and overuse:** The inappropriate use of antimicrobial drugs in both human and animal health settings contributes significantly to the development of resistance. This includes prescribing antibiotics for viral infections (where they are ineffective) and using antibiotics in animal feed for growth promotion rather than treating infections.

4. Addressing rigidity in following AMR guidelines requires striking a balance between adherence to evidence-based guidelines and providing individualized patient care. Here are some strategies to achieve this balance:

- **Flexibility in clinical decision-making:** Encourage healthcare providers to consider patient-specific factors, such as the severity of illness, clinical presentation, and underlying conditions, when determining the need for antimicrobial treatment.
- **Continued education:** Regularly update healthcare professionals with the latest evidence and guidelines on AMR and appropriate antibiotic use. This can help them make informed decisions based on the most current information.
- **Local surveillance:** Establish and maintain local surveillance of AMR patterns to tailor treatment decisions to the specific resistance patterns in a given area.
- **Shared decision-making:** Involve patients in treatment decisions and educate them about the appropriate use of antibiotics. When patients are well-informed, they are more likely to accept evidence-based treatment recommendations.
- **Support antibiotic stewardship programs:** Encourage healthcare providers to actively participate in antibiotic stewardship programs that promote the responsible use of antibiotics while still allowing for individualized patient care.

5. Correct diagnosis and appropriate management of infections are crucial in preventing AMR. When infections are promptly and accurately diagnosed, healthcare providers can implement targeted therapy timelier, reducing the unnecessary use of antimicrobial drugs. Here are some key aspects to consider the same in the context of preventing AMR through correct diagnosis:

- **Accurate diagnostic testing:** Utilizing accurate and reliable diagnostic tests is essential for identifying the causative agent of infection and determining its susceptibility to antibiotics. State-of-the-art diagnostic solutions like automated identification & antimicrobial susceptibility testing using commercial AST systems (cASTs), MALDI-TOF and molecular assays can provide timely actionable results to guide therapy.
- **Differentiating bacterial from viral infections:** Many infections are caused by viruses, against which antibiotics are ineffective. Differentiating between bacterial and viral infections is crucial to avoid unnecessary antibiotic prescriptions. Rapid diagnostic tests can aid in making this distinction.

- **Syndromic management:** In settings where diagnostic resources are limited, syndromic management can be employed. This approach involves treating certain infections based on the observed clinical symptoms, reducing the overuse of broad-spectrum antibiotics.
- **Antibiotic stewardship:** Implementing antibiotic stewardship programs in healthcare facilities helps optimize antibiotic use. These programs involve guidelines, education, and monitoring to ensure that antibiotics are prescribed appropriately and only when necessary.
- **Public education:** Educating the general public about the appropriate use of antibiotics and the consequences of AMR is essential. Empowered patients are more likely to cooperate with healthcare providers and follow treatment recommendations.
- **Infection prevention and control:** Robust infection prevention and control measures in healthcare settings help reduce the spread of infections and, consequently, the need for antimicrobial treatment.
- **One health approach:** Recognizing that AMR is a multifaceted problem, the One Health approach involves collaboration among human health, animal health, and environmental sectors to address AMR comprehensively.
- **New diagnostic technologies:** Investing in research and development of innovative diagnostic technologies can lead to faster and more accurate identification of pathogens and their resistance patterns.

6. One Health is a collaborative and holistic approach that recognizes the interconnectedness of human health, animal health, and environmental health. It acknowledges that the health of humans, animals, and ecosystems are closely linked and that addressing health challenges effectively requires collaboration and cooperation among multiple disciplines and sectors.

7. The One Health approach is highly relevant and essential in addressing the complex and multifaceted problem of AMR. AMR is a global health crisis that affects both humans and animals, and its emergence and spread are in fuenced by factors at the human-animal-environment interface. The One Health approach recognizes the interconnectedness of human health, animal health, and environmental health, making it a valuable framework for combating AMR effectively. Here's how the One Health approach can be applied to tackle AMR:

- **Surveillance and data sharing:** One Health emphasizes the importance of surveillance systems that monitor AMR in humans, animals, and the environment. This involves collecting and sharing data on antibiotic use, resistance patterns, and the transmission of resistant microbes among different species. Integrated data sharing helps identify emerging AMR threats and informs evidence-based interventions.

- **Responsible antibiotic use:** The One Health approach advocates for responsible and judicious use of antibiotics in both human and veterinary medicine. By promoting appropriate antibiotic prescribing practices and implementing guidelines for antibiotic use in animals, the approach aims to reduce the selective pressure that drives the development of AMR.
- **Infection control and prevention:** Effective infection control measures are vital in preventing the spread of resistant bacteria. One Health encourages the implementation of robust infection control practices in healthcare settings, animal husbandry, and food production to limit the transmission of resistant pathogens.
- **Linking human and animal health:** Zoonotic diseases, which are infections transmitted between animals and humans, are a significant concern for AMR. The One Health approach fosters collaboration between human and veterinary health professionals to address zoonotic diseases effectively and prevent their spread, including zoonotic AMR.
- **Environmental considerations:** The environment serves as a reservoir for antibiotic-resistant bacteria, where it can spread between humans, animals, and the wider ecosystem. One Health takes into account the environmental factors influencing AMR, such as antibiotic pollution in water systems, and encourages sustainable practices to mitigate its impact.
- **Research and innovation:** The One Health approach supports interdisciplinary research that spans human and animal health, microbiology, ecology, and environmental sciences. This collaborative research can lead to innovative solutions for tackling AMR, including the development of new antimicrobial drugs and alternative treatment strategies.
- **Policy and advocacy:** One Health advocates for evidence-based policies and interventions that address AMR comprehensively. It involves collaboration among policymakers, healthcare professionals, veterinarians, environmentalists, and other stakeholders to implement coordinated and effective strategies.

8. Inappropriate antimicrobial use is a significant concern in India, contributing to the growing problem of AMR in the country. Studies show that up to 75% of antibiotic prescriptions in India are from the WATCH and reserve groups. Several factors contribute to the misuse and overuse of antibiotics in India, leading to the development and spread of resistant bacteria:

- **Over-the-counter availability:** Antibiotics are often available without a prescription in India, making it easy for patients to access and self-medicate with these anti-microbials. This practice leads to the improper use of antibiotics, including using them for viral infections where they are not effective.

- **Lack of awareness:** Public awareness about the appropriate use of antibiotics and the consequences of AMR is relatively low in India. Patients may demand antibiotics for minor infections, and healthcare providers might prescribe them without considering the necessity.
- **Weak regulatory enforcement:** Regulations around antibiotic use and sale in India are sometimes not strictly enforced, contributing to the easy over-the-counter access and misuse of antibiotics.
- **High burden of infectious diseases:** India faces a high burden of infectious diseases, and in certain cases, healthcare providers might feel compelled to prescribe antibiotics as a precautionary measure, even when not warranted.
- **Antibiotic use in agriculture and veterinary:** The use of antibiotics as growth promoters in livestock and poultry farming is prevalent in India. This practice can lead to the emergence of resistant bacteria in animals and, subsequently, in humans through the food chain.
- **Limited access to diagnostic testing:** In many parts of India, access to accurate diagnostic testing for infections is limited. This can result in empirical antibiotic treatment without knowledge of the causative pathogen or its susceptibility.

9. Addressing inappropriate antimicrobial use in India requires a multi faceted approach involving various stakeholders:

- **Public education:** Increasing awareness among the public about the proper use of antibiotics, the consequences of AMR, and the importance of completing prescribed courses of treatment.
- **Healthcare provider training:** Educating healthcare professionals on evidence-based prescribing practices and the importance of appropriate antibiotic use.
- **Antibiotic stewardship programs:** Implementing antibiotic stewardship programs in healthcare facilities to optimize antibiotic use and promote rational prescribing.
- **Regulatory actions:** Strengthening and enforcing regulations on antibiotic sale and use, including over-the-counter availability.
- **Improved diagnostic capacity:** Enhancing access to accurate diagnostic testing to guide appropriate antibiotic treatment.
- **Surveillance and data collection:** Establishing and expanding surveillance systems to monitor AMR patterns and track changes over time.
- **One health collaboration:** Promoting collaboration between human health, animal health, and environmental sectors to address AMR comprehensively.

10. Zoonotic diseases and AMR are interconnected global health challenges that share several key aspects:

- **Transmission between humans and animals:** Zoonotic diseases are infections that can be transmitted between animals and humans. The transmission of zoonotic pathogens, including bacteria, viruses, and parasites, can occur through direct contact, consumption of contaminated food or water, exposure to infected animal vectors or the environment.
- **AMR in zoonotic pathogens:** The misuse and overuse of antimicrobial drugs in both human and veterinary medicine can lead to the development of AMR in zoonotic pathogens. Resistant strains of zoonotic bacteria and other microorganisms can pose a significant threat to public health, as they may become more challenging to treat in both human and animal populations.
- **Increased human-animal interaction:** Urbanization, agricultural expansion, and changes in land use have led to increased interactions between humans and animals, facilitating the transmission of zoonotic pathogens. This close contact can contribute to the spread of infections and AMR.
- **Environmental factors:** Zoonotic diseases and AMR can also be influenced by environmental factors. Antibiotics used in agriculture can lead to the development of resistant zoonotic bacteria in livestock, which may enter the environment through runoff or waste disposal.
- **One health approach:** Given the complex interplay between humans, animals, and the environment in the transmission of zoonotic diseases and AMR, the One Health approach is crucial. This collaborative and interdisciplinary approach involves human health, veterinary health, environmental health, and other relevant sectors working together to address both zoonotic diseases and AMR effectively.

11. The lack of adequate AMR monitoring facilities in Indian hospitals is a significant concern that hinders efforts to combat AMR effectively. Monitoring AMR is crucial for understanding the prevalence of resistant pathogens, identifying emerging resistance patterns, and guiding evidence-based treatment decisions. Several factors contribute to the lack of AMR monitoring facilities in Indian hospitals:

- **Infrastructural constraints:** Lack of physical infrastructure (e.g. water supply, ventilation, etc.) in many hospitals in LMICs.
- **Resource constraints:** Many hospitals in India, particularly those in rural and underserved areas, face resource constraints, including limited funding, infrastructure, and skilled personnel. Establishing and maintaining sophisticated AMR monitoring facilities can be challenging in such settings.

- **Limited diagnostic capacity:** Some hospitals may lack the necessary diagnostic equipment and expertise to conduct AMR testing accurately. Diagnostic tests to determine antibiotic susceptibility often require specialized equipment and well-trained laboratory staff.
- **Priority and awareness:** In resource-limited settings, AMR monitoring might not be perceived as a top priority compared to other pressing healthcare challenges. Awareness about the importance of AMR monitoring and its impact on patient outcomes may need to be improved.
- **Data collection and reporting challenges:** Establishing a robust AMR monitoring system requires consistent data collection, analysis, and reporting. This process can be complex and resource-intensive, especially in hospitals with already strained healthcare systems.
- **Limited compliance:** Limited compliance by a section of healthcare personnel is a major concern.
- **Limited collaboration:** Collaboration between healthcare facilities, public health agencies, and research institutions is essential for a comprehensive AMR monitoring network. The lack of collaboration and data-sharing mechanisms can hinder efforts to monitor AMR on a larger scale.

12. Diagnostic tools for antimicrobial resistance (AMR) play a crucial role in identifying the presence of resistant pathogens and guiding appropriate treatment decisions. These tools help healthcare professionals select the most effective antibiotics and avoid those to which the pathogens are resistant, thereby improving patient outcomes and contributing to the overall effort to combat AMR. The choice of diagnostic tool depends on factors such as the type of infection, available resources, turnaround time, and laboratory expertise. Advances in technology continue to expand the range and capabilities of diagnostic tools for antimicrobial resistance detection. Here are some common diagnostic tools and methods used for detecting antimicrobial resistance:

- **Antimicrobial Susceptibility Testing (AST):** Antimicrobial susceptibility testing (AST) is an in vitro diagnostic test to identify which antimicrobial agent/s is specifically effective for individual patients. Clinical laboratories currently deploy several methods which may include the disk diffusion and minimum inhibitory concentration (MIC) methods. Commercial systems are also widely available for automated antimicrobial susceptibility testing.
- **Molecular Diagnostics:** Molecular methods directly detect specific genetic markers associated with antibiotic resistance. Polymerase chain reaction (PCR) and DNA sequencing are commonly used techniques. These methods provide rapid results and can identify resistance genes even before cultures are completed.

- **Next-Generation Sequencing (NGS):** NGS technologies can provide a comprehensive genetic profile of bacterial strains, including the presence of resistance genes. This allows for the simultaneous detection of multiple resistance mechanisms.
- **Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS):** This technique identifies bacterial species based on their unique protein profiles. It can also detect specific resistance mechanisms, enabling rapid identification of pathogens and their resistance profiles.
- **Phenotypic Tests for Specific Resistance Mechanisms:** Some tests are designed to detect specific mechanisms of resistance. For example, the Modified Hodge Test can identify carbapenemase-producing bacteria.
- **Biomarker Detection:** Detection of certain biomarkers released in response to pathogen invasion can help guide treatment decisions. Certain markers may help in differentiating between bacterial and viral etiologies (e.g. procalcitonin).
- **Point-of-Care Tests:** Rapid diagnostic tests that can be performed at the point of care are increasingly valuable in providing quick results, allowing healthcare providers to make timely treatment decisions.
- **Bio-informatics and Data Analysis:** Advanced data analysis techniques help identify patterns of resistance and track the spread of resistant strains. Bio-informatics tools can analyze large datasets, predict resistance mechanisms, and inform clinical decisions.
- **Phenotypic Assays for Resistance Detection:** Some newer assays focus on phenotypic changes associated with resistance, such as changes in bacterial growth rates or metabolic profiles.
- **Lab-on-a-Chip Technologies:** These micro-fluidic devices can rapidly analyze patient samples for resistance markers and deliver results within a short time frame.

13. Real-time diagnostics play a crucial role in preventing AMR by providing timely and accurate information about infectious agents and their susceptibility to antibiotics. These diagnostic tools enable healthcare providers to make informed and evidence-based decisions, leading to more targeted and appropriate use of antimicrobial drugs. Here are some ways in which real-time diagnostics contribute to AMR prevention:

- **Rapid identification of pathogens:** Real-time diagnostic tests, such as molecular assays and point-of-care tests, can rapidly identify the causative agents of infections. This allows healthcare providers to start appropriate treatment promptly, reducing the need for broad-spectrum antibiotics or empirical therapy.

- **Guided antibiotic therapy:** Real-time diagnostics provide information about the susceptibility of pathogens to specific antibiotics. With this knowledge, healthcare providers can choose the most effective antibiotic, ensuring that patients receive the right treatment from the beginning and reducing the risk of treatment failure.
- **Minimizing inappropriate antibiotic use:** By accurately identifying viral infections or non-bacterial causes of illnesses, real-time diagnostics help avoid unnecessary antibiotic prescriptions. This prevents the overuse of antibiotics, which is a major driver of AMR.
- **Avoiding delayed treatment:** Delayed or inappropriate treatment of bacterial infections can lead to the progression of the disease and the development of more severe infections. Real-time diagnostics enable timely initiation of appropriate antibiotic therapy, preventing complications and the need for more potent antibiotics later.
- **Monitoring treatment response:** Real-time diagnostics can be used to monitor the response to antibiotic therapy. If the chosen antibiotic is not effective, healthcare providers can switch to an alternative treatment promptly, preventing the development of resistance during prolonged ineffective therapy.
- **Identifying multidrug-resistant pathogens:** Some real-time diagnostics can detect specific resistance genes or mechanisms, allowing for the rapid identification of multidrug-resistant pathogens. This information is critical for infection control measures and for preventing the spread of resistant strains.
- **Surveillance of AMR patterns:** Real-time diagnostic data can be aggregated to create real-time surveillance systems for AMR. These systems provide up-to-date information on resistance trends, helping public health authorities to identify emerging resistance and tailor interventions accordingly.
- **Facilitating antibiotic stewardship:** Real-time diagnostics support antibiotic stewardship efforts by providing evidence to guide appropriate antibiotic use. This ensures that antibiotics are used judiciously and only when necessary, minimizing the risk of resistance development.

14. Behavioral change plays a critical role in reducing AMR as it addresses the root causes of inappropriate antibiotic use and fosters responsible practices among individuals, healthcare providers, and communities. Here are some key areas where behavioral change can contribute to AMR reduction:

- **Public awareness and education:** Increasing public awareness about AMR and the consequences of inappropriate antibiotic use is essential. Public education campaigns can inform people about the importance of using antibiotics only when prescribed, completing the full course of treatment, and not sharing antibiotics with others.

- **Proper self-medication practices:** Encouraging individuals to avoid self-medication with antibiotics and to seek professional medical advice when experiencing symptoms of infection can help reduce the misuse of antibiotics.
- **Empowering healthcare providers:** Behavioral change initiatives can focus on empowering healthcare providers with knowledge about appropriate antibiotic prescribing practices and the importance of avoiding unnecessary antibiotic prescriptions.
- **Antibiotic stewardship programs:** Implementing antibiotic stewardship programs in healthcare facilities can promote responsible antibiotic use. These programs involve monitoring and optimizing antibiotic prescribing, promoting guidelines, and educating healthcare professionals about best practices.
- **Shared decision-making:** Encouraging shared decision-making between healthcare providers and patients can lead to a better understanding of the need for antibiotics and more informed treatment choices.
- **Monitoring and feedback:** Providing healthcare providers with feedback on their antibiotic prescribing practices can help them become more aware of their prescribing patterns and encourage appropriate use.
- **Regulation and policy:** Implementing and enforcing regulations and policies related to antibiotic use in healthcare settings and agriculture can shape behavioral norms and practices.
- **Behavioral interventions:** Behavioral change interventions, such as nudges and social norming, can be employed to influence healthcare providers and patients to adopt responsible antibiotic use practices.
- **Healthcare facility culture:** Fostering a culture of responsible antibiotic use in healthcare facilities, emphasizing the importance of infection prevention and control measures, can help prevent unnecessary antibiotic prescriptions.
- **Community engagement:** Engaging communities in AMR awareness and prevention programs can create a sense of responsibility and collective action in addressing the issue.

15. AMR Diagnostic stewardship, also known as AMR diagnostic optimization, refers to the systematic and coordinated approach to ensure the appropriate and responsible use of diagnostic tests for the detection of antimicrobial-resistant infections. This stewardship complements antibiotic stewardship efforts by guiding healthcare providers to use diagnostic tests effectively to improve patient care, reduce unnecessary antimicrobial use, and combat the spread of AMR. Here are some key aspects of AMR Diagnostic stewardship:

- **Test selection and interpretation:** AMR diagnostic stewardship involves selecting the most appropriate diagnostic tests to identify the causative pathogen and its susceptibility to antibiotics. The ideal diagnostic tool should be fast, accurate, affordable, accessible, and of the highest quality. It also emphasizes the correct interpretation of test results to guide targeted and effective antimicrobial therapy. It should be available at the point of care.
- **Optimizing test utilization:** Healthcare providers are encouraged to use diagnostic tests judiciously and only when clinically indicated. Overuse or misuse of diagnostic tests can lead to unnecessary antimicrobial prescriptions, contributing to AMR.
- **Access to diagnostics:** Ensuring access to reliable and timely diagnostic tests is crucial for AMR diagnostic stewardship. Adequate infrastructure, equipment, and trained personnel are needed to perform accurate and timely testing.
- **Timely reporting of results:** Rapid reporting of diagnostic test results can lead to more timely and appropriate treatment decisions, reducing the use of broad-spectrum antibiotics and the potential for AMR development.
- **Feedback and education:** AMR diagnostic stewardship involves providing feedback to healthcare providers on their diagnostic testing practices and offering educational resources to improve their understanding of AMR and appropriate test utilization.
- I**ntegration with antibiotic stewardship:** AMR diagnostic stewardship should be integrated with antibiotic stewardship efforts to ensure that diagnostic testing complements appropriate antibiotic use and treatment decisions.
- **Surveillance and monitoring:** Monitoring the patterns of AMR and diagnostic testing practices is essential to identify areas of improvement and guide targeted interventions.
- **Laboratory quality assurance:** Ensuring the accuracy and reliability of diagnostic test results through rigorous quality assurance measures is vital for AMR diagnostic stewardship.
- **One health approach:** Adopting a One Health approach that involves collaboration between human health, animal health, and environmental sectors is essential for addressing AMR effectively and improving diagnostic practices across different settings.

16. Clinical microbiologists play a crucial role in reducing AMR by actively contributing to various aspects of AMR surveillance, diagnosis, treatment, and prevention. Their expertise and efforts are essential in combatting the global threat of AMR. Here are some key roles that clinical microbiologists play in reducing AMR:

- **AMR surveillance:** Clinical microbiologists are responsible for monitoring and identifying the prevalence of AMR in clinical isolates. They conduct antimicrobial susceptibility testing to determine the effectiveness of antibiotics against specific pathogens. This data is vital for tracking AMR trends and guiding appropriate treatment decisions.
- **Diagnostic testing:** Clinical microbiologists are involved in the accurate and timely identification of infectious agents causing illnesses. They use various laboratory techniques, such as culture, molecular testing, and serology, to identify pathogens and provide valuable information for targeted therapy.
- **Appropriate antibiotic use:** Clinical microbiologists collaborate with healthcare providers to guide appropriate antibiotic selection based on susceptibility testing results. This ensures that patients receive effective treatment, reducing the likelihood of treatment failure and the development of AMR.
- **Antibiotic stewardship programs:** Clinical microbiologists actively participate in antibiotic stewardship programs. They provide valuable input on laboratory diagnostic algorithms, interpret microbiology results, and contribute to the development of evidence-based guidelines for appropriate antibiotic use.
- **Outbreak investigations:** During outbreaks of AMR-related infections, clinical microbiologists are instrumental in investigating the source and transmission of the resistant pathogens. Their findings inform infection control measures to prevent further spread.
- **Education and training:** Clinical microbiologists play a role in educating healthcare professionals about AMR and the importance of responsible antibiotic use. They provide training on proper specimen collection, laboratory techniques, and interpretation of diagnostic results.
- **Research and innovation:** Clinical microbiologists engage in research to study AMR mechanisms, identify emerging resistance patterns, and explore new diagnostic methods. Their research findings contribute to the development of novel strategies to combat AMR.
- **Quality assurance:** Clinical microbiologists ensure the accuracy and reliability of laboratory results through rigorous quality assurance measures. This ensures that diagnostic testing is consistently reliable and effective in guiding treatment decisions.
- **Advocacy and collaboration:** Clinical microbiologists collaborate with other healthcare professionals, policymakers, and public health authorities to advocate for the implementation of AMR control measures. They actively support interdisciplinary collaboration, including the One Health approach, to address AMR holistically.

17. Antimicrobial stewardship in tuberculosis (TB) refers to a comprehensive and coordinated approach to ensure the appropriate and responsible use of antimicrobial drugs, specifically antibiotics used to treat TB infections. TB is caused by the bacterium Mycobacterium tuberculosis and remains a significant global health threat. Early diagnosis and antimicrobial stewardship in tuberculosis is a key to treatment response, elimination of the disease and tackle drug resistance. Antimicrobial stewardship efforts in TB focus on optimizing treatment regimens, improving patient outcomes, preventing the emergence of drug resistance, and minimizing the adverse effects of antimicrobial therapy. The key components of antimicrobial stewardship in TB are:

- **Treatment guidelines:** Development and dissemination of evidence-based treatment guidelines for TB management, including drug dosages, treatment durations, and drug interactions.
- **Drug susceptibility testing (DST):** Utilizing DST to identify the susceptibility of M. tuberculosis to various antimicrobial drugs. DST helps tailor treatment regimens to the specific drug susceptibilities of the infecting strain, reducing the risk of treatment failure and drug resistance.
- **Individualized treatment plans:** Antimicrobial stewardship in TB involves tailoring treatment plans to individual patients, considering factors such as drug resistance profiles, co-existing medical conditions, and medication tolerability.
- **Adherence support:** Ensuring patient adherence to the full course of TB treatment is essential to prevent treatment failure and the development of drug-resistant strains. Antimicrobial stewardship programs provide support to patients to enhance treatment adherence.
- **Monitoring and follow-up:** Regular monitoring of patients' response to treatment and clinical progress is critical. Close follow-up helps detect treatment failures or the emergence of resistance promptly.
- **Management of drug interactions and side effects:** Antimicrobial stewardship programs address potential drug interactions and side effects, ensuring that patients receive safe and effective treatment.
- **Preventing overuse of second-line drugs:** Second-line TB drugs are reserved for the treatment of drug-resistant TB. Antimicrobial stewardship efforts ensure that these drugs are used appropriately to prevent the further development of resistance.
- **Infection control:** Implementing infection control measures in healthcare settings to prevent the transmission of drug-resistant TB strains and protect vulnerable patients.
- **Education and training:** Antimicrobial stewardship in TB includes educating healthcare providers, patients, and communities about TB prevention, treatment, and the importance of adherence to treatment plans.

- **Surveillance and data collection:** Regular surveillance of TB cases and drug resistance patterns helps identify emerging resistance and informs policy and treatment guidelines.

18. A hospital antibiotic policy, often referred to as an Antimicrobial Stewardship Program (ASP) or Antibiotic Management Program, is a structured and comprehensive approach implemented by healthcare institutions to promote the appropriate and responsible use of antibiotics. The primary goal of such a policy is to optimize patient outcomes while minimizing the development of antibiotic resistance and reducing the risk of adverse events. Implementing a hospital antibiotic policy is an essential step in addressing antimicrobial resistance, improving patient care, and ensuring the responsible use of antibiotics. It requires commitment from hospital leadership, effective communication among healthcare teams, and ongoing monitoring and evaluation of outcomes. Here are some key components and elements commonly found in a hospital antibiotic policy:

- **Multidisciplinary Team:** An ASP is typically led by a multidisciplinary team that includes infectious disease specialists, clinical pharmacists, microbiologists, infection preventionists, and other relevant healthcare professionals.
- **Guidelines and Formularies:** The policy outlines guidelines and recommendations for antibiotic prescribing based on evidence-based practices. It includes an approved list of antibiotics (formulary) that healthcare providers are encouraged to use.
- **Education and Training:** Healthcare professionals are educated about appropriate antibiotic use, resistance patterns, and the principles of antimicrobial stewardship. Ongoing training helps providers make informed decisions when prescribing antibiotics.
- **Review and Approval Process:** The policy may require that certain high-risk or restricted antibiotics be approved by an infectious disease specialist or the ASP team before they are prescribed.
- **Preauthorization and Restriction:** Certain antibiotics, especially those at high risk for resistance development, may require preauthorization or have usage restrictions to ensure their appropriate use.
- **Dose Optimization:** Guidelines for dosing, frequency, and duration of antibiotic therapy are provided to ensure optimal treatment outcomes while minimizing unnecessary exposure to antibiotics.
- **De-escalation:** Healthcare providers are encouraged to reassess and adjust antibiotic therapy based on culture and sensitivity results to narrow the spectrum of treatment whenever possible.
- **Infectious Disease Consultation:** The policy may recommend or require consultation with infectious disease specialists for certain complex cases or infections.

- **Monitoring and Surveillance:** The ASP team monitors antibiotic usage, resistance patterns, and clinical outcomes. This helps identify trends and areas for improvement.
- **Feedback and Reporting:** Healthcare providers receive regular feedback on their antibiotic prescribing practices, which can include individual and hospital-wide performance reports.
- **Patient Education:** Patients are educated about the appropriate use of antibiotics, the importance of completing prescribed courses, and the risks associated with antibiotic resistance.
- **Data Collection and Analysis:** Data on antibiotic use, resistance rates, and patient outcomes are collected, analyzed, and used to refine the antibiotic policy and intervention strategies.
- **Collaboration and Communication:** The ASP team collaborates with various departments within the hospital, including pharmacy, laboratory, infection control, and quality improvement, to ensure effective implementation.
- **Research and Continuous Improvement:** The hospital policy should evolve based on new evidence, best practices, and lessons learned. Research initiatives and quality improvement projects may be conducted to enhance antibiotic stewardship efforts.

19. Next-generation sequencing (NGS) is a powerful diagnostic tool that has the potential to significantly reduce AMR. NGS allows for the rapid ancomprehensive analysis of genetic material, including microbial genomes, enabling more precise identification of pathogens and their resistance mechanisms. Here's how NGS can contribute to AMR reduction:

- **Accurate pathogen identification:** NGS can accurately identify the causative pathogens of infections, even in cases where conventional diagnostic methods fail. This ensures that patients receive appropriate and targeted treatment, avoiding the unnecessary use of broad-spectrum antibiotics.
- **Detection of AMR genes:** NGS can detect specific genes associated with AMR. This allows healthcare providers to identify the presence of resistance mechanisms and make informed decisions about antibiotic selection.
- **Comprehensive resistance profiling:** NGS provides a comprehensive view of the resistance profile of a pathogen, including both known and novel resistance genes. This information can guide treatment choices and help avoid antibiotics to which the pathogen is resistant.
- **Monitoring treatment response:** NGS can be used to monitor the response of infections to antibiotic treatment. This enables healthcare providers to identify treatment failures early and adjust therapy promptly, reducing the risk of further resistance development.

- **Surveillance of AMR patterns:** NGS can be applied in surveillance programs to track AMR patterns in different pathogens. This information helps public health authorities identify emerging resistance trends and design targeted interventions.
- **Detection of co-infections and mixed infections:** NGS can identify cases of co-infections or mixed infections with multiple pathogens, each potentially requiring different treatments. Tailoring therapy based on NGS results improves patient outcomes.
- **Outbreak investigations:** During outbreaks of resistant infections, NGS can rapidly identify the source and transmission pathways of resistant pathogens. This information is crucial for implementing effective infection control measures.
- **Genomic epidemiology:** NGS can provide insights into the spread of resistant strains and their transmission dynamics, aiding in the development of strategies to contain AMR.

20. Pre-analytical handling of samples is a critical step in reducing AMR as it directly impacts the accuracy and reliability of diagnostic results. Proper sample collection, transportation, and storage are essential to ensure that microbiological tests provide accurate information for guiding appropriate antibiotic treatment. Here are key considerations for pre-analytics handling of samples to reduce AMR.

21. Eco-friendly initiatives in France. In France, antimicrobial use in animals has been reduced by 40% in 5 years from 2012 to 2017. Before prescribing critical antibiotics to animals, test results are needed. Antimicrobial resistance (AMR) is a significant global health concern, and countries like France are taking various measures to combat it. Here are some of the measures that France has been implementing to reduce antimicrobial resistance:

- **Promoting Rational Use of Antibiotics:** France has been focusing on raising awareness among healthcare professionals and the public about the appropriate use of antibiotics. This includes promoting the importance of completing prescribed antibiotic courses and discouraging unnecessary or improper antibiotic use.
- **Surveillance and Data Collection:** The French government has been actively involved in collecting and analyzing data on antimicrobial resistance patterns. Surveillance helps in understanding the extent of the problem, identifying emerging resistance trends, and guiding intervention strategies.
- **Infection Prevention and Control:** Improving hygiene practices in healthcare settings and promoting infection prevention and control measures can help reduce the spread of infections and consequently the need for antibiotics.

- **Education and Training:** Healthcare professionals, veterinarians, and pharmacists are being trained to make informed decisions about antibiotic prescriptions. Continuing education programs help them stay updated on the latest guidelines and best practices.
- **Regulating Antibiotic Use in Agriculture:** France, like many other countries, has been working to regulate and reduce the use of antibiotics in agriculture, especially in livestock farming. This includes implementing measures to limit the prophylactic use of antibiotics and encouraging responsible use. The use of antibiotics as growth promoters is prohibited, as in all EU countries.
- **Research and Innovation:** Investing in research to develop new antibiotics, alternative treatment options, and diagnostics is crucial. France has been supporting research initiatives aimed at finding novel solutions to combat antimicrobial resistance.
- **Public Awareness Campaigns:** Public awareness campaigns have been launched to educate the general population about the importance of responsible antibiotic use, the risks of antimicrobial resistance, and the role of individuals in preventing its spread.
- **International Collaboration:** France actively participates in international efforts to address antimicrobial resistance, working with organizations such as the World Health Organization (WHO), the European Centre for Disease Prevention and Control (ECDC), and other relevant entities.
- **Hospital Stewardship Programs:** Hospitals are implementing antimicrobial stewardship programs that involve a multidisciplinary approach to optimize antibiotic use, improve patient outcomes, and reduce the development of resistance.
- **Policy and Regulation:** France has been enacting policies and regulations to control the availability and distribution of antibiotics. These measures may include prescription requirements for certain antibiotics and stricter regulations on over-the-counter antibiotic sales.

22. An antibiogram is a laboratory test that provides information about th susceptibility profile of bacteria or other microorganisms to different ant. It help guide healthcare professionals in choosing the most appropriate antibiotic treatment for infections. The hospital antibiogram is a periodic summary of antimicrobial susceptibilities of local bacterial isolates submitted to the hospital's laboratory. Antibiograms play a critical role in antibiotic stewardship and patient care, as they aid in tailoring treatment to specific pathogens and preventing the development of antibiotic resistance. Antibiograms are essential tools for guiding evidence-based antibiotic therapy and promoting the responsible use of antibiotics, which is crucial for combating antimicrobial resistance and ensuring optimal patient outcomes. Key points about antibiograms:

- **Purpose:** Antibiograms help determine which antibiotics are effective against a particular bacterial strain. This information assists doctors in choosing the most appropriate antibiotic for treating infections and avoiding the use of ineffective drugs.
- **Testing Process:** In an antibiogram, bacteria isolated from a patient's sample (such as blood, urine, or wound discharge) are tested for their susceptibility to various antibiotics either manually or on automated systems.
- **Zone of Inhibition:** The area around each antibiotic disc where bacterial growth is inhibited is called the "zone of inhibition." The size of this zone provides an indication of the bacteria's susceptibility to the antibiotic as per standard guidelines (like CLSI/EUCAST).
- **Minimum Inhibitory Concentration (MIC):** In addition to measuring the zone of inhibition, some laboratories provide the minimum inhibitory concentration (MIC) value for each antibiotic. MIC represents the lowest concentration of the antibiotic that prevents visible growth of the bacteria.
- **Interpretive Criteria:** Clinical microbiology guidelines provide interpretive criteria that define whether a bacterium is susceptible, intermediate, or resistant to a specific antibiotic. These criteria are used to determine appropriate treatment options.
- **Data Collection and Analysis:** Antibiogram data are collected and analyzed over time to monitor trends in antibiotic resistance and guide antibiotic stewardship efforts. This information helps healthcare facilities make informed decisions about their antibiotic prescribing practices.
- **Infection Control and Outbreak Management:** Antibiograms can be valuable tools for infection control and management during outbreaks. They help identify patterns of resistance and guide strategies to contain and prevent the spread of resistant strains.
- **Local Epidemiology:** Antibiograms reflect the local prevalence of antibiotic resistance in a specific healthcare facility or community. This information is important for tailoring empiric antibiotic therapy to local resistance patterns.

- **Antibiotic Stewardship:** Antibiograms are a key component of antibiotic stewardship programs, which aim to promote the appropriate and responsible use of antibiotics to preserve their effectiveness and prevent the development of resistance.
- **Continual Updates:** Antibiograms are typically updated regularly to reflect changes in bacterial resistance patterns. This ensures that healthcare providers have access to the most current information when making treatment decisions.

23. bioMérieux is fighting infectious diseases. bioMérieux is a multinational biotechnology company headquartered in Marcy-l'Étoile, France. The company specializes in providing diagnostic solutions for clinical laboratories, industrial applications, and food safety. biomérieux is a major player in the field of in vitro diagnostics and microbiology, with a focus on developing innovative diagnostic tests and instruments to aid in the detection and monitoring of various diseases and infections. The history of bioMérieux is directly linked to the fight against infectious diseases. The In Vitro Diagnostics company provides tests for the early detection of infectious diseases. In addition, bioMérieux also has extensive expertise in the fields of antimicrobial resistance and healthcare associated infections. The company also has designed research programs for emerging diseases. They have in vitro diagnostic solutions. 12% of revenue is spent on R&D.

24. Role of India in AMR: Govt. of India initiatives are taken under PSA and NITI Ayog. Integrated disease control is needed within and across compartments. Sustainable infrastructure development is required. Data integration, ground-level training, and preparedness are needed. ICMR has created a nationwide AMR surveillance network. NABL and NABH accreditation should be mandatory for all teaching medical colleges. Collaborations among lab scientists, clinicians, and policymakers are needed.

25. Government of India has undertaken several initiatives to address antimicrobial resistance (AMR) and promote responsible antibiotic use. These initiatives are part of India's broader efforts to improve healthcare, strengthen surveillance, and mitigate the impact of AMR. Here are some key initiatives and actions taken by the Indian government:

- **National Action Plan on Antimicrobial Resistance (NAP-AMR):** The Ministry of Health and Family Welfare launched the NAP-AMR in 2017. The plan outlines a multi-sectoral approach to address AMR in human health, animal health, and the environment. It focuses on strengthening surveillance, infection prevention and control, improving access to quality-assured antibiotics, and promoting awareness.
- **Integrated Disease Surveillance Program (IDSP):** The IDSP is a comprehensive disease surveillance program that tracks various infectious diseases, including those caused by antimicrobial-resistant pathogens. The program aims to improve disease detection, reporting, and response.

- **National Centre for Disease Control (NCDC):** NCDC is involved in monitoring, surveillance, and outbreak investigations related to AMR. It plays a key role in coordinating efforts to combat AMR and conducts research on resistant pathogens.
- **Indian Council of Medical Research (ICMR):** ICMR is engaged in research related to AMR, including studies on resistance patterns, mechanisms, and alternative treatment options. It promotes collaborative research projects and supports capacity building.
- **Surveillance Network and Laboratories:** India has established a network of laboratories for monitoring AMR and conducting antimicrobial susceptibility testing. This network helps collect data on resistance patterns and informs treatment guidelines.
- **Standard Treatment Guidelines and Essential Medicines List:** The government regularly updates standard treatment guidelines and the National List of Essential Medicines to guide healthcare professionals in appropriate antibiotic prescribing.
- **Regulation of Antibiotics:** The government has introduced regulations to control the sale of antibiotics, including stricter prescription requirements for certain classes of antibiotics. This aims to reduce over-the-counter availability and promote responsible use.
- **Awareness Campaigns:** The Ministry of Health and Family Welfare conducts awareness campaigns to educate healthcare professionals, patients, and the general public about the responsible use of antibiotics, the risks of AMR, and the importance of completing prescribed courses.
- **One Health Approach:** The government recognizes the One Health approach and emphasizes collaboration between the human health, animal health, and environmental sectors to address AMR holistically.
- **Research and Innovation:** The government supports research and innovation in AMR-related areas through funding and grants to promote the development of new antibiotics, diagnostics, and treatment alternatives.
- Training and Capacity Building: Various government agencies, including medical colleges and health institutions, provide training to healthcare professionals on rational antibiotic use and infection prevention and control.

26. Here are some of the other roles and efforts that India has been undertaking to combat AMR:

- **National Action Plan:** India has developed a National Action Plan on AMR, which outlines strategies and initiatives to address antimicrobial resistance in healthcare, agriculture, and the environment. The plan focuses on improving surveillance, strengthening infection prevention and control, promoting rational use of antibiotics, and fostering research and innovation.

- **Surveillance and Data Collection:** India is working on enhancing its surveillance systems to monitor the prevalence of resistant pathogens, track resistance trends, and identify emerging hotspots. This data is crucial for informed decision-making and targeted interventions.
- **Rational Use of Antibiotics:** India is promoting the responsible and judicious use of antibiotics through awareness campaigns targeting both healthcare professionals and the general public. This includes educating prescribers about appropriate antibiotic use and the importance of completing prescribed courses.
- **Infection Prevention and Control:** Improved hygiene practices and infection prevention and control measures in healthcare settings can help prevent the spread of infections and reduce the need for antibiotics. India has been working to strengthen these measures.
- **Regulation of Antibiotics:** India's regulatory agencies are working to regulate the use of antibiotics in both human and animal health. This includes measures to control over-the-counter sales of antibiotics and promote proper prescription practices.
- **One Health Approach:** India recognizes the interconnectedness of human, animal, and environmental health in the context of AMR. The "One Health" approach emphasizes collaborative efforts among multiple sectors to address AMR comprehensively.

  Capacity Building: Training healthcare professionals, veterinarians, and other stakeholders about AMR, infection prevention, and appropriate antibiotic use is essential. India is investing in capacity-building programs to enhance knowledge and skills.
- **Research and Innovation:** India is supporting research to develop new antibiotics, diagnostics, and treatment alternatives. Efforts are being made to encourage domestic research and innovation in the field of AMR.
- **International Collaboration:** India actively participates in global efforts to combat AMR. The country engages with international organizations, collaborates on research projects, and shares experiences and best practices with other countries.
- **Awareness Campaigns:** Public awareness campaigns raise awareness about AMR, educate the public about responsible antibiotic use, and emphasize the role of individuals in preventing the spread of resistant infections.

27. The Indian Council of Medical Research (ICMR) collaborates with various medical and healthcare organizations to develop and update clinical practice guidelines, including those related to the management of infectious diseases. These guidelines are aimed at providing evidence-based recommendations to healthcare professionals for the diagnosis, treatment, and prevention of various infections. ICMR's standard treatment guidelines on infections might cover a range of topics, including:

- **Common Bacterial Infections:** Guidelines for the management of common bacterial infections such as respiratory tract infections (pneumonia, bronchitis), urinary tract infections, skin and soft tissue infections, and bacterial gastroenteritis.
- **Tuberculosis:** Recommendations for the diagnosis, treatment, and management of tuberculosis (TB), including drug-resistant TB cases.
- **HIV/AIDS:** Guidelines for the treatment of HIV/AIDS, including antiretroviral therapy (ART), management of opportunistic infections, and prevention strategies.
- **Sexually Transmitted Infections (STIs):** Guidelines for the diagnosis and management of STIs like syphilis, gonorrhea, and chlamydia.
- **Malaria and Other Vector-Borne Diseases:** Recommendations for the diagnosis and treatment of malaria and other vector-borne diseases prevalent in India.
- **Viral Infections:** Guidelines for managing viral infections such as hepatitis (including hepatitis B and C), influenza, and emerging infections.
- **Antimicrobial Resistance and Stewardship:** Recommendations for the appropriate use of antibiotics to combat antimicrobial resistance, including guidance on empirical antibiotic therapy, dosing, and duration of treatment.
- **Vaccination:** Guidelines for vaccination schedules and recommendations for different age groups, including routine immunizations and special populations.
- **Infection Prevention and Control:** Strategies and measures for infection prevention and control in healthcare settings to reduce the spread of infections.
- **Pediatric Infections:** Guidelines specific to managing infections in pediatric patients, including neonatal infections and childhood immunizations.
- **Hospital-Acquired Infections:** Recommendations for preventing and managing infections acquired in healthcare facilities.
- **Zoonotic Diseases:** Guidance on managing diseases that can be transmitted between animals and humans.

KEY TAKE AWAYS

- Today's health issues (including AMR concern) are transboundary, multifactorial, and across species, and therefore mitigation strategies need to be devised through the One Health approach. This necessitates interdisciplinary collaboration. The symposium identified key stakeholders in this collaborative approach.
- One of the key roles of this collaboration shall be awareness creation on AMR and widespread dissemination of accurate information on judicious antimicrobial use.
- The attributes of an ideal diagnostic test can be summed up by the acronym 4 A- Accurate, Accessible, Actionable in a timely fashion and Affordable.
- The laboratory has an indispensable role in pathogen identification, AMR detection and reporting and therefore training of all users across all levels (including elementary level) is necessary in optimal utilization of diagnostic tests to curb AMR.
- Right test at the right time on the right patient is essential for diagnostic stewardship that translates to right antimicrobial selection and informed prescription on a timely basis for improved patient outcome. The hand-in glove integrative Diagnostic and Antimicrobial stewardship can be brought about by effective communication between the lab and the prescriber.
- Training of health-care personnel on evidence based antimicrobial prescription is pivotal in promoting rational antimicrobial usage.
- The need for accurate and timely AMR surveillance data from the community level up to the tertiary level cannot be overemphasized. The same is instrumental in policy making and implementation.

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