NATIONAL ANTIMICROBIAL STEWERDSHIP PROGRAM

Ministry of health

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FOREWORD

Antimicrobial resistance is a threat for global health which has no respect for national borders. Misuse and excessive use of antimicrobial drugs have led to rapid development of resistance to these drugs. These treatments that have paved the way for numerous medical advancements in the modern world is now challenged. Development of antimicrobial resistance (AMR) has resulted in ineffectiveness of several commonly used antimicrobials. Time is running out, especially when new resistance mechanisms are emerging and spreading globally, but not enough new antimicrobial drugs are being developed to fight the resistant organisms. Hence, the use of existing antimicrobials must be optimized and managed to extend the lifespan of these antimicrobials.

To combat the spread of AMR the 68th World Health Assembly (WHA) adopted a Global Action plan on containment of antimicrobial resistance. In support of this united cause, Maldives successfully endorsed the National Action Plan for containment of Antimicrobial Resistance 2017-2022. One of the objectives of the action plan was to optimize the use of antimicrobial medicines and to develop a National Antimicrobial Stewardship Program to achieve this objective, within healthcare settings.

The National Antimicrobial Stewardship Program (NAMSP) intends to optimize the treatment of infections and minimize development of resistance to antimicrobials. This document provides the structure towards implementation of antimicrobial stewardship throughout the country. It will assist clinicians in the efforts to improve quality of patient care and patient safety through increased cure rate for infections whilst reducing any unnecessary use of these valuable therapeutics. Successful implementation of this program will thus strengthen public trust in the healthcare system and reduce the economic health burden from treatment failures.

Implementation of the stewardship programme for each health institution based on this national guideline will foster prudent use of antimicrobials, thus minimizing the development of antimicrobial resistance within the human healthcare system. Furthermore, it will also ensure prescribing and administration of the most appropriate antimicrobial treatment regimen for each individual patient resulting in successful patient outcomes. Collective efforts from all healthcare practitioners and institutions in accordance to this programme will contribute to the effort in curbing the escalation in resistance to antimicrobials.

It is my sincerest hope that this NAMSP is yet another step taken to support the containment of antimicrobial resistance at a national level, particularly in optimizing the use of antimicrobials and implementation of proper prescribing practices. It is my sincere hope that all healthcare facilities will commit to the objectives of this program and contribute to the efforts in curbing the development of antimicrobial resistance.

Dr. Shah Abdulla Mahir

Minister of State for Health

FOREWORD

Antimicrobial resistance (AMR) is a growing public health and development threat of major concern and is becoming a serious political, social and economic challenge globally. Currently, at least 700,000 people die each year due to drug-resistant diseases in what is termed as "slow tsunami". The health care costs for patients with resistant infections is higher than the non-resistant infections due to longer illness, additional laboratory tests and use of more expensive drugs. If current trends continue, AMR could reduce the GDP in low-income countries by 5%.

It's clear that AMR is occurring everywhere in the world and is compromising our ability to treat infectious diseases, as well as undermining many other advances in health and medicine including achievement of SDGs. Addressing such challenges, the draft global action plan was developed with the aim to ensure continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality-assured, used in a responsible way, and accessible to all who need them.

In line with SEAR Flagship Priority on AMR, WHO Country Office assisted Food and Drug Authority in identifying vulnerabilities, opportunities and prioritize the activities for AMR containment which are outlined in Maldives National Action Plan (NAP) for AMR. The NAP on AMR highlights the importance of national policies and treatment guidelines according to the national AMR patterns.

I am pleased to note development of **Antimicrobial Stewardship Guidelines** for the health facilities with assistance from WHO. Antimicrobial stewardship (AMS) describes a coherent set of actions that ensure optimal use of antimicrobials to improve patient outcomes, while limiting the risk of adverse events. It provides practical guidance to support the implementation of optimal use of antimicrobial medicines including prescribing practices to improve patient outcomes and thus to reduce the overall burden of antimicrobial resistance. It strives to implement evidence-based approaches in collaboration with health-care providers to ensure that the right patient is prescribed the right antimicrobial in the right dosage via the right route for the right duration with timely de-escalation.

The AMR Stewardship guidelines are critically important as countries respond to COVID-19 pandemic which has the potential to accelerate AMR. For example, antibiotics could be prescribed to individuals presenting with mild COVID-19 disease which are not needed. These guidelines covering the aspects of leadership, accountability, drug expertise, tracking, antimicrobial time out and reporting will therefore act as appropriate reference for local policies and actions to increase clinical competences of health workers in appropriately treating COVID-19.

I believe the successful implementation of these guidelines will enable health workers as "Antimicrobial Stewards" who will carefully and responsibly manage antimicrobials and will continue to define the responsible use of these critical resources.

WHO Country Office Maldives considers it a matter of great privilege for extending technical support to Food & Drug Authority (MFDA) and Ministry of Health for development of AMR Stewardship Guidelines. As a trusted and reliable partner, I assure continued support to ensure that the country remains geared and fully equipped to combat the threat of AMR.

Dr Arvind Mathur
WHO Representative to Maldives

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List of Abbreviations

AMR: Antimicrobial Resistance

AMS: antimicrobial stewardship

AMSP: Antimicrobial Stewardship Program:

AST: Antibiotic Sensitivity Testing

ATCC: American Type Culture Collection

CAUTI: Catheter Associated Urinary Tract Infection

CDC: Center for Disease Control

CDI: Clostridium difficile infections

CLSI: Clinical and Laboratory Standards Institute

CRE: Carbapenem Resistant Enterobacteriacae

CSF: Cerebrospinal Fluid

DDD: Daily Defined Dosage

DG: Director General

DOT: Days of Therapy

ESBL: Extended Spectrum Beta-lactamase

EUCAST: European Committee on Antimicrobial Susceptibility Testing

GAP: Global Action Plan

GLASS: Global Antimicrobial Resistance Surveillance System

HAI: Healthcare Associated Infections

HCF: Healthcare Facility

HCW: Healthcare worker

HICC: Hospital Infection Control Committee

HPI: Hospital Pharmacy Initiative

ICU: Intensive Care unit

ID: Infectious Disease

IQC: Internal Quality Control

IV: Intravenous

MALDITOF: Matrix-Assisted Laser Desorption/ionization Time of Flight

MDRO: Multidrug resistant organism

MFDA: Maldives Food and Drug Authority

MIC: Minimum inhibitory Concentration

MOH: Ministry of Health

MRSA: Methicillin Resistant Staphylococcus aureus

NAMRC: National Antimicrobial Resistance Committee

NAMSP: National Antimicrobial Stewardship Program

NAP: National Action Plan

NMSC: National Multi-Sectoral Steering Committee

OPAT: Outpatient Parenteral Antimicrobial Therapy

OPD: Outpatient Department

OTC: Over the counter

PCR: Polymerase Chain Reaction

PO: Per oral

POC: Point Of Care

QI: Quality Improvement

SOP: Standard Operating Procedure

SSI: Surgical Site Infections

TSC: Technical Sub Committee

VAP: Ventilator Associated Pneumonia

VRE: Vancomycin Resistant Enterococci

WHA: World Health Assembly

WHO: world Health Organization

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SECTION 1.: BACKGROUND

1.1 Maldives: Country Introduction

Republic of Maldives is an island nation comprising of more than 1190 islands in the Indian Ocean-Arabian Sea region. Of these, only 182 islands are inhabited. The country is made up of 27 atolls between the Chagos Archipelago and Minicoy Island, 250 miles southwest of India. In 2018, Maldives has an estimated population of 444,259, which ranks 175th in the world. Maldives is the smallest Asian country, both by land area and population. Its estimated population of 444,259 live on a total land area of just 298 square kilometres (206th in the world). However, the Maldives Islands has a high population density of 1,102 people per square kilometre, making it the 11th most densely populated country on earth. The largest city and capital in Maldives is Male, with an estimated population of 63,000. This is followed by Addu City (32,000) and Fuvahmulah (12,000). These are the only cities with a population surpassing 10,000. More than 65% of the population resides in rural areas[1].

1.2 The health system in Maldives

The public sector conforms to the largest share of the health system in Maldives. Public Health System is the major health service provider with facilities stratified into Primary, Secondary and Tertiary level of care. Primary care facilities are represented by Health Centres and Secondary care is provided by Atoll and Regional Hospitals. The public sector is supported by private health care providers, mainly providing curative and diagnostic services, and medicines and medical products located within the country. Another key sector that forms part of the health system is the voluntary nongovernmental parties working on specific health issues. While the public system extends to all inhabited islands, private and voluntary services are concentrated in Male'. The health system is also supported by external foreign development partners.

The health-care delivery system of Maldives is organized into a three tier system, the first being at the island level primary health centres, the second at the higher level of health facilities which include specialty care hospitals (at the atoll level), and tertiary care services at the urban level. Each of these 165 island hospitals are manned by a team of doctor, nurses and public health workers. The centres provide emergency and primary healthcare.

There are 11 Atoll Hospitals which have indoor and laboratory facilities and aim to provide secondary level care. The doctors of various specialties are available round the clock. Secondary care is also provided by 6 Regional hospitals. Administratively, the regional or

atoll hospital in each atoll acts as the main coordinating body in providing primary and curative health care in that atoll and each atoll covers a population of 5,000 to 15,000 people. Each atoll and island health facility has a public health unit that provides immunization, health awareness and advice, and reproductive health services. It also conducts surveillance and manages the control of communicable diseases. In each atoll, the public health unit of the atoll hospital supervises the public health staff at each island health centre. There are big hospitals like IGMH and ADK Hospitals located in Male' which aims to provide well equipped tertiary level healthcare. The private health sector in the Maldives, although small, is vigorous and distributed widely across the islands. Among the private hospitals, the ADK hospital is the main private hospital located in

Male'.

The health care workforce is dominated by expatriate health workforce. There are a total of 443 and 446 doctors working in Male' and Atoll islands respectively[2]. Providing healthcare to its citizens spread across various islands has always been a challenge but Maldives has risen to this challenge and spends more than 9% of its GDP on healthcare. It has limited institutional capacity and total import based medical supplies including antimicrobial agents. In spite of all odds Maldives is a front runner in improved health outcomes in South East Asia region. This is evident in the fall of infant mortality rate from 34 in 1990 to just 8 in 2014, Maternal mortality ratios from 677 per 100,000 live births in 1990 to 41 per 100,000 live births in 2014. Progress in control of communicable disease has been a major factor responsible for this change. This progress has seen huge milestones such as declaration of Maldives as malaria Free State in 2015, elimination of lymphatic filariasis in 2016 and elimination of measles in 2017. High coverage of immunization, safe water supply, better management of diarrheal disease, and a better general, and referral health services all contribute to this improved picture. Vaccination coverage remains consistently above 98% for all childhood vaccines, and vaccine preventable diseases have been controlled [3, 4].

Aasandha is the national healthcare insurance scheme of the Maldives which was developed to provide free medical assistance to all Maldivian Citizens. The current model (2014) of Aasandha is based on an unlimited package with no ceiling limits placed for Maldivian Nationals from hospitals and health centres operated by health corporations as well as private hospitals ADK in Male' and IMDC in Addu City and the private operations Central Clinic and Central Medical Centre. The scheme is administered to a state-owned company 'Asandha Pvt Ltd', for which the Ministry of Health (MoH) is the main provider of health

care and the National Social Protection Agency (NSPA) is the governing agency of this scheme. The private sector provides curative services on a fee-for-service basis and package prices for curative care received from health facilities abroad. The scheme does not cover expatriate population in the country. Under the health insurance system, the rural population has access to free public health care with free referrals to the nearest hospital including sea transport in emergencies as well as treatment abroad for services not available in the country [5].

1.3 Overview of Antimicrobial resistance

Antimicrobial resistance is the ability of microbes to grow/multiply in the presence of drug that would normally kill them or limit their growth. Some bacteria inherently do not respond to certain drugs (intrinsic resistance) while others may stop responding to a drug to which it is originally sensitive (acquired resistance). Development of AMR leads to infections that are harder to treat or control; the risk of the spread of infection to others is increased; prolonged hospital stays with added economic and social costs causing increase in complications and death. As per CDC estimations more than two million people are infected with antibiotic resistant organisms causing 23,000 deaths world-wide [9].

Antimicrobial usage has increased over the year, and there are several factors that lead to this. **Error! Reference source not found.** demonstrates the common drivers to antimicrobial usage.

Overuse of antimicrobials has increased the rate at which resistance is developing and spreading. The lack of new drugs to challenge these antibiotic resistant organisms has created superbugs. AMR has emerged as a major public health problem all over the world. Infections caused by resistant microbes fail to respond to treatment, resulting in prolonged illness and greater risk of death. Treatment failures also lead to longer periods of infectivity, with increased numbers of infected people moving in the community. This in turn exposes the general population to the risk of contracting a resistant strain of microorganisms. When these become resistant to first-line antimicrobials, the prohibitive high cost of the second-line drugs may result in failure to treat these diseases in many individuals.

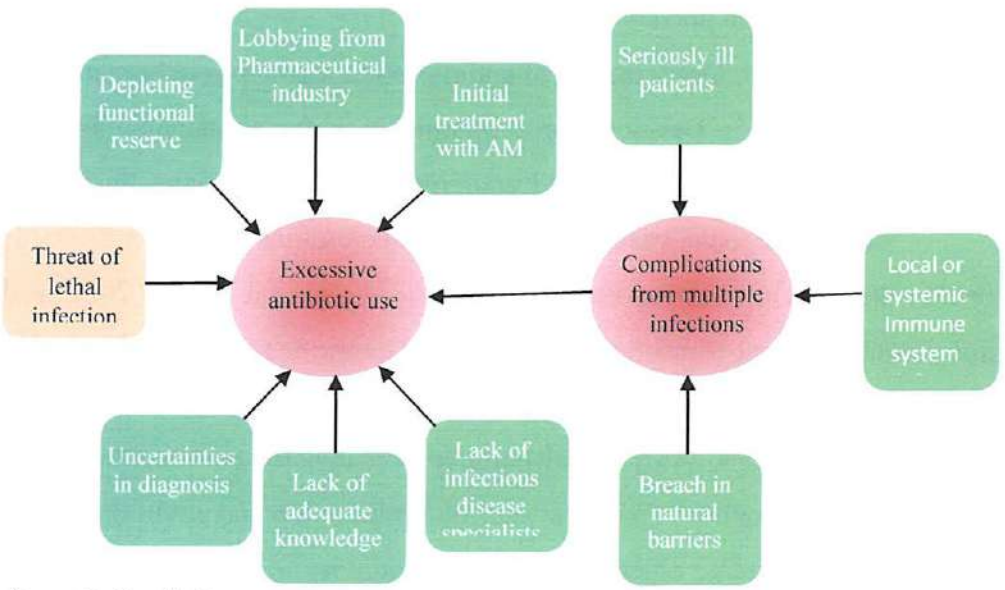


Figure 1: Drivers for antimicrobial usage

1.4 AMR containment efforts in Maldives

Antimicrobial resistance is the biggest public health care problem which the world faces today. At the Sixty-eight World Health Assembly (WHA) in May 2015, a global action plan was endorsed to tackle antimicrobial resistance. The goal of the draft global action plan (GAP) is to ensure, for as long as possible, continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality-assured, used in a responsible way, and accessible to all who need them. One of the overarching requirements outlined by the GAP AMR was that all Member States should develop their own, tailor-made National Action Plans on AMR (NAP AMR), duly aligned with the principles and approaches mentioned in the GAP AMR by May 2017. Keeping in view of the WHA resolution the Ministry of Health (MOH), Maldives accorded highest priority to AMR containment. WHO country office for Maldives, has provided technical support to develop National Action Plan (NAP-AMR). MOH designated the Maldives Food and Drug Authority (MFDA) as the National AMR focal agency and the NAP AMR was endorsed on May 16th, 2017 with five strategic objectives [10].

- Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training
- Objective 2: Strengthen the knowledge and evidence base through surveillance and research

- Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures
- Objective 4: Optimise use of antimicrobial medicines in human and animal health
- Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions

Further, the National Action Plan on AMR for the period 2017 – 2022 lead to set up of a High Level National Multi-Sectoral Steering Committee (NMSC) supported by a National AMR Coordinating Committee (NACC) and multi-sectoral (TSC). Director General (DG) of MFDA is the National AMR focal point responsible for coordinating AMR activities and tasks in the health, animal, fisheries, and food production and environment sectors.

As outlined in Strategic objective 4.1 it is mandatory to establish a National Antimicrobial Stewardship Programme on a national scale to improve and measure the appropriate use of antimicrobials. A situational analysis was undertaken with the aim of understanding the country context and capacity so as to structure an Antimicrobial Stewardship Program for Maldives.

1.5 Antimicrobial Stewardship Program in human health

An effective strategy to limit the effect of multidrug resistance must be multifaceted and must include the education of patients and physicians about appropriate drug, dose and duration, use of effective infection-control practices to prevent transmission from infected to uninfected patients, surveillance of antimicrobial resistance and antimicrobial use, and improved use of immunization.

"The primary goal of antimicrobial stewardship is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, the selection of pathogenic organisms (such as *Clostridium difficile* infection), and the emergence of resistance."

Antibiotic stewardship has been defined as *"coordinated interventions designed to improve and measure the appropriate use of antibiotic agents by promoting the selection of the optimal antibiotic drug regimen including dosing, duration of therapy, and route of administration"* [12]. It is a systematic approach to optimizing antimicrobial therapy, through a variety of structures and interventions. Antimicrobial stewardship includes not only limiting inappropriate use but also optimizing antimicrobial selection, dosing, route, and duration of therapy to maximize clinical cure or prevention of infection, while limiting the

unintended consequences, such as the emergence of resistance, adverse drug events, and cost [13].

Stewardship and access cannot be dealt with in isolation. Any stewardship framework must also ensure that access to antibiotics is not compromised and is expanded where needed. A wider recognition of antimicrobial medicines, in particular antibiotics, as a global public good is needed to undertake stewardship at the various levels.

The goals of antimicrobial stewardship programmes are:

1. To ensure the best clinical outcome, for treatment or prevention of infection.
2. To minimize unintended consequences of antimicrobial use
3. To minimize healthcare costs without compromising quality of care

To ensure the best clinical outcome, for treatment or prevention of infection:

Antimicrobial stewardship programs (AMSP) have a direct responsibility to ensure prudent antimicrobial prescribing. Multiple studies have shown that antibiotics are prescribed unnecessarily in around one third to half of the patients, and that they are prescribed inappropriately (timing, molecule, dose, route, duration) in the same proportions. Inadequate initiation of antibiotics can increase mortality by up to 50%.

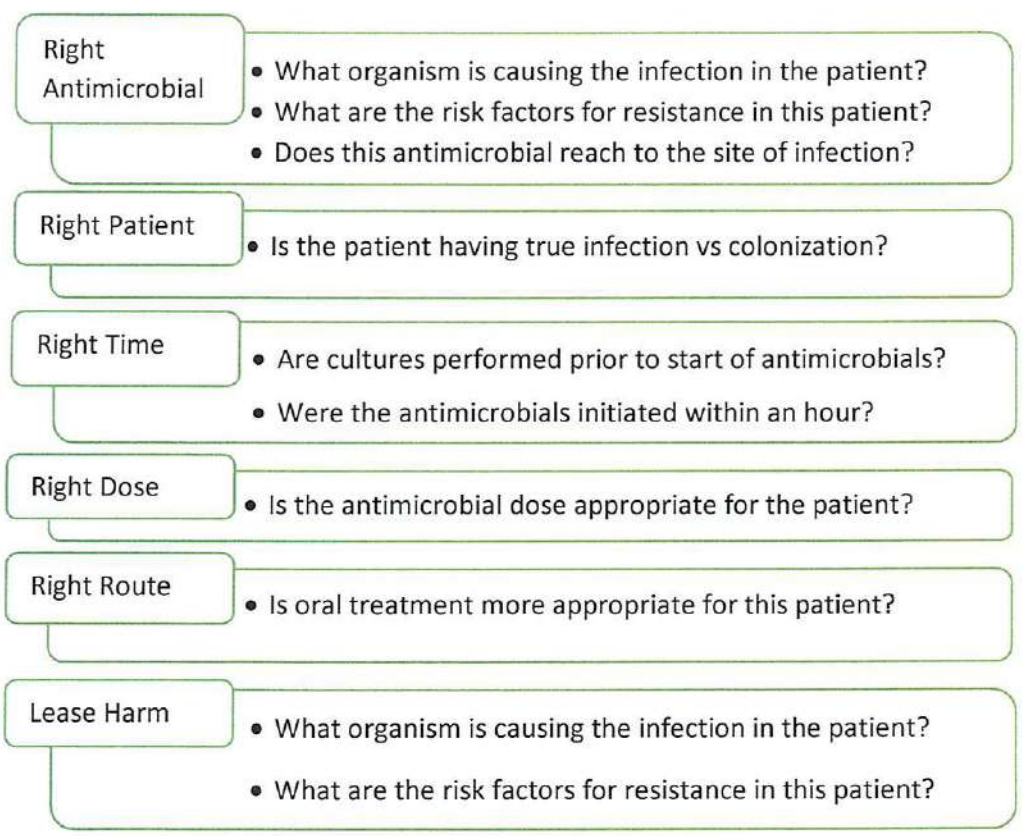


Figure 2: Guidance to appropriate prescribing of antibiotics

In addition to timely and appropriate antibiotic initiation, stewardship programs may minimize risk for adverse events and even mortality by implementing interventions for timely review or renal dose adjustment. Timely de-escalation will minimize patient exposure to broad spectrum antimicrobials and therefore reduce their risk for associated events such as resistance or *C. difficile* infection. Renal dose adjustments will ensure patients are not over- or under-dosed which may increase their risk for adverse effects, infection relapse, or development of resistance.

Antibiotics cause disruption in the normally "diverse" intestinal flora or gut microbiome. One of the goals of antimicrobial stewardship is to minimize or prevent unnecessary changes in the gut biome to prevent the development and transmission of antimicrobial resistance among our commensal biome. Reducing antibiotic exposure will minimize the duration and extend of disruption of the microbiome thereby ultimately reducing collateral damage and improving patient outcomes.

Moreover, prolonged courses of antibiotics increase the risk of colonization with multidrug resistant organisms. These colonized organisms then spread to other patients in healthcare settings. Interrupting this chain of transmission is as important as preventing the development of resistance. Reducing unintended consequences by practicing rational prescribing and limiting the duration of therapy to appropriate treat each infection with the safest, effective course of antibiotics is an important stewardship goal.

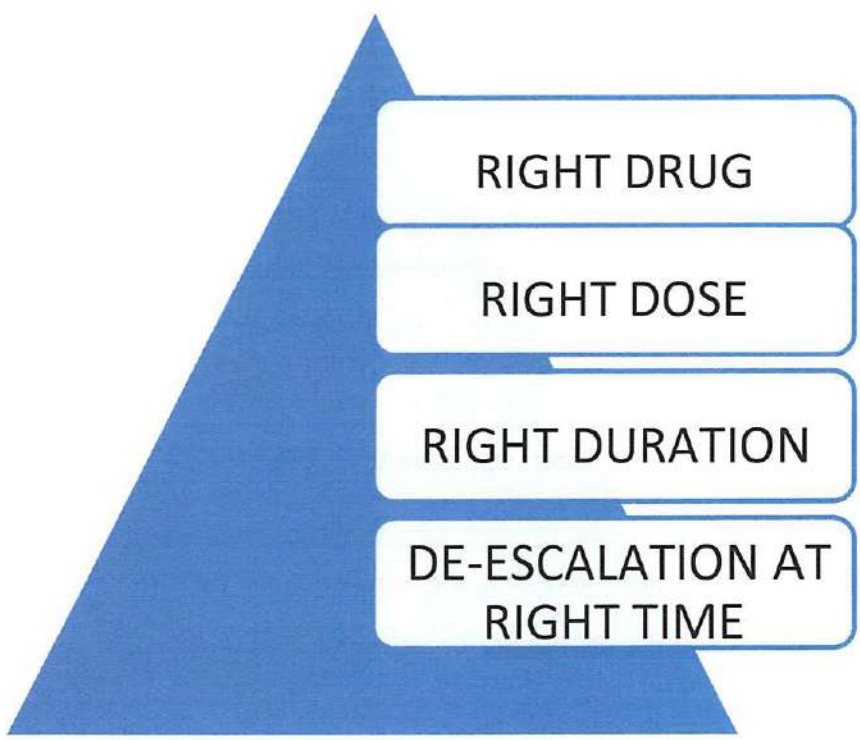


Figure 3: Antimicrobial stewardship programs focus on "4Ds" of prescribing antimicrobials.

To minimize unintended consequences of antimicrobial use

Antimicrobial use is often associated with indirect consequences. These could be in form of selection of pathogenic organisms such as Clostridium difficile, adverse drug reactions and high levels of antimicrobial resistance in individual, community and country.

a. Adverse drug reactions: When contemplating antibiotic use, prescribers must consider possible beneficial and harmful drug interactions. After antibiotics are instituted, adverse reactions must be anticipated. Acute illness, comorbidities, and concurrent medications affect the presentation and management of antibiotic-related adverse events. AMSP aims to help prescribers choose antibiotics rational agents that maximize antimicrobial activity and minimize potential drug interactions and adverse reactions. A study from India has reported that antibiotics were responsible for 40.9% of adverse drug reactions reported in a tertiary care hospital [14].

b. Selection of pathogenic organisms: *C. difficile* is the leading cause of hospital-acquired

gastrointestinal illness and has been associated with increased length of stay, morbidity, and mortality. Most cases of *C. difficile infections (CDI)* are associated with prior antibiotic use. Although most classes of antibiotics have been identified as risk factors for CDI, penicillins, cephalosporins, clindamycin and quinolones are the most frequently implicated agents[15]. Limiting the use of antimicrobials in right dose and duration tends to minimize the alternations in intestinal microbiome and hence offer protection against this deadly pathogen. Stewardship programs have an opportunity for intervention by ensuring compliance to rational prescription guidelines to minimise CDI and patient exposure to unnecessary antibiotics.

c. Emergence of antimicrobial resistance: Meta-analysis of more than 200 studies found a significant association between antibiotic consumption and the subsequent development of bacterial resistance at both the individual and community level. High antibiotic resistance was observed at community, country and regional level. Hence, responsible prescribing at the individual level as well as public policy that addresses the problem at the national or regional level are critical components of any strategy to reduce bacterial resistance[16]. The prevalence of resistance to multiple antibiotic classes among Gram-negative pathogens, such as *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, has increased in recent years, and has been closely linked to levels of antimicrobial consumption. Prior exposure to beta-lactam antibiotics has been shown to be a risk factor for acquisition of

extended-spectrum beta lactamase producing strains of *E. coli* and *K. pneumoniae* in hospitalised adults and children[17].

To minimize healthcare costs without compromising quality of care

A Cochrane review of 221 studies reported reduction in duration of antimicrobial therapy by 1.95 days with a similar risk of death. This was also associated with moderate-certainty evidence of a decreased length of stay. Both of these outcomes directly impact overall healthcare costs and can be used to validate further efforts for AMS program expansion[18].

In order to reduce antibiotic consumption and costs without increasing mortality or infection related re-admissions, an accurate diagnosis at the time of prescribing is vital. AMS programs may assist in accurate diagnosis by providing clinical pathways which quickly summarize guidelines, or by ensuring access to rapid diagnostic options (e.g. rapid influenza or Procalcitonin for sepsis). If positive, rapid influenza tests may decrease antibiotic consumption as patient has a clear diagnosis of viral infection. If negative, they may reduce anti-viral agent prescribing or inpatient isolation costs. Rapid identification using MALDI-TOF from positive blood culture bottles can result in a shorter duration of intravenous antimicrobial therapy thereby reducing costs and improving patient outcomes. Switching from intravenous to oral antimicrobials also tends to reduce costs, morbidity and overall reduction in healthcare associated infections. Once a provider has determined that a patient truly has a non-self-limiting bacterial infection, an effort must be made to choose the narrowest spectrum agent that is appropriate for the disease state.

AMS programs may help providers by identifying infections with the highest risk of overprescribing and targeting those patient populations whether they practice in a clinic or ambulatory healthcare setting, an acute care hospital or a long-term care facility antimicrobial stewardship programs may also focus on length of therapy to ensure that patients are treated for the minimum duration supported by the literature.

1.6 Economics of AMSP

Implementing an AMSP in any hospital may appear to bring extra financial burden on the hospital. However, it has been shown that the AMSP often are cost effective in the long run saving more money for hospitals then the actual expenditure on running the program. Firstly, cost savings would result from improved antimicrobial use by applying the evidence-based principles of feedback auditing and prior authorization resulting in some reductions in overall antimicrobial costs. Secondly, reduced incidence of complications such as multi drug resistant organisms (MDRO) infections and *Clostridium difficile* are reduced which

indirectly reduce the days of hospitalizations and treatment bringing down the overall cost. Also, the additional reductions in targeted MDROs by integrating the AMSP with ongoing infection control activities tends to bring down costs especially in ICUs. Overall the AMSP interventions tend to reduce the length of stay in hospitals which in turn would allow lower costs for patient care given fixed reimbursement, thereby enhancing the institution's revenue under prospective payment. This was a direct application of the cost efficiency strategy described and was likely the most important cost factor that we considered.

"Effective antimicrobial stewardship programs can be financially self-supporting and improve patient care. Comprehensive programs have consistently demonstrated a decrease in antimicrobial use (22% -36%), with annual savings of $200,000 -$900,000 in both larger academic hospitals and smaller community hospitals."[13]. In England the Hospital Pharmacy Initiative (HPI) facilitated the employment of Antimicrobial Pharmacists in 88% of Hospital Trusts and consequently experienced a reduction in overall expenditure on antimicrobials, with a projected decrease of £30million (E34 million) in 1 year; almost three times the outlay for the HPI provided from central funds[19]. Various studies across globe have reduced costs by implementing AMSP interventions. Reduction in hospital overall costs by € 12 for each € spent has been reported by Van Daalen et al [20]. Also, return of investment to the tune of 1:5 has been found in various studies[21].

1.7 Core Elements of Hospital Antibiotic Stewardship Program

For the implementation of a successful Antibiotic Stewardship Program it is important that certain criteria are met

- There must be a well-defined structure of Antibiotic Stewardship Program with clear objectives and guidelines. There must be clear accountability in terms of members and their roles and responsibilities.
- The Antibiotic Stewardship Program team members, prescribers, health care workers and nursing staff have to be motivated enough to bring about changes to improve patient outcomes.
- The leadership support has to be provided to overcome economical, organizational and professional barriers

The U.S. Centers for Disease Control and Prevention have established core elements necessary for developing a successful antimicrobial stewardship program[22].

Table 1: Core elements

Leadership Commitment	**Dedicating necessary human, financial and information technology resources.**
Accountability	Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician leader is effective
Drug Expertise	Appointing a single pharmacist leader responsible for working to improve antibiotic use.
Action	Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. "antibiotic time out" after 48 hours), IV to PO programs, prospective audit and feedback, antibiotic restrictions, etc.
Tracking	Monitoring antibiotic prescribing and resistance patterns
Reporting	Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff
Education	Educating clinicians about resistance and optimal prescribing

It is extremely important that healthcare providers recognize the need for and the value of Antibiotic Stewardship Programs and support their existence in healthcare facilities. The optimal structure and components of the program will vary according to the specific institution's needs. However, a successful program requires the involvement of well trained, motivated and enthusiastic physicians and pharmacists and the strong support of the healthcare administration and medical staff. Interested physicians and pharmacists can usually demonstrate to institutions that an ASP can pay for itself in short order by reducing pharmacy costs and reducing length of stays.

It is vital to have supporters and champions who will promote and support the work of the AMSP group in the wider organization. In addition, the group should be able to promote the benefits of its activities in terms of patient safety, reduced harm, reduced length of stay and reduced morbidity.

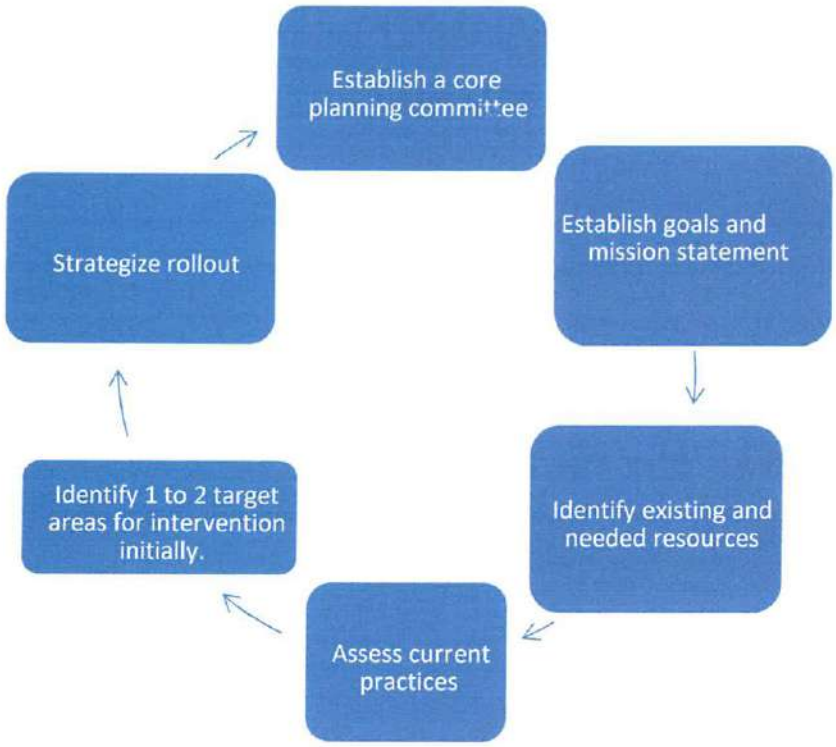


Figure 4: Establishing an AMSP in healthcare facility

SECTION 2. : NATIONAL MICROBIAL STEWARDSHIP PROGRAM IN THE MALDIVES

2.1 Vision

Optimization of antimicrobial prescribing practices to improve patient outcomes so as to reduce the overall burden of antimicrobial resistance.

2.2 Mission

National Antimicrobial Stewardship Program in Maldives strives to implement evidence based approaches in collaboration with healthcare providers to ensure that the right patient is prescribed the right antimicrobial in the right dosage via the right route for the right duration with timely de-escalation.

2.3 Goals of the project

1. Decrease selective pressure for the emergence of antibiotic resistance microbes.
2. Optimize utilization of antimicrobial agents in order to realize improvement in patient outcomes and economic benefit. This program should be coordinated with existing infection control efforts in order to significantly decrease the prevalence of antibiotic resistant pathogens at both hospital and community level.
3. Increase effectiveness and timeliness of antimicrobial formulary management by various interventions and process managements.
4. Eliminating redundant/unnecessary antimicrobials by implementing stewardship interventions such as:
    a. Responding to emergence of resistance to antimicrobial drugs by recommending alternations to the formulary of available antimicrobial drugs,
    b. Instituting therapeutic interchanges where appropriate and advantageous, and
    c. Instituting antibiotic restrictions/usage guidelines where appropriate and advantageous (e.g. approval process for colistin, carbapenem, vancomycin stops orders)
    d. Expanding and Optimizing of parenteral to oral conversion plan
5. Initiate, implement and monitor infection control program.
6. Development and enforcement of national regulations to restrict over-the-counter (OTC) sales of antibiotics without a prescription, and to restrict or prohibit the use of antimicrobials as growth promoters in order to promote rational use in the human and animal health sector.

7. Ensure access to life saving antimicrobials is not compromised to all who need them while restricting overuse.

2.4 Initiation of the program

The program will by initiated as a focused program in one high use area and then implemented in the entire hospital/facility in graded manner. This program would be individualized for the specific unit or patient population and would include protocols for prophylaxis, guidelines for empiric therapy, formulary restriction, conversion of parental to oral route, or innovative utilization programs (cycling, selective decontamination, etc.). Outcome determinants in the specific unit would include measures of infectious morbidity, antibiotic use per 1000 patient days for outpatients and 100 bed days for inpatients, rates of resistance, length of stay. As AMR and infection control go hand in hand the CDC 12-step antimicrobial utilization campaign will be initiated throughout each healthcare facility (HCF) for both inpatient as well as outpatients [23]. 5.1Annexure A gives the assessment tool to assess the capacity and preparedness of the hospital for AMSP.

2.5 Elements of the program

The program personnel will spend their time monitoring specifically monitoring, evaluating and intervening on management of antimicrobial therapy. Program personnel will include:

a) **One program leader**: Senior hospital physician with interest and motivation in field of AMR who is already working in the hospital. In island hospitals, senior physician or medical doctor can be appointed as program leader.

b) **One physician with expertise in infectious diseases:** The physician will commit more than 50% of his/ her budgeted time to the program. Some role redefining can be done so as to limit his/her ability to distract the individual's focus on the program. For island hospitals with no such expertise, nursing in-charge can be appointed for this post.

c) **One nurse/physician with knowledge of pharmacology of antimicrobials:** The person will commit 100% of his/ her time to the program. This work managed by a trained nurse/physician in infection control. Although it is always better to hire pharmacist but it should not stop the implementation of the program until fresh hiring is done.

d) **One data entry operator:** He/she will commit 100% of his/her time to the program. He/she will enter the data related to antimicrobial use and resistance. He/she under guidance of

5. Create formulary decisions, including antibiotic restrictions.
6. Develop policy/guidelines to streamline/de-escalate therapy.
7. Develop antimicrobial order forms with algorithms for common entities.
8. Provide continuous prospective review with feedback and interventions.
9. Communicate recommendations via chart, pamphlets, stickers, notes, or face-to-face
    - Prescribers education initiatives: Staff and providers involved in antibiotic orders from initiation to administration and monitoring should receive education about antibiotic resistance and stewardship
    - Patient education program: Patients and their families should be educated, as needed, regarding appropriate use of antimicrobials

2.9 Process of Antimicrobial Stewardship program

The AMSP committee must be constituted and sensitization meeting must take place within two weeks of roll out of the program. The committee must meet at least monthly in the initial 6-12 months of initiation, then the quarterly meetings can be held after one year.

The following table depicts the recommended structure and process of Antimicrobial Stewardship Program at various levels of health care in Maldives. Developing an AMSP for individual facilities depends on the available capacity of resources, resources and bed number. Smaller island hospitals with limited capacity can adopt relevant procedures from the Atoll or Regional hospitals.

Table 2: Structure and process of Antimicrobial Stewardship Program at various levels of health care in Maldives

Parameter	Island Hospital	Atoll Hospital	Regional Hospital	Tertiary care hospital
Beds	Nil	15-20	<100	>100
AMSP team	Hospital in-charge	Hospital in-charge	Full committee	Full committee
	Prescriber (1)	Prescriber (1-2)		
	Nurse	Infection control Nurse		
		Pharmacist (optional)		
Documents	Use National Treatment guidelines	Prepare own guidelines and AMR surveillance data or adapt National guidelines	Prepare own guidelines, AMR surveillance data and other documents	Prepare own guidelines, AMR surveillance data and other documents
	Use National AMR surveillance data			
Interventions	Prescription audit	Prescription audit	All	All

	with individual feedback	with individual feedback		
	Restricted antimicrobial list	Parenteral to oral switch		
	Antibiotic time out decisions with 48 hours review	De-escalation with dose optimization at 48 hours		
	Delayed prescription with restriction telephonic consult	Formulary		
		Antibiotic review		
Suggested meeting frequency	Quarterly	Quarterly	Monthly	Monthly
Laboratory support	Rapid POC tests to rule out/in bacterial causes	AST at least by manual method	AST manual or automated	AST preferably automated MIC reporting for ICU/sick patients
Education	Prescriber and patient education	Prescriber and Prescriber and patient education	Prescriber and patient education	Prescriber and patient education
Data sharing	With TSC	With TSC	With TSC	With TSC & NAMRC
Review by NAMRC	Annual	Annual	Annual	Half yearly

All hospitals need to submit the antibiotic usage to TSC on Antibiotic usage, AMR surveillance data to TSC on AMR Surveillance which will then submit data after preliminary analyses to National AMR committee on quarterly basis. This data will then be analysed and used for improvement in program by National AMR Committee. The TSC on AMR awareness & Education will develop training and education material required in AMSP. Antimicrobial usage data from STO pharmacies and Aasandha can be sent quarterly to TSC on antimicrobial usage. This data will reflect overall consumption data from all sources except the private pharmacy dispensing.

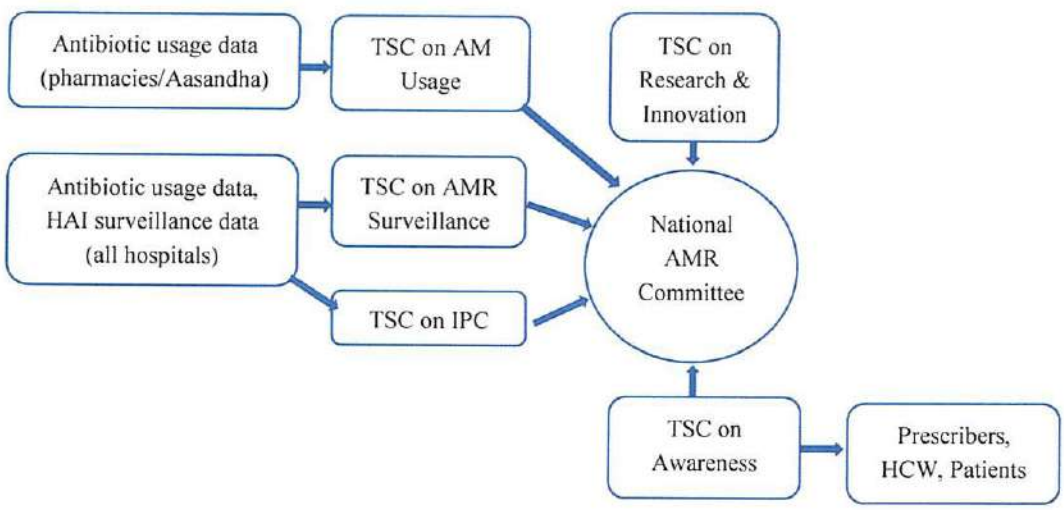


Figure 5: Flow of data related AMSP

2.10 Process of Antimicrobial Stewardship program

The program can initially be implemented at a tertiary care hospital and later expanded to include Regional, Atoll and Island Hospitals.

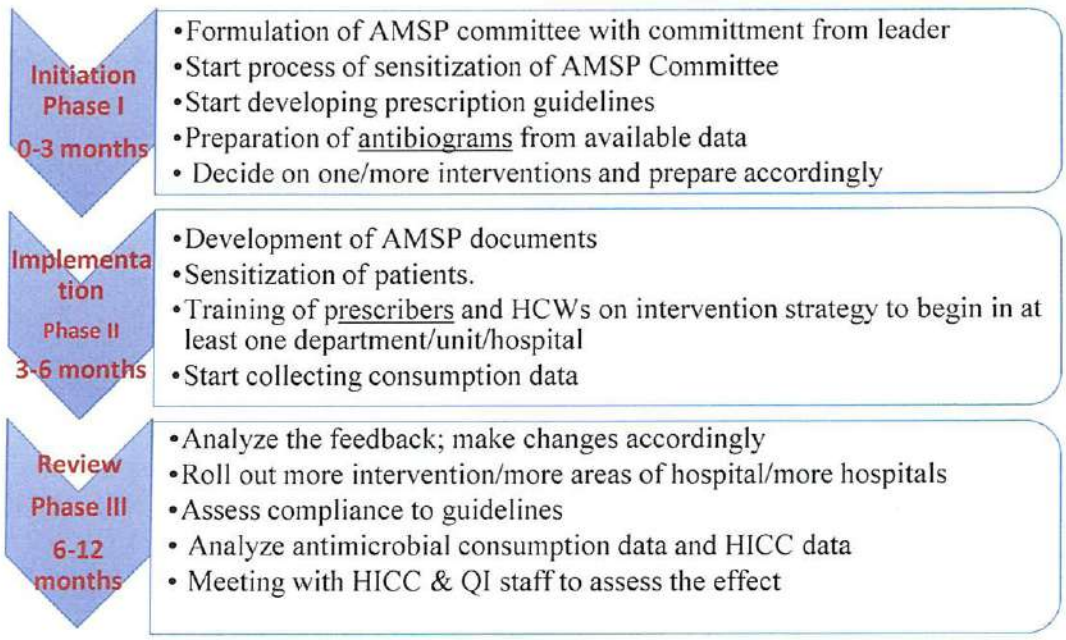


Figure 6: AMSP implementation plan

SECTION 3. GUIDELINES FOR NATIONAL ANTIMICROBIAL STEWARDSHIP

3.1 National leadership initiative in Antimicrobial Stewardship Program

The National AMR containment committee has to ensure control and prevention of antimicrobial resistance with, reduction of medication-related adverse events, and reduction of unnecessary financial costs through having an effective antimicrobial stewardship programme. It has to ensure the following:

- All hospitals to have an antimicrobial stewardship programme in place. It will be the responsibility of the Hospital in charges/leaders/managers/chief executives to ensure its implementation and functioning. They will be required to provide evidence, on an annual basis to NAMRC to show that such a programme is in place, that clear targets and objectives for the programme have been set, and that these targets and objectives are being realized. NAMRC must conduct review of antimicrobial stewardship programme at least annually so as to review progress and modify goals to be included in the hospital's annual plan.
- The provision of adequate funding for appropriate personnel, information technology resources and educational initiatives. The committee must make provisions that the stewardship-related duties are included in job descriptions and annual performance reviews. It should prioritize and fund the appointment of key personnel if required to implement antimicrobial stewardship programs in hospitals

- Establishment of working groups to develop National treatment guidelines relating to antimicrobial use including empirical therapy and surgical prophylaxis, infection control and prevention guidelines, surveillance of healthcare associated infections for all levels of healthcare and monitor their implementation at all levels.
- Establishment of committee to suggest changes in curriculum regarding antimicrobial resistance and its control at undergraduate and postgraduate education of all healthcare workers. Later to ensure that these changes are made in curriculum.
- Must coordinate with TSC on Antibiotic usage and TSC on AMR Surveillance in order to generate country wide data on AMR surveillance and antibiotic usage.
- Incorporation of principles of rational prescribing and hazards of AMR in training programs for healthcare workers to ensure that all healthcare professionals who recommend, prescribe, handle and administer antimicrobials receive adequate training and education in the proper use of antimicrobials, in line with the principles of rational antimicrobial prescribing. An induction program should be made mandatory for all healthcare workers. Principles of rational antimicrobial prescribing should be a mandatory core module for training and be included in examinations.
- Development of a structured training programme delivered at a national level which could be accessed by all personnel working in AMSP. NAMRC must develop educational material in coordination with TSC on AMR awareness & Education related to AMSP and rational usage of antibiotics for patients, prescribers and other healthcare workers.

- Prioritization of the development of electronic patient records, electronic prescribing and computer-based surveillance in hospitals; all of which will enhance the implementation of antimicrobial stewardship programmes.
- Prioritization of the provision of pharmacy information technology systems, which can provide the audit and surveillance requirements outlined in these guidelines.
- Cooperation with other ministries and departments for development and enforcement of national regulations to restrict over-the-counter (OTC) sales of antibiotics without a prescription, and to restrict or prohibit the use of antimicrobials as growth promoters to promote rational use in the human and animal health sector.
- The access to life saving antimicrobials is not compromised to all who need them while restricting overuse.

3.2 Structure and organization of stewardship programs at hospitals with inpatients (Atoll hospitals, regional hospitals and referral hospitals)

All hospitals should ensure the recommendations included in the AMSP section dealing with structure and organization of stewardship programs at hospital level is implemented. An effective antimicrobial stewardship program should ensure control and prevention of antimicrobial resistance, the reduction of medication-related adverse events, and the reduction of unnecessary financial costs and must be a strategic goal for all hospitals.

3.2.1 Resources

- All hospitals must constitute an AMSP committee/team. The chair of the committee must be hospital manager/chief executive, or a

designated senior member of the hospital management team. He should have responsibility for ensuring that an effective antimicrobial stewardship program is in place, including the provision of funding for appropriate personnel, information technology and educational initiatives.

- All hospitals should have a multidisciplinary Drugs and Therapeutics Committee. Larger hospitals require their own in-house committee, while regional committees may be set up to service smaller institutions or develop regional guidelines. These regional committees can liaison with Regional and Atoll Hospitals.
- All hospitals should have the infection control committee in place with proper guidelines.
- All hospitals must have a medical microbiologist with a formal on-site commitment, including designated hours for managing the antimicrobial stewardship programme. At least one medical microbiologist for 250 beds is suggested as per International norms. Prescribers should have ready access to clinical microbiology or infectious diseases expertise on a 24- hour basis. Such contact should be encouraged for all serious or complicated infections. In places where microbiologists are not available, laboratory technologists can undertake work to provide feedback and perform tests.
- All hospitals must have at least one nurse/physician/clinical pharmacist with dedicated responsibility for antimicrobial stewardship.
- All hospitals should have access to a laboratory-based antimicrobial surveillance data developed and disseminated by microbiologist working with AMSP team.

- All hospitals should have administrative and information technology to support the antimicrobial stewardship programme.
- All hospitals should have a pharmacy information technology system (e.g. STO Pharmacy of each hospital) that can provide antimicrobial prescribing data, in line with local and national surveillance requirements.

3.2.2 The AMSP team

The AMSP team must therefore comprise of following members:

i. Hospital Director/chief executive (or designated senior member of management team) as chair
ii. Medical microbiologist
iii. Physician with some training in infectious diseases
iv. Nurse/Physician/Pharmacist
v. Infection prevention and control nurse
vi. Consultant surgeon
vii. Consultant physician
viii. Consultant paediatrician
ix. Consultant Obstetrician & Gynaecologist
x. Nursing administrator or Representatives from other specialist areas, as appropriate (e.g. intensive care, emergency room, Labour Room, etc.)
xi. Member of Drugs and Therapeutics Committee

The antimicrobial stewardship team should work closely with the institution's infection prevention and control team to ensure that prevention of healthcare associated infection and antimicrobial resistance are integrated with the antimicrobial stewardship programme. Infection prevention and control nurse specialists should be members of the antimicrobial stewardship team.

3.2.3 Roles and responsibilities of various members of team

- The role of the team is to implement the antimicrobial stewardship programme, which may include:
    - Pre-authorization of restricted antimicrobials.
    - Review of patients on intravenous antimicrobials so as to assess for potential to switch to oral therapy.
    - Review of patients receiving antimicrobials with duplicate spectra, or other potentially inappropriate drug combinations.
    - Review of patients on selected broad spectrum antimicrobials.
    - Review of patients with documented sterile site infections (e.g. bloodstream infection, meningitis), to ensure appropriate antimicrobial therapy is in place.
    - Review of patients receiving antimicrobials for a duration that exceeds recommendations in the hospital antimicrobial guidelines.
    - Participation in the infection prevention and control programme. Provision of education on prudent antimicrobial use to consultant, non-consultant and nurses.

- The nurses should link with the antimicrobial stewardship team, helping them to target their activities efficiently.
- The antimicrobial stewardship team should have sufficient administrative and information technology support, to allow it to implement stewardship initiatives

a. Hospital Director/chief executive (or designated senior member of management team as chair)

- To provide effective leadership to the antimicrobial stewardship team to plan and manage the program.
- To issue formal statement that "This hospital supports efforts to improve and monitor antibiotic use".
- To incorporate the detection, prevention and control of antimicrobial resistance into institutional strategic goals and provide the required resources.
- To establish policy and practices for rational use of antimicrobials.
- To develop the annual plan for the program, review strategies and set goals and targets.
- To coordinate with in charge Hospital Infection Control Committee, Drugs and Therapeutics committee and National AMR Committee.
- To regularly organize meetings with members to discuss progress, solve issues related to the program and submit the regular surveillance/audit reports to TSC and National AMR Committee Chair.
- To ensure that the staff from relevant departments are given sufficient time to contribute to stewardship activities.
- To undertake initiatives to educate prescribers, patient and healthcare workers.

b. Medical microbiologist

- To ensure that there is access to a high quality diagnostic microbiology service.
- To provide quality assured services related to identification and antimicrobial sensitivity testing.
- To prepare and disseminate antibiograms and antimicrobial resistance surveillance reports to clinicians.

- To ensure that there is restrictive reporting of antimicrobial susceptibilities and interpretative reporting of microbiology test results.
- To ensure provision of appropriate rapid diagnostic tests to assist prescribers.

c. Physician

- To assist in developing antimicrobial prescribing guidelines, surgical prophylaxis guidelines, surveillance of HAI etc. in association with prescribers and infection control committee.
- To assist in developing syndromic clinical treatment guidelines and encourage their compliance.
- To provide expert advice on antimicrobial use, to promote the safe, effective and cost-efficient use of antimicrobials.
- To assist in patients and healthcare professional's education initiatives about optimal antimicrobial use.
- To ensure that the prescribed antimicrobials reflect local and national guidelines, as relevant.
- To perform day to day tasks related to AMSP such as:
    - Identification of patients for stewardship interventions,
    - Initiation of streamlining or sequential therapy,
    - Dose adjustments,
    - Approval of restricted antimicrobials, in conjunction with microbiologist or clinical pharmacist,
    - Assess compliance with policies and prescribing errors,
    - Undertake audit and provide feedback.

d. Nurses including Infection prevention and control nurse (In addition to her duties in HICC)

- To ensure that adequate microbiological samples for culture and sensitivity are obtained taking all precautions prior to start of any antimicrobial therapy.
- To make sure that the laboratory results are communicated in a timely manner.
- To ascertain that the antimicrobial doses are not missed and are administered according to optimal dose intervals. Also ensure that the antimicrobial administration is adapted to clinical needs as well as patient condition (i.e. evaluating oral routes if clinically appropriate).
- To perform audits and point prevalence surveys to assess compliance to AMSP interventions.
- To assist in patients and healthcare professional's education initiatives about optimal antimicrobial use.
- To analyse and share infection control data with AMSP members.

e. Prescribers (Consultant surgeon, physician, in charge emergency medicine)

To ensure rational antimicrobial prescribing as part of routine prescribing.

- To ensure compliance of treatment guidelines.
- To make sure that the cultures are ordered before start of antibiotics.
- To keep themselves updated with newer diagnostic strategies and their interpretation.
- To ensure that the rational antimicrobial prescribing is included in education for other prescribers as well as healthcare workers.
- To assist AMSP team members in carrying out audit and take appropriate action on feedback provided.

f. Nurse/physician with clinical pharmacology training/Pharmacist

- To assist in developing the policy, clinical guidelines and restricted antimicrobials list and review periodically.
- To perform day to day tasks related to AMSP.
- To collect, analyse and provide feedback on local consumption and expenditure on antimicrobials to the AMSP team and prescribers.
- To take part in education of health care workers and prescribers in rational antimicrobial prescription.

g. Quality improvement staff

- To assess all audit and feedbacks using quality indicators.
- To assist and provide training to staff involved in healthcare at all levels.

3.3 Guidelines and documents

AMS Program must develop core documents

a. Antibiotic policy
b. Guidelines for surgical prophylaxis
c. Guidelines for parenteral to oral conversion/ to streamline/de-escalate therapy
d. Infection control document from HICC
e. Checklists to monitor appropriateness of prescription of antibiotics
f. Guidelines for surveillance of AMR and antimicrobial usage
g. Syndromic treatment guidelines
h. Audit forms to audit interventions
i. List of restricted antibiotics and process for prescribing same.

5.6 Annexure F and 5.7 Annexure G list the principle of rational prescribing and surgical prophylaxis. 5.9 Annexure I is a suggested guide for developing prescription guidelines. National guidelines may be adapted till

such local guidelines are in place. These guidelines should be developed in partnership with all treating departments and must be updated at least every two years. These guidelines should be easily accessible and should be developed as a pocket book or in electronic version for easy accessibility.

Both AMSP and the infection control program are strategic partners in efforts to reduce healthcare associated infections and antimicrobial resistance. HICC has to actively interact with the AMSP team to ensure control of AMR. The guidelines for infection control and surveillance of HAI (Surgical site infection, Catheter associated blood stream infections, catheter associated urinary tract infections etc.) must be developed.

3.4 Antimicrobial Stewardship interventions

Interventions in AMSP can be introduced in phased manner or in whole hospital depending upon the decision of AMSP team. Broadly following interventions can be introduced:

Table 3: Types of antimicrobial stewardship interventions

S. no.	Stewardship Interventions
1.	Prospective audit
2.	Antibiotic Timeouts
3.	Antibiotic consumption analysis
4.	Formulary Restriction
5.	Dose optimization
6.	Streamlining or de-escalation of therapy
7.	Parenteral to oral conversion
8.	Guidelines and clinical pathways
9.	Laboratory surveillance and feedback
10.	Combination therapies

3.4.1 **Core intervention**

a. Prospective audit

- Members of AMSP team need to conduct regular bedside review of the patients to analyse the prescriptions related to antimicrobial prescribing. 5.11 Annexure K suggests criteria for selection and flow of review of patients requiring bedside review.
- After reviewing the AMSP team must provide feedback to the prescriber advising change if required on the optimal antimicrobial therapy. The feedback should preferably be provided by direct conversation with the clinician/team. This allows a rapport building and builds trust of prescriber in AMSP team. The feedback can also be provided by using a standard form (5.12 Annexure L) in patient's case record or electronically also.
- The changes/advice by AMSP team should be construed as optional advice, so that the prescription autonomy is not lost and the advice is not seen as interference with patient care. The AMSP team member should always try to deliver this advice in a non-confrontational and non-critical manner.
- **Antibiotic "Time outs"**: Antibiotics are often started empirically in hospitalized patients while diagnostic information is being obtained. However, this decision is often not reviewed in the next 48-72 hours by the prescribers. An antibiotic "time out" prompts a reassessment of the continuing need and choice of antibiotics when the culture reports and other investigation results are available. All prescribers should review antibiotics prescription after 48

hours to assess all 4Ds of antimicrobial stewardship. The AMSP team in prospective audit must focus on antibiotic time outs as well.

b. Antimicrobial prescribing surveillance and audit

- The only way to determine if antibiotic use is improving is through measurement. Measurement firstly to set the baseline and then repeated measurement to check if things are improving. Antimicrobial prescribing analysis form backbone of any AMSP. These can be quantitative to assess the overall antimicrobial consumption in a ward/unit/hospital or qualitative to assess the appropriateness of prescribing.

- **Quantitative surveillance of antibiotic use**: For hospitals with electronic antimicrobial prescribing this data can be collected easily. This data can also be collected from Aasandha dispensing/STO pharmacy online data. In many hospitals without electronic prescribing the hospital pharmacy system or the patient case records can provide information on antimicrobials supplied to wards and other clinical areas. These data can be used as a proxy for antimicrobials given to patients. In the community data on antimicrobial use can come from medicine sales data from pharmacies or from Aasandha. Since all antimicrobials in Maldives are imported, the import data also gives proxy data of overall consumption of antibiotics by the population.
- The most common, standardized measure for antimicrobial usage is defined daily doses (DDD). The basic definition for a DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. In simple terms,

the DDD is the amount of antibiotic that a typical adult patient will receive each day for treatment of an infection. DDDs are used for monitoring trends of antibiotic use over time (e.g. is use going up or down) in a ward, hospital or group of hospitals. These can may be undertaken on a monthly or quarterly basis depending on the setting and the antibiotics included.

- To calculate the total DDDs for a period, the total number of grams of each antibiotic used in a ward (or whole hospital) during a defined period is divided by the WHO assigned DDD value for that antibiotic. DDD cannot be used for paediatric patients as they are typically assigned for adult patients.
- An alternative is the Days of Therapy (DOT). One DOT represents the administration of a single antibiotic on a given day regardless of the number of doses administered or dosage strength
- **Qualitative assessment of appropriateness of prescription**: A qualitative approach is required to provide information on which patients are being given which antibiotics, their indication, which antibiotics are being used for treatment of particular infections and whether the antibiotics prescribed are in accordance with local prescribing guidelines. Remembering the principle that we need to measure to improve, the use of Point Prevalence Surveys (PPS) enables assessment of the quality of antibiotic use and identification of targets for quality improvement (as detailed in 3.1). The

antimicrobial stewardship team in each hospital should have a system of regular surveillance and audit of antimicrobial use.

c. Formulary Restriction

The AMSP team in consultation with the Drugs and Therapeutics Committee should make a list of restricted and unrestricted antibiotics. The restricted antibiotics can only be prescribed by approval chair of AMSP. This list should be periodically reviewed every 12 months based on antimicrobial usage data and rates of antimicrobial resistance. Restrictions may have to be reinforced, or applied to additional antimicrobial agents, in the setting of outbreaks caused by antimicrobial-resistant pathogens (e.g. *C. difficile*, VRE, MRSA) in special settings.

Antimicrobials included on the hospital formulary can be divided into three groups:

1. Unrestricted: may be prescribed by any clinician
2. Consultant only: may only be prescribed by a consultant
3. Restricted: may only be prescribed following prior discussion with, and approval by, the antimicrobial stewardship team

Preauthorization for antimicrobials must be given all restricted antibiotics by a designated member of the AMSP team. The process for preauthorization should complete the following steps shown in figure 3.1.

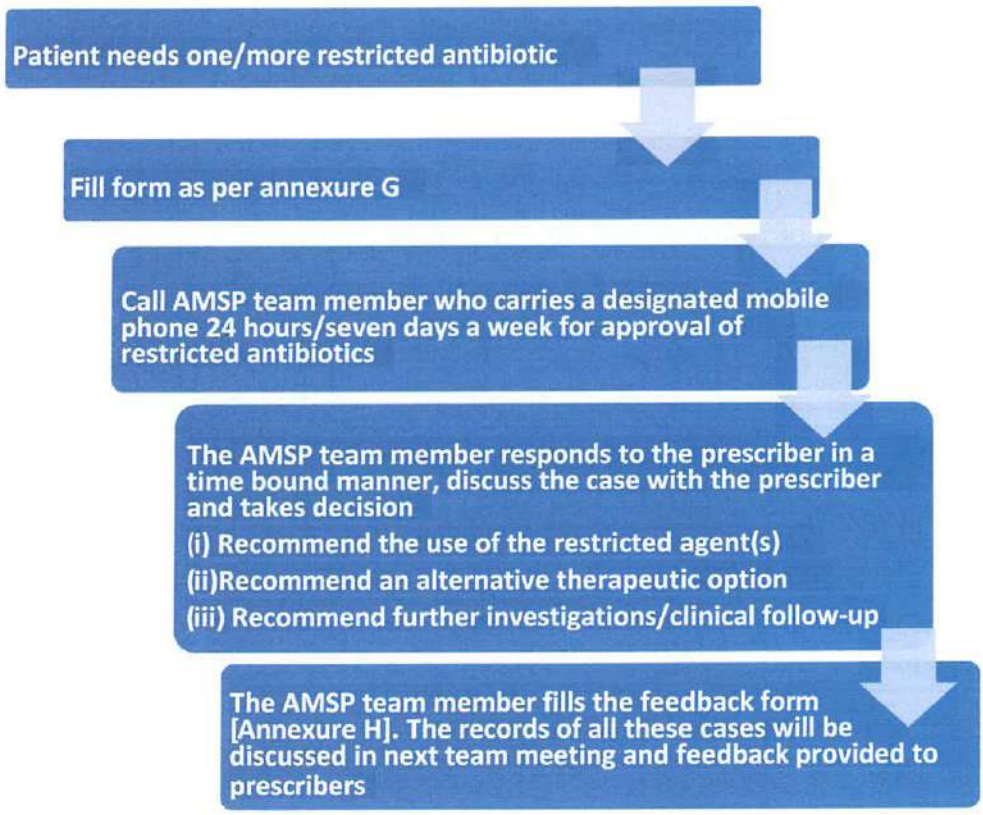


Figure 7: Pre-authorisation system for restricted antimicrobials

3.2.4 Supplemental interventions

a. Optimisation of therapy

- AMSP teams should ensure that antimicrobial is given at the optimal dose, frequency and duration, based on individual patient characteristics such as age, weight, renal function, likely causative organism, site of infection, and pharmacokinetic and pharmacodynamics characteristics of the antimicrobial agent(s).
- It must be ensured that antimicrobials requiring adjustments according to patient's renal and hepatic function are monitored and changed accordingly.

b. Streamlining or de-escalation of therapy

- Often the empirical therapy is started without much evidence. AMSP team must streamline empirical therapy on the basis of on-going clinical review, laboratory results, and diagnostic imaging, as soon as possible.
- All empiric antimicrobial therapy should be reviewed on a daily basis by the clinician responsible for the patient's care. AMSP teams should liaison with prescriber to identify antimicrobial regimens that are likely to require streamlining, such as:
    - Antimicrobial combinations with overlapping spectrum of activity
    - Prolonged use of broad spectrum antimicrobials
    - Unauthorised use of restricted agents
    - Antimicrobial agents or combinations of agents, those are not in accordance with hospital antibiotic policy.

c. Parenteral to oral conversion

- Many intravenous agents have equivalent oral preparations. The administration of oral medications relies upon a functioning gastrointestinal tract for adequate absorption of the medication. Early switch from intravenous (IV) agents to the equivalent oral preparation offers several benefits:
    - o Decreased total cost of therapy,
    - o Decreased potential for line associated infections,
    - o Potential for decreased length of stay and patient preference,
    - o Increased patient comfort and mobility,
    - o Savings in nursing time spent preparing and administering intravenous doses.

- A key factor in the conversion from IV to PO therapy is the bioavailability of the oral preparation. An oral agent that is well absorbed is considered equivalent to intravenous preparation. However, each case is unique as the patient specific factors are also important determinants in this decision.

Table 4: Criteria for parenteral to oral antimicrobials

PARENTERAL TO ORAL CONVERSION PROGRAM
AMSP member will assess a patient's ability to convert to oral antimicrobial therapy on the basis of the following criteria:
Patient Inclusion Criteria □ The patient is receiving an oral diet, or is receiving tube feeds of at least 50% of their goal rate, or is receiving and tolerating oral medication
• A suitable oral form of antimicrobial or oral antimicrobial with similar profile is available • Prolonged course of antimicrobial therapy not required • Afebrile for the past 24-48 hours • Definite clinical improvements as assessed clinically • White cell count returning decreasing/normalizing
Patient Exclusion Criteria • Patients designated 'nil orally' for any reason • Haemodynamically unstable • Presence of a deep-seated/high risk infection, for which continued IV therapy is required (e.g. osteomyelitis, septic arthritis, deep tissue abscess, meningitis, intracranial abscess, endocarditis, severe or necrotising soft tissue infections) • Being prescribed scheduled anti-emetics • Patients with mucositis and/or receiving chemotherapy that causes mucositis/ being treated for active gastrointestinal bleed/GI disorder which will affect absorption of drug.

- The AMSP team member will provide advice on converting patients meeting the above criteria from IV to equivalent oral dose and frequency, using a standardized form [Annexure I].
- If the IV agent has not been converted to the recommended oral equivalent within 24 hours of the recommendation being made, a member of the antimicrobial stewardship team will contact the treating physician responsible for the patient's care directly, to discuss the recommendation.
- Regular audits of compliance with parenteral to oral conversion recommendations will be carried out, and the feedback given to prescribers.

d. Outpatient Parenteral Antimicrobial Therapy (OPAT) programs

OPAT programs tends to minimize the hospital stay thereby offering reducing risk of healthcare associated infections but they require good health team, robust communication systems, documented policies and guidelines. OPAT program can be developed as per standard guidelines available from Infectious Diseases Society of America [24].

3.2.5 Laboratory Interventions

a. High quality laboratory service

- It is important to have a high quality 24-hour access microbiology laboratory preferably accredited to implement a successful AMS Program. The communication between the AMSP team members and laboratory is vital. The positive culture reports must be conveyed rapidly to prescribers and AMSP team members so that the therapeutic interventions can be made in desired time frame.
- The laboratory should use standard guidelines for antibiotic sensitivity testing (AST) such as Clinical and Laboratory Standards Institute (CLSI) or EUCAST. The AST laboratory must routinely perform standard Internal Quality Control (IQC) for AST utilizing

ATCC strains. This includes IQC for culture media as well as antibiotic discs used in AST. The laboratory must be part of External Quality Assurance Program to validate its results.

- The laboratory must train and emphasize on correct sample collection techniques to improve the significance of reporting of clinical isolates. This may require regular training programs and interactions with treating doctors and nursing staff.
- The AST reporting should be done in restricted manner, reporting only when clinically indicated. AST should not be reported for suspected colonizers. Microbiologists should not hesitate to call the clinician to clarify such cases.
- The laboratory should maintain narrow spectrum agents as first line of reporting. In case the organism is susceptible to first line antibiotics it should be reported first. Restricted antibiotics/second line antibiotics should be reported only in cases of resistance to first line/unrestricted antibiotics. Some interpretive comments on reports must be included in reports to guide prescribers (As suggested in 5.9 Annexure I)

b. Standard bacteriology and antimicrobial susceptibility testing methods

- Isolation, identification and antimicrobial susceptibility testing should be performed according to bacteriology standard operating procedures (SOPs) developed in house updated with revised breakpoints from CLSI)/EUCAST.
- Antimicrobial susceptibility testing of pathogens should be conducted by one of the following methods:

1. **Kirby Bauer Disc Diffusion**: AST should be performed using the Kirby-Bauer disk diffusion method. Results should be reported as zone inhibition diameters.

2. **Screen Agar**: AST for vancomycin for Enterococcus species and for

Staphylococcus aureus should not be done by disc diffusion. Screening AST for vancomycin

in Staphylococcus aureus and Enterococcus species requires testing by vancomycin screen agar (Brain Heart Infusion agar with vancomycin 6µg/ml).

3. **Broth Microdilution**:

a. AST for colistin in blood isolates of *E. coli*, Klebsiella species, Acinetobacter species, and Pseudomonas species requires testing by broth microdilution. Results should be reported as minimum inhibitory concentration (MIC) breakpoint.

b. AST for vancomycin in all isolates of S. aureus and Enterococcus species in which growth has been detected (positive growth) on vancomycin screen agar requires repeat AST testing by broth microdilution. Results should be reported as MIC breakpoint.

c. Automated AST systems (Vitek, Phoenix, Microscan): If a facility performs AST using an automated AST system, results should be reported as MIC breakpoints for all pathogen-antibiotic (i.e. "bug-drug") combinations tested. If AST by both manual disc diffusion and automated testing methods are performed, MIC results should be reported.

3.2.6 AMR Surveillance

- The laboratory must collect AST surveillance data to generate antibiograms. The suggested organisms for which surveillance can be performed and the appropriate antibiotic panels for these organisms are given in 5.17 Annexure Q. While the antibiotics listed in the surveillance AST panels are critical for public health purposes, microbiology laboratories may wish to perform AST for additional antibiotics to guide clinical decision making.
- Pus "swabs" and "wound swabs" should not be included in AMR surveillance reporting.
- When several cultures are collected during patient management, duplicate findings for the same patient should be excluded (de-duplication) for surveillance purposes. For each surveillance period, only one result should be reported for each patient per surveyed specimen type and surveyed pathogen. The surveillance can be carried out using excel or a special software such as WHONET™.
- Annual antibiograms for selected pathogens using surveillance data must be generated and circulated in the hospital to guide empirical therapy. Stratified antibiograms (location based or age based) give better information to prescribers and are a great help in revising antibiotic policy.

3.2.7 Rapid diagnostics

Rapid testing for inflammatory markers such as Procalcitonin, C Reactive Protein etc. guide prescribers to institute rational therapy especially in sepsis cases. Rapid identification and direct sensitivity from blood culture bottles flagged positive can save 24 hours as compared to conventional AST. However, it is recommended that the results of direct sensitivity testing are reconfirmed after AST from isolates the next day.

In sepsis cases, a preliminary report can be generated by Gram stain from positive flagged bottle in automated culture systems. This can help in institution of more specific therapy so as to reduce the antibiotic prescribing. MALDI-TOF if available is able to specifically identify the pathogen in less than 30 minutes.

Rapid diagnostic tests rapidly confirm the presence of a bacterial pathogen or help to rule out a bacterial infection (e.g. PCR identification of respiratory viruses in children with lower respiratory tract infection) help to monitor response to therapy, and guide the duration of antibiotic therapy.

3.2.8 Educational interventions

a. Education regarding Antimicrobial Stewardship Program

All hospitals should organize training programs for prescribers and AMSP team members to sensitize them on aspect of rational prescription, prescription guidelines, infection control and surveillance strategies.

b. Prescriber education

All new medical, nursing and pharmacy staff must have a mandatory induction program in rational prescribing of antimicrobials, infection control and control of healthcare associated infection. Modules to training of trainers need to be developed to deliver standard training in all aspects. It is also essential to have an on-going education programme for all prescribers in AMSP. This training MUST be made mandatory for all prescribers by senior management. As all doctors prescribe antibiotics, a strong input is needed from academia to transfer the knowledge in the undergraduate curriculum.

Monthly meetings must be held by AMSP team with prescribers to share data related to AMSP surveys and analysis.

Educational aids to guide prescribers at the point of prescribing such as clinical algorithms for the diagnosis of infection, or methods to standardise documentation of treatment decisions must be displayed at important locations in hospitals.

AMSP and rational prescription must be included in curriculum of undergraduate and postgraduate education of all healthcare workers. Flow charts (Annexure L) reminding prescribers about rational prescribing can be displayed in doctors working areas.

c. Patient and caregiver education

All outpatient areas should have educational material such as posters/pamphlets etc. to educate patients about use of antibiotics. Face to face training and sensitization can be provided in patient waiting area, in vaccine clinics. In addition to health care workers, peers or opinion leaders can be utilized for this interaction. Antibiotic awareness campaigns in schools and offices should be carried out to bring about this behaviour change.

Some topics which should be included in these awareness programs are suggested below:

- When antibiotics are not needed. For example, patients should be informed that most upper respiratory tract infections are viral and do not require antimicrobials.
- Damage caused by antibiotics such as antibiotic associated diarrhoea, allergic reaction etc.
- Disturbance caused by antibiotics to useful bacteria in body. For example, use in infancy and childhood is associated with allergic, infectious, and autoimmune diseases, likely through disturbing the microbiome.

- Patients should not ask the doctor for antibiotic prescription. If antibiotic is prescribed, then they must finish complete course.

3.2.9 Information technology support in AMSP

Computer-based surveillance should be used to target antimicrobial stewardship interventions, track antimicrobial resistance patterns, and identify healthcare-associated infections and treatment related adverse events. Software for patient records, computerised prescribing, laboratory reports and clinical decision support make implementation and functioning of AMSP convenient and more accessible.

3.2.10 Antimicrobial surveillance, audits and feedback

a. Point prevalence surveys

Prevalence surveys of antimicrobial use should be carried out at least every twelve months, and ideally every six months. These surveys should focus on high risk areas, or on aspects of antimicrobial use that are likely to be targeted for stewardship interventions. The antimicrobial audits should be undertaken as point prevalence surveys to analyse specific antimicrobial use on prefixed days decided by team (e.g. Every third Monday). The data set should be kept to a minimum, to facilitate completion of the surveys, and only include data that is likely to be acted upon. Aim of these surveys is to

- Establish baseline antimicrobial use data for the hospital
- Examine prescribing patterns (e.g. use of reserved antimicrobials, route of administration and potential for intravenous/oral switch, duration of use, combinations prescribed, review date, indication etc.)
- Identify areas for intervention
- Check compliance to interventions in AMSP.
- Provide data to target antimicrobial stewardship initiatives
- Benchmark practice over time in each hospital and with other hospitals.

b. Antimicrobial resistance data

Antimicrobial resistance surveillance data has to be entered in GLASS from January 2018 by all countries aligned with Global action plans. AMR data must be generated using guidelines outlined in 5.17 Annexure Q. The WHONET should be used to generate data such as:

- Data on bloodstream isolates.
- Rates of detection of selected antimicrobial resistant bacteria (e.g. new isolates of extended spectrum beta-lactamase (ESBL) producing Gram negative bacteria)
- Antibiograms for selected pathogens (e.g. urinary tract isolates), or for specific high-risk units (e.g. intensive care unit)
- Rates of C. difficile associated disease
- Use of specific agents by ward or unit

c. Prescribing audits

Detailed audits of antimicrobial use may be carried out by ward-based nurses/AMSP team member/pharmacists. The frequency with which such audits are carried out will vary according to local resources and needs. Examples of such audits include [5.19 Annexure S]:

- Audit of surgical antimicrobial prophylaxis
- Audit of antimicrobial use on selected wards or units where an increase in antimicrobial resistant organisms has been identified (e.g. ESBL-producing Gram negative bacteria, VRE)
- Monthly audit of antimicrobial use on selected high risk units (e.g. ICU, transplant unit)
- Audit of use of restricted antimicrobials
- Audit of parenteral to oral conversion programmes
- Audit of therapeutic drug monitoring if done

The data thus collected will be used to generate quarterly and then annual report on antimicrobial use and the report be submitted to the hospital Chief

and circulated to all clinicians. To encourage a whole team approach it is beneficial to share data at multi-professional meetings and this should be done informally at ward meetings or via hospital or directorate level audit meetings or in a community setting with all staff in a clinic.

3.2.11 Feedback data to individual clinical services or prescribers

The data on antimicrobial prescribing should be shared with each clinical service or prescriber on a regular basis. In hospitals with more than 200 beds this data can be shared quarterly while for less than 200 beds this can be done at 6-12 months. Initially this data will be shared in face to face meetings so that sensitization and understanding of AMSP can be developed. Later this can be done electronically with only one yearly meeting. An attempt should be made to include following in feedback report:

- Antimicrobial use, expressed as DDD per 100 in-patients admitted or discharged under that prescriber's care per quarter. Breakdown of antimicrobial use by risk groups and iv/oral route, as detailed under quarterly report
- Antimicrobial costs for inpatients admitted or discharged under that prescriber's care per quarter
- Comparison of antimicrobial use and cost with overall data for hospital and, where appropriate, with overall data for the relevant discipline (e.g, medicine, surgery, paediatrics etc.)
- Analysis of dose and duration of antimicrobials on basis of PPS.
- An indication of the proportion of antimicrobial use that was in line with hospital prescribing guidelines

3.2.12 Process indicators

A variety of measurements, taken from prevalence surveys or prescribing audits, may be used that can act as process indicators for the

success of antimicrobial stewardship programmes. Examples of useful process indicators include

- Quarterly measure of overall antimicrobial consumption, or consumption of selected agents, expressed as DDD per 100 bed days
- Proportion of single dose pre-operative antimicrobial prophylaxis for clean surgery
- Proportion of patients with parenteral to oral switch within stipulated time.
- Proportion of restricted antimicrobial use that is in accordance with hospital prescribing guidelines
- Proportion of patients with community-acquired pneumonia, UTI, GPC or GNB infection who have been assessed using a validated measure of severity
- Proportion of patients who have received antimicrobial therapy in concordance with hospital prescribing guidelines

3.5 Antimicrobial Stewardship programme at island hospitals

According to CDC the Antimicrobial Stewardship program for outpatient department has four core elements [25]. These are:

- Commitment: Demonstrate dedication to and accountability for optimizing antibiotic prescribing and patient safety.
- Action for policy and practice: Implement at least one policy or practice to improve antibiotic prescribing, assess whether it is working, and modify as needed.
- Tracking and reporting: Monitor antibiotic prescribing practices and offer regular feedback to clinicians, or have clinicians assess their own antibiotic prescribing practices themselves.

- Education and expertise: Provide educational resources to clinicians and patients on antibiotic prescribing, and ensure access to needed expertise on optimizing antibiotic prescribing.

3.5.1 AMSP team

The 165 island hospitals have mostly outpatients and emergency services. They have a minimum basic laboratory service and may not usually provide culture and antimicrobial sensitivity. There are few medical personnel with support of nursing and other healthcare workers. The team at these centres will function under leadership of in-charge/director of hospital and will comprise of physician, surgeon, nursing in-charge and pharmacist. 4-5 such hospitals can be linked together under a single leadership from regional or Atoll Hospital.

3.5.2 AMSP documents

All centres should develop their own empirical antimicrobial treatment guidelines, list of restricted antibiotics for outpatients, audit forms of outpatient antibiotic use and syndromic treatment guidelines. 5.20 Annexure T gives common syndromes for which specific guidelines and interventions should be developed.

3.5.3 Interventions

Prescribers can implement at least one of the following actions to improve antibiotic prescribing:

- **Use evidence-based diagnostic criteria and treatment recommendations**: When possible, these criteria and recommendations should be based on national or local clinical practice guidelines informed by local pathogen susceptibilities.
- **Use delayed prescribing practices or watchful waiting, when appropriate**: Delayed prescribing can be used for patients with conditions that usually resolve without treatment but who can benefit from antibiotics if the conditions do not improve (e.g., acute

- Patients also should be informed that certain bacterial infections (e.g., mild ear and sinus infections) might improve without antibiotics. Also it is important to provide recommendations for when to seek medical care if patients worsen or do not improve.
- Educate patients about the potential harms such as nausea, abdominal pain, diarrhea, *C. difficile* infection, allergic reactions, and other serious reactions of antibiotic treatment.

SECTION 4. WAY FORWARD AND RECOMMENDATION

Training modules are a must for prescribers and other staff engaged in antimicrobial stewardship programs. Such toolkit or case based modules must be created for training of trainers which can be used as an educational intervention in AMSP, sample collection and transport techniques, surveillance of healthcare associated infections and principles of infection control.

It is recommended that each organisation draw up a local antimicrobial stewardship policy and develop local antimicrobial guidelines based on national guidance.

Infection control and antimicrobial resistance are two sides of same coin. Effective control of AMR requires rigorous infection control practices. In order to train healthcare workers, it is important to form consensus guidelines and training modules in surveillance of healthcare associated infections and principles of infection control.

Laboratory strengthening is backbone of any good AMSP. Rapid quality assured reports are mandatory to run a stewardship program. Hence it is recommended to designate a Microbiology reference laboratory and develop Standard Operating Procedures for bacterial identification and Antibiotic sensitivity testing.

Considering the unique geographical profile of Maldives, it is recommended to create training modules which can be used for online training and certification.

SECTION 5. ANNEXURES

5.1 ANNEXURE A: SITUATION ASSESSMENT OF HOSPITAL

SITUATION ASSESSMENT OF HOSPITAL

1. Name of the hospital:
2. Bed Strength of Hospital:
3. Type of Hospital: Tertiary ☐ Regional ☐
   Atoll ☐ Island ☐
4. Administrative Head of the Hospital:
5. Governance: Private ☐ Public ☐ Combined ☐
6. Occupancy index (2017):
7. OPD Attendance (2017):
8. Number of doctors (Full time):
9. Number of doctors (Part Time):
10. Number of nurses:
11. Broad Specialty/Super specialty available in the hospital:
    Tick as applicable

☐	Medicine	☐	Otorhinolaryngology
☐	Psychiatry	☐	Microbiology
☐	Pathology	☐	Maternity
☐	Surgery	☐	Anaesthesia
☐	Ophthalmology	☐	Immunology
☐	Biochemistry	☐	Respiratory disease
☐	Paediatrics	☐	Gynaecology
☐	Radiology	☐	Obstetrics
☐	Cardiology	☐	Paediatric Surgery

Others please specify:

12. Are any of the following available in the hospital?
Indicate names of persons willing to be part of AMSP team.

Infectious disease specialist	
Microbiologists	
Infection control nurse	
ID Physician	
Pharmacist	
Junior doctor representative	
Data analyst/IT representative	
Primary/secondary care representative	

13. In case any of the above not available, is the hospital willing to hire them? Yes No
14. Number of ICUs: 15. Beds in each ICU:
16. Total ICU bed Strength:
17. Is there a formulary to dispense antibiotics in hospital?
Yes No
18. Is a pharmacist available in hospital? Yes No
If yes, how many?
19. Does hospital have an ID specialist? Yes No
20. Is there a drugs and therapeutics committee available in the hospital?
Yes No *If yes, go to section B*
21. Is there a hospital infection control committee in the hospital?
Yes No *If yes, then go to Section C*
22. Is there a functional microbiology department?
Yes No *If yes go to section D*
23. How are all OPD and IPD prescriptions dispensed in the hospital?
Manual Electronic Printed
24. Are all prescriptions available online for review? Yes No
25. Are there any points of care tests available in the hospital round the clock (e.g. Procalcitonin assay, CRP, Direct Microscopy of samples etc.)?
Yes No

5.2 ANNEXURE B: ASSESSMENT OF INFECTION CONTROL PRACTICES

SITUATION ASSESSMENT OF INFECTION CONTROL PRACTICES

1. Is there a hospital Infection Prevention and Control Committee (HICC)?

If no: skip to Section B: Assessment of antimicrobial stewardship program

Yes ☐ No ☐

2. Who is the in charge of HICC?

3. How frequently does HICC meet?

4. Total number of members in HICC

5. Do you have Hospital infection control nurses in your institution?

Yes ☐ No ☐ If yes, number of HICNs in your hospital ☐

6. Do you have hospital Infection control and prevention coordinators in your hospital?

Yes ☐ No ☐

7. Any training organized for infection control / hand hygiene compliance / biomedical waste management rules?

If Yes; which group of healthcare workers have been trained?

Doctors ☐ Nurses ☐ Workers ☐

8. Do you measure any of the following: (if yes, enclose data)?

MRSA rates ☐ *C. difficile* colonization/infection rates ☐ CRE/ESBL rates ☐

9. Does hospital conduct surveillance for healthcare-associated infections?

Yes ☐ No ☐

If yes, which HAIs? VAP ☐ SSI ☐ CAUTI ☐ CABSI ☐

10. What is the mechanism of sharing this data in your institute?

Electronic ☐ Printed ☐ Any other:

5.3 ANNEXURE C: ASSESSMENT OF ANTIMICROBIAL STEWARDSHIP PROGRAM

(Please enclose relevant documents to support s no. 1-37 wherever applicable)

SITUATION ASSESSMENT OF ANTIMICROBIAL STEWARDSHIP PROGRAM

1. Is there any AMSP in the hospital?

Yes ☐ No ☐ If No, this is the end of the assessment.

2. Has the hospital a formal written statement, from leadership, that supports the antibiotic stewardship program?

Yes ☐ No ☐

3. Is there a medical doctor responsible for the antibiotic stewardship program?

Yes ☐ No ☐

4. Do you have AMSP team available in your hospital?

Yes ☐ No ☐

If Yes; is any of the staff below involved in the antibiotic stewardship program?

Medical Doctors ☐

Infection's Prevention and Control Team ☐

Quality and Management ☐

Microbiology ☐

Pharmacy ☐

Informatics Systems ☐

Nurses ☐

5. Does hospital have an antibiotic policy? Yes ☐ No ☐

If Yes, How frequently is it updated? ☐

6. Is there a policy that requires prescribers to document the dose, duration,

and indication for all antibiotic prescriptions? Yes ☐ No ☐

7. Are there recommendations, based on national guidelines and local susceptibility, to assist antibiotic prescription on common clinical conditions?

Yes ☐ No ☐

8. Is there a formal procedure to review the appropriateness of all antibiotics

48 hours? Yes ☐ No ☐

9. Do specified antibiotic agents need to be approved by the leader (medical

doctor) prior to dispensing? Yes ☐ No ☐

10. Does the leader (medical doctor) participate on review courses of therapy for specified antibiotic agents? Yes ☐ No ☐

11. Are there specific interventions in place to ensure optimal use of antibiotics to treat the following infections?

Community-acquired pneumonia ☐

Urinary tract infection ☐

Skin and soft tissue infections ☐

Surgical prophylaxis ☐

Empiric treatment of methicillin-resistant Staphylococcus aureus ☐

Clostridium difficile infections ☐

Culture-proven invasive infections ☐

12. Are there automatic changes from intravenous to oral antibiotic therapy in appropriate situations? Yes ☐ No ☐

13. Are there dose adjustments in cases of organ dysfunction?

Yes ☐ No ☐

14. Are there dose optimizations (pharmacokinetics/pharmacodynamics) to optimize the treatment of organisms with reduced susceptibility?

Yes ☐ No ☐

15. Are there automatic alerts in situations where therapy might be unnecessarily duplicative? Yes ☐ No ☐

16. Are there time-sensitive automatic stop orders for specified antibiotic prescriptions? Yes ☐ No ☐

17. Does the Pharmacy participate in ward meetings?

Yes ☐ No ☐

18. Does the hospital monitor the adherence to antibiotic use policies (dose, duration and indication)? Yes ☐ No ☐

18. Does the hospital monitor the adherence to facility-specific treatment recommendations? Yes ☐ No ☐

19. Does the hospital monitor the compliance of the specific interventions in place? Yes ☐ No ☐

20. Do you have online prescription system in your hospital?

Yes ☐ No ☐

21. Do you conduct antibiotic prescription audit in your hospital?

Yes ☐ No ☐

22. Do you conduct antibiotic consumption studies in your hospital?

Yes ☐ No ☐

23. Do you have restricted antibiotic usage policy in your hospital?

Yes ☐ No ☐

If Yes, please elaborate how?

24. Do you have antibiotic de-escalation policy in your hospital?

Yes ☐ No ☐

25. Does the hospital track rates of C. difficile infection?

Yes ☐ No ☐

26. Does the hospital produce an annual antibiogram report?

Yes ☐ No ☐

27. Does the hospital monitor antibiotic consumption at the unit/hospital?

Yes ☐ No ☐

Is yes; which by which of the following metrics:

☐ By counts of antibiotic(s) administered to patients per day (Days of Therapy; DOT)?

☐ By number of grams of antibiotics used (Defined Daily Dose, DDD)?

☐ By direct expenditure for antibiotics (purchasing costs)?

28. Does the antibiotic stewardship program share facility-specific reports on antibiotic use with prescribers? Yes ☐ No ☐

29. Has a current antibiogram been distributed to the prescribers?

Yes ☐ No ☐

30. Do prescribers receive direct and personalized communication about how they can improve antibiotic prescription?

Yes ☐ No ☐

31. Does the antibiotic stewardship program provide education to clinicians and other relevant staff on improving antibiotic prescription?

Yes ☐ No ☐

If yes; how often is it done;

32. Does the hospital have any compliance checklists to check for compliance to any of the following?

- ☐ Surgical prophylaxis guidelines
- ☐ Antibiotic prescription guidelines
- ☐ Infection control practices guidelines
- ☐ Hand hygiene compliance by healthcare workers

5.4 ANNEXURE D: ASSESSMENT OF MICROBIOLOGY LABORATORY

SITUATION ASSESSMENT OF MICROBIOLOGY LABORATORY

1. Number of Microbiologists
2. Number of laboratory technicians
3. Number of bacterial cultures/sensitivity received in 2017
4. Any accreditation available for any test in the laboratory?

   Yes No
5. Methods of conducting routine microbiologic culture:

   Manual Automated
6. Methods of routinely performing identification of clinical isolates:

   Manual Automated
7. Routine internal quality control mechanisms for culture media, reagents in place: Yes No
8. Does lab participate in external quality assurance for microbiology?

   Yes No If yes, which one;
9. Does lab utilize a SOP for Antibiotic sensitivity testing (AST)?

   Yes No If standard SOP, then specify;
10. Methods of routinely performing AST for clinical isolates (Specify each that applies)

    Disc diffusion

    MIC by Micro broth dilution

    MIC by automated gradient systems
11. Do you use McFarland standards for all AST?

    Yes No
12. Which standard guidelines are followed in AST? CLSI/ CLSI EUCAST

5.5 ANNEXURE E: Documents to be included from the respective hospital

1) Hospital antibiotic policy
2) AMSP document
3) HAI surveillance data for 2017
4) AMR data 2017
5) Prescribing guidelines if any
6) Antibiotic consumption data
7) Any other (specify)

5.6 ANNEXURE F: Principles of rational prescription

(Adapted from UK Specialist Advisory Committee on Antimicrobial Resistance (SACAR)[26].

- Do NOT use antimicrobials
    - To treat colonization or contamination unless there is clear indication such as immunosuppression or post splenectomy.
    - As general prophylaxis or "Feel good" factor.
    - To treat infections which have high suspicion of viral causes such as influenza
- Use Antimicrobials only
    - In cases of high degree of suspicion of infection.
    - After a treatable infection has been recognized
    - Prevention of infection where evidence has demonstrated that the potential benefits outweigh the risks.
- Empirical therapy must be based on local/national prescribing guidelines formed by recent information about trends in antimicrobial sensitivities.
- Use targeted therapy instead of broad-spectrum antimicrobials unless there is a clear clinical reason (for example, mixed infections or life-threatening sepsis).
- Review broad spectrum antimicrobials as early as possible and promptly switch to narrow spectrum agents when sensitivity results

become available. Choose antibiotics as determined by the sensitivity of identified causative organism.

- The timing, regimen, dose, route of administration and duration of antimicrobial therapy should be optimised and documented. The indication for which the patient is being prescribed the antimicrobials should be documented in the drug chart and case notes by the prescriber.
- Prefer oral antimicrobials then intravenous. Clear criteria should be defined for when intravenous therapy is appropriate.
- Always review intravenous prescription after 48 hours at least and switch to oral if possible.
- Always have a stop/review date on antibiotic order form/patient chart. No antibiotic should be written for indefinite time.
- Ensure that the patient receives antibiotics in correct dosage in correct form for correct duration.

5.7 ANNEXURE G: principles of surgical prophylaxis

The following recommendations are related to surgical prophylaxis guidelines (Adapted from Bratzler et al)[27]:

Optimum surgical antibiotic prophylaxis is a high-impact intervention, and it is a good starting point for institutions beginning an antimicrobial stewardship program. Improvements in delivery of antibiotic prophylaxis may reduce the incidence of surgical site infections, lowering patient morbidity, mortality and costs.

Selection of antimicrobial agent for surgical prophylaxis should be based upon following criteria:

1. Characteristics of the ideal agent
2. The comparative efficacy of the antimicrobial agent for the procedure

3. The safety profile
4. The patient's medication allergies
5. Adequate serum levels achieved during whole procedure with good post antibiotic effect.

Choice of drug

- A single dose of antibiotic with a long enough half-life to achieve activity throughout the operation is recommended.
- Usually, a single first-generation cephalosporin for operations not expected to encounter anaerobes or a single second-generation cephalosporin with anaerobic operations based on local susceptibility patterns is sufficient.
- For clean operations on the skin and subcutaneous tissues that do not involve any portion of the gastrointestinal tract, a semi synthetic penicillin resistant to penicillinases, such as oxacillin or cloxacillin, is probably effective.
- Administration of antibiotics that are active against enteric anaerobes for procedures involving the lower gastrointestinal tract should be considered routine.
- Procedures on the upper gastrointestinal tract should involve use of antibiotics with activity against Gram-positive cocci and common Gram-negative organisms but which are not active against anaerobes.
- Procedures that do not enter any portion of the intestinal or genitourinary tract are sufficiently covered with antibiotics that are primarily active against Gram-Positive cocci.
- β-Lactam allergies are often cited as a contraindication for antibiotic prophylaxis

- For operations in which the risk is primarily from skin organism's vancomycin or teicoplanin is a common choice for patients allergic to β-Lactam. If local susceptibility patterns are favourable, clindamycin can be used.
- First-generation cephalosporins are the most commonly used agents for prophylaxis in caesarean section. Concern about neonatal exposure to antibiotics and the effect on neonatal sepsis have led to delays in administering antibiotics until after the umbilical cord has been clamped. In caesarean section procedures, antimicrobial prophylaxis should be administered before skin incision.
- Prophylactic antibiotic is solely given for prevention of infections following surgery and are not recommended for UTI or respiratory tract infection following surgery.

Timing

- Antimicrobial therapy should be initiated within the 30 minutes prior to surgical incision to optimize adequate drug tissue levels at the time of initial incision. The half-life of the antibiotic should be considered: administration of Vancomycin or a fluoroquinolone should begin within 120 minutes before surgical incision because of the prolonged infusion times requires for these drugs

Dose and duration

- For surgeries less than 4hrs: Single dose
- For surgeries greater then 4hrs: 2-3 doses
- For open heart surgeries: duration of prophylaxis should not be more than 48 hours.
- In general, repeat antimicrobial dosing following wound closure is not necessary and may increase the risk for the development of antimicrobial resistance

5.8 ANNEXURE H: Ready Reckoner for Surgical Prophylaxis in common surgeries

(based on ASHP, IDSA and SHEA report 2013)[27]

Surgical Procedure	1st Line agents	Alternative Agents in Patients With βLactam Allergy
Colorectal	Cefazolin + metronidazole, cefoxitin/ cefotetan/ ampicillin sulbactam/ceftriaxone + metronidazole, ertapenem	Clindamycin + aminoglycosideg or aztreonam or fluoroquinolone, metronidazole + aminoglycoside or fluoroquinolone
Gynaecology surgery	Cefazolin/ cefotetan/ cefoxitin/ ampicillin–sulbactamh	Clindamycin or vancomycin + aminoglycoside or aztreonam or fluoroquinolone Metronidazole + aminoglycoside or fluoroquinolone
Laparoscopic procedure		
Elective, low-risk	None	None
Elective, high-risk	Cefazolin/cefoxitin/ cefotetan/ ceftriaxone/ampicillin–sulbactam	Clindamycin or vancomycin + aminoglycoside or aztreonam or fluoroquinolone/Metronidazole + aminoglycoside or fluoroquinolone
Urologic Procedures		
Lower tract instrumentation with risk factors for infection (includes trans rectal prostate biopsy	Fluoroquinolone/ trimethoprim Sulfamethoxazole/cefazolin	Aminoglycoside with or without clindamycin
Clean with entry into urinary tract	Cefazolin	Aminoglycoside or aztreonam Fluoroquinolone, aminoglycoside with or without clindamycin
Clean contaminated	Cefazolin + metronidazole, cefoxitin	Fluoroquinolone, aminoglycoside + metronidazole or clindamycin
Vascular and cardiac surgery	Cefazolin	Clindamycin/ vancomycin
Total joint replacement	Cefazolin	Clindamycin, vancomycin

5.9 ANNEXURE I: Guide for developing antimicrobial prescribing guidelines

(Adapted from SACAR[24])

Antimicrobial guidelines should be evidence-based and prepared in line with best practice recommendations for treatment guidelines. The provision of costing information within the guideline should be discussed locally.

The guidelines must be prepared by a multidisciplinary team comprising of members from various departments. The guidelines must mention whether the guideline is mandatory or for guidance only. It should provide guidance on the local procedure for microbiological samples.

Wherever feasible, reference should be made to relevant national or international guidelines.

Choice of therapy is based on:

- The site of infection.
- Common pathogens encountered.
- Local epidemiology and resistance patterns.
- Evidence and clinician consensus.
- Antimicrobial stewardship principles.
- Formulary availability.
- Antimicrobial costs

There are mainly three types of antibiotic treatment regimens:

Prophylactic Therapy: Treatment given to prevent an infection that has not yet developed.

Empiric Therapy: Patients who have a proven or suspected infection, but the responsible organism(s) have or have not yet been identified.

Definitive Therapy: After culture and sensitivity results are known, the definitive therapy phase of treatment can begin.

The antimicrobials that are recommended in the guidelines should be listed, with clear indications to the route of administration and should state whether they are:

- Unrestricted
- Restricted (approval of a specialist is required)
- Permitted for specific conditions (for example, co-trimoxazole for Pneumocystis)

The guidelines must be reviewed regularly and changes done as per prevalent antibiogram and evidence. Empiric prescribing guidelines are appropriate for most patients, but they do not replace clinical judgment. It is recommended that, as minimum, guidelines for treatment or prophylaxis should be made available for the conditions listed below.

Specific treatment guidelines should cover the following:

- Urinary tract infections
- Upper respiratory tract infections
- Lower respiratory tract infections, including, community and health-care associated pneumonia and exacerbations of chronic obstructive pulmonary disease
- Soft tissue infections including injuries or bites, cellulitis, chronic ulcers and necrotising fasciitis
- Central nervous system infections: bacterial meningitis, viral encephalitis
- Gastro-intestinal infections: food poisoning and intra-abdominal sepsis
- Genital tract infections
- Blood stream infections
- Eye, ear, nose and throat infections
- Sepsis of unknown origin

- Specific confirmed infections: for example, treatment regimens for MRSA, *C. difficile* and tuberculosis
- Endocarditis

For treatment, guidelines must clearly mention first-line recommendation followed by second line recommendation, timing, dose, route of administration, duration of treatment, rules for parenteral to oral switch.

Prophylaxis

- Prevention of bacterial endocarditis (procedure-specific criteria should be agreed to identify which patients should receive prophylaxis)
- Endoscopic procedures (details should be given of which individuals, considered at high risk, should receive prophylaxis (for example neutropenic patients))
- Surgical prophylaxis (recommendations should be made for all common surgical interventions including timing of initial dose and exceptional circumstances for repeat doses)
- Splenectomy patients (provide details of both the immunization and antimicrobial prophylaxis requirements)
- Patients with immunosuppression such as neutropenic/on steroids/anticancer drugs/post-transplant

For prophylaxis, guidelines must clearly mention first-line recommendation followed by second line recommendation for empirical therapy, dose, timing of initial dose, route of administration and details/indications of repeat dosing if required.

5.10 ANNEXURE J: Sample empirical antimicrobial prescribing guidelines for few common infections

(Adapted from: NHS Foundation Trust. Empirical antibiotic guidelines for the management of common infections in adult inpatients 2018)[28].

Syndrome	1st Line	Alternate/2nd Line
Septicaemia (unknown source)	Piperacillin/ tazobactam 4.5g IV TDS + Gentamicin 5mg/kg IV stat	Ciprofloxacin 400mg IV BD + Teicoplanin 400mg IV BD for 3 doses then 400mg IV OD + Gentamicin 5mg/kg IV stat
Mild CAP (CURB-65 score 0 - 1) for 57 days	Amoxicillin 500mg PO	Clarithromycin 500mg PO BD
Moderate CAP (CURB-65 score 2) for 7-10 days	Amoxicillin 500mg - 1g PO TDS + Clarithromycin 500mg PO BD	Clarithromycin 500mg PO BD
Severe CAP (CURB -65 score ≥ 3) for 10-14 days Switch to oral as per policy	Co-amoxiclav 1.2g IV TDS + Clarithromycin 500mg PO/IV BD	Teicoplanin 400mg IV BD for 3 doses then 400mg OD + Clarithromycin 500mg IV/PO BD
Hospital acquired pneumonia (HAP) for 5-7 days	1st line: Piperacillin/ tazobactam 4.5g IV TDS	Teicoplanin 400mg IV BD for 3 doses, then 400mg IV OD + Gentamicin 5mg/kg IV OD
Infective exacerbation of COPD	Doxycycline 100mg PO BD for 7 days	If intolerant to tetracyclines, amoxicillin can be used
Uncomplicated, Lower UTI	Nitrofurantoin 100mg PO QDS for 3 days for women, 7 days for men	Trimethoprim 200mg BD for 3 days (men 7 days)
Complicated UTI & Pyelonephritis	Gentamicin 5mg/kg IV OD	

Meningitis	Ceftriaxone 2g IV BD for 714 days	Chloramphenicol 1g IV QDS for 714 days
Intra-abdominal infections	Cefazolin 2 g IV q8h + Metronidazole 500 mg PO/IV q12h	Ciprofloxacin750 mg PO BID or 400 mg IV q12h + Metronidazole500 mg PO/IV q12h

Anti-pseudomonas antibiotics: Piperacillin-tazobactum, Ceftazidime, Cefepime, aztreonam, imipenem, Meropenem, doripenem, ertapenem, gentamicin, tobramycin, ciprofloxacin, levofloxacin.

Anaerobic Coverage: Imipenem, Meropenem, doripenem, ertapenem, Metronidazole, ampicillin sulbactum, Moxifloxacin, Tigecycline, Clindamycin, Piperacillin –Tazobactam and Cefotetan provide coverage against anaerobic organism and will such patients will not require additional anaerobic cover. Anaerobes here include GI anaerobes except *Clostridium difficile*, for which the only antibiotics with good clinical activity on this list are vancomycin and metronidazole.

ANTIBIOTIC	MSSA	MRSA	Enterococci	Streptococci	GNB
Penicillin G			+	++	
Ampicillin			++	++	+
Ampicillinsulbactum	++			++	+
Piperacillin-Tazobactum	++		++	++	++
Cefazolin	++			++	+
Cefuroxime	+			+	++
Cefotetan	+			+	++

Ceftriaxone	+			++	++
Cefepime	+			++	++
Ceftaroline	++	++		++	++
Imipenem/ Meropen**em/ doripenem/**ertap**enem**	++		+	++	++
Gentamicin / Tobram**ycin**	Synergistic	-	Synergistic	Synergistic	++
Ciprofloxacin	+/-				++
Levofloxacin	++		+/-	++	++
Moxifloxacin	++		+/-	++	++
Doxycycline	+	+/-	+/-	+	+
Tigecycline	++	++	++	++	++
Clindamycin	++	+		++	
Vancomycin	++	++	++	++	
Azithromycin	+/-			+	+
Linezolid	++	++	++	++	
Quinopristin / Dalfop**ristin**	++	++	++	++	
Cotrimoxazole	++	+		+/-	
Daptomycin	++	++	++	++	

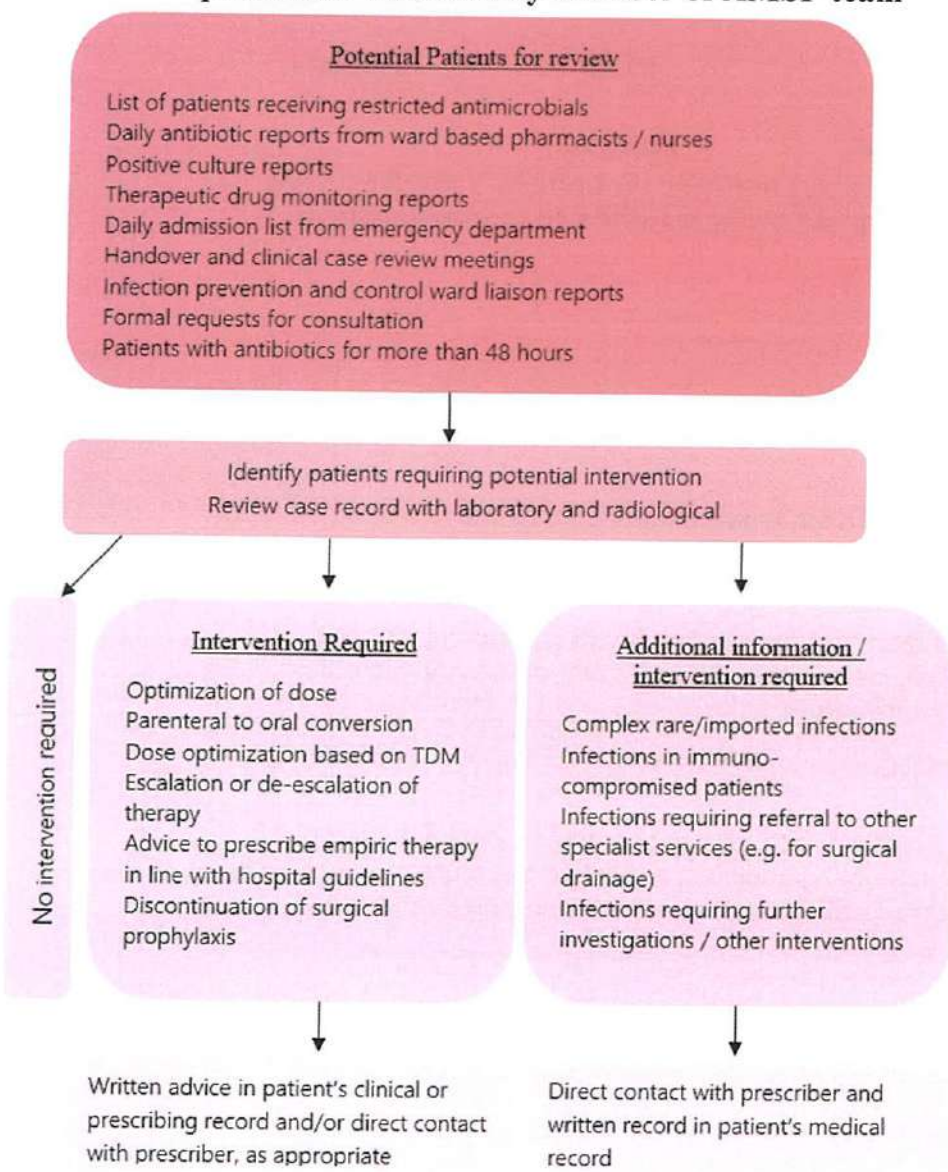
Key:

MSSA: Methicillin sensitive *Staphylococcus aureus*,

MRSA: Methicillin resistant *Staphylococcus aureus*,

GNB: Gram Negative Bacteria

5.11 ANNEXURE K: Flow chart for patient review and prescriber feedback by member of AMSP team



5.12 ANNEXURE L: Format of Standard Antibiotic Review Form

Patient name:		ID no:		Location:	
Date:	Time:		Allergies:		

This patient's antimicrobial therapy has been reviewed by a member of the AMSP Team and the advice given below is suggested to provide optimal antimicrobial therapy:

Rationale/supporting evidence for above recommendations*:

These recommendations are not mandatory. If you wish to discuss the recommendations further, please contact a member of the Antimicrobial Stewardship Team (contact details below)

Reviewer name	Signature	Contact no:

*Rationale may include reference to relevant section in local antimicrobial prescribing guidelines, national guidelines, published literature, websites etc. Retain one copy in the medical/prescribing record and one by the AMSP team

5.13 ANNEXURE M: Format of Preauthorization form for restricted antimicrobials

Name :		Weight:		Height:	
Hospital ID no:		Ward/Unit/Bed no:			
Clinical indication for antimicrobial therapy :					
Microbiology culture results, *if available* ;					
Drug allergies and side effects to previous antimicrobials :					
Renal and hepatic function status :					
Restricted agent asked for					
Recommendation of AMSP team:			Dose:		Duration:
Yes		No			
If No then alternate agent suggested:					
Signature :		Contact details :			

5.14 ANNEXURE N: Format for information card for all restricted antimicrobials requests

Patient's name:		ID no:		Location:	
AMSP team member's name, designation and contact number					
Prescribing consultant's name and designation					
Reason for calling					
If for pre-authorization, reason for authorization					
Recommendations given					
Rationale for recommendations given					
Contact details				Signature	

5.15 ANNEXURE O: Parenteral to oral conversion order

<table>
<tr><td colspan="3">The patient name:_____ of ward/unit/bed no._____
Is being given antibiotic(s)_____
for past _____ days. By chart review the patient is tolerating an oral diet/tube feeding, or oral medication, and does not have any identifiable contraindications to oral antimicrobial therapy.</td></tr>
<tr><td colspan="3">The antimicrobial stewardship team recommends converting the above agent to:</td></tr>
<tr><td>Oral agent</td><td>Dose</td><td>Duration</td></tr>
<tr><td colspan="3">Kindly Contact for any clarification</td></tr>
<tr><td>Date</td><td>Signature</td><td>Contact no</td></tr>
</table>

5.15 ANNEXURE O: Parenteral to oral conversion order

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<tr><td colspan="3">Kindly Contact for any clarification</td></tr>
<tr><td>Date</td><td>Signature</td><td>Contact no</td></tr>
</table>

5.16 ANNEXURE P: Sample restrictive AST reporting form

Patient ID no;	Lab no.	Sample	
Name:	Age/Sex	OPD/Ward/ICU/Clinic	
Direct microscopy:			
Organism isolated:		MRSA/VRE/HL GR/ESBL/CRE*	
1st line Antibiotic	Sensitive/Intermediate/ Resistance Or MIC	2nd line Antibiotic	Sensitive/ Intermediate/ Resistance or MIC
Penicillin/Ampicillin/ Amoxycillin /piperacillin		Linezolid	
Amoxy-clavulanate/ piperacillin-Tazobactum/ Piperacillin Sulbactum		Vancomyci/ Teicoplanin	
Cefazolin/ Cephalexin/ Ceftriaxone/ Cefexime/ Ceftazidime		Meropenem/ Imepenem	
Erythromycin/azithromycin/ Clindamiycin/Lincomycin		Colistin/ Polymyxi B	
Gentamicin/Tobramycin/ Amikacin		Tigecycline	
Ciprofloxacin/norfloxacin/ oflacin/levofloxacin		Aztreonam	
Tetracycline			
Chloramphenicol			

Note: ^ ***will be given only on demand or in exceptional circumstances as discussed with clinician.***

****MRSA; Methicillin resistant Staphylococcus aureus, HLGR: High level gentamicin resistant, VRE: Vancomycin resistant enterococci, ESBL: extended spectrum beta lactamase, CRE: carbapenems resistant enterobacteriacae***

- Organism isolated is part of normal flora at site of infection/skin. Kindly correlate clinically before prescribing antibiotics.
- Interpretive criteria of susceptibility based on standard dosing in a patient with normal renal function tests and in absence of co-morbidities.
- **Inducible clindamycin resistance**: present (antibiotic therapy may fail clinically)/ absent/ not applicable.

- **Enterococci:** combination therapy with vancomycin/penicillin with aminoglycoside recommended for life threatening infections. However with HLGR present, this combination therapy may be clinically ineffective.
- If clinical evidence of infection or bacteraemia present then please contact to discuss options for therapy. Antibiotic susceptibilities are available if clinical assessment suggests infection in following situations:
    - **Urine:** The urine of patients with indwelling catheters frequently becomes colonised. Unless the patient becomes systemically unwell, treatment is not indicated
    - **Sputum:** Antibiotic therapy may be indicated if clinical or radiological evidence of lower respiratory tract infection present. Otherwise this probably represents upper airways colonisation, for which antibiotic therapy is not required.
    - **Pus Swab:** If cellulitis or deep-seated infection, antibiotic therapy may be indicated. Otherwise this represents colonisation, and likely to respond to topical antiseptic therapy alone.

Date: _____

Reported by: Signature

5.17 ANNEXURE Q: Suggested antimicrobial panel for pathogens under surveillance

The list can be expanded later to include other organisms such as *Streptococcus pneumoniae, Shigella species* and *Neisseria gonorrhoeae* as per the GLASS panel.

Suggested Guidelines for organisms inclusion in AMR Surveillance		
Clinical specimen	**Laboratory Case definition**	**Priority pathogens for surveillance**
Blood	Isolation of pathogen from blood	Enterococcus species *Staphylococcus aureus* *Escherichia coli* Klebsiella species Acinetobacter species Pseudomonas species Salmonella enterica Typhi Salmonella enterica Paratyphi
Urine	Clinically significant growth in urine specimen[1]	Enterococcus species *Escherichia coli* Klebsiella species
Pus Aspirate	Significant growth from aspiration of purulent material from a closed infected site	Enterococcus species *Staphylococcus aureus* *Escherichia coli* Klebsiella species
Other Sterile Body Fluid (CSF, pleural fluid, peritoneal fluid, synovial fluid, pericardial fluid)	Significant growth from a sterile body fluid specimens	Enterococcus species *Staphylococcus aureus* *Escherichia coli* Klebsiella species Acinetobacter species Pseudomonas species
Stool	Isolation of pathogen from stool	Salmonella enterica Typhi Salmonella enterica Paratyphi

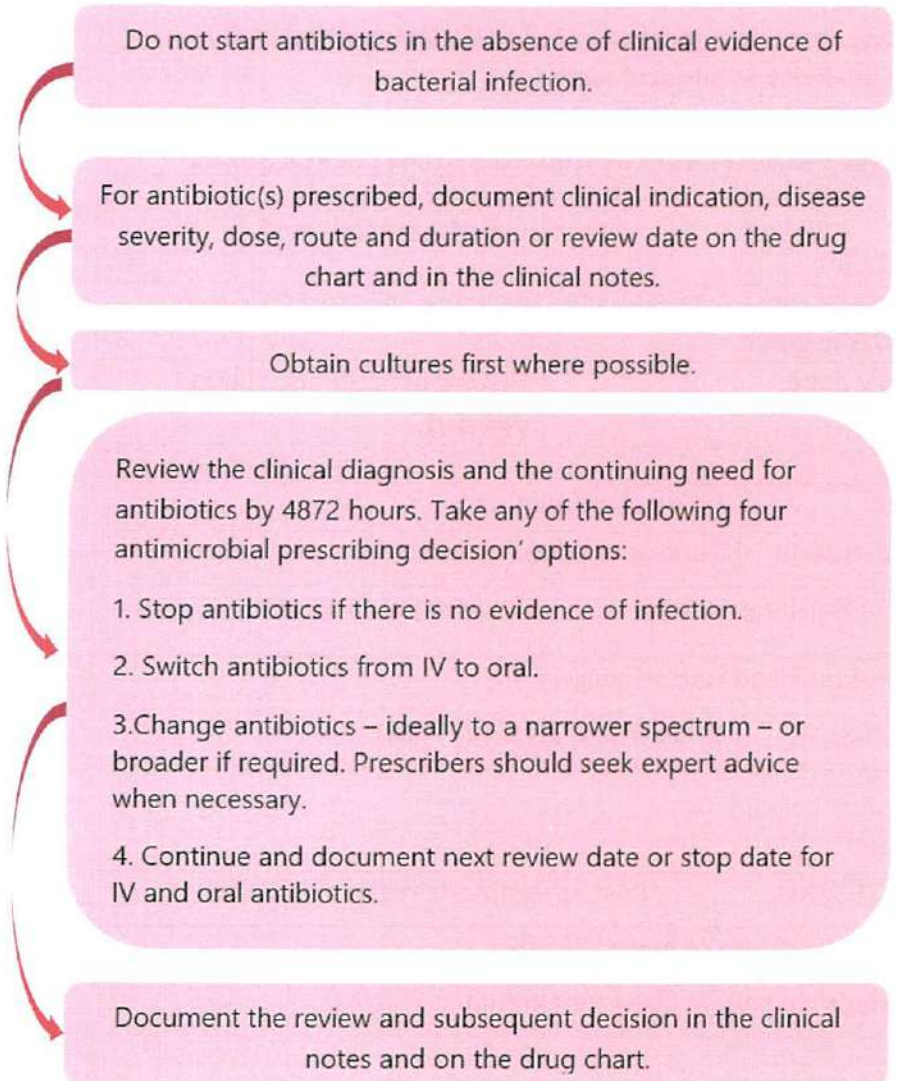
*Colistin testing for MIC by Microbroth dilution only, Cotrimoxazole: Trimethoprimsulphamethoxazole

[1] Pure culture according to local laboratory practice. Catheter samples should be excluded if possible

Organism	*Staphylococcus aureus*	Enterococcus species	Enterococcus species
Site	Blood, pus aspirate, other sterile body fluids	Blood, pus aspirate, other sterile body fluids	Urine
Antimicrobial agent with strength	Cefoxitin (30µg)	Ampicillin (10µg)	Ampicillin(10 µg)
	Erythromycin(15 µg)	Erythromycin (15µg)	Tetracycline(30 µg)
	Ciprofloxacin(5 µg)	Ciprofloxacin(5 µg)	Ciprofloxacin 5 µg
	Gentamicin(10µg)	Gentamicin (120µg)	Gentamicin (120 µg)
	Vancomycin screen agar	Vancomycin screen agar	Vancomycin screen agar
	Linezolid(30 µg)	Linezolid(30 µg)	Linezolid (30 µg)
	Doxycycline(30 µg)		
	Clindamycin (2 µg)		
	Cotrimoxazole (1.25/23.75 µg)		

Suggested panel of antimicrobials (disc strength) for Gram negative organisms to be included in AMR surveillance				
Organism	*Escherichia coli* *Klebsiella species*	*Acinetobacter* species	*Salmonella enterica* Serotypes Typhi and Paratyphi	*Pseudomonas* species
Site	Blood, urine, pus aspirate, other sterile body fluids	Blood, pus aspirate, other sterile body fluids	Blood, stool	Blood, pus aspirate, other sterile body fluids
Antimicrobial with strength	Ampicillin(10µg)	Piperacillin-tazobactam (100/10 µg)	Ampicillin(10 µg)	Piperacillin-tazobactam (100/10 µg)
	Cotrimoxazole(1.25 /23.75 µg)			
	Cefotaxime(30µg)	Ertapenem/Mero pe nem(10µg)	Chloramphen icol(30µg)	Ceftazidime(10 µg)
	Cefepime(30µg)	Amikacin(30µg)	Ceftriaxone(30µg)	Amikacin(30µg)
	Ertapenem(10µg)	Imipenem(10µg)	Nalidixic acid(30µg)	Imipenem(10µg)
	Ciprofloxacin(5µg)	Ciprofloxacin(5µg)	Ciprofloxacin (5µg)	Ciprofloxacin(5 µg)
	Cotrimoxazole (1.25/23.75µg)	Minocycline(30µg)	Cotrimoxazol e (1.25/23.75µ g)	Tobramycin(10 µg)
	Nitrofurantoin 300µg (E.coli urine isolates only)	Gentamicin(10µg)	Azithromycin(15µg)(only for S Typhi blood isolates)	Gentamicin(10µ g)
	Colistin*	Colistin	-	Colistin

5.18 ANNEXURE R: Steps to antimicrobial prescribing



5.19 ANNEXURE S: Audit forms

Can be carried out as point prevalence survey or the audit sheet can be attached with patient case sheet. It is recommended to do short period audits at regular interval with feedback to surgical team.

<table>
<tr><th colspan="6">FORM M1: SURGICAL PROPHYLAXIS GUIDELINES COMPLIANCE SHEET</th></tr>
<tr><td colspan="2">Patient ID no:</td><td>Age:</td><td>Patient weight:</td><td colspan="2">Type of surgery: clean/clean contaminated/contaminated</td></tr>
<tr><td colspan="6">Surgical department: General surgery/Orthopedics/Pediatric surgery/ Gynecology/ Maternity/ ENT/Eye/ER/Any other:</td></tr>
<tr><td colspan="2">Date of surgery:</td><td colspan="2">Surgery done:</td><td colspan="2">History of antibiotic allergy:
YES/NO</td></tr>
<tr><td colspan="6">Name of antibiotic given:</td></tr>
<tr><td colspan="3">Dose of pre-op antibiotic:</td><td colspan="3">Route of antibiotic:</td></tr>
<tr><td colspan="3">Time of antibiotic administration:</td><td colspan="3">Time of incision:</td></tr>
<tr><td colspan="2">Time of start of surgery:</td><td colspan="2">Time of finishing surgery:</td><td colspan="2">Duration of surgery:</td></tr>
<tr><td colspan="6">Time between dose of antibiotic and start of surgery:</td></tr>
<tr><td colspan="3">Second dose indicated: YES/NO</td><td colspan="3">Second dose given: YES/NO</td></tr>
<tr><td colspan="6">Reasons for same:</td></tr>
<tr><td colspan="6">Post op antibiotic indicated:</td></tr>
<tr><td colspan="3">Post op antibiotic given: YES/NO</td><td colspan="3">Post op antibiotic regimen dose for ___</td></tr>
<tr><td colspan="6">Antibiotic prophylaxis continued for>24 hours: YES/NO</td></tr>
<tr><td colspan="6">Documentation as "once only" in patient chart for antibiotic: YES/NO</td></tr>
<tr><td colspan="6">Name of Surgeon:</td></tr>
<tr><td colspan="6">Name of Anesthetic:</td></tr>
<tr><td colspan="6">Antibiotic irrigation YES/NO If yes then name of antibiotic:</td></tr>
<tr><td colspan="6">Compliant with guidelines: YES/NO</td></tr>
<tr><td colspan="6">Reason for noncompliance:</td></tr>
<tr><td colspan="6">Date of audit:</td></tr>
<tr><td colspan="6">Signature of auditor:</td></tr>
</table>

FORM M2: ANTIBIOTIC STOP ORDER/REVIEW DECISION/ PRESCRIBER CHECKLIST		
Patient ID no:		**Department/Ward/OPD:**
Drug		
1	Is the antibiotic indicated?	YES/NO
2	Have the cultures been sent before staring antibiotic?	YES/NO
3	Are any Gram staining results available before starting antibiotic?	YES/NO
4	If yes have they been considered in selection of antibiotic?	YES/NO
5	Is it essential to give double or broad spectrum antibiotic?	YES/NO
Dose		
1	Is the appropriate for age/indication?	YES/NO
High		
Appropriate Low		
2	Is the dose adjusted for any co-morbidities such as renal or hepatic disorder?	YES/NO
Route		
1	Does the antibiotic have high bioavailability?	YES/NO
2	Is the route appropriate?	YES/NO
3	Is it possible to deescalate from iv to oral with this antibiotic?	YES/NO
Still needs IV		
Can tolerate oral Stable but not ready for oral route		
4	Is the dosing interval appropriate?	YES/NO
5	Has the dosing frequency adjusted for any co-morbidities such as renal or hepatic disorder?	YES/NO
Duration		
1	Is the duration of antibiotic appropriate for the indication?	YES/NO
2	Has the dosing duration specified in the prescription right from start?	YES/NO
Signature		Contact details

FORM M3: POINT PREVALENCE SURVEY FOR INDIVIDUAL PATIENT						
Patient ID:	Department:					
	Ward:					
Name of drug(S)						
Route						
Unit dose						
Dosage frequency						
Indication						
Complies with (local) guidance		YES		NO		
Cultures sent prior to start of therapy		YES		NO		
Concurrent use of >3 antibiotics		YES		NO		
Antibiotics continued for more than 7 days		YES		NO		
Dose & duration adjusted for comorbidity		YES		NO		
Concurrent double cover (anaerobic/GPC/GNB)		YES		NO		
Intravenous to oral switch done in 48 hours		YES		NO		
Date of survey:	Done by:					

FORM M4: POINT PREVALENCE SURVEY FOR TOTAL ANTIBIOTIC USE		
Department: **WARD:**	**Date of review:** **Done by:**	
Total no of patients on day of survey in ward:		
S. no.	Indicator	No. of patients
1.	Cultures sent prior to start of therapy	
2.	Concurrent use of >3 antibiotics	
3.	Patients with antibiotics continued for more than 7 days	
4.	Patients with antibiotics continued for more than 14 days	
5.	Patients on concurrent double cover (anaerobic/GPC/GNB)	
6.	Patients with intravenous to oral switch done in 48 hours	
7.	Patients on surgical prophylaxis>48hours	
8.	Complies with local/national guidance	

9.	Dose & duration adjusted for comorbidity	
Signature		Contact details

FORM M5: FEEDBACK FORM FOR PRECRIBER/TREATING FACILITY			
Department:		**WARD:**	**Period of review:**
Review Done by:		Total no of patients during period of review in ward:	
S. no.	Indicator	Proportion or percent of patients (as advised by Prescriber in charge of patient)	Proportion or percent of patients (as Advised by AMSP team)
1.	Cultures sent prior to start of therapy		
2.	Concurrent use of >3 antibiotics		
3.	Patients with antibiotics continued for more than 7 days		
4.	Patients with antibiotics continued for more than 14 days		
5.	Patients on concurrent double cover (anaerobic/GPC/GNB)		
6.	Patients with intravenous to oral switch done		
7.	Patients on surgical prophylaxis>48hours		
Signature of AMSP team leader			

9.	Dose & duration adjusted for comorbidity	
Signature		Contact details

FORM M5: FEEDBACK FORM FOR PRECRIBER/TREATING FACILITY			
Department:		**WARD:**	**Period of review:**
Review Done by:		Total no of patients during period of review in ward:	
S. no.	Indicator	Proportion or percent of patients (as advised by Prescriber in charge of patient)	Proportion or percent of patients (as Advised by AMSP team)
1.	Cultures sent prior to start of therapy		
2.	Concurrent use of >3 antibiotics		
3.	Patients with antibiotics continued for more than 7 days		
4.	Patients with antibiotics continued for more than 14 days		
5.	Patients on concurrent double cover (anaerobic/GPC/GNB)		
6.	Patients with intravenous to oral switch done		
7.	Patients on surgical prophylaxis>48hours		
Signature of AMSP team leader			

5.20 ANNEXURE T: Infection and syndrome specific interventions

Develop syndrome based specific interventions, clearly documenting the treatment options and criteria for prescribing antimicrobials.

Community-acquired pneumonia. Interventions for community-acquired pneumonia have focused on correcting recognized problems in therapy, including: improving diagnostic accuracy, tailoring of therapy to culture results and optimizing the duration of treatment to ensure compliance with guidelines.

Urinary tract infections (UTIs). Many patients who get antibiotics for UTIs actually have asymptomatic bacteriuria and not infections. Interventions for UTIs focus on avoiding unnecessary urine cultures and treatment of patients who are asymptomatic and ensuring that patients receive appropriate therapy based on local susceptibilities and for the recommended duration.

Skin and soft tissue infections. Interventions for skin and soft tissue infections have focused on ensuring patients do not get antibiotics with overly broad spectra and ensuring the correct duration of treatment

Empiric coverage of methicillin-resistant *Staphylococcus aureus* (MRSA) infections. In many cases, therapy for MRSA can be stopped if the patient does not have an MRSA infection or changed to a beta-lactam if the cause is methicillin-sensitive *Staphylococcus aureus*.

***Clostridium difficile* infections.** Treatment guidelines for Clostridium difficile infections (CDI) urge providers to stop unnecessary antibiotics in all patients diagnosed with CDI, but this often does not occur. Reviewing antibiotics in patients with new diagnoses of CDI can identify opportunities to stop unnecessary antibiotics which improve the clinical response of CDI to treatment and reduces the risk of recurrence.

Treatment of culture proven invasive infections. Invasive infections (e.g. blood stream infections) present good opportunities for interventions to improve antibiotic use because they are easily identified from microbiology results. The

culture and susceptibility testing often provides information needed to tailor antibiotics or discontinue them due to growth of contaminants.

Format for Assessment of Appropriateness of Antibiotics for Urinary Tract Infections (UTIs)			
Patient ID		Sex: M/F	Ward/unit
Does the patient have any of the following underlying co-morbidities? (Tick all that apply) __kidney stones ___Urologic abnormality __Pregnancy __neutropenia __history of renal transplant __other: __urinary catheter in place at the time of diagnosis or in the 48h preceding diagnosis?			
Were any of the following signs or symptoms documented? (Check all that apply) __dysuria __flank pain __urgency __fever (>38°C) or rigors __frequency __WBC >11,000 cells/µl __suprapubic pain __nausea and/or vomiting __new onset delirium* __other (please document below) (*Criteria should not be used alone. Should be taken into account with other signs and symptoms)			
Urine culture report: YES/NO Pyuria (≥ 5-10 WBCs/high power field): Epithelial cells noted? (number/high power field):			
Organism isolated		Sensitive to	
Method of urine collection __ Clean catch __ Straight catheterization__ Indwelling catheter __Not specified			
Was the patient receiving antibiotics prior to collection of the urine culture?			YES/NO
Were empiric antibiotics (started prior to culture results) consistent with institutional/national guidelines? Document antibiotic with dose and duration			YES/NO
Was the urinary catheter removed after a diagnosis of CA-UTI or catheter-associated asymptomatic bacteriuria (CA-ASB)? If Not, give reason			YES/NO
Were empiric antibiotics stopped if no organism was isolated by culture? If No, give reason for continuation			YES/NO
If an organism was isolated by culture, was it susceptible to the prescribed antibiotic?			YES/NO
Were antibiotics changed after culture results were available? If YES,			YES/NO

please document antibiotic change:	
Total duration of antibiotic therapy for UTI while an inpatient?___ Days	YES/NO
Was AMSP team/ID consult team involved the patient's care?	YES/NO

Format for Assessment of Appropriateness of Antibiotics for Community Acquired Pneumonia (CAP)

Patient ID	IPD/OPD	Sex: M/F	Ward/unit

Was the patient hospitalized in an acute care hospital for ≥ 2 days within 90 days of the diagnosis of pneumonia?	YES/NO
History of ____Intravenous antibiotic therapy ____intravenous chemotherapy,____wound care ____attend a hemodialysis clinic within 30 days of diagnosis	
Did the patient have a documented pulmonary infiltrate on chest radiograph or other chest imaging?	YES/NO
Patient meets criteria for CAP	YES/NO
Was the patient admitted to an ICU due to complications of CAP? If Yes, Were blood cultures sent?	YES/NO
Was a sputum and/or endotracheal aspirate sent for Gram stain and culture?	
Were cultures sent before antibiotics were administered?	
Any Rapid/POC done for diagnosis?	
Were initial antibiotics consistent with institutional/national guidelines?	YES/NO
Was an organism isolated by culture within 72 hours of the first dose of antibiotics	YES/NO
If an organism was isolated by culture, was it susceptible to the prescribed antibiotic?	YES/NO
Were antibiotics changed after culture results were available? If **YES**, please document antibiotic change: _____	YES/NO
Was the patient initially prescribed an intravenous (IV) antibiotic with good oral bioavailability If **YES**, was the antibiotic changed to an oral formulation (PO), or was the patient started on a different oral antibiotic within 24 hours of being eligible for oral medications?	YES/NO
Total planned duration of antibiotics	

SECTION 6. RESOURCES

Suggested reading:

1. Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines. WHO 2011; available at apps.who.int/medicinedocs/documents/s19184en/s19184en.pdf
2. European Antibiotic Awareness Day: 2014 resources: https://www.gov.uk/government/collections/european-antibiotic-awareness-day-resources
3. Prescribing competencies: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/253094/A RHAIprescrcompetencies__2_.pdf
4. Start Smart Then Focus Prescribers checklist: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/366944/Se condary_care_prescribers_checklist.pdf
5. Antimicrobial Self-Assessment Toolkit: http://imperial-asat.herokuapp.com/
6. Sepsis clinical toolkit and audit tools: http://www.collemergencymed.ac.uk/ShopFloor/Clinical%20Standards/Sepsis http://sepsistrust.org/info-for-professionals/clinicaltoolkits/
7. TARGET Antimicrobial prescribing toolkit for Primary Care: http://www.rcgp.org.uk/clinical-and-research/target-antibiotics-toolkit.aspx
8. Treatment Guidelines for Antimicrobial Use in Common Syndromes. ICMR, 2017 at https://icmr.nic.in/guidelines/treatment%20guidelines%20for%20antimicrobial.pdf
9. Hospital infection prevention and control guidelines NCDC, 2016 at http://www.ncdc.gov.in/WriteReadData/l892s/File571.pdf
10. Antimicrobial Stewardship in Australian Health Care, 2018 at https://www.safetyandquality.gov.au/wp-content/uploads/2018/04/AMSAH-Book-WEBCOMPLETE.pdf https://www.safetyandquality.gov.au/wpcontent/uploads/2018/04/AMSAH-Book-WEB-COMPLETE.pdf
11. Ontario Agency for Health Protection and Promotion (Public Health Ontario).
    Antimicrobial Stewardship Strategy: Surgical antibiotic prophylaxis optimization. Toronto, ON: Queen's Printer for Ontario; 2016. Available at https://www.publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/AntimicrobialStewardshipProgram/Documents/ASP_Strategy_Surgical_Antibiotic_Prophylaxis.pdf
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4. Start Smart Then Focus Prescribers checklist: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/366944/Se condary_care_prescribers_checklist.pdf
5. Antimicrobial Self-Assessment Toolkit: http://imperial-asat.herokuapp.com/
6. Sepsis clinical toolkit and audit tools: http://www.collemergencymed.ac.uk/ShopFloor/Clinical%20Standards/Sepsis http://sepsistrust.org/info-for-professionals/clinicaltoolkits/
7. TARGET Antimicrobial prescribing toolkit for Primary Care: http://www.rcgp.org.uk/clinical-and-research/target-antibiotics-toolkit.aspx
8. Treatment Guidelines for Antimicrobial Use in Common Syndromes. ICMR, 2017 at https://icmr.nic.in/guidelines/treatment%20guidelines%20for%20antimicrobial.pdf
9. Hospital infection prevention and control guidelines NCDC, 2016 at http://www.ncdc.gov.in/WriteReadData/l892s/File571.pdf
10. Antimicrobial Stewardship in Australian Health Care, 2018 at https://www.safetyandquality.gov.au/wp-content/uploads/2018/04/AMSAH-Book-WEBCOMPLETE.pdf https://www.safetyandquality.gov.au/wpcontent/uploads/2018/04/AMSAH-Book-WEB-COMPLETE.pdf
11. Ontario Agency for Health Protection and Promotion (Public Health Ontario).
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5. Antimicrobial Self-Assessment Toolkit: http://imperial-asat.herokuapp.com/
6. Sepsis clinical toolkit and audit tools: http://www.collemergencymed.ac.uk/ShopFloor/Clinical%20Standards/Sepsis http://sepsistrust.org/info-for-professionals/clinicaltoolkits/
7. TARGET Antimicrobial prescribing toolkit for Primary Care: http://www.rcgp.org.uk/clinical-and-research/target-antibiotics-toolkit.aspx
8. Treatment Guidelines for Antimicrobial Use in Common Syndromes. ICMR, 2017 at https://icmr.nic.in/guidelines/treatment%20guidelines%20for%20antimicrobial.pdf
9. Hospital infection prevention and control guidelines NCDC, 2016 at http://www.ncdc.gov.in/WriteReadData/l892s/File571.pdf
10. Antimicrobial Stewardship in Australian Health Care, 2018 at https://www.safetyandquality.gov.au/wp-content/uploads/2018/04/AMSAH-Book-WEBCOMPLETE.pdf https://www.safetyandquality.gov.au/wpcontent/uploads/2018/04/AMSAH-Book-WEB-COMPLETE.pdf
11. Ontario Agency for Health Protection and Promotion (Public Health Ontario).
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Suggested reading:

1. Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines. WHO 2011; available at apps.who.int/medicinedocs/documents/s19184en/s19184en.pdf
2. European Antibiotic Awareness Day: 2014 resources: https://www.gov.uk/government/collections/european-antibiotic-awareness-day-resources
3. Prescribing competencies: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/253094/A RHAIprescrcompetencies__2_.pdf
4. Start Smart Then Focus Prescribers checklist: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/366944/Se condary_care_prescribers_checklist.pdf
5. Antimicrobial Self-Assessment Toolkit: http://imperial-asat.herokuapp.com/
6. Sepsis clinical toolkit and audit tools: http://www.collemergencymed.ac.uk/ShopFloor/Clinical%20Standards/Sepsis http://sepsistrust.org/info-for-professionals/clinicaltoolkits/
7. TARGET Antimicrobial prescribing toolkit for Primary Care: http://www.rcgp.org.uk/clinical-and-research/target-antibiotics-toolkit.aspx
8. Treatment Guidelines for Antimicrobial Use in Common Syndromes. ICMR, 2017 at https://icmr.nic.in/guidelines/treatment%20guidelines%20for%20antimicrobial.pdf
9. Hospital infection prevention and control guidelines NCDC, 2016 at http://www.ncdc.gov.in/WriteReadData/l892s/File571.pdf
10. Antimicrobial Stewardship in Australian Health Care, 2018 at https://www.safetyandquality.gov.au/wp-content/uploads/2018/04/AMSAH-Book-WEBCOMPLETE.pdf https://www.safetyandquality.gov.au/wpcontent/uploads/2018/04/AMSAH-Book-WEB-COMPLETE.pdf
11. Ontario Agency for Health Protection and Promotion (Public Health Ontario).
    Antimicrobial Stewardship Strategy: Surgical antibiotic prophylaxis optimization. Toronto, ON: Queen's Printer for Ontario; 2016. Available at https://www.publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/AntimicrobialStewardshipProgram/Documents/ASP_Strategy_Surgical_Antibiotic_Prophylaxis.pdf
12. National Treatment Guidelines for Antimicrobial Use in Infectious Diseases. NCDC Available at

http://ncdc.gov.in/WriteReadData/l892s/File622.pdf **Massive Online Open Courses available from:**

1. Infection control: https://www.futurelearn.com/courses/infection-control-antimicrobialresistance
2. Antibiotic stewardship : https://www.futurelearn.com/courses/antimicrobial-stewardship
3. Antimicrobial Stewardship: A competency-based approach at https://openwho.org/courses/AMR-competency

SECTION 7.BIBLIOGRAPHY

1. Maldives Population 2018. World Population Review. Available at http://worldpopulationreview.com/countries/maldives-population/.
2. Statistical Yearbook of Maldives. National Bureau of Statistics, Ministry of Finance and Treasurery. Available at {http://statisticsmaldives.gov.mv/yearbook/2018/Health.
3. World Health Organization. Maldives. Available at http://www.searo.who.int/maldives
4. NEHAP Maldives 2015-2020. Available at http://www.searo.who.int/maldives/mediacentre/nehap2015-2020.pdf
5. Health Master Plan 2016-2025, Ministry of Health, Republic of Maldives(2014). Available at health.gov.mv
6. Fair RJ, Tor Y. Antibiotics and Bacterial Resistance in the 21st Century. *Persp Med Chem.* 2014; 6:25-64.
7. Freedberg DE, Salmasian H, Cohen B, Abrams JA, Larson EL. Receipt of antibiotics in hospitalized patients and risk for *Clostridium difficile* infection in subsequent patients who occupy the same bed. JAMA Intern Med 2016; 176:1801–1808.
8. Talbot et al. Bad Bugs Need Drugs: An Update on the Development Pipeline from the Antimicrobial Availability Task Force of the Infectious Diseases Society of America Clin Infect Dis 2006; 42:657–668.
9. Antibiotic resistant threats in the United States. CDC 2013. Available at https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf
10. National Action Plan on containment of antimicrobial resistance, Maldives. Available at http://www.searo.who.int/maldives/antimicrobial-resistance/maldives-amr-plan-201722.pdf
11. Mendelson M. et al. Antibiotic resistance has a language problem. Nature Reviews 2017; 545: 23-25.
12. Fishman N. Policy statement on antimicrobial stewardship by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Diseases Society PIDS). Infect Control Hosp Epidemiol 2012; 33:322–7.
13. Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP 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. Clin Infect Dis. 2007;44(2):159-77.
14. Sharma S, Khajuria V, Mahajan V, et al. Adverse drug reactions profile of antimicrobials: A 3-year experience from a tertiary care teaching hospital of India. Ind J Med Microbiol 2015; 33:393.

SECTION 7.BIBLIOGRAPHY

1. Maldives Population 2018. World Population Review. Available at http://worldpopulationreview.com/countries/maldives-population/.
2. Statistical Yearbook of Maldives. National Bureau of Statistics, Ministry of Finance and Treasurery. Available at {http://statisticsmaldives.gov.mv/yearbook/2018/Health.
3. World Health Organization. Maldives. Available at http://www.searo.who.int/maldives
4. NEHAP Maldives 2015-2020. Available at http://www.searo.who.int/maldives/mediacentre/nehap2015-2020.pdf
5. Health Master Plan 2016-2025, Ministry of Health, Republic of Maldives(2014). Available at health.gov.mv
6. Fair RJ, Tor Y. Antibiotics and Bacterial Resistance in the 21st Century. *Persp Med Chem.* 2014; 6:25-64.
7. Freedberg DE, Salmasian H, Cohen B, Abrams JA, Larson EL. Receipt of antibiotics in hospitalized patients and risk for *Clostridium difficile* infection in subsequent patients who occupy the same bed. JAMA Intern Med 2016; 176:1801–1808.
8. Talbot et al. Bad Bugs Need Drugs: An Update on the Development Pipeline from the Antimicrobial Availability Task Force of the Infectious Diseases Society of America Clin Infect Dis 2006; 42:657–668.
9. Antibiotic resistant threats in the United States. CDC 2013. Available at https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf
10. National Action Plan on containment of antimicrobial resistance, Maldives. Available at http://www.searo.who.int/maldives/antimicrobial-resistance/maldives-amr-plan-201722.pdf
11. Mendelson M. et al. Antibiotic resistance has a language problem. Nature Reviews 2017; 545: 23-25.
12. Fishman N. Policy statement on antimicrobial stewardship by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Diseases Society PIDS). Infect Control Hosp Epidemiol 2012; 33:322–
    7.
13. Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP 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. Clin Infect Dis. 2007;44(2):159-77.
14. Sharma S, Khajuria V, Mahajan V, et al. Adverse drug reactions profile of antimicrobials: A 3-year experience from a tertiary care teaching hospital of India. Ind J Med Microbiol 2015; 33:393.

SECTION 7.BIBLIOGRAPHY

1. Maldives Population 2018. World Population Review. Available at http://worldpopulationreview.com/countries/maldives-population/.
2. Statistical Yearbook of Maldives. National Bureau of Statistics, Ministry of Finance and Treasurery. Available at {http://statisticsmaldives.gov.mv/yearbook/2018/Health.
3. World Health Organization. Maldives. Available at http://www.searo.who.int/maldives
4. NEHAP Maldives 2015-2020. Available at http://www.searo.who.int/maldives/mediacentre/nehap2015-2020.pdf
5. Health Master Plan 2016-2025, Ministry of Health, Republic of Maldives(2014). Available at health.gov.mv
6. Fair RJ, Tor Y. Antibiotics and Bacterial Resistance in the 21st Century. *Persp Med Chem.* 2014; 6:25-64.
7. Freedberg DE, Salmasian H, Cohen B, Abrams JA, Larson EL. Receipt of antibiotics in hospitalized patients and risk for *Clostridium difficile* infection in subsequent patients who occupy the same bed. JAMA Intern Med 2016; 176:1801–1808.
8. Talbot et al. Bad Bugs Need Drugs: An Update on the Development Pipeline from the Antimicrobial Availability Task Force of the Infectious Diseases Society of America Clin Infect Dis 2006; 42:657–668.
9. Antibiotic resistant threats in the United States. CDC 2013. Available at https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf
10. National Action Plan on containment of antimicrobial resistance, Maldives. Available at http://www.searo.who.int/maldives/antimicrobial-resistance/maldives-amr-plan-201722.pdf
11. Mendelson M. et al. Antibiotic resistance has a language problem. Nature Reviews 2017; 545: 23-25.
12. Fishman N. Policy statement on antimicrobial stewardship by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Diseases Society PIDS). Infect Control Hosp Epidemiol 2012; 33:322–7.
13. Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP 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. Clin Infect Dis. 2007;44(2):159-77.
14. Sharma S, Khajuria V, Mahajan V, et al. Adverse drug reactions profile of antimicrobials: A 3-year experience from a tertiary care teaching hospital of India. Ind J Med Microbiol 2015; 33:393.

15. Baxter R, Ray GT, Fireman BH. Case-control study of antibiotic use and subsequent Clostridium difficile-associated diarrhea in hospitalized patients. Infect Control Hosp Epidemiol. 2008;29(1):44-50.
16. Bell BG, Schellevis F, Stobberingh E, Goossens H, Pringle M. A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance. BMC Infectious Diseases. 2014; 14:13.
17. Skippen I, Shemko M, Turton J, Kaufmann ME, Palmer C, Shetty N. Epidemiology of infections caused by extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella spp.: a nested case-control study from a tertiary hospital in London. J Hosp Infect. 2006; 64(2):115-23.
18. Davey P, Marwick CA, Scott CL, Charani E, McNeil K, Brown E, Gould IM, Ramsay CR, Michie S. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database of Systematic Reviews 2017; 2: Art. No.: CD003543. DOI: 10.1002/14651858.CD003543.pub4
19. Cooke J, Davey P, Wickens H, Jacklin A, Jamieson C, Gourlay Y, Hand K, Wellsteed S. Improving Practice – Working together to improve the use of antimicrobials. J Antimicrobial Chemother 2007; 60(4):712-4.
20. Van Daalen FV, Opmeer BC, Prins JM, Geerlings SE, Hulscher MEJL.The economic evaluation of an antibiotic checklist as antimicrobial stewardship intervention. J Antimicrob Chemother 2017;72(11):3213-3221
21. Dik JWH, Hendrix R, Friedrich AW, Luttjeboer J, Nannan Panday P, Wilting KR, et al. Cost-Minimization Model of a Multidisciplinary Antibiotic Stewardship Team Based on a Successful Implementation on a Urology Ward of an Academic Hospital. PLoS ONE 2015;10(5): e0126106. https://doi.org/10.1371/journal.pone.0126106
22. CDC. Core Elements of Hospital Antibiotic Stewardship Programs. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. Available at http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html.
23. CDC. CDC Campaign to Prevent Antimicrobial Resistance in Healthcare Settings. 12 Steps to Prevent Antimicrobial Resistance Among Long-term Care Residents Atlanta, GA: US Department of Health and Human Services, CDC; 2014. Available at https://kodu.kliinikum.ee/infektsioonikontrolliteenistus/doc/oppematerjalid/longterm.pdf
24. Tice AD, Rehm SJ, Dalovisio JR, Bradley JS, Martinelli LP, Graham DR et al. Practice guidelines for outpatient parenteral antimicrobial therapy. IDSA guidelines. Clin Infect Dis 2004; 38(12):1651-72.
25. Sanchez, G.V., Fleming-Dutra, K.E., Roberts, R.M., Hicks, L.A. Core Elements of Outpatient Antibiotic Stewardship. MMWR Recomm Rep 2016; 65(No. RR-6):1–12.

26. Specialist Advisory Committee on Antimicrobial Resistance (SACAR) Antimicrobial Framework. J Antimicrob Chemother 2007; 60 Suppl 1: i87-i90.
27. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health-Syst Pharm. 2013; 70:195-283.
28. NHS Foundation Trust. Empirical antibiotic guidelines for the management of common infections in adult inpatients 2018. Available at http://www.kingstonformulary.nhs.uk/download/158/antibiotic-guidelines-for-theempirical-management-of-common-infections-in-adult-inpatients