MINISTRY OF HEALTH

&

MINISTRY OF AGRICULTURE & FISHERIES

SULTANATE OF OMAN

ANTIMICROBIAL RESISTANCE (AMR) NATIONAL ACTION PLAN

VERSION 1

Forward

The Antimicrobial Resistance (AMR) is a major public and global health security threat. Antimicrobials saved millions of lives since the discovery of Penicillin over the last eighty years. The emergence and the widespread of AMR will compromise all modern medicine interventions and take us back to the pre-antibiotics era, unless well-coordinated strategies are implemented aggressively at the global and national levels.

Oman national action plan is providing a road map to all stakeholders in the country to combat the threats of AMR. It will also support World Health Assembly resolution 67.25 (Antimicrobial Resistance) and WHO Global Action Plan (WHA 68.7), which urges countries to take urgent action at the national, regional, and local levels to combat antimicrobial resistance.

The plan is focusing on five major elements with defined objectives, activities and monitoring tools by adopting the One Health approach. It will coordinate efforts for raising awareness among health care providers, veterinary and agriculture professionals and the public. Surveillance and monitoring of AMR trends in human and animal health will be implemented to assess the magnitude of the problem and help in planning the interventions to reduce the incidence of AMR in both sectors. It will also support implementation of antimicrobial stewardship programs in all healthcare settings and elimination of the use of medically-important antibiotics for growth promotion in food animals.

The success of this national action plan will require high level coordination and all stakeholders' commitment. The Ministry of Health and the Ministry of Agriculture and fisheries will provide all the resources required for the implementation of the strategy and will ensure that efforts and activities are monitored and sustained.

Dr. Ahmed Al-Saidi
Minister of Health

Dr. Fuad Bin Jaafer Al Sajwani
Minister of Agriculture & Fisheries

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Abbreviations

AMR	Antimicrobial Resistance
CIA	Critically Important Antimicrobials (as identified by the AGISAR document)
CRE	Carbapenam Resistant Enterobactriaceae
DDD	Daily Drug Dosage
DOT	Days Of Therapy
EU	European Union
GCC	Gulf Corporation Council
HAI	Healthcare Associated Infection
HCW	Healthcare Worker
MDRO	Multi Drug Resistant Organism
MDR TB	Multi Drug Resistant Tuberculosis
XDR TB	Extensively Drug Resistant Tuberculosis
MRSA	Methicillin Resistant *Staphylococcus aureus*
VISA	Vancomycin Resistant *Staphylococcus aureus*
VRE	Vancomycin Resistant *Enterococcus*
WHA	World Health Assembly
WHO	World Health Organization

1. Executive Summary

Antimicrobial Resistance (AMR) is becoming a global health security threat compromising all modern medicine interventions. Infections are becoming harder to treat, the risk of spread of infections to others is increased, and morbidity and length of hospital stays are prolonged, which create an economic burden on health care system. In addition, the risk of death is markedly higher in patients infected with multidrug resistant organisms. Effective antimicrobials are essential for preventative and curative medicine. Misuse and abuse of antimicrobials in human, animals and food production is worsening the magnitude of the crisis and putting our health at a major risk.

The current threats of AMR in Oman are similar to those global threats. This includes an increasing rates of multidrug resistant Gram negative such as multidrug resistant *Acintobacter*,the Carbapenamse producing *Enterobacteriaecae ,MRSA*, enteric pathogens such as *Salmonella*, and Multidrug resistant TB. The actual magnitude of these organisms need to be addressed by implementing the national surveillance system .

A nationally coordinated effort and adopting the ONE HEALTH approach by all concerned sectors and the whole society is crucial and mandatory to combat the resistance in the country. The national action plan detailed the strategic national objectives to fight AMR through national coordination, it emphasizes on the role of awareness, surveillance, optimization of antibiotic consumption and use, the infection prevention and control measures, research and international collaboration with WHO, FOA and OIE. It addresses the need to establish a National reference center and a national AMR committee with defined roles and responsibilities to coordinate, follow up the implantation of National Action Plan.

2. Background

Antibiotic resistance bacteria are in rise globally especially with extensive travel and medical tourism**.** Antimicrobial resistance develops when the microorganisms adapt and grow in the presence of antibiotics. The development of AMR is related to the frequency of use and can affect different antibiotics in the same class rendering them ineffective. AMR that develop in one organism and one location can rapidly and unpredictably spread. Drug resistant bacteria can circulate widely in humans, animals, through food, water and the environment. Resistant bacteria can be found in food animals and food product used for human consumption.

This emergence and the spread of MDROs is challenging epidemic with great impacts on health economy, adversely affect the patient's outcomes with increasing mortality and morbidity.

There is an alarming increase of antimicrobial resistance especially among Gram negative bacteria. Although MDRO surveillance are conducted in some tertiary care hospitals in Oman, the national magnitude of this problem is not known due to the variations in antimicrobial susceptibility methods and lack of national mandatory surveillance for MDROs (Multi Drug Resistant Organisms).

The aim of this report is to give an overview of AMR in Oman, highlight the challenges and provide a proposed strategy and a roadmap for the national stakeholders to combat the threat of AMR in human and animal sectors .The principles of One health will be adopted and implemented. Taking into considerations the challenges present, and adapting certain well evident intervention based on international recommendations such as WHO,EU, and the GCC Infection control working group .

Current Antimicrobial Threats in Oman

Multidrug-Resistant *Acinetobacter baumannii* (MDRA)

Multidrug-Resistant *Acinetobacter baumannii* (MDRA) is an important pathogen known to cause health care associated outbreaks in many parts of the world and is associated with high mortality. A recent surveillance data at the Royal hospital showed that there an increasing trend of the incidence on Multidrug resistant *Acinetobacter buamannii*.In 2015 54% were acquired from other hospitals**.** 35.5 % of the MDRA isolated were from clinical samples**.** Between 2008 -2015 Several outbreaks in different units and wards of the hospital have been reported leading to closures of ICU and other wards*. (**See appendix I).***

The molecular epidemiology of MDRA have been assessed in a collaborative study between six GCC (Oman, KSA, Bahrain, Kuwait, Qatar and UAE) countries and Queensland university in Australia. Typing of these strains by molecular testing and PCR showed that 69% of the resistant *Acinetobacter* are equipped with two types of enzymes OXA 23 and OXA 40, an enzyme which can destroy majority of antibiotics used to treat *Acinetobacter baumannii* including carbapenems. These strains are epidemic strains and can spread rapidly (spread between patients leading to outbreaks (1)

CARBAPENEM RESISTANT ENTEROBACTERIACEAE (CRE)

The rapid spread of CRE is considered a major public health threat as these have become virtually resistant to all antibiotics. Infections with CRE are associated with increased morbidity and mortality**.**

Similarly Carbapenem resistant Enterobacteriaecae strains (CRE) are increasing in Oman.

The first report of CRE from the Arabian Peninsula came from Oman, when two strains of *Klebsiella pneumoniae* were isolated from two patients who were admitted at Khoulah Hospital. Those strains were typed by molecular methods and found to carry the NDM1(New Delhi Metallo beta lactamase) gene. The first patient had history of travel to India but the other did not have any history of travel.(2)

A laboratory based survey of isolates submitted to Central Public Health Laboratory between 2013-2015, where total 1468 strains were submitted from different hospitals in the country. Majority of the strains are mainly reported by the Royal and Khoulah Hospitals. The dominant strains are *Klebsiella pneumoniae* accounting for 60 % of the isolates. These strains are commonly isolated from patients >50 years of age. The sources of these isolates are mainly form infection control samples where hospitals are implementing active surveillance for CRE among high risk patients. However significant portion still isolated from clinical samples such urine 17.3 %, wounds 14.1%, respiratory samples 10.4% and from blood cultures 5.8%.

Recently, molecular analysis of such strains (1,2,3), showed the spread of new and novel resistance markers nationally. This include the NDM-1 and OXA carbapenamases and their genes. Possession of such novel markers have rendered them resistant to virtually all available antibiotics. Also, such MDR-organisms have been implicated in healthcare associated infections such as central lines associated blood stream infections, ventilator associated pneumonias and UTIs. (see appendix I for details).

Salmonella Resistance

The World Health Organization has reported recently an alarming increase in the incidence of resistant strains of *Salmonella*, which is mainly due to increasing use of antibiotics in animal husbandry and agriculture.

The Central Public Health Laboratories have launched in 2014 national antimicrobial resistance surveillance among enteric isolates including *Salmonella.* Data collected during July 2014 till May 2015, showed a total of 207 isolates of *Salmonella spp*. Ampicillin, cotrimoxazole and chloramphenicol sensitive strains were 75 %,79% and 93% respectively. A concerning finding that 50 % of the total Salmonella strains were resistant to Ciprofloxacin which is a drug that is commonly use in intensive breeding of animals. (Appendix I)

Methicillin-Resistant *Staphylococcus Aureus* (MRSA)

Methicillin-Resistant *Staphylococcus Aureus* (MRSA) causes a wide range of infections ranging from mild skin infections such as impetigo to pneumonia, blood stream infections, toxic shock syndromes that are associated with increased morbidity and mortality. MRSA is one of the common cause of health care associated infections (HA-MRSA). There is also an increasing trend of community MRSA (CA-MRSA).

National data on the MRSA trend and burden are lacking. A point prevalence survey by the Infection Prevention and Control Department at DGDSC, have shown that MRSA accounted for 30.8% among the *Staphylococcus aureus. (11)*

Active surveillance conducted in the Royal Hospital between 2007 to 2015 showed an overall increasing trend. Majority are from skin and soft tissue and 20 % are Community Associated where patients had no prior exposure to health-care setting.Fig.7&8(Appendix I).

Drug Resistant TB

Multi Drug Resistant (MDR) – TB is a global health security risk and carries grave consequences for those affected therefore actions needed on all fronts from prevention to cure. WHO therefore called for MDR- TB to be addressed as a public health crisis in 2013.

Among 1372 newly diagnosed TB from 2011 to 2015 at Central Public Health Laboratories, 20 multidrug resistant (MDR) cases were detected which represent 1.5 % whereas 10.5% were resistant to any of first line drugs. The drug resistance cases of tuberculosis observed more in non-national compare to nationals. (see appendix I).

Data on Antimicrobial use and consumption

Scarce data on the actual consumption of antimicrobials in the country. Several audits have been conducted by some hospitals and the Department of Rational Drug Use at the MOH. A recent audit regarding the use of Surgical Antimicrobials Prophylaxis (SAP) at Khoulah Hospital, showed that

antimicrobials were widely used (97%) in surgical departments whether therapeutic or prophylactic. Cefuroxime was the most commonly used antibiotic for SAP (58%), However the type of antibiotics used for SAP varied among different departments, and the most striking finding was that about 69% of SAP were inappropriately given for more than 24 hours.

In another study to review patterns of antimicrobial prescribing for hospitalized patients in the acute care setting and assess the appropriateness of antimicrobial use among prescribers in a tertiary care hospital in Oman, concluded that there is a variability in the use of antimicrobials. There were 178 patients discharged from acute medical teams over the study period. Sixty-four percent of the patients received a total of 287 antimicrobial agents during admission. The average number of antimicrobials prescribed per patient in those prescribed antimicrobials was 2.5+-1.1. The most commonly prescribed antimicrobial agent was piperacillin/tazobactam. Most patients had infections from gram-negative organisms, and high rates of extended spectrum beta-lactamase producing organisms were observed. Cultures were obtained before antimicrobial initiation in only 25% of patients. Variability in antimicrobial selection for common infections was observed. (13)

National Antimicrobial Resistance (AMR) Action Plan to Combat Antimicrobial Resistance:

Vision

To halt the spread and the rise of antimicrobial resistance(AMR) in Oman.

Mission

To combat antimicrobial resistance through nationally coordinated efforts between different sectors and stakeholders through the following objectives:

1. To reduce the spread of antimicrobial resistance

2. To reduce the adverse impact on patient's outcomes

3. To monitor the trend of AMR through well-established surveillance system

4. To promote rational use of antimicrobial agents at all healthcare levels, and veterinary settings

5. To advocate for research on antimicrobial resistance detection, or on optimal use of antimicrobials

Elements of the National Strategy

1. Awareness

Enhance awareness among patients, health care works, and agriculture and veterinary professionals of the impact and the magnitude of the problem through improved communication, coordination, education and training.

Activities:

- Conduct training courses for residents, primary health care physicians, other healthcare workers and veterinarians and agriculture professionals.

- Include the importance of rationale use of antimicrobials and the impact of antimicrobial resistance in the curricula of nursing, pharmacy, dental, medical and veterinary and agricultural schools.

-Include the use and resistance of antimicrobials in school curricula to promote awareness and understanding of the children and public.

- Conduct Regular National campaigns to increase and improve the awareness among HCW, veterinary and agriculture and the Public.

- Educate all groups of prescribers on disease prevention (including immunization) and infection control issues.
- Encourage prescribers and dispensers to educate patients on antimicrobial use and the importance of adherence to prescribed treatments.

- Educate patients on the importance of measures to prevent infection, such as immunization, hygiene and cough etiquette.

2. Surveillance

Surveillance of the incidence and trend of MDROs and the Healthcare Associated Infections (HAIs) is very crucial to understand and assess the national magnitude of the problem and needed to plan interventions and monitor their effectiveness.

Activities:

2.1 MDRO Surveillance: Both in Human and Animal

-Standardization of Antimicrobial Laboratory testing and unifying the MDROs definitions.

-Upgrade the Laboratory capacity in all hospitals with qualified human resources and needed to tools to accurately identify MDROs and to identify newly or emerging mechanisms of resistance.

-Ensure the quality of laboratory methods used for identification and antimicrobial susceptibility testing by ensuring the adherence to standard operating procedures (SOP), internal and external quality control schemes

-Establish and upgrade the molecular bacteriology section at the Central Public Health Laboratories to cater as a national reference laboratory for MDROs.

-Adapt a national MDROs surveillance using the Global Antimicrobial Surveillance framework.

-Establish national antibiogram to help in developing treatment guidelines

-Establish national benchmarking for MRSA,MDRA,CRE,VRE….

-Establish benchmarking for HAIs caused by MDROs

- Conduct point prevalence studies at the animal and agriculture sectors to assess the prevalence of MDROs.

- Implement food borne pathogens AMR surveillance in animal health and agriculture sectors using the standards published by OIE.

-Adapt the FAO/WHO Codex Alimentarius Code of practice to minimize and contain AMR in these sectors.

-Collaborate and participate in regional and global networks for exchange of expertise in surveillance and research in both human and animal sectors.

2.2 Surveillance of Antimicrobial consumption and use in Humans and Animals

Collect and report data on use of antimicrobial agents in human and animal health and agriculture so that trends can be monitored and the impact of intervention can be assessed

Activities:

-Monitor the trend of antimicrobial consumption by DDD/DOT

-Monitor the trend of antimicrobial consumption in animal and agriculture.

3. Rational use of Antimicrobials in human and animal health

3.1 Human

3.1.1 Legalizations:

-link dispensing of all antimicrobial agents to a prescription and unique prescriber/pharmacist identifiers

-Prohibit over the counter sale of antimicrobials

- Develop standards for selecting and using generic antimicrobial agents.

- Ensure that only antimicrobials meeting international standards of quality, safety and efficacy grant marketing authorization.

-Introduce legal requirements for manufacturers to collect and report data on antimicrobial distribution (including import/export).

-Introduce requirements for pharmaceutical companies to comply with national or international codes of practice on promotional activities.

-Develop antimicrobials restriction for community.

3.1.2 Guidelines

-Encourage development and use of guidelines and treatment algorithms to foster appropriate use of antimicrobials.

-Improve antimicrobial use by supervision and support of clinical practices, especially diagnostic and treatment strategies.

- Audit prescribing and dispensing practices and utilize peer group or external standard comparisons to provide feedback and endorsement of appropriate antimicrobial prescribing.

- Encourage the use of point-of-care diagnostics to identify where antimicrobials are required, as well as to reassess the appropriateness of the diagnosis and treatment. e.g rapid streptococcal antigen detection for pharyngitis or use of rapid molecular assays for influenza.

3.1.3 Antimicrobials Stewardship programs (AMS)

Establish antimicrobial stewardship programs in all hospitals that ensure rational use of antibiotics through several interventions including feedback and education

It is highly recommended that all hospitals implement an Antibiotic Stewardship Programs.

The core elements AMS program:

1) Leadership support

Hospital leadership support is essential to support all the activities and interventions of the program to improve the antibiotics use in the facility.

2) Leadership accountability

The program should be led by a senior physician who will be responsible for the program outcomes of the stewardship activities.

3) Antimicrobials Expert

Whenever possible, the team running the Antimicrobial Stewardship (AMS) program should be composed of clinical pharmacy, senior clinician, microbiologist, infection prevention and control, nursing representative, quality improvement officer, Information technology personnel.

4) Surveillance and feedback mechanism on specific antimicrobial consumption

Surveillance and feedback on antibiotic utilization should be conducted regularly or at least twice a year (every 6 monthly). Report of this surveillance and feedback must be submitted to the hospital leadership and reported to the central antimicrobial unit at Directorate General of Disease Surveillance &Control (Fig.1) Necessary action should be taken based on surveillance finding and local resistance pattern.

5) Implementation of prospective audit and feedback

Prospective Audit and Feedback such as antibiotic point prevalence survey should be conducted.

6) Formalize regular antimicrobial rounds by AMS team

Identify and suggest streamlining of antimicrobial (e.g. Choice of antimicrobial; de-escalation; dose optimization; IV to oral switch) during the rounds. Impact on antibiotic utilization data and acceptance rate should be documented.

7) Specific interventions to improve antibiotic use

Several interventions can be implemented to ensure the rational antibiotic use including: Antibiotic time-out pre-authorization policy, prospective audits on appropriate use and feedback in addition to establishing pharmacist driven interventions such as automatic switch of IV to PO, Time-sensitive automatic stop orders for specified antibiotic prescriptions

8) Education on AMS program via continuous medical education (CME) and antibiotic awareness campaign.

Provide regular updates on antimicrobial prescribing, practice and usage for healthcare professionals.

3.2 Animals

3.2.1 Legalizations:

-prohibit the use of the Critically Important Antibiotics (CIA) in animals**.**

- All antimicrobials used for disease control in food animals require obligatory prescriptions by licensed veterinarians.

-Terminate or rapidly phase out the use of antimicrobials for growth promotion.

-Create national systems to monitor antimicrobial usage in food animals according to OIE standards.

-To have scientific recommendations on the use in the veterinary sector of last resort antimicrobials for humans (e.g. tigecycline and colistin) sector

-To reduce the overall use of antimicrobials in veterinary medicine (better targeted treatments, guided by best practice guidelines …. etc)

-To regulate and reduce the use of medicated feeds.

-Upgrade the capacity the national animal laboratories to effectively monitor for residues of antimicrobials of concern (critically important antimicrobials including fluoroquinolones, third and fourth generation cephalosporins and macrolides).

3.2.2 Guidelines:

-Enhance availability of veterinarians to prioritize diagnosis of disease in livestock and companion animals, and to encourage early use of appropriate diagnostic testing, in particular, bacterial culture and sensitivity tests**.**

-Encouraging retailers to review their standards for meat and animal products and to set clear specifications, concerning bio-security, antimicrobial stewardship and good husbandry throughout the supply chain for overseas as well as nationally sourced meat and animal products, working with suppliers and veterinarians to ensure compliance.

-Implement standard screening protocols for animal trading.

4. Infection prevention and control

High standards of infection prevention and control will remain crucial to minimize the risk of infection, limit the emergence and spread of multi drug resistant organisms in human and animals.

Activities:

Human :

Ensure Capacity building and training of infection prevention and control physicians and nurses

- Identify IPC programs in the hospital as separate departments reporting to the highest authority and make them accountable to lead the surveillance of MDRO & HAIs activities

- Enhance surveillance of MDROs and establish national benchmarking for MRSA, MDRA, CRE, VRE….

-Mandate ongoing national surveillance program for Health Care Associated Infections (HAIs) caused by MDROs

-Reduce infection by immunization.

-Adopt National Adult Vaccination program especially those at risk such as patients with chronic lung diseases, immunosuppressed etc

- Maintain high compliance with adult vaccines for HCWs

- Implement the standards of infection prevention and control as mandated by the national code of conduct. (14)

-Establish ongoing health care workers education and training program that focus on importance of the adherence of infection prevention measures.

- Establish an inter hospital transfer system that ensures the identification of patients with MDROs between hospitals the country and transfer of patients between hospitals; to place on proper isolation precautions.

- Mandate a mandatory program for Hand hygiene in all healthcare setting that focus on continuous education, monitoring of compliance, feedback and improvement strategies.

Animal:

Activities:

-Monitor and improve infection prevention and control practices in animal health, both through enhanced dissemination and implementation of best practice and better use of data and diagnostics.

- Make available the use of vaccines in husbandry.

- Adopt and adhere to government guidance on bio-security, animal husbandry and on farm health

planning for each of the major farming sectors and to take proactive action to reduce the risk of disease occurring in their animals under experienced veterinarian supervision.

-Consider the use of 'farm assurance schemes' as a mechanism to increase adherence to best husbandry including isolation of sick animals, testing of new stock and responsible use of antibiotic principles by veterinarians only, while ensuring animal health and welfare.

5. Research

-Develop a collaborative research sectors including, healthcare, drug regulatory agencies, veterinarian care and agriculture.

- Involve Research council (TRC)and the national academic centers and make them aware of AMR and consideration for AMR research funding as priority. This will help mapping the national magnitude of the problem and assess the effectiveness of the interventions.

Governance

The National AMR Committee will lead the implementation of this Strategy as a comprehensive, integrated Programme across government. The committee will be composed of all the stakeholders including:

1-Ministry of Health

2-Private sector (Hospitals & pharmacies)

3-Ministry of Agriculture and Fisheries wealth

4-Sultan Qaboos University, Armed Forces hospitals, Royal Oman Police

5- Research council and other agencies supporting research

6-Media

7-Community leaders

8-Consumer protection

9-Ministry of Municipality (Food Safety Center)

10-Ministry of Environment

11.Oman Medical Specialty Board (OMSB)

The National Antimicrobial Resistance Committee will have the following roles and responsibilities:

-Ensure political commitments of all stakeholders to the national AMR strategy.

-Address in a collaborative way all the actions and activities stated in the national strategic plan to combat AMR.

-Ensure that strategic goals are adopted and implemented by all stakeholders

-Regularly meet and review trends of AMR in all sectors involved

-Seek international collaboration with organization such as WHO, FAO, OIE…

-Foster and encourage national AMR research projects.

-Monitor regularly key performance indicators of the strategic goals and activities.

-Develop regulations and national policies with regards to the use of antimicrobials in health and animal husbandry.

Central Antimicrobial Resistance Unit (National reference Center) :

Central AMR unit as the responsible body accountable to the prompt action and follow up of implementation of the strategic plan.
All surveillance data of MDROs and antimicrobial consumption should be reported to this unit. The unit will be receiving data from antimicrobial stewardship teams in the hospital, the MDRO surveillance data, the consumption data from both health and animal sectors. The unit should coordinate national activities with regards to audits, feedback, education and awareness. The unit will be responsible for developing the national operational plan of the strategy and sets the key indicators for monitoring. Annual report of all the activities should be submitted to the National AMR committee Fig.1

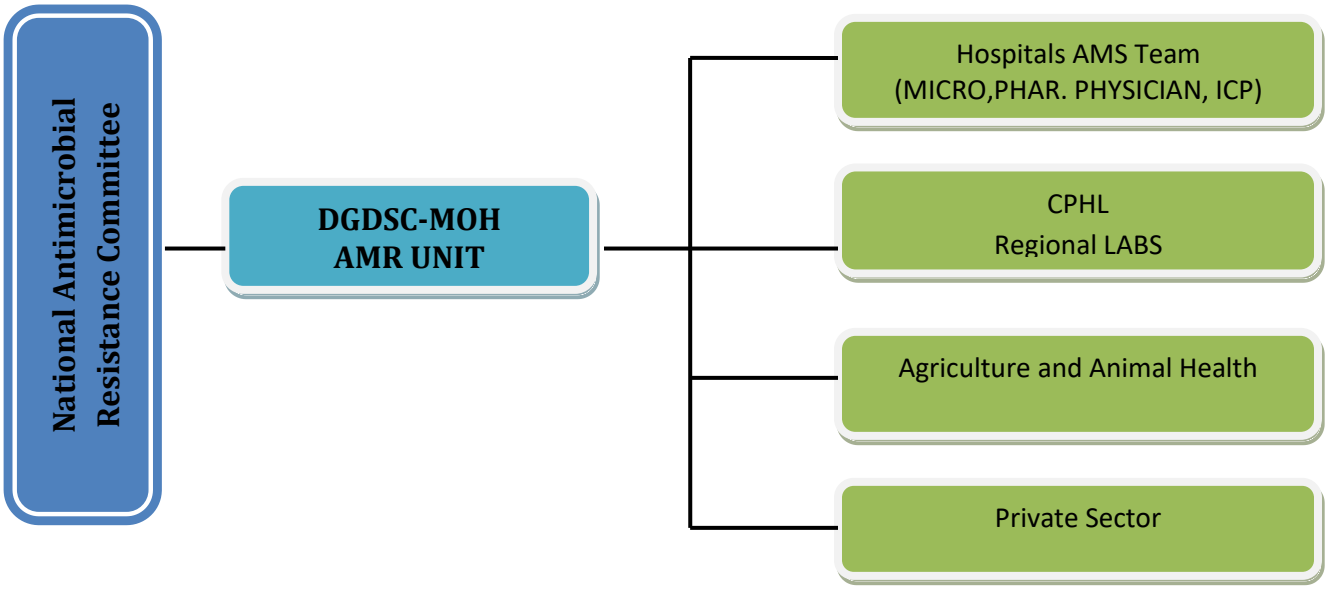

Fig 1 -Organization structure of AMR National reference Center and Committee.

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Appendix I: Current AMR threats in Oman

Multi Drug Resistant Acinetobacter (MDRA):

Multidrug-Resistant *Acinetobacter baumannii* is an important pathogen known to cause health care associated outbreaks in many parts of the world and is associated with high mortality.

The recent surveillance data at the Royal hospital showed that there an increasing trend of the incidence on Multidrug resistant *Acinetobacter buamannii*.In 2015 54% were acquired from other hospitals (not Royal hospital cases).Fig 2

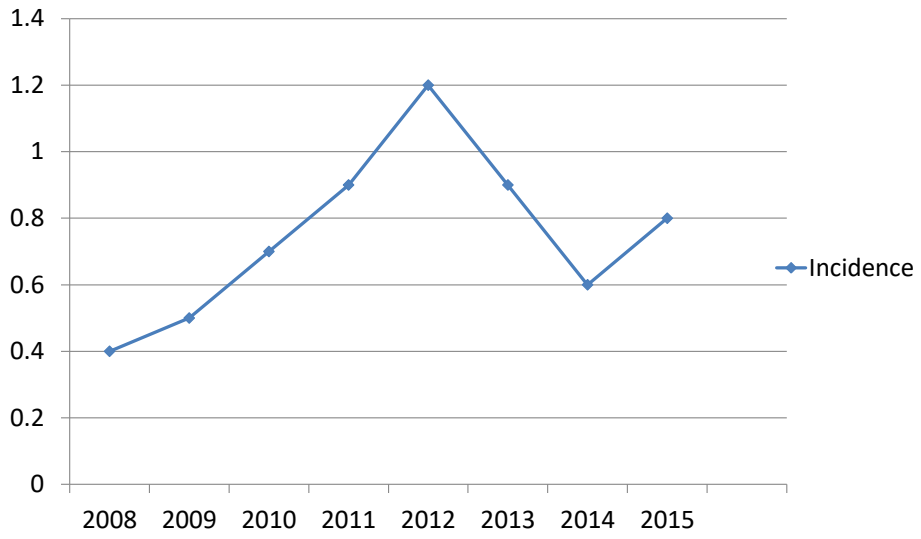

Fig.2 Incidence rate of MRAB /100 admissions in royal hospital 2008-2015

35.5% of the MRAB isolated were are from clinical samples, while 65.5 % represent colonization. Between 2008 -2015 Several outbreaks in different units and wards of the hospital have been reported leading to closures of ICU and other wards. Fig 3

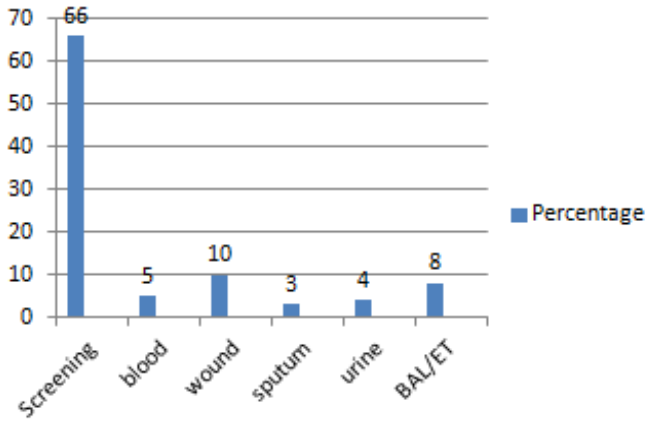

Fig.3 Percentage of MRAB by source at Royal Hospital in 2015.

The molecular epidemiology of MDRA have been assessed in a collaborative study between six GCC (Oman,KSA,Bahrain,Kuwait ,Qatar & UAE) countries and Queensland university in Australia. Typing of these strains by molecular testing and PCR showed that 69% of the resistant *Acinetobacter* are equipped with two types of enzymes OXA 23 and OXA 40, An enzyme which can destroy majority of antibiotics used to treat *Acinetobacter baumannii* including carbapenems. These strains are epidemic (strains and can spread rapidly spread between patients leading to outbreaks 1)

CARBAPENEM RESISTANT ENTEROBACTERIACEAE (CRE)

Similarly, Carbapenem resistant Enterobacteriaceae strains (CRE) are increasing.

The rapid spread of CRE is considered a major public health threat as these have become virtually resistant to all antibiotics. Infections with CRE are associated with increased morbidity and mortality.

Laboratory based survey of isolates submitted to Central Public Health Laboratory between 2013-2015 .A total of 1468 strains were submitted from different hospitals in the country. Majority of the strains are mainly reported by the Royal and Khoulah Hospitals (table1 & fig 4). The dominant strains are *Klebseilla pneumoniae* accounting for 60 % of the isolates (Fig.6). These strains are commonly isolated from patients >50 years of age (fig 5).The source of these isolates are mainly form infection control samples where hospitals are implementing active surveillance for CRE among high risk patients. However significant portion still isolated from clinical samples such urine 17.3 %, wounds 14.1%, respiratory samples 10.4% and from blood cultures 5.8% (Fig. 4)

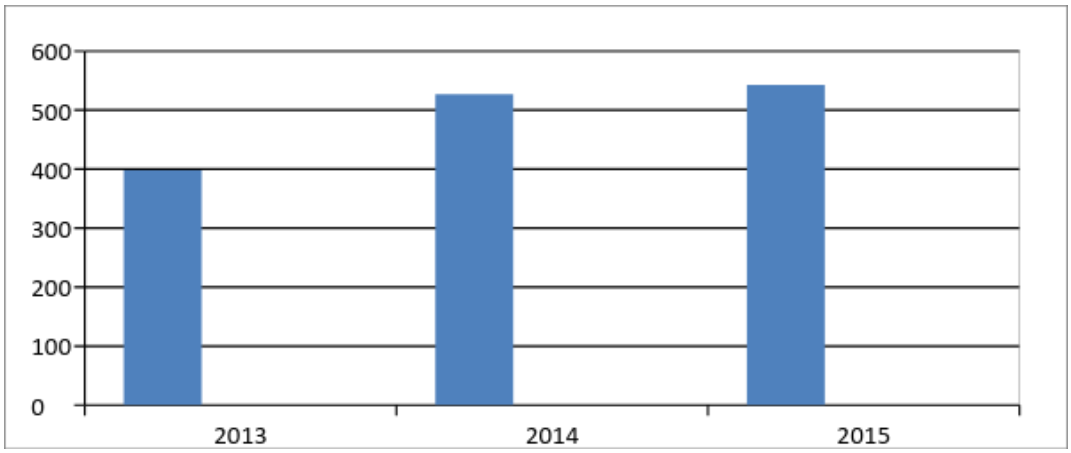

Fig.4 Annual CRE strains submitted to CPHL 2013-2015.

Hospitals	2013	2014	2015
Al Masarra H.	0	1	21
Al Nahdha H.	11	6	8
Buraimi H.	2	9	4
Ibri H.	2	3	10
Khoula H.	137	165	196
Nizwa H.	10	42	113
Royal H.	183	174	38
Sohar H.	2	10	14
SQH	9	78	95
Sur H.	42	38	44
Total	398	527	543

Table-1 CRE strains submitted by different hospital in the country 2013-2015

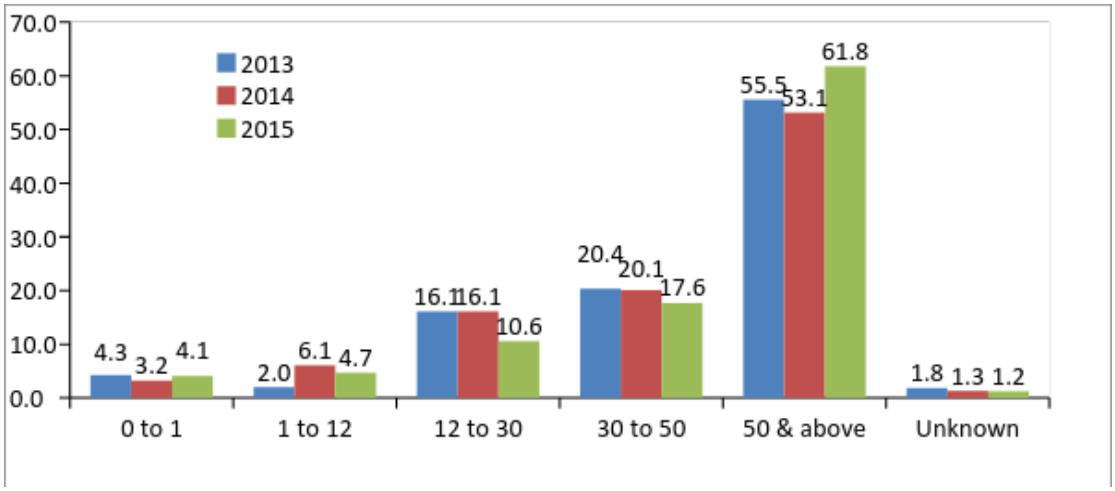

Fig.5 Age group affected by CRE acquisition

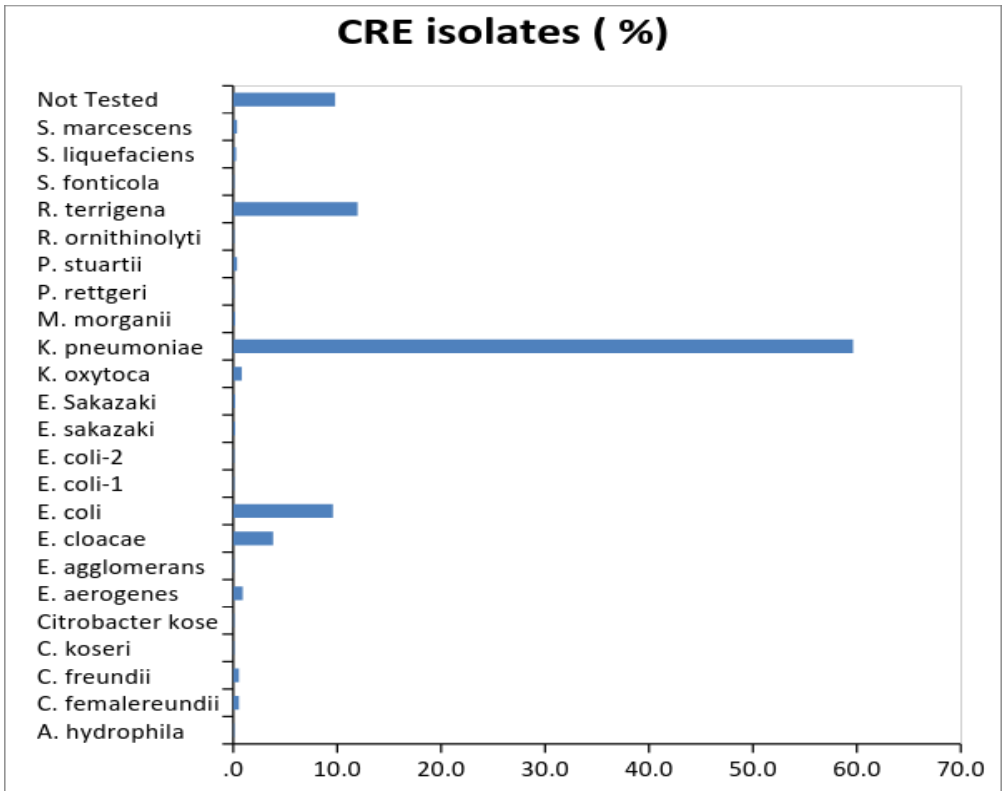

Fig.6 Frequency of CRE isolates (%) between 2013-2105

Source	CRE isolates Frequency (%)
Biopsy	2.3
Blood	5.8
Catheter	2.0
Endotracheal secretions	7.6
Infection Control screening samples	36.0
Pus	3.0
Sputum	2.8
Tissue	.4
Urine	17.3
Wound	14.1
Others	8.8

Table 2.Frequency of CRE isolates by source or sample (2013-2015)

The first report of CRE from the Arabian peninsula came from Oman, when two strains of *kelbsiella pneumoniae* were isolated from two patients who were admitted at Khoulah Hospital.Those strains were typed by molecular methods and found to carry the NDM1(New Delhi Metallobetalactamase) gene .The first patient had history of travel to India but the other did not have any history of travel.(2)

Typing of 22 isolates isolated at the Royal Hospital isolated in 2010-2011, revealed the presence of OX4 48 AND NDM1 and the combination of OXA 48 AND 181.
In addition, the majority of the strains were harboring other enzymes such as ESBL (Extended Spectrum Beta-lactamases) mainly CTXM-15 and other genes encoding for aminoglycosides quinolones, tetracyclines and sulphonamides rendering the organism resistant to all classes of antibiotics (3)

Recently, molecular analysis of such strains(1,2,3) ,showed the spread of new and novel resistance markers nationally .This include the NDM-1 and OXA carbapenamases and their genes .Possession of such novel markers have rendered them resistant to virtually all available antibiotics. Also, such MDR-organisms have been implicated in healthcare associated infections such as central lines associated blood stream infections, ventilator associated pneumonias and UTIs.

Methicillin-Resistant *Staphylococcus Aureus* (MRSA)

Methicillin-Resistant *Staphylococcus Aureus* (MRSA) causes a wide range of infections ranging from mild skin infections such as impetigo to pneumonia, blood stream infections, toxic shock syndromes that are associated with increased morbidity and mortality. MRSA is one of the common cause of health care associated infections (HA-MRSA). There is also an increasing trend of community MRSA (CA-MRSA).

National data on the MRSA trend and burden are lacking. Active surveillance conducted in the Royal Hospital between 2007 to 2015 showed an overall increasing trend. Majority are from skin and soft tissue and 20 % are Community Associated where patients had no prior exposure to health-care setting.Fig.7 & 8

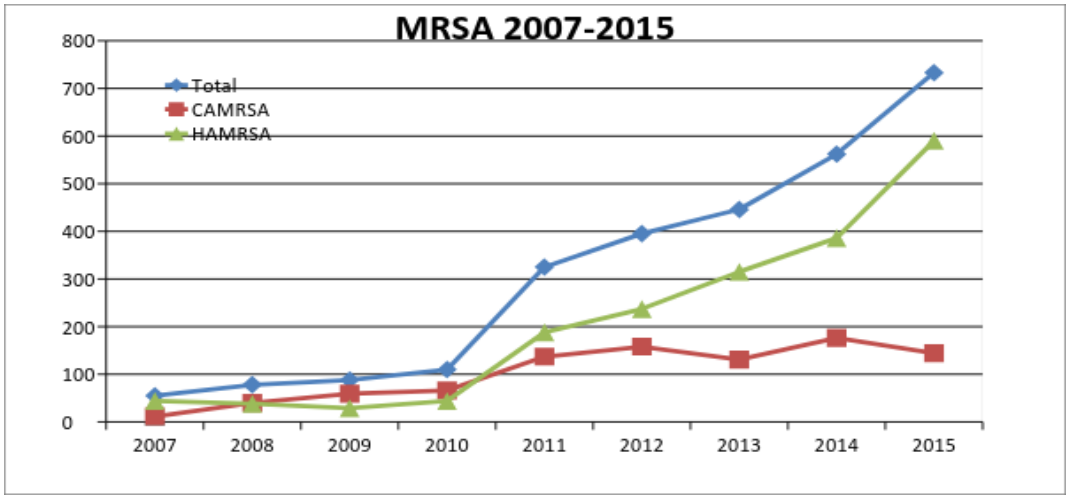

Fig.7 Surveillance of MRSA at Royal Hospital 2007-2015

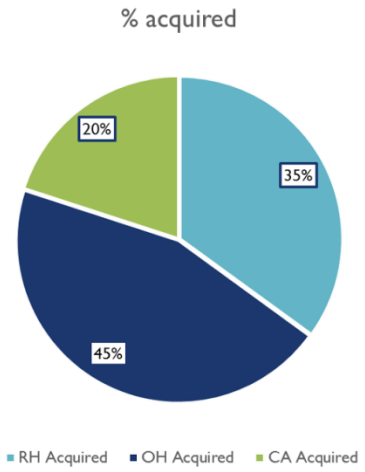

Fig.8 MRSA by origin of acquisition- Royal Hospital 2015

Salmonella Resistance:

The World Health Organization has reported recently an alarming increase in the incidence of resistant strains of *Salmonella*, which is mainly due to increasing use of antibiotics in animal husbandry and agriculture.

The Central Public Health Laboratories have launched in 2014 a national antimicrobial resistance surveillance among enteric isolates including *Salmonella.* Data collected during July 2014 till May 2015, showed a total of 207 isolates of Salmonella spp.Ampicillin ,cotrimoxazole and chloramphenicol sensitive strains were 75 %,79% and 93% respectively (Fig 9). A concerning finding that 50 % of the total Salmonella strains were resistant to Ciprofloxacin which is a drug that is commonly use in intensive breeding of animals.

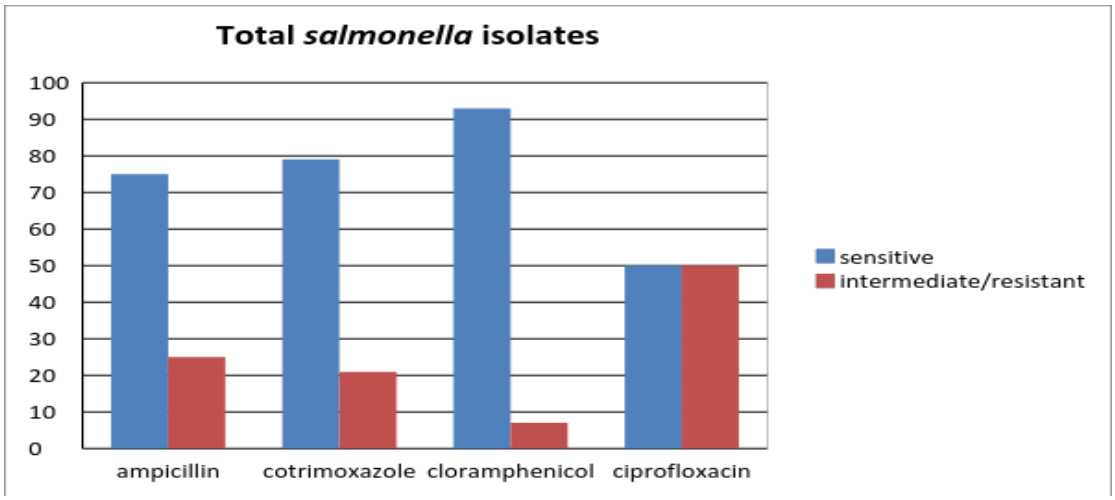

Fig.9 Susceptibility of Salmonella isolates

Among the 27 strains of extra intestinal *Salmonella* spp. isolated from bloodstream infections,7.4 % were resistant to ceftriaxone fig.10

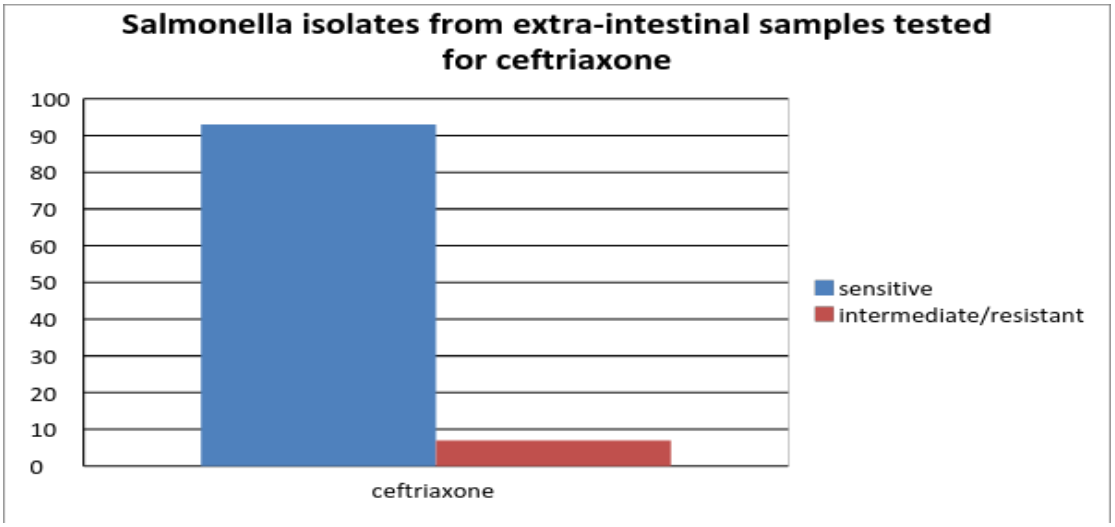

Fig.10 Susceptibility of extra intestinal Salmonella isolates

Drug Resistant TB:

Multi Drug Resistant (MDR) – TB is a global health security risk and carries grave consequences for those affected therefore actions needed on all fronts from prevention to cure. WHO therefore called for MDR- TB to be addressed as a public health crisis in 2013.

Five priority actions are crucial to accelerate the response against the MDR-TB epidemic:

1. Prevent the development of drug-resistance through high quality treatment of drug-susceptibility TB.
2. Expand rapid testing and detection of drug resistant TB cases.
3. Provide immediate access to effective treatment and proper care.
4. Prevent transmission through infection control.
5. Increase political commitment with financing.

The national TB reference laboratory in Oman has an important role in controlling the spread of infections, through the early detection, isolation, identification and susceptibility testing. Molecular tests were implemented to provide rapid diagnosis of TB which can help in patient care and public health management.

In 2014 total 280 new TB cases were reported including national and non-national in Oman, among them 28, or 10%, antibiotic resistance were identified. The drug resistance cases of tuberculosis observed more in non-national compare to national.

	Number of cases	Cases per 100,000 population	Percent of all TB cases in OMAN
Any first-line resistance	28	0.69	10%
INH resistance	22	0.54	8%
MDR	6	0.025	2%
XDR	0	0	0%

Table3: Shows drug resistance tuberculosis cases in 2014 among national and non-national

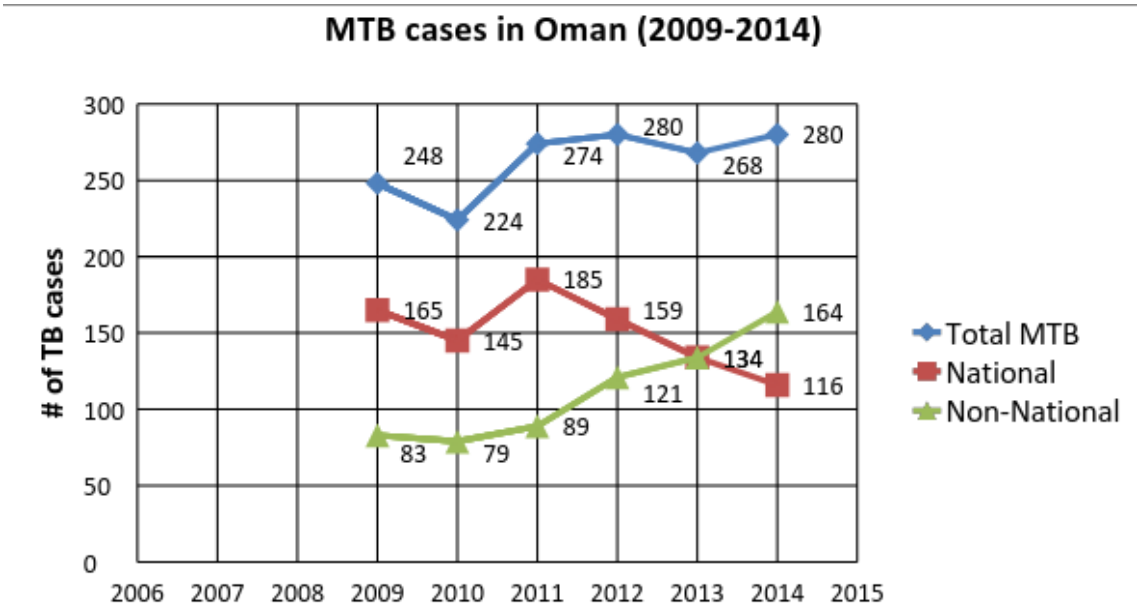

Fig.11: Shows Total TB cases from 2009-2014 (National – Non -National). On the other hand, national TB cases decreased since 2012 where non - national residence increased. This effect the total number of MTB recorded.

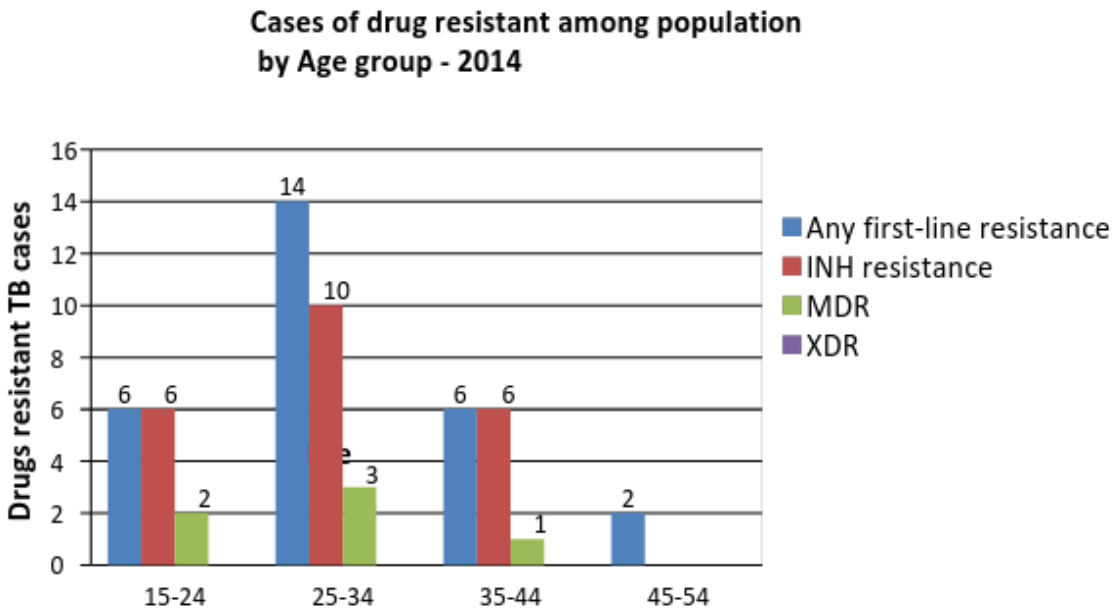

Fig 12: Shows distribution of drug resistant tuberculosis among population in 2014- Oman. Antibiotic resistance occurs most often among age group 25-34.

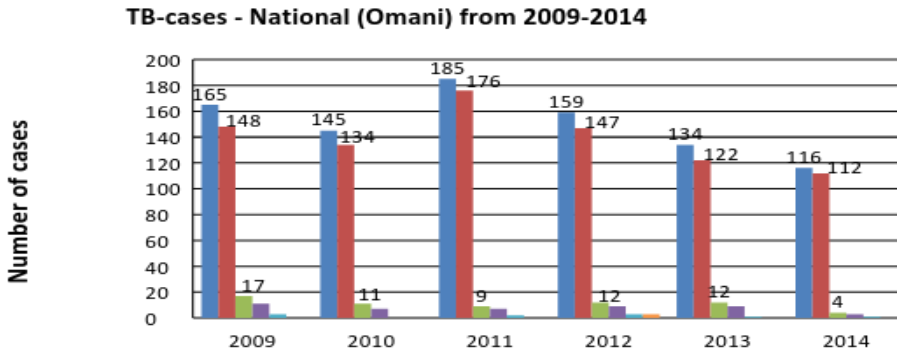

Fig.13 : TB Drug- resistant cases for National (Omani) from 2009-2014.The graph shows significant decrease in TB cases and multi-drug resistant. Three cases of XDR were reported in 2012.

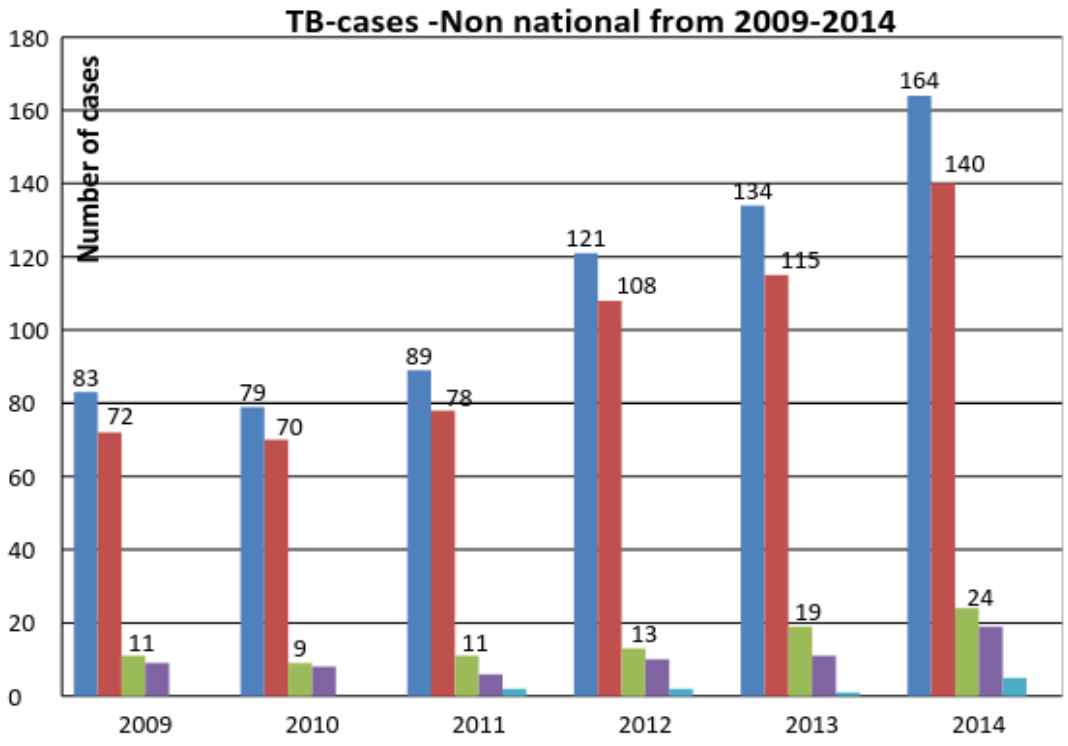

Fig.14: Shows TB Drug- resistant cases for Non-national from 2009-2014

Multi-drug resistant cases increased from 2009 to 2014. No XDR cases reported among non-national.

APPENDIX: II

PROPOSED OPERATIONAL NATIONAL AMR ACTION PLAN

National Strategic Objective	Activities	Time frame
1. Improves awareness and understanding of antimicrobial resistance through effective communication, education and training	**Education**	
	• Develop curricula on antimicrobial resistance for professionals in the healthcare, veterinary and agriculture sectors (including infection prevention and control, rational use of antimicrobial medicines, surveillance) and implement pre-service and in-service training	
	• Conduct regular training courses to increase and improve the awareness among HCW, veterinary and agriculture professionals	
	• Conduct National campaigns awareness for patients and public on the importance of measures to prevent infection, such as immunization, hygiene and cough etiquette.	
2. Strengthen the national surveillance system	**National antimicrobial resistance surveillance system**	
	• Establish a national reference centre for antimicrobial resistance with the ability to systematically collect, analyse and report data on antimicrobial use and resistance in order to inform decision making at national and international levels	
	• Establish or strengthen surveillance on antimicrobial resistance in animal health and agriculture sectors	
	• Collect and report data on use of antimicrobial agents in human and animal health and agriculture	
	• Establish mechanisms for regular sharing of antimicrobial resistance data across human and animal health environmental sectors at the national, regional and global levels as per global standards	
	Laboratory capacity	
	• Designate at least a national reference laboratory for antimicrobial resistance capable of quality assured identification and susceptibility testing and reporting, including on newly emerged resistance	
	• Establish an antimicrobial resistance surveillance network integrating all laboratories	
	• Involve all the national health laboratories in external quality assurance programmes	
3. Reduce the incidence of infection through effective infection prevention measures	**Community level prevention**	
	• Promote personal hygiene through social mobilization and behavior change activities	
	• Promote vaccination among the communities and health care providers	
	Infection prevention and control in healthcare settings	
	• Develop national policies, strategies and plans for health care waste management	
	• Develop and implement national infection prevention and control programmes	
	• Establish or strengthen infection prevention and control programmes in health care facilities at all levels with emphasis on tertiary hospitals	
	• Develop systems for safe collection, storage, transportation and final disposal of healthcare waste	
	Animal Health	
	• Strengthen animal health and agricultural practices through implementation	

	of the standards published in the terrestrial and aquatic animal health codes of the organization for Animal Health(OIE) and Codex Alimentarius code of practice to minimize and contain antimicrobial resistance	
	• Develop recommendations for the use of vaccines as a method of preventing infections in animals and reduction of antimicrobial use	
4. Optimize the use of antimicrobial medicines in human and animal health	**Access to quality antimicrobial medicines**	
	• Develop and enforce legislation and regulations on prescription and dispensing of medicine including antibiotic (self- regulation by professional association) informed by identification of barriers	
	• Strengthen pharmaceutical supply chain (procurement, supply and management systems)	
	• Establish or strengthen mechanisms for registration of antimicrobial medicines within relevant national authorities according to global standards (e.g International Cooperation on Harmonization of Technical Requirement for registration of Veterinary Medicinal Products)	
	• Establish national mechanisms (e.g market surveillance) for identification and report on sub- standard/falsified/counterfeit medicines and link with the global mechanisms	
	• Develop and enforce regulations to control promotional practices by industry	
	• Develop and implement evidence-based standard treatment guidelines to guide stewardship programmes in human health	
	• Establish antimicrobial stewardship programs in all hospitals that ensure rational use of antibiotics through several interventions including feedback and education.	
	Animal health sector	
	• Identify and consider banning non-health use of critically important antibiotics for humans in the animal sector	
	• Promote the prudent use of antimicrobials and legalize the distribution and dispensing of antimicrobials by prescription, carried out by accredited veterinary professionals	
	• Adopt policies on the use of antimicrobial agents in terrestrial and aquatic animals, and agriculture, including: implementation of Codex Alimentaruis and OIE intergovernmental standards and guidelines such as the List of Antimicrobials of Veterinary Importance as well as WHO/OIE guidance on the use of critically important antibiotics, phasing out of the use of antibiotics for animal growth promotion and crop protection and crop protection in the absence of risk analysis, and reduction in nontherapeutic use of antimicrobial medicines in animal health	
	• Assess the investment needs for implementation of the national action plan on research and development	
5.Research	• Identify operational research priorities for promoting responsible use of antimicrobial medicines, defining improved practices for preventing infection in human and animal health and agricultural practice	
	• Identify the possibilities and feasibility of developing novel diagnostic tools for low resource settings	
	• Conduct research to identify the economic burden due to antimicrobial resistance at the national level(to use as advocacy material)	