

Antimicrobial Resistance: Identifying the Major Conflicts of Interest and Way Forward

Samridhi Sharma^{1,*}, Kemesha Govender¹, Kiran Nagaraju², Pratik Chhetri³, Sunitha Chandrasekhar Srinivas¹

¹Faculty of Pharmacy, Rhodes University, Grahamstown, SOUTH AFRICA.

²Department of Pharmacy Practice, Visveswarapura Institute of Pharmaceutical Sciences, Bengaluru, Karnataka, INDIA.

³Director, Authentic Leadership Institute Nepal, Kathmandu, NEPAL.

ABSTRACT

Consistent and sustainable actions in the right direction to address the current public health challenges of antimicrobial resistance (AMR) is crucial to avert the severe negative impact on health and development of the global population. Inadequate knowledge on the appropriate use of antibiotics in humans as well as in food production (meat and plant-based), lack of hygiene, and poverty are some of the major contributing factors to the emergence and spread of AMR. While existing antimicrobials are becoming ineffective at an alarming rate and the discovery void in new classes of antibiotics has remained for decades, specific attention on the rational use of available antibiotics is crucial. While low- and middle-income countries (LMICs) address their double burden of diseases with inadequate healthcare systems and lack of preparedness to address AMR, the commercial interests of the market forcing for the irrational use of antimicrobials will also remain a major trigger. Hence, LMICs require greater commitment in operationalizing their national AMR action plan which have all been adopted from the WHO's Global Action Plan. This review article provides a summary of global events for AMR, HIV/AIDS and NCDs, to draw out the disparity of resolutions and conflicts of interest. Increased knowledge and education on the rational use of antimicrobials is key for agricultural industries, health care professionals as well as patients and communities. The implementation of national and international policies along with youth participation is bound to lead to positive health and development outcomes.

Key words: Antimicrobial resistance, HIV/AIDS, India, Non-communicable diseases, South Africa, Sustainable Development Goals, Youth.

INTRODUCTION

“We find ourselves on the brink of a post-antibiotic era” – *Department of Health Republic of South Africa, 2015*.¹

According to the World Health Organization (WHO), antimicrobial resistance (AMR) is a global threat to public health.² AMR causes around 700 000 deaths every year and is projected to lead to 10 million deaths annually by 2050.^{3,4} By 2050, 4730000 deaths in Asia and 4150000 deaths in Africa will be attributable to AMR.³ Over-prescription and irrational use of antimicrobials result in the development and spread of AMR, which is worsened by poor infection control in clinics and hospitals as well as by poor sanitation.² AMR results in more infections, for longer durations; increased duration and frequency

of hospital admissions; and increased health-related expenses. Inadequate knowledge is partly responsible for inappropriate prescription, which may further increase morbidity and mortality rates.⁵⁻⁷ Poverty contributes to the increase of AMR, as patients tend to share antimicrobials or use leftovers to treat infections.⁸ Patients require counselling and education on the correct use of antimicrobials and the importance of hygiene to prevent AMR and to maintain healthy living.⁷ Widespread use of antimicrobials in the agricultural industry also contributes significantly to the emergence and spread of AMR. Large quantities of antibiotics are used for growth promotion, as well as for prophylaxis and to treat infections in intensively farmed animals, to prevent economic losses.^{9,10} Therefore, due to a potential conflict of commercial interest,

DOI: 10.5530/ijopp.13.4.51

Address for

correspondence:

Ms. Samridhi Sharma

Faculty of Pharmacy, Rhodes University, Grahamstown, SOUTH AFRICA.

Phone no: +27 (0) 46 603 8381

Email Id: samridhi1sharma@gmail.com



www.ijopp.org

the risk of policies failing to tackle AMR is also high.¹¹ While existing antimicrobials are becoming ineffective at a high rate, there is slow to minimal development of new antimicrobial agents.¹²

AMR has a major negative impact on some major diseases such as TB, pneumonia, malaria and HIV, especially in developing nations such as South Africa and India. As antimicrobial agents become more ineffective, treatment of these diseases becomes more difficult.^{7,13,14} Antimicrobials do not possess a unilateral role of therapy. They are required for successful treatment of various communicable and non-communicable diseases (NCDs),² further complicating the double burden of diseases in developing countries.¹⁵ Without effective antimicrobials, death due to infectious diseases will continue to rise, while NCD related issues such as chemotherapy and heart surgery would increasingly become high risk as prophylaxis antibiotics would be unavailable.¹⁶

Although AMR is a major threat to public health, aggressive and effective actions in developing countries are yet to begin. Below is a summary of events, in the form of a timeline, for HIV/AIDS, AMR and NCDs, to depict the disparity of resolutions. A few important milestones in the three aspects - AMR, HIV/AIDS and NCDs - are shown. Table 1 below shows some of the important milestones achieved as an outcome of global, regional and national responses.

Table 1: Timeline for HIV/AIDS Resolutions.

HIV/AIDS
2030
<ul style="list-style-type: none"> Target year for ending AIDS epidemic¹⁷
2020
<ul style="list-style-type: none"> The UNAIDS “90-90-90” targets for 2020 - 90% of HIV positive population to know their HIV status, 90% of patients diagnosed with HIV to receive antiretroviral therapy and 90% of those on antiretroviral therapy to achieve viral suppression¹⁷
2017
<ul style="list-style-type: none"> WHO launched the first Global Action Plan on HIV Drug Resistance¹⁷
2016
<ul style="list-style-type: none"> WHO launched its “treat all” consolidated guidelines on the strategic use of antiretroviral therapy for both treatment and prevention¹⁷ WHO prequalified over 250 pharmaceutical products for treating HIV-related conditions, 29 active pharmaceutical ingredients (APIs) and two devices for male circumcision¹⁷
2015
<ul style="list-style-type: none"> MDG 6’s target of 15 million people on HIV treatment by 2015 was met nine months ahead of schedule^{18,19} Declaration of Sustainable Development Goals (SDGs); SDG 3 targeting to fully eradicate AIDS epidemic by 2030^{18,20}

2010

- UNITAID established the Medicine Patent Pool (MPP) to increase access to HIV, viral hepatitis C and TB treatments in low- and middle-income countries (LMICs)²¹
- WHO introduced a new treatment framework of a five-pronged programmatic approach, to increase accessibility, safety, effectiveness and efficiency of antiretroviral therapy¹⁷

2008

- At the 17th International AIDS Conference in Mexico City, WHO launched a set of priority interventions to assist LMICs achieve universal access to HIV prevention, treatment, care and support¹⁷

2004

- The Oral Health and Disease in AIDS Conference in Phuket, Thailand issued the Phuket Declaration to encourage research and strengthen oral health promotion and the care of HIV-infected persons²²

2002

- Global Fund to Fight AIDS, TB and Malaria founded¹⁸

2001

- Heads of State and Representatives of Governments issued Declaration of Commitment on HIV/AIDS at the United Nations General Assembly Special Session (UNGASS)²³
- The Doha Declaration by World Trade Organisation, allowing developing countries to buy or manufacture generic medicines for public health crises such as HIV/AIDS¹⁸
- The South African law allowed the government to purchase any brand-named AIDS medicines at the lowest rates, provided the medicines complied with international trade agreements²⁴
- WHO prequalification established as a response to the HIV/AIDS pandemic to guide UN and others to procure quality ARVs²⁵

2000

- U.S National Security Council and UN Security Council both declared HIV/AIDS a security threat^{18,26}
- Declaration of 8 Millennium Development Goals (MDGs); MDG 6 was to combat HIV/AIDS, malaria and other diseases^{18,27}

1987

- First antiretroviral (ARV) medicine, zidovudine, approved by U.S. FDA^{18,26}
- WHO launched Global Programme on AIDS^{18,26}

1985

- First International AIDS Conference which took place in Atlanta²⁶

1980s

- People first became aware of HIV/AIDS²⁸

While antibiotics are considered one of the most significant discoveries of the 20th century, the real challenge is the increased prevalence of AMR seen in hospitals, communities, as well as the environment in which antibiotics are used.²⁹ Table 2 highlights some of the major milestones in AMR resolutions.

Progress in managing this major global public health problem is shown using an NCD related example. A clear conflict of interest emerges when considering economic

Table 2: Timeline for AMR Resolutions.

AMR	
2017	<ul style="list-style-type: none"> The World Health Assembly resolution 68.7 requested for all national action plans to be completed by May³⁰ WHO issued a list of the 12 most important antibiotic-resistant bacteria, in addition to <i>Mycobacterium tuberculosis</i>, requiring urgent research and development^{31,32}
2016	<ul style="list-style-type: none"> The Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) established an international partnership to tackle antimicrobial resistance³³ Davos Declaration at World Economic Forum by Pharmaceutical, Biotechnology and Diagnostics Industries on combating antimicrobial resistance³⁴ Leading pharmaceutical companies presented industry roadmap with key commitments to be delivered by 2020 to reduce antimicrobial resistance³⁴ United Nations General Assembly held the first high-level meeting on antimicrobial resistance and passed a political declaration^{35,36} The Drugs for Neglected Diseases initiative along with WHO launched a global research and development partnership to develop and promote the rational use of new antibiotics³⁰
2015	<ul style="list-style-type: none"> Governments at the World Health Assembly adopted a global action plan to tackle antimicrobial resistance³⁰
2014	<ul style="list-style-type: none"> The 67th World Health Assembly resolution WHA67.25 called for the development of the global action plan on antimicrobial resistance³⁷
2011	<ul style="list-style-type: none"> APUA, WHO, Rajasthan Society for Promotion of Rational Use of Drugs (RSPRUD) and International Society for Pharmacoeconomics and Outcomes Research (ISPOR) offered an "International Training Course on Promoting Rational Use of Drugs in the Community" at the Institute of Health Management Research in Jaipur, India³⁸
2009	<ul style="list-style-type: none"> Launch of WHO 'SAVE LIVES: Clean Your Hands' campaign³⁹
2006	<ul style="list-style-type: none"> Establishment of APUA South Africa⁴⁰
1996	<ul style="list-style-type: none"> Establishment of APUA India³⁸
1981	<ul style="list-style-type: none"> Dr Stuart B. Levy founded Alliance for the Prudent Use of Antibiotics (APUA) as a global non-profit organisation, aiming to improve antimicrobial use and contain antibiotic resistance⁴¹
1977	<ul style="list-style-type: none"> Emergence of multidrug resistance was first reported in Soweto, South Africa⁴²
1960	<ul style="list-style-type: none"> Appearance of antibiotic resistance in most developed countries^{29,43}
1928	<ul style="list-style-type: none"> Discovery of penicillin by Sir Alexander Fleming¹⁶

generation and job creation among the food, beverage, alcohol and cigarette industries and demonstrates how the United Nations (UN) and governments have to manage the conflict of revenue generation of these major industries against the NCD pandemics they cause, especially in developing countries. Table 3 below highlights some of the major milestones in NCD resolutions.

Table 3: Timeline for NCDs Resolutions.

NCDs	
2025	<ul style="list-style-type: none"> To achieve the WHO Global NCD Action Plan⁴⁴
2016	<ul style="list-style-type: none"> The United Nations Economic and Social Council (ECOSOC) encouraged Task Force members to support nations in bringing upon the new NCD-related targets mentioned in the 2030 Agenda for Sustainable Development into their national responses⁴⁵ The Global Hearts Initiative was launched by WHO, the US Centres for Disease Control and Prevention and other partners to reduce salt intake⁴⁵ WHO issued its first Global report on diabetes⁴⁵
2015	<ul style="list-style-type: none"> The WHO Model List of Essential Medicines included 16 low- and high-cost medicines which could either increase survival periods for common cancers or successfully cure up to 90% of patients with rare cancers⁴⁵ WHO issued new guidelines, which recommend limiting daily intake of free sugars to below 10% of total energy intake⁴⁵
2014	<ul style="list-style-type: none"> The Global Coordination Mechanism to prevent and control NCDs established by the WHO Member States⁴⁵ The WHO Commission on Ending Childhood Obesity established by the WHO Director-General⁴⁵
2013	<ul style="list-style-type: none"> The World Health Assembly adopted a comprehensive global monitoring framework for NCDs⁴⁵ WHO issued a Global brief on hypertension and made blood pressure monitoring the theme for World Health Day to increase public awareness⁴⁵
2011	<ul style="list-style-type: none"> The UN General Assembly held a high-level meeting on NCDs and adopted a far-reaching Political Declaration⁴⁵
2010	<ul style="list-style-type: none"> A set of recommendations on the marketing of foods and beverages containing high sugar, salt and fats to children was approved by the World Health Assembly⁴⁵ WHO issued its first Global recommendations on physical activity for health purposes⁴⁵
2007	<ul style="list-style-type: none"> WHO issued a comprehensive approach towards surveillance, prevention and control of chronic respiratory diseases at a global level⁴⁵

Impact on South Africa and India

South Africa is a unique country which suffers from a quadruple burden of disease. AMR has a mass effect on the people of this country, as 7 700 000 people in South

Africa are living with HIV and 51% of the country's total deaths are attributed to NCDs.^{46,47} Furthermore, the country's negative GDP growth rate of -17.1% does not provide for forays towards more expensive medications.⁴⁸ In India, 2100000 people are living with HIV,⁴⁹ and 63% of total deaths are due to NCDs.⁵⁰

The issue of AMR comes into play when the infrastructure and support system of the health care system is weak. Figures 1 and 2 below illustrate the health care personnel per 1000 population in South Africa and India, respectively.

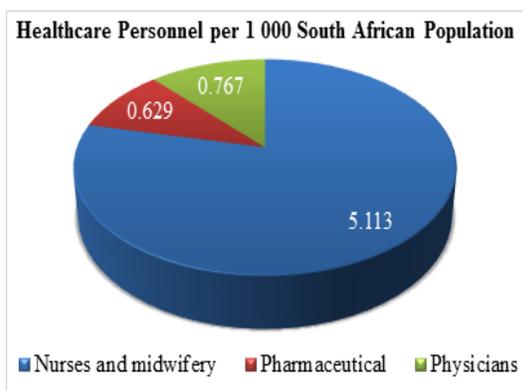


Figure 1: Pie Chart for Healthcare Personnel per 1 000 South African Population.⁵¹⁻⁵³

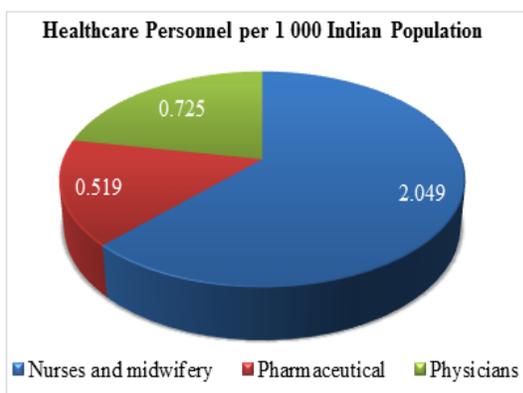


Figure 2: Pie Chart for Healthcare Personnel per 1 000 Indian Population.⁵¹⁻⁵³

Health care providers fall short in prevention and control of AMR, along with other diseases. Along with insufficient staff compliments, the budget allocated to the health care sector poses further problems. South Africa and India spend 8.8% and 4.7% of their GDP on health care, respectively, which is much less than the 15% annual budget agreed by the Abuja Declaration.⁵⁴⁻⁵⁶ Unsustainability is introduced when there is disproportionate sharing of the funds. In South Africa, less than 50% of the total GDP allocated to health

expenditure is provided to the public sector,^{55,56} which caters for 84% of the country's population.⁵⁷ AMR is a burden which could be prevented with sufficient health promotion and pharmaceutical care.

These are challenges and shortcomings in South Africa and India, as well as in other LMICs. The UN has put forward the Global Goals to end poverty, protect the planet and ensure that all people enjoy peace and prosperity.⁵⁸ There is also a relationship between health beliefs and the increased demand for antimicrobial medicines. Use of antimicrobial medicines is strongly influenced by social constraints and cultural views of infectious diseases requiring antimicrobial treatment. Therefore, several countries have launched national campaigns to educate physicians and patients about the irrational use of antimicrobials and the risk of AMR.⁵⁹

Why the Slow Movement for AMR?

AMR is a major global problem, yet relatively few actions have been taken to combat it.² A comparison between Tables 1-3 highlights the challenges with regards to correcting the potential crisis. It took decades before HIV/AIDS was given the attention it needed and, ever since, the momentum to reduce its prevalence has been ongoing. Since HIV/AIDS has a negative impact on public health and the economy, stringent policies were implemented.^{60,61} As compared to NCDs and AMR, HIV/AIDS did not face similar challenges with regards to self-serving and conflicts of interest of industries, other than the pharmaceutical industry. NCDs are the leading cause of death globally, although this too was an area which took time before major players like the UN pushed for resolutions.⁶² Management and prevention of NCDs are challenging, as the significance of policy implementation is strongly influenced by the commercial interests of tobacco, alcohol, beverage and processed food industries. These industries play an active role in influencing the public through advertisements and policy-makers minimise regulation in order to maximise profits.^{63,64} Antimicrobials indirectly affect the mortality rates of both HIV/AIDS and NCDs. Therefore, AMR requires a greater force towards prevention as well as Research and Development (R&D) of new antimicrobials.

According to pharmaceutical manufacturers, the lack of development of new antimicrobials is owed to the law of supply and demand. Since NCDs are the current focus of health concerns, the demand for treating these diseases is resulting in sufficient profits for manufacturers.¹² The pharmaceutical industry is a key stakeholder in manufacturing and distributing antimicrobials, as well

as in R&D of new antimicrobials. However, there is potential conflict of interest where profits are prioritized over patients' welfare, which acts as a limiting factor in combating AMR.^{65,66} AMR affects everyone around the world; therefore, there is a demand for new antimicrobials, particularly in LMICs. However, LMICs cannot afford to fund expensive R&D projects themselves, nor can they afford the expected high prices of these new antimicrobials.

If one considers the trend, and particularly the goal of stakeholders, it would become clear that action was taken against HIV/AIDS and NCDs only when the diseases progressed to and severely impacted high-income countries (HICs). As HICs can afford quality therapy, pharmaceutical industries are willing to develop and manufacture new treatment to meet the demand. According to the Access to Medicine Index, the top five pharmaceutical industries in providing access to medication for the year 2016 are GlaxoSmith Kline plc., Johnson & Johnson, Novartis AG, Merck KGaA and Merck & Co Inc. All five of these pharmaceutical industries mainly manufacture pharmaceutical products for NCDs and communicable diseases such as HIV/AIDS, which further indicates disease prevalence and increased demand⁶⁷⁻⁷¹

The Access to Medicines Index stimulates and guides pharmaceutical industries to cater more for populations in LMICs, which do not have access to essential medicines or vaccines. The Index analyses how the top 20 research-based pharmaceutical corporations make medicines, vaccines and diagnostics more accessible in LMICs.⁷² Excellent changes are being driven and integrated worldwide due to the rigorous analysis of best practices by multinationals⁷³ with the production of 20 company report cards on six sections.⁷⁴ Engaging with the pharmaceutical industry in strategic collaborations has resulted in the development of 420 products to respond to 51 of the most burdensome diseases identified in LMICs by the top 20 multinationals.⁷⁵ To make products available and affordable, some pharmaceutical industries are demonstrating good practice in approaches towards needs-responsive product registration, and are also considering affordability to a greater extent. However, only 25% of the countries with high-need have product registration, and only 5% of pharmaceuticals are covered by pricing strategies that meet the Index's criteria. And though there is increased licensing, large middle-income countries such as Mexico and Thailand, home to the majority of the world's poor, are excluded.⁷⁶

Despite ongoing policies and support provided by the WHO since late 1970s with regards to essential medicines,

one third of the global population (close to two billion people) to date do not have access to essential medicines. This aspect is now being propelled by the 'Towards Access 2030' supported by the Sustainable Development Goals⁷⁷

Do the Sustainable Development Goals Help?

The 8 Millennium Development Goals (MDGs) focused on health to a large extent, as MDG 4 – reduce child mortality; MDG 5 – improve maternal health; and MDG 6 – combat HIV/AIDS, malaria and other diseases, were solely aimed at health-related issues. Furthermore, MDG 1 – eradicate extreme poverty and hunger, and MDG 6 both indirectly favoured the battle against AMR.⁷⁸ Poverty is a huge risk factor to AMR, and influences responses to HIV/AIDS. It would involve the control of opportunistic diseases, which require the use of antimicrobials. The use of antimicrobials to control the opportunistic diseases would mean promoting the correct use of medication, so that mortality resulting from HIV is low. It may have also probed the development of new antimicrobials. MDGs have now passed, therefore we need to scrutinize the new way forward, as embodied in the Sustainable Development Goals (SDGs).

The SDGs comprise of 17 goals and 169 targets,⁷⁹ but the focus is more generic than the MDGs. SDGs hold one goal dedicated to health; SDG 3 – good health and well-being.⁵⁸ If equal efforts are being put into various types of diseases, then this may result in unsustainability and higher mortality rates, because the number of deaths in the world is owed to various diseases, but in different capacities. If SDG 3 and SDG 10 – reduced inequality – were yolked together, justice for health will be served. SDG 10 aims to create preferential treatment in trade for developing nations and least developed nations, which can help reduce inequalities by creating more export opportunities.⁸⁰ If this is made possible, then LMICs would be able to import medications at more affordable rates, and increase the access to medicines, consequently reducing mortality rates and increasing sustainability. Since the effect of AMR is more pronounced in LMICs, and affordability is an abundant issue, this may create opportunity to address the problem. Furthermore, SDG 4 – quality education – when combined with SDG 3 and SDG 10, can create an even larger difference. Quality education at an early stage allows for children to develop basic cognitive and language skills, as well as EQ.⁸¹ SDG 4 also strongly supports the reduction of persistent disparities, which further supports SDG 1, and will indirectly aid in achieving SDG 3, as health education may result in better self-care and self-management, and thus improve health outcomes.^{81,82}

WHO's Role in Combating AMR

Dr Marc Sprenger, WHO Director of the Antimicrobial Resistance Secretariat, stated that many low-income countries require greater support in tackling AMR. Over 90% of the global population resides in countries that have developed, or are currently developing, a national action plan on AMR. More than 80% of high-income countries have a national action plan in place, or are developing one. They are thus in a better position to tackle the challenges of AMR. In comparison, only about 30% of low-income countries either have or are developing a national action plan. Low-income countries require greater support, as they lack expertise to develop a national action plan, and face greater exposure to infectious diseases, as their health systems are much weaker and lack preparedness. The WHO Director-General, Dr Tedros Adhanom Ghebreyesus, also considers AMR as one of the most complex global challenges faced by his leadership.⁸

In September 2016, global leaders met at the United Nations General Assembly to tackle the threat of AMR. This was the fourth time in history that a health-related problem was discussed in the meeting, which indicates the worldwide significance of AMR. A resolution was drafted which called for action, ensuring the appropriate use of antimicrobials across human as well as animal health.^{35,36}

To tackle the challenges of AMR, the WHO, Food and Agriculture Organization of the United Nations (FAO), and World Organisation for Animal Health (OIE) launched the Global Database for Antimicrobial Resistance Country Self-Assessment. This database presents information from a questionnaire which was distributed to nations in November 2016, and provides open access to nations' statutes regarding their action towards implementation of the global action plan on AMR.⁸⁴

In 1977, the World Health Assembly of "Health for All" was used as a guiding principle, along with health policies to launch the *WHO Model list of essential medicines*. The WHO Essential Medicines List (EML), which is updated and revised biennially, is used by many nations as a measure to increase access to and availability of medicines. Many nations also use the EML as a guide to develop their own lists. The *WHO Model list of essential medicines* for 2017 includes information on which antibiotics to use for common infections, as well as which to use for more serious conditions. WHO experts grouped antibiotics into three categories – Access, Watch, and Reserve – and recommended when each category of antibiotics should be used, as shown in Table 4. This is to ensure availability of the required antibiotics and

the appropriate prescription of antibiotics for a specific infection, further enhancing treatment outcomes and reducing the development of AMR.⁸⁵

Table 4: Categories of Antibiotics and their Recommendations.^{85,86}

Category of Antibiotics	Recommendations	Examples of Antibiotics
Access	<ul style="list-style-type: none"> Widely available, affordable and quality-assured Treat wide range of common infections 	<ul style="list-style-type: none"> Amoxicillin Benzylpenicillin Clindamycin Doxycycline Metronidazole
Watch	<ul style="list-style-type: none"> First- or second-choice treatments for smaller number of infections Relatively high resistance potential 	<ul style="list-style-type: none"> Ceftriaxone Erythromycin Levofloxacin Meropenem Vancomycin
Reserve	<ul style="list-style-type: none"> Last-resort; only used in most severe conditions when all other alternatives fail Used for life-threatening infections due to multidrug-resistance bacteria 	<ul style="list-style-type: none"> Aztreonam Colistin Fosfomycin (IV) Linezolid Polymyxin B

In 2017, the WHO also published the fifth revision of the Critically Important Antimicrobials for Human Medicines (CIA list). This CIA list is intended for all stakeholders involved in managing AMR and ensures that all antimicrobials are used appropriately in human and veterinary medicine.⁸⁷ On 27 February 2017, upon requests by Member States, WHO published a priority pathogens list of antibiotic-resistant bacteria. The list is a catalogue containing 12 families of bacteria that pose the highest threat to public health and promotes R&D of new and effective antibiotics.⁸⁸ Table 5 below shows the WHO priority pathogens list, along with their priority status and the antibiotics to which the pathogen is resistant.

The grave concerns AMR carries is the reason the WHO recently announced the formation of an *ad hoc* Interagency Coordination Group (IACG) in March 2017, co-chaired by the UN Deputy Secretary-General and the WHO Director-General. Using expertise from appropriate stakeholders, the IACG guides required approaches to ensure sustained effective global actions to tackle and combat AMR.⁸⁹ WHO continues to encourage individuals to engage in hand hygiene and infection prevention and control programmes by participating in the 'SAVE LIVES: Clean Your Hands' campaign, which is held annually on or around 5 May. For the 2017 campaign, the materials were co-branded with 'Antibiotics, handle

Table 5: WHO Priority Pathogens List for R&D of New Antibiotics.⁸⁸

Priority Status	Pathogen	Resistant Antibiotic
Priority 1: Critical	<i>Acinetobacter baumannii</i>	carbapenem-resistant
	<i>Pseudomonas aeruginosa</i>	carbapenem-resistant
	<i>Enterobacteriaceae*</i>	carbapenem-resistant, 3 rd generation cephalosporin-resistant
Priority 2: High	<i>Enterococcus faecium</i>	vancomycin-resistant
	<i>Staphylococcus aureus</i>	methicillin-resistant, vancomycin intermediate and resistant
	<i>Helicobacter pylori</i>	clarithromycin-resistant
	<i>Campylobacter</i>	fluoroquinolone- resistant
	<i>Salmonella spp.</i>	fluoroquinolone- resistant
	<i>Neisseria gonorrhoeae</i>	3 rd generation cephalosporin-resistant, fluoroquinolone- resistant
Priority 3: Medium	<i>Streptococcus pneumoniae</i>	penicillin-non- susceptible
	<i>Haemophilus influenzae</i>	ampicillin-resistant
	<i>Shigella spp.</i>	fluoroquinolone- resistant

with care' as hand hygiene is key for effective infection prevention and control to combat AMR.⁹⁰ Furthermore, the World Antibiotic Awareness Week aims to raise awareness on AMR and encourage optimum practices amongst the public, health workers, farmers, food-producing companies, veterinarians and policy makers, in order to avoid AMR from developing further.⁸⁷

Youth Empowerment

Youth and young health care professionals have been excellent examples in bringing about change and driving progressive solutions. Innovation, access and empowerment have become the three pillars for Universities Allied for Essential Medicines⁹¹ responsible for several positive changes in the area of access to essential medicines,⁹²⁻⁹⁴ including antibiotics.⁹⁵ Young professionals are driving this process, while gathering evidence and increasing their outreach in the form of publications⁹⁶⁻⁹⁹ as well, to coordinate focussed activities on essential medicines. While literature surrounding adult leadership focusses on “issues of authority (voice, influence and decision-making power)”, youth leadership

tends to focus on “issues of ability (skills, knowledge and talents)”.¹⁰⁰ Youth leadership positively influences community participation as knowledge of policies is put into action for the well-being of society.¹⁰¹

CONCLUSION

Education on the rational use of antimicrobials is key for agricultural industries, health care professionals and patients. AMR awareness is essential for the public, as health education positively affects individuals' health and well-being. Youth participation demonstrates a positive effect on outcomes, including its effect on community change.¹⁰¹

As advocated by WHO, policies at a national and international level are needed to tackle AMR. Coordinated initiatives are needed to convince the public and policy-and decision-makers of the medical as well as economic advantages of combating AMR.⁹ There is also an urgent need for R&D addressing newly prioritised antibiotic resistant-pathogens.³²

ACKNOWLEDGEMENT

Rhodes University is acknowledged for all of its support.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

AMR: Antimicrobial Resistance; **APIs:** Active pharmaceutical ingredients; **APUA:** Alliance for the Prudent Use of Antibiotics; **ARV:** Antiretroviral; **CARB-X:** Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator; **CIA:** Critically Important Antimicrobials; **ECOSOC:** Economic and Social Council; **EML:** Essential Medicines List; **FAO:** Food and Agriculture Organization of the United Nations; **HICs:** High-income countries; **IACG:** Interagency Coordination Group; **ISPOR:** International Society for Pharmacoeconomics and Outcomes Research; **LMICs:** Low- and middle-income countries; **MPP:** Medicine Patent Pool; **MDGs:** Millennium Development Goals; **NCDs:** Non-communicable diseases; **OIE:** World Organisation for Animal Health; **R&D:** Research and Development; **RSPRUD:** Rajasthan Society for Promotion of Rational Use of Drugs; **SDGs:** Sustainable Development Goals; **UN:** United Nations; **UNGASS:** United Nations General Assembly Special Session; **WHO:** World Health Organization.

REFERENCES

- Department of Health Republic of South Africa. Implementation Plan for the Antimicrobial Resistance Strategy Framework in South Africa: 2014-2019. 2015 [cited 2017 Jun 26]. Available from: <http://www.health.gov.za/index.php/antimicrobial-resistance?download=1175:implementation-plan-for-the-antimicrobial-resistance-strategy-framework-in-south-africa-2014-2019>
- WHO. Antimicrobial resistance. Who Int. 2016. [cited 2017 Jun 20]. Available from: <http://www.who.int/mediacentre/factsheets/fs194/en/>
- Review on Antimicrobial Resistance. Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations. 2014. [cited 2017 Jun 20]. Available from: https://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations_1.pdf
- Robinson TP, Bu DP, Carrique-Mas J, Fèvre EM, Gilbert M, Grace D, *et al.* Antibiotic resistance is the quintessential One Health issue. *Trans R Soc Trop Med Hyg.* 2016;110(7):377-80.
- Smith RD, Coast J. Antimicrobial resistance: A global response. *Bull World Health Organ.* 2002;80(2):126-33.
- WHO. 10 Facts on Antimicrobial Resistance. Who Int. 2017. [cited 2017 Jun 20]. Available from: http://www.who.int/features/factfiles/antimicrobial_resistance/facts/en/index9.html
- WHO. Antibiotic resistance. Who Int. 2016. [cited 2017 Jun 20]. Available from: <http://www.who.int/mediacentre/factsheets/antibiotic-resistance/en/>
- Planta MB. The role of poverty in antimicrobial resistance. *J Am Board Fam Med.* 2007;20(6):533-9.
- Roca I, Akova M, Baquero F, Carlet J, Cavaleri M, Coenen S, *et al.* The global threat of antimicrobial resistance: Science for intervention. *New Microbes New Infect.* 2015;6:22-9.
- Chang Q, Wang W, Regev-Yochay G, Lipsitch M, Hanage WP. Antibiotics in agriculture and the risk to human health: How worried should we be?. *Evol Appl.* 2015;8(3):240-7.
- Lhermie G, Gröhn YT, Raboisson D. Addressing Antimicrobial Resistance: An Overview of Priority Actions to Prevent Suboptimal Antimicrobial use in Food-Animal Production. *Front Microbiol.* 2017;7:2114. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5216048/>
- Powers JH. Antimicrobial drug development – the past, the present and the future. *Clin Microbiol Infect.* 2004;10:23-31.
- Mendelson M, Matsoso MP. The South African Antimicrobial Resistance Strategy Framework. 2015. [cited 2017 Jun 20]. Available from: http://www.fidssa.co.za/Content/Documents/2015_01.pdf
- South African Department of Health. Antimicrobial Resistance Background Document. 2017. [cited 2017 Jun 20]. Available from: http://www.fidssa.co.za/Content/Documents/AMR_Background_document_FINAL_March15.pdf
- Gutiérrez-Delgado C, Guajardo-Barrón V. The double burden of disease in developing countries: The Mexican experience. *Adv Health Econ Health Serv Res.* 2009;21:3-22.
- Ventola CL. The Antibiotic Resistance Crisis. *Pharm Ther.* 2015;40(4):277-83.
- WHO. HIV: From a devastating epidemic to a manageable chronic disease. Who Int. 2017. [cited 2017 Jun 21]. Available from: <http://www.who.int/publications/10-year-review/hiv/en/>
- Henry J. Kaiser Family Foundation. Global HIV/AIDS Timeline. Kff.Org. 2016. [cited 2017 Jun 25]. Available from: <http://www.kff.org/global-health-policy/timeline/global-hivaids-timeline/>
- UNAIDS. UNAIDS announces that the goal of 15 million people on life-saving HIV treatment by 2015 has been met nine months ahead of schedule. 2015. [cited 2017 Jun 25]; Available from: http://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2015/july/20150714_PR_MDG6report
- United Nations. Sustainable Development Goals-Goal 3. Un Org. 2017. [cited 2017 Jun 25]. Available from: <http://www.un.org/sustainabledevelopment/health/>
- MPP. About the Medicines Patent Pool (MPP). Medicinespatentpool Org. 2017. [cited 2017 Jun 25]. Available from: <http://www.medicinespatentpool.org/about/>
- Petersen PE. Policy for prevention of oral manifestations in HIV/AIDS: The approach of the WHO Global Oral Health Program. *Adv Dent Res.* 2006;19(1):17-20.
- UNAIDS. Keeping the Promise - Summary of the Declaration of Commitment on HIV/AIDS. 2002;35. [cited 2017 Jun 21]. Available from: http://www.unaids.org/sites/default/files/sub_landing/files/jc668-keepingpromise_en.pdf
- Swarns RL. Drug Makers Drop South Africa Suit over AIDS Medicine. The New York Times. 2001. [cited 2017 Jun 21]; Available from: <https://www.nytimes.com/2001/04/20/world/drug-makers-drop-south-africa-suit-over-aids-medicine.html>
- WHO. Essential Medicines and Health Products: Prequalification of Medicines Programme. Extranet Who Int. 2017. [cited 2017 Jun 25]. Available from: <https://extranet.who.int/prequal/content/overview-history-mission>
- CDC. CDC Global HIV/AIDS Milestones: On the Path to an AIDS-Free Generation. Cdc Gov. 2017. [cited 2017 Jun 25]. Available from: <https://www.cdc.gov/globalaids/global-hiv-aids-at-cdc/aids-free-generation.html>
- Millennium Project. About the MDGs [Internet]. unmillenniumproject.org. 2006 [cited 2017 Jun 25]. Available from: <http://www.unmillenniumproject.org/goals/>
- AVERT. Origin of HIV and AIDS. Avert Org. 2017. [cited 2017 Jun 21]. Available from: <https://www.avert.org/professionals/history-hiv-aids/origin>
- Davies J, Davies D. Origins and Evolution of Antibiotic Resistance. *Microbiol Mol Biol Rev.* 2010;74(3):417-33.
- Inoue H, Minghui R. Antimicrobial resistance: translating political commitment into national action. *Bull World Health Organ.* 2017;95(4):241-312.
- WHO. WHO publishes list of bacteria for which new antibiotics are urgently needed. Who Int. 2017. [cited 2017 Jun 26]. Available from: <http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/>
- WHO. WHO stresses urgent need for R&D for drug-resistant TB alongside newly-prioritized antibiotic-resistant pathogens. Who Int. 2017. [cited 2017 Jun 25]. Available from: <http://www.who.int/mediacentre/news/releases/2017/drug-resistant-tb/en/>
- California Life Sciences Institute. International Partnership Established To Tackle Antimicrobial Resistance. 2016. [cited 2017 Jun 25]; Available from: <http://califesciencesinstitute.org/international-partnership-established-to-tackle-antimicrobial-resistance/>
- IFPMA. Leading Pharmaceutical Companies Present Industry Roadmap to Combat Antimicrobial Resistance. 2016. [cited 2017 Jun 25]. Available from: https://www.ifpma.org/wp-content/uploads/2016/09/AMR-Roadmap-Press-Release_FINAL.pdf
- Thursky K. Milestones, challenges in antimicrobial stewardship. *Doctorportal Com Au.* 2017. [cited 2017 Jun 25]. Available from: <https://www.doctorportal.com.au/mjainsight/2017/2/milestones-challenges-in-antimicrobial-stewardship/>
- WHO. United Nations high-level meeting on antimicrobial resistance. Who Int. 2016. [cited 2017 Jun 25]. Available from: <http://www.who.int/mediacentre/events/2016/antimicrobial-resistance/en/>
- WHO. Global Action Plan on Antimicrobial Resistance. 2015. [cited 2017 Jun 25]. Available from: http://www.wpro.who.int/entity/drug_resistance/resources/global_action_plan_eng.pdf
- APUA. India - Alliance for the Prudent Use of Antibiotics. Apua Org. 2016. [cited 2017 Jun 25]. Available from: <http://apua.org/india/>
- WHO. About SAVE LIVES: Clean Your Hands. Who Int. 2017. [cited 2017 Jun 25]. Available from: <http://www.who.int/gpsc/5may/background/en/>
- APUA. South Africa: Alliance for the Prudent use of Antibiotics. Apua Org. 2016. [cited 2017 Jun 25]. Available from: <http://apua.org/south-africa/>
- APUA. Our History: Alliance for the Prudent use of Antibiotics. Apua Org. 2016. [cited 2017 Jun 25]. Available from: <http://apua.org/ourhistory/>
- Gelband H, Duse AG. GARP: Executive summary. *S Afr Med J.* 2011;101(8):552-5.
- ECDC. European challenges on antimicrobial resistance from a one health perspective. 2012. [cited 2017 Jun 26]. Available from: http://ecdc.europa.eu/en/aboutus/who-we-are/Director%20Speeches/20120314_AMR_presentation_Copenhagen_EUpresidency.pdf
- WHO. Global NCD Action Plan. 2014. [cited 2017 Jun 25]. Available from: <http://www.who.int/nmh/publications/ncd-infographic-2014.pdf>
- WHO. Noncommunicable diseases: The slow motion disaster. Who Int. 2017. [cited 2017 Jun 25]. Available from: <http://www.who.int/publications/10-year-review/ncd/en/>
- UNAIDS. South Africa | UNAIDS. Unaid.org. 2018. [cited 2020 August 28]. Available from: <http://www.unaids.org/en/regionscountries/countries/southafrica>
- WHO. Noncommunicable Diseases (NCD) Country Profiles: South Africa. 2018. [cited 2020 August 28]. Available from: https://www.who.int/nmh/countries/2018/zaf_en.pdf?ua=1
- Trading Economics. South Africa GDP Annual Growth Rate. [cited 2020 August 28]. Available from: <https://tradingeconomics.com/south-africa/gdp-growth-annua>

49. UNAIDS. India | UNAIDS. Un aids Org. 2017. [cited 2017 Jun 25]. Available from: <http://www.unaids.org/en/regionscountries/countries/india/>
50. WHO. Noncommunicable Diseases (NCD) Country Profiles: India. 2018. [cited 2020 August 28]. Available from https://www.who.int/nmh/countries/2018/ind_en.pdf?ua=1
51. WHO. Density of Nursing and Midwifery Personnel. Gamapserver Who Int. 2017. [cited 2017 Jun 25]. Available from: http://gamapserver.who.int/gho/interactive_charts/health_workforce/NursingMidwiferyDensity/tablet/atlas.html
52. WHO. Density of Pharmaceutical Personnel. Gamapserver Who Int. 2017. [cited 2017 Jun 25]. Available from: http://gamapserver.who.int/gho/interactive_charts/health_workforce/PharmaceuticalDensity/tablet/atlas.html
53. WHO. Density of Physicians. Gamapserver Who Int. 2017. [cited 2017 Jun 25]. Available from: http://gamapserver.who.int/gho/interactive_charts/health_workforce/PhysiciansDensity_Total/tablet/atlas.html
54. WHO. The Abuja Declaration: Ten Years On. Who Int. 2011. [cited 2017 Jun 25]. Available from: http://www.who.int/healthsystems/publications/abuja_declaration/en/
55. Trading Economics. South Africa: Health expenditure, total (% of GDP). Tradingeconomics Com. 2017. [cited 2017 Jun 25]. Available from: <https://tradingeconomics.com/south-africa/health-expenditure-total-percent-of-gdp-wb-data.html>
56. The World Bank. Health expenditure, total (% of GDP). Data Worldbank Org. 2017. [cited 2017 Jun 25]. Available from: <http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS>
57. South African Department of Health. National Health Insurance in South Africa - Policy Paper. 2011. [cited 2017 Jun 25]. Available from: <http://www.gov.za/sites/www.gov.za/files/nationalhealthinsurance.pdf>
58. United Nations. Sustainable Development Goals. Un Org. 2017. [cited 2017 Jun 25]. Available from: <http://www.un.org/sustainabledevelopment/sustainable-development-goals/>
59. Harbarth S, Samore MH. Antimicrobial Resistance Determinants and Future Control. *Emerg Infect Dis.* 2005;11(6):794-801.
60. Whiteside A. How HIV / AIDS impacts on the health sector. *AIDS Anal Afr.* 1997;7(2):8-11.
61. Bayer R, Edington C. HIV Testing, Human Rights, and Global AIDS Policy: Exceptionalism and Its Discontents. *J Health Polit Policy Law.* 2009;34(3):301-23.
62. WHO. Noncommunicable diseases.. Who Int. 2017. [cited 2017 Jun 25]. Available from: <http://www.who.int/mediacentre/factsheets/fs355/en/>
63. Smith K, Dorfman L, Freudenberg N, Hawkins B, Hilton S, Razum O, *et al.* Tobacco, Alcohol and Processed Food Industries – Why Do Public Health Practitioners View Them So Differently?. *Front Public Health.* 2016;4:64. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4826885/>
64. WHO. Unhealthy commodity producers, conflict of interest and effective health governance. 2017. [cited 2017 Jun 25]. Available from: <http://www.who.int/global-coordination-mechanism/dialogues/Private-sector-role-Conflicts-Interst.pdf?ua=1>
65. Durrant C. The responsibility of the pharmaceutical industry. *Clin Microbiol Infect.* 2001;7:2-4.
66. Aiello AE, King NB, Foxman B. Ethical Conflicts in Public Health Research and Practice. *Am J Public Health.* 2006;96(11):1910-4.
67. Access to Medicine Foundation. Merck and Co., Inc. *Accesstomedicineindex Org.* 2016. [cited 2017 Jun 25]. Available from: <https://accesstomedicineindex.org/report-cards/merck-co-inc/>
68. Access to Medicine Foundation. GlaxoSmithKline plc. *Accesstomedicineindex Org.* 2016. [cited 2017 Jun 25]. Available from: <https://accesstomedicineindex.org/report-cards/glaxosmithkline-plc/>
69. Access to Medicine Foundation. Johnson and Johnson. *Accesstomedicineindex Org.* 2016. [cited 2017 Jun 25]. Available from: <https://accesstomedicineindex.org/report-cards/johnson-johnson/>
70. Access to Medicine Foundation. Novartis AG. *Accesstomedicineindex Org.* 2016 [cited 2017 Jun 25]. Available from: <https://accesstomedicineindex.org/report-cards/novartis-ag/>
71. Access to Medicine Foundation. Merck KGaA. *Accesstomedicineindex Org.* 2016. [cited 2017 Jun 25]. Available from: <https://accesstomedicineindex.org/report-cards/merck-kga/>
72. Access to Medicine Foundation. Access to Medicine Index. *Accesstomedicineindex Org.* 2016. [cited 2017 Jun 26]. Available from: <http://accesstomedicineindex.org/>
73. Access to Medicine Foundation. Best and innovative practices [Internet]. *Accesstomedicineindex Org.* 2016. [cited 2017 Jun 26]. Available from: <http://accesstomedicineindex.org/best-innovative-practices/>
74. Access to Medicine Foundation. Report cards. *Accesstomedicineindex Org.* 2016. [cited 2017 Jun 26]. Available from: <http://accesstomedicineindex.org/report-cards/>
75. Access to Medicine Foundation. Collaborative research models appear effective in engaging the industry in developing urgently needed products with low commercial potential. *Accesstomedicineindex Org.* 2016. [cited 2017 Jun 26]. Available from: <http://accesstomedicineindex.org/key-findings/collaborative-research-models-appear-effective-in-engaging-the-industry-in-developing-urgently-needed-products-with-low-commercial-potential/>
76. Access to Medicine Foundation. Good practice in making products affordable and available is limited. *Accesstomedicineindex Org.* 2016. [cited 2017 Jun 26]. Available from: <http://accesstomedicineindex.org/key-findings/good-practice-making-products-affordable-available-limited/>
77. WHO. Towards Access 2030: WHO Medicines and Health Products Programmed Strategic Framework 2016-2030. 2017. [cited 2017 Jun 26].
78. United Nations. Millennium Development Goals. Un Org. 2017. [cited 2017 Jun 25]. Available from: <http://www.un.org/millenniumgoals/>
79. United Nations. Sustainable Development Knowledge Platform: Transforming our world: the 2030 Agenda for Sustainable Development. Sustainabledevelopment Un Org. 2017. [cited 2017 Jun 25]. Available from: <https://sustainabledevelopment.un.org/post2015/transformingourworld>
80. United Nations. Sustainable Development Knowledge Platform: Sustainable Development Goal 10. Sustainable Development un org. 2017. [cited 2017 Jun 25]. Available from: <https://sustainabledevelopment.un.org/sdg10>
81. United Nations. Sustainable Development Knowledge Platform: Sustainable Development Goal 4. Sustainable Development Un org. 2017. [cited 2017 Jun 25]. Available from: <https://sustainabledevelopment.un.org/sdg4>
82. Adams RJ. Improving health outcomes with better patient understanding and education. *Risk Manag Healthc Policy.* 2010;3:61-72.
83. WHO. Superbugs: The world is taking action, but low-income countries must not be left behind. Who Int. 2017. [cited 2017 Jun 25]. Available from: <http://www.who.int/mediacentre/commentaries/2017/superbugs-taking-action/en/>
84. WHO. Antimicrobial resistance: Country progress in the implementation of the global action plan on antimicrobial resistance: WHO, FAO and OIE global tripartite database. Who Int. 2017. [cited 2017 Jun 25]. Available from: <http://www.who.int/antimicrobial-resistance/global-action-plan/database/en/>
85. WHO. WHO updates Essential Medicines List with new advice on use of antibiotics, and adds medicines for hepatitis C, HIV, tuberculosis and cancer. 2017. [cited 2017 Jun 25]. Available from: <http://www.who.int/mediacentre/news/releases/2017/essential-medicines-list/en/>
86. WHO. WHO Model List of Essential Medicines - 20th List. 2017. [cited 2017 Jun 25]. Available from: http://www.who.int/medicines/publications/essentialmedicines/20th_EML2017.pdf?ua=1
87. WHO. World Antibiotic Awareness Week. 2017. [cited 2017 Jun 25]. Available from: <http://www.who.int/campaigns/world-antibiotic-awareness-week/2017/event/en/>
88. WHO. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. Who Int. 2017. [cited 2017 Jun 25]. Available from: <http://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/>
89. WHO. Report of the First Meeting of the Interagency Coordination Group on Antimicrobial Resistance. 2017. [cited 2017 Jun 25]. Available from: <http://www.who.int/antimicrobial-resistance/interagency-coordination-group/IACG-firstMtgReport.pdf?ua=1>
90. WHO. Save lives: Clean Your Hands 2017. Who Int. 2017. [cited 2017 Jun 25]. Available from: <http://www.who.int/infection-prevention/campaigns/clean-hands/2017/en/>
91. UAEM. Universities Allied for Essential Medicines. Uaem Org. 2017. [cited 2017 Jun 26]. Available from: <https://uaem.org/>
92. Maciag K, Kishore SP. A step in the right direction. *Nat Rev Microbiol.* 2010;8(4):244.
93. Kishore SP, Tavera G, Hotez PJ. The Global Health Crisis and Our Nation's Research Universities. *PLoS Negl Trop Dis.* 2010;4(2):e635.
94. Chokshi DA. Improving Access to Medicines in Poor Countries: The Role of Universities. *Plos Med.* 2006;3(6):e136.

95. Greenberg A, Kiddell-Monroe R. Re Routing biomedical innovation: observations from a mapping of the alternative research and development (R&D) landscape. *Glob Health*. 2016;12(1):54.
96. UAEM. Cases of UK government using compulsory licenses [Internet]. UAEM Evidence. 2014. [cited 2017 Jun 26]. Available from: <https://uaemevidence.wordpress.com/2014/11/03/cases-of-uk-government-using-compulsory-licenses/>
97. UAEM. Drug price increases are common in the USA. UAEM Evidence. 2016. [cited 2017 Jun 26]. Available from: <https://uaemevidence.wordpress.com/2016/05/16/drug-price-increases-are-common-in-the-usa/>
98. UAEM. Ever greening is common. UAEM Evidence. 2016. Available from: <https://uaemevidence.wordpress.com/2016/05/16/evergreening-is-common/>
99. UAEM. MSF 3P (Push, Pull, Pool) Project for TB. UAEM Evidence. 2014. [cited 2017 Jun 26]. Available from: <https://uaemevidence.wordpress.com/2014/10/14/msf-3p-push-pull-pool-project-for-tb/>
100. MacNeil CA. Bridging generations: Applying 'adult' leadership theories to youth leadership development. *New Dir Youth Dev*. 2006;2006(109):27-43.
101. Checkoway BN, Gutierrez LM. Youth Participation and Community Change: An Introduction. *J Community Pract*. 2006;14(1-2):1-9.