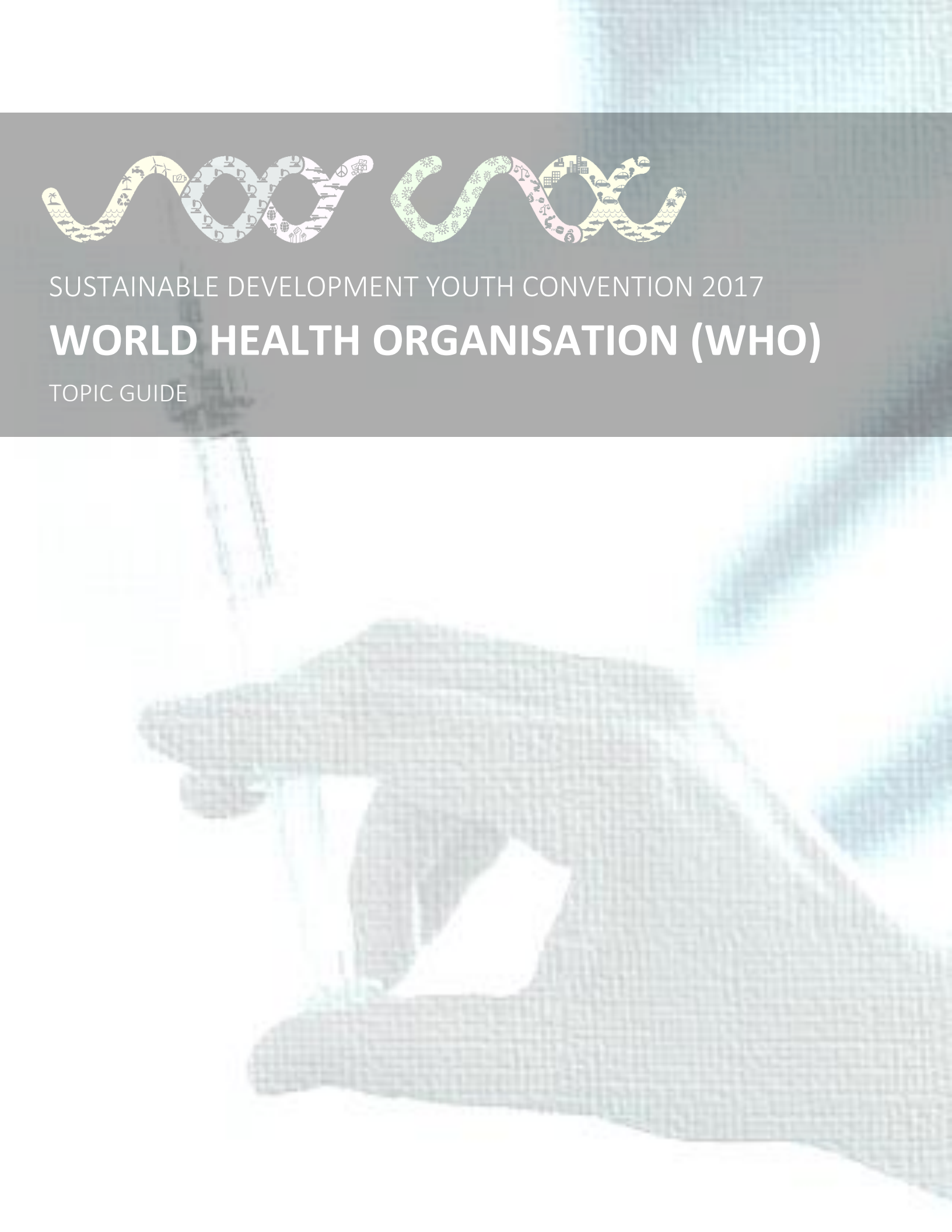
SUSTAINABLE DEVELOPMENT YOUTH CONVENTION 2017

WORLD HEALTH ORGANISATION (WHO)

TOPIC GUIDE



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ABOUT THE CHAIRS

TEOH JING YANG
HEAD CHAIR

Jing Yang sincerely wonders how the life of a Chinese health minister might be. Indeed, writing this topic guide has drained away his chakra and life energy, and reduced him to incoherent ponderings so please take the effort to read it. In other news, Jing Yang enjoys being picked up by fourteen-year old German girls during his free time and hopes to have similar opportunities in the near future. With a love for exotic hair and asking questions, he continues to search for people with similar interests. Jing Yang looks forward to a lively council where everyone speaks, and everyone speaks. If you see him looking at you, raise your placard. (Note: Points of personal privilege for "the Chair to stop staring creepily at me" are not in order.)

CHO HYUNMIN
VICE CHAIR

Hyunmin is blessed with an extensive knowledge of Korean, but please do not ask him to translate KPOP lyrics for you because he is very lazy. Hyunmin is right at home kayaking through gushing river trails or cycling through Pasir Ris park at one in the morning, but occasionally he will step indoors and grace his fellow chairs with his hatred for biology. As Hyunmin's second chairing experience, SDYC 2017 promises to be an interesting challenge he is excited to face. Hyunmin is looking forward to seeing extensively researched (haha) position papers and hopes for interesting arguments in council.

TAN ZHI HUA JOSHUA
VICE CHAIR

In his natural habitat with his headphones on and his gaming computer in front of him, Joshua may not appear like your typical, eloquent MUNner. Slap on a suit and some misplaced issues with sovereignty, however, and you will see a fearsome terror dominate conversations with his dry humour and concise arguments. President to the NUS High VC Club and a connoisseur of MUNs with 6 conferences under his belt, Joshua is looking forward to chairing for the first time during SDYC 2017. He hopes that all delegates will be informed and engaged in debating on antibiotics - and hopefully find a replacement for his waifu Emila-tan. Note: Memes are highly encouraged.

COMMITTEE INTRODUCTION

Established in 1948, the World Health Organization (WHO) is a specialized agency of the United Nations (UN), concerned with international public health. With 194 Member States, the WHO's primary role today is to direct and coordinate international health within the United Nations' system. The areas in which WHO work in includes health systems, non-communicable diseases, promoting health through life-course, communicable diseases, preparedness, surveillance and response, and corporate service. WHO coordinates international outbreaks response using resources from the Global Outbreak Alert and Response Network (GOARN), which is a collaboration of existing institutions and networks. This network pools human and technical resources for rapid identification, confirmation and response to outbreaks of international importance.

On the issue of antibiotic resistance, WHO has played a vital role in information collection, provision of guidelines and assessing the national regulatory capacities of member states. Articles 19 to 23 of the WHO constitution is of importance in authorising the World Health Assembly (herein called the Health Assembly) of WHO with the legal mandate:

a) to 'adopt conventions or agreements with respect to any matter within the competence of the Organization' with a two-third vote of the Health Assembly(Article 19),
b) to 'adopt regulations concerning: (a) sanitary and quarantine requirements and other procedures designed to prevent the international spread of disease; … (c) standards with respect to diagnostic procedures for international use; (d) standards with respect to the safety, purity and potency of biological, pharmaceutical and similar products moving in international commerce; … .',
c) to 'make recommendations to Members with respect to any matter within the competence of the Organization'

with Member States required to take necessary actions for compliance within eighteen months of an adoption of a convention or agreement.[1]

[1]"CONSTITUTION OF THE WORLD HEALTH ORGANIZATION." Accessed June 24, 2017. http://www.who.int/governance/eb/who_constitution_en.pdf.

KEY QUESTION

In response to the spread of antibiotic resistance, what are the domestic and international policies that the global community can undertake to suppress the spread and ensure the long-term accessibility of antibiotics and relevant medicine for future generations? Resolutions should realistically address challenges arising in: (i) the rational use of medicine, (ii) infection control measures, and (iii) innovation and development.

TOPIC INTRODUCTION

Discovered by Alexander Fleming in 1928, Penicillin is regarded as the world's first antibiotic, a type of drug that works by either killing the bacteria or inhibiting its reproduction. Frequently called the Miracle Drug, penicillin is believed to have saved at least 200 million lives since its first medicinal use. Today, antibiotics are able to treat patients suffering from all types of diseases and infections, continuously demonstrating their effectiveness. However, the perceived security derived from their ubiquitous use understates the development of antibiotic resistance in rapidly mutating bacterial strains and growing concerns for the future of antibiotics.

Antibiotic resistance stems from the selective pressure that antibiotic drugs impose on bacterial populations, where random mutation confers a spectrum of antibiotic resistance – when antibiotics are admitted into the body, a small proportion of the bacteria population that is resistant to the specific antibiotic survives while the rest are inhibited. These survivors soon multiply to constitute a larger portion of the population. The cycle repeats itself until the bacterial strain is completely resistant to the antibiotics in question. A different drug must then be used to treat persons infected with the resistant strain.

However, for a portion of the population to be resistant in the first place, a random mutation must have occurred by chance to one bacterial individual that conferred weak resistance. Proper treatment courses of antibiotics are often sufficient to eliminate these few weakly resistant bacterial individuals. Nonetheless, in the event that they do survive to pass down the resistance, more mutations can occur that improves the bacteria's resistance against the antibiotic. Random mutation and development of resistance in bacteria is inevitable but the rapid proliferation of resistant bacteria is usually escalated by mankind – overprescription by physicians, misuse by patients, susceptible practices and environments within hospitals, overuse in livestock, and lack of commitment by the government provide the necessary conditions for resistant bacterial strain to develop.

Antibiotic resistance currently poses a grievous threat towards global health security. In the United States of America alone, resistant bacteria infect at least two million people and kill more than 23,000 each year.[2] Alarmingly, the danger of antibiotic resistance lies in the resistant bacteria's ability to travel across borders with ease. As bacteria are microorganisms and symptoms are often slow to show, infected persons or carriers of antibiotic-resistant bacteria are able to escape detection by customs authorities. Indeed, studies have shown that though thousands of air travelers have been routinely screened, few disease cases have been detected. As the resistance spreads across borders, countries are unable to keep up with necessary changes in their domestic strategies for clinical management. Infected individuals would take the ineffective antibiotics without knowledge of the contraindicating circumstances, while research into new antibiotics struggle to keep up with the fast pace of growing antibiotic resistance.

According to World Health Organisation (WHO), resistance in *Klebsiella pneumoniae* which causes lethal pneumonia has already spread to all nations. A widely used fluoroquinolone antibiotic against *E.Coli* is no longer effective in more than half of patients in several countries. Gonorrhoea has been found to be resistant to even the last resort medicines in at least 10 countries, while *P.falciparum* (malaria) is resistant to almost all available drugs in Cambodia and Thailand, the spread of which would present a critical threat to combatting malaria and retard significant achievements that had been made against malaria and its spread. As of February 2017, WHO has also introduced a priority pathogen list for resistant bacteria in urgent demand for research and development of new antibiotics.[3] In the long term, there is an unsettling risk of a multidrug resistant disease epidemic where no treatment options are available, which could potentially generate irreversible damage to the global health and economy. Antibiotic resistance in animal agriculture will also have negative implications in food production standards.

The necessity for international cooperation in combatting antibiotic resistance is clear - just as a successful national regime against antibiotic resistance can reap benefits for neighbouring countries, the lack thereof poses a security threat to human health in other countries too. 'The WHO's Policy Package to Combat Antibiotic Resistance' has emphasised the immediate need for 'regulating and promoting rational use of medicine, including in animal husbandry, and ensure proper individual care', '[enhancing] infection prevention and control [measures]' and '[fostering] innovation and development for new tools'.[4] Although the targets are straightforward, the international community faces challenges

[2] "Antibiotic / Antimicrobial Resistance | CDC". 2017. *Cdc.Gov*. https://www.cdc.gov/drugresistance/.
[3] "Bacteria and Antibiotics Needed". 2017. *World Health Organization.* http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/.
[4] "WHO | The WHO Policy Package To Combat Antimicrobial Resistance". 2017. *Who.Int*. http://www.who.int/bulletin/volumes/89/5/11-088435/en/.

in direct implementation - increased regulation comes at the cost of discouraging innovation and research, and compromising animal health in agricultural settings; countries with large pharmaceutical markets or animal agriculture-based economies would support deregulation instead. In addition, developing countries also lack the resources to achieve designated targets and will require international support.

While some countries have seen varying degrees of success in implementing the aforementioned policies on a national level, a vast majority lack a domestic legal framework, hence prompting the need for international dialogue regarding guidelines for domestic strategies. In a WHO report "*Worldwide country situation analysis: Response to antimicrobial resistance"*, dated April 2015, it was found that only 34 out of 133 countries participating in the survey had comprehensive national plans to fight antibiotic resistance. The same report revealed a lack of effective surveillance or standard treatment guidelines in many countries that the sales of antibiotics without prescription remained widespread, public awareness remains low and measures to prevent and control hospital infections are not put in place[5]. The unprecedented use of international mechanisms and cooperation within WHO's constitution, be it binding legal frameworks or unequivocal recommendations could engender significant progress on the issue.

[5] "WHO report finds systems to combat antibiotic resistance lacking." World Health Organization. Accessed June 23, 2017. http://www.who.int/mediacentre/news/releases/2015/antibiotic-resistance-lacking/en/.

KEY DEFINITIONS

LMIC

LMICs are Low and Middle Income Countries, which are distinguished from high income countries within each of the six WHO regions: African Region, Region of the Americas, South-East Asia Region, European Region, Eastern Mediterranean Region, and Western Pacific Region.[6]

Misuse & Overuse of Antibiotics

In this topic guide, the 'misuse and/or overuse of antibiotics' is to be interpreted and understood as the use of antibiotics under unreasonable or unnecessary circumstances. Such circumstances of overuse extend but are not limited to cases such as the prescription of antibiotics for viral infections, the prescription of antibiotics which serve no medical purposes, and over-the-counter purchases and consumption of antibiotics in nonbacterial infections. The line that distinguishes reasonable from unreasonable circumstance is blurred, especially in cases such as animal agriculture where it is debatable whether the use of antibiotics as growth promoters can be considered unreasonable or unnecessary.

Substandard and Counterfeit (Falsified) Medicine

Member states of the WHO have previously agreed on the definition of substandard medicine as that of "genuine medicines produced by manufacturers authorized by the National Medicines Regulatory Authority (NMRA) which do not meet quality specifications set for them by National standards."

In contrast, "a counterfeit medicine is one which is deliberately and fraudulently mislabeled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient (inadequate quantities of ingredient(s) or with fake packaging."[7]

In this topic guide and in the course of debate, 'counterfeit medicine' can be used synonymously with 'falsified medicine' which according to WHO definitions, refers to 'Medical Products that deliberately/fraudulently misinterpret their identity, composition or source'. Although previous documents makes use of the term 'counterfeit medicine', WHO has decided to adopt the Definition of

[6] "Definition Of Regional Groupings". 2017. *World Health Organization.* http://www.who.int/healthinfo/global_burden_disease/definition_regions/en/.
[7] "WHO | The WHO Policy Package To Combat Antimicrobial Resistance". 2017. *Who.Int*. http://www.who.int/bulletin/volumes/89/5/11-088435/en/.

Substandard and Falsified Medical Products for future documentation of medical products requiring the aforementioned categorisation[8]. For the purpose of the SDYC WHO council 2017, any submitted resolution should be consistent in the use of the following terms, sticking to either 'counterfeit' or 'falsified', but not both, to refer to such medical products.

KEY CONCEPTS

Antibiotics

Antibiotics are drugs that target pathogenic bacteria. Penicillin derivatives are examples of bactericidal antibiotics, which kill microorganisms by preventing the synthesis of or destroying their cell walls. On the other hand, bacteriostatic agents like tetracycline and sulphonamides work by slowing down or stopping bacterial reproduction by impeding microorganism processes such as DNA replication, protein synthesis and enzyme activities. In high volumes, bacteriostatic drugs can often be bactericidal.

Development of Antibiotics

Antibiotics can be made from living organisms including fungi and bacteria, or produced synthetically. The development of antibiotics is an especially time and money consuming process. First, thousands of species or materials are screened for signs of antibacterial action against several known bacteria. Second, the drugs must be isolated and purified into an active ingredient. Third, the drugs must be clinically tested to prove that their harmlessness to the user, after which they are approved for public use.

Natural Selection

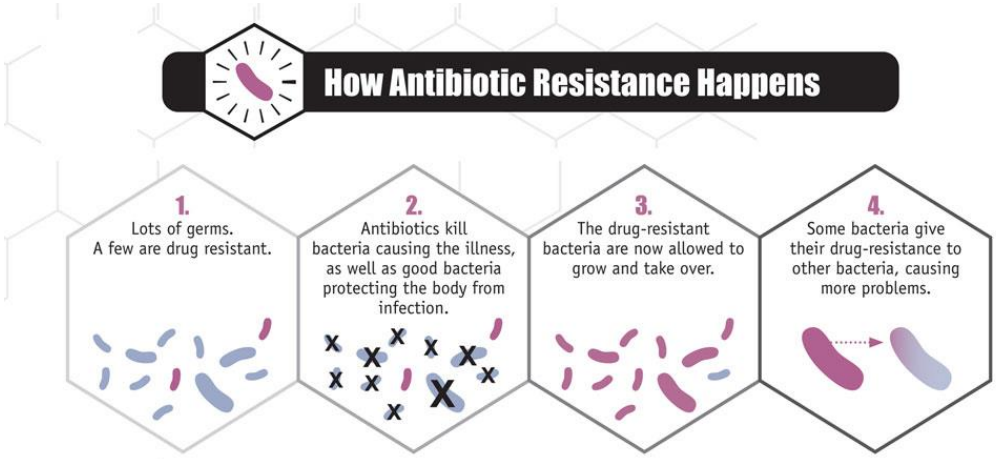
Natural selection works based on variation of traits in a given population. As the environment cannot support endless growth, there is inevitably a competition for resources. Individuals with traits or mutations that allow them to adapt better to the stress survive with a higher chance, and pass down the characters to their offspring. In the end, the traits that lead to a better survivability of the organisms becomes more common in the population.

Antibiotic Resistance / Antibacterial Resistance

Like other organisms, bacteria can undergo random mutation. Sometimes, these mutations could be advantageous to the bacteria by letting them develop resistance to certain antibiotics. When non-resistant microorganisms are killed by drugs, resistant ones enjoy a greater supply of food and room to

[8] "Definitions of Substandard and Falsified (SF) Medical Products." World Health Organization. Accessed June 24, 2017. http://www.who.int/medicines/regulation/ssffc/definitions/en/.

multiply. These resistant individuals could spread their beneficial characters horizontally - conjugation, transformation and transduction - or vertically, from parent to daughter. Over time, new strains of super bacteria that are resistant to certain types of antibacterial are created, pressuring development of new agents that can combat these microorganisms. It is of note that antibiotic resistance is a distinct subset of the overarching antimicrobial resistance that is the resistance of microbes such as bacteria, viruses and fungi in general.



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[9]

Causes of Antibiotic Resistance[10]

While selection pressure placed on bacteria by antibiotics is the prime factor of antibiotic resistance, humans can accelerate the proliferation of resistant strains. Over-prescription or incorrect prescription by physicians that due to diagnostic uncertainty, lack of knowledge and patient demand can lead to an excessive usage of antibiotics, placing a greater selection pressure on the microorganisms and consequently speeding up natural selection of microorganisms. Patients who do not adhere to strict medical guidelines and prematurely stop their intake increase the chances of bacteria surviving the dose and developing resistance. Furthermore, patients may wish to self-medicate through over the counter purchases without correct prescription from registered physicians. This, coupled with the significant possibilities of poorly manufactured or counterfeit antibiotics, magnifies the risk of incorrect dosage or usage of agents, ultimately leading to antibiotic resistance.

Hospitals, especially those residing in rural or developing countries, can provide conducive environments for breeding of resistant microbes due to them attending to many patients in close

[9] "Alliance For The Prudent Use Of Antibiotics". 2017. *ALLIANCE FOR THE PRUDENT USE OF ANTIBIOTICS.* http://apua.org/.

[10] Infections, Institute, Stacey Knobler, Stanley Lemon, Marjan Najafi, and Tom Burroughs. 2017. "Factors Contributing To The Emergence Of Resistance". *Ncbi.Nlm.Nih.Gov.* https://www.ncbi.nlm.nih.gov/books/NBK97126/.

proximity. Patients who often experience weak immune systems particularly can act as fertile breeding grounds for resistant microorganisms. Moreover, negligence of proper sanitation measures can inflame the situation by assisting airborne or contact transmission of resistant bacteria.

Vaccinations

Vaccines are inactivated or weaker forms of pathogens, priming the immune system of the subject so that subsequent exposures to the pathogen leads to a ready and strong immune response from the body.

Endemic Nature of Superbugs

The major setback of superbugs is their ability to linger in communities and regions for long periods of time. This is especially true for less developed regions and medical facilities, considering the poor regulation of antibiotic sales in the former, and the susceptibility of the latter to provide an optimum environment for superbugs to reproduce and spread. Furthermore, their growing resistance to antibiotics makes the elimination of such bacteria both costly and tedious.

KEY ISSUES

1. Rational Use of Antibiotics

The largest contributing factor towards antibiotic resistance has been the irrational use of antibiotics in agriculture and therapeutic settings of both industrialised and developing countries. The need for 'rational use of medicine' garners increasing attention in World Health Assembly (WHA) resolutions and its particular relevance to antibiotic resistance was also discussed in a WHO report[11] for the 58th World Health Assembly.

The irrational use of medicine is characterised by misuse or overuse by consumers and prescriber, often leading to the lack of quality-assured medicine or incomplete courses of treatments that creates the preconditions for resistant bacterial strains to proliferate. Substandard, counterfeit and lack of quality-assured medicine and incomplete treatment courses fail to completely eradicate the bacterial population. As a result, slightly resistant bacteria survive to populate the gene pool. In this manner, the irrational use of medicine creates a selective pressure for antibiotic resistance in the bacteria which over a sufficient period of time can lead to complete resistance to commercial drugs in the entire species. Overuse of antibiotics also exacerbates the situation by creating more opportunities for the bacterial population to develop antibiotic resistance.

[11] "Antimicrobial Resistance: A Threat To Global Health Security". 2005. *Apps.Who.Int.* http://apps.who.int/medicinedocs/index/assoc/s16338e/s16338e.pdf?ua=1.

Usage in therapeutic settings

In developed countries, misuse often occurs in the form of overprescription by physicians, even in the absence of appropriate indication, primarily due to factors such as diagnostic uncertainty, lack of opportunity for patient follow-up, lack of knowledge regarding optimal therapies, and patient demand.[12]

Underlying these factors, there is insufficient training and supervision of health personnel, a lack of access to the necessary diagnostic facilities that can empower clinical management decision, and a lack of standard treatment guidelines for healthcare professionals to refer or adhere to that has taken antibiotic resistance into adequate consideration. In the case of acute otitis media - the inflammation of the middle ear - the physician is obliged to meet the immediate needs of his patient (by dispensing antibiotics as a rapid cure) as he is obliged to be concerned for the health of future patients to come. Because prescribing decisions are often made on blurred lines like such, where the drug offers a small but significant clinical benefit, if not psychological aid to both physician and patient, but at the expense of larger selective pressure for antibiotic resistance, doctors become hard-pressed to make the appropriate judgement call without the assistance of standard guidelines[13].

From one perspective, the issue of antibiotic resistance is one of greater significance to developing countries, many of which have infectious bacterial diseases listed as their main cause of death[14] and still lack equitable access to antibiotics. It is not contradictory to speak of the regulation of use alongside providing universal access in these context, as the rise of antibiotic resistance exists in a vicious cycle with lack of access in these countries. For instance, the common case of counterfeit or substandard drugs poses a severe economic burden to both the nation and the individuals as households have to pay for the replacement or repeated course of inadequate drugs while shouldering a loss of income due to illness[15]. As the cost of antibiotics constitute a large proportion of household income, individuals are in this manner, excluded from rudimentary healthcare that they are entitled to on the basis of human rights.

Reasons cited for a lack of access also includes low economic status, inappropriate use, high cost of most recent and efficacious antibiotics, extensive “over the counter” usage, an increasing number of

[12] Infections, Institute, Stacey Knobler, Stanley Lemon, Marjan Najafi, and Tom Burroughs. 2017. "Factors Contributing To The Emergence Of Resistance". *Ncbi.Nlm.Nih.Gov.* https://www.ncbi.nlm.nih.gov/books/NBK97126/.

[13] Lipsitch, M., R. S. Singer, and B. R. Levin. "Antibiotics in agriculture: When is it time to close the barn door?" *Proceedings of the National Academy of Sciences* 99, no. 9 (2002): 5752-754. doi:10.1073/pnas.092142499.

[14] Planta, M. B. 2007. "The Role Of Poverty In Antimicrobial Resistance". *The Journal Of The American Board Of Family Medicine* 20 (6): 533-539. doi:10.3122/jabfm.2007.06.070019.

[15] Johnston, Atholl, and David W. Holt. "Substandard drugs: a potential crisis for public health." *British Journal of Clinical Pharmacology* 78, no. 2 (2014): 218-43. doi:10.1111/bcp.12298.

counterfeit drugs, and a dramatic increase in antibiotic resistance.[16] In Vietnam for instance, a 500-mg capsule of antibiotic ciprofloxacin obtained locally was found to have effectively only 20mg. Similar studies in other developing countries have also demonstrated the presence of counterfeit drugs with few or no active ingredient.[17] Indeed, self-medication, counterfeits, and inappropriate use from ignorance and inappropriate marketing of pharmaceuticals exacerbate the problem by creating stronger selective pressure within the population for resistance, causing new antibiotics to quickly phase into redundancy. It is of irony that these behaviours result from the very same poverty conditions and lack of healthcare infrastructure that has left millions denied of access to affordable and quality-assured medicine.

The economic, social and public health consequences of substandard and counterfeit medicine alone, even without discussing prescription practices, are of enormous concerns. Ineffective treatment of this nature incurs unnecessary yet heavy drug cost to both patients and healthcare systems, while creating preconditions for the spread of drug resistance. Drug resistance leads to a shorter clinical utility of the drug in question, requiring society to shoulder the cost of investing more resources in drug development. In addition, consumers lose confidence in the healthcare system, and sales from counterfeits goes to funding the corrupt and the criminal. The same study on the effects of falsified and substandard drugs indicates the possibility of toxic doses of dangerous ingredients in such medicine. It also corroborates with other studies on the verisimilitude that poor-quality medicine compromises the clinical treatment of chronic and infectious disease, resulting in disease progression, drug resistance, and death[18]. Such discussions are definitely not isolated in only the theoretical dimension, as evidenced by patients died despite antimalarial treatment after receiving antimalarial drugs of subpar manufacture[19].

The prevalence of substandard and counterfeit medicine on a global scale is unknown. Isolated reports notwithstanding, there are no definitive statistics on poor-quality medicine. Nonetheless, scholars have pointed to southeastern Asia and Africa as facing the problem to a larger extent. Indeed, member states with weak or no regulatory systems for drug quality control are perfect environments for the production and circulation of counterfeit and substandard medicine to thrive. A 2004 WHO survey on the African Region identified only 4% of member states as having developed national regulatory

[16] Carlet, Jean, and Didier Pittet. 2013. "Access To Antibiotics: A Safety And Equity Challenge For The Next Decade". *Antimicrobial Resistance And Infection Control* 2 (1): 1. doi:10.1186/2047-2994-2-1.
[17] Planta, M. B. 2007. "The Role Of Poverty In Antimicrobial Resistance". *The Journal Of The American Board Of Family Medicine* 20 (6): 533-539. doi:10.3122/jabfm.2007.06.070019.
[18] "Countering the Problem of Falsified and Substandard Drugs." 2013. doi:10.17226/18272.
[19] Newton, Paul N., Rose Mcgready, Facundo Fernandez, Michael D. Green, Manuela Sunjio, Carinne Bruneton, Souly Phanouvong, Pascal Millet, Christopher J. M Whitty, Ambrose O. Talisuna, Stephane Proux, Eva Maria Christophel, Grace Malenga, Pratap Singhasivanon, Kalifa Bojang, Harparkash Kaur, Kevin Palmer, Nicholas P. J Day, Brian M. Greenwood, François Nosten, and Nicholas J. White. "Manslaughter by Fake Artesunate in Asia—Will Africa Be Next?" *PLoS Medicine* 3, no. 6 (2006). doi:10.1371/journal.pmed.0030197.

capacity. A majority were found with gaps in their national medicine regulatory system, with limited capacity to ensure quality manufacture, distribution of quality medicine, and import of quality medicine at ports of entry. WHO has also estimated that 30% of 191 member states to have effectively no drug regulation in place, and only 20% to have well-developed drug regulations.

As 'Preventing and controlling substandard and counterfeit medical products in the WHO African region'[20], 'Substandard drugs: a potential crisis for public health'[21], and 'Effective Drug Regulation: A Multicountry Study'[22] provides in more extensive detail, eradicating substandard and counterfeit antibiotics will require effective drug laws, quality control guidelines, national drug regulatory authorities with the legal mandate, independence, and institutional capacity, as well as human, financial and technical resources. International collaboration mechanisms will also be crucial for information exchange, enforcing and monitoring the status of regulations, and combatting organised crimes of circulating counterfeit medicine. Indeed, the challenge of eradicating substandard and counterfeit medicine is complex in itself, and intricately intertwined with efforts to combat the spread of antibiotic resistance. In this aspect, they border on the same front; progress on one front is progress on both.

In Resolution WHA60.16, 2007 on the Rational Use of Medicine, WHO has urged the implementation of national programmes and a drug regulatory authority for the rational use of medicine as aforementioned, including the financing of, and capacity building of institutions in the public and private sector. However, national regimes for the management of antibiotic resistance has been deemed unrealistic for many developing countries in the absence of financial, legal, political and technical support from the international community.[23] The global scope of antibiotic resistance demands for global cooperation; multidrug resistant tuberculosis that develops in Africa can pose a health threat to countries in America as well. Hence, it is imperative that WHO member states develop an integrated framework for dispensing support to meet the specific challenges that different states may face in the concerted effort at antibiotic resistance management.

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[20] "Preventing and controlling substandard and counterfeit medical products in the WHO African region." African Health Observatory. Accessed June 24, 2017. https://www.aho.afro.who.int/en/ahm/issue/15/reports/preventing-and-controlling-substandard-and-counterfeit-medical-products-who.

[21] Johnston, Atholl, and David W. Holt. "Substandard drugs: a potential crisis for public health." *British Journal of Clinical Pharmacology* 78, no. 2 (2014): 218-43. doi:10.1111/bcp.12298.

[22] Ratanawijitrasin, Sauwakon, Eshetu Wondemagegegnehu, and World Health Organization. "Effective drug regulation : a multicountry study." Apps.who.int. January 01, 1970. Accessed June 24, 2017. http://apps.who.int/iris/handle/10665/42470.

[23] Fidler, David. 1998. "Legal Issues Associated With Antimicrobial Drug Resistance". Emerging Infectious Diseases 4 (2): 169-177. doi:10.3201/eid0402.980204.

Usage in Animal Agriculture

The causal factors of antibiotic resistance are not entirely limited to medical treatment in humans, but also extend to overuse in agriculture and animal husbandry. For instance, In the US, half of all antibiotics are used in agriculture.[24] As livestocks are consumed for food, strict health standards and veterinary oversight are required to prevent health risks caused by animal-borne or plant-borne diseases. Antibiotics are used to treat infected livestock and control the spread of a disease outbreak.[25] Aside from medicinal purposes, antibiotics are also used to boost the growth of livestock, improve feed efficiency and routinely prevent diseases.[26]

The rationale behind the extensive and ostensibly imprudent use of antibiotics lies in the goal of food animal production - "to deliver a safe, affordable, nutritious high-quality food product to the consumer" in bulk. Intensive animal farming has seen large quantities of livestock being grouped on a single farm, and hence requires the use of herd health measures to prevent epidemic disease outbreaks that could decimate the population. Under specific criteria, other measures such as vaccination and appropriate nutrition among various technologies are arguably insufficient at preventing and controlling diseases alone; under the same circumstances, the administration of antibiotic agents as part of the preventive medicine strategy becomes warranted.[27]

However, for reasons of animal welfare, logistical challenges and efficiency, herd medicine is practiced on a population basis as compared to individual treatment in humans. Hence, routine use of antibiotic drugs by food producers is more likely to escalate the growth of resistance in animal-borne diseases. This would result in the export of contaminated food that could pose a threat to animal, plant and human health.[28]

In addition, the use of antibiotics in agricultural settings is arguably incompatible with expectations that antibiotics will cure life-threatening infections[29] - excessive usage for non-medicinal purposes may hamper future performance in the clinical setting and therefore, the elimination of non-judicious use

[24] Lipsitch, M., R. S. Singer, and B. R. Levin. 2002. "Antibiotics In Agriculture: When Is It Time To Close The Barn Door?". *Proceedings Of The National Academy Of Sciences* 99 (9): 5752-5754. doi:10.1073/pnas.092142499.
[25] "The Facts About Antibiotics In Livestock & Poultry Production". 2017. *Meatinstitute.Org.* Accessed June 23. https://www.meatinstitute.org/index.php?ht=a/GetDocumentAction/i/99943.
[26] J Guidos, Robert. 2011. "Combating Antimicrobial Resistance: Policy Recommendations To Save Lives". *Clinical Infectious Diseases 52* (Supplement 5): NP-NP. doi:10.1093/cid/cir154.
[27] Infections, Institute, Stacey Knobler, Stanley Lemon, Marjan Najafi, and Tom Burroughs. 2017. "Factors Contributing To The Emergence Of Resistance". *Ncbi.Nlm.Nih.Gov.* https://www.ncbi.nlm.nih.gov/books/NBK97126/.
[28] Fidler, David. 1998. "Legal Issues Associated With Antimicrobial Drug Resistance". *Emerging Infectious Diseases* 4 (2): 169-177. doi:10.3201/eid0402.980204.
[29] Nathan, Carl, and Otto Cars. 2014. "Antibiotic Resistance — Problems, Progress, And Prospects". *New England Journal Of Medicine* 371 (19): 1761-1763. doi:10.1056/nejmp1408040.

should be considered in light of the pressing need for conservation of antibiotics.[30] It is of note that much of the antibiotics is used for growth promotion and disease prevention[31], which might or might not constitute as non-judicious use.

However, the argument inherently posits that antibiotic abuse in agriculture contributes to the antibiotic resistance in human-borne diseases, a fact that remains subject to dispute. Hitherto, it is important to mention that certain important facts concerning antibiotic use and effects on human health remains unclear after three decades of research, and in the cases where the facts are clear, interpretation differs. For instance, resistant bacteria on farms can be transmitted even in the absence of antibiotic-mediated selection.[32] This suggests that humans can acquire resistant infections even when antibiotics is not used in food animal production, which casts doubts over the extent of contribution that antibiotics use has over human antibiotics resistance.

The antibiotics that are used in clinical and agricultural setting is clearly an undisputed fact. WHO have provided a list of antibiotics of relative importance to humans, with remarks on their use in food animal production.[33] The list demonstrates a huge degree of overlap between antibiotic use in humans and animals. However, statistics provided by the FDA suggested that based on population proportions, vast majorities of antibiotics are not used in both humans and animals[34]. The question of overlap in antibiotic use of humans and animal depends on the interpretation of known facts regarding antibiotic use, and although deceivingly trivial at first, the facts plays a crucial role in determining the plausibility of antibiotic use contributing to resistance in bacteria that infect animals and humans.

The determination of relevant facts will be necessary for stakeholders to make informed decisions in the regulation of antibiotic use. Hence, there is a need for leadership and coordination of international efforts in researching the global impact of antibiotic use. In the meantime, states must also make preparation for future eventualities.

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[30] J Guidos, Robert. 2011. "Combating Antimicrobial Resistance: Policy Recommendations To Save Lives". *Clinical Infectious Diseases 52* (Supplement 5): NP-NP. doi:10.1093/cid/cir154.

[31] Chang, Qiuzhi, Weike Wang, Gili Regev-Yochay, Marc Lipsitch, and William P. Hanage. 2014. "Antibiotics In Agriculture And The Risk To Human Health: How Worried Should We Be?". *Evolutionary Applications* 8 (3): 240-247. doi:10.1111/eva.12185.

[32] Marshall B, Petrowski D, Levy S B(1990) Proc Natl Acad Sci USA 87:6609–6613.

[33] "Examples Of Antimicrobials Important In Human Medicine Being Used For Animal Treatment, Metaphylaxis Or Growth Promotion — Antimicrobial Resistance Learning Site For Veterinary Students". 2011. *Amrls.Cvm.Msu.Edu.* http://amrls.cvm.msu.edu/veterinary-public-health-module/i.-introduction/examples-of-important-antimicrobials-in-humans-used-in-animals-for-treatment-metaphylaxis-or-growth-promotion.

[34] Medicine, Center For Veterinary. "Animal Drug User Fee Act (ADUFA) - ADUFA Reports." U S Food and Drug Administration Home Page. Accessed June 24, 2017. https://www.fda.gov/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/ucm042896.htm.

Legal and Political Challenges in Introducing Regulations

Although state legislatures hold authority in regulating prescription of antibiotic drugs, further attempts to legislate rational use of drugs might invite negative responses from medical professionals who deem such national strategies as interfering with professional judgement.[35] Indeed, enforcement of rigid prescription guidelines may prevent medical professionals from providing the best possible, sometimes necessary treatment to their patients.

In regulating clinical use of antibiotics, the issue of overprescription cannot be resolved only on the physician's end alone. Some countries lack regulations on the sales of antibiotics, with antibiotic agents being available as a commodity to be bought without prescription from a relevant authority. This is a common occurrence in developing countries where opportunity to improve legislature have not been presented. The combination of over-the-counter access in these countries with the misaligned financial incentives for providers has effectively shifted the responsibility of rational use from the prescriber and healthcare professional to the unknowing consumer. This has lead to unsatisfactory outcome concerning the abuse of antibiotics and hence forms the basis for controlling access to antibiotics. Evidently, stricter regulations need to be imposed on the sales of antibiotics. However, it would come at the cost of the pharmaceutical sector, which would face increased development risks with new market restrictions. Therefore, balance is important in crafting policies that succeed in regulatory action without discouraging pharmaceuticals from leaving the antibiotics market altogether. Tighter regulations will also pose economic concerns for countries with huge pharmaceutical industries. The United States (US) for instance have a pharmaceutical market valued at $339,694 million USD[36] and would have reason to oppose implementation of regulatory measures in favor of market deregulation.

The regulation of antibiotics for agricultural use also proves controversial, as each restriction will come at the cost of animal health in the short term and the loss of economic benefits to food producers, pharmaceutical companies as well as consumers.[37] The threat to human health is intangible as a result of being difficult to quantify and document. However, to introduce a dilemma to the challenging enough task of balancing economic and health benefits, research has suggested that once the medical impact of antibiotic use is evident, regulations of animal use would become redundant in preventing the spread of resistance to the drugs in pathogenic bacteria of humans.[38] As with policies on infectious disease and global climate, waiting on conclusive evidence would result in ineffective mitigation of

[35] Fidler, David. 1998. "Legal Issues Associated With Antimicrobial Drug Resistance". *Emerging Infectious Diseases* 4 (2): 169-177. doi:10.3201/eid0402.980204.
[36] Wee. 2017. "Biggest Pharmaceutical Markets In The World By Country". *Worldatlas.* http://www.worldatlas.com/articles/countries-with-the-biggest-global-pharmaceutical-markets-in-the-world.html.
[37] Lipsitch, M., R. S. Singer, and B. R. Levin. 2002. "Antibiotics In Agriculture: When Is It Time To Close The Barn Door?". *Proceedings Of The National Academy Of Sciences* 99 (9): 5752-5754. doi:10.1073/pnas.092142499.
[38] Ibid.

damage; therefore the need for a scientific basis prior to introducing regulation must be weighed against the potential risk of inaction in designing policy.

For reasons aforementioned, the regulation of agricultural antibiotics is often not maintained in many nations, especially LMICs. The WHO has repeatedly called for action on this issue, but it is seemingly not within the jurisdiction of WHO to create regulations concerning drug use.[39] The ability of the international community to convince or pressure countries into compliance with the proper use of antibiotic drugs is severely compromised by the lack of legal support from international law. For example, in the event of animal-borne or plant-borne diseases developing antibiotic resistance, trade restrictions can be imposed on exports of contaminated food by countries applying sanitary and phytosanitary (SPS) measures under the World Trade Organisation and other international trade agreement. However, international trade law has dictated that the basis for such trade restrictions only extends to the protection against specific health dangers conferred by the product rather than the production process.[40] Therefore, trade restrictions cannot be legally used against countries that neglect proper use of antibiotics if they continue to produce food that meets safety standards set by the Codex Alimentarius Commission. In the context of ensuring global adherence to recognised principles and practices of antibiotic use, the necessity of finding appropriate international legal instruments cannot be further emphasised.

Lastly, underlying the challenges of regulations for rational use of medicine is the demand for accountability and transparency from regulatory bodies on both the domestic and international level. The irrational use of antibiotics across the globe calls for tighter but fair and feasible regulations across different settings, with the need for member states of WHO to increase national efforts to achieve the end goal of ending misuse. Missing transparency or accountability, member states cannot possibly address their commitment to the success of both domestic and international frameworks in a tangible manner.

[39] "Constitution Of The World Health Organisation". 2006. *Who.Int.* http://www.who.int/governance/eb/who_constitution_en.pdf.
[40] Fidler, David. 1998. "Legal Issues Associated With Antimicrobial Drug Resistance". *Emerging Infectious Diseases* 4 (2): 169-177. doi:10.3201/eid0402.980204.

2. Infection Control

Surveillance

The extent of the lack of data on antibiotic resistance throughout the globe is troubling indeed. A 2015 report by the WHO on the extent of global antibiotic resistance reflected an enormous lack of data on the spread of antibiotic resistance due to infrequent monitoring, which stemmed from poor laboratory capacity and data management. The situation is most grim in Africa and the Eastern Mediterranean, as the data in these regions is largely incomplete due to a lack of information and political framework. However, the Western Pacific and European region have displayed more complete surveillance programs, seeing that 70% of West Pacific nations have a surveillance system and European nations have a joint surveillance system; the European antibiotic Resistance Surveillance Network.[41]

Furthermore, antibiotic resistance is not just a regional problem, but an international one. Superbugs are often able to travel across regions and take root in different parts of the globe.[42] Clearly, this concerns the international audience and requires cooperation between nations in order to tackle this problem. In order to monitor the spread and severity of antibiotic resistant bacteria, several international surveillance systems have been set up.[43] The WHO has listed out that surveillance systems would provide essential details on antibiotic resistance and may be utilized to create infection control strategies and antibiotic usage policies. These systems also specify the needs of different regions around the world and can detect and predict new resistance mechanisms. In short, the WHO has specified that antibiotic resistance data can provide crucial information to combat antibiotic resistance. Infrastructure employed to collect and share data includes software (e.g. WHONET), microbiology laboratories and local healthcare facilities (e.g. Hospitals and clinics), and many developing countries lack this sort of infrastructure.

The Global Antibiotic Resistance Surveillance System (GLASS) is an initiative by the WHO as part of their global action plan on antibiotic resistance.[44] Although it has not made any actions concerning antibiotic resistance, the WHO has called for member nations of the UN to participate and contribute to the system, by collecting and sharing data to foster national surveillance system through international

[41] "WHO Report Finds Systems To Combat Antibiotic Resistance Lacking". 2015. *World Health Organization.* http://www.who.int/mediacentre/news/releases/2015/antibiotic-resistance-lacking/en/.
[42] Gale, More, and More Pearson. 2017. "Indian Travel Boom Is Sending Tourists Home With Superbugs". *Bloomberg.Com.* https://www.bloomberg.com/news/articles/2017-01-19/superbug-stowaways-india-travel-boom-spreads-dangerous-microbes.
[43] Critchley, I.A., and J.A. Karlowsky. 2017. "Optimal Use Of Antibiotic Resistance Surveillance Systems".
[44] "Global Antimicrobial Resistance Surveillance System (GLASS)". 2015. *World Health Organization.* http://www.who.int/antimicrobial-resistance/global-action-plan/surveillance/glass/en/.

standards.[45] The system is expected to combine clinical and laboratory data on the most threatening superbugs around the world, and determine optimal steps to be taken to combat antibiotic resistance. Moreover, the system will create a global standard for antibiotic resistance surveillance and data collation. In addition, the WHO has added flexibility to the system, by allowing nations to submit data that only fulfils certain requirements of GLASS, hence enabling them to contribute information and work on other areas of antibiotic resistance surveillance synonymously. The system will submit its first report in the last quarter of 2017. As this system is relatively young compared to other already established systems, its efficacy is somewhat unclear. Nevertheless, this system is much more extensive than other regional surveillance systems, observing that it intends to collate antibiotic resistance data from around the globe instead of simply focusing on one specific locality.

EARS-Net, or the European Antibiotic Resistance Surveillance Network is the largest publicly funded antibiotic resistance surveillance system in Europe. EARS-Net conducts surveillance on the 7 bacterial pathogens susceptible to antibiotic resistance commonly causing infections and collates data from medical institutions and research facilities from 30 European nations. EARS-Net has proven effective in showing the severity of antibiotic resistance throughout Europe. A 2015 report showed that a strain of superbug, *Klebsiella pneumoniae,* had an increase of resistance towards 2 of the "last-line antibiotics" from 6.2% in 2012 to 8.1% in 2015.[46] However, EARS-Net is only restricted to the collection and use of antibiotic resistance information in Europe. Less developed regions such as Africa are in need of surveillance networks and research infrastructure, in order to provide essential information on the spread of antibiotics resistance. In addition, emerging antibiotic resistance surveillance systems may follow a standardised system of data collection as shown in EARS-Net.

By establishing antibiotic resistance surveillance networks, more information can be gathered on the mechanisms of superbugs and new strategies and policies can be drawn up to combat the spread of antibiotic resistance. However, many countries, especially developing nations, lack the resources and political frameworks to set up such surveillance systems, which includes the use of expensive infrastructure such as microbiology laboratories. Standardised data collection techniques need to be implemented as well, so as to preserve the accuracy of the data. Furthermore, international surveillance systems like GLASS require the consent of individual nations to share national data.

[45] Mitchell, Cristina. 2015. "PAHO WHO | World Health Assembly Closes With Approval Of New Resolutions". *Pan American Health Organization / World Health Organization.* http://www.paho.org/hq/index.php?option=com_content&view=article&id=11016&Itemid=135&lang=en.

[46] "News - Last-Line Antibiotics Are Failing". 2017. *Ecdc.Europa.Eu.* http://ecdc.europa.eu/en/press/news/_layouts/forms/News_DispForm.aspx?ID=1510&List=8db7286c-fe2d-476c-9133-18ff4cb1b568.

Sanitation Measures

Often, the prevention of a disease is better than researching a cure for it. For example, a 2016 study linked the overuse of antibiotics in India to the lack of basic sanitation measures and immunization rates.[47] Thus, billions of dollars of federal budget and taxpayer money, and years of research on antibiotics can be easily avoided by simply employing proper sanitation measures and sustaining clean living conditions. Moreover, ReAct, an NGO dedicated to preventing the spread of antibiotic resistance, has stated that poor sanitation may also result in the increase in spread of resistant bacteria.[48] Simply put, good sanitation and health practices curb the emergence of antimicrobial resistance and reduce the extent of infection spread.[49]

Proper sanitation measures maintain efficient and sterile healthcare facilities which would not require the use of antibiotics. One such occurrence is the Kiomboi hospital in Tanzania, where medical staff had to make a crucial decision to resort to antibiotics during a childbirth, or risk infection to the patient, due to a lack of clean water in the facility during a 2015 drought. This lack of clean water increases the risk of infection during surgical operations and other healthcare procedures, which antibiotics have to be employed to mitigate this risk. Furthermore, this situation is not limited to Tanzania alone. In many hospitals in Africa and South Asia, antibiotics are frequently overused to make up for poor water sanitation and childbirth infections. Up to one in five infant deaths in these regions can be attained to sepsis, tetanus and meningitis, all resulting from the lack of clean water in healthcare facilities. Unfortunately, this contributes to the proliferation of antibiotic resistance.

However, supplying clean water to hospitals in LMICs is easier said than done. Drought, polluted rivers and economic scarcity of water[50] [51] all create obstacles for local governments in South Asian and sub-Saharan African nations to ensure efficient clean water distribution to their people. The issue of drought and polluted rivers in Africa is easily made clear; seasonal rains determine when these nations are able to obtain their water, thus a continuous supply of clean water needs to be established. In South Asia, however, the situation is much more complicated. Due to conflict and geopolitics in the region, there is scarcity amidst abundance of water. Despite major rivers such as the Ganges, Indus and

[47] Laxminarayan, Ramanan, and Ranjit Roy Chaudhury. 2016. "Antibiotic Resistance In India: Drivers And Opportunities For Action". *PLOS Medicine* 13 (3): e1001974. doi:10.1371/journal.pmed.1001974.
[48] "Infection Prevention And Control: National Action Pans – React". 2017. *React.* https://www.reactgroup.org/toolbox/policy/national-action-plans/elements-of-a-national-action-plan/infection-prevention-and-control/.
[49] "Infection Prevention And Control: National Action Pans – React". 2017. *React.* https://www.reactgroup.org/toolbox/policy/national-action-plans/elements-of-a-national-action-plan/infection-prevention-and-control/.
[50] "What'S Really Causing Water Scarcity In Africa South Of The Sahara? | IFPRI". 2013. *Ifpri.Org.* http://www.ifpri.org/blog/what%E2%80%99s-really-causing-water-scarcity-africa-south-sahara.
[51] "South Asia's Water Crisis: A Problem Of Scarcity Amid Abundance - The Asia Foundation". 2015. *The Asia Foundation.* http://asiafoundation.org/2015/03/25/south-asias-water-crisis-a-problem-of-scarcity-amid-abundance/.

Brahmaputra running through the region, an estimated 22 out of 32 Indian cities face daily water shortage problems, as nations refuse to cooperate in sharing hydrological information and water resources. In addition, the construction of dams have restricted water access in some areas, while flooding others. To tackle the issue of antibiotic resistance, individual states must discover methods to secure clean water access to their populations or find other

As observed, the sanitation measures that are to be taken up to combat antibiotic resistance differ from nation to nation. Countries such as Brazil may require the management of slums and drainage systems, whereas nations such as Tanzania are in desperate need for clean water supply and distribution. Nations need to cooperate in a way such that the needs of each individual nation are addressed, while ensuring that local governments are open to aid from the international audience. By doing so, the prevention of infection and disease spread may potentially reduce the proliferation of global antibiotic resistance.

Public Education and Awareness

Another obstacle in the issue of antibiotic resistance is public education and awareness of the issue. This is not simply restricted to awareness about the presence of antibiotic resistance, but also the extent of the severity of the problem. A 2015 report by the WHO revealed that in many regions around the globe, especially the Eastern Mediterranean region, local governments do not have an action plan against antibiotic resistance. This displays that many nations do not even posses the political framework to fight antibiotic resistance. Furthermore, another survey conducted by the WHO in 2015 across 12 countries[52] revealed that 65% of respondents had taken antibiotic resistance in the past 6 months and 93% revealed that their main source of antibiotics were pharmacies/drug stores. However, the survey also revealed that 35% of people felt that they should stop taking antibiotics when they felt better. 57% of responders also believed that people like them could not contribute anything in the fight against antibiotic resistance.The above report and survey both reveal unawareness by both the public and governments on the issue of antibiotic resistance, despite the major role that antibiotics play in their daily lives. The survey also mentioned that the public plays a huge role in preventing antimicrobial resistance, by taking actions including but not limited to preventing infections to avoid the use of antibiotics and always completing the course of antibiotics as prescribed. Thus, it further emphasises on the need for public awareness in most countries on the significance of antibiotic resistance.

Past initiatives have been taken by international governmental and non-governmental agencies such the WHO and the Alliance for the Prudent Use of Antibiotics (APUA), to educate the public on the

[52] ANTIBIOTIC RESISTANCE: MULTI-COUNTRY PUBLIC AWARENESS SURVEY. 2015. World Health Organisation.

proper use of antibiotics, and individual nations to recognise the severity of the issue and enact appropriate policies to deal with it. The World Antibiotic Awareness Week is a startup by the WHO to encourage good antibiotic health practices in developed and developing countries. The campaign makes use of posters, fact sheets and even a social media campaign, to spread awareness and inform the public about antibiotic resistance.[53] Moreover, the campaign toolkit points out key areas of development to policy makers and other stakeholders with respect to the matter. The APUA also releases a complimentary triannual newsletter to over 10,000 disease practitioners over more than 100 countries.

It may seem that developing countries are lagging behind in terms of antibiotic resistance awareness, but that is gradually changing. Organisations such as ReAct, which are mainly based in developing regions including Southeast Asia, Africa and Latin America, provide continuously updated online toolboxes to provide inspiration and guidance on fighting antibiotic resistance.[54] However, much more still needs to be done to reach out to many others in developing nations to inform them about antibiotic resistance.

As observed, many of these resources are directed at policymakers and healthcare professionals. Very few of the resources provided by NGOs are directly addressed to the general populace of developing nations. It is up to the initiative of member nations to recognise the severity of the spread of antimicrobial resistance and educate their own citizens on the issue. Considering that many obstacles such as language and cultural barriers[55] and lack of internet access[56] prevent citizens from accessing the much-needed resources, NGOs and local governments need to play their part to overcome these problems.

[53] "World Antibiotic Awareness Week 2016". 2016. *Who.Int.* http://www.who.int/campaigns/world-antibiotic-awareness-week/Toolkit2016.pdf.
[54] "About The Toolbox – React". 2017. *React*. https://www.reactgroup.org/toolbox/about-the-toolbox/.
[55] Fatahi, Nabi, and Ferid Krupic. 2016. "Factors Beyond The Language Barrier In Providing Health Care To Immigrant Patients". *Medical Archives* 70 (1): 61. doi:10.5455/medarh.2016.70.61-65.
[56] "4 Billion People Still Don'T Have Internet Access. Here'S How To Connect Them". 2016. *World Economic Forum.* https://www.weforum.org/agenda/2016/05/4-billion-people-still-don-t-have-internet-access-here-s-how-to-connect-them/.

3. Innovation & Development

To ensure that we stay ahead of the evolving microorganisms, continuous development of novel antibiotics is essential. According to the World Health Organisation, today a perilous multitude of multidrug- resistant bacteria such as *Acinobacter*, *Pseudomonas* and *E. coli* pose significant threats to humanity through bloodstream infections and pneumonia.[57] Yet, there has been a steady decline of pharmaceutical firms. In 2011, Pfizer, a major giant since the 19th century, shut down its antibiotic research facilities in Connecticut, USA, terminating its long research into gram-negative bacteria that are prone to developing antibiotic resistance. Other firms – Sanofi-Aventis, Eli Lily, Bristol-Myers Squibb – have all followed suit, quitting the market due to failing profits and leaving only a handful of companies like Marck & Co. and GlaxoSmithKline remaining. Furthermore, the number of new antibiotics approved by Food and Drug Administration of America (FDA) have been steadily dwindling.[58] Much of these results is due to limitations of antibiotic research, both monetary and regulatory.

The biggest problem that obstructs innovation and development of novel antibiotics is the astounding financial costs of researching and developing a pharmaceutical product for clinical use. Per a new study by the Tuft Centre for the Study of Drug Development, the process often takes longer than a decade and costs around $2,558 million.[59] Furthermore, it costs another $312 million to test effects of new formulas and dosage strengths, and monitor safety of patients and look for possible long-term side effects. Indeed, the cost of development and approval for public use for a new drug in 2013 had rose by a staggering 145% of that in 2003. The question of revenue potential of antibiotics is also a complication – unlike drugs for diabetics or high cholesterol that must be taken for life, antibiotics are meant to be taken for just a few days, severely limiting the extent of recoupment that the firm can enjoy.

Another rein that firmly holds back development of new antibiotics is strict regulations on drug development by regulatory bodies such as FDA. After the administration was closely scrutinised over Ketek scandal (where the antibiotic manufactured by Sanofi-Aventis was approved by FDA management despite warnings of fraudulent research papers by scientists and resulted in liver failures in public patients), the bar for approval by FDA was raised[60]. Yet, many pharmaceutical companies

[57] "Bacteria and Antibiotics Needed". 2017. *World Health Organization.* http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/.
[58] Shlaes, D. M., D. Sahm, C. Opiela, and B. Spellberg. 2013. "The FDA Reboot Of Antibiotic Development". *Antimicrobial Agents And Chemotherapy* 57 (10): 4605-4607. doi:10.1128/aac.01277-13.
[59] "PR Tufts CSDD 2014 Cost Study | Tufts Center For The Study Of Drug Development". 2014. *Csdd.Tufts.Edu.* http://csdd.tufts.edu/news/complete_story/pr_tufts_csdd_2014_cost_study.
[60] DM Shlaes, RC Moellering Jr. 2002. The United States Food and Drug Administration and the end of antibiotics. *Clin Infec Dis 34*, 420-422

believe its requirements to be impractically high[61]. For instance, since it is hard to know for sure whether the experimental drug played a role in deaths of patients already suffering from lethal conditions, trial sizes have to be large, requiring large manpower and financial support. Moreover, per FDA guidelines, patients must not have had any other antibiotics other than the experimental drug, yet these subjects are decidedly hard to find. Consequently, companies begin to shy away from developing and submitting new antibiotics. In fact, the number of new systemic antibiotics approved by FDA plunged from 16 from 1983 to 1987, to just two from 2007 to 2012 according to Infectious Diseases Society of America.

Still, thanks to efforts by many agencies, governments and policy makers are trying to incentivise drug development and reduce regulatory barriers. The European Medicines Agency announced in 2013 that it would provide additional guidance to companies and aid their development of antibiotics. The Centre for Disease Control and Prevention (CDC) funded 34 innovative projects in 2016 to target antibiotic resistance, spending more than $14 million to encourage both state and private drug developers to implement tracking, prevention and antibiotic stewardship that are in line with its action roadmap. Partnerships between companies, universities and individuals are also becoming more common, as the commitment to the same target by many researchers make development much more efficient. In 2012, the Bill and Melinda Gates Foundation expanded its Tuberculosis Drug Accelerator program, newly recruiting drug companies, academic institutions, and government laboratories. In June 2014, AstraZeneca signed a research and development agreement to work on novel antibiotics against gram negative bacteria.

Political winds are also changing regarding legislative regulation on drugs. In May 2012, FDA Director Janet Woodcock acknowledged the ineffectiveness of guidelines and promised to reboot it. Indeed, in its 2013 guidance on antibacterial therapies, FDA exhibited more willingness in accepting externally or historically controlled studies, and reduced its suggested safety database to as small as 300 patients[62], in order to attract more investments by firms in research for new drugs. The FDA Safety and Innovation Act was also put in place in 2012, aiming to stimulate development of new antibiotics, one of the titles being Generating Antibiotic Incentives Now (GAIN Act). Through this legislation, chosen firms are given extended exclusivity period where antibiotics for serious infections can be sold without competition by five years, increasing the profits from the new antibiotics and thus giving innovative firms higher profits to make up for their investment and development costs. GAIN Act also provides fast track and priority review status to innovative drugs that are covered, lowering the regulatory bar for qualifying firms. Furthermore, FDA has created an Antibacterial Drug Development Task Force – made up of scientists

[61] Ledford, Heidi. 2012. "FDA Under Pressure To Relax Drug Rules". *Nature.Com.* http://www.nature.com/news/fda-under-pressure-to-relax-drug-rules-1.11936.
[62] "Guidance For Industry Antibacterial Therapies For Patients With Unmet Medical Need For The Treatment Of Serious Bacterial Diseases". 2013. https://www.fda.gov/downloads/Drugs/Guidances/UCM359184.pdf.

and clinicians – to evaluate existing FDA guidelines and brainstorm new methods of facilitating development of antibiotics.

Proper and extensive vaccination is another way that can cripple the rapid proliferation of antibiotic resistant bacteria. By preventing the bacterial infections from even happening, vaccination can greatly diminish the need for antibiotics, consequently lowering the rate of development of antibiotic resistance. Indeed, per WHO, if every child around the globe were properly vaccinated from Streptococcus pneumoniae bacteria, an estimated 11 million days of antibiotic use could be avoided. Vaccines that are effective against viruses could help, too; by curtailing the frequency of viral infections – during which patients often take antibiotics unnecessarily, the expansion of resistant pathogens could be decelerated.

However, simply providing monetary incentives or giving subsidies to firms can be expensive. Excessive lowering of regulatory bars can also lead to public health risks, as less time and effort are put in place to test new, untested antibiotics that may bring long-term side effects after approval for public use. Relying on vaccines is a bad idea as there are still several pathogens that vaccines are ineffective against, vaccines take a long time to develop and their success rates are low. Therefore, other backup incentives re still required to more effectively slow down the crisis of antibiotic resistance.

LINKS TO SUSTAINABLE DEVELOPMENT

Antibiotic resistance is not an issue we can simply ignore. Since the first use of antibiotics, we have been struggling to stay in front in the race against the constant evolution of bacteria. The first cases of antibiotic resistance was detected 15 years after the initial distribution of penicillin to the masses. Now, a mere year after the use of linezolid and ceftaroline began, bacteria resistant to each antibiotic were identified[63]. Evidently, the possibility of an unsustainable 'antibiotic apocalypse' is looming closer and closer.

Sustainable development can be defined as meeting the needs of the present generation without compromising the ability of the future generations to meet their own. Antibiotic resistance is an ever-growing obstacle that today already kills thousands of people around the world yearly, and alarmingly, the current measures implemented to reduce antibiotic resistance have not yet measurably slowed the progression of antibiotic resistance. Without dependable antibiotics, many medical procedures will be rendered complicated and delicate, such as childbirth and invasive surgery. A simple cut, if infected by an aggressive strain of antibiotic-resistant bacteria, may prove fatally dangerous. The responsibility to ensure that such an antibiotic apocalypse remains a possibility rather than a reality therefore lies in the current generation of medical, governmental and non-governmental leaders.

The third goal of the United Nation's Sustainable Development is to "Ensure healthy lives and promote well-being for all at all ages."[64] The World Health Organisation should therefore aim to develop and promote long-term solutions to ensuring that antibiotics are still effective and accessible to future generations.

[63] https://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf#page=28
[64] "Goal 3 .:. Sustainable Development Knowledge Platform". 2017. *Sustainabledevelopment.Un.Org*. Accessed June 23. https://sustainabledevelopment.un.org/sdg3.

PAST INTIATIVES

Low and Middle Income Countries (LMICs)

Even though the major cause of antibiotic resistance is excessive use of antibiotics especially in rich nations, low and medium income countries (LMICs) are not mere third parties – antibiotic consumption in LMICs are steadily growing at the highest rate, adding to the selection pressure placed on pathogens and contributing to antibiotic resistance. In fact, according to the IMS Health MIDAS database, from 2000 to 2010, consumption of antibiotics in LMICs rose by 36%, three quarter of which can be traced to the 5 BRICS countries (Brazil, Russia, India, China, South Africa).

The gravity of the crisis is further emboldened by the widespread lack of resources present in many LMICs, especially rural areas. Hospitals are few, understaffed and underfinanced, with staff to population ratio reaching nearly 1 to 1000. Healthcare workers often neglect proper sanitation measures, providing a conducive area for antibiotic resistant strains to breed and manifest. The low purchasing power for newer antibiotics that must be taken promptly to halt the spread means it is notably hard to contain these antibiotic resistant bacteria. Developments and innovations of drugs are also hard to come by, as laboratory capacities are limited and expensive, and skilled are lacking due to the poor levels of public education.

These bleak outlooks stress the necessity for immediate and strong counter measures not just by the international community but also by the governments of LMICs themselves. Yet, there is a visible lack of policies and regulations at the individual nation levels.

According to a 2014 survey by CDDEP (Center for Disease Dynamics, Economics and Policy), in the African regions where 26 low income and 20 middle income countries are located at, only 6 LMICs have governmental bodies that deal specifically with antibiotic resistance by formulating appropriate policies. Furthermore, although around three quarter of the Africa region countries have at least one medicine policy that emphasises rational use of antibiotics and restricts use of antibiotics without prescription, in every case enforcement is poor. In the South-East Asia region, while nearly all countries had policies aimed to contain antibiotic resistance, strong laboratory capacities, prescription auditing, public education campaigns and infection control procedures, only Sri Lanka had regulations placed on antibiotic use in humans or animals.

In the international level, there have been some actions to improve the situation of antibiotic resistance in LMICs, namely the Global Antibiotic Resistance Partnership (GARP). A project of CDDEP that began in 2008 with funding from Bill and Melinda Gates Foundation, it aims to promote locally

relevant policies related to antibiotic use and resistance in LMICs. Through GARP, local experts in each country are identified, assembled into a working group, then offered resources to ultimately work towards development of policies that are customised for local use. GARP's work in its first four countries – Kenya, India, Vietnam and South Africa – is deemed largely successful, as it has managed to create a hub of antibiotic resistance expertise and activity, focusing on policy research that is tailored to individual nations. Today, GARP has expanded its partnerships to four additional countries: Mozambique, Tanzania, Nepal and Uganda.

An example of GARP's success can be seen in its first partnership, Kenya 2009, where it funded two small projects. The first project, antibiotic use in food animals, revealed that there was a rampant overuse of antibiotics like penicillin and tetracycline among all surveyed farmers and herders. While most antibiotics were purchased directly at stores without a proper veterinarians' –often scarce and inaccessible near farm areas – prescription, some were obtained when non governmental organisations (NGOs) provided farmers free antibiotics as means of support, unknowingly raising the risk of antibiotic resistance. Ultimately, the study showed that most bacteria cultured from beef, about half from chicken and a smaller number from pigs were resistant to commonly used antibiotics. The second project, researching the knowledge, attitude and pricing of antibiotics in hospitals in areas of Kenya, confirmed that the frequent inadequacy of antibiotics in hospitals in rural areas was because hospitals, underfinanced, were forced to purchase antibiotic drugs in small quantities, even though larger sums would result in economies of scale that yield lower costs per drug. Today, armed with these findings and having acquired necessary funding and leadership, GARP-Kenya is an independent group that acts as a trusted advisor to the government in regards to policies on antibiotic resistance.

ReACT is another project that supports and conducts many antibiotic resistance related activities in LMICs all around the world. A project funded mainly by Swedish International Development Cooperation Agency (SIDA) and to a some extent WHO, it advocates for global engagement on antibiotic resistance through collaboration with organisations, individuals and even governments. One of its notable successes include its work on Ghana, where a technical task team for antibiotic resistance was established in 2013 to develop extensive national policies on drug use and resistance. Today, Ghana is the first African nation to develop and submit a national policy to address antibiotic resistance.

The successes in GARP and ReACT programs show that with the right incentives and funding provided, LMICs can combat antibiotic resistance effectively. However, there is still a grave need for governments of many LMICs to engage more actively by placing more focus on the crisis.

International Non-Governmental Organisations (INGOs)

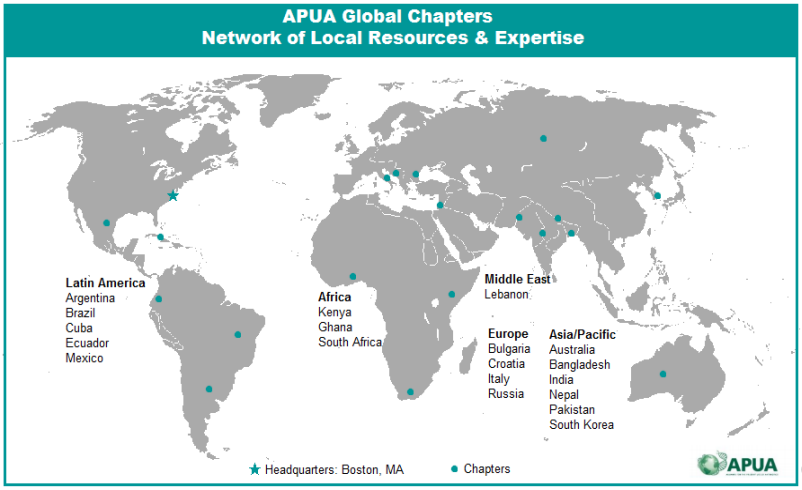
APUA

The Alliance for the Prudent Use of Antibiotics (APUA) is a US-based NGO which was founded in 1981 to combat antibiotic resistance. APUA seeks to strengthen international defenses to prevent the spread of infectious diseases by regulating access to antibiotics and promoting effective and efficient treatment. The organisation has an network of agencies in 16 countries across the globe, and dedicates itself to spreading awareness about antibiotic resistance.

In addition, research and surveillance information about antibiotics is gathered and processed by the organisation, which is then used to generate counter-measures against disease spread and the growth of superbugs. This information comes from sources such as an International Scientific Advisory Board and research centers focused on antibiotic resistance.

APUA agencies also work hand-in-hand with international and local governing bodies to create proper policy guidance on the issue of antibiotic resistance. The organisation uses evidence from a range of research fields such as microbiology, pharmacoeconomics and behavioral studies to back their views and claims on their policies. APUA also facilitates discussions between private corporations and local governments to ensure policies that can cater to multiple stakeholders.

The network of APUA affiliated agencies across the globe also assist in spreading the message about the significance of antibiotic resistance. Some of their activities include sponsorship of antibiotic resistance related research, public education on antibiotic resistance and cooperation with local health ministries and other health organisations to improve healthcare in these nations.



[65]

[65] "Alliance For The Prudent Use Of Antibiotics". 2017. ALLIANCE FOR THE PRUDENT USE OF ANTIBIOTICS. http://apua.org/.

World Health Organisation (WHO)

Established in 1948, the World Health Organisation (WHO) is the United Nations' specialised agency for global health. Since its inception, WHO has strived towards the "attainment by all peoples of the highest possible level of health"[66], by serving as the coordinating authority on international health work, with its functions including but not being limited to establishing and promoting cooperation between relevant stakeholders, assisting governments on request, advancing work towards the eradication of endemics and epidemics. Over the past two decades, WHO has shown increasing concern towards the imminent challenge of evolving antibiotic resistance, with a first resolution passed in 1998[67] during the Fifty-first World Health Assembly urging action from member states.

Among other subsequent resolutions[68], WHO has of 2015 released a Global Action Plan on Antibiotic Resistance[69], in which five main objectives were outlined; to improve awareness and understanding of antibiotic resistance through effective communication, education and training; to strengthen the knowledge and evidence base through surveillance and research; to reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures; to optimize the use of antibiotic medicines in human and animal health; and to develop the economic case for sustainable investment that takes account of the needs of all countries and to increase investment in new medicines, diagnostic tools, vaccines and other interventions.

By and large, WHO has taken the role of producing suitable guidelines for member states to adhere to developing national action plans against antimicrobial resistance. For example, in the five countries situated in the Greater Mekong subregion, resistance in *P. falciparum* malaria against first-line treatment was confirmed as of July 2016, and resistance towards all available antimalarial medicine being observed along the Cambodia-Thailand border. Subsequently, a "*WHO Strategy for Malaria Elimination in the Greater Mekong subregion (2015-2030)*"[70] was produced and endorsed by all 5 stakeholder countries.

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[66] "Constitution Of The World Health Organisation". 2006. *Who.Int.* http://www.who.int/governance/eb/who_constitution_en.pdf.
[67] "Emerging And Other Communicable Diseases: Antimicrobial Resistance". 1998. *Apps.Who.Int.* http://apps.who.int/medicinedocs/index/assoc/s16334e/s16334e.pdf?ua=1.
[68] "WHO | Resolutions On Antimicrobial Use And Resistance". 2017. *Who.Int.* Accessed June 23. http://www.who.int/drugresistance/AMR_DC_Resolutions/en/.
[69] "Global Action Plan On Antimicrobial Resistance". 2015. *World Health Organization.* http://www.who.int/antimicrobial-resistance/publications/global-action-plan/en/.
[70] "WHO Strategy For Malaria Elimination In The Greater Mekong Subregion (2015-2030)". 2015. *Iris.Wpro.Who.Int.* http://iris.wpro.who.int/bitstream/handle/10665.1/10945/9789290617181_eng.pdf?sequence=1.

It is difficult to comment on the efficacy of these initiatives for a few specific reasons. Firstly, the challenge of antibiotic resistance is a recent one and not enough studies have been produced to examine the effectiveness of existing policies. The main criterion to judge existing policies ultimately is their ability to keep AMR under control in the long term. In addition, WHO's role as an advisory and coordinating body ties its success to the effort of individual member states instead of its policies alone. One may see positive results arise of policy in one region but not in another.

To encourage more rational prescriptions and adequate supplies of cheaper drugs, WHO has also implemented the Essential Drugs Programme (EDP), where lists of essential medicines and appropriate guidelines are compiled. Four decades after its first publishment in 1977, the list includes around 430 drugs that satisfy the priority healthcare needs of the population[71]. Together, the medicines not only provide effective treatment for much of diseases, but also ensures regular updates, quality of drugs and continued development for better agents[72]. Furthermore, the programme highlights guidelines regarding acquisition and supplies of medicines especially in the public sector, medicine donations and local productions. Indeed, today the WHO lists are seen relevant in not just low and middle income countries, but in all nations, and more than 155 countries have created their national lists based on those released by WHO.
exploitation.[34] Therefore, tackling poverty and promoting equality will reduce the number of child exploitation cases significantly.

The Council's main objective during the committee sessions is to ensure that children's safety and well-being are not compromised due to various forms of child exploitation such as child trafficking, slavery and sexual exploitation. For this aim to be achieved, sufficient laws and regulations need to be in place with adequate enforcement by the relevant authorities so that justice is meted out to those who exploit children, and would-be perpetrators are deterred. However, developing countries and remote areas generally lack the resources to effectively implement and enforce child protection laws.

[71] http://www.who.int/medicines/publications/essentialmedicines/EML_2017_ExecutiveSummary.pdf?ua=1
[72] http://www.who.int/medicines/services/essmedicines_def/en/

KEY STAKEHOLDERS

Similar to other topics being discussed and resolved in the UN General Assembly, the issue of antibiotic resistance has multiple points of contention. Although there exists general agreement that antibiotic resistance is a pressing issue requiring solutions for the long term, member states may differ on the exact measures needed to achieve the same goal. The major bloc positions concerning the resolution of antibiotic resistance will fall under nations with large pharmaceutical corporations and markets, nations with large livestock sectors, and the less economically developed countries (LEDCs).

People's Republic of China (PRC)

The six decades since the establishment of the PRC in 1949 have seen remarkable improvement in the country's public health. Life expectancy more than doubled from 35 years before 1949 to 74.8 years in 2010, and infant mortality has fallen to 9.5% in 2013.[73] The widespread use of antibiotics played a crucial role in achieving these success. However, bacterial resistance has become a relevant concern for the chinese, with surveillance data indicating a widespread prevalence of methicillin-resistant *Staphylococcus aureus* and other antibiotic-resistant bacteria in the region. China has quickly recognised the problem's severity and has introduced a vast amount of regulations and management strategies to curb the problem, as part of its current healthcare reforms. A recent policy of note is China's National Action Plan to Contain Antimicrobial Resistance (2016 -2020)[74], which aim to achieve important milestone goals in all areas, from public education to research, sales management to surveillance. The effectiveness of the bulk of China's policy is hard to determine, with conflicting academic opinions. While China's healthcare campaign has decreased antibiotic sales and effect a reduction in prescription of antimicrobials for hospitalised patients and outpatients, other issues such as unregulated use in animal husbandry, over-the-counter purchase, and elimination of economic incentives in drug sales awaits attention[75]. Nevertheless, China's active involvement has poised itself to lead the international community in tackling the complex global issue of antibiotic resistance.

France

Through an extensive public awareness campaign on antibiotic resistance using the catchphrase 'Antibiotics are Not Automatic', France has succeeded in lowering antibiotic prescription by 26.5% from 2002 to 2007[76]. More recently, on November 2012, France introduced a national action plan called

[73] Wang, Li, Xiulan Zhang, Xiaoyun Liang, and Gerald Bloom. 2017. "Addressing Antimicrobial Resistance In China: Policy Implementation In A Complex Context".
[74] National Action Plan to Contain Antimicrobial Resistance (2016-2020). Accessed June 24, 2017. http://en.nhfpc.gov.cn/2016-08/26/c_70276.htm.
[75] Xiao, Yonghong, Jing Zhang, Beiwen Zheng, Lina Zhao, Sujuan Li, and Lanjuan Li. "Changes in Chinese Policies to Promote the Rational Use of Antibiotics." *PLoS Medicine* 10, no. 11 (2013). doi:10.1371/journal.pmed.1001556.
[76] "Are antibiotics still automated." WHO. Accessed June 24, 2017. http://www.who.int/bulletin/volumes/89/1/11-030111/en/.

"Ecoantibio 2017", highlighting five priorities to reduce antibiotic use in veterinary medicine[77]; restrictions in prescription of antibiotics, making antibiotics a public good, promotion of new methods of breeding practices, tax reforms and reflection on business practices to modify related regulations and incentives accordingly.

The initiatives have largely been rewarding - the exposure of antibiotics to animals was lowered by 20%, while the use of critical antibiotics was cut by 21% in just two years[78]. Building on this success, France is creating a new, updated plan from 2017 to 2021, called "Ecoantibio 2", one oriented more towards incentives than regulations. The plan, through joint efforts of Ministries of Health, Agriculture and Environment, also focuses on access to alternatives, improvements of current preventive measures and better diagnostic tools for detection of antibiotic resistant pathogens.

Germany

Germany lists 3rd on the list of largest agricultural exporters in the world, and is one of the major consumers of agricultural antibiotics. Despite the government banning the use of antibiotics to promote growth in livestock in 2005, veterinarians often administer antibiotics on a large scale. This has led to an excessive use of antibiotics in the region, and a proliferating resistance to even the strongest antibiotics available. In addition, farmers also group livestock together in cramped barns, further amplifying the spread of superbugs among livestock and increasing the opportunity for bacteria to gain multiple resistances.

As a developed scientific and economic hub, Germany is looking to enhance and encourage national research and development of new antibiotics. In 2015, the Federal Cabinet of Germany adopted a policy to counter the growth of antibiotic resistance, named DART 2020. The action plan aims to further develop the EU's One Health approach, incentivise research and development in respective studies, and promote awareness and vital skills of both the general populace and medical professionals.

[77]Malvezin, Christophe. "Antibiotic Resistance: Recap of the French Plan." RSS. May 06, 2015. Accessed June 24, 2017. http://frenchfoodintheus.org/852.
[78]Ffus-wpadmin. "Ecoantibio II plan to reduce use of antibiotics released." RSS. May 15, 2017. Accessed June 24, 2017. http://frenchfoodintheus.org/3556.

India[79][80]

India tops the world when it comes to being the country with the highest infectious disease burden and the largest consumer of antibiotics for human health (at 12.9 million units with 10.7 units per person; beating both china and the US in total consumption). It is without a doubt, both a large driver of antibiotic resistance and a victim of the consequential lapse in public health. Indeed, irrational and inappropriate use of medicine is high with pervasive practice of over-the-counter nonprescription sales of most antibiotics such as carbapenem which have contributed to carbapenem resistance in gram-negative bacteria. The problem is one that cannot be removed from the country's poor healthcare infrastructure. As of 2013, India had no national data on antibiotic resistance in different pathogens except for when a national program was already present. Hospitals mostly lack infection control measures, and doctors are poorly trained or not aware of the rational use of medicine. Antibiotic residues have been detected in various food animal products, suggesting widespread antibiotic use in the growing livestock industry. The OECD projects that withdrawing antimicrobial growth promoters in India would come at an estimated cost of US$$1.1 billion, without accounting for the health benefit of less antibiotic resistance. The need for improved drug regulation, physician training and compensation, standard treatment guidelines and national plans for containment is present in India. The indian government has of recent years, taken progressive steps with or without WHO support to rectify the problem. This includes establishing INSAR (Indian Network for Surveillance of Antimicrobial Resistance) to collect key data regarding antimicrobial resistance, and the publication of a 'National Treatment Guidelines for Antimicrobial Use in Infectious Diseases' by the National Centre for Disease Control. Without commenting on the success of these policies, it is acknowledged that the indian government is in all likelihood prepared to take the appropriate action in combatting antimicrobial resistance.

South Africa

Antibiotic use in South Africa is increasing as a result of multiple reasons, including inappropriate prescribing, patient insistence and doctors' knowledge on correct usage of antibiotic agents[81], not to mention South Africa's staggering frequency of infectious diseases among its people. Furthermore, the huge income inequality in South Africa amplifies the need to address the issue of antibiotic resistance promptly - second-line treatments, which are often more expensive, are virtually impossible to obtain to the poor majority of the population. Antibiotics have also been greatly used by the agriculture

[79] Kumar, Sganesh, C. Adithan, Bn Harish, Gautam Roy, A. Malini, and S. Sujatha. "Antimicrobial resistance in India: A review." *Journal of Natural Science, Biology and Medicine* 4, no. 2 (2013): 286. doi:10.4103/0976-9668.116970.
[80] Laxminarayan, Ramanan, and Ranjit Roy Chaudhury. "Antibiotic Resistance in India: Drivers and Opportunities for Action." *PLOS Medicine* 13, no. 3 (2016). doi:10.1371/journal.pmed.1001974.
[81] Desai, Dr Safwaan. "South Africa is facing a superbug epidemic." Health24. December 11, 2015. Accessed June 24, 2017. http://www.health24.com/Medical/Meds-and-you/Antibiotics/south-africa-is-facing-a-superbug-epidemic-20151211.

industry in treating infectious illnesses in animals for years, speeding up the rate of antibiotic resistance[82].

Still, there have been stepping up their efforts in combatting antibiotic resistance. The South African Society for Clinical Microbiology, the Group for Enteric, Respiratory and Meningeal diseases surveillance (GERMS) and their partners have been performing routine, nationwide checks on relevant pathogens and antibiotics[83]. Moreover, with help and recommendations from Global Antibiotic Resistance Partnership (GARP), South Africa has modified and updated their regulations on antibiotics and prescriptions. However, there are obstacles - surveillance in South Africa is laboratory based, and are not easily correlatable to resistant bacteria outside labs; there are essentially no credible measurement of resistance in the communities. To improve South Africa's position in the war against antibiotic resistance, it is clear that collaboration of multiple stakeholders will be necessary.

United States of America

Being the largest pharmaceutical market in the world, the United States shows great promise in leading research on antibiotics. However, the field of antibiotics development has largely been neglected due to the lack of profits and high research costs. A growing superbug resistance reflects the grim reality of the ever-decreasing efficiency and lifespan of current antibiotics [84]. Furthermore, the number of newly approved antibiotics by the Food and Drug Administration continue to dwindle, as a result of pharmaceutical companies leaving the antibiotics development sector.

Another area in desperate need of policy reform is the infection surveillance sector [85] in national healthcare. Government industries and medical personnel often oversee the need to state superbug infection as a cause of death, resulting in the lack of accountability of the spread and severity of superbugs. However, there is no legal basis for not doing so, except for the states of Washington and Illinois. Furthermore, the healthcare sector may view this as detrimental to their reputation and business, as listing a superbug infection under causes of death would not only risk legal liabilities, but

[82] "Situation Analysis: Antibiotic Use and Resistance in South Africa." Center for Disease Dynamics, Economics & Policy (CDDEP). Accessed June 24, 2017. http://www.cddep.org/publications/situation_analysis_antibiotic_use_and_resistance_south_africa#sthash.Xvs2jENo.MilPhKmN.dpbs.

[83] "The Paradox of South Africa: How Antibiotic Resistance Fits into the Health Picture." Center for Disease Dynamics, Economics & Policy (CDDEP). Accessed June 24, 2017. http://www.cddep.org/blog/posts/paradox_south_africa_how_antibiotic_resistance_fits_health_picture#sthash.OeDrRGSW.Otwwt35u.dpbs.

[84] Sukkar, Elizabeth. "Why are there so few antibiotics in the research and development pipeline?" The Pharmaceutical Journal. November 13, 2013. Accessed June 24, 2017. http://www.pharmaceutical-journal.com/news-and-analysis/features/why-are-there-so-few-antibiotics-in-the-research-and-development-pipeline/11130209.article

also reflect their failure to treat the patient. Government institutes such as the Centre for Disease Control and Prevention also lack the financial and political infrastructure to reliably track the death toll caused by respective superbugs and the extent of the spread. This hinders federal and state governments from properly allocating manpower and funds to limit the spread of the disease.

GlaxoSmithKline

GSK is a London-based pharmaceutical corporation and is the one of the largest of its kind in the world. Despite the growing epidemic of superbugs and other such companies leaving the sector due to a lack of returns, GSK, along with several other pharmaceutical giants, have pledged to remain committed to the research and development of new antibiotics [86]. Furthermore, the corporation participated as a signatory in the joint industry declaration [87] on combating antibiotic resistance as of January 2016.

The company has also released a declaration of their public policy positions on antibiotic resistance [88], promising the prevention of improper industrial acts to increase profits and save costs, such as the dumping of antibiotic waste into water bodies and licensing newer antibiotics for agricultural use. Furthermore, it recognises the urgent need for relevant stakeholders to combat antimicrobial resistance, and has called for them to research on alternative solutions such as vaccines, and provide incentive models for the creation of new antibiotics in various regions around the globe.

Having products in agricultural antibiotic sector, GlaxoSmithKline has not stated its stance on the use of older antibiotics to treat livestock. However, it has expressed concern in this field, and seeks to avoid licensing future antibiotics meant for human therapeutic purposes to the agriculture industry. As for current products, the corporation has much to work on the regulation and prescription of these products, so as to ensure that it does not contribute to the spread of antimicrobial resistance.

FOOD FOR THOUGHT

1. How can member states achieve greater accountability in the use of antibiotics?
2. What will be a feasible framework for the promotion of rational use of medicine that encompasses challenges faced in both industrialised and developing countries?
3. How can innovation and research on the international level be stimulated?
4. In the event of epidemic or endemic, what are necessary measures to consider for implementation?
5. How will member states implement and enforce strict international guidelines for infection prevention and control measures?
6. How can member states stimulate more firms to start researching and developing innovative antibiotics?
7. How can the international community ensure well-connected and continuous checks on resistant bacteria?
8. How can the international community inform itself accurately on important facts surrounding antibiotic resistance?
9. How can data collected from surveillance infrastructure be effectively utilised?
10. How can the the frequency of use of antibiotics be regulated without compromising the health of citizens who actually need them promptly?
11. How can the international community effectively quarantine existing strands of resistant bacteria to minimise early casualties?
12. How can the use of antibiotics in the agriculture industry be effectively managed for the best outcome?
13. Is WHO doing an effective job at slowing down the manifestation of antibiotic resistance? If not, which aspects of WHO should be altered or removed?
14. How can domestic policy and international mechanism seek to address inappropriate prescription practices as well as substandard and counterfeit medicine?
15. On what level is regulation for drug quality and use justified, necessary and/or sufficient?
16. Will there be alternative forms of treatment that the international community can transition into? If so, what are the necessary steps at present to prepare for such a transition?

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