

Risk Management and Prevention of Antibiotics Resistance: The PREVENT IT Project

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Running title: Combating antibiotics resistance through education and awareness

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Abstract

Background: Globally, a significant increase in the emergence of antibiotic resistant (ABR) pathogens has rendered several groups of antibiotics ineffective for the treatment of life-threatening infections. **It is an endemic in hospital settings and a major concern while handling pathogens involved in an epidemic or pandemic. ABR is a matter of great concern due to its recusant impact on public health and cost to the healthcare system, especially in developing country like India.** An indiscriminate and inappropriate usage of antimicrobials, poor infrastructure and sanitation are the major factors driving the evolution of ABR in such countries. Therefore, in addition to the development of novel therapeutics and safeguarding the efficacy of existing antibiotics, there is an urgent need for a programme focussed on the education in risk management and prevention of ABR.

Aim: **To promote qualitative teaching activities in academia and society to visualize a future where every individual is aware of ABR and empowered with right education to address the issue.**

Method: The project, ‘Risk Management and Prevention of Antibiotics Resistance - PREVENT IT’, funded by the ERASMUS+ Programme of the European Union converges academicians and non-government organizations (NGOs) to inculcate a sense of awareness towards the increase in the frequency of ABR pathogens, judicious usage of antimicrobials and the economic/health burden of ABR, in students, academicians, clinicians and population at large.

Expected Outcome: The project commissioned envisages a behavioural change in individuals and attempts to support policymakers by executing stable changes in the curricula of institutes of higher education, developing advanced workshop modules for the training of academicians and disseminating ABR-related information through conferences/seminars, social media campaigns and an online platform dedicated to ABR. In addition, the project aims to develop a European-Indian network for the management of risk and prevention of ABR.

Key words: Antibiotic resistance, Education, Erasmus plus, Europe, Global Action plan, , India,.

Introduction:

Of the various health issues faced by the world today including COVID 19, antimicrobial resistance (AMR) is a growing problem that poses a grave threat to global public health (1). The term AMR pertains to the inability of the antibiotic to treat or cure the infection caused by microorganisms. Reports from the World Health Organization (WHO), have also declared AMR being the sole factor to be responsible for approximately 10 million deaths by 2050 (2). Given the fact that AMR is not constricted by demography or geography, it needs to be addressed globally (3). The global AMR response is listed in the WHO's core mandate, stressing the importance and priority to seek its remedy. The Global Action Plan on Antimicrobial resistance by WHO (4) and the National Action Plan on Antimicrobial Resistance NAP-AMR (5) by the Govt. of India are some of the global and local initiatives to combat the predicted adverse conditions. These action plans hinge on a multi-pronged approach that includes-

1. Creating awareness through education and training
2. AMR Surveillance
3. Prevention and Control Measures, including
 - 3a. Rational use of antibiotics
 - 3b. Research and Innovative Practices like improved diagnostics for reducing use of antibiotics
 - 3c. Therapeutics; that minimizes use of antibiotics
4. Collaboration facilitation

Though, all the approaches mentioned above are equally significant, creating awareness through education, targets the problem at the base level. As per a review conducted in 2016 by O'-Neill (6), the emphasis was laid on the urgency of creating global awareness campaign to educate the public, particularly youngsters about the ramifications of drug resistance. These initiatives have the potential to bring about behavioral change in the mindset of the youth. It is said that developing countries, such as India, with their enormous youth population could see their economies rise, only if they invest profoundly in young people's education and health (7). An innovative project initiated to address these challenges, named Risk Management and Prevention of Antibiotics Resistance - PREVENT IT, is being undertaken in India, in alignment with the National Action Plan (NAP) and funded by the European Commission under the Erasmus+ scheme. The project comprises of seven Indian partners and four European partners. The vision of the project is a future where every individual is aware of antibiotic resistance (ABR) and empowered with the right education to address and seek remedial course of action to prevent the further development of drug resistance. It is imperative for all the key stakeholders - academicians, researchers and non-governmental organizations - to coordinate and collaborate to ensure that health systems are better prepared to prevent and tackle the AMR threat.

Background:

The year 1928 ushered in the modern era of medicine with the discovery of the first antibiotic, Penicillin (8) that transformed the consequence of infections. However, unfortunately the bacteria evolved to become resilient to antibiotic/s leading to ‘resistance’ viz. antibiotic resistance (ABR). The likely causes of the increasing resistance are multifactorial including the involvement of three parties: humans, animals and the environment. It spans inappropriate antibiotic prescription, over-the-counter sale of antibiotics, disproportionate use of antibiotics in food of animals (livestock, aquatic, pets), and poor sanitation and hygiene (13). Further, hospital effluents, water from wastewater treatment plants (WWTP), industrial effluents appear to act as reservoir for ABR in soil and aquatic environment (14, 15). One cannot also ignore the contribution of other factors such as release of unused antibiotics or their non-metabolized residues into the environment via manure/feces and increased international travel. Thus, it is vital to apprehend that AMR is a multi-faceted problem which can only be tackled by employing the “One Health Approach” so that collaborative efforts can be made by the health authorities dealing with these spheres (16).

A report by World Health Organization states that there will be approximately 10 million deaths worldwide due to Antimicrobial resistance (AMR), mostly due to resistant bacterial infections by 2050 (18). The problem is, if the present condition is not tackled rightly, the global economic burden may reach about \$120 trillion (2). Recent data suggests that at least 700,000 people die each year due to drug-resistant diseases (6). Out of this, at least 230,000 people die only from multidrug-resistant tuberculosis (18).

Of all the developing countries, India bears the highest burden of resistant bacterial infections with a crude mortality rate from infectious diseases of 417 per 100,000 persons (19). At the same time, India ranks first in worldwide consumption of antibiotics for human use, with 10.7 units of antibiotics consumed per person in 2010. A rise of about 67% has been projected in antibiotic consumption by the year 2030 (20). Also, the incidence will double in BRICS countries (Brazil, Russia, India, China, and South Africa), which are developing at fast pace and are amongst the vastly populated countries of the world. In the absence of real data reflecting the current effect of ABR Indian scenario, few reports (21) have identified it as an emerging threat to public health. One of the major sources for environmental pollution in India are the hospital effluents and pharmaceutical waste waters which are passed into the nearby water bodies. Moreover, there is no ample treatment and improper disposal of unused antibiotics which is thrown in water or landfill. A study conducted by Akiba et al. (22) in South India found resistant *Escherichia coli* strains to third generation Cephalosporin in both domestic water and hospital effluents. Not only this, 100% resistance to cephalosporin (third generation drug) was seen in case of 283 *E. coli* isolates obtained from Indian river Cauvery located in Karnataka (23). Furthermore, a variable percentage of Oxytetracycline resistant Gram-negative bacilli and *Staphylococcus aureus* were detected in cow and buffalo milk in West Bengal and Gujarat. Another study by Sudha et al. (24) in shellfish and crabs in Kerala found strains of *Vibrio cholera* and *V. parahaemolyticus* 100% resistant to Ampicillin. Further, it has been reported that India will be contributing to the major relative rise in antibiotics consumption between 2010 and 2030, especially for use in livestock (25).

Various initiatives have been introduced both at global level and national level to fight against this adverse and alarming situation of AMR. Emphasizing the threat AMR poses to human health in May 2015, the World Health Assembly (WHA) recommended a Global Action Plan (GAP) on

AMR - comprising ABR (4). These initiatives include vigilant use of antibiotics and surveillance of antibiotics by engaging the “One Health Approach”. The WHA resolution also emphasized on practical measures and requested the Member States to align their national action plans with GAP-AMR by May 2017. In this framework, India has approved the National Action Plan on Antimicrobial resistance in alignment with global action plan (2017-2021) (5). The initiative was coordinated by Ministry of Health & Family Welfare, Government of India. Also, India has given due cognizance to the problem of AMR and launched “National Programme on the Containment of Antimicrobial Resistance” prior under the aegis of the National Centre for Disease Control (NCDC) in twelfth five year plan (2012 - 2017) (26). Further, recently in the year 2019, Indian Council of Medical Research published “Treatment Guidelines for Antimicrobial Use in Common Syndromes” (27). However, in spite of taking measures at the basal level, the final output could not stop the development of AMR (28).

Both global and national action plan call for an increased awareness, hence it is very important the education sector must also be included strategically to make a difference. Today this is a glaring gap. As at grassroot level – the communities, students both in school and higher education sector are not currently recipients/beneficiaries of this awareness programme. Academic institutions across the globe including India need to introduce and modify the content of its courses to enable their students to grow intellectually, politically, socially and culturally. Education of this type needs a new pedagogy where beings can develop skills to find out critically and contemplate systematically about difficulties/problems (29). A further study conducted by Fien (30) has suggested that making change in curriculum will directly influence the overall political, economical, and social development. Another approach is ‘capacity building’ which is one of the key prerequisites for its successful implementation, involving strategies, resources aiming to increase collective power of people. Thus, there is an urgent need to influence curriculums by incorporating information related to risk management and prevention of AMR/ABR. The project entitled; “**Risk Management and Prevention of antibiotics resistance - PREVENT IT**” aims to address these challenges via educational initiatives.

Context

Looking at the current scenario, it would not be wrong to say that India is becoming a hub of resistant infections not only for humans but animals as well. The poor sanitation, lack of infrastructure and huge population density are the contributing factors towards this situation. Though historically, AMR did not receive much attention in India, today tremendous efforts are being made in this direction. For instance, the initiation of a National Action plan aligned to a global action plan and active participant in GLASS. However, even after such initiatives, the dearth of financial help in developing countries acts as barrier in the implementation of these plans. Thus, use of primordial measure of prevention working at the grass root level with an aim to prevent any infection with low cost involvement is the need of the hour. One such initiative is creating awareness amongst society, especially youth of a country through education. In this regard, the innovative character of the PREVENT IT project is to create the first Indo-European collaboration aimed at developing ABR specific curricula and disseminating expertise in ABR prevention. The experts from academia will reach students from different background while Non-Governmental Organizations (NGOs) will be spreading awareness among citizens. The project will bring sustainable change by creating awareness both at organizational and societal level.

Functioning of the PREVENT IT Project:

Goal

The goal of the project is to create a future where every individual will be aware of antibiotic resistance (ABR) and empowered with the right education to address the issue of ABR.

Therefore, the project aims to promote qualitative learning activities in academia as well as in the society.

Objectives

- 1.** To establish the first European-Indian network for risk management and prevention of ABR by developing interdisciplinary curricula on Risk Management and Prevention of ABR at Indian partner universities.
- 2.** To spread awareness in academicians, students, policy makers and general public through public events and awareness campaigns on social media.
- 3.** To create super-expertise in delivering ABR advanced vocational training to young Indian academicians.
- 4.** To create an interdisciplinary free online course for spreading awareness, enlarging the target groups empowered in the framework of the project.
- 5.** To promote informative events at community level in cooperation with projects' NGOs.

Funding agency and cohort of the project

The Erasmus+ programme of the European Commission has opportunities for individuals as well as organizations aiming for research, teaching mobility, and policy reform acts. Out of these key actions, PREVENT IT was granted under the category of **Capacity-building** in the field of **higher education** (CBHE) to support modernization, accessibility, and internationalization of higher education in developing and transition countries. The project is a consortium of partners from five countries, namely India, Portugal, Latvia, Italy and Netherlands. There are nine higher education institutions and two Non-Governmental Organizations involved, making a total of eleven partners. Of these, seven partner organizations are situated in different states of India, thus justifying the diversity of the group (**Figure 1**). The Health Sciences team of the project comprises of the experts from each Higher Education Institutes (HEIs)/organizations responsible to undertake the academic and scientific tasks of the project. The detailed description of other stakeholders is given in Figure 1.

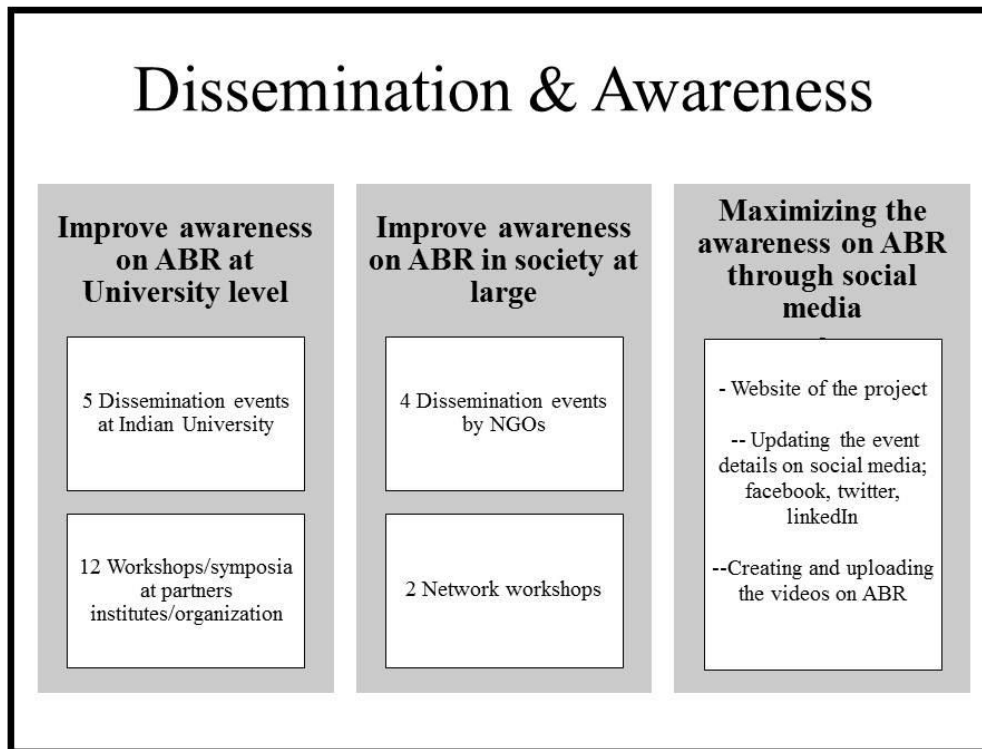
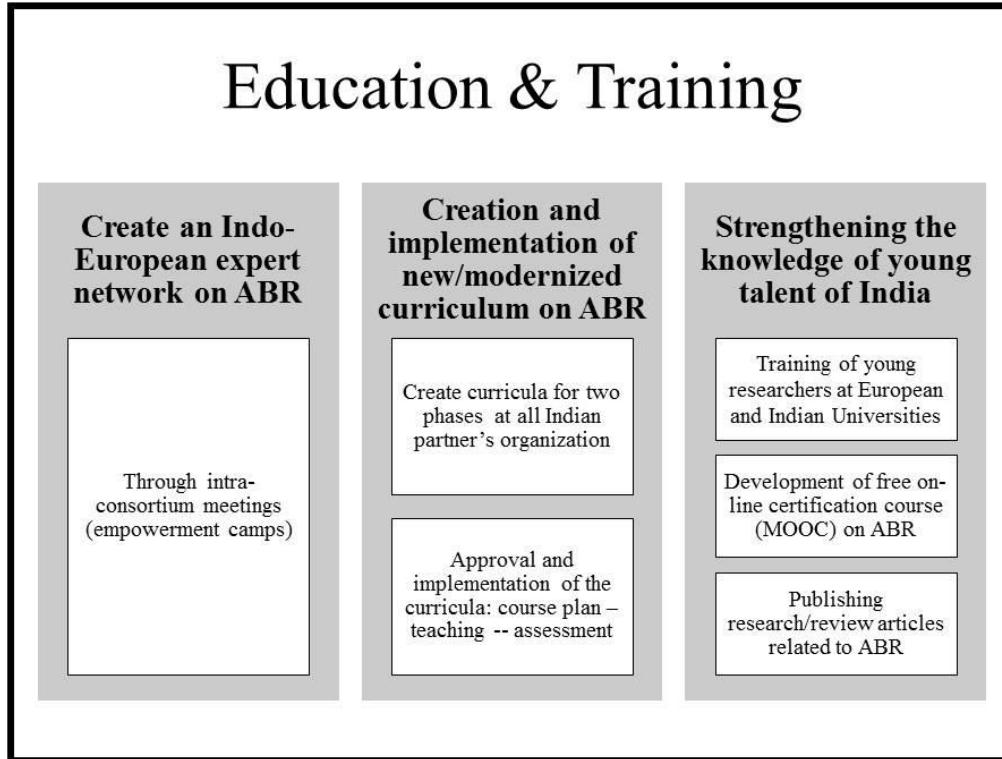
Figure 1: Geographical distribution of the partners



Strategic priorities

The PREVENT IT project outlines interventions and priorities planned to be executed over 2019-2021 to combat the public health challenge of ABR not only in India but globally too. The key strategic priorities include “Education & Training” and “Dissemination & Awareness” – which are in line with the global and national action plan. As it is said, “One always has time enough, if one applies it well”, the key activities (**Figure 2a & 2b**) involved in achieving the strategic priorities are planned on yearly basis.

Figure 2a and 2b: Strategic priorities of PREVENT IT project



➤ *Education and Training*

Education

This project seeks to influence education by modifying the existing curriculum, or creating new course/s at the graduate, post graduate and doctoral level at Indian Universities, as well as NGOs. This will serve to ensure the sustainable application of the knowledge on ABR. An expert review committee was also established called the Indo-European network whose functioning was to ensure a robust curriculum.

Create an Indo-European expert network on ABR

In order to create an Indo-European network on ABR, the first milestone of the project was to organize three intra-consortium empowerment camps of four days each comprising a total of eighty four hours. These empowerment camps are very crucial in terms of skills and team building. The mission is to create the Health Sciences team of interdependent experts from HEIs and NGOs with a great ingenuity in antibiotics prevention and risk management – with specific knowledge on Indian milieu. The key role of the first two empowerment camps is to create the new/modernized curricula for the Indian Universities as well as NGOs.

Creation and implementation of new/modernized curriculum on ABR

First of all, the existing curricula of health-care programs will be reviewed by the respective partner organizations for the existence or non-existence of relevant topics that must be taught on ABR. The gaps observed in curriculum will be enlisted and proposed revised or new curricula will be shared and presented in front of Indo-European network during the empowerment camps. The feedback/s (online) on the curricula will be provided by Indo-European expert group depending on the field of expertise (Allied Health Sciences, Optometry, Physiotherapy, Microbiology, Pharmacy, Biotechnology, Bachelor of Medicine and Bachelor of Surgery (MBBS), Nursing, Public Health, Bachelor of Dental Surgery (BDS), Doctorate level). The discussion/s will aim at evolving the teaching methodology and assessment pattern followed at different HEIs.

For the sustainable implementation of the curricula, attempt will be made to ensure the incorporation of the proposed curricula as part of the existing syllabus. The curricula to be implemented at Universities will be subjected to the approval from board of studies and Academic councils while NGOs need approval from their respective personnel/entities. The expected key outcomes of the first two camps is to finalize the list of teaching modules with details of updated course plan – including course nomenclature; target audience; teaching methodologies; assessment pattern; bibliography pattern at academic and community level.

Key output:

The implementation of the finalized curricula is planned to begin at respective organizations by June, 2020, aiming to modernize the multidisciplinary courses in Health Sciences, thus influencing approximately nine hundred students.

Training

The term “training” corresponds to strengthen the knowledge of young researchers in India so that they can emerge as the future experts in the field of ABR. These experts will have capacity to conduct teaching activities and develop sustainable tools for creating awareness on ABR besides developing online course, social media campaign, and carry out focused ABR publications. Also, the selection of young scientists on projects for their post-graduation and doctoral work based on AMR is significant.

Strengthening the knowledge of young researchers of India

For this, five full time (Associate Researchers) will be engaged at the Indian Universities from the second year onwards. They will be trained through various capacity building trainings to emerge as subject experts engaged in teaching and creating online courses and publications dedicated to ABR. The training to be imparted in two phases-

The first phase- Training at Chitkara University and the second phase- Training at the partner European Universities, while training at host institutions will be there throughout. The training at Indian University will be to understand the goal, objectives and key activities of the project along with team building.

The exhaustive training will be provided at European universities for about four weeks. The content of the training will include expert talks on ABR by European faculties, learning of new teaching methodology such as problem based learning, exposure to organization of the hospital/pharmacy prescribing antibiotics etc. The key idea is to use these subject specialists to further train the trainers at their respective host and intra-consortium organizations.

It has also been observed that younger people wish to have health information via the internet or electronic means, thus attempts to update and stimulate a sub-group of a population by means of organized communication actions through explicit channels will be done (30). An interdisciplinary open access course will be developed by the young researchers under the guidance of Health Science expert group. The technical portion of the on-line course will be supervised by the European experts from Maastricht University. The effort will be made to write and publish minimum six research/review articles in peer reviewed journal/s on ABR in order to create awareness on the risk management and prevention of ABR.

Key output:

To prepare and equip ABR experts to further share the knowledge on ABR through teaching activities. Further, there will be development of a free on-line certificate course for healthcare professionals. Also, to publish minimum six research/review articles in peer reviewed journal/s on ABR in order to spread awareness on the risk management and prevention of ABR.

➤ ***Dissemination & awareness***

Recent literature on social marketing campaigns, including online campaigns, advocate that the campaigns can impact people to bring out change in their behavior and can also inspire policy-makers (32). Also, awareness campaigns are being documented as one of the most proficient means of communicating information especially to the general public. According to the state of change model, if the awareness campaign is propagated effectively for a specific issue, it will bring change in the attitudes of the society, finally reflecting the change in person's perception about his/her own capacity to perform an act. However, it has been observed that often campaigns on health have been funded on short time-scales but in order to achieve behavior change, long term strategies are needed (33). Thus, a series of comprehensive events are being planned to make students, academicians, policy makers and general public aware about the alarming situation on ABR. The events will be planned in a way so that the intra-consortium mobility of Europeans as well as Indians is promoted. The key aim is to strengthen the network and understanding of team work for the noble cause.

Improve awareness on ABR at University and societal level

In total, nine dissemination events and fourteen network workshops will be conducted during the tenure of the project. The key activities involved will be the more or less common for both the categories. The steps involved will be to: identify and consolidate existing communication/information resources/products on AMR in various sectors/stakeholder groups; map the expertise of individual, stakeholders plus organizations (public/ private) to develop

communication strategy. The content and teaching methodology for the event will vary according to the targeted stakeholders. The target audience varies from students of intra-consortium, students from other universities policy makers, academicians, accredited social health activist (ASHA) workers, self-help groups, farmers, pharmacists etc.

Maximizing the awareness on ABR through social media

A multifaceted approach will be undertaken to ensure the awareness and visibility via social media campaigns. One of the key activities will be website hosting which will be updated periodically, in order to share ABR news, articles, information – which will boost visitor's figures. Social media will be used intensely for the visibility and outreach of the PREVENT IT project. The communication will be done on three social sites viz. Facebook, Twitter and LinkedIn. The social media of the project handle will be shared by the young researchers and will do the needful for its further promotion.

Key output:

Outreach maximum population and spread the awareness to lower the incidence of ABR

Expected outcome/s of the project:

- Help create a consensus amongst scientists working across the globe on the problem of AMR and its remedies in an atmosphere of urgency and mutual cooperation.
- Develop and implement international, interdisciplinary teaching curricula at Indian Universities on risk management and prevention of ABR.
- Invest in young talents, empowering Indian super-experts having an international outlook.
- Spread awareness among academicians, students, policy makers and general public through events and social media campaigns.
- Create an interdisciplinary online course to educate a multidisciplinary audience.
- Establish the first European-Indian network to develop further initiative for risk management and prevention of ABR.

Perspective

The proposal is the direct output of the collective preliminary-assessment study conducted since September 2016. In accordance with recent statement of the Indian Ministry of Health & Family Care, historically antimicrobial/antibiotics resistance (AMR/ABR) did not receive adequate focus and attention in India (26). The topic was selected due to numerous scientific publications warnings – and reiterated World Health Assembly resolutions - on global risks of antibiotics resistance. It is worthy to note that India, a developing country, is one of the nations with highest burden of bacterial infections (19). Further, the emergence of resistant bacterial infections event to the newer class of antibiotics is making situation more worrisome (34).

Moreover, the preliminary research conducted by PREVENT IT team has identified the following problems: I) Lack of awareness in HEIs, Civil Society organizations and citizens; II) Lack of compulsory curricula for HEIs' students which requires antibiotics resistance prevention skills; III) Lack of projects in Asia tackling antibiotics resistance at grassroots level; IV) Legislative gap in Indian context: absence in the legislation of restrictions on pharmacological pollution in water sources; V) Few Indian HEIs' scientific publication on ABR – correlation to brain drain; VI) Lack of Asian-centered MOOC on ABR – and skills' glitches in MOOC creation at Indian HEIs. Thus, in order to bridge the gap, this project will act as a stepping stone.

Key strengths:

Geographical spread and inter-disciplinary experts:

The primary strength of the project is the diversity of the partners and collaboration amongst European and Indian experts. Creating a pool of super-expertise from different health sciences backgrounds with a great heterogeneity of geographical distribution is the key weapon of the project. There is involvement of the partners from Europe (Latvia, Netherlands and Portugal), who are known worldwide for being the countries with lowest and controlled incidence of ABR (35). Further, University of Maastricht is well known for creating online courses (MOOC) as well as the famous learning methodology i.e. problem based learning. Another partner, University of Milan is one of the largest universities in Europe and is ranked among top five universities of Italy. The Pharmaceutical Sciences Departments have great experience both in the development of new antibiotics and studying antibiotic resistance mechanisms and in regulatory aspects and quality control. This inter-exchange of knowledge would definitely ensure in creating breakthrough knowledge bank, resources and expertise that would prove consequential in targeting the ABR threat.

All the Indian universities have been associated with the Erasmus Plus funded projects at some point of time. The associated Indian universities have well established departments and prowess in various domains to be influenced by the project. The range varies from Public Health – Microbiology – Nursing – Medical doctors – Dentists - Allied health sciences – Biotechnology – Pharmacy etc. The three universities, Amrita Vishwa Vidyapeetham University, Manipal Academy of Higher Education and Kalinga Institute of Industrial Technology are already contributing to the clinical care and academic training seamlessly. The focus is on infection prevention and control (IPC) activities and antimicrobial stewardship (AMSP) initiatives to combat hospital associated infections in association with WHO and Quality Council of India (QCI). Both the NGOs are well equipped to provide capacity building through training and programs to be delivered to general public. Looking at the dissimilitude of competence and geographical distribution of Indian partners (including Higher Educational Institutions and Non-Governmental Organizations) within consortium needs no further explanation.

Empowering young talent: Capacity building:

One of the major outcomes of the project is training the young associate researchers to become subject expert on ABR. These experts will be responsible for training the trainers, students and conducting different dissemination events for general public.

Sustainable goals and outcomes:

The endeavor is to bring about sustainable changes in the form of curriculum, publication and MOOC course. The curriculum is so created that it can be incorporated in the academic program guide to make sure the pervasive implementation of the same. This will definitely sensitize the students, ensuring the fact that when they enter the health care sector, they are honed enough to contribute in decreasing the incidence of ABR. Another approach is to encourage reflection amongst academicians working in different fields of health care through publications. An effort will be made to bring on plate the sad reality of the current situation of ABR and highlighting the steps involved in risk management and prevention of ABR. Last but not the least, in order to outreach student population at large, a free online certification course will be created using interdisciplinary approach. This initiative will enable the project to reach out to the students across India as well as other parts of the world.

Creating awareness:

One of the major outcomes of the project is to sensitize healthcare, non-healthcare students and general public. The mode of delivery will be through expert talks, skits, dramas, posters, etc. during dissemination events. However, the content of the delivery will change according to the

target audience. This is setting in motion a very sustainable process as the students who are being trained are the ones entering healthcare workforce tomorrow as well as will become the future academicians and researchers.

Limitations:

A major limitation of this project, similarly to every other project promoting capacity building activities in a vast country as India, is the financial shortcoming vis-à-vis the magnitude of the challenges addressed. The project although targets a wide audience of students and general public but measures to involve farmers and animal husbandry, covering all hemispheres of ‘One health’ is lacking and the execution of the curriculum programme is restricted to regions within India. Despite the direct involvement of five Indian higher education institutions – and two non-governmental organizations, risk management and prevention of antibiotics resistance in India require an integrated approach, involving an enlarged and differentiated platform of stakeholders, combining the bottom-up approach utilized in the project, with coordinated top-down initiatives. Also, at present, government agencies involved in policy making are not directly involved in the execution of the project.

PREVENT IT is expected to generate a major improvement in the capabilities of Indian universities - and NGOs - to educate different target groups with foundational and advanced skills in ABR. Due to the Erasmus+ funding scope, the activities financed are only marginally focusing on research, partially hampering the scientific credibility – and visibility – of the project in the international academic community.

Conclusion:

Projects like PREVENT IT unify the researchers, students, academicians, non-governmental organizations from different parts of the world and provide them a common platform to work in unison for the noble cause assuring good health. These types of projects will accelerate the pace of curriculum change globally, keeping in line with changes in healthcare trends. Preventing ABR through a behavioural change is the first step of this collaborative process and the success of the project would open up further novel alternatives to combat ABR. As it is rightly said, ‘ *He who has health, has hope; and he who has hope, has everything.* ’; it is high time we should collaborate across disciplines to bring sustainable changes in the healthcare sector for better, happier and healthier future.

Conflict of Interest: None.

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