Antibiotic resistance: Prioritising the patient
THE GLOBAL INFECTION PARTNERSHIP DECLARATION

“We, the Global Respiratory Infection Partnership (GRIP), recognising the imminent onset of the post-antibiotic era and taking full cognisance of the declining numbers of new antibiotics in development hereby commit to:

1. Consistent, sustainable evidence-based advocacy and intervention for rational antibiotic use and antimicrobial stewardship;
2. Formulating a framework for non-antibiotic treatment options for respiratory tract infections (RTIs), such as sore throat, common colds, influenza and cough;
3. Facilitating multi-stakeholder commitment to antibiotic stewardship and rational antibiotic use.”

GRIP MEETING ATTENDEES

GRIP meeting attendees (left to right): Dr Martin Duerden, Dr Aurelio Sessa, Mr John Bell, Dr Alike van der Velden, Prof. Sabiha Essack, Dr Laura Noonan, Prof. Attila Altiner, Prof. Roman Kozlov, Prof. Dr Ayşe Willke Topcu, Prof. John Oxford, Mr Adrian Shephard, Dr Ashok Mahashur, Dr Doug Burgoyne, Professor Antonio Carlos Pignatari.
INTRODUCTION

In 2015, the GRIP partnership met to establish the global status of antibiotic resistance and recognise the local challenges in each country. The aim of the meeting was to assess the progress of GRIP and the success of previous initiatives, and to discuss possible solutions to target the specific challenges facing each country. The group also aimed to determine a focus for 2015 activations.

Chair of the meeting, Professor Oxford gave an insightful overview on the diminishing usefulness of antibiotics and the ongoing global challenges surrounding their stewardship.

The resolutions put forward by Dame Sally Davies (UK Chief Medical Officer), who has called for global action on antimicrobial resistance (AMR) to antibiotics, were presented. Professor Oxford highlighted the need for the involvement of global organisations supporting the cause — “Her task is to get the World Health Organisation behind them, because without them it’s not going to move anywhere”. The action plan contains four main resolutions:

1. “Global action on AMR – preparing for the diminishing usefulness of antibiotics and antivirals”

2. “Push to agree on a global plan for AMR research, surveillance and action, and for this to be passed by the World Health Assembly with overwhelming support”

3. “Advocate laboratory surveillance of drug-microbe combinations and antibiotic-stewardship programmes – at the local, national and regional level”

4. “Practice what I preach in 2015 – the need to increase one’s own physical fitness”

Another point of discussion was the new discovery of teixobactin – an antibacterial isolated from a bacterium that has not previously been cultured. Professor Oxford noted that while the discovery is exciting — “they’re pushing it forward as a potential for a resistance-free antibiotic” — it could be many years until this antibiotic is available for clinical use. He emphasised that it is vital that we protect the antibiotics we presently have as it may be many years until new antibiotics are approved for clinical use.

“There are new discoveries which will eventually provide us with new antibiotics, but that isn’t to say that we don’t need to look after them properly and that requires changes at many levels.”

[Dame Sally Davies’] task is to get the World Health Organisation behind them, because without them it’s not going to move anywhere

Prof. Oxford

EXECUTIVE SUMMARY

- Antibiotic resistance continues to be an escalating global health threat

- The current media coverage and drive to increase awareness offers an opportunity to further instigate behavioural change at a government policy level, and through to grass roots initiatives

- The recent discoveries in the field of antibiotics will hopefully provide us with alternatives in the future; however, antibiotic stewardship must become the norm

- Throughout 2014, GRIP accelerated their efforts in the fight against AMR through both global and local activations

- Future GRIP initiatives will have to contend with the complexity of country contexts in terms of the challenges and barriers they are facing. Countries will need to join forces to combat the scale of the issue and drive real change

- Patient education should be the focus of 2015 initiatives — either by producing materials that target them directly, or by developing pharmacy materials that can be used during patient consultations

For more information on the Global Respiratory Infection Partnership and to access the materials referred to in this report please visit www.GRIP-initiative.org
GRIP ACHIEVEMENTS

In 2011, European healthcare professionals (HCPs) met to understand the landscape and the challenges that lie behind antibiotic resistance. This formed the foundation of GRIP and defined future aims and objectives. The first GRIP advisory board was held in 2012; the meeting highlighted the multifactorial nature of the problem, including patients, pharmacy, microbiology and doctors, as well as geographical differences. During 2013, knowledge was turned into practice – the pentagonal 5P framework (policy, patients, prescribers, prevention and pharmacy) was introduced and GRIP materials were developed and released.

2014 activations

In 2014, GRIP further accelerated their efforts with a number of global and local activations. The Geneva Forum, WHO response and GRIP Summit were used to seek engagement, while the GRIP YouTube channel, Summit and the Summit meeting report (accepted for publication in the International Journal of Pharmacy Practice [IJPP]) were used to drive awareness.

The 2014 Summit, entitled ‘Antibiotic stewardship: more action, less resistance’, was chaired by Professor Oxford and examined the latest science regarding the impact of inappropriate antibiotic use. The new GRIP 1,2,3 toolkit was released, receiving positive feedback from attendees:

- Attendees came from 18 different countries
- 100% of attendees stated that the educational content of the presentations was either excellent, very good or good
- 95% of attendees expressed an interest in sharing the GRIP materials, the 5P framework, and the 1,2,3 approach

New GRIP materials were released at the GRIP 2014 Summit. The new materials focused on:

- Expanding the 1,2,3 approach
- Improving patient/parent information
- Enhancing healthcare provider education

The patient video, developed by GRIP, was also released. It follows the character of Bob who is suffering from a upper respiratory tract infection (URTI). The video explains the importance of effective symptomatic relief in a clear, concise and humorous format.
GRIP ACTIVATIONS AT A LOCAL LEVEL

Since the last GRIP meeting, members have been working to further disseminate GRIP messages at a local level. Members were asked to give an update on the current status of antibiotic resistance in their country and the initiatives they have been working on in the last year.

Germany

Both public and media interest in antibiotic resistance in Germany has increased. In an effort to change GP prescribing behaviour, a trial analysing the effect of educating GPs on appropriate antibiotic use and prescription rates was set up. The CHANGE-2 trial uses an algorithm to help diagnose URTIs and recommend when to refer patients for further investigation if there is uncertainty. Tests like the rapid strep test and the C-reactive protein test are common tools used in Germany to identify serious infections. Although the validity of the tests has been questioned, scientists argue that they can provide reassurance if the result is normal. The results of CHANGE-2 will be available by mid/late 2015 and, following the success of the CHANGE-2 intervention trial, the second phase of Germany’s antibiotic resistance strategy – DART – is expected to get underway in 2015.

Australia

Awareness of antibiotic resistance in Australia is a growing concern for GRIP. Data from the NPS MedicineWise Research conducted in September 2014 and released in November during Antibiotic Awareness Week shows that 17% of patients expect an antibiotic to be prescribed when treating a URTI. However, doctors believe that 50% of patients expect to receive an antibiotic prescription. These shocking statistics are particularly worrying considering that GPs are often challenged by their patients and, when pushed for time and to avoid conflict, they prescribe antibiotics, even when they feel they are unnecessary. It has been noted that although Australian GPs are aware of the problem of antibiotic resistance and acknowledge the issue to be serious, most feel the responsibility is not theirs. The release of a national initiative report by the Australian Commission on Safety and Quality in Health Care on Antimicrobial Resistance in 2013 hopes to tackle these issues through governance and surveillance, as well as communication, which includes education, stakeholder engagement and partnerships.

South Africa

In 2014, South Africa made the most of opportunities to raise awareness of antibiotic resistance, with presentations by Professor Sabiha Essack at the Geneva Health Forum, the FIP World Congress and the Conference of the Independent Community Pharmacy Association on the role of the pentagonal 5P framework for antibiotic stewardship. The South African Department of Health also released a framework document outlining their AMR strategy, which includes prevention strategies focusing on IPC and vaccination programmes, interventions that are underpinned by education of HCPs and sustained multi-pronged communication and information campaigns.

This looks set to continue with plans for a 2015 Honours Research Project, which will determine the appropriateness and adaptability of interventions/tools aimed at minimising antibiotic use in the treatment of self-limiting URTIs. Looking in a South African context within the private sector, the project will:

- Assess the knowledge, attitudes and practices of community pharmacists with regard to the use of antibiotics in the treatment of URTIs
- Determine the appropriateness and adaptability of the GRIP toolkit via a questionnaire survey of pharmacists and patients, and
- Recommend modifications and adaptations to the toolkit to suit the South African context in the treatment of URTIs
Future publications in 2015, such as Prescriber Practices for Common Community-Acquired Infections in South Africa, hope to further promote awareness of AMR in South Africa.

Russia

Increasing awareness and knowledge of antibiotics is still very much the focal point in Russia’s fight against AMR. Their main aim is to reduce unnecessary use of systemic antimicrobials in outpatients with RTIs, which involves improving the knowledge of physicians and medical students, decreasing the frequency of self-treatment with systemic antimicrobials, and reducing dispensing of systemic antimicrobials without prescription, among others. A key target group, recommended by Professor Kozlov is medical students, as they seem to have a keen interest in the topic. Results from a survey undertaken among Smolensk students show that, although 63.3% are aware of the fact that antibiotics are often used inappropriately, over half (55.7%) of students had taken antibiotics without a prescription. However, promisingly, 70% of students asked were interested in understanding more about AMR. Other target groups include GPs and ENT specialists, pharmacists, patients and parents of children with a RTI and Smolensk residents. To present the campaign in a unified style, a website has been set up to cover the problems of AMR in Russia and inappropriate antibiotic use. With the campaign in full swing, Russia anticipates an increase in awareness of antibiotic resistance, further prompting a call to action in the fight against AMR.

Ireland

From 2003 to 2013, the rate of antibiotic consumption in Ireland was shown to increase from 20.34 to 23.66 DDD (defined daily dose), prompting an audit in 2014 of the Personal Antibiotic Prescribing and Irish Antimicrobial Prescribing guidelines. Results from the initial data collection showed that 10% of sore throat patients received an inappropriately prescribed antibiotic. Following an intervention and a re-audit, results indicated a reduction in inappropriate prescribing from 10% to 3.7% and the use of appropriate antibiotics increased from 80% to 100%, highlighting the fact that awareness of best practice guidelines can reduce antibiotic overuse.

With this in mind, one area of the ‘Play Your Part’ initiative aims to tackle the problem of GPs overestimating the value patients place on antibiotics during consultations, and consists of a forum, website and a resource pack. The resource pack has already been distributed to 2,530 GPs, with over 300 GPs also receiving a pack at the annual Irish College of General Practitioners winter meeting. A ‘Play Your Part’ pharmacy pack has also been handed out to 1,500 pharmacists. Focusing on an effort to tackle awareness in pharmacies, a partnership with the Irish Pharmacy Union has also been set up to reduce unnecessary antibiotic usage in Ireland. The success of the campaign is evident; ‘Play Your Part’ received a commendation for Best Education Project – General Practice/Pharmacy at the 2012 Irish Healthcare Awards.

In 2015, Ireland will focus on national guidelines and building a stronger antibiotics campaign. An emphasis will be placed on education and reinforcing guidelines for GPs and students, as for many doctors, it is easy to let things slip over time; therefore an awareness of guidelines can help maintain good practices.

Brazil

Dr Pignatari reported that the campaign against AMR in Brazil is moving steadily, with a main focus on targeting patients and pharmacists in 2015. As 200 million people in Brazil speak Portuguese, it is imperative that materials are translated to communicate their messages effectively, beginning with abstracts of articles previously published in the International Journal of Pharmacy, following which they will be published in Brazilian journals. A week-long public health awareness event held in April 2015 will also be a main focus of the campaign in which the issue of URTIs will be discussed.

Italy

Many think of “resistance as a problem of the hospital not the community” highlighted Dr Sessa, who stressed that everyone is responsible. Italy’s main targets for raising awareness of AMR are GPs and pharmacists. This has included audits of small group GP practices or local health districts, and local seminars directed at pharmacists. Increasing awareness of AMR in Italy looks to be on track; plans for 2015 include preparing a study protocol aimed at collecting qualitative data regarding URTIs in pharmacy and the pharmacist-patient relationships that sit behind antibiotic use, as well as releasing the GRIP toolkit containing an introductory letter, leaflet and poster to doctors and local pharmacies.

Netherlands

Although antibiotic use in the Netherlands had been increasing over the last 5 years, it has decreased in the last year. Dr van der Velden, however, warns not to become too complacent as this could be attributed to a mild winter. Unnecessary antibiotic use tends to occur during the winter months and this is one area in which the Netherlands needs to focus to reduce unneeded prescriptions. Nevertheless, results from the ARTI-4 trial that looked at the effect of educational materials for GPs and patients demonstrated that GPs who received educational intervention prescribed antibiotics nearly 8% less compared with the control group. Moreover, significant results from year one of the study showed that over-
under-prescribing for RTIs decreased from 44% to 28% and 2.8% to 1.5%, respectively.

A 2014 ministerial meeting held in the Netherlands further exemplifies the country’s efforts to tackle AMR. Conclusions such as developing and implementing “national and global measures and intergovernmental standards for infection prevention” and recognising “the need for a stepwise multi-sectoral approach to enable all countries, especially developing countries to strengthen their capacities and to make progress to achieve better control of antimicrobial use and resistance at all levels”, among others, were drawn at the meeting, which they hope to action in 2015.

Four guest speakers attended the GRIP advisory board to provide case studies from different countries and highlight their local challenges and the impact antibiotic resistance has in their markets.

EXPANDING HORIZONS: ANTIBIOTIC RESISTANCE CHALLENGES FROM AROUND THE WORLD

Resistance snapshot – USA

The USA has many activities and initiatives currently in action to raise awareness of AMR, the main being the national ‘Get Smart’ campaign, which has a multi-faceted approach of creating guidelines and educational materials aimed at HCPs and patients, as well as campaigns that run on TV and radio.

However, despite these successes, the USA still has much to do. Worryingly, some have argued that an improvement in healthcare will only occur if there is a resulting increase in revenue or cost saving. Although doctors receive remuneration for avoiding antibiotic use, they actually receive more from writing a prescription. This may be why antibiotics are often prescribed as they are inexpensive and there is no unease associated with prescribing them. Perhaps further contributing to unnecessary prescribing is the referral to ‘patients’ as ‘consumers’, leading to many HCPs assuming they must give patients what they want rather than what is right. Moving towards prescriptions for symptomatic relief so that doctors are still benefitting from the associated revenue, is one method to avoid inappropriate antibiotic prescriptions suggests Dr Burgoyne.

Targeting employers may also prove to be a successful reach for the campaign as many larger companies often vaccinate their staff against the flu, and can provide an opportunity for many people to speak to HCPs about cold and flu, as well as educate them on antibiotic use. Future campaigns targeting Minute Clinics may also be planned as 65% of URTI diagnoses are made there. Focusing on communication efforts to HCPs and pharmacists on symptomatic relief and alternatives to antibiotics, as well as collaborating with private employers and state programs such as Medicaid, will most certainly provide results in the USA’s fight against AMR.

Resistance snapshot – Saudi Arabia

There are many factors contributing to antibiotic resistance in Saudi Arabia; one main problem being that it seems to be relatively simple to access antibiotics. As well as through prescriptions and pharmacy, antibiotics can be sourced from leftovers, relatives and neighbours, and samples and donations. The need to provide education to patients, doctors and HCPs in Saudi Arabia is even more evident when taking into account the influences on antibiotic use within the country. Many patients still hold misbeliefs regarding the use of antibiotics, and can often be demanding. A lack of knowledge within physicians and in policies and regulations of antibiotic use, coupled with the financial benefit for pharmacies prescribing antibiotics, can all lead to incorrect antibiotic use.

A study by Bin Abdulhak et al., published in 2011 in BMC Public Health, investigated the non-prescription sale of antibiotics in one region of Saudi Arabia. Results showed that 77.6% of the pharmacies included in the study dispensed antibiotics without prescription, and 95% of these sales were made without patient request. It was also noted that ciprofloxacin is the most common antibiotic given for a URTI (in 86% of cases), even though it may not be the most appropriate. Another study by Abdallah et al. in 2011 in the Research Journal of Medical Science assessed the attitudes of 50 patients with antibiotic-resistant Staphylococcus: 24% of doctors or pharmacists said they felt ignored by the patient; 64% of patients exaggerated symptoms to get an antibiotic; 64% of patients purchased antibiotics based on quality; and 44% of patients had <50% compliance to treatment.

Saudi Arabia recognises their need to implement and enforce guidelines and regulations, as well as educate doctors, pharmacists and the general public in an effort to raise awareness and effect change in antibiotic use.

Resistance snapshot – Turkey

A study by Versporten et al. published in 2014 comparing antibiotic use within ESAC-Net countries showed that Turkey has the highest consumption of antibiotics in Eastern Europe. There are several factors contributing to the inappropriate and widespread use of antibiotics in Turkey, which include the attitudes and behaviours of family physicians, over-the-counter selling by pharmacists, high rates of self-medication, patient or family requests, and poor infection prevention and control practices. One particular trend increase was noted after implementation of the Social Security Reform, which allowed the prescription and consumption of drugs much easier. The issue of compliance also seems to be a major factor, with many not finishing their course or using leftover antibiotics.

Before responsible antibiotic use can occur in Turkey, there are many barriers to overcome said Dr Topcu. Insufficient national guidelines and surveillance systems for antibiotic resistance and consumption of drugs need to be addressed, as well as poor enforcement of regulation. Investigating the lack of laboratory
facilities that contribute to the diagnosis in primary care and the widespread practice of selling antibiotics over the counter are also major focal points. However, Turkey has already begun to tackle a few of these issues with many initiatives currently taking place. These include a policy released in 2003 that restricts the prescription of antimicrobials so that some prescriptions can only be made by infectious disease specialists, and an action plan that contains quantitative targets to reduce antibiotic use by 2017. Furthermore, the Turkish Ministry of Health established an educational programme for Rational Antibiotic Use in 2014. With the actions of medical associations such as the Turkish Clinical Microbiology and Infectious Diseases Society at several related conferences and their involvement in creating and preparing guidelines, Turkey looks set to place a concerted and coordinated effort in tackling the spread of AMR.

Resistance snapshot – India

A total of 15.7% of the drug market in India is attributable to antibiotics and antibiotic consumption in India is currently estimated to be the largest worldwide, with statistics indicating that there was a 36% increase in antibiotic consumption between 2000 and 2010. Consumption of antibiotics peaks in September and seems to correlate with the increase in dengue fever in the post monsoon season. A study by Boeckel in 2014 showed that 51–69% of patients hospitalised due to dengue fever were prescribed antibiotics, with most receiving third-generation cephalosporins or fluoroquinolones.

There are many reasons why antibiotics are misused in India comments Dr Mahashur, who explains that the top determinants of irrational antibiotic prescribing are a lack of knowledge about appropriate use and an inability to access reliable laboratory results. On the other hand, antibiotic dispensing occurs as a desire to meet consumer demand and because of economic incentives. Stressing the importance of educating people about antibiotics, Dr Mahashur highlights that with bacterial infections increasing, 400,000 people die of pneumonia each year; however, due to misuse, antibiotics are often not available when they are truly needed. There is also an issue with the copying of prescriptions and a lack of regulation into the production of antibiotics – patients are more likely to choose the cheap, poor quality medicines.

Although government controls regarding AMR have been lax, Dr Mahashur reports that they have significantly improved since a new controller has been appointed. Now, prescriptions must be noted down and dated; as a result, many pharmacies have closed down. With the government’s support and cooperation from associations targeted to tackling AMR, India’s main objectives to reduce inappropriate use of antibiotics in the near future will be to monitor antibiotic use and resistance patterns, reduce disease incidence and prevent spread of bacteria, improve diagnostics and appropriate usage of antibiotics, and improve the management of non-medical usage. Having these goals in mind will surely aid India into running a successful campaign against AMR.

GRIP INITIATIVES AND GETTING ANTIBIOTIC RESISTANCE ON THE GLOBAL RADAR

Following a number of global initiatives, GRIP has helped in successfully placing antibiotic resistance on the radar. GRIP recognises that the challenge is to maintain this presence and sustain strategies for its containment. Principles of the WHO 2014 draft global action plan that supports GRIP’s presented objectives were summarised: whole-of-society engagement, prevention first, access not excess, sustainability, and incremental targets for implementation. It was noted, however, there would be difficulty ensuring that every member state commits and, while some countries may be ready to implement an action plan, others do not have a strategic framework or protocols in place.

One particular aim of GRIP is to effect behaviour change regarding people’s attitudes to AMR. The Group notes that effecting change, large or small, in some countries will be challenging; however, GRIP can provide a “multi-pronged attack” since its many initiatives are international and can target multiple audiences says Dr Duerden. GRIP materials are particularly beneficial as they recommend an alternative to antibiotics, notes Dr Burgoyne – it is much easier to engender a behavioural shift when there is another option.
In order to maintain focus, Professor Essack highlights the need for sustained, innovative messages resulting in the behavioural change GRIP is trying to induce; it is important to be consistent, but to keep interest by reiterating the same message differently every time. However, work needs to be carried out to determine how to get these messages across; there is a need for both simple translation of current materials into more languages, but also innovative tactics that challenge the norm, highlighted Dr Pignatari.

On the issue of prevention first, Professor Oxford notes that a better understanding on the viruses that cause the common cold and flu will place GRIP in a better position to educate HCPs and patients and make them more confident in not needing to take antibiotics.

**DISCUSSION: DEFINING THE FOCUS OF INITIATIVES FOR 2015**

**The 5P framework for the non-antibiotic management of URTIs**

The five-part framework is an innovation that was developed to highlight key areas of focus for antibiotic stewardship to include prescribers, pharmacy staff, patients, policy and prevention. The framework presents rationale for focusing on URTIs to promote appropriate antibiotic use in primary care.

![Figure 1: Factors influencing the global status of antibiotic resistance](image)

**Figure 2: The GRIP’s pentagonal framework for change encompasses five key areas—Policy, Prevention, Prescriber, Pharmacy and Patient**

Policy endorsed by local governments and clinical communities of practice that advances antibiotic stewardship and conservation and encourages the symptomatic management of URTIs

Prevention of resistance by the rational use of antibiotics

Patient empowerment on self-management and education about appropriate symptomatic treatment options

Pharmacy guidance on their stewardship role as community antibiotic educators providing patients with advice and support on symptomatic management and guidance on when to consult a doctor

Prescriber guidance on antibiotic stewardship and effective dialogue with patients

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CONCLUSION: WHAT’S NEXT FOR GRIP?

Antibiotic resistance is now firmly on the global radar. For 2015, GRIP has reaffirmed it is committed to maintaining its prominence and sustaining strategies for its containment.

The GRIP strategy was initially global but has since focused on both global and local initiatives, after recognising that there are specific challenges and opportunities in certain regions. The 2015 initiatives will be centered on maximising awareness through educating and driving implementation at a local level. This will be achieved through new local antibiotic awareness campaigns in all regions, and by providing markets with the knowledge and tools to implement their local campaigns.

Throughout the forthcoming year, GRIP intends to further disseminate its messaging surrounding the inappropriate use of antibiotics in the management of URTIs. Identification of the key challenges in each country and tailoring initiatives put in place in each of these countries will be imperative. It was agreed by the group that GRIP materials are important in increasing outreach to patients, pharmacists and prescribers.

Prioritising patient education is an important step in the fight against antibiotic resistance. Patients can put pressure on doctors for a prescription, and currently their needs are often misunderstood by HCPs. In 2015, all initiatives will take a patient-centric approach and will focus on educating patients on how to get better without using antibiotics and why antibiotics will not be effective. Efforts will also be placed on empowering patients to take control of their care and protecting themselves against URTI. Promoting effective patient consultations with HCPs will be at the heart of these initiatives.