



GRIP
Meeting report
2017



Attendees

Prof. John Oxford, Emeritus Professor of Virology at St Bartholomew's and the Royal London Hospital, Queen Mary's School of Medicine and Dentistry, UK (Meeting Chair)

Mr John Bell, Principal Advisor to the Pharmaceutical Society of Australia Pharmacy Self Care Programme; Practitioner/Teacher in Primary Health Care at the Graduate School of Health, University of Technology Sydney, Australia

Dr Doug Burgoyne, President of Veridicus Health, Salt Lake City, Utah, USA

Dr Martin Duerden, Clinical Adviser on Prescribing to the UK Royal College of General Practitioners and Honorary Senior Research Fellow, Bangor University, Wales, UK

Prof. Sabiha Essack, South African Research Chair in Antibiotic Resistance and One Health and Professor in Pharmaceutical Sciences, University of KwaZulu-Natal (UKZN), South Africa

Dr Ashok Mahashur, President of the Indian Chest Society and Consultant Chest Physician, Mumbai, India

Prof. Antonio Carlos Pignatari, Professor of Infectious Diseases and Director of the Special Clinical Microbiology Laboratory of the Division of Infectious Diseases, Federal University of São Paulo, Brazil

Dr Aurelio Sessa, Family Physician and Senior Partner, Arcisate, Italy

Dr Alike van der Velden, Assistant Professor, University Medical Center Utrecht, Netherlands

Prof. Roman Kozlov, Director of the Institute of Antimicrobial Chemotherapy, Smolensk State Medical University; Chief Specialist of the Ministry of Health of the Russian Federation on Clinical Microbiology and Antimicrobial Resistance; President of the Inter-regional Association for Clinical Microbiology and Antimicrobial Chemotherapy, Smolensk Russia

Guest attendees

Dr Direk Limmathurotsakul, MD MSc PhD, Wellcome Trust Intermediate Fellow for Public Health and Tropical Medicine, Mahidol-Oxford Tropical Medicine Research Unit, Mahidol University, Thailand

Assoc. Prof. Dr. Paraya Assanasen, Rhinology and Allergy Division, Department of Otolaryngology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand

Dr Devendra Soni, ENT Specialist, Prime Healthcare Group, Dubai

RB

Mr Adrian Shephard, Senior Global Professional Manager, RB

Dr Atif Rizvi, Medical Marketing Manager, RB

EXECUTIVE SUMMARY

There has been much progress over the last 5 years in terms of getting antimicrobial resistance on the global agenda, supported by initiatives like the Global Respiratory Infection Partnership (GRIP).

The 2015 WHO Health Organization's 'Global Action Plan on Antimicrobial Resistance' published in 2016, together with the WHO 'Global Framework for Development & Stewardship to Combat Antimicrobial Resistance, Draft Roadmap', published in May 2017, fuelled the sense of urgency and the need for a collaborative, multi-stakeholder approach. These initiatives have been further championed among individual countries, for example, Dame Sally Davis, the Chief Medical Officer of the UK, has put the issue as one of her central ambitions for her tenure in office.

Despite this multiple challenges remain. Across the developed world, while there is increased awareness of the need for better stewardship, higher pressure on prescribers not to provide antibiotics and an overall increased understanding of the implications of inappropriate antibiotic usage, patient 'pester power' remains an issue, with a high volume of patients presenting to physicians still requesting antibiotics for conditions which will not be made better by antibiotic usage, i.e. sore throats.

In developing markets, open/OTC access to antibiotics seems to be one of the biggest issue, as experienced by the GRIP advisors who were in Thailand for this year's annual meeting. In virtually all cases, when describing the symptoms of a sore throat, antibiotics were freely available and recommended/dispensed within pharmacy, without a prescription. However, knowledge about the alarm symptoms requiring antibiotic treatment and (a sub-set of) symptomatic treatments was present in the pharmacies.

Since its creation, the GRIP advisors have promoted the '5 P Pentagon' which looks at Policy, Prevention, Prescriber, Pharmacy and Patient. Today it is clear that these initiatives complement the WHO strategy, particularly around improving awareness and understanding of antimicrobial resistance through effective communication, education and training.

Looking to the future, priorities remain, including:

- **Policy:** to ensure appropriate policies and guidelines are in place, not least to limit availability without prescription and that pharmacy remains the first point of call in managing self-limiting conditions
- **Prescribers:** to reduce the number of inappropriate prescriptions provided for conditions like sore throat infections, which are minor and self-limiting
- **Pharmacy:** to ensure pharmacy can confidently manage the needs of patients presenting with upper RTI, and endeavour to limit unnecessary physician consultations
- **Patients:** to reduce 'patient pester' power around the need for antibiotics for these self-limiting conditions; to empower self-management instead

In terms of patients, where access to healthcare is based on patient choice or tied to a fee for service, there remains increased pressure from patients. This is a clear factor in inappropriate prescribing. While the digital world has some challenges for health information, it provides clear educational opportunities to drive awareness that for vast majority of patients with these self-limiting conditions like sore throats outcomes will not be enhanced by the use of antibiotics. This applies for illness with a viral origin, which most often occur. For bacterial sore throat, antibiotics modestly shorten symptom duration.

Veterinary and agricultural use remains a huge issue but is outside the GRIP remit. However, it has important implications for how organisms resistant to antibiotics may make their way into the food chain and how genes for resistance are transferred into bacteria infecting humans.

Across all stakeholder groups, the need for initiatives to drive awareness and understanding remain paramount. Building initiatives based around global understanding, but driven by local nuances and needs is critical. GRIP continues to show how the '5 P Pentagon', supported by partnerships and passion to affect change locally, can deliver results.

This year, the Global Respiratory Infection Partnership (GRIP) moved location to Thailand to enhance the focus on disparities between the developed and the developing world.

Opening the meeting, Professor John Oxford began his session by challenging the audience to think about the generation of new consumers emerging: the 'Game of Thrones' generation, prominent in Time magazine, he said. This cluster of consumers are vastly different from previous generations. They communicate in different ways, they are not connected to the mainstream media, and they pose a challenge for us to engage. Yet they are a powerful force, as governments around the world are recognizing, and therefore connecting with this audience is critical to future success.

“ I suspect this is the group that’s going to change things scientifically as well

Professor Oxford

When it comes to looking at the bigger picture, Professor Oxford drew the GRIP advisers to a painting called the Triumph of Death, by Bruegel, from the 16th century. The critical image is the pale horse and the pale rider which represent infection. Infection is the critical thing that history can teach us: death will always triumph. Here the WHO have created a threat list, based on all bacteria, and the threat to human health, said Professor Oxford.

Hope is on the horizon, however, with articles published in Cell recently, illustrating how soil microbes could play a positive role in infection control. Phages have equally become more interesting to the scientific community and may provide innovative treatments beyond the antibiotic era.

“I think strongly a modified virus will deliver death to antibiotic resistant bacteria, and these are genetically modified viruses and phages, engineered using CRISPR. Basically, to take a phage and genetically modify them using this editing technique, is totally amazing concluded Professor Oxford. That is a huge step forward.”

PAST, PRESENT & FUTURE

Following on from Professor Oxford's reflections, the GRIP meeting set out to look at achievements to date, activities that are happening now and those that will deliver results in the future. To begin, long-term members were asked to give an update, reflecting on progress and forthcoming activities.

Setting the scene, Mr Adrian Shephard, from RB, said GRIP was based around an era where a number of antibiotics are useless in clinical practice, primarily because of their inappropriate usage. GRIP has consistently shown its commitment to sustainable, evidence-based interventions for the rational use of antibiotics and antibiotics stewardship.

Focus on an area where antibiotics really shouldn't play much of a role – upper respiratory tract infections – has paid dividends through the multi-stakeholder group that is GRIP. Partnerships between policy makers, prescribers, pharmacists and patients has achieved much, but the rise in resistance continues.

The stark headlines around operations that won't be possible in the future, the needless deaths caused by resistance and continual spread of infectious disease point continuously to the need for more action. “Progress has been made,” Mr Shephard concluded, “But there is still much more that can be done. Challenges exist around resistance, mass availability and animal usage. Education of professionals and patients is vital. There remains much to be done.”



Australia **John Bell**

Australia still has quite a high use of antibiotics and this is not something we are proud of, said John Bell. One group, NPS Medicinewise, has had a concerted effort to encourage the appropriate use of antibiotics in Australia. The program had some notable successes, said Mr Bell, encouraging consumers to become 'Resistance Fighters'. While this initiative has come to a close, Mr Bell said he would continue to be lobby for investment in educating consumers.

As part of the Australian Government's National Antimicrobial Resistance Strategy 2015–2019, the Australian Commission on Safety and Quality in Health Care was funded by the Department of Health to establish and coordinate a national surveillance system for Antimicrobial Use and Resistance in Australia (AURA).

Published this year, the Second Australian Report on Antimicrobial Use and Resistance in Human Health found that, while antibiotic usage declined 9.2% between 2010 and 2015 in hospitals, challenges remained.

- Some 23.3% of prescribing did not comply with guidelines; 21.9% of prescriptions were assessed as inappropriate. Of surgical prophylaxis prescriptions, 27.4% were continued for longer than 24 hours (less than 5% is considered best practice).
- The most common reasons that hospital prescriptions were deemed to be inappropriate were:
 - An antimicrobial was not needed (19.6%)
 - The antimicrobial chosen was incorrect (spectrum too broad: 25.2%)
 - The duration of treatment (17.7%) or the dose was incorrect (19.5%).

Looking at community-based healthcare, the report also found that there had been little reduction in the 30 million antimicrobial prescriptions dispensed through the Pharmaceutical Benefits Scheme/Repatriation Pharmaceutical Benefits Scheme since 2008.

In particular, prescribing antimicrobials to treat respiratory tract infections remains common, with more than 60% of patients prescribed an antimicrobial, despite the fact that antimicrobials are usually not recommended for these conditions.

As a result, the report authors have called for an intensification of community-efforts to control prescribing.

“ More than 60% of patients were prescribed an antimicrobial to treat respiratory tract infections, despite the fact that antimicrobials are usually not recommended for these conditions



Italy Dr Aurelia Sessa

Annually 1 in every 4 people in Italy has a respiratory tract infection. In total, 85% of antibiotic prescriptions come from primary care, said Dr Sessa. This is the reason why

education and interventions on antibiotic management are so important in Italy. Fuelled by historical data, the initiative, called Progetto G.A.I.A. (Gestione Appropriata In Antibioticoterapia), looked to:

- Improve prescribing appropriateness (efficiency, efficacy and safe) of treatment of the URTI and LRTI
- Adopt logical and rational empiric therapy in out-patients
- Choose the appropriate medication for that RT infection, in that patient, with the right dosage and in the right duration to optimize outcomes
- Identify appropriateness and inappropriateness indicators for correct or incorrect use of antibiotics.

“ We are adopting a logical and rational, empirical approach to the patient for the therapy.

To date the team have created a scientific board, defined the content of educational material, and are sharing this with over 100 GPs. The group have also looked to retrospectively collect prescription data to look at indicators of appropriate prescribing in this area.

To date some 20 indicators of inappropriate prescribing have been identified including:

- Number of patients who received an antibiotic prescription (numerator) of the total of patients of diagnosis of URTI (denominator)
- Number of patients who received a prescription of quinolones, cephalosporins or macrolides (numerator) in bacteria URTI in patients with no asthma, chronic obstructive pulmonary disease (COPD) or penicillin allergy (denominator)
- Number of patients who received a prescription of quinolones, cephalosporins or macrolides (numerator) in acute bronchitis in patients with no asthma or COPD (denominator)
- Number of patients who received a first-line prescription of quinolones (numerator) in patients with exacerbation of COPD age <65 year and with no comorbidity without a prescription of penicillin or cephalosporin in the previous 30 days for another COPD exacerbation (denominator)

Appropriate indicators included:

- Number of patients with exacerbation of COPD (GOLD 1 and 2) without comorbidity (asthma, heart failure, CHD/stroke, diabetes), age ≤ 65, who received a prescription of penicillins or oral cephalosporin (numerator) of the total of patients with exacerbation of COPD who received any antibiotic prescription (denominator)
- Number of patients with exacerbation of COPD (GOLD 3 and 4) age > 65, with any comorbidity (heart diseases, stroke, diabetes) who received a prescription of protected penicillin, cephalosporin, macrolides, parenteral antibiotic or quinolones (numerator) of the total of patients with exacerbation of COPD who received any antibiotic prescription (denominator)
- Number of patients with community acquired pneumonia (CAP) without comorbidity (asthma, COPD, heart failure, CHD/stroke, diabetes) who received a prescription of penicillins or macrolides or tetracyclins (numerator) of the total of patients with CAP who received any antibiotic prescription (denominator)

When the project ends in 2018, Dr Sessa says the team hope to be able to:

- Collect the data of RTI of all GPs participants, including therapies, investigations and other related prescriptions and compare appropriateness and inappropriate indicators over time
- Show how this innovative model is capable of impacting on professional performances of the GPs of the network
- Drive adoption among other GPs
- Influence health authority policies



USA Doug Burgoyne

The USA has been approving a host of new anti-infectives, said Mr Burgoyne, with nine in 2015 and four so far this year in 2017.

While the majority of these are antivirals, they have received a lot of publicity in the USA, often due to their high cost. Access to these products, including the new antibiotics, is controlled through the managed care plans, meaning that the insurance companies and the pharmacy benefit management companies are putting restrictions into place on usage.

There are two reasons for this, Dr Burgoyne said: firstly an attempt to control resistance to these new products, and secondly, and probably more influential, cost. “When there’s an antibiotic that’s \$5, for example, compared to one that’s \$500, then it’s in the payer’s best interest to use the lower cost one.” As a result, while the resistance message is shared within the United States community, it is generally ignored by the managed care industry.

Finding the right place to start campaigns around appropriate usage is difficult, Dr Burgoyne said. If you start an antibiotic resistance campaign with an employer group, you can influence 500 or 5,000 or 50,000 people, however if you start with an insurance company, you can influence a couple of million people. But, he continued, if people change jobs and subsequently insurance schemes, then those efforts may be lost, and people stop hearing the message about antibiotic resistance. So managed care has generally taken a step back away from doing too much.

“ There’s this strange world where we talk about antibiotic resistance, we know it’s a problem, the community knows it’s a problem, physicians recognise there are issues, but nobody is really putting enough effort into doing anything about it outside of the hospital.

One growing trend that may also have an impact on antibiotic resistance is a change in how consumers engage with retail pharmacy. Large chains like CVS which are attempting to be a ‘one stop shop’, replacing the GP office. Services offered include drop in clinics, where patients can go to the pharmacy, see a nurse practitioner, and be diagnosed for one of about 25 different conditions, including respiratory tract infections.

“While we haven’t analysed the data yet, our hypothesis is that nine times out of ten, someone with a respiratory infection will walk out with an antibiotic,” said Dr Burgoyne. Customer satisfaction is the number one driver of care, he continued, and every pharmacy will want to have a good score on Google or on some other type of consumer website, and this may lead to inappropriate demands.

On the positive, every pharmacy offers a wide arrange of products that offer effective symptom relief. Consumers may also be more willing to listen to pharmacists telling them they don’t need an antibiotic because “there’s a different level of trust with a pharmacist; in fact, when a pharmacist tells a

patient you don’t need something, it generally improves the trust relationship between patient and pharmacist,” Dr Burgoyne concluded.



India Dr Ashok Mahashur

Within India, the responsibility for antimicrobial prescriptions lies firmly with physicians, said Dr Mahashur. This situation is complicated however by the different types of practitioners in India, from qualified practitioners, to an equal number of unqualified practitioners who remain outside of the regulatory authorities’ control, yet may still dispense antibiotics if requested by patients.

To address this, a pilot project involving some 992 patients was run in India in three localities:

- A slum area because this is often where the number of non-qualified doctors exceeds the number of qualified doctors, but also because this population experience poor hygiene conditions and are very prone to infections
- A mid-class locality because these populations are often very concerned about their health and visit doctors frequently
- And a wealthy locality with five star hospitals

The pilot placed interns or final year students in the Pharmacy to review doctors’ prescriptions. Patients were also questioned around their symptoms to check the diagnosis of upper respiratory tract infection. In many cases on reviewing prescriptions it was difficult to determine what the prescription was for. While the highest number of prescriptions for antibiotics came from the non-qualified doctor group (21%), some 17% came from the middle group populated by qualified doctors. Quinolones and macrolides topped the prescribing list.

“ What makes this most worrying, said Dr Mahashur, was the use of these drugs in respiratory tract infections given a background of rampant tuberculosis in India and resistance to these valuable drugs.

Summarising the study, Dr Mahashur said evidence suggests that acute, uncomplicated upper respiratory tract infections frequently are treated with antibiotics in the Indian settings. The question then remains why do the doctors prescribe these antibiotics indiscriminately? There could be financial considerations, doctors are keen not to lose the patient to another doctor; there could be diagnostic uncertainty, due to a lack of facilities to diagnose viral infections; and there is pressure on a doctors time.

In conclusion, Dr Mahashur said the development of guidelines and doctor and patient education were critical in preventing antimicrobial resistance.



Brazil
Professor Antonio Carlos Pignatari

While the general practitioner role seen in many other markets around the world doesn't exist in Brazil, inappropriate antibiotic prescribing remains an issue among clinical specialists, said Professor Pignatari.

Initiatives in hospitals are delivering some results, supported by those with an interest in antimicrobial stewardship, with a focus on "giving the right antibiotic at the right dose for individual patients". Part of this has been ensuring that doctors understand prescribing mistakes are happening in hospital and the implications of errors.

Looking at the pharmacy environment in Brazil, legislative challenges have had a major impact. Previously, pharmacists were able to dispense products such as antibiotics without a prescription. This means that in terms of pure inappropriate supply challenges, this issue has been resolved in the pharmacy setting. However there is still much work to be done to ensure other healthcare provider settings continue to be educated, said Professor Pignatari.

“ Policy change has had a major impact on inappropriate prescribing



Netherlands
Dr Alike van der Velden

The Netherlands has done a lot to control inappropriate prescribing. However in a drive to improve efficiencies, online training has become a new focus areas for educating GPs, said Dr van der Velden. The RAAK project (Rational Antibiotic Use in Kids) is an online training programme for GPs with material for parents to enhance proper antibiotic use for children with respiratory tract infection (<http://www.rationeelantibiotica.nl> - <http://www.rationeelantibiotica.nl/public/raak-informatie-brochure.pdf>).

The team set out to understand the effectiveness of these interventions and how they impacted consultations. Antibiotic prescribing rates were 21% in those that had had an intervention vs 33% in the control group. So this concise online training appeared to be effective in reducing antibiotic prescribing.

Separately in the Netherlands, the team have also been looking at out of hours service, trying to establish whether there was a pattern to these consultations and if they impacted in quality of care or inappropriate prescribing. Results showed that the quality of antibiotic prescribing during out-of-hours care was comparable to office-hours. Tied to this was the investigation of an app called 'Should I see a doctor?', which was designed to help patients decide if they really needed physician care for acute symptoms.

"The app was meant as a self-triaging system for acute symptoms and to empower patients to make informed decisions about the need to consult," said Dr van der Velden.

It encouraged patients with problematic symptoms to consult, but for others offered reassurance, on self-care advice and guidance on when to see a doctor.

Using a built-in questionnaire, it appeared that the app was used by patients of all ages and the majority of patients received the advice to call their own GP (the same day, or when app was used in the evening or weekend, the next day or Monday), or to call the out-of-hours clinic. Overall, 65% of patients intended to follow the advice.

One of the most important questions was the diagnostic accuracy of the app - did the app provide the correct advice? Overall in 81% of cases, the app advice corresponded to the results of the triage call done by a nurse.

“ I think a number of countries are looking for alternative ways to communicate with patients, importantly, patients do like these kinds of apps, so long as they are evidence-based and endorsed by GPs



South Africa
Prof Sabiha Essack

Professor Essack focused her presentation on the GRIP ambassador work conducted over 2016 and 2017. Since the GRIP initiation, Professor Essack has been appointed as an expert consultant to the World Health Organisation Regional Office for Africa. A critical enabler of local action plans is education and awareness. To date, as part of this, 5 workshops have been held covering almost all of the 47 countries in the WHO AFRO region.

In the context of global pharmacy, Professor Essack participated in a stakeholder roundtable on the responsibility with antimicrobial medicines, prior to the FIP meeting in Argentina 2016. GRIP's Pentagonal Framework featured here. Interviews were also held with Eduardo Savio, chairperson of the AMR working group of FIP. In exploring a potential partnership with FIP, Professor Essack was able to present the pharmacy practice and pharmacy resources, the need for pharmacy optimisation and communications. A key challenge to GRIP as a result of these meetings was proving the impact of these resources and improved outcomes to drive adoption more widely.

Separately, Professor Essack reflected on the keynote presentation she gave on the on the appropriate use of antibiotics at the 2nd National Pharmacy Conference in Durban, South Africa. This webinar went out live to 1,769 pharmacists in 12 African countries.

“ I was able to showcase GRIP resources in all of my presentations nationally, regionally in Africa and internationally

Looking closer to home, Professor Essack acknowledged that the pharmacy advisory group was formalised in South Africa in 2017 to discuss ways in which pharmacy could be advanced. Leveraging existing resources, such as those of GRIP, has already been acknowledged as an important step forward.



Russia **Professor Roman Kozlov**

Russia is making substantive steps in surveillance and research, said Professor Roman Kozlov, greatly influenced by support from the Russian Minister of Health (who has been elected chairman of the World Health Assembly for the coming year).

A pilot project that ran from February 2017 to June 2017 looked at reducing systemic antimicrobial use in outpatients linked to respiratory tract infections, concentrating on educating healthcare teams who engage patients at a primary care level, as well as public education. A number of channels were used to deliver the educational activities including a website for physicians, pharmacists and the general public, and social media channels, as well as colouring books for children. Information was provided on the classical pathway for a diagnosis of sore throat, how to use diagnostic aids like throat cultures as well as lectures from experts, such as clinical microbiologists, together with advice on how to manage patients.

Learnings from this pilot, supported by the Minister of Health, have applicability elsewhere, said Professor Kozlov. Pharmacists also remain an important target, he said, with opportunities to train through the pharmacy chains. The chains have also agreed to put posters in their pharmacies to help educate consumers. However, messaging has also gained support from other channels including the Russian Post Office and the Russian Tax agency who have been displaying information to help educate the public as well.

Students were also particularly interested, especially military and physical education students, through lectures and ‘flash mobs’ activations.

Measuring the impact of these initiatives is challenging, Professor Koslov concluded because there are many variables that may impact on overall reduction in antimicrobial prescribing, however there is a high degree of transferability of these initiatives and government support will aid future uptake.

“ The Russian Ministry of Health is very motivated by antimicrobial stewardship



United Kingdom **Dr Martin Duerden**

Barely a week goes by in the UK without some mention of the challenges caused by antibiotic resistance in the media, said

Dr Duerden. In part this is triggered by the focus of Dame Sally Davis, the UK Chief Medical Officer, who has made the issue her life’s ambition to tackle.

Nonetheless, in the UK 60% of all antibiotic usage is for respiratory tract infections, said Dr Duerden, the vast majority of all those prescriptions come from the primary care setting. To tackle this, guidelines have been established which try to address prescribing behaviours, as well as other initiatives such as comparative prescribing information within an area, and comparative resistance information within areas.

Public Health England (PHE) has been highly active, said Dr Duerden, helping to deliver a consistent message and encouraging everyone to work together in this field. In collaboration with PHE, the Royal College of General Practitioners has issued a set of TARGET resources designed to provide education and advice on the use of antibiotics, including a website, and training resources, feeding into the personal development plans that now guide GPs fitness to practice. Resources also target patients, encouraging self-care, and include posters and leaflets for patients as well as online advice around whether antimicrobials are required, and other treatment options.

The role of the community pharmacist has also been highlighted, not least because of an emerging issue with a shortage of doctors in primary care. Pharmacists could play an increasing role here, said Dr Duerden, helping to manage patients with symptoms and avoiding them unnecessarily presenting to GPs with upper respiratory tract infections.

In terms of impact, to date there has been a 7% reduction in prescribing between 2014 and 2015, but Dr Duerden questioned, is this real and will it be sustained?

“ The problem is there is such a wide variation on the use of antibiotics and, it very much depends how bad the winter is. So, if we have a mild winter, you will get the 7% reduction in antibiotic usage. If we have a hard winter, I think that we’ll lose that benefit.

PAST, PRESENT & FUTURE: GUEST PRESENTATIONS

To help the GRIP members become orientated to Thailand and the developing markets, a number of guest speakers were invited to give their interpretation of current work around antimicrobial resistance and the overall public, prescriber and policy activation plans.

Holding the GRIP meeting in Thailand allowed GRIP members to get a wider perspective of some of the challenges that were happening in different countries around the world, with a view to understanding how future efforts could be directed to maintain focus on this global health priority.

UNDERSTANDING LOCAL CHALLENGES: A THAI PERSPECTIVE

Guest Speaker 1:

Burden of AMR and Thailand National Strategic Plan

Dr Direk Limmathurotsakul, MD MSc PhD, Wellcome-Trust Intermediate Fellow for Public Health and Tropical Medicine, Mahidol-Oxford Tropical Medicine Research Unit, Mahidol University, Thailand

Mortality attributable to antibiotic resistance is as much of an issue in Thailand as it is in many other large countries in the world, said Dr Limmathurotsakul, with estimates of some 19,122 deaths attributable to multidrug-resistant bacterial infection from 2004 to 2010, increasing over time. Comparing the mortality rates with those of the USA (23,000), it is clear to see quite how big an issue this is for Thailand with a population substantively smaller than the USA.

This is the reason why a National Committee has been formed, supported by the Government and the Prime Minister, to investigate the challenges further.

Currently, ambitious goals within the National Strategic Plan for Antimicrobial Resistance 2017 – 2021 in Thailand include:

- 50% reduction in AMR morbidity
- 20% reduction in antimicrobial use in humans
- 30% reduction in antimicrobial use in animals
- 20% in public knowledge and awareness of appropriate use of antimicrobials
- Improvements in the capacity of the national AMR management system

Thinking practically, initial focus would have to be around monitoring and measurement, said Dr Limmathurotsakul, which will inform success in future years based on international monitoring systems such as the WHO Global Antimicrobial Resistance Surveillance System (GLASS), although there has been much debate on collating incidence vs. prevalence data.

When it comes to the reduction in human usage of antibiotics, part of the challenge in Thailand is the free availability of antibiotics over the counter from a pharmacy.

Such easy access poses a challenge because it is difficult to get a clear picture of actual antibiotic use in Thailand in a given year. The same is true for animal usage.

A new taxation system will allow better data collection, however this will not deliver results for the next two to three years. Given the paucity of data, Dr Limmathurotsakul and his teams started to look at a concept called 'Activity Footprint'. Working in collaboration with the UK and the USA, the team started to look for cities with a similar footprint – following the impact of a general carbon footprint: "The more you use, the worse you make it for the world but it's still necessary and you need to use something when you really need it."

The team are looking at an antibiotic consumption survey to understand more about overall usage figures, including importantly the ex-pat community that resides in Thailand. Early reads of median data suggest that most people surveyed took an antibiotic within the last six months. As a result, one focus of the messages has been around the fact that antibiotics aren't required annually.

Recent data on usage in animals is also interesting. Dr Limmathurotsakul found that in some cases antibiotics are routinely added to feeding systems in small amounts. This is an entirely different issue to address but it is a major focus for the Thai government.

In the areas of awareness and education, Thailand has supported Antibiotic Awareness Week and activations are happening. One particular area is the miswording between 'antibiotics' and 'anti-inflammatories' which isn't helping consumer understanding. A further challenge is the availability of antibiotics at no charge from hospitals, and patient demand for the strongest, and therefore what they perceive to be the most effective drugs.

Guest Speaker 2:
Overview of Thai perspective on the challenges of managing upper RTI locally, hospital policy, prescriber behaviors and action plans and key motivators

Associate Professor Dr Paraya Assanasen

Providing an additional perspective on the challenges in Thailand, Associate Professor Dr Paraya Assanasen began by telling GRIP members the challenge for Thai healthcare providers. While respiratory tract infections are well understood and recognized as self-limited conditions that often resolve within two weeks, they do have an impact on patients' lives, often leading to a reduction in overall productivity. As a result, patients frequently presented with these respiratory infections in the hospital where Dr Assanasen worked, he said. "They are common, acute infections, for which antibiotics are prescribed, even though these are available without a prescription at a low cost over the counter from pharmacies."

Nonetheless the majority of antibiotics in Thailand are bought by the patients, followed by those that come from seeing a doctor through the universal coverage scheme, or privately. Data from a study in 2008 showed that the most commonly prescribed antibiotic in the case of fever was amoxicillin. Presence of a fever was a key indicator for prescription of an antibiotic. This data was also replicated in a recent study from 2016, with Thai nationals most often being given an antibiotic to treat fever.

Looking back historically, from 2000 onwards, Thailand has data that there was relatively high penicillin resistance to *Streptococcus pneumoniae* but at that time it was still sensitive to amoxicillin and clavulanic acid. Looking at the hospital where Dr Assanasen works, data suggests that from 2010 to 2016 there was a decrease in sensitivity of *Streptococcus pneumoniae* in the hospital, and resistance increased from 64% to 67%.

Reflecting on the action plan from the Thai Government, Dr Assanasen said much work was being done to engage prescribers, including work looking at databases to audit and access compliance. The primary focus was on reducing unnecessary antibiotic use in common diseases such as upper respiratory tract infection and acute ear infection. Work was happening to create de-centralised, collaborative networks between national and local stakeholders, to deliver a national policy on antibiotic prescribing in the context of AMR. This included prescriber education and managing patient expectations.

One such focus was designed to reduce the number of patients who receive antibiotics by 20%. By implementing effective education, the team were able to show real impact on prescribing trends, alongside an improvement in patients' health perceptions.

Concluding his presentation, Dr Assanasen said data have shown that it was possible to deliver a large decrease in inappropriate prescribing for antibiotic prescriptions through education initiatives. It is vital however to address educational initiatives at the pharmacy based on the free availability of these products without a prescription. Mentoring is critical in this context.

“ If you provide more knowledge to the doctor, they can understand and they can prescribe less antibiotic. ”

■ Guest Speaker 3:

*Dr Devendra Soni, ENT Specialist,
Prime Healthcare Group, Dubai*

Antibiotics are an important front-line instrument in the fight against various infectious diseases in the Middle East, however, the irrational use and prophylactic use of antibiotics is big problem in the region.

Part of the issue is that many patients seek out antibiotics around the second or third day of symptoms. Citing a study conducted in 2010 done in Kuwait, Dr Soni said out of 270 patients, 50% were prescribed antibiotics for upper respiratory tract infections.

To tackle the misuse of antibiotics, authorities in the region are looking at six priorities.

1. **Reduce** use of antibiotics by improved water, sanitation and immunization.
2. **Educate** health care professionals, policy makers and the public on sustainable antibiotic use.
3. **Improve** hospital infection control and antibiotic management.
4. **Reduce** the sub therapeutic use of antibiotics in agriculture.
5. **Change** incentives that encourage antibiotic misuse and overuse.
6. **Ensure** political commitment to meet the threat of antibiotic resistance.

One of the key challenges is that in many Middle Eastern countries antibiotics can easily be obtained over the counter. Issues are also complicated by use in animals, which then makes its way into the food chain. Guidelines may also be important in reducing inappropriate use over the counter.

The affluence of different countries in the Middle East region also impacts on access, said Dr Soni. People have easy access to specialists, so there is an opportunity for more patient demand, and there is no shortage of pharmacies, so populations from higher socio-economic groups can afford to pay for treatment and will likely not have issues getting access to antibiotics, said Dr Soni.

Looking at the importance of public awareness and the need for broader education, pharmacists can play a significant role in promoting prescriber change through education, decision support and treatment recommendation, audit and feedback mechanism, said Dr Soni. "Studies have shown that provider education efforts are most effective when they are viewed as assistance rather than restriction," he concluded. "Education directed toward small groups appears to be most beneficial, when compared with mass mailing."

Summing up, Dr Soni said political commitment is critical. Until there are policies in place, it's difficult to implement successful action plans: this means a co-ordinated effort from doctors, pharmaceutical companies and big pharmaceutical chains to define the appropriate measures to control antibiotic misuse.

■ Guest Speaker 4:

Dr Atif Rizvi, Regional Medical Marketing Manager, RB

Dr Atif Rizvi, who co-ordinates professional marketing efforts for RB across the developing markets, was also asked to provide GRIP members with an overview of the scenario in some of the other markets.

Looking at the challenges and commonalities in the developing markets, Dr Atif began by explaining that in RB terms the developing market included all of Asia, Africa and Latin America. Some 78% of the world's population is the developing market, and discussions about antimicrobial resistance really matter here. Approximately 25% of the deaths in these regions are caused by infections and diseases relevant to this discussion. This figure rises to around 98% of deaths in children.

In the Philippines, the usage of antibiotics is similar to Thailand, where some 1500 different preparations are available. Approximately every two out of three purchases are not on prescription. Like Thailand again, the Philippines has started a campaign to educate the people about not using antibiotics where they are not required.

Across all these markets, there is a common availability challenge with two components. Antibiotics are in scarce supply, such as in parts of Africa, or antibiotics have become commodities and are freely available from pharmacies. The third type of market reflects those like Japan and Hong Kong where regulations control access more effectively.

The single biggest area where impact can be made in these regions, said Dr Atif, was through education of healthcare professional and patients. Citing an example where GRIP member Dr Martin Duerden had visited Saudi Arabia, Dr Atif said these efforts created impact, with more than 20 meetings (covering 400 doctors) and some 22 pharmacy education programmes. This triggered a further cascade of activities. A similar activation programme was seen in Dubai. Further in Dubai some 35,000 leaflets were distributed to patients.

In terms of evaluating impact around 93% of healthcare professionals engaged in these activities reported they had made it clear on when to prescribe and not to prescribe antibiotics.

Summing up the challenges for the developing markets, Dr Atif encouraged the GRIP members to do more to help keep conversations alive at a government level, continuing to influence medical societies and medical opinions through the use of things like protocols, and ensuring that the public continued to be educated in the field of AMR.

PLANNING FOR THE FUTURE

Despite a substantial increase in efforts to harmonise global initiatives around microbial resistance and the intensity of focus being exerted, challenges remain, with inappropriate antibiotic usage still a central issue, particularly in conditions like respiratory tract infections, and often won't relieve the symptoms that are driving consultations.

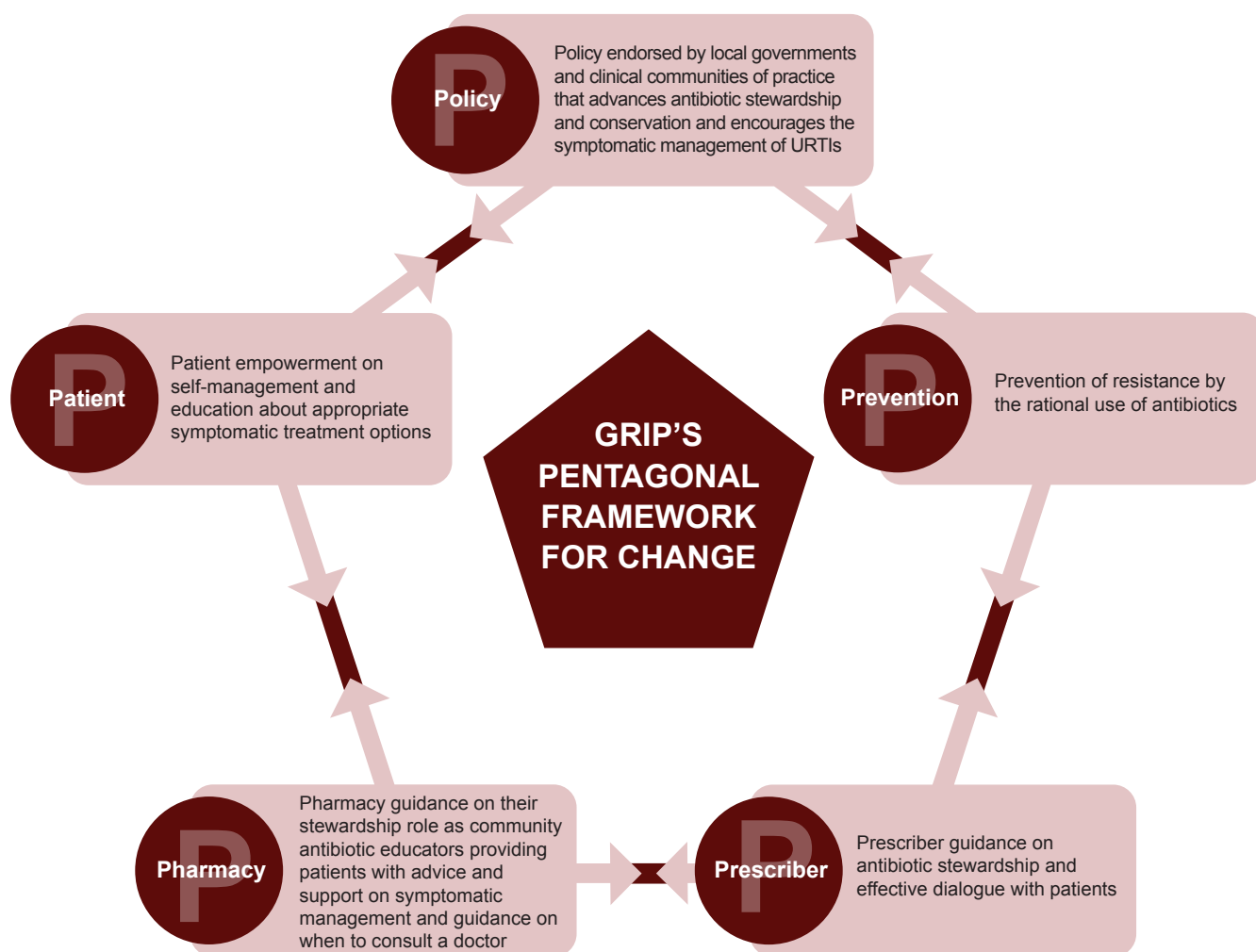
The GRIP declaration, as outlined below remains relevant, as does the Pentagonal Framework.

THE GLOBAL RESPIRATORY INFECTION PARTNERSHIP DECLARATION

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

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



Visiting pharmacies in Thailand illustrated challenges in terms of free access, and for which policy is a critical driver. In the absence of regulations or the enforcement thereof, it remains clear that many consumers still believe that upper respiratory tract infections may require antibiotics, if not immediately, rapidly after early onset of symptoms to reduce the risk of potential further complications.

In almost all cases, antibiotics were freely sold OTC upon presentation of symptoms, or when asked for directly by name. This isn't unique to Thailand however in terms of pharmacy accessibility.

In some cases, OTC access is also linked to where patients pay to see healthcare professionals, where evidence from the GRIP members and guest participants illustrate the ongoing impact of patient demands and the increased likelihood of antibiotics being dispensed.

For every stakeholder group, education remains critical, particularly for minor self-limiting conditions. Given the symptoms that appear to be most troublesome to patients in areas like respiratory tract infections, guidance on how to obtain symptomatic relief can play a major role in helping alleviate patient concerns.

Guidelines for the management of upper respiratory tract infections can help drive educational efforts and deliver a consistent approach, however, their value only becomes apparent if they are widely adhered to – hence the issue of policy change.

↔ CHANGING BEHAVIOURS

In terms of direct action it is clear that although policy changes help influence the environment and trigger conversations, targeted action is key to success among specific groups. Evidence from this year's GRIP meeting showed that there are still some key areas to address at a community level.

Prescribers: Among prescribers, education on antibiotic resistance and better stewardship remains of primary importance. Equipping prescribers with a repository of techniques for managing patient expectations around the need for antibiotics would help sometimes difficult conversations. Affordable diagnostic tools and treatment guidelines will further enforce appropriate prescribing practice around upper respiratory tract infections. Comparative data among prescribers has also been shown to be effective, exerting some peer to peer pressure. A better understanding of microbiology and enhanced understanding of stewardship will help deliver clinically meaningful changes in behaviour.

Pharmacists: Among pharmacists the willingness to sell antibiotics is a challenge in many countries. Policy changes such as those seen in Brazil are key enablers. While acknowledging individual responsibility is important, regulation and guidelines would enable a consistent approach. Giving pharmacists a greater sense of their leadership in managing community health at this level through better research on outcomes, educational efforts and clarity on the effectiveness of symptomatic solutions in upper respiratory conditions would be key actions to implement.

Patients: Patient demand remains a key barrier to successfully reducing the inappropriate use of antibiotics in largely self-limiting conditions. While guidelines and restrictions can reduce access, ultimately in many cases persistent demand from patients still results in antibiotics being issued or sold. While publicity campaigns are being evidenced around the world, there is still much work to be done to reduce 'pester power', and to convince patients that while their symptoms may be causing them distress, in conditions like upper respiratory tract infections, treatment with an antibiotic is extremely unlikely to make them feel better sooner. The detrimental effect to society because of individual actions, i.e., "a tragedy of the commons", should also be emphasized.

These messages need to be consistently delivered across multiple stakeholders to ensure that everyone recognizes that antibiotics need to be protected for the future health of everyone.