More action, less resistance: report of the 2014 summit of the Global Respiratory Infection Partnership

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Abstract
‘Antimicrobial resistance is a global health security threat that requires concerted cross-sectional action by governments and society as a whole,’ according to a report published by the WHO in April 2014[1]. On 24–25 June 2014, the Global Respiratory Infection Partnership (GRIP) met in London, UK, together with delegates from 18 different countries to discuss practical steps that can be taken at a local level to address this global problem in an aligned approach.

This was the second annual summit of GRIP. The group, formed in 2012, includes primary care and hospital physicians, microbiologists, researchers, and pharmacists from nine core countries. GRIP aims to unite healthcare professionals (HCPs) around the world to take action against inappropriate antibiotic use, focussing on one of the most prevalent therapy areas where antibiotics are inappropriately prescribed – upper respiratory tract infections (URTIs).

Chaired by GRIP member, Professor John Oxford (UK), the 2014 summit included engaging presentations by guest speakers examining the latest science regarding the impact of inappropriate antibiotic use.

Guest Speaker Presentations

Antibiotic stewardship: more action, less resistance

Opening the meeting, guest speaker Professor Stuart Levy, Professor of Molecular Biology and Microbiology and of Medicine, and Director of the Centre for Adaptation Genetics and Drug Resistance at Tufts University School of Medicine, made a strong case for antibiotic resistance being an environmental and societal problem, as well as a medical one.

Professor Levy reinforced the fact that resistance to multiple antibiotics is now not just a problem in the hospital but common in the community, making it difficult to control its spread. The consequences of this spread are alarming. Resistance leading to treatment failure and/or deaths affects a vast array of medical conditions and procedures including cancer, pneumonia, infant bloodstream infections and organ transplantations. Use of a single antibiotic can result in multidrug resistance, as bacteria tend to accumulate resistances. Once selected, a drug resistance will not disappear again, he emphasised, although it may drop in frequency.

Antibiotic resistance develops wherever antibiotics are used – in agriculture as much as in healthcare. A major contributor is the use of antibiotics at subtherapeutic doses to promote growth in food animals. ‘Given enough antibiotic and time, resistance will appear,’ said Professor Levy.

The effect of antibiotic resistance on both humans and agriculture – and their interaction – makes this an environmental problem. Resistant bacteria are transmitted from humans to animals and vice versa; they also enter water and soil; are dispersed to fruit, vegetables and wildlife; and are transferred back to humans and food animals (Figure 1).
'Antibiotics are societal drugs', said Professor Levy. People in close contact with a person using antibiotics have been found to carry bacterial strains resistant to both single and multiple antibiotics, he explained. This implies that individual use of antibiotics affects family, the community and society as a whole.

Professor Levy called for greater antimicrobial stewardship by preventing infections, tracking resistance patterns, developing rapid diagnostic methods, and improving the use of antibiotics. Conversely, regarding the frequent use of the term 'war on antibiotics', Professor Levy suggested an alternative view of the challenge: 'We have to make peace with bacteria. They are the ones that have survived and that will survive.'

The human microbiome and antibiotics

Professor Thomas MacDonald, Professor of Immunology and Dean for Research at Barts and The London School of Medicine and Dentistry, gave a presentation on the effects of antibiotics on the highly balanced ecosystem of the commensal bacteria in the gut.

The huge surface area of the gut is populated by some 500 species of bacteria, with the whole microbiome having a population of approximately $10^{14}$ organisms. The specific composition of the microbiota community differs from individual to individual and is imprinted early in life.

The commensal bacteria in the gut have a variety of structural, metabolic and protective functions including barrier fortification, vitamin synthesis, salvage of energy from food and pathogen displacement. They are also essential for a healthy immune system, with gut-associated lymphoid tissue comprising 70% of the entire human immune system. Evidence from germ-free mice shows that bacterial colonisation of the gut is prerequisite for the development of the immune system, in particular the early induction of immunoglobulin A in neonates. ‘There is absolutely no doubt that the activation and development of systemic and mucosal immunity and the tissues involved in it are driven by the presence of the microbiota', said Professor MacDonald.

What does this mean for treatment with antibiotics? Professor MacDonald presented research showing that the use of antibiotics leads to a loss of diversity and a shift in community composition of the gut microbiota. The microbiota stabilise again once the antibiotics have stopped, but it never returns to its original state.

The exact consequences of this shift are unknown, but there is mounting evidence that the composition of the gut microbiota has a direct impact on the body's ability to fight infections, said Professor MacDonald. For example, signals from the microbiota promote the differentiation of T cells residing in the intestinal epithelia – in particular the population of Th17 cells. Ironically, this subset of T helper cells is responsible for protecting the body against bacteria and fungi.

This implies the paradox that taking antibiotics to clear an infection will simultaneously destroy the body's natural defence mechanisms against infection, and in some individuals, this damage may be permanent. It is therefore crucial to
avoid the use of antibiotics unless this is clearly indicated by the nature and severity of the infection.

**Sessions Led by GRIP Members**

**Global guidance in URTI management**

GRIP’s approach to tackling antibiotic resistance is based on the premise that inappropriate use of antibiotics for URTIs, in particular sore throat, is a key driver for increasing antibiotic resistance rates in the community and that effective action requires a consistent approach across healthcare professions and countries.[6,7] GRIP members, Dr Alike van der Velden (the Netherlands) and Professor Roman Kozlov (Russia), addressed the challenges that make it necessary to establish a unified approach.

**The challenges to a unified approach**

National guidelines on the management of sore throat vary enormously between countries to the extent that different strategies are recommended for the symptoms around the world. For example, the American Association of Family Practitioner guidelines[8] recommend that patients with positive throat cultures should be treated with antibiotics regardless of severity of infection or ability of the patient to fight off the infection, whereas guidelines in the Netherlands (NHG guideline) focus on the distinction between mild and severe throat infections.

A second challenge is the variation in antibiotic resistance rates between countries, highlighting the influence of social and cultural factors on attitudes towards antibiotic use.

Thirdly, there is a gap between the knowledge and skills required by HCPs and the education they receive on prudent antimicrobial prescribing. Topics such as bacterial resistance; diagnosis, treatment and prevention of infection; antimicrobial stewardship and communication skills receive insufficient attention in the curricula of HCPs’, said Professor Kozlov.

Additional challenges include differences between countries in time allocated for patient consultations and variations in knowledge level regarding antibiotics and the natural course of URTIs among the general public.

**5P framework – a global collaborative approach**

To address the variation in global antibiotic use guidelines, GRIP has developed a framework for the management of URTIs in primary care that can be adapted across countries. The framework involves a collaborative approach by multiple stakeholders and focuses on five key areas: policy, prevention, prescribers, pharmacy teams, and patients (Figure 2).[9]

GRIP believes that much can be achieved by addressing the interaction between HCPs and their patients. The group has developed the 1, 2, 3 approach in order to provide a structured approach for the consultations, and to help the HCP effectively treat and communicate with their patients (Table 1).

Briefly, step 1 involves identifying and addressing patient concerns and expectations. During step 2, the severity of the condition is assessed, with attention being paid to risk factors for complications. In step 3, the HCP provides counselling on effective self-management options.

Dr van der Velden emphasised that this universal approach can be adapted for use in any local environment, regardless of guideline variations between countries, resistance patterns or medical curricula. She presented to the delegates a consultation algorithm designed to assist prescribers and pharmacists in applying the 1, 2, 3 approach when engaging with sore throat patients. The algorithm includes questions and prompts for each step of the approach and is developed in line with the structured 1, 2, 3 approach. The algorithm – along with other GRIP materials – is available on the GRIP website at www.grip-initiative.org.

**More action – the latest support from GRIP**

Throughout the past 3 years, GRIP has developed a series of resources for HCPs and patients to support their initiative. GRIP members Dr Martin Duerden (UK) and Professor Sabiha Essack (South Africa) provided an overview of these materials and how they can help support HCPs in managing patients with URTIs (Figure 3).
GRIP’s 1, 2, 3 toolkit resources – launched last year – provide a plethora of useful materials that help educate the HCP on the need to change behaviour, the value of managing symptoms and guidance on communicating with patients in line with the GRIP 1, 2, 3 approach. The resources also included patient materials, which help provide guidance on the realistic duration of URTI symptoms, reassurance that appropriate symptomatic relief can meet their needs and guidance on when to seek further advice. The resources are designed to be adaptable for local use while maintaining the consistency of GRIP’s approach.

Dr Duerden and Professor Essack launched new GRIP 2014 materials, which aim to complement the existing 2013 materials. The new 2014 materials included continuing professional development (CPD) modules, covering antibiotic resistance, URTI management in primary care and communication skills – the activities of which can be logged as part of healthcare provider personal development points. Patient materials were also launched, further helping to shape shared decision-making during the consultation. Much of these patient materials not only helped provide the relevant reassurance and reasoning for why antibiotics do not help manage symptoms in the majority of cases, but also empowered the patients in providing the right tools to help HCPs choose the most appropriate treatment for their condition.

### Consultation skills

An interactive session run by GRIP members Dr Duerden and Mr John Bell (Australia) looked into consultation skills. Dr Duerden emphasised that effective communication between the HCP and the patient is a skill that can be learnt, just as much as other medical skills. He recommended giving a structure to the consultation, for example using the Calgary–Cambridge model: (1) initiating the session; (2) gathering information; (3) building the relationship; (4) explaining and planning; and (5) closing the session.[10,11]

Mr Bell discussed the role of pharmacy engagement in treating patients with URTIs, emphasising the need for pharmacy teams to move away from a paternalistic approach to a collaborative partnership that endeavours to place the patient at the centre of the decision-making process. He re-enforced the importance of explaining symptom duration – along with reasoning as to why a visit to the doctor was not important—and how it is vital to advise the patient on the most effective symptomatic relief options in order to cater for specific symptoms and preferences. Mr Bell touched on the importance of medicine optimisation when antibiotics are needed, re-enforcing messaging on antibiotic resistance with reasoning for appropriate course fulfilment.

Observation of certain ground rules can also help to make the interaction more effective by helping elicit the patient’s problems and concerns. Tips included sitting at a right angle from the patient, maintaining a comfortable level of eye contact and using verbal signposting to separate listening from note reading. A particularly powerful skill is to allow the patient to complete the opening statement without interruption – this can lead to a significant reduc-

<table>
<thead>
<tr>
<th>Table 1 Using the 1, 2, 3 step approach for sore throat</th>
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<tbody>
<tr>
<td>1. Address the patient’s concerns</td>
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<tr>
<td>• Identify the patient’s main symptom or concern and ascertain how unwell they are</td>
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<tr>
<td>• Doctors should perform a clinical assessment of the head and neck. Check glands and tonsils</td>
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<tr>
<td>2. Be vigilant – assess severity</td>
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<tr>
<td>• For doctors: use the Centor criteria to identify risk of group A beta-haemolytic streptococci (GABHA) and identify potential risk factors</td>
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<tr>
<td>• For pharmacy: identify risk factors, co-morbidities and/or red flag symptoms and refer when needed</td>
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<tr>
<td>3. Counsel on effective self-management</td>
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<tr>
<td>• Provide reassurance for the patient with information on the duration of symptoms, recommend symptomatic relief and, if required, advise the patient when they should see a doctor or return for a reconsultation</td>
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<tr>
<td>• Explain why antibiotics are not needed together with the benefits that symptomatic relief can provide</td>
</tr>
<tr>
<td>• The pharmacy can help explain to patients the range of symptomatic relief products available</td>
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**Figure 3** Global Respiratory Infection Partnership (GRIP)’s 1, 2, 3 toolkit materials, available on the GRIP website: www.grip-initiative.org.
tion in late-arising problems. After a review of the phrases that HCPs can use to explore patient’s ideas, concerns and expectations (the ICE approach), the speakers demonstrated in two role play scenarios how physicians and pharmacists can apply GRIP’s 1, 2, 3 approach during a patient consultation for sore throat.

**Interventions in practice**

In another interactive session, GRIP members Dr Laura Noonan (Ireland) and Dr Aurelio Sessa (Italy) encouraged delegates to implement and evaluate interventions to reduce antibiotic prescribing in their local community practices.

Dr Noonan described her experience of testing the effectiveness of a take-home patient information leaflet that contained information on viral illnesses, antibiotics and antibiotic resistance, the likely duration of symptoms, and information on when to reconsult; the leaflet could be personalised and signed by the general practitioner (GP).

**What were the results of the study?**

Use of the leaflet resulted in a reduction of immediate antibiotic prescriptions from 47.5% to 13.3%; it also reduced the mean duration of consultations from 11 min to 10 min, and reconsultation rates dropped from 7.5% to 6.6%. These are the results of a study Dr Noonan conducted at two rural GP practices in Ireland, involving a 1-week control period during which consultations for URTIs proceeded as usual, and a 1-week intervention period during which the information leaflet was used. The findings confirmed the value of giving patients something tangible to take home to support a nonantibiotic management approach.

Dr Sessa reported on the impact of introducing the use of the GRIP toolkit materials in his GP group practice in northern Italy. He conducted a study in which GPs could choose to use materials from the GRIP toolkit or to conduct the consultation without such materials. The results found that the use of the toolkit materials halved the number of antibiotic prescriptions, as shown in Table 2.

The study protocol used by Dr Sessa, together with template data collection forms, is available from the GRIP website (www.grip-initiative.org). The group are keen for other practitioners to use it to gather further data on the differences that the materials can make in actual practice. The study results can also help GP practices to evaluate whether their current level of antibiotic use is appropriate.

**Local Activation**

In this session, practitioners from three different countries shared their efforts to promote the principles of antibiotic stewardship at a local level. These talks gave insight into how strategies can be tailored to local needs and opportunities, and how successful implementation can result in substantial success within localities.

**Brazil**

In Brazil, a new regulation was introduced in 2010 to stop the widespread sale of antibiotics without prescription. Given this relatively recent change in policy, GRIP member Professor Antonio Pignatari and ENT specialist Professor Mônica Menon decided to target opinion makers and prescribers by holding interactive symposia at key congresses in the country. The first symposium took place at a national congress for ENT specialists in November 2013 and the second at a regional congress for GPs in April 2014. Delegates received information about appropriate antibiotic prescribing and the GRIP initiative (Table 3).

Both symposia were well received, and Professor Menon and Professor Pignatari are planning further talks at congresses and other relevant meetings, in addition to introducing the concept of antibiotic stewardship in training programmes for hospital staff. There are also plans to reach

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<th>Table 3 Feedback of the GRIP message in Brazil</th>
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<td>• ABORL Symposium</td>
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<td>† Regional Congress for GPs in São Paulo – 4–5/4/2014*</td>
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<th>Table 2 Impact of GRIP toolkit use on antibiotic prescribing at a GP group practice in Italy</th>
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<tr>
<td>Toolkit use</td>
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GP, general practitioner; GRIP, Global Respiratory Infection Partnership.

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wider audiences by publishing short articles in professional journals and hospital magazines.

**United Kingdom**

Dr Terry Maguire, a community pharmacist and health commissioner from Northern Ireland, spoke about the promotion of antibiotic stewardship collaborating with existing public health initiatives. Examples for Northern Ireland include the Minor Ailments Scheme (promoting self-management of minor ailments) and the Choose Well campaign (promoting better use of medicines, including antibiotics).

In addition, the Primary Care Intranet and other health authority websites in Northern Ireland are being used to give GPs access to relevant patient information leaflets. GPs can also download an audit template that has been adapted for the audit of antibiotic prescribing.

Finally, Antibiotics Awareness Day 2013 offered the opportunity to launch a CPD module for pharmacists and to send antibiotic awareness resources to GP surgeries across the UK; the materials had been adapted from the GRIP 1, 2, 3 toolkit and were rated as good or excellent by 98% of responders.

**5P Debate**

The meeting ended with a stimulating debate that focussed on the question ‘which of the five Ps in GRIP’s pentagonal framework for change will have the biggest impact on countering inappropriate antibiotic use in management of URTIs in primary care’. In an election panel style, each P was represented by two GRIP members seeking to show the merits of their P over the other Ps.

In an audience vote before the debate, there was a clear winner, with 33% of the audience feeling that the ‘prescriber’ has the most influence on inappropriate antibiotic use, ahead of ‘patients’ (27%), ‘policy’ (23%), ‘prevention’ (10%) and, finally, ‘pharmacy’ (6%) (Figure 4).

Subsequently, the discussion began with a short opening presentation for each P, followed by a debate in which each team defended its P.

- **Policy:** The policy team argued that it is not possible to substantially affect antibiotic prescribing and purchasing behaviours without national guidelines supported by regulation and antibiotic surveillance systems.
- **Prevention:** Those campaigning for prevention called for a greater ‘use of prevention strategies (so that) you won’t need to treat the patient’.
- **Prescriber:** The prescriber team said that ‘[d]octors hold the key’, and that ‘[t]hey are the ones who stand between the patient and the antibiotic’.
- **Pharmacy:** The defenders of pharmacy asserted that pharmacists are more accessible than any other health professionals and are most suited to provide individualised and tailored treatment advice.
- **Patients:** Arguments in favour of the P for patients included the fact that patients are often driving prescribing, and ultimately, they make the decision of whether to take the antibiotic. ‘If we teach [a patient] to treat one sore throat symptomatically, a large number of subsequent infections will also be treated without antibiotics.’

The debate ended with another vote by the audience, which resulted in a tie between prescribers and patients (26% each), followed closely by pharmacy (23%) and policy (19%), and finally prevention (6%) (Figure 5).
‘We have seen an equalisation and that’s a very good result,’ said GRIP member Professor Attila Altiner (Germany). He emphasised that all Ps are important, confirming the need for partnership – a topic that came up repeatedly during the debate and in audience contributions. ‘We have to work hand in hand,’ concluded Professor Altiner.

You can access the edited recordings of the debate from the GRIP Summit at www.grip-initiative.org.

**Localisation of Approach**

The GRIP 2014 materials were reviewed by the assembled audience of international HCPs. The attendees were broken down into regions and discussed in detail how these materials could be utilised and implemented in order to engage and deliver a sustainable message to enact change. Feedback from all the materials was positive, with many countries discussing how to adapt and evolve the existing materials in order to cater for their region’s specific barriers to change.

The GRIP patient leaflet, URTI guide for patients and GRIP video brought significant praise from the audience. It was felt that the GRIP patient leaflet and URTI guide for patients (a guide which the patient fills out prior to the consultation and allows them to detail their symptoms, durations and reasons for visiting the HCP) were excellent tools to help drive the joint decision-making process. It was felt that the GRIP video – which follows the character of Bob who is suffering from an URTI – resonates with the apprehension felt by many patients and greatly explains the importance of effective symptomatic relief in a clear, concise and humorous format.

The GRIP resources are available for download by all HCPs on the GRIP website: www.grip-initiative.org. There are additional resources on the website including the 2013 GRIP materials, podcasts (Table 4) and the debate footage. A bespoke GRIP YouTube channel page has also been launched, which includes interactive footage on the GRIP members’ thoughts on the 5P framework and the 1, 2, 3 approach, the threat of antibiotic resistance, and the challenges facing effective and appropriate URTI management (Table 4).

**Declarations**

**Conflict of interest**

The Author(s) declare(s) that they have no conflicts of interest to disclose.
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**Authors’ contributions**

All Authors state that they had complete access to the study data that support the publication. All listed individuals were attendees at the meeting and members of the Global Respiratory Infection Partnership.

**References**