Fighting antimicrobial resistance

The contribution of pharmacists

2015

International Pharmaceutical Federation

Colophon

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Executive summary

Antimicrobial resistance (AMR) is one of the greatest threats facing humanity. Action to confront and help overcome the problem must be taken now. Policies already exist or are being formulated at international, regional and national levels. Pharmacists are increasingly being involved in providing their expertise when AMR policies are being created, evaluated and implemented. This can be seen in the World Health Organization (WHO) Global Action Plan to tackle AMR (1) and in the expansion of antimicrobial and infection control programmes that require approaches from both hospital and community settings.

The International Pharmaceutical Federation (FIP) is a global federation of national associations of pharmacists and pharmaceutical scientists. In order to support these associations in their fight against AMR, FIP has prepared this briefing document. It is an overview of the different activities that community and hospital pharmacists are involved in.to prevent AMR and to reverse AMR rates.

Pharmacists work to protect and promote the health, safety and well-being of patients and the public, making them more resilient to infections.

Pharmacists' unique position in health care systems makes them the most accessible health care professional. Through a process of triage, pharmacists evaluate whether or not they can offer a solution via treatment of minor ailment symptoms. Furthermore, when antibiotics are not needed, pharmacists can reassure patients and correct any misunderstandings.

When antibiotics are needed, pharmacists, ideally supported by available diagnostic tools, supply antibiotics in specific legally defined cases, or refer to a physician or a specialist.

Pharmacists are experts in medicines. In their advisory and clinical role they ensure optimal management of antimicrobial treatment. This includes prescribing and/or use of antibiotics with regard to indication, choice, dose, duration and dose adjustment, as well as interaction and adverse effect minimisation, and adherence support tailored for short- or long-term regimens — all with medicines safety and responsible use in mind. Pharmacists adjust formularies when special support is needed to address specific patient needs.

Pharmacists ensure the quality of medicines and their safe disposal, and contribute to reduction of antimicrobials in the environment.

In hospitals, pharmacists are leading stewardship programmes and are heavily involved in their implementation, maintenance and promotion. They provide expertise on sterilisation and hygiene. Specific emphasis is given to collaborative approaches as part of interprofessional teams or interdisciplinary management of antimicrobial strategies and to engagement with stakeholders.

These examples of pharmacists' activities are illustrated by campaigns and programmes developed by pharmacists and their associations around the world. The objective of this document is not to provide an exhaustive list of all activities, but to stimulate and nurture discussion between various stakeholders and different FIP partners, providing a foundation for the formulation of recommendations and policy in the future.

1 Antimicrobial resistance: Global health threat

1.1 Background

Since the discovery of penicillin in 1928, antimicrobials have enabled many of the greatest medical advances. (2) Penicillin, with its excellent safety and efficacy profile, saved the lives of many people during the Second World War. (3) Without antibiotics, procedures such as surgery would carry a much higher risk owing to an increased likelihood of sepsis. (2)

Antibiotics or, more accurately, antimicrobials are active substances of synthetic or natural origin which destroy microorganisms (bacteria, viruses, fungi and parasites), suppressing their growth or their ability to reproduce in animals or humans. (4)

Antimicrobial resistance (AMR) is a natural process. It occurs when microorganisms evolve to be able to resist the medicine that has been used to combat them. (5) Resistant microorganisms can survive or even grow in the presence of a concentration of antimicrobial that is usually sufficient to inhibit or kill non-resistant microorganisms of the same species. (4) This important feature was foreseen by Alexander Fleming who, in his speech when receiving the Nobel Prize in Medicine for the discovery of penicillin, issued a warning about the possibility of creating resistant organisms if antibiotics were used irresponsibly. (6) It is likely that AMR began as soon as mass use of antimicrobials by the population began, soon after industrialised production became possible.

1.2 Why is AMR a problem?

1.2.1 Individual consequences: Burden on health

AMR has a particular impact on tuberculosis because this disease has a long-term treatment regimen. (5) Because AMR is a natural process, some degree is expected to develop against all antimicrobials, even when treatments are optimal. (7)

Treatment failure caused by AMR contributes to: additional side effects; longer hospital stays; psychological disorders due to reduced quality of life; burden on families; and a greater likelihood of death as a result of inadequate or delayed treatment. (8) An example is the treatment of patients with multidrug-resistant TB, who have to undergo a two-year treatment programme. (9)

AMR also affects patients who are not infected with resistant organisms. Because of the increasing rate of resistance among common pathogens, broader-spectrum agents are now required for the empirical therapy of many common infections. These agents are usually more expensive, have more deleterious effects on protective microflora, and can be more toxic or less effective. (10)

Resistant infections currently claim at least 50,000 lives each year across Europe and the USA, and hundreds of thousands of deaths are being caused in other areas of the world. (5)

1.2.2 Population consequences: Economic burden

The latest report from the World Health Organization (WHO), "AMR — Global report on surveillance 2014", (7) shows estimates of economic burden. In the EU alone costs of treatment of resistant pathogens are estimated at about EUR 1.5bn annually. (11) The current overall medical costs of antibiotic resistance to the Canadian health care system, predominantly the institutions, may be as much as CAD 200m annually. (12) By comparison, the US Office of Technology Assessment has estimated that the costs of managing antibiotic resistance in the USA range from USD 0.1bn to USD 10bn per year. (12)

1.3 Future trends

AMR may be the greatest challenge to face health care in the 21st century (10). Four factors that will largely determine the future extent of AMR have been analysed: pathogen and microbial ecology; prescribing and dispensing practices;

population characteristics; and health care policy. (13) (14) In addition, the 2001 WHO Global Strategy alluded to a country's health system and medicines regulatory framework as well as incentives and interplay between patients and prescribers to be the influential factors. (15) This strategy was later renewed with the 2015 WHO Global Action Plan. (1)

AMR is also influenced by the massive increases in trade and human mobility brought about by globalisation. In the 1990s, for example, a resistant *Streptococcus pneumoniae* first identified in Spain quickly spread to Argentina, Brazil, Chile, China Taiwan, Colombia, Malaysia, Mexico, the Philippines, the Republic of Korea, South Africa, Thailand, the USA and Uruguay. (16). A more recent example is the New Delhi metallo-β-lactamase (NDM) resistant gene that was first detected in 2008 in a *Klebsiella pneumoniae* isolate from a patient repatriated to Sweden after being treated in a hospital in New Delhi, India. It quickly spread all over Europe and to Africa, Asia, Australia and, nowadays, it is believed to be present in countries all over the world. (17)

AMR also indirectly affects the treatment of non-communicable diseases, making it more difficult. For example, modern cancer treatments often suppress patients' immune systems, making them more susceptible to infections. Without an effective antimicrobial to prevent or treat infection, chemotherapy for cancer would not be ethical. (5)

Some 300 million people are expected to die prematurely because of AMR over the next 35 years, costing the world economy up to USD 100tn by 2050 if we do not take action. (5)

2 Need for better management

2.1 Responsible vs irresponsible use of antimicrobials

2.1.1 Current use of antimicrobials

The emergence of AMR is a complex problem driven by many interconnected factors, in particular the overuse and misuse of antimicrobials. (18) Antimicrobials have been used in inappropriate ways all over the world and the widespread impact and increasing prevalence of AMR has been well documented. (19)

Much work has been done to look at the association between the level of use of antibiotics in different countries, and the incidence of resistant bacteria that are isolated. Figure 1 provides data from a 2004 study (20) that looked at total antibiotic use in 20 industrialised countries by defined daily dose per 1,000 population per day, and showed how increased antibiotic consumption correlated with a higher percentage of *Streptococcus pneumoniae* isolates that were resistant to penicillin.

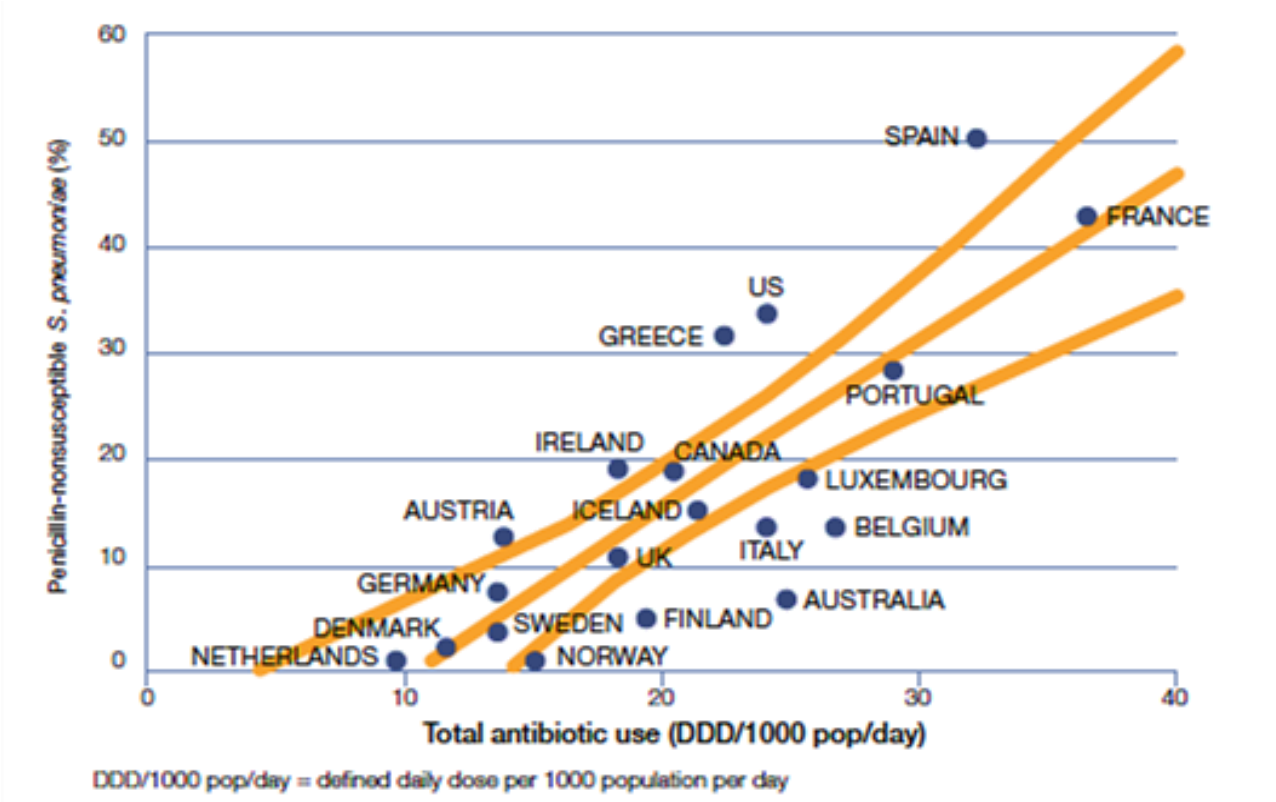

Figure 1. Relationship between total antibiotic consumption and *Streptococcus pneumoniae* resistance to penicillin in 20 industrialised countries in 2004

When looking at the consumption of antibiotics for systemic use in the community, for example in Europe, according to the most recent data released by European Centre for Disease Prevention and Control (ECDC) in 2013, (21) usage ranges from 10.8 defined daily doses (DDD) per 1,000 inhabitants and per day (the Netherlands) to 32.0 DDD per 1,000 inhabitants and per day (Greece); this is a 2.9-fold difference, which is similar to that seen in previous years. The population-weighted EU/EEA mean consumption was 22.4 DDD per 1,000 inhabitants and per day, representing a continuing increase over the past five years for the EU as a whole. (See Figure 2.)

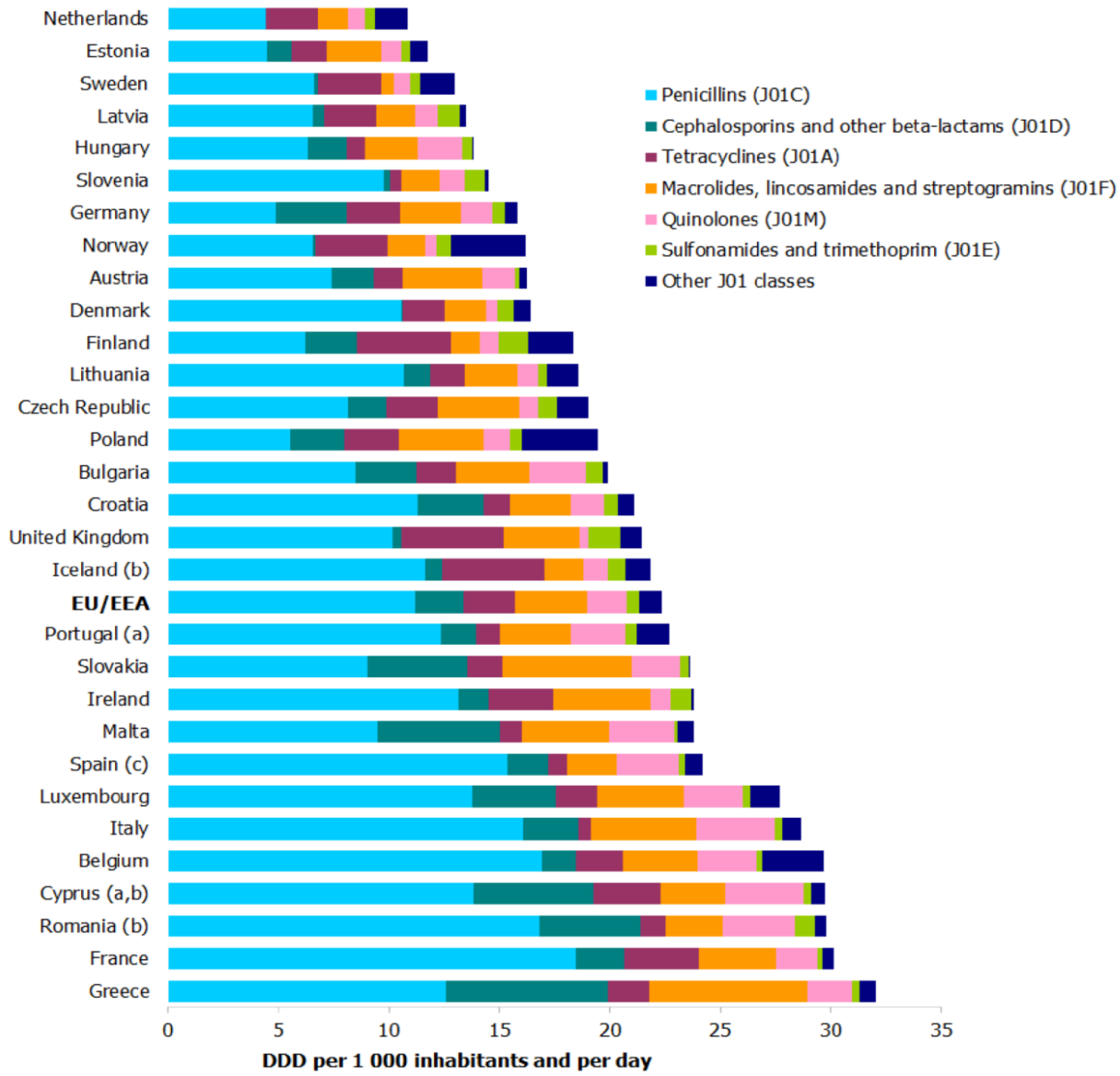

Figure 2. Consumption of antibiotics for systemic use in the community by antibiotic group in 30 EU/EEA countries, 2013 (expressed in DDD per 1,000 inhabitants and per day) (21)

Most antibiotic consumption occurs in the community (outside hospitals). However, hospitals, by their very nature, are prone to AMR because of extensive use of antimicrobials in contained environments. Antibiotic use in hospitals is a main driver for the spread of multidrug-resistant bacteria responsible for health care associated infections. (21)

Although irresponsible use of medicines is the main cause of AMR, as described in a recent WHO report, (7) there are other important factors to consider, for example, practices in the agricultural industry and animal husbandry. In these activities, antimicrobials are given to animals as growth promoters or as additives to feeds and are not considered as medicines. (22) Antimicrobial-resistant bacteria arising from agricultural practices enter human environments and are transferred to people and goods, thus creating a possibility for AMR to cross national borders. (23)

Bacteria of international concern are summarised in Table 1 below. (7) (24)

Table 1. Resistant bacteria of international concern

Escherichia coli	Resistance to third-generation cephalosporins; Resistance to fluoroquinolones
Klebsiella pneumoniae	Resistance to third-generation cephalosporins; Resistance to carbapenems
Staphylococcus aureus	Resistance to meticillin (MRSA)
Streptococcus pneumoniae	Resistance, or non-susceptibility, to penicillin
Non-typhoidal salmonella (NTS)	Resistance to fluoroquinolones
Shigella species	Resistance to fluoroquinolones
Neisseria gonorrhoeae	Decreased susceptibility to third-generation cephalosporins
Enterococcus faecalis	Resistance to vancomycin (VRE), to aminopenicillins
Pseudomonas aeruginosa	Resistance to carbapenems, to amikacin, to ceftazidime
Acinetobacter baumannii	Resistance to carbapenems, to third-generation cephalosporins

2.1.2 Responsible use of antimicrobials

The cost to people's lives and to health care systems resulting from suboptimal antimicrobial medicines use cannot be afforded. (25)

Evidence presented at FIP's 2012 ministers summit on the benefit on the responsible use of medicines indicates that the status quo is no longer an option given that almost USD 54bn (or 0.9% of the global total health expenditure) can be avoided annually from preventing antibiotic misuse or overuse. (25)

Responsible use of medicines implies that health system stakeholder activities and capabilities are aligned to ensure that patients receive the right medicines at the right time, use them appropriately, and benefit from them. Bringing the right medicines to patients who need them requires the engagement of all actors, including governments, and a vision on how to integrate public and private interests and mobilise resources. (25)

2.2 Gaps in research and development

While the development of AMR has been accelerating, the development of new antimicrobial agents has slowed substantially in past decades. (26) For example, the ageing of the USA population has shifted medicine discovery efforts towards agents for chronic medical conditions that are more prevalent among the elderly, such as hypercholesterolaemia, hypertension, mood disorders, dementia, arthritis and cancer. (18)

This situation could explain why only two classes of new antimicrobials (oxazolidinones and lipopeptides) have come to market over the past 30 years. (11) It is noteworthy that these are designed to treat infections caused by multidrug-resistant Gram-positive bacteria. The other systemically administered antibiotics that have reached the market during this period belong to existing classes of antibiotics and are not efficacious against the majority of organisms already resistant to other agents in the same class.

As of early 2012, 109 antibiotics were in the pipeline and 70% of these were in early stages of development. In contrast, only 31 potential candidates were in phase II trials and only nine candidates had reached phase III trials. (26) And there is no guarantee of any of these reaching the market.

However, even an increase in development of new antimicrobials is no guarantee that the system problems associated with AMR will be stopped, since microorganisms are constantly evolving resistance mechanisms. There have even been reports of resistance before some newer antimicrobials have been approved for human use. Figure 3 shows estimated time lag between an antibiotic being introduced to clinical use and the first appearance of resistance. (27)

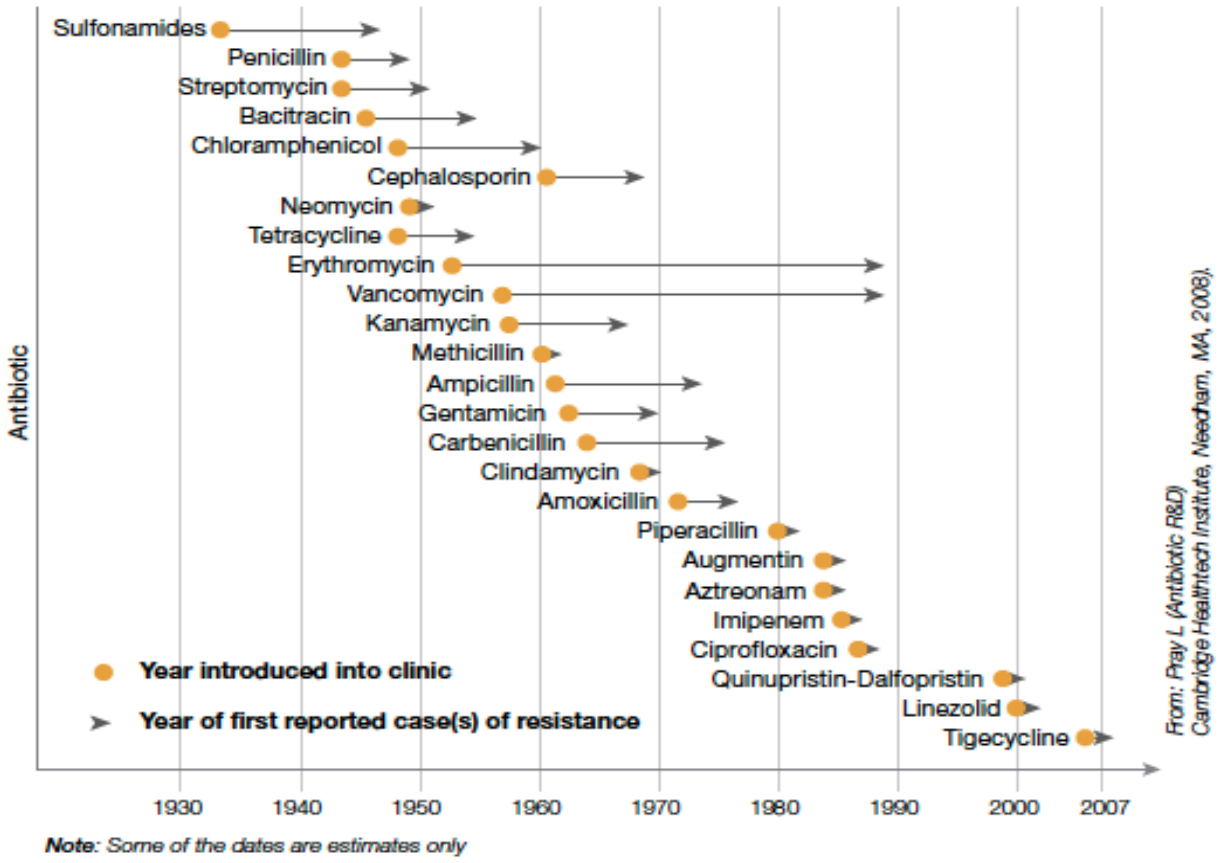

Figure 3. Time lag between an antibiotic being introduced to clinical use and the first appearance of resistance (27)

The responsible use of antimicrobials remains crucial or new medicines may become ineffective too soon.

3 Translating needs into policies

Reducing AMR requires global action, education and promotion. Guidelines and policies can provide tools for physicians and dispensers to educate patients on antimicrobial use and the importance of adherence to prescribed treatments, and to ensure patients receive medicines appropriate to their clinical needs at doses that meet their individual requirements for an adequate period and at the lowest cost to them and their community. (6) Surveillance and prudent use of antibiotics by medical, pharmacy, dental and veterinary professionals are urgently needed. So are the provision of the correct type of consultations and advice to the patient, delving into the reasons for non-adherence to regimens, and acting upon them.

Economic incentives combined with increasing R&D initiatives leading to interest in the development of new antimicrobial medicines may also be part of a solution. (28)

Control of the development of AMR can be achieved via collaborative health personnel practice and the involvement of all stakeholders. (29)

3.1 Policy at international level

International AMR policies aim at prudent use of antimicrobials and infectious disease prevention, combined with surveillance of resistance and antimicrobial use. (29) In 2001, the WHO published its Global Strategy for Containment of Antibiotic Resistance, (30) which involves all these factors. In 2004, the WHO investigated which diseases are considered a health threat with a pharmaceutical gap. The results were reported in its "Priority medicines for Europe and the world" document, which lists the antimicrobials needed to address these threats. (26)

FIP has been monitoring WHO policies. In response to AMR rising up the global health agenda, in 2008 FIP issued its "Statement of policy — control of antimicrobial resistance", (31) through which FIP takes responsibility for professional leadership through a range of AMR activities.

In 2014, the WHO invited FIP and other stakeholders to contribute to its report "Antimicrobial resistance: Global report on surveillance 2014". (7) It provided, for the first time, an accurate picture of the magnitude of AMR and the current state of surveillance globally. It called for a coordinated approach and formulated a base for a Global Action Plan on AMR.

The Global Action Plan on AMR was approved in May 2015 by the WHO. (1) The highlights of the plan are summarised in Appendix 1. Through the process of development of this plan, FIP promoted best practices and the role of pharmacists in the selection, procurement, distribution of antimicrobial medicines and shared how pharmacists contribute to infection prevention and control, surveillance, and improving the prescribing and use of antimicrobials (i.e. antimicrobial stewardship). (32)

Several organisations have a dedicated focus to AMR, for instance Action on Antibiotic Resistance (ReAct). ReAct brings together stakeholders towards action on antibiotic resistance through a variety of means, including translation of scientific evidence to policymakers, helping to develop national policy platforms and mobilising civil society groups to take action on AMR. (33)

3.2 Policy at regional or national level

3.2.1 Governmental policies

An important step in providing better surveillance or management in AMR is to develop strategies or plans involving different areas, including government, health authorities and health care associations. In some countries, AMR policies or plans have been developed to cope with different AMR scenarios and/or prevention.

At present, Australian, British, German, Swiss, Indian, American, Canadian, Chinese, Israeli, Brazilian, European and South American policies (among other national policies) cover these specific issues:

- Taking action in main areas such as surveillance, prevention of communicable diseases and infection control through the responsible use of antimicrobial agents. (26) (34) (35) (36) (37) (38) (39) (40) (41)
- Research and development of alternative products and/or new antimicrobial medicines. (37) (38) (42)
- Protection and promotion of public and animal health evaluation and supervision of medicines for human and veterinary use. (4) (34) (37) (38) (43)
- Comprehensive collaboration between government and health professionals to improve antimicrobial stewardship. (38) (44) (45) (40)
- Control of antimicrobials in food from animal production that is not beneficial to public health. (4) (39) (40)
- Factors influencing the development of AMR and the interactions between them. (46)

Since Australia's consumption of antibiotics is among the highest in the developed world, there have been moves by the Australian Federal Government to address AMR. The issue is to be targeted in an upcoming national strategy that promises better prescribing and greater surveillance to combat the threat of so-called superbug resistance. (47) For the first time, the Australian Federal Departments of Health and Agriculture have vowed to work together to limit the risk to human health. The 2015–19 policy calls for a "one health" surveillance system, collecting data on antibiotic use in humans and animals and evidence of resistance in food and patients, and identifying emerging problem areas, with Australia set to engage international networks.

An example of a national body working for interdisciplinary collaboration to ensure the effective use of antibiotics in human and veterinary bacterial infections is STRAMA (the Swedish Strategic Programme against Antibiotic Resistance). (40)

3.2.2 Policies on pharmacists' roles

A 2014 WHO report, "The role of pharmacist in encouraging prudent use of antibiotics and averting antimicrobial resistance: a review of policy and experience in Europe", (48) presents a number of issues that policymakers may wish to consider with a view to strengthening their efforts to tackle AMR, such as enhancing the prudent use of antibiotics. The report was developed by the Health Technology and Pharmaceutical Programme in collaboration with WHO-EURO regional office, the Pharmaceutical Group of the European Union (PGEU), Europharm Forum, and the WHO Collaborating Centre for Drug Development and Pharmacy Practice at Pharmakon (Denmark). Besides this, a paper "Pharmacists have decisive role in combating antibiotic resistance, says new WHO European survey" (49) highlighted pharmacists' roles in AMR prevention and control, following a survey carried out by the WHO-EURO regional office.

The PGEU in its statement "Community pharmacists' contribution to the control of antibiotic resistance" (50) focused on the pharmacist's role in correcting the misconception that antibiotics are needed to treat colds and other minor ailments.

In March 2015, the American Pharmacists Association (APhA) adopted the following statements (51) as part of its official policies:

1. APhA supports the role of pharmacists in antimicrobial stewardship in all practice settings.
2. APhA supports pharmacists working in collaboration with others to lead the development and implementation of antimicrobial stewardship programs and initiatives.
3. APhA supports pharmacists advising prescribers and educating patients on the appropriate use of antimicrobials.

The UK Pharmacy Infection Network (PIN) has worked closely with hospital pharmacists for many years developing and leading on UK antimicrobial stewardship initiatives solely and in collaboration with other UK infection societies and government agencies. (52) The Society of Hospital Pharmacists of Australia (SHPA) Infectious Diseases Committee of Speciality Practice has performed a similar role in Australia over recent years.

4 Community pharmacists fighting AMR

Community pharmacists are often the first point of contact for the public and they have a pivotal role in advising patients on minor ailments and referring them to their physician when required. They are often the entry gate to the health system on account of their easy accessibility.

That accessibility has been evaluated in Australia, where a recent study indicates that, between July 2011 and July 2012, 94% of Australians aged 18 years and over reported visiting a community pharmacy. This proportion increases to 99% for Australians aged 65 years and over. (19) This situation gives pharmacists the unique opportunity to offer an effective medication therapy management and counselling on consumption of medicines and also engage patients in their appropriate, efficacious, safe and responsible use, as well as consulting and collaborating with physicians to ensure optimal and responsible use of antibiotics. (53)

Due to their special position in the community, pharmacists can educate and lead the general public in their (antimicrobial) medication-related needs. Roles played by community pharmacists include health promotion and infection minimisation or control, triage and optimal treatment management.

4.1 Health promotion

Health promotion events and campaigns that are having a positive impact on population immunity, resilience to infections and overall community health are indirectly helping to reduce the need for use of antimicrobials.

In this regard, pharmacists as communicators on healthy lifestyles have taken part in health promotion campaigns on a wide range of topics, including encouraging the choices that help to keep the immune system healthy, e.g., smoking cessation and healthy eating (getting enough vitamins, etc).

In Australia, National Prescribing Service (NPS) MedicineWise (54) involved pharmacists and other health care professionals in a campaign to raise public awareness about AMR as a public health issue that uses health promotion approach (e.g., good hygiene, isolation of infected patients in the family, advice on how to overcome infections, including common viral infections, etc). (See Activity 1.) In India, the theme of National Pharmacy Week, which usually covers public health and health promotion topics, was planned to be AMR-related in November 2015.

4.2 Infection prevention and control

4.2.1 Educating on infection prevention

Infection prevention and control is an essential strategy to reduce infection and the subsequent increased use of antimicrobials. It supports a broader public health and infection minimisation agenda, with educating the community on hand washing and hygiene practices, correct sneezing/coughing protocols, isolation of infected patients etc. Pharmacists are involved in such strategies.

In Great Britain, the Royal Pharmaceutical Society encouraged people to visit local pharmacies for sexual health advice and protection against sexually transmitted infections. (See Activity 2.) Moreover, pharmacists continuously lead the control of infectious diseases such as chlamydia and syphilis through the simple action of selling condoms.

The Scottish Antimicrobial Prescribing Group (SAPG) has developed a plan, "Self help guide to treating your infection" for use by community pharmacies. (See Activity 3.)

In Canada, a public education programme called "Do bugs need drugs?" focuses on community education about hand washing for infection prevention to stay healthy and stop the spread of the infection. (See Activity 4.)

4.2.2 Infection control via immunisation

Immunisation is an important part of any infection control strategy. It helps reduce the misuse of antimicrobials. In the case of viral vaccines, protection from a virus will reduce the number of viral infections (and, consequently, bacterial

superinfections), which in some cases are mistakenly diagnosed as a bacterial infection and so treated with antimicrobials. For example, there is a common misuse of antibiotics against influenza. (55)

Currently, however, opportunities to vaccinate are being missed. Increasing numbers of vaccine providers, such as pharmacists, create new opportunities to widen access to immunisation services and improve coverage among adults. (56) There is growing evidence that vaccination by pharmacists increases vaccination rates in hard-to-reach groups, but also among people eligible for vaccination but who have not received it. (57) (58)

In Ireland, pharmacists supported by the Irish Pharmacy Union delivered seasonal influenza vaccinations to eligible at-risk groups (e.g. pregnant women and people with chronic illnesses). It was found that 23% of those immunised by their pharmacist had never received an influenza vaccine before; 81% were considered to be at risk. Some 90% of all patients who received an immunisation were in this "at-risk" group. (58) (59) (See Activity 5.) Pharmacy-based influenza immunisation services are running in England (60), Portugal (see Activities 6 and 7), and in Belgium where they targeted patients with chronic disease such as diabetes. (See Activity 8.)

All 50 states of the USA and the District of Columbia have statutes that permit pharmacists to administer vaccines. (61) They are functioning as vaccine advocates, vaccine facilitators and vaccine administrators, with the support of the American Pharmacists Association and the US Centers for Disease Control and Prevention's National Immunisation Programme, which have developed a training course to prepare pharmacists for active participation in immunisation programmes. (57) (62) Following a successful pilot, legislation is being introduced in Australia to allow pharmacists to administer influenza vaccine.

Programmes involving immunisations are evidence of a significant leap toward pharmacists' involvement in direct patient care. (63) Furthermore, increasing pharmacists' vaccine recommendations and educating patients about vaccine benefits may increase vaccination rates in future pandemics. (64)

Pharmacists have also developed specific activities targeting health professionals. The American Society of Health-System Pharmacists launched an initiative to help pharmacists promote the immunisation process among their colleagues, and to improve influenza immunisation rates among other health care workers. (See Activity 9)

4.3 Triage

In the context of this document, triage is a process of assessing whether patients in a community pharmacy can be successfully treated by the pharmacist or whether they need to be referred to another health care professional. The stages of triage are described below.

4.3.1 Appropriate treatment of symptoms without antimicrobials

People suffering from influenza or other respiratory problems may think treatment with antibiotics is needed. Pharmacists can give proper counselling for symptoms and ensure that patients have a good understanding of their illness and realistic expectations of its progression.

The Community Pharmacists Association of Thailand developed a campaign to prevent unnecessary use of antibiotics for non-bacterial infections and to tackle increasing antibiotic resistance under the slogan "Mirror, mirror on the wall, do I need antibiotics at all?" People were encouraged to check their throats in a mirror and decide, with support from pharmacists, if the symptoms of illness were viral or bacterial. (See Activity 10.)

Pharmacists in Spain launched a communication campaign with the slogan: "Do not ask us for antibiotics but for information". The aim was to discourage patients from using antimicrobials without prescription and to improve responsible use of antimicrobials. (See Activity 11.) Similar campaigns were developed in Costa Rica by the College of Pharmacists (see Activity 12) and in Czech Republic (see Activity 13), supported by patient leaflets and poster on AMR and ways to prevent it.

The General Pharmaceutical Council of Spain organised a campaign to raise awareness among the population of the risks of self-medication to treat flu symptoms. (See Activity 14.) The National Association of Pharmacies in Portugal organised a workshop for children, entitled "Protect yourself from Influenza A!" to educate them on H1N1 influenza and how to avoid catching it. (See Activity 15.) It focused on improving community knowledge about diseases that do not need antimicrobial treatments.

The Pharmaceutical Society of Australia (PSA) has co-produced a continuing education module for pharmacists on best practice treatment of upper respiratory tract infections and a consumer information brochure and poster on appropriate use of antibiotics to be distributed to pharmacies and physicians' surgeries. PSA has also developed a programme "PSA's Pharmacy Self Care", which provides education modules for pharmacists and their assistants, via fact cards, covering over 85 most-frequently-asked-about health topics. (See Activity 16.)

Pharmacists in the UK led an "Ask your pharmacist week" campaign to encourage people to avoid unnecessary visits to the physician and, instead, seek the support of local pharmacies to stay well during the winter. (See Activity 17.)

In Scotland, a minor ailments service provided by community pharmacies supported patients through the sale or supply of medicines for the treatment of symptoms where infection is considered to be viral, e.g. upper respiratory tract infection. (65) A similar minor ailments service is evolving in England. (66)

4.3.2 Direct supply of antimicrobials by pharmacists

In some countries pharmacists are legally allowed to prescribe antimicrobials in clearly specified cases.

Some provinces in Canada have given pharmacists the authority to prescribe antimicrobials for certain minor ailments. Although the list of approved minor aliments varies among provinces, the treatment of certain fungal and bacterial infections are often included. For instance, pharmacists in Saskatchewan are able to prescribe for impetigo, folliculitis and various tinea infections. Through their interventions, pharmacists are able to facilitate the quick and appropriate use of antimicrobials for their patients. (67)

In New Zealand, pharmacists can prescribe and dispense (without reference to a medical practitioner) trimethoprim for short-term treatment of an uncomplicated urinary tract infection. (68) (See Activity 18.)

Pharmacists in the UK dispensed azithromycin to patients with a positive result for chlamydia. Their sexual partners received the medicine too. (See Activity 19.)

A study (69) conducted by the University of Rhode Island and published in the *Journal of the American Pharmacists Association* showed the value of pharmacist-initiated antibiotic therapy for Lyme disease. Pharmacists dispensed two 100mg doxycycline tablets to people who had been exposed to *Ixodes scapularis* (deer tick) as a prophylactic treatment, and provided counselling on medicine intake regimen, signs and symptoms of Lyme disease and strategies for possible future tick prevention. (See Activity 20.)

Fast and reliable diagnostic tests are required to help pharmacists identify an infection as bacterial rather than viral and guide the appropriate use of antimicrobials. In Great Britain, according to the Royal Pharmaceutical Society, the Longitude Prize is on offer to those who can develop quick and reliable diagnostic tests. In addition, there has been recent publicity around the use of a C-reactive protein test to help identify antibacterial infections. (70)

4.3.3 Referral to appropriate health professionals

After an accurate assessment, pharmacists can offer to treat minor health problems or infections with an over-the-counter medicine. If a serious health problem is identified and the person needs to see a physician or specialist, pharmacists refer the patient to an appropriate professional.

For example, in India, TB is estimated to cost society approximately USD 3bn. (71) The Government, in its plan to fight TB, uses the DOTS (directly observed treatment, short-course) strategy, ensuring that patients complete the course of treatment and helping to reduce the chances of development of AMR. Since 43% of presumptive TB cases come to the pharmacy for advice or to buy medicine, DOTS is led by pharmacists. Pharmacists refer patients properly to DOTS facilities to increase their chance of correct diagnosis and treatment. The Indian Pharmaceutical Association in collaboration with PSG College of Pharmacy conducted a DOTS-TB training programme for pharmacists from the hospital and community sectors with emphasis on responsible use, no sale of antibiotics without a prescription, counselling patients for adherence, etc.

A similar initiative to engage pharmacies in making contributions to the case detection and cure rates in community areas has been implemented in the Philippines. (72)

4.4 Optimal treatment management

Pharmacists are trained in the management and responsible use of medicines and they play a major role in improving outcomes for patients taking antimicrobials through encouraging adherence in short- and long-term treatments.

4.4.1 Adherence support

4.4.1.1 Short-term infections

A new antibiotic adherence programme in the Newfoundland province of Canada began in January 2015. Pharmacists are reimbursed by conducting an initial consultation with patients receiving antibiotics and follow-up phone call to resolve any potential issues. (67)

The Association of Danish Pharmacists developed a campaign with the slogan "Unless you take your antibiotics to the end, you might believe that the treatment does not work". The core targets of this campaign were the parents of young children. (See Activity 21.) In a similar campaign in 2014, Danish pharmacists provided parents with a checklist chart for antibiotics. They could use that chart to put small stickers with "smileys" indicating that the child has already taken the medicine. (See Activity 22.) In Ireland, the Irish Pharmacy Union sought to improve responsible use and adherence, and to highlight the potential side effects of antibiotics and how they might be avoided via posters and booklets. (See Activity 23.)

In the UK, NHS Wales developed a "Choose Pharmacy Programme", software that allowed dispensing to registered patients of medicines for common ailments free of charge without a physician's prescription. This gave pharmacists an opportunity to guide people with regard to their antimicrobial treatment, if necessary. (See Activity 24.)

4.4.1.2 Long-term infections

In the control of diseases that require long-term treatment, the most important challenge is adherence. Directly observed treatment supervised by pharmacists is the best option for TB. As an example, a study compared adherence by DOT under pharmacy supervision with self-administered TB treatment (SAT) in Spain. DOT implemented through pharmacy offices was much more effective than SAT. In the DOT group, 75.2% of patients completed treatment and were cured compared with only 26.7% in the SAT group (73).

In the Philippines, pharmacists involved in "Pharmacy DOTS Initiatives" are trained to carry out interventions geared towards the provision of information about TB, about why the dispensing of anti-TB medicines without a valid prescription must be discouraged and about the role of the pharmacy to refer patients to DOTS facilities. (72) They provide wide access and convenience for patients seeking TB information or medicines.

4.4.1.3 Specific cases

The dose and formulation of a medicine needs to be appropriate to patients' needs. For example, in order for the most effective antibiotic to be given to a child, child-specific formulations (where the dose can be easily measured and the medicine is easy to swallow) are often needed. (74) In many countries, pharmaceutical formulations can be prepared extemporaneously in the pharmacy. (See Activity 25.)

FIP is currently working on FIP-WHO technical guidelines covering points to consider in the provision by health care professionals of children-specific preparations that are not available as authorised products. The subject of the document is the compounding technique applied by pharmacists to produce medicines from active pharmaceutical ingredients or using authorised medicines when no commercially available, authorised, age-appropriate or adequate dosage form exists.

Sometimes the challenge of taking medicines is the medicine itself. For example, where a child does not like the flavour. In those situations, pharmacists must support parents and make them aware of how important it is for the treatment to be completed. Pharmacists can adjust the dosage forms by using syrups, for example, in which the medicines can be mixed and dissolved, so that children are more likely to take them.

4.4.2 Minimising interactions

Medicines interactions (75) may occur as a result of accidental misuse or a lack of knowledge about the active ingredients. Pharmacists advise on how to use medicines correctly, adverse side effects and potential interactions with

other medicines, treatments, food or drinks. For example, calcium in milk decreases the absorption of ciprofloxacin. (76) Pharmacists are ideally placed to counsel people on when and how to take medicines, and the optimal timing in relation to meals.

Pharmacists can provide evidence-based advice to ensure appropriate antimicrobial doses are administered so that AMR does not emerge from sub-therapeutic concentrations.

4.5 Ensuring quality of medicines

Quality of medicines is a crucial factor in the prevention of AMR. Counterfeit medicines are a major threat to public health and antibiotics are one of the most counterfeited groups. (77) Counterfeit medicines may have no therapeutic effect or may even be toxic. Moreover, if the medicine has the correct active antimicrobial ingredient but it is not in sufficient quantity, this can increase AMR. Pharmacists protect the integrity of the supply chain, and procure medical products only from reputable sources. They are alert to differences in quality of packaging, labelling or leaflets and in physical appearance of medicinal products. (78) Pharmacists are a vital asset in assuring the safety of patients through their active participation in the fight against counterfeit medicines.

That antimicrobial dispensing must be always with a prescription and also in certified pharmacies or drugstores was a simple but important message in a campaign developed by the General Pharmaceutical Council of Spain to raise public awareness on procuring antimicrobials only from reliable sources. (See Activity 26.)

5 Hospital pharmacists fighting AMR

As well as dispensing medicines, in some countries hospital pharmacists are also responsible for their purchase, manufacture and quality testing. (79) Pharmacists work closely with medical and nursing staff to ensure that patients receive the best treatment, advising on the selection, dose and administration route. They also provide help and advice to patients in all aspects of their medicines.

These activities make pharmacists strong supporters in the fight against the threat of AMR in hospitals. Their work in multidisciplinary teams puts them in a good position to coordinate strategies for better antimicrobial stewardship and develop processes with regard to such activities as sterilisation and hygiene.

5.1 Pharmacist-led stewardship programmes

Antimicrobial stewardship programmes in hospitals seek to optimise antimicrobial prescribing in order to improve individual patient care and slow the spread of antimicrobial resistance. (80) Pharmacists in the UK, Australia and the USA have been integral to the development of antimicrobial stewardship guidance for both primary and secondary care (81) and hospitals (82) (83) and the development of antimicrobial prescribing standards.

In secondary care, short-term funding from the UK Department of Health in 2003 (84) established antimicrobial pharmacists to work across teams and networks to ensure antimicrobial stewardship was embedded into hospital infection control practice. This has enabled pharmacists to play important and leading roles in National Health Service hospital antimicrobial teams to ensure antimicrobial guidelines are evidence based, that patients are reviewed daily to stop treatment if appropriate or to de-escalate to less powerful antibiotics and that regular antimicrobial audits and reviews of antibiotic use are performed. Furthermore, some published studies have reviewed behavioural change interventions for antimicrobial stewardship in hospitals and have proposed using games to develop stewardship initiatives. (85) (86)

UK hospital pharmacists have been instrumental in reducing prescribing of high-risk broad-spectrum medicines (notably cephalosporins and fluoroquinolones) associated with *Clostridium difficile* infection and coinciding with a reduction in *C. difficile* infections and stabilisation in resistance to these antimicrobial agents. Guidance, "Start smart — then focus: Antimicrobial stewardship toolkit for English hospitals", (87) was published by the Department of Health in England in 2011 and was updated in March 2015. The document was authored by pharmacists with support from infectious diseases physicians and microbiologists.

Researchers at University College London have been identifying worldwide resources and guidance available for health care professionals which support education and training in antimicrobial stewardship. Working in partnership with the Royal Pharmaceutical Society, they will develop this into a multidisciplinary open-access database that signposts existing published material around education and development of antimicrobial stewardship. The final database has been launched as a website "amsportal.org".

Expert practice curricula for infection and antimicrobial stewardship have been produced by the UK Clinical Pharmacy Association Infection Management Group, with the Royal Pharmaceutical Society as an affiliated group, to support pharmacists with the knowledge skills, experience and behaviours to advance in their practice, which will include reducing the spread of AMR. (88) Similar educational seminar series were provided by the Society of Hospital Pharmacists of Australia (SHPA; see Activity 27). An online antibiotic stewardship programme (89) has also been developed in Ireland by the Irish Institute of Pharmacy (see Activity 28).

Furthermore, the SHPA has also published standards of practice for clinical pharmacy (90) that detail the role and responsibilities of pharmacists in the care of patients, which includes the management of infections and the use of antimicrobials.

In the same way, the Australian Commission for Safety and Quality in Health Care coordinates and leads a number of programmes which aim to address AMR and support antimicrobial stewardship, for example, the Commonwealth AMR and AU Surveillance Project, (91) the Healthcare Associated Infection Prevention Programme and Antimicrobial Stewardship Initiative, (92) and the Antimicrobial Stewardship Clinical Care Standard. (93) In addition, NPS

Medicinewise is currently running a five-year campaign to reduce prescribing of antibiotics by 25%, to bring Australia in line with the European average. The campaign targets both health professionals and consumers. (94)

All hospitals should have an antimicrobial lead pharmacist who promotes antimicrobial stewardship. (82) This is a perfect scenario where pharmacists can manage the correct use of antimicrobials, and have a remarkable and positive impact on AMR prevention.

In the UK, a smartphone application for antimicrobial guidelines (MicroGuide) was developed by pharmacists and medical microbiologists in an NHS hospital and has been licensed to over 45 other hospitals. The app content can be edited by clients according to local resistance patterns and clinician preferences. In February 2015, MicroGuide was awarded the NHS Innovation Challenge Prize in the Infection Control category, providing investment for the development of a decision-support system within the app to better tailor antibiotic therapy to individual patients according to severity of illness and risk of resistance. (95) Another smartphone application "IAPP" was found to have a positive effect on antimicrobial prescribing in hospitals in both medicine and surgery. (96)

5.2 Sterilisation

Many hospital sterilisation services are not provided by a fully-fledged department but by a sub-department under the hospital's surgical or nursing services. However, pharmacists, with their training in microbiology and aseptic technique, are competent in the functions sterilisation services are expected to perform. Hospital pharmacists may also have the responsibility of implementing training programmes for hygiene personnel.

5.3 Hygiene in hospitals

Evidence suggests that adherence to handwashing protocols by hospital visitors can be as low as 25%, and could be increased to up to 77% through the introduction of a novel intervention, for example, the use of disposable gloves during contact with patients and their environment. (97) In a study conducted to determine the rate of nosocomial diarrhoea caused by *C. difficile*, it was shown that this rate was three times lower in hospitals with "universal use of gloves". (98) In a similar study focusing on vancomycin-resistant enterococci, 39% of staff became contaminated with these organisms, and the cross-contamination of staff decreased by 71% when disposable gloves were used. (98) There is an opportunity here for pharmacists, working alongside their hospital to colleagues, to promote the use of disposable gloves in hospitals.

6 Collaborative practice

The level of collaboration between pharmacists and other health care professionals ranges from simple contact through to pharmacists being seen and recognised as core members of the multidisciplinary team with the authority and responsibility to manage and modify medicines therapy. FIP established a Working Group on Collaborative Practice in 2009, which led to the adoption of the FIP Statement of Policy on Collaborative Pharmacy Practice the following year. (99) The main purpose was to develop a robust definition of collaborative practice, identifying the current status and integrating pharmacists into a collaborative health care team to improve patient outcomes.

Furthermore, according to the "Statement on Interprofessional Collaborative Practice" by the World Health Professions Alliance in 2013, (100) improved access to health interventions, efficient use of resources, and reduced increase of AMR occur when health systems embrace interprofessional collaborative practice across the full range of the problem (health promotion, infection control and medicines management).

The embedding of an interprofessional approach could also be considered in the provision of education and training to engender enhanced professionalism and interprofessional collaborative best practice in the area of antimicrobial resistance.

6.1 Interprofessional collaboration model

In 1997, the Clinical Research Team (now called the Microbiology and Infectious Diseases Reference Laboratory, MIRL) at the National Health Research Institute of China Taiwan took on the role of promoting the importance of fighting against AMR while facilitating the work between the government, scientists and practitioners. Further to this, the China Taiwan Surveillance of Antimicrobial Resistance programme (TSAR) started to run in a two-year cycle and was completed by the eighth cycle in 2013. The outcomes include the results of sensitivity testing of all microbes, allowing the monitoring of new emerging microbes, and the listing of indicators for measuring the progression of infection control (e.g., defined daily dose). This programme was later passed to the Antimicrobial Stewardship Programme chaired by the Centre of Disease Control of China Taiwan, scheduled from 2013 to 2015. Data of the outcomes of this collaborative programme, such as decrease (in percentage) of medication cost, reduction of antimicrobials consumption, minimisation of infections and secondary infections, etc. will be released in 2016.

According to the China Taiwan Society of Health-System Pharmacists (TSHP), the results of the TSAR served as background for accreditation guidelines developed by China Taiwan Joint Commission on Hospital Accreditation. These guidelines underline the role of pharmacists and emphasise the importance of their involvement in the infection control teams.

In Switzerland, physicians and pharmacist quality circles (PPQCs) formed of five physicians and one pharmacist, evaluated a number of medical attitudes, including attitudes to prescribing antibiotics for common infections in outpatient treatment. They agreed on a set of treatment options based on fixed objectives: first improving care quality, and secondly finding the most economical solutions. Afterwards the prescribers put these strategies into practice. Findings included that the overall cost of antibiotic and hypertensive drug prescriptions was higher in 1998 than in 1997, but less so in circle prescribers than reference groups. (101) An evaluation over nine years (1999–2007) showed that there was a decrease of 42% in the cost of medicines in the PPQC group compared with the reference group, which represents a USD 225,000 saving by general practitioners alone in 2007. These results are explained by compliance with guidelines, pharmacovigilance, greater use of generics, and continuing education on the responsible use of medicines. (102) (See Activity 29.)

Interdisciplinary collaboration has a positive impact on medicines stewardship, including antimicrobial management. Furthermore, it can be applied in any country and can achieve the savings expected by political authorities without compromising quality or patient safety.

6.2 Feedback on prescribed antimicrobial regimens

Pharmacists engaged in near-patient clinical roles are able to intervene in the event of inappropriate antimicrobial use. (103) They can work as part of multidisciplinary clinical teams to ensure the correct use of antimicrobials, and can also verify if the choice of agent and treatment plan comply with the national standards that apply in their countries.

In the community, pharmacists can ensure that antimicrobials are appropriate by asking patients handing in prescriptions why they have been prescribed. They can also work with local GPs, or contacts in the primary care organisations or commissioning bodies, to improve prescribing habits. For example, providing delayed prescriptions could provide patients with an option to initiate antimicrobials only if their condition aggravates. (103)

In the UK, a hospital pharmacist chaired a government advisory committee working group to propose quality measures for antimicrobial prescribing in primary and secondary care. (104) The primary care measures have been adopted by the NHS in England through the Quality Premium initiative whereby primary care health care commissioning groups are incentivised to reduce total antimicrobial prescribing and prescribing of broad-spectrum agents in particular. (105)

The International Classification of Diseases (ICD) registered on every antimicrobial prescription is also a way to facilitate the monitoring of antimicrobial use so that action can be taken when these medicines are not used in an optimal way.

7 Engaging stakeholders

Multiple interventions are needed to tackle AMR. The contribution of pharmacists may not be obvious at first glance, since collaboration usually happens within research teams, institutions or organisations. However, pharmacists are an important partner and should be involved in initiatives concerning AMR.

7.1 Monitoring AMR threats

Surveillance is essential to determine the magnitude of AMR, to establish trends, and to seek strategies to lessen its impact. Clinical and research laboratories throughout the world generate resistance data but few submit these data to appropriate databases that could allow local analysis or linking with a surveillance network. (106)

Furthermore, the effectiveness of surveillance data can be enhanced by integrating evidence that identifies vulnerability to certain infections. This way infection control strategies can become more focused on reaching those who need the services the most, facilitating a more effective response. (107) Groups especially vulnerable to certain infections vary. For example, poor and vulnerable groups are at greater risk of TB infection compared with the general population because of overcrowded and substandard living conditions, poor nutrition, interaction with other diseases, and migration from or to higher-risk communities or nations. Factors such as social isolation, reduced access to health services, lack of trust in the health system and lack of a voice in the community all have a negative impact on health. In this context, TB control cannot be achieved by concentrating on improving averages across the general population, but needs to address the specific needs of vulnerable communities. (107) There is an opportunity for dialogue among all stakeholders on how to best identify such groups to improve their access to medication and pharmaceutical expertise, as well as to improve adherence, and therefore treatment outcomes.

7.2 Pharmacists engagement in R&D

Developing new medicines involves a great deal of time, effort, scientific research and expense. Pharmacists and pharmaceutical scientists employed in R&D engage with stakeholders via academia and other institutions.

A body with a strong public health mandate is needed to govern and run the R&D process by publishing the priority product targets based on predicted areas of medical need, assessing products against those criteria, negotiating purchase agreements and managing the ethical and practical challenges of global use. (26) Patent policy could help to resolve the conflict between the private profit motives of companies and public interest in conserving antibacterial effectiveness. (108) Collective action involving all stakeholders, including those representing pharmaceutical expertise, is therefore necessary. Similar approaches to the Multilateral Initiative on Malaria, which coordinates research on antimalarial products, (109) (110) should be considered for research into new antimicrobials.

7.3 Reducing antimicrobials in food and the environment

Antimicrobial use in food-producing animals may affect human health through the presence of pharmaceutical residues in foods and particularly by the selection of resistant bacteria in animals (15). Currently there is no real understanding of the extent of the use of antimicrobials in animals. They are used in animals for prophylaxis, treatment and growth promotion and those animals serve as a reservoir of resistant pathogens and resistance mechanisms that can directly or indirectly result in antibiotic resistant infections in humans. In North America and Europe, it is estimated that about 50% in tonnage of all antimicrobial production is used in food-producing animals and poultry. (111)

Currently, the WHO is working closely with the Food and Agriculture Organization (FAO) and the World Organization for Animal Health (OIE) to tackle AMR issues at the animal-human interface through better coordination at global level and improved intersectoral and multidisciplinary collaboration. The WHO, the FAO and the OIE have established a formal tripartite alliance to enhance global coordination and to promote intersectoral collaboration between the public health and animal health sectors as well as in food safety. (7)

It is noteworthy that the OIE has undertaken an update of all relevant standards on AMR including the OIE list of antimicrobial agents of veterinary importance in the guidelines for risk analysis of foodborne AMR adopted by the Codex Alimentarius Commission in July 2011 and since 2010. (7)

Many patients store antibiotics from uncompleted courses, well beyond their expiry date, and later take them for self-diagnosed conditions or give them to family members and friends. (112) Pharmacists can help to prevent this. In Belgium, an activity carried out by the Belgian Pharmaceutical Association in 2011 invited patients to return their unused antibiotics (see Activity 30).

Pharmacists organised take-back collections of expired and unused medicines, for instance, by appointment with pharmacists in Malaysia (see Activity 31), via an in-pharmacy campaign in Argentina (see Activity 32) and by bringing the medicines to the pharmacy directly (e.g. in France, Spain, Slovakia and Canada). (113) In the USA, the public could ask their pharmacists for an envelope to mail their medicines directly to the appropriate disposal centre (see Activity 33).

There is a new concern regarding the presence of antimicrobials in wastewater. Treatments to "clean up" wastewater may be modifying the antibiotics and, by doing so, triggering a rise in antibiotic-resistant bacteria. (114) In this regard, FIP is developing a report "Green pharmacy practice" expected to be released in 2015. It has as an underlying premise that pharmacists should accept a degree of responsibility for changing the entire medication-use process so as to minimise the environmental effects of prescribing, dispensing, pharmaceutical care, disposal of unused medicines and, ultimately, reducing metabolic waste discharge into the environment. The report will provide practising pharmacists with the necessary information and tools for taking environmental aspects into consideration in their daily professional activities.

8 Summary

Pharmacists are the most accessible health care professionals, and are fully competent in all aspects of medicines. They possess scientific knowledge for the entire medicines-use process, including procurement, preparation, storage, security, distribution, dispensing, administration and safe disposal.

Pharmacists are on the front line of community health services, and are the entry point for patients to health care and the health system. This position gives them various opportunities. Pharmacists serve as communicators and educators on healthy behaviours and infection prevention. They increase the coverage of immunisation in hard-to-reach groups, and they are in good position to explain the importance of using antimicrobials only when needed.

The pharmacy is a place where pharmacists evaluate the needs of patients and provide a sort of triage. In this process pharmacists assess whether they can successfully treat the patient or whether the patient needs to be referred to another health care professional. Depending on the results of the assessment, there are three possible outcomes: the patient can be treated by the pharmacist without antibiotics, the patient can be treated by the pharmacist with antimicrobial treatments where this is legally allowed to happen, or the patient can be referred to another health care professional, usually a physician or a specialist.

Where pharmacists are legally allowed to prescribe antibiotics, fast and reliable diagnostic tests can support them in the proper diagnosis of common infections such as chlamydia or Lyme disease.

Pharmacists provide effective medication management for both short- and long-term treatments. They support adherence, minimise interactions and ensure quality of medicines. In hospitals, pharmacists lead stewardship programmes and are competent in hygiene and sterilisation. Pharmacists collect unused medicines, reducing the presence of antimicrobials in the environment.

Pharmacists are fully committed to supporting the development of programmes to combat AMR, through promotion, prevention and control of antimicrobial treatments, and providing access to high quality treatments in the community and at all levels or care. Pharmacists encourage the commitment of all health care professionals to fight the AMR threat via programmes developed in collaboration with stakeholders.

All of the above can help to prevent AMR in the community and in hospitals, and increases the likelihood of successful antimicrobial policies being implemented. This document clearly articulates the important role of pharmacists in addressing this public health issue and can provide a foundation for discussion among various stakeholders.

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Appendices

Appendix 1. Objectives of the WHO Global AMR Action Plan

The WHO Global AMR Action Plan has the following objectives:

1. To improve awareness and understanding of AMR;
2. To strengthen knowledge through surveillance and research;
3. To reduce the incidence of infection;
4. To optimise the use of antimicrobial agents; and
5. To ensure sustainable investment in countering antimicrobial resistance.

Development of this plan has been guided by the advice of countries and key stakeholders, based on several multi-stakeholder consultations at different global and regional forums.
It urges Member States (and, where applicable, regional economic integration organisations):

1. To implement the proposed actions for Member States in the global action plan on antimicrobial resistance, adapted to national priorities and specific contexts;
2. To mobilise human and financial resources through domestic, bilateral and multilateral channels in order to implement plans and strategies in line with the global action plan;
3. To have in place, by [...] 2017, national action plans on antimicrobial resistance that are aligned with the global action plan on antimicrobial resistance and with standards and guidelines established by relevant intergovernmental bodies.

And invites international, regional and national partners to implement the necessary actions in order to contribute to the accomplishment of the five objectives of the global action plan on antimicrobial resistance.

Appendix 2. Examples of activities organised by pharmacist associations

These summaries have been developed by FIP, based on a set of references (publications, materials of the activities, newspaper articles etc.). The list of references for a specific activity is available on request.

Activity 1 - Actions against lifestyle diseases and promotion of good health (Australia)

In Australia, National Prescribing Service (NPS) Medicines Wise involved pharmacists and other health care professionals in campaign to raise public awareness about AMR as a public health issue that uses health promotion approach, e.g., good hygiene, isolation of infected patients in the family, advice on how to overcome infections (including common viral infections, etc.). Furthermore, the NSP provides tools and guidelines for pharmacists and health care professionals with the latest evidence to help health professionals further understand the issues around wellbeing and AMR. It also includes tools and resources to help educate patients and carers, and contains posters and brochures with advice on how to better manage their health and get the best from their medicines.

Activity 2 - Campaign on sexual health advice from pharmacies (Great Britain)

More than 100,000 copies of the "Ask about sexual health" leaflet were distributed to community pharmacies and primary care organisations in 2005 as part of a campaign that coincided with "Ask about medicines week" led by Great Britain's Royal Pharmaceutical Society. The aim was to drive home the message that community pharmacists are ideally placed to provide expert help and advice on all aspects of sexual health. This leaflet, designed to encourage people to visit local pharmacies for sexual health advice, was so successful that the RPS had to reprint it. Copies were available from the RPS's public relations unit during the entire year.

Activity 3 - Self help guide to treating your infection (Scotland)

The Scottish Antimicrobial Prescribing Group (SAPG) has developed a "Self help guide to treating your infection" for use by community pharmacies. The SAPG carried out an online survey of all community pharmacists in early 2015 to seek their feedback on the usefulness of the materials and identify any learning needs with respect to providing advice on self-limiting infections. This will be followed up by a more in-depth qualitative study of pharmacist attitudes and behaviours in collaboration with Robert Gordon University, Aberdeen.

Activity 4 - "Do bugs need drugs?"(Canada)

In Canada, a public education programme called "Do bugs need drugs?" is being implemented in certain provinces. The programme is focused on community education about hand washing for infection prevention and the responsible use of antibiotics. The programme is not only for health care professionals, but also for workplaces, parents, children and teachers. Participants learn the importance of washing their hands to stay healthy and to stop the spread of infections, the difference between viruses and bacteria, and when antibiotics should be used.

Activity 5 - Flu vaccinations (Ireland)

In Ireland, pharmacists have been delivering flu vaccinations since 2011, when close to 1,400 pharmacists were trained to do so. Subsequently in 2013, the Irish Pharmacy Union led an activity where pharmacists have delivered seasonal flu vaccinations to eligible patients. The service was available free-of-charge to those in an at-risk group who had a medical card. Eligible at-risk groups included elderly people, pregnant women and people with chronic illnesses. Pharmacists could also provide the service to any patient over the age of 18 who was not in the at-risk category. As a result, 23% of the patients who received an immunisation from their pharmacist had never received a flu vaccine before, 81% of these patients were high-priority (or groups of patients considered at risk), and 90% of all patients who received an immunisation were in this "at-risk" group. Statistical data revealed that community pharmacies contributed to reducing the number of flu cases in Ireland and consequently reduced care costs.

Activity 6 - Establishing seasonal flu vaccination in community pharmacy: an enabling service (England)

In June 2009, in order to prepare pharmacists in offering seasonal flu vaccination services to their patients, the National Pharmacy Association in England launched a new service in association with an established flu vaccination provider, The Health Station. This service consisted of a one-day training course specific to vaccination, an operation manual and guidelines for the delivery of this service, a window poster and patient leaflets to promote this service at the community pharmacy. There was also a clinical governance programme with pharmacist support available seven days a week via telephone, and a separate patient helpline.

Activity 7 – Flu immunisation campaign in community pharmacies (Portugal)

In October 2008, the National Association of Pharmacies (ANF) in Portugal organised for the first time a nationwide pharmacy-based influenza immunisation campaign to organise and promote the flu vaccination provided in community pharmacies. The activity was supported with models and tools, including an administration record to support pharmacists in the provision of this new service. Fifty-three training sessions for pharmacy-based immunisation delivery and 264 sessions for basic cardiac life support took place in 11 districts across Portugal during 12 weeks. This campaign aimed to increase the coverage of flu vaccines for population with higher risks. A similar campaign was organised in 2010–11, highlighting that immunisation at the community pharmacy is simple and easy. The campaign is repeated annually.

In 2008, 1,588 pharmacies took part, leading to the vaccination of 159,700 patients (i.e., between 5.5% and 11.3% of all vaccinated patients who are older than 65 years). Half of the vaccines were administered in the first 10 days of October. Almost every patient was satisfied with the immunisation provider, with the service operating hours, with the waiting time, with the privacy, and with the information provided. Some 13.1% of the patients were being vaccinated for the first time. A total of 1,842 community pharmacies took part in this flu vaccination campaign in 2009.

Activity 8 - Reminding diabetic patients to be immunised against flu (Belgium)

In Belgium in autumn 2007, a pilot project was run by the Belgian Pharmaceutical Association to make the community pharmacy a medium for raising awareness among diabetic patients on the importance of being immunised against influenza and for improving the influenza immunisation rate among these patients.

Later, in 2009, another pilot project was launched: Belgian pharmacists were asked to identify diabetic patients for whom no sale of vaccination against influenza was recorded, to talk with them about the benefits of influenza vaccination, to disseminate brochures and to refer them to their physicians for a vaccine prescription. For the general population, the vaccination rate increased from 14.8% to 17.3% from 2006–09. Among diabetic patients, the rate increased from 45.6% to 48.6%.

Activity 9 - Pharmacists advocating for immunising health care workers against influenza (USA)

The American Society of Health-System Pharmacists launched an initiative in 2009 to help pharmacists advocate among their colleagues for influenza immunisation for health care workers. This initiative consisted of an online resource centre with the following tools available: a campaign planning checklist; an "Influenza Myths vs. Facts" document; a list of possible immunisation incentives; an online quiz to evaluate knowledge on influenza immunisation;

and key links to evidence-based information. Pharmacists have been invited to relay (and adapt) this campaign within their hospitals.

Activity 10 - "Mirror, mirror on the wall, do I need antibiotics at all?" campaign (Thailand)

The Pharmaceutical Association of Thailand organised a campaign to prevent unnecessary use of antibiotics for non-bacterial infections and to battle increasing antibiotic resistance in the country. This initiative started in March 2014 and aims to lower consumption of antibiotics. A simple concave mirror and a picture of a human throat with bacterial infection are made available to consumers trying to buy antibiotics for treating the common cold and cough; consumers can check their throats in the mirror to see if it resembles the throat in the picture and decide whether or not they think antibiotics are needed. This campaign is by Community Pharmacists Association of Thailand called "Mirror, mirror on the wall, do I need antibiotics at all?". The initiative is part of the Antibiotics Smart Use policy implemented by the Thai Ministry of Public Health.

Activity 11 - "Do not ask us for antibiotics but for information!" (Spain)

In November 2003, the Pharmacy Chamber of Ciudad Real in Spain launched a communications campaign whose slogan was: "Do not ask us for antibiotics but for information!". This campaign aimed to discourage patients from using antibiotics without prescription and to improve responsible use of antibiotics.

Activity 12 -"Ask for advice, not for antibiotics!" (Costa Rica)

To raise awareness and educate patients about responsible use of antibiotics and antimicrobial resistance, the College of Pharmacists of Costa Rica ran a communications campaign where patients were invited to ask for advice instead of asking for antibiotics in 2009. This campaign aimed to provide basic information on antibiotics and antimicrobial resistance and how to prevent it. This campaign was supported by patient leaflets and a poster.

Activity 13 - Antibiotic resistance awareness campaign (Czech Republic)

"The Pharmacy Day", a campaign organised on 29 October 2009 in the Czech Republic, focused on antibiotic resistance. The campaign slogan was: "Responsible use of antibiotics — pharmacists advise you" This campaign included the display of posters in all community pharmacies and the distribution of leaflets to patients. The key information provided in the leaflets was: why antibiotics should be prescribed by a physician; when and how long the antibiotic should be taken for; what food and beverages should be avoided during a treatment; what side effects to expect; when to stop taking antibiotics; and why antibiotics should not be taken on the patient's own initiative.

Activity 14 - "Seasonal flu: don't take medicines without proper advice" (Spain)

In January 2007, the Pharmacy Chamber of A Coruña, in Spain, organised a campaign to raise public awareness of the risks of self-medication (especially antibiotics) to treat flu symptoms. The campaign also highlighted the responsible use of medicines and the effectiveness of measures such as frequent hand-washing to prevent the spread of contagious diseases. This campaign also reinforced the role of the pharmacist as an adviser on which treatment is best for a particular case.

Activity 15 - H1N1 workshop for children (Portugal)

The Pharmacy Museum (branch of National Association of Pharmacies in Portugal) organised a workshop in autumn 2009 entitled "Protect yourself from Influenza A" for schoolchildren. The workshop aimed to educate them on the characteristics of the H1N1 virus, and situations of everyday life where they may be exposed to contagion. The correct techniques for washing hands, and other measures to prevent the spread of influenza A virus, were some of the practices addressed in the playful and fun workshop.

Activity 16 - Self-care — health advice for life (Australia)

The Pharmaceutical Society of Australia launched in 1990 a programme to improve counselling and health promotion by pharmacists. The programme called "Pharmaceutical Society of Australia's Pharmacy Self Care (PSC)" is a membership based programme for pharmacies providing education modules and health campaign tools for pharmacists and pharmacy assistants, and consumer health information resources. This programme consists of fact cards which cover more than 85 most-frequently-asked-about health topics, classified in 14 different categories. All these resources are reviewed, updated and written by pharmacists for pharmacists.

Activity 17 - Ask your pharmacist: "Come to pharmacy first" campaign (UK)

In 2013, a National Pharmacy Association "Ask your pharmacist" campaign took place in the UK to encourage people to avoid unnecessary GP and accident and emergency visits by instead seeking the support of local pharmacies to stay well during the winter. The theme of the week was "Come to pharmacy first". The week was followed by a major new public awareness initiative, in which Pharmacy Voice is a partner, called "Treat yourself better without antibiotics". It sustained "pharmacy first" messages right the way through winter and beyond.

Activity 18 - Pharmacist-led treatment of urinary tract infections (New Zealand)

In New Zealand pharmacists can prescribe and dispense (without reference to a medical practitioner) trimethoprim for short-term treatment of an uncomplicated urinary tract infection. The trimethoprim is supplied in oral dosage units containing 300mg or less per dose unit, and in a pack of three dosage units, to women aged 16–65 years by a registered pharmacist who has successfully completed the New Zealand College of Pharmacists' training in the treatment of urinary tract infections.

Activity 19 - Screening and treatment of chlamydia infections (UK)

To facilitate the screening and the treatment of chlamydia infections, especially among young adults, the National Pharmacy Association in the UK instigated a "Chlamydia Test and Treat" service in 2008. It was offered after azithromycin was officially launched as an over-the-counter Pharmacy medicine. Between five and 10 tests a day were received by GLG Laboratories, the NPA partner in this service. Pharmacists can only supply tablets to individuals who are confirmed as having a positive Nucleic Acid Amplification Technique (NAAT) chlamydia test result, and to their sexual partners without them having to take a test. Some 70% of NPA members are now signed up to provide the service. The service is free for 16 to 24 year olds.

Activity 20 - Pharmacist-initiated doxycycline for Lyme disease prophylaxis (USA)

A study (69) conducted by the University of Rhode Island, under a collaborative practice agreement with an infectious diseases specialist physician, trained pharmacists at an independent pharmacy. It was published in the *Journal of the American Pharmacists Association*. It showed the value of pharmacist-initiated antibiotic therapy of Lyme disease to improve public access to Lyme disease prophylaxis following an established *Ixodes scapularis* (deer tick) bite. Pharmacists dispensed two 100mg doxycycline tablets to people who had been exposed to *Ixodes scapularis* as a prophylactic; and provided counselling on how to take the medicine (a broad-spectrum antibiotic of the tetracycline class), signs and symptoms of Lyme disease and prevention strategies for possible future tick attachment. Eight patients participated in the study and completed a follow-up survey. No patients enrolled in the study developed any symptoms of Lyme disease or the disease itself.

Activity 21 - Taking antibiotics until the course is finished (Denmark)

A campaign organised by the Association of Danish Pharmacists between 28 October and 1 December 2007 had the slogan "Unless you take your antibiotics to the end, you might believe that the treatment does not work". The targets of this campaign were the parents of young children. Parents could obtain brochures on common illnesses such as impetigo and inflammation of the middle ear, throat, sinuses, lungs and bladder. They were also offered a brochure entitled "Medicines and child". For the children, the pharmacy association reprinted the story of Kalle Kanin, a rabbit who had pain in his ears. In addition to providing these brochures, pharmacies offered advice on how to give antibiotics to children.

Activity 22 - Smiley chart for antibiotics (Denmark)

Pharmacies in Denmark provided medication checklist charts for antibiotics for European Antibiotic Awareness Day on 2014. Parents of children taking antibiotics can use this chart to put small stickers with smileys indicating that the child has already taken the medicine. The chart can be used for other medicines as well. It has been made available on the Danmarks Apotekerforening website so parents can print it.

Activity 23 - Campaign on the importance of correct use of antibiotics (Ireland)

A campaign was run by the Irish Pharmacy Union in 2008 to highlight the importance of correct use of antibiotics. Posters and booklets were displayed in pharmacies, advising patients on antibiotics, how to take them, what side effects to expect, and what to do if a dose was missed.

Activity 24 - Choose pharmacy — common ailments scheme (Wales)

In 2012, NHS Wales started a "Choose Pharmacy — Common Ailments Scheme" programme to encourage patients to consult a participating community pharmacy, rather than their GP for common ailments. The goal is to free time by making pharmacies the first stop for common minor conditions. Thirty-two pharmacies are participating in this programme. Registered patients can be given free medicines without a physician's prescription for conditions such as hay fever, threadworm and conjunctivitis. The software used creates a pharmacy health record and includes information about the prescription, and any advice given by the pharmacist. The programme is being advertised via posters, postcards and leaflets.

Activity 25 - "Don't Rush to Crush" Handbook (Australia)

The Society of Hospital Pharmacists of Australia (SHPA) developed a comprehensive guide for pharmacists in order to support them by administering solid oral medicines to patients who are unable to swallow.
When administering tablets and capsules to patients who have difficulty swallowing or an enteral feeding tube, health care professionals need answers to these questions:

- Can I crush it?
- Can I dissolve it?
- Can I open the capsule?
- Is there a liquid formulation?
- Can I give the injection orally?

The Handbook provides answers to these questions and offer advice for pharmacists on how to manage administration of medicines in people with swallowing difficulties unable to take solid oral medicine.

Activity 26 - Antibiotics: always with a prescription (Spain)

In late 2010, the Pharmacy Chamber of Castille and Leon in Spain organised an information campaign to educate patients on antibiotics and their responsible use. This campaign was entitled: "Antibiotics: always with a prescription in the community pharmacy". It aimed to raise awareness on AMR and the importance of a proper diagnosis (and thus a prescription) before receiving any antibiotic.

Activity 27 - Education of pharmacists in infectious diseases (Australia)

The Society of Hospital Pharmacists of Australia (SHPA) provide an educational seminar series that provides pharmacists with the basic skills required to optimise the use of antimicrobials and manage patients with infection diseases. The Infectious Diseases Clinical Seminars focus on the principle of antimicrobial use, interpretation of microbiology laboratory results, and the pharmacology, pharmacokinetics and pharmacodynamics of antimicrobials. The SHPA has also published standards of practice for clinical pharmacy that detail the role and responsibilities of pharmacists in the care of patients, including the management of infections and the use of antimicrobials.

Activity 28 - Online Antibiotic Stewardship Programme (Ireland)

In Ireland, the Irish Institute of Pharmacy has developed a self-directed training course for pharmacists titled "Online Antibiotic Stewardship Programme". This course is delivered fully online and looks at the principles of antimicrobial prescribing, pharmacology of antibiotics and the role of the pharmacist in implementing antimicrobial stewardship in the workplace. On successful completion of this programme it is envisaged that participants will be able to identify the key areas where pharmacists can make interventions to promote the safe and responsible use of antibiotics at hospital and community level and minimise risk of development of antimicrobial resistance.

Activity 29 - Physicians and Pharmacist Quality Circles (Switzerland)

In Switzerland, "Physicians and Pharmacist Quality Circles" (PPQCs) were established. These are formed by five physicians and one pharmacist, backed by four health insurance funds.
When the quality circles team launched its project, with the backing of four health insurance funds, its objectives were clear. It wanted to: improve the quality of care; improve the relationship between local physicians and pharmacists; evaluate a method of interdisciplinary, locally run continuing education; and make the savings expected by political authorities and health insurance funds without sacrificing quality of care.
Initially, they studied 12 therapeutic groups, including antimicrobials. (101) The costs were examined during 2006 and 2007, comparing the price of prescriptions with a control or reference group. It was shown that the costs were lower while quality of care and patient outcomes improved when PPQC strategies were applied. An evaluation over a nine-

year period (1999–2007) showed that there was a decrease of 42% in the cost of medicines in the PPQC group in comparison with the reference group, which represents a USD 225,000 saving by GPs alone in 2007. (102) These results are explained by compliance with guidelines, pharmacovigilance, greater use of generics, and continuing education on the responsible use of medicines. (78)

Activity 30 - Bring left-over antibiotics (Belgium)

The Belgian Pharmaceutical Association led a campaign in 2011 to encourage patients to return their unused antibiotics to a pharmacy. Leftovers create a double concern: not only do they encourage self-medication, even when antibiotics are not appropriate, they also seldom contain sufficient quantities for an effective therapy. They are therefore useless and could even add to the emergence and spread of antimicrobial resistance.
Pharmacists were asked to label all dispensed antibiotics with a sticker, provided by the government, that urged the patient to return any leftovers, stating that antibiotics do not belong in a family medicine cabinet. A popup-message was shown at every antibiotic dispensing act to remind pharmacy staff of the sticker. Only 14% of the pharmacies blocked the message during the six-day project, indicating a high acceptance rate.

Activity 31 - Know your pharmacist – Medicine cabinet clean-up (Malaysia)

A medicine cabinet clean-up campaign organised by the Malaysian Pharmaceutical Society was a month-long event consisting of public forums, health campaigns and road shows, media/radio exposures and "walk-in" invitations for the public to consult the community pharmacists regarding their health and medicine issues. The public was invited to call pharmacies directly to schedule a consultation with the pharmacist and asked to bring to the pharmacy all medicines stored at home. Pharmacists checked for expired or damaged drugs, and re-label the non-expired drugs if necessary. Pharmacists collected and disposed of all unwanted medicines. Pill boxes were given to selected customers to improve adherence. A medicines summary card was also filled out by the pharmacist so that the customer would know the name, dosage and usages of the medicines they were taking. Pharmacists checked all the medication for proper dosage and times, possible polypharmacy, medicine interactions, side effects etc. Initiatives like these help to prevent misuse of medicines and addictions, and also contribute to building a patient-pharmacist relationship, which is important, especially for mental conditions. Some 244 pharmacists took part in this campaign.

Activity 32 - Don't throw away your medicines (Argentina)

In Argentina, 6 June 2015 was celebrated as "Environment Protection Day". The public was invited to go to pharmacies with expired or unused drugs so that they could be disposed of safely.

Activity 33 - Dispose My Meds campaign (United States, 2009)

On 19 April 2010, the National Community Pharmacists Association in the USA co-organised a national programme to provide people living with mental illness with a safe and effective solution to dispose of their unused medicines, which can be a potential risk of addiction. This programme was initially implemented in over 300 pharmacies in the state of Ohio in a medicines disposal programme launched in November 2009. This programme was then extended at a national level to 800 participating pharmacies. They were referenced in a dedicated website: www.disposemymeds.com, which invited the public to either dispose of their unused medicines in their community pharmacies or ask their pharmacists for a special envelope to mail their unused medicines directly to appropriate disposal centres.

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