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**title** Antibiotic resistance: how did we get here and what can we do?

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# Executive summary

### Does antibiotic resistance exist?

Yes. It is a worsening phenomenon seen all over the world, including Australia.

### What are the implications of antibiotic resistance?

Infection with antibiotic-resistant bacteria is associated with longer length of stay in hospitals and higher death rates. This amounts to significant financial costs; the European Union, for example, spends €1.5 billion annually on antibiotic-resistant infections. Significant indirect costs can also arise from antibiotic-resistant infections when they adversely affect other areas of medicine, for example, transplant medicine, surgery and chemotherapy.

### How did we get here?

Antibiotic resistance has many causes but the most important ones include: excessive and inappropriate antibiotic use among humans and animals (including 'over-the-counter' antibiotic use), global trade, global travel, medical tourism, environmental contamination with antibiotics, and a decline in new antibiotic development.

### What can we do?

Because there are multiple causes, a multi-pronged solution is required. The 'EVADES BUGS' strategy seeks to address the core problems: Education, Vaccine development, Animal health, Diagnostics, Environmental controls, Surveillance, Better antibiotics, Universal infection control and hand hygiene, Government and political will, Stewardship of antibiotics in hospitals.

Many superbugs arrive here from overseas as a consequence of global trade and global travel. As a result, Australia must play a global role in addressing the issue as well as a local one.

Implementing the EVADES BUGS strategy would require activity across portfolios (for example, Health, Trade, Agriculture, Environment, Tourism, Customs). Therefore, it is worth considering the establishment of a single coordinating body, such as an Australian Centre for Disease Control, to take responsibility for the strategy as part of a broader focus on monitoring and responding to communicable diseases.

# Antibiotic resistance: the challenge for Australian health policymakers

'Antimicrobial resistance poses a catastrophic threat. If we don't act now, any one of us could go into hospital in 20 years for minor surgery and die because of an ordinary infection that can't be treated by antibiotics.'

Professor Dame Sally Davies, United Kingdom Chief Medical Officer, March 2013.[1]

## The problem

Bacteria have always had the ability to become resistant to antibiotics. However it wasn't until the introduction of antibiotics last century that this started to have clinical implications. For example, the antibiotic methicillin was introduced in 1960 and it was only in 1962 that staphylococci resistant to methicillin were found. Erythromycin was introduced in 1950 and tetracycline-resistant strains of Shigella were identified by 1959. In 1972, vancomycin was introduced and vancomycin-resistant enterococcus was identified in 1988. Even with rapid advances in medical technology, antibiotic resistance remains a major problem. Linezolid and ceftaroline are two relatively new (and expensive) antibiotics that were introduced in 2000 and 2010 respectively: both had generated resistant bacteria within a year of their appearance.[2]

Antibiotic resistance is a major health problem that can have a devastating impact on individual patients. The case study below in Box 1 illustrates one such devastating case where a relatively young, healthy man had an accident and ended up dying because he contracted an infection that was resistant to all antibiotics.

> A 40-year-old man, previously healthy, had an accident and was admitted to intensive care with lung bruising and fractures. It was discovered that he had a urine infection that was resistant to most antibiotics. He was initially treated with an extremely powerful antibiotic and improved. Three days later, however, he developed pneumonia, which was also resistant to antibiotics. Medical staff treated him with two other powerful and dangerous antibiotics, but his condition did not improve. Further testing revealed that he had a new bacterium that was resistant to all the previously used antibiotics. There was only one antibiotic available that could work. He was given this antibiotic but the bacterium even became resistant to it as well. Without any antibiotics at all to treat him, he died.

Box 1. Fatal case of multi-resistant infections in a young man.[3]

While obviously devastating for this patient and his family, this scenario also has a terrible impact on healthcare workers who, despite having access to expensive and extensive antibiotics, are helpless to intervene.

Unfortunately, cases such as the one outlined above are not rare. In the United States, 23,000 deaths and over two million illnesses due to antibiotic-resistant bacteria are reported every year.[2] Similarly in Europe, rates of antibiotic resistance among an important group of bacteria (Gram-negatives) have been steadily increasing.[4] And here in Australia, there has been a rise in multi-resistant bacteria (for example, Gram-negatives, vancomycin-resistant enterococcus (VRE), and community-acquired methicillin-resistant staphylococcus aureus (MRSA)).[5-7] Some of the most common strains of multi-resistant bacteria are listed below:

- MRSA (Methicillin-resistant Staphylococcus aureus or methicillin-resistant 'golden staph')
- VRE (Vancomycin-resistant enterococci)
- Clostridium difficile infection (C. diff)
- MROs (Multiresistant Organisms)
- Ceftriaxone-resistant gonorrhoea
- Drug-resistant Streptococcus pneumoniae

Further details about each of these bacteria are provided in Appendix A.

## What are the implications of antibiotic resistance?

There are direct and indirect costs from multi-resistant bacteria, and both are significant.

The human cost of an antibiotic-resistant infection can be death. And this is not just for isolated cases. In fact, people with a relatively common ailment – for example, a bloodstream infection (or septicaemia) – are much more likely to die from the infection if it is caused by a resistant bacterium than a non-resistant one (60% versus 20%).[8,9]

In terms of financial cost, antibiotic resistance is an expensive affair. The European Union spends €1.5 billion on antibiotic-resistant infections each year. The costs are attributed to healthcare expenses and lost productivity.[10] In the United States, a study recently estimated the costs associated with treating people with antibiotics when they had a sore throat (antibiotics do not need to be used in 90 per cent of cases but they were used in about 60 per cent of them). Researchers found that between 1997 and 2010, using antibiotics in the United States to treat sore throats cost about US$500 million. That was a conservative estimate, so the authors speculated that it could have cost up to 40 times more.[11]

The costs associated with antibiotic resistance, however, do not only come from treating people unnecessarily with antibiotics. It also costs more to treat people with antibiotic-resistant infections than it does to treat people with non-resistant infections. Take, for example, the case of a 40 year-old woman with a urinary tract infection. Upon discovering that she has a multi-resistant infection, her general practitioner sends her to the emergency department for treatment. She is not that unwell, but because there are no oral antibiotic treatment options available, she needs to be treated in hospital with intravenous antibiotics.

In this case, the extra costs for treating this woman arise because:

- more expensive antibiotics are required
- she needs hospital treatment instead of treatment at home
- she needs to be treated in a single room in hospital
- extra consumables, such as gowns and gloves, are required by staff in order to prevent cross-infection.[12,13]

Many other direct costs are associated with treating patients who have antibiotic-resistant infections. They largely arise because the patient becomes a much higher risk, particularly in areas of medicine where infections are common complications – surgery and chemotherapy, for example. When antibiotic-resistant infections take hold, treatment options can be rendered ineffective, and the outcomes catastrophic.

## What causes antibiotic resistance?

A number of problems have contributed to antibiotic resistance, both in Australia and globally. They are outlined briefly below.

### *Unnecessary or inappropriate antibiotic use in humans*

While antibiotics are a vital weapon in the war against disease, they do not need to be used all the time. And when required, the antibiotic with the narrowest spectrum of antibacterial activity should be prescribed. Unfortunately, these practices are often ignored. This happens in the hospital and community, resulting in excessive and unnecessary use of antibiotics to which bacteria get exposed. Data at both the community and hospital level show that there is a strong correlation between antibiotic use and antibiotic resistance.[14-20] 2010 data from the Organisation for Economic Co-operation and Development (OECD) show that Australia was one of the highest consumers of antibiotics, coming in eighth out of twenty nine countries. Australia used 24.1 defined daily doses per 1000 people per day. The OECD average was 20.5 with the biggest consumer being Greece at 39.4 and the lowest being Chile at 9.7.[21]

A common example of the overuse of antibiotics is in the treatment of sore throats. In 90 per cent of cases, sore throats are due to a virus so there is no need for antibiotics. However an American study recently found that in 60 per cent of cases, patients received antibiotics even though it was warranted in only 10 per cent of them. To compound the problem, instead of using a simple narrow-spectrum antibiotic like penicillin, more expensive and broader-spectrum antibiotics were often used.[11] Australian doctors appear to be prescribing less antibiotics (just over 30%) for acute upper respiratory tract infections (URTI). They are also seeing less patients with acute URTIs in their practice compared to just over a decade ago. While this is heartening, there is still room for improvement.[22]

There are a number of reasons why antibiotics are inappropriately prescribed, and they involve patients, doctors and suppliers.

Among doctors, there are some that continue to believe that antibiotic resistance is not a major problem. One Swedish study, for example, surveyed doctors about their treatment of urine infections, and identified two groups who said that either antibiotic resistance was not a problem at all, or that it was a problem, but not in their practice.[23]

Doctors also sometimes prescribe antibiotics unnecessarily because of a perceived patient demand for it. This practice is particularly concerning because there is some research showing that doctors are not good at determining whether or not patients are expecting them to prescribe an antibiotic.[24] Nevertheless, patients do come to the doctor with the expectation that they will receive antibiotics. They often believe that antibiotics will hasten their recovery or make them better. This may be because they were given antibiotics previously for the same condition and felt that it helped, or perhaps because friends or family were given antibiotics for a similar illness.[25] However, a patient's desire for antibiotics is a poor reason to prescribe them. Research on patients presenting to the doctor with an acute cough, for example, has shown that the patients that come with expectations or hopes for antibiotics are often not the ones who would benefit from them.[24]

A survey of 1,013 Australians by the National Prescribing Service's MedicineWise showed that four in five expect a prescription from their general practitioner for an ear, nose, throat or chest infection. Over half (51%) said that they would ask their doctor for one. Parents would be twice as likely to ask for antibiotics to treat their child's cold or cough than their own (14% vs 6%), with fathers more likely to ask than mothers (22% vs 9%). The survey also identified a number of misconceptions related to antibiotics. For example, only half of respondents knew that bacteria are becoming resistant to antibiotics, only 40 per cent knew that antibiotics should not be taken for viruses and 40 per cent did not know that taking antibiotics when they're not needed contributes to antibiotic resistance. More than 50 per cent were not aware that resistance increases when an antibiotic course is not completed as directed. Young people were less knowledgeable on the matter.[26]

In many parts of the world, antibiotics are available over-the-counter or without a prescription. The rates of non-prescription use of antibiotics by the general population vary: three per cent in the UK, Netherlands and Denmark, 18 per cent in India, 36 per cent in China, 46 per cent in Brazil, 62 per cent in Vietnam and 100 per cent in Sudan and Nigeria. This practice means that often the wrong antibiotic is used, the wrong dose is taken, or the course of antibiotics is too short. All of these problems contribute to antibiotic resistance, so it should come as no surprise that antibiotic resistance is an issue in regions with high non-prescription antibiotic use.[27]

### *Antibiotic use in animals*

Antibiotic use in animals is very common; they are used to promote growth, to prevent illness and treat it. Antibiotic use in animals is far greater than it is in humans. In the United States, for example, 80 per cent of the total volume of antibiotics sold in 2011 was for use in meat and poultry production.[28]

As with humans, when animals take antibiotics, it causes resistant bacteria to appear. This becomes a problem for humans in a number of ways. Most obviously, people consume meat that contains resistant bacteria. Resistant bacteria can also spread via animal waste into the water supply and fertilisers, and some studies have found resistant bacteria in farm workers, food animal transport trucks and non-domesticated animals.[28]

When resistant bacteria grow in animals, there is a flow-on effect in humans because the antibiotics used to treat animals come from the same families as those used to treat humans. In other words, cross-resistance can develop. For example, in countries such as the United States, most antibiotic-resistant E. coli in humans is derived from food animals.[29] This is of great significance considering that E. coli is the most common cause in humans of urine infections and one of the leading causes of bloodstream infections.

### *Global travel and medical tourism*

Every year, around two billion people travel across large distances, with about one billion travelling internationally.[30] All this global travel helps spread antibiotic-resistant bacteria.

Because some nations have very high rates of antibiotic resistance, no country can develop an effective strategy for controlling antibiotic-resistant bacteria by acting alone.[3,31-33] The hard work done by a country controlling antibiotic-resistant bacteria within its own borders can easily be undone when overseas travellers return with undeclared superbugs in their bowels. Numerous international studies show this.[34-37] One Australian study, for example, looked at the number of travellers leaving Australia with antibiotic-resistant E. coli and compared it to rates among those returning to Australia. They found that travellers were six times more likely to be carrying antibiotic-resistant E. coli when returning to Australia, especially from Asia. While most travellers got rid of the antibiotic-resistant E. coli six months after returning to Australia, 18 per cent still had the bacterium, heightening the risk that it will move from people into our local environment and become established here.[37]

'Medical tourism', where people go overseas for a medical procedure, is also becoming increasingly common. People go overseas seeking treatment for a variety of reasons (for example, treatment costs might be lower overseas or they think they will get better care), and for a variety of procedures (for example, cosmetic surgery, orthopaedic surgery, transplant surgery or dental procedures). They are travelling from developing countries to developed ones and vice versa.

Australian media have reported that medical tourism is on the rise here with Australians travelling overseas for a variety of procedures.[38] There are companies in Australia that arrange medical procedures overseas somewhat like a travel agency. Even a local health fund is participating.[39,40]

There are two reasons why medical tourism heightens the risk of picking up antibiotic-resistant bacteria. First, some of the popular destinations for medical tourism have higher rates of antibiotic-resistant bacteria than Australia.[32,38] And second, unlike other tourists, medical tourists will be exposed to healthcare facilities in these countries where there are more antibiotic-resistant bacteria. Cases of antibiotic-resistant infections associated with medical tourism have already been reported in the scientific literature.[41]

***Lack of new antibiotics***

The emergence of bacteria resistant to antibiotics would be much less of a problem if there were plenty of alternative antibiotics available to treat people. Unfortunately, the development of new antibiotics has also slowed down. American data show an almost 20-fold drop in submissions for new antibiotics between 1980-84 and 2010-12.[2] The lack of new antibiotics being developed is especially problematic in some areas. For example, in the case of a common gram-negative bacterium (pseudomonas), only one effective oral antibiotic has been available in the last 20 years.

***Environmental contamination***

Antibiotic-resistant bacteria are contaminating the environment; they have been found in waterways and sewage outlets, even in Australia. One of the reasons this problem has emerged is that antibiotic-resistant bacteria are sometimes excreted directly into the environment, for example in hospital wastewater.[42] Another is that antibiotics in the water coexist with antibiotic-sensitive bacteria, which can cause them to become resistant. One of the main problems with excreting antibiotics into the environment is that they can survive for long periods of time; some have been shown to persist in the environment for over a year.[43]

## What can be done to prevent antibiotic resistance?

The term “EVADES BUGS” was developed for the purposes of this report. Its components are recognized in both international literature and practice.[2,10,44]

The EVADES BUGS Strategy:

- **E**ducation
- **V**accine development
- **A**nimal health
- **D**iagnostics
- **E**nvironmental controls
- **S**urveillance

- **B**etter antibiotics
- **U**niversal infection control and hand hygiene
- **G**overnment and political will
- **S**tewardship of antibiotics in hospitals

***Education***

Most antibiotic consumption occurs in the community, so it is vital to continue to educate doctors, nurse practitioners and patients about the appropriate use of antibiotics. Many programs have been developed to reach these key stakeholders. In Australia, the National Prescribing Service's MedicineWise website has an e-learning tool to promote antibiotic awareness.[45]

Australia is also part of a global initiative held every November called 'Antibiotic Awareness Week' that highlights issues related to antibiotic resistance and the responsible use of antibiotics.[46]

A number of other educational tools are also available internationally. The United Kingdom, for instance, has developed a tool for patients and healthcare workers called TARGET (Treat Antibiotics Responsibly, Guidance and Education Tool). It is promoted by the Royal College of General Practitioners on its website.[47] In the United States, the Centers for Disease Control and Prevention (CDC) has its own 'Get Smart' program aimed at educating people about appropriate antibiotic use.[2] Studies examining the impact of these education tools have shown that they lead to improvements in antibiotic prescribing.[48,49] However the CDC points out that while these programs might be effective, they are not widely used.[2]

***Vaccine development***

Immunizing the population against infection from antibiotic-resistant bacteria is one of the best ways of preventing it. This strategy has been used quite successfully against some antibiotic-resistant bacteria like Streptococcus pneumoniae (the most common cause of pneumonia and middle ear infections in children), but less so in others (for example, golden staph).[50,51] Ongoing development of vaccines against antibiotic-resistant bacteria is also recommended by authorities in the United Kingdom.[10]

***Animal health***

The World Health Organization's Advisory Group on Integrated Surveillance of Antibiotic Resistance published a document on the critically important antibiotics used in both humans and animals. The aim of the document is to provide a reference to develop risk management strategies in this area. Key uses of the document include:[52]

- Prioritizing for most urgent development of risk management strategies those antibiotics characterized as critically important in order to preserve their effectiveness in human medicine.
- Ensuring that critically important antibiotics are included in antibiotic susceptibility monitoring programs.
- Refining and prioritizing risk profile and hazard analysis activities for interventions by species or by region.
- Developing risk management options such as restricted use, labelling, limiting or prohibiting extra-label use, and making antibiotics available by prescription only.
- For the development of prudent use and treatment guidelines in humans and animals.
- To direct special research projects to address prevalence data gaps on existing or potential future critically important antibiotics.

Another worldwide innovation has been 'One Health', which is a global network of veterinarians and healthcare workers for humans who are working closer together in recognition of the link between animal and human health.[53]

In Australia, the Australian Commission on Safety and Quality in Health Care has examined the issue of antibiotic use in the animal industry. It found that the Department of Agriculture, Fisheries and Forestry monitors the scientific literature and is increasingly aware of the complexities between animal and human health. It also noted that Meat and Livestock Australia is funding an investigation into antibiotic-resistant bacteria in red meat, which is due for completion in 2014. The Australian Veterinary Association is also promoting the judicious use of antibiotics in animals through its guidelines for prescribing, authorising and dispensing veterinary medicines.[54,55]

Like global travel, global trade means that animal products from overseas come into Australia, and antibiotic use may not be as strictly regulated in some of the countries they are coming from. For example, last year, consignments of fish from Vietnam were found to contain an antibiotic that is banned in Australia.[56] Therefore, Australia has a vested interest in ensuring that other nations are successful when it comes to antibiotic regulation in their food and crop industry.

***Diagnostics***

Developing more rapid and accurate diagnostic tests will help health professionals to differentiate between viral infections that do not need antibiotics, and bacterial infections that might. Such tests must also be able to quickly determine if any bacteria present are antibiotic-resistant or not. This is important at a community level because there are some infections (for example, ceftriaxone-resistant gonorrhoea) where patients can be given an ineffective antibiotic and think that they are cured, which allows them to unwittingly spread the superbug to other people.

At a hospital level, the ability to accurately diagnose bacterial infections and detect antibiotic-resistant bacteria would have enormous benefits. It would allow staff to quickly determine whether a patient needed to be isolated to prevent the infections spreading. It would also mean that the best antibiotic could be started as soon as possible.[10]

***Environmental controls***

A multidisciplinary approach involving hospitals, pharmaceutical companies and sewage plants is needed to prevent the spread of antibiotic-resistant bacteria in the environment. Whether this has happened yet or not is unclear. Even individuals can make a difference by not disposing of drugs "down the drain".[43]

***Surveillance***

Routinely collected surveillance data can be used to highlight problem areas that need urgent action. In Australia, the data on golden staph bloodstream infections on the MyHospitals website is possibly one example of how the inclusion these data may stimulate improvements in infection control overtime.[57] The number of golden staph bloodstream infections in a hospital is a surrogate marker for infection control problems. When high infection rates are publicly reported, it should prompt hospitals to review and improve their infection control practices.

Many countries have surveillance programs in place for antibiotic-resistant bacteria – in Australia, there is the Australian Group on Antimicrobial Resistance (AGAR), and in Europe there is EARS-Net .[58,59] AGAR is a non-governmental organisation made up of laboratory-based doctors from around Australia that periodically publishes data on the number of antibiotic-resistant bacterial infections. While it serves a valuable role, it is not able to be a single surveillance centre capable of capturing data on all community and hospital cases of antibiotic-resistant bacterial infections. As the American Centers for Disease Control and Prevention has pointed out, the lack of routine surveillance of antibiotic resistance internationally is also a major problem.[2]

Surveillance should not be exclusive to humans. Antibiotic resistance patterns in agriculture and aquaculture should also be monitored because of their implications for human health.

***Better antibiotics***

Pharmaceutical companies must be encouraged to develop new antibiotics, especially to treat Gram-negative bacteria. Potential obstacles to this include the perception that development in this area has a poor return on investment compared with drugs for cholesterol or hypertension. For example, a new antibiotic, at discovery, is worth “minus” $50 million to a pharmaceutical company. This is in comparison to discovery of a drug for musculoskeletal pain, which is worth “plus” $1 billion.[60] Other obstacles for companies to develop new antibiotics are uncertainty about the regulatory environment for developing new antibiotics and the cost and complexity of dealing with the regulatory process.[10]

In the United States, one strategy to deal with this has been the passage of the GAIN Act - “Generating Antibiotic Incentives Now”. It uses a number of mechanisms, including prolonged exclusivity, to make the development of antibiotics more attractive to a pharmaceutical company. In concert with this, the Infectious Diseases Society of America has proposed the Special Populations Limited Medical Use scheme which seeks to fast-track the approval of newly developed antibiotics by minimizing their regulatory processes.[60]

***Universal infection control and hand hygiene***

As well as preventing antibiotic-resistant bacteria from developing, measures must be taken to stop infections from spreading. This is crucial in hospitals where spreading antibiotic-resistant bacterial infections to vulnerable patients can be catastrophic. One way of doing this is to have appropriately skilled and resourced infection control units in hospitals.

Although there are many facets to infection control (for example, isolation in single rooms, education, and wearing personal protective equipment), the importance of hand hygiene in clinical settings cannot be overstated. The World Health Organization is taking a leading role in promoting hand hygiene. Locally, Hand Hygiene Australia is promoting the National Hand Hygiene Initiative, which is based on the World Health Organization’s hand hygiene advice. The initiative promotes cleaning hands with soap and water or an alcohol-based hand rub to reduce bacteria.[61] Regular hand hygiene audits are conducted in hospitals around Australia, and the results are published on the MyHospitals website.[57]

***Government and political will***

Because there are many causes of antibiotic resistance, tackling it effectively requires strong leadership at a senior government level. It needs coordinated action across portfolio areas, including health, agriculture, environment, customs, tourism, science, immigration, and trade. There are positive signs internationally that the necessary steps are being taken.

Over a decade ago, the World Health Organization issued its strategy to combat antibiotic resistance.[62]

In the United States, an interagency task force on antibiotic resistance has been established with members from 12 federal agencies, including Defence, Veterans Affairs, and Agriculture.[63]

In India, a multi-pronged approach to addressing antibiotic resistance has been put in place – the Chennai Declaration. It was born out of the negative press generated when a very resistant superbug, NDM-1, was discovered in the New Delhi water supply.[64] The Chennai Declaration lists goals and sets out one, two and five-year targets for achieving them, and has since been endorsed by respected international organisations.[65]

In the United Kingdom, the Chief Medical Officer recently recommended adding antibiotic resistance to the National Risk Register of Civil Emergencies alongside other civil threats such as pandemic influenza, terrorism and coastal flooding.[10,66]

And most recently, in June 2013, the G8 joint Science Ministers discussed antibiotic resistance, naming it as one of the leading health security challenges of this century.[67]

***Stewardship of antibiotics in hospitals***

Antimicrobial stewardship (AMS) programs are a systematic way of rationalising antibiotic use in healthcare institutions. Studies have shown that AMS programs improve antibiotic and patient outcomes while reducing adverse events and costs.[68-71]

Because patients in Australian hospitals are prescribed more antibiotics than they are in Europe, and up to half of antibiotic regimens prescribed are regarded as inappropriate, the Australian Commission for Safety and Quality in Health Care has made it mandatory for all hospitals to have an AMS program.[71] The objectives of the program are to:

- Provide clinicians prescribing antibiotics with access to current, endorsed therapeutic guidelines on antibiotic usage
- Undertake monitoring of antibiotic usage and resistance
- Take action to improve the effectiveness of antibiotic stewardship.[72]

Accreditation of such programs in Australian hospitals began in January 2013. An AMS program often consists of a multidisciplinary team of pharmacists, infectious diseases physicians and clinical microbiologists. A recent analysis of AMS programs in public and private health facilities in regional and metropolitan Victoria was performed. The investigators found that AMS programs in metropolitan public hospitals were more advanced than their counterparts in private hospitals or regional public hospitals. In particular, these latter groups fell behind in establishing formulary restriction and approval systems. But even the public hospitals fell short in having a dedicated antibiotic management team, performing regular audits and giving feedback to prescribers. Three barriers to implementing a better AMS program that they identified included a lack of resources, lack of leadership and a reluctance of doctors to change their prescribing habits.[73]

## Conclusion

Antibiotic resistance is a global concern that has already led to people dying from untreatable infections, bringing back memories of the pre-antibiotic era. The problem is caused by a variety of factors encompassing both animal and human health and affects many different bacteria.

There has been a global push to address antibiotic resistance, but only some countries have classified it as a priority issue. Australia needs to be part of global efforts to tackle antibiotic resistance, if for no reason other than global travel and trade mean superbugs will be introduced here from overseas.

Because the origins of antibiotic resistance are complex, so is the solution. Australia should adopt the EVADES BUGS strategy, which seeks to address the key drivers of resistance. Coordinated cross-government action will be required to ensure the effectiveness of the EVADES BUGS strategy. The best way to achieve this is to coordinate action under a single body, capable of monitoring real-time progress. To this end, Australia should consider establishing an Australian Centre for Disease Control that is dedicated to monitoring communicable diseases.

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## Appendix A – Common types of antibiotic-resistant bacteria

Some of the most problematic antibiotic-resistant bacteria are listed here. Of those discussed below, the American Centers for Disease Control and Prevention this year classified three of them as belonging to the most serious threat level: Clostridium difficile, Carbapenem-resistant Enterobacteriaceae and Drug-resistant Gonorrhoea.

**MRSA (Methicillin-resistant Staphylococcus aureus or methicillin-resistant "golden staph")**

There are two types of MRSA: one that is strongly associated with hospitals and the other that is more common in the community. MRSA lives on the skin and in the nose. The community form of MRSA is well known for causing aggressive pneumonia in children and serious skin infections that often need a combination of surgical drainage and antibiotics. On the other hand, the hospital strain of MRSA is harmless if it is just colonising the skin or the nose. But, if it gets inside a person, then it is extremely dangerous. And hospitals are full of vulnerable patients with 'passageways' from the skin to their insides e.g. intravenous cannulas and surgical wound infections. In Australia, even with the best medical care, the overall death rate from MRSA in the bloodstream is more than 20 per cent.

**VRE (Vancomycin-resistant enterococci)**

Enterococcus is a normal member of the bacteria in our bowel. VRE occurs when it becomes resistant to an important intravenous antibiotic called vancomycin. VRE is a growing problem in Australia that is associated with antibiotic use and being in regular contact with the healthcare system due to chronic illnesses e.g. dialysis for kidney failure. When infection due to VRE occurs, expensive antibiotics with serious side effects have to be used.

**Clostridium difficile infection ("C. diff")**

Whenever an antibiotic is taken (e.g. for a sore throat), it wipes out billions of bacteria in the bowels, leaving only more resistant ones behind. One of these resistant bacteria is C.diff. When C. diff is left unchecked, it can cause diarrhoea, dehydration, and may require surgical treatment. More than 15 per cent of people may die. In 2012 in the United States, there were 250,000 cases of C. diff cases with 14,000 deaths and one billion dollars excess in costs. Not surprisingly, the Americans have classified C. diff within its most serious threat level.

**MROs (Multiresistant Organisms)**

Under the banner of MROs comes a large group of superbugs such as CRAB, ESBL, ESCAPPM, NDM-1, KPC and CRE, multidrug-resistant Pseudomonas, to name but a few. Foodborne threats such as drug-resistant Salmonella and drug-resistant Campylobacter are no less important. Their evolution has been complex. CRE (or Carbapenem-resistant Enterobacteriaceae) cause 9000 cases and 600 deaths every year in the United States. The Centers for Disease Control and Prevention has classified it amongst its highest threat group.

**Ceftriaxone-resistant gonorrhoea**

In Australia last year, gonorrhoea was one of the leading notifiable diseases. If untreated, gonorrhoea can cause a variety of problems, including urethritis, infertility, and death. Currently, there are limited antibiotics with which to treat gonorrhoea. The situation worsened when Japanese health authorities announced the first case of ceftriaxone-resistant gonorrhoea in 2011. If this drug-resistant strain of gonorrhoea were to spread, the results would be devastating. And given the prevalence of gonorrhoea and the ease with which sexually-active individuals can travel the world, it is no surprise that the American Centers for Disease Control and Prevention has included drug-resistant gonorrhoea as one of three bacteria in its highest threat level of action.

**Drug-resistant Streptococcus pneumoniae**

Worldwide, this bacterium is the commonest cause of community-acquired pneumonia and bacterial middle ear infections. Growing resistance to penicillin and a related group of antibiotics called cephalosporins is of great concern. However, this is one area where vaccine development has been very helpful.

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