



ANTIBIOTIC RESISTANCE – MORE THAN A MEDICAL PROBLEM



Impact Objectives

- Gain a more comprehensive understanding of what drives the inappropriate use of antimicrobials across society and which drivers are most problematic
- Develop and coordinate a feasible health strategy to eradicate, or at the very least, slow down the rate of antimicrobial resistance (AMR)
- Re-educate society at all levels as to the appropriate use of antimicrobials

Antibiotic resistance – more than a medical problem

Professors Mitchell Byrne and Antoine van Oijen discuss their unique collaboration and efforts toward addressing the global challenge of antimicrobial resistance



Professor Mitchell Byrne



Distinguished Professor Antoine van Oijen

Could you offer a brief summary of the extent of the problem globally of antimicrobial resistance (AMR)?

AvO: Previous reports have stated that unless solutions are found to stop the spread of antimicrobial resistance (AMR), today's estimated 700,000 deaths per year would grow to an enormous 10 million deaths per year by 2050; more than caused by cancer or cardiovascular diseases. The root causes of the problem lie in: overuse of antibiotics in primary health and agriculture; a resultant rapid bacterial resistance against existing antibiotics; the spread of so called 'superbugs'; a lack of point-of-care diagnostic technology to follow such spread; and lack of novel antibiotics to combat resistant infections. To date, there has been no coordinated effort to understand and tackle all the underlying drivers in an integrated effort. With the highly interconnected nature of the factors underlying AMR, such a holistic approach is a critical next step in solving what will likely be society's major 21st-century health challenge.

As a clinical psychologist, why did you feel it was important to get involved in this issue?

MB: Much of my previous research activity has centred on health and health behaviours. I developed a clear understanding early in my career that human behaviour is the primary driver of both health and ill-health, and that neither professional advice nor medical technology can influence health outcomes in the absence of understanding the social and psychological drivers of decision-making. When Professor van Oijen convened a cross-disciplinary meeting to discuss the challenge of AMR, I attended with the view that pure science alone was ill-equipped to tackle the problem and that partnership between disciplines would be needed.

Could you explain the key objectives of the AMR Global Challenges Programme and any gaps you are trying to fill?

AvO: Broadly speaking, we know what causes and facilitates AMR; the accelerated pace of microbial reproduction causes evolutionary adaptation of bacterial resistance to occur very quickly. Merely developing new antimicrobials therefore does not solve the problem and strategies to hinder the transmission of microbial infections and promote the appropriate use of antimicrobials are required.

MB: The questions to address are, first, what drives the inappropriate use of antimicrobials across society and second, which drivers are most problematic, how can we effect change on these, and how can

we implement a sustainable community-wide programme. The Wollongong Antimicrobial Resistance Research Alliance (WARRA) seeks to answer these questions, whereby the Illawarra & Shoalhaven population can serve as a test bed for a nationally and internationally feasible health strategy to halt, or at least slow down, AMR.

You mention WARRA as a key part of your programme. Can you explain what this is?

WARRA is a grouping of researchers and clinicians from various disciplines formed in 2017 with the mission to tackle the AMR problem. One aspect of the programme specifically focuses on establishing community-based cohort studies to characterise AMR and provide a test bed for holistic interventions. The team has formed partnerships between the University of Wollongong in Australia, and local health authorities, clinicians, community stakeholders and industry to develop new approaches to tackle AMR. One important cohort is the Illawarra & Shoalhaven region, which represents a microcosm of Australia and is ideally positioned for studies of AMR. A wide range of stakeholder groups are already on board and engaged in the project from an extensive range of industry, biotechnology, research, health and clinical backgrounds, creating the perfect environment to tackle AMR from a holistic perspective. ●

The right team in the right place

The Wollongong Antimicrobial Resistance Research Alliance (WARRA) is a unique collaboration of life and social scientists in the perfect position to develop and test new strategies to combat antimicrobial resistance

The growing issue of antimicrobial resistance (AMR) is poised to be one of the major health challenges of the 21st century. Since the discovery of antibiotics such as penicillin in the 1940s, the widespread and uncontrolled use of antibiotics in human and animal health, agriculture and industry has pushed microbes to become resistant to most classes of drugs currently available. Without effective antibiotics, society will return to an age where even routine medical procedures become potentially lethal. Furthermore, many treatments now deemed common, such as chemotherapy, will become more problematic due to risks of infection.

We have been using antibiotics to fight bacteria for decades, but, like any organism, the bacteria have adapted to these antibiotics and have become resistant. To make matters worse, the rapid rate at which bacteria replicate means any bacteria surviving a course of antibiotic treatment rapidly reproduce, spreading this resistance quickly across communities. Unfortunately, there is no sole strategy to combat the process of resistance because bacteria have been through many adaptations, effecting resistance. Therefore, whilst identifying how bacteria are evolving to bring about drug resistance and combating this is an important aspect, it can't stand alone. The strategy of only developing new drugs is also flawed because simply producing new drugs that kill microbes in new ways

only pushes the problem down the road. Because this issue is one of bacterial evolution, any strategy put forth by humans will eventually be overcome. Faced with seemingly insurmountable challenges, many researchers have begun to acknowledge that this issue is not simply about medical technology. Rather, it will require a multidisciplinary effort to reduce the spread of infections and re-educate all levels of society in the ways that antimicrobials should be appropriately used. In this way, the selection pressures on bacteria to evolve resistance are weakened and drugs remain effective for longer.

A UNIQUE PARTNERSHIP

At the forefront of these efforts are the AMR Global Challenges Research Programme and the Wollongong Antimicrobial Resistance Research Alliance (WARRA). WARRA itself is headed up by prominent researchers Distinguished Professor Antoine van Oijen and Professor Mitchell Byrne of the University of Wollongong in Australia. This is a unique partnership that reflects the interdisciplinary nature of the problem; van Oijen is a life scientist developing novel microscopy tools to study how bacteria work and Byrne is a clinical psychologist/social scientist. While a clinical psychologist may seem out of place in an antimicrobial resistance research programme, many of the challenges surrounding this issue are people based and require an understanding of human behaviours

regarding antimicrobial usage. 'I am a behavioural scientist whose approach to the problems and solutions in life focus on the environmental drivers or contingencies governing human behaviour, including the internal cognitive environment,' explains Byrne. He brings with him extensive experience in funded clinical research trials. Together the two researchers have assembled a diverse team and partnerships between the University of Wollongong and local health authorities, clinicians, community stakeholders and industry, to develop new approaches to tackle AMR.

Australia, believes Byrne, can be at the heart of this new approach. 'As one of the world's most developed nations, with access to some of the highest quality healthcare and research institutions, Australia has an opportunity to inform international governments,' he says. To do so, the WARRA programme has set out to find a testing ground for their new approaches and ideas. The ideal testing ground needed to be representative of the broader population and have the infrastructure, funding and expertise available to carry out the research programmes and interventions, and subsequently analyse and disseminate the data globally. According to Byrne, they have found the right spot in the Illawarra and Shoalhaven region: 'Here we have one local Health District, one major research University which is investing heavily with \$1.2 billion in its health strategy (including ►



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\$80 million into Molecular Horizons), and the majority of pathology tests completed by one provider.' The region also closely resembles the overall make-up of Australia, explains Byrne, saying: 'the Illawarra and Shoalhaven region is a microcosm of the Australian community, traversing all socioeconomic and demographic groups.'

TARGETING MULTIPLE POTENTIAL FACTORS

With the appropriate testing ground established, the team now has a great opportunity to study the drivers of the resistance problem, identify which require the most attention and test interventions. 'For example,' says Byrne, 'there is a general consensus amongst researchers that the overuse of antibiotics is one of the key drivers of resistance, but what isn't well understood is how we might be able to change these drivers.' Using a variety of approaches is key. So far the programme has already begun investigating patient healthcare service utilisation rates and clinical outcomes in relation to AMR. Several other pilot projects are underway, including a study to examine the community behaviours contributing to antibiotic use and resistance. As Byrne describes, projects are also aimed at healthcare workers and educators: 'We have two projects undertaking qualitative analyses of the perceptions of nursing students, primary care nurses and acute care nurses about the role of nursing in reducing inappropriate antibiotic use and of early childhood educators' attitudes and behaviours with respect to hygiene maintenance in early childhood education and care settings.'

With so many projects underway, coordination and collaboration has become a big part of the project's success. 'Collaboration is essential and a significant component of our initial work has involved establishing collaborative relationships,' says Byrne, adding: 'given the broad range of stakeholders, coordination between service providers has been a significant challenge.' However, by basing their efforts within the Illawarra region, Byrne and his colleagues believe any successful public health policy changes enacted here have the ability to be disseminated across larger communities. With this goal of sharing the knowledge and message behind the resistance problem, the project team has also created the AMR Education Series, a workshop series boasting a line-up of presentations and interactive case studies by infectious disease physicians, pharmacists, psychologists and microbiologists. According to Byrne: 'By engaging with primary healthcare providers, we can understand the challenges and hurdles faced in prescribing antibiotics, and help them overcome these challenges.'

A TRULY GLOBAL PROBLEM

Like many of the issues facing society in the 21st century, AMR is a global challenge. Infection knows no borders and so conditions in any one nation will affect the rest. The WARRA programme represents one of the first that is explicitly designed to export the knowledge gained to the world. The programme, in its interdisciplinary make-up and efforts to form a representative, real-world testing ground, truly represents the multifaceted nature of this global issue and is therefore poised to address the problem in an all-encompassing fashion. ●

Project Insights

FUNDING

Funding provided by the University of Wollongong, University of Wollongong Global Challenges and the Illawarra Health and Medical Research Institute.

COLLABORATORS

Illawarra Shoalhaven Local Health District • NSW Health Pathology • Southern IML Pathology • Centre for Health Research Illawarra Shoalhaven Population • Colleagues at the University of Wollongong and other universities

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Professor Mitchell Byrne is an endorsed Clinical and Forensic Psychologist with over 35 years applied experience. He is currently Associate Dean – Education for the University of Wollongong's Into Health Primary and Community Health Centre. Professor Byrne's favourite epithet is: 'all behaviour has meaning' and believes that understanding the meaning of a behaviour is the first step in changing that behaviour.

Distinguished **Professor Antoine van Oijen** led research groups at Harvard Medical School, US and Groningen University in the Netherlands, before moving to the University of Wollongong in 2015 as an Australian Research Council Laureate Fellow. He is interested in studying the mechanisms of antimicrobial resistance, from developing novel molecular diagnostics to understanding how resistance travels through the community.



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