



Newsletter

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In this issue...

2 Global burden of bacterial antimicrobial resistance in 2019: an advocacy to intensify efforts for antimicrobial stewardship in low-and-middle income countries

Armel Poda, Jean-Baptiste Guiard-Schmid, Abdoul-Salam Ouédraogo and Pierre Tattevin

 3 - 4 Developing multi-disciplinary and context specific solutions to tackle antimicrobial resistance

Erica Westwood, Lisa Haagensen and Mirfin Mpundu

5-6 The French interventional research plan developed to tackle antimicrobial resistance

Patricia Renesto, Erica Telford, Guia Carrara, Yazdan Yazdanpanah and Evelyne Jouvin-Marche

7 BSAC and Pfizer collaboration to improve patient outcomes by addressing access disparities in antimicrobial stewardship Jacqueline Sneddon and Andy Townsend

ISAC & APUA and Other Antimicrobial Resistance News

- 8-9 Antimicrobial Resistance in the News
- 10 12 ISAC Society News
- 13 About ISAC / APUA









Global burden of bacterial antimicrobial resistance in 2019: an advocacy to intensify efforts for antimicrobial stewardship in low-and-middle income countries

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A landmark paper was published in February 2022 in The Staphylococcus aureus and Klebsiella pneumoniae. Lancet, entitled 'Global burden of bacterial antimicrobial A combination of data with heterogeneous methods and resistance in 2019: A systematic analysis¹. A consortium of quality, and the lack of data from many parts of the world, experts in the field of antimicrobial resistance (AMR) are limitations to consider. But this paper provides an collected and analysed a broad range of data from the insightful assessment of the current burden of AMR literature for 23 pathogens and 88 pathogen-antibiotic worldwide, with better awareness of the large combinations, in 204 countries in 2019. It included hospital heterogeneity between areas. It depends not only on AMR and surveillance systems; and other sources worldwide; to prevalence but also on the tools available to fight AMR; estimate deaths and disability-adjusted life-years (DALYs) including surveillance, antimicrobial stewardship (AMS)

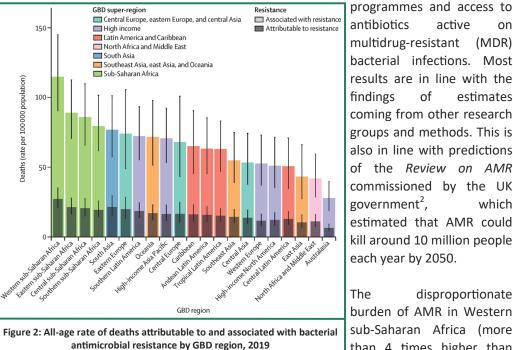
attributable to, and associated with, AMR. They estimated two different primary criteria, based on two counterfactuals:

- attributable 1. Deaths to AMR;
- Deaths 2. associated with AMR;

(each comparing the current situation to а situation where infections with drug-resistant bacteria would be replaced by no infection).

Their main findings were that around 5 million associated deaths were with AMR in 2019; including 1.3 million attributable to

AMR. Of note, the burden of AMR was the highest in most striking and sobering result of this study. Efforts to Western sub-Saharan Africa (27.3 deaths attributable to improve access to diagnostic tools and appropriate AMR per 100,000 inhabitants) and the lowest in treatment for infections due to MDR bacteria, as well as Australasia (6.5 deaths attributable to AMR per 100,000 capacity building of key stakeholders (physicians, inhabitants). Lower respiratory tract infection was the microbiologists and pharmacists) are therefore urgently most burdensome infectious syndrome (>1.5 million required in that part of the world taking into account the deaths attributable to AMR), and the three primary aspect of One Health. pathogens in terms of AMR burden were Escherichia coli,



each year by 2050. disproportionate The burden of AMR in Western sub-Saharan Africa (more than 4 times higher than Australasia) is probably the

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Developing multi-disciplinary and context specific solutions to tackle antimicrobial resistance

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Antimicrobial Resistance Solutions (ICARS) published an article and transmission in a setting. in the 38th volume of the APUA Newsletter¹. It introduced ICARS as a recently launched partnership that would codevelop "pilot intervention and implementation research projects" with ministries and stakeholders in low- and middleincome countries (LMICs). The ambition was to develop costeffective and context specific solutions for antimicrobial resistance (AMR) that are owned, led and eventually scaled by LMIC ministries. Since then, ICARS has evolved into an independent self-governed organisation with a Board of This philosophy is at the heart of the ICARS model and project Directors; a Technical Advisory Forum; and 23 employees and consultants with relevant expertise to deliver on ICARS' vision and mission. Importantly, ICARS has now approved and launched several projects, and is in the process of initiating additional projects and partnerships to mitigate AMR (Figure 1). This article provides an update on ICARS' portfolio and approach for multi-stakeholder partnerships to tackle specific AMR challenges.

In the winter of 2020, the International Centre for drivers and influencing factors that impact AMR emergence

Implementation research is "the scientific inquiry into questions concerning implementation — the act of *carrying an intention into effect*^{"2,3.} This means there should be adaptation to the study setting and investigation of how the intervention works within the wider social, political, economic and health context.

portfolio. Dialogues with various ministries in LMICs have shown a clear desire from governments to collaborate on a range of topics including human health antimicrobial stewardship (AMS) challenges. Based on best-practice guidance, stewardship in healthcare settings could benefit from a multidisciplinary approach within the healthcare team⁴. For stewardship interventions to be sustainable and scalable, however, a wider perspective is required - including but not limited to - social sciences. For example, projects

Why ICARS?

While evidence exists on how to best tackle AMR, there is still a critical gap in translating such evidence into Many countries have action. developed AMR National Action Plans (NAPs), but in resource poor settings the challenge remains for how best to implement initiatives to reduce AMR; example due to competing for

priorities, limited funding and often a need for more technical and/or infrastructure capacity, amongst other factors.

ICARS uses top-down and bottom-up approaches to codevelop context-specific solutions for tackling AMR across the One Health spectrum. This ensures that expertise from both ministries, central policy agencies and local researchers are included to support a holistic approach to tackling AMR.

ICARS Demonstration Projects

ICARS' project portfolio currently focuses on small-scale demonstration research projects that aim to develop and test interventions to mitigate AMR. These are usually 2-3 years in duration, with a budget of \$500-750k per project. Projects adopt intervention and implementation research approaches, to develop and test solutions within a specific setting. Successful projects are intentionally designed to meet local needs and complexities, and therefore benefit from multidisciplinary approaches to fully understand the different

Dialogues with various ministries in economic LMICs have shown a clear desire from governments to collaborate on a range of topics including human health antimicrobial stewardship challenges.

across the ICARS portfolio include expertise to assess intervention cost effectiveness, as well as behaviour change expertise to support sustainability in prescribing and use practices.

It is clear from the literature that antimicrobial use, particularly in LMICs, is highly influenced by selfmedication and non-prescribed usage

through informal channels and is also driven by complex systems within the health care setting and outside of $it^{5,6}$. Understanding drivers and developing relevant interventions require project development and delivery by local stakeholders and researchers, with appropriate support and resources to bring forward the implementation research perspective for more effective interventions. ICARS intends to move the dial by supporting nationally developed, multidisciplinary and complementary approaches designed to recognise and tackle real-world challenges.

Case Study: ICARS Partnerships in Zambia

ICARS is collaborating with the Government and a range of stakeholders in Zambia through different avenues to address antimicrobial prescribing and use practices. Like other countries, overuse and misuse of antimicrobials is a driver of AMR in Zambia⁷. In the human sector, selling or dispensing antimicrobials does not always adhere to best-practice⁸. In the community, antibiotics are also accessed from informal

providers and use practices can be inconsistent. Therefore, policies are implemented. This participatory approach this requires interventions and solutions that are developed recognises the complex role antibiotics play in societies and within the health system and the community.

To tackle this challenge, ICARS is collaborating with the Zambia National Public Health Institute (ZNPHI) and Lusaka University Teaching Hospital to co-develop a project that aims to address inappropriate antibiotic use in blood stream infections (BSIs) and urinary tract infections (UTI) along the challenge may need to be addressed from different angles, continuum of care from primary to tertiary healthcare with a wide set of stakeholders who can help elucidate the facilities. This project has a multipronged approach to complexities of antimicrobial use patterns, as well as implement a stewardship intervention that will adapt the core components of the WHO's Practical Toolkit on Antimicrobial Stewardship Programmes In Low- and Middle *Income Countries,* as well as CDC recommendations^{4,9}. It also builds on ReAct Africa's work on piloting AMS in some health facilities. Focusing on BSIs and UTIs will, by proxy, strengthen stewardship efforts and committees in the hospitals critical to AMS. The aim is to adapt this best-practice approach from the toolkit to local context, e.g. through existing laboratory

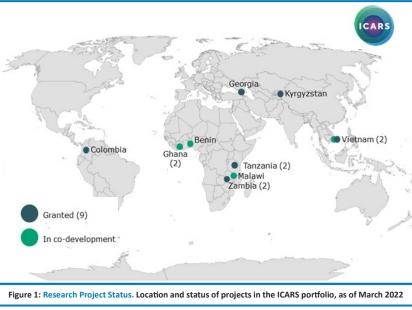
uses dialogue, learning and solutions to address the gap between local realities and policies.

Partnerships for Sustainable Solutions

Together, these partnerships in Zambia show how one AMR solutions that are feasible and have potential to scale up. Through developing relationships with national stakeholders to co-develop projects that address country-identified priorities and using complementary methodologies, the ambition is to support a deeper set of interventions that can support sustainable AMR mitigation.

This is a mission that cannot be achieved alone, and partnerships are at the heart of ICARS' model¹¹. Each partner and expertise that brings has unique capacities

infrastructure or accessible resources such as reagents and antibiotics. Another critical aspect of this project is to assess the economic impact of adapted AMS the programme and activity understand affordability beyond the pilot area. In this context, inappropriate antimicrobial use for BSIs will need to be addressed through health care settings antibiotic susceptibility results, resistance profiles and evidence-



us closer to our goal of tackling drug-resistant infections across the One Health spectrum.

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launched its Standard Treatment Guidelines based on local susceptibility patterns supported by ReAct Africa and the University of Maryland. The same approach will be used for addressing UTIs.

To compliment the project led by the Zambian Ministry, and to strengthen solutions that are developed and owned by the community, the Wellcome Trust in partnership with ICARS, is supporting Eden University to test and implement a Responsive Dialogue toolkit to tackle AMR in three Hygiene & Tropical Medicine community settings in Zambia¹⁰. The intention of this approach is to adopt a participatory methodology with a wide range of community stakeholders, including e.g. policy makers, research institutions, civil society, women's groups, non-governmental organisations, the general public and community pharmacies. Through community conversations, the project will gather evidence on antibiotic-seeking behaviour, identify drivers of antibiotic use in relation to UTIs, and develop community-informed and contextually relevant solutions that not only address AMR and antibiotic use, but also inform how the Zambian AMR NAP and associated

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The French interventional research plan developed to tackle antimicrobial resistance

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Introduction

It is widely known that, together with climate change, antimicrobial resistance (AMR) is one of the most urgent global health challenges for the next decade. Overuse of these wonder drugs, which revolutionised medicine in the late 1930s, has been accompanied by the rapid appearance of AMR strains¹. A recent report estimated that AMR could be responsible for at least 10 million deaths / year globally by 2050 if measures are not taken². For several years, in response to the global AMR challenges, many countries launched priority initiatives. In this article, we discuss the recent strategies set out by the French Government, which promptly recognised the importance of tackling this health emergency.

The French National Priority Research Programme against AMR

As the burden of AMR infections in France was recognised as one of the highest in the European Union, the One Health inter-ministerial roadmap of 2016 prompted the French Government to dedicate one of its strategic research instruments, the French National Priority Research Programme (Programme Prioritaire de **R**echerche - PPR), to tackling AMR³. This French national AMR PPR, which started in 2019, aims to bring together the strengths of all relevant public research expertise to reduce AMR over the next 10 years. See the professional community network involved here. To address this, the action plan promotes

multidisciplinary research initiatives that take a One Health approach.

This ambitious research programme aims to reduce and optimise antibiotic use in human and veterinary medicine and to propose new public health strategies and environmental control measures. It is based on an innovative framework supporting an interconnected / integrated approach(Figure 1).

The French AMR PPR plan, which combines One Health principles with digital technology, data mining and artificial intelligence, comprises four main challenges:

- 1. Dynamics and control of the emergence, transmission and dissemination of AMR.
- 2. Optimisation of antibiotic use in human and veterinary medicine.
- 3. Individual, ethnological, sociological, economic, political and cultural determinants of AMR.
- 4. Therapeutic innovation.



To achieve the aforementioned goals, the three different actions detailed below have been already funded.

Call 1: Antibiotic resistance: understand, innovate, act

This action (€25 million) launched by the French National Research Agency (ANR) led to the selection of 11 long-term research projects (3 to 6 years) with expected impact at both the national and international level. The projects (**Table 1**) should undoubtedly contribute to tackling the four key AMR PPR challenges.

Several results regarding *the optimisation of antibiotic use* are expected and are detailed in **Table 1**. They come under the headings: dynamics and control of the emergence, transmission and dissemination of AMR / Optimisation of

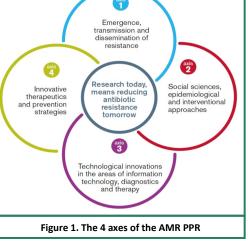
antibiotic use / Individual, ethnological, sociological, economic, political and cultural determinants of AMR / Therapeutic innovation. The main features of these projects are also presented in short movies (in French).

Call 2: Structuring tools

This action (€4 million) launched by Inserm aimed to structure research on AMR in metropolitan France and in overseas departments and territories while applying a One Health approach. Three projects were funded with ambitious objectives (**Table 1**).

Call 3: An Antibiotic Resistance network in partnership with LMICs

Within the framework of the AMR PPR, a budget of €1.5 million was allocated to the structuring and coordination of an AMR network in partnership with low- and middle-income countries (LMICs), designated as **the AMR-Sud network**. Since the burden of AMR is disproportionately higher in such countries, international cooperation must indeed be considered as a key element of the AMR action plan.⁵ To this aim, two complementary research projects were developed fostering collaborations within the AMR-Sud network and will be carried out in Burkina Faso, Cambodia, Côte d'Ivoire and Madagascar. The first project focuses on the transmission factors of antibiotic resistance in various environments and in the three One Health sectors (**CircUs**), while the other focuses on the economic and social factors of antibiotic resistance (**RAMSES**).



Acronym and project title	Coordinator	PI institution
Call 1- Antibiotic resistance: understand, innovate, act		
ANORUTI Analysis of NOn-Response to antibiotics <i>in vivo</i> : application to Escherichia coli Urinary Tract Infection	Bruno Fantin	Inserm UMR 1137, Université de Paris IAME
DREAM Dynamics of REsistance to Antibiotics within the human gut, Microbiota: combining diet informed population cohort and quantitative <i>in vitro</i> gut studies	Olivier Tenaillon	Inserm UMR1137, IAME, Université Paris, Université Paris Nord
DYASPEO Dynamics of AMR spread, persistence and evolution between humans, animals and their environment	Jean-Yves Madec	Anses EPA
MicroFlu4AMR Characterisation and high-throughput screening of bacterial communities in the soil: mechanisms of antibiotic resistance and discovery of new antibiotics	Andrew Griffiths	ESPCI Paris EPA
Mustart Multiparametric Strategies against Antibiotic Resistance in Tuberculosis	Alain Baulard	Institut Pasteur de Lille, IPL Autre Fondation de recherche reconnue d'utilité publique
NAILR	Vincent Cattoir	Université de Rennes 1 UR1 EPSCP
NASPEC Narrow spectrum antibiotics to fight the emergence of bacterial resistance	Michel Arthur	Université de Paris ; EPSCP
OrA-NEAT Development and evaluation of a tailored antibiotic stewardship programme in nursing homes based on an in-depth qualitative assessment of organisations, health professionals' attitudes, and needs	Nelly Agrinier	Université de Lorraine - APEMAC EPSCP
PHAG-ONE Development, production and clinical use of therapeutic phages to treat infections due to antibiotic resistant bacteria	Fréderic Laurent	Hospices civils de Lyon HCL Autre CHU
Seq2Diag Whole genome sequencing and artificial intelligence to characterise and diagnose antibiotic resistance and capacity to escape treatment	Philippe Glaser	Institut Pasteur IP Autre Fondation de recherche
TheraEPI Epigenetic-based Therapy to bypass resistance	Paola B. Arimondo	Institut Pasteur IP Autre Fondation de recherche
Call 2- Structuring Tools		
ABRomics-PF A numerical platform on antimicrobial resistance to store, integrate, analyse and share multi-omics data	Claudine Médigue Philippe Glaser	French Institute of Bioinformatics (IFB), Institut Pasteur (IP)
PROMISE Professional community network on antimicrobial resistance	Marie-Cécile Ploy Bruno François	Inserm UMR 1092, CHU and CIC1435 of Limoges
DOSA Digital Observatory of Social dimensions of Antimicrobial resistance	Nicolas Fortané	Inrae CNRS UMR IRISSO, Université Paris-Dauphine

Call 4: Call for junior and senior researcher positions

The AMR PPR funding (€7.5 million) will also provide the opportunity to attract outstanding senior scientists recognised as leaders in the field of AMR and motivated to develop, in France, multi-disciplinary research projects of excellence favouring a One Health approach. The aim of this programme is also to recruit promising young scientists to set up and lead a research team within an established French laboratory. The selection process is ongoing.

Conclusion

Over the past decade, the frequency and spectrum of antibiotic-resistant microorganisms have increased dramatically worldwide and some infections have proven untreatable with antimicrobial drugs^{1,2}. As summarised above, the French government has taken AMR seriously and the scientific community is now mobilised in a One Health approach, integrating aspects of molecular epidemiology to References understand on a global scale the evolution of AMR in the host 1. (human / animal) and the associated environment³. addition to the fundamental and clinical research focusing on emergence, transmission, dissemination, prevention, control, 3. and therapeutic and diagnostic innovation, the PPR aims to strengthen the social sciences and digital sciences. While the 4. first will allow the identification of underlying drivers of antibiotic misuse, raising awareness and encouraging 5. behavioural changes at all levels, the latter will fill a research gap in the development of digital capabilities and machine

learning. This national strategy intends to fully integrate international research agendas and WHO priorities, and to strengthen ongoing international cooperation (e.g. European Joint Programming Initiative on Antimicrobial Resistance, European Innovative Medicines Initiative, EU Joint Action on Antimicrobial Resistance and Healthcare Associated Infections). Furthermore, an appropriate communication strategy has been developed: a dedicated website for the scientific community, the National Antibiotic Resistance Portal.

This tool is a common, cross-sectoral and interactive entry point, identifying public and private actors, platforms, networks, and research coordination activities, and listing research projects and scientific events focusing on antibiotic resistance. This portal is highly visited by many actors not only in France but also abroad and will undoubtedly contribute to strengthening France's place in the global AMR landscape.

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BSAC and Pfizer collaboration to improve patient outcomes by addressing access disparities in antimicrobial stewardship (AMS)

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Around the world, many patients face barriers to equal and quality care based on factors that include their age, gender, ethnicity, socioeconomic status and even geographic proximity leading to poor health outcomes. Unfortunately, the response to the global pandemic has exacerbated this issue and has put health disparities in the spotlight. Antimicrobial resistance (AMR) has also been adversely impacted by the pandemic due to increased use of antibiotics¹.

AMR affects all countries, but the burden is disproportionately higher in LMICs². Factors such as poor hygiene and sanitation, limited access to adequate healthcare infrastructures, and lack of regulations contribute to AMR and the COVID-19 pandemic has exacerbated the problem³. Patients in resource-limited settings are more likely to be prescribed antibiotics inappropriately to treat common infections. AMS is important to help control, contain and mitigate AMR by supporting the appropriate use of antimicrobials. Patients receiving care in low resource facilities may not have equitable access to effective and holistic AMS programmes while underserved populations in high income countries often receive suboptimal care with respect to use of antibiotics due to racial and socioeconomic inequalities^{4,5,6}. The inequitable access to AMS programmes increases the inappropriate use of antimicrobials, hinders access to new medicines, and, consequently, disproportionately impacts the burden of AMR.

Pfizer has been a leader in tackling some of the most persistent healthcare challenges, including infectious disease. The company has a long and proud heritage addressing evolving infectious disease challenges, stemming from its pioneering work on penicillin in the 1940s. Pfizer continues to pursue a collaborative, multi-pronged approach to help drive industry-leading solutions across the areas of active stewardship, innovative surveillance, global policy, manufacturing and R&D. Pfizer is also committed to building a more equitable future for patients and taking action to address disparities that have long hindered accessible treatment and care. This includes a new initiative to tackle pressing healthcare disparities impacting patients today including higher morbidity and mortality rates due to AMR in underserved populations.

Pfizer Hospital Chief Medical Officer, Dr Pol Vandenbroucke, said, "All patients, no matter who they are or where they live, deserve the best possible treatment. I'm proud of the work Pfizer is undertaking in collaboration with British Society of Antimicrobial Chemotherapy (BSAC) to help tackle these pressing healthcare References disparities and raise the standards of care for vulnerable patients."

As a learned society with 50 years' experience in infection and antimicrobial use, and over 3,000 members across 76 countries, BSAC's position as a world leader in education provision has attracted partnerships with a variety of organisations including 4. Global Antibiotic R&D Partnership (GARDP), International Centre for Antimicrobial Resistance Solutions (ICARs) and Médecins Sans 5. Frontières (MSF). Recent initiatives to provide free open access education courses that are relevant and multilingual to meet the needs of healthcare professionals in LMICs have built the

foundation for supporting development of new AMS programmes globally.

In 2022, BSAC is progressing development of a Global Antimicrobial Stewardship Accreditation Scheme (GAMSAS) which will be a sustainable, points-based accreditation scheme to drive improvements in AMS in all healthcare settings. The scheme will use self-assessment surveys together with expert support to Identify areas of practice requiring improvement and identify good practice that can be shared. A key contribution from BSAC will be educational support through utilisation of resources and bespoke training to support AMS practice. The scheme will also create awareness of variation in AMS provision amongst healthcare payers and users, facilitating research to address this and providing evidence to bridge the gap between policy and practice. The aim is to create a network of Centres of Excellence to support and encourage other organisations to build sustainable AMS programmes.

To start this GAMSAS journey, BSAC has collaborated with Pfizer to focus on areas of greatest need, building upon the strengths and ambitions of both organisations. The focus will be to establish AMS Centres of Excellence and support the creation of holistic education and training programmes on optimal use of antibiotics in facilities with limited resources and / or underserved populations. Our hope is that these programmes will raise awareness of AMR among healthcare professionals to improve outcomes for patients and address a long-standing health inequity. Our multi-step standards will accommodate the wide range of staff and facility resources available across different countries.

BSAC President Dr David Jenkins said, "I am excited to see this collaboration launched and we look forward to supporting hospitals with disparities to improve antimicrobial use and to share learning with local networks via our GAMSAS initiative." Pfizer and BSAC jointly released a Quality Improvement Request for Proposals (RFP) for Establishing Antimicrobial Stewardship (AMS) Centres of Excellence to Improve Patient Outcomes by Addressing Access Disparities in January 2022. Following consideration of applications by an Expert Review Panel, the initiative will commence in June 2022 with 10 centres from a variety of low-, middle- and high-income countries to implement improvement actions supported by the independent grant and establish BSAC's first tranche of AMS Centres of Excellence.

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Antibiotic Resistance in the News

Beef labelled "raised without antibiotics" contains antibiotics

Antibiotics have been found in beef labelled as "raised without antibiotics" (RWA) according to a new study in <u>Science</u>.

The authors tested 699 cattle from 312 lots and 33 different feed yards (all RWA certified) for 17 antibiotics commonly used in feed and water. At least one animal tested positive for antibiotics in 42% of feed yards and 15% of lots had at least one positive test.

Meat labels in the United States (including "Raised Without Antibiotics," "No Antibiotics Administered," "No Added Antibiotics," "Raised Antibiotic Free," and "No Antibiotics Ever") must be approved by the Department of Agriculture (USDA) but although UDSA-approved labels give RWA claims credibility, the agency does not require empirical testing to validate claims. Therefore, consumers are reliant on producers labelling their products appropriately.

Finding antibiotics in RWA beef, call the integrity of such labels into question. The authors recommend policy reforms by the UDSA to ensure accuracy of labelling.

Pharmaceuticals detected in rivers in all continents

Authors of a global study in <u>Proceedings of the National Academy</u> <u>of Sciences</u> analysed active pharmaceutical ingredients (APIs) in 258 rivers in 104 countries across all continents (representing the pharmaceutical fingerprint of 471.4 million people).

Samples were obtained from 1,052 locations and analysed for 61 APIs. Authors found the highest concentrations of APIs at sites in Lahore (Pakistan), La Paz (Bolivia) and Addis Ababa (Ethiopia). The most contaminated sites were in low- to middle- income countries and associated with poor wastewater areas and waste management infrastructure and pharmaceutical manufacturing. Carbamazepine, metformin and caffeine (a compound also arising from lifestyle use) were most frequently detected at over 50% of sites. Concentrations of at least one API at 25.7% of the sampling sites were greater than levels considered safe for aquatic organisms or which are of concern in terms of selection for antimicrobial resistance.

Oral carbapenem antibiotic possible option for treating UTIs

Authors of a phase 3 trial published in <u>NEJM</u> compared orally administered tebipenem pivoxil hydrobromide with intravenous ertapenem in patients with complicated urinary tract infection (cUTI) or acute pyelonephritis.

1,372 patients were enrolled from 95 hospitals across 15 countries from June 2019 to May 2020.

868 patients were included in the Microbiologic Intention-to-Treat Population of whom 449 received oral tebipenem pivoxil hydrobromide and 419 received intravenous ertapenem for 7 to 10 days (or up to 14 days in patients with bacteremia).

An overall response was seen in 58.8% of patients who received tebipenem pivoxil hydrobromide compared with 61.6% who received ertapenem. Overall response at end-of-treatment was 97.3% in the tebipenem pivoxil hydrobromide group and 94.5% in the ertapenem group.

Similar safety profiles were noted for both groups with adverse events observed in 25.7% of patients receiving tebipenem pivoxil hydrobromide and in 25.6% of patients receiving ertapenem.

Cognitive decline linked to long-term antibiotic use

Researchers have found a link between chronic use of antibiotics in midlife and minor cognitive decline seven years later according to a study in <u>PLOS One</u>.

The authors conducted a study amongst 14,542 women in the Nurse Health Study II (an ongoing nationwide cohort study that began in 1989 which investigates risk factors for major chronic diseases in women). Participants completed a self-administered computerised neuropsychological test between 2014–2018 comprising four tasks to test psychomotor functions and information processing speed.

Participants (mean age 54.7) were classified by antibiotic use: no use, less than 15 days, 15 days to 2 months and over 2 months. Women who used antibiotics for at least 2 months in midlife had small decreases in global cognition (-0.11 standard units [SU]), psychomotor speed and attention (-0.13 SU) and working memory and learning (-0.10 SU) compared with those who had not used antibiotics. The authors concluded that the data emphasise the importance of antibiotic stewardship, especially among aging populations.

Childhood antibiotic exposure high in some LMIC

Authors of a study in <u>Clinical Infectious Diseases</u> studied antibiotic treatments in children in the first five years of life in 45 low- and middle- income countries (LMICs) using Demographic and Health Survey data. The authors estimated the number of children aged 0-59 months who received antibiotics for fever, diarrhoea or a cough over two weeks and aggregated this to estimate cumulative illness and antibiotic treatment for each country.

Of the 438,140 child-observations contributed, 38.7% of children were ill in the 2-weeks prior to the study, with 38.4% of these illnesses treated with antibiotics. The number of illnesses treated with antibiotics ranged across countries from 10% (Niger) to 72% (Jordan). 42% of febrile and 32.9% of non-febrile illnesses were treated with antibiotics. The authors estimated that children in LMICs received an average of 18.5 antibiotic treatments in their first five years of life. Again, this varied across countries from 3.7 (Niger) to 38.6 (Republic of the Congo).

A median of 68.7% of antibiotic treatments were attributed to medical care, 9% to informal care and 16.9% to self-medication. The authors concluded that the high and likely unjustified use of antibiotics in children in some LMICs is concerning—the balance between access to antibiotics and appropriate antibiotic use needs to be addressed.

AMR communications toolkit

The Center for Infectious Disease Research and Policy Antimicrobial Stewardship Project (CIDRAP-ASP) has launched a free communications toolkit for antimicrobial resistance (AMR).

The AMR Communication Toolkit (which includes posters, infographics, a video etc) aims to equip doctors and patients with key facts in an accessible format, giving them the resources to raise AMR awareness in their communities.

Download the resources here.

Stewardship intervention reduced vancomycin use in children

A quality improvement (QI) intervention reduced overall vancomycin use in a paediatric intensive care unit (PICU) according to a study in *Pediatrics*.

The authors quantified the prevalence of infections caused by organisms requiring vancomycin therapy, including methicillinresistant *Staphylococcus aureus* (MRSA), among patients with suspected bacterial infections. Based on these data, the authors performed three QI interventions over 3-years (1) stakeholder education, (2) generation of a consensus-based guideline for empiric vancomycin use and (3) implementation of this guideline through clinical decision support.

Among 1,276 episodes of suspected bacterial infection, 19 cases of bacteraemia due to organisms requiring vancomycin therapy were identified, including 6 MRSA bacteraemias. During the 3-year QI project, overall vancomycin days of therapy (DOT) per 1,000 patient days in the PICU decreased from a baseline mean of 182 DOT per 1,000 patient days to 109 DOT per 1,000 patient days, representing a 40% reduction. No adverse impact was observed on clinical outcomes or inadequate empiric coverage of organisms causing bacteraemia in this population.

Provider education and consensus building among key stakeholders were associated with the reduction in vancomycin use.

RSV vaccine in pregnant mothers reduced antibiotics in babies

In a randomised, double-blind trial, researchers found that administering a respiratory syncytial virus (RSV) vaccine to pregnant mothers reduced antibiotic prescribing in their infants by 12% compared with those who received the placebo. The study (published in Proceedings of the National Academy of Sciences) included 4,500 pregnant women across 11 countries, two thirds of whom received the RSV vaccine. Vaccine efficacy was 12.9% against all new antimicrobial prescription courses and 16.6% against lower respiratory tract infection (LRTI)-associated new antimicrobial prescription courses among infants in the first 90 days of life. Over the first 90 days of life, maternal vaccination prevented 3.6 antimicrobial prescription courses for every 100 infants born in high -income countries and 5.1 courses per 100 infants in low- and middle-income countries, representing 20.2% and 10.9% of all antimicrobial prescribing in these settings, respectively. While LRTIs accounted for 69-73% of all antimicrobial prescribing prevented by maternal vaccination, high vaccine efficacy was observed against acute otitis media-associated antimicrobial prescription among infants in high-income countries.

Increase in Fluoroquinolone sales and resistance in Salmonella

Authors of a study in Journal of Global Antimicrobial Resistance found correlation between quinolone а resistant Nontyphoidal Salmonella (NTS) and fluoroquinolone sales in food animals. NTS resistant to fluoroquinolone drugs (including ciprofloxacin, а first-line antimicrobial used to treat severe Salmonella infections in humans) were isolated from retail meats. The authors reviewed data for 4,318 NTS isolates from 2009 to 2018 through the FDA National Antimicrobial Resistance Monitoring System programmes.

Fluoroquinolone sales increased by 41.67% from 2013 to 2018. The prevalence of quinolone-resistant NTS from retail ground beef increased from 5% in 2014 to 11% in 2018. The increase of quinolone-resistant isolates in retail meats since 2016 was mostly related to *Salmonella Infantis* and *Salmonella enteritidis*.

AMR in Eastern Mediterranean Region countries is high

A study in <u>Emerging Infectious Diseases</u> reports data on bloodstream infections (BSIs) from the Global Antimicrobial Resistance Surveillance System (GLASS) during 2017–2019 from 11 – 14 countries in the World Health Organization (WHO) Eastern Mediterranean Region to assess AMR.

The authors BSIs report caused by carbapenemresistant Acinetobacter spp. (CRAsp), third-generation cephalosporin (3GC)-resistant Enterobacteriaceae (Escherichia coli and Klebsiella pneumoniae), methicillinresistant Staphylococcus aureus (MRSA), and carbapenemresistant Enterobacteriaceae (CRE) (E. coli [CREC] and K. pneumoniae [CRKP]). The median proportion of bloodstream BSIs was highest for carbapenem-resistant Acinetobacter spp. (70.3%) and lowest for carbapenem-resistant Escherichia coli (4.6%).

The authors also evaluated data on antimicrobial use in hospitalised patients from seven countries (Jordan, Sudan, Pakistan, United Arab Emirates, Tunisia, Lebanon and Iraq). They found 53% of 16,551 hospitalised patients received one or more antimicrobial (the largest proportion for respiratory infections).

Authors also evaluated regional capacities of antimicrobial stewardship (AMS) programmes and infection prevention and control (IPC) programmes and found that few countries have capacity for IPC and AMS programmes to prevent emergence and spread of AMR. These findings emphasise the need for regional political leadership in addressing AMR.

Gram stain effective in guiding treatment for pneumonia

Gram stain guided antibiotic therapy was slightly more effective than guideline-based broad-spectrum antibiotic treatment in patients with ventilator-associated pneumonia (VAP) according to a study in <u>JAMA Open Network</u>.

The authors randomised 206 patients (mean age 69 years old) with VAP in Japanese ICUs from 2018 – 2020. Clinical response occurred in 76.7% patients in the Gram stain guided group and 71.8% in the guideline-based group. There was a decrease in antipseudomonal agent use and anti-MRSA agents in the Gram stain guided group.

The 28-day mortality rate was 13.6% in the Gram stain guided group versus 17.5% in the guideline-based group. There were no significant differences between the groups in ICU-free days, ventilator-free days and adverse events.

EU report calls for a One Health approach to tackling AMR

The European Center for Disease prevention and Control (ECDC), European Food Safety Authority (EFSA), European Medicines Agency (EMA) and the Organisation for Economic Co-operation and Development (OECD) have released a joint report on antimicrobial resistance (AMR) in the European Union (EU) and European Economic Area (EEA).

Despite reductions in antibiotic consumption in humans and food-producing animals between 2011–2020, AMR in bacteria from humans in the EU and EEA has increased for many antibiotic-bacterium combinations since 2011. The rise in resistance to critically important antibiotics is of particular concern. The report presents trends in antibiotic consumption and AMR from a One Health perspective and sets out policy options for national governments and the EU.

Society News

32nd International Congress of Antimicrobial Chemotherapy (ICC)

On behalf of the Organising Committee of the 32nd International Congress of Antimicrobial Chemotherapy (ICC 2022), we are delighted to invite you to participate in the Congress, which will take place at the Perth Convention and Exhibition Centre, Perth, Australia from **27 – 30 November 2022**.

We are delighted to be able to host the ICC as a face-to-face meeting. The ICC will be an excellent opportunity to interact with leading experts and meet with your international colleagues once again. And where better to reconnect but in the beautiful city of <u>Perth</u>, the capital of Western Australia.



The programme comprises plenary & keynote lectures, symposia and

workshops by international speakers in the field of infectious diseases and clinical microbiology. Oral and poster sessions will be an integral part of the programme as well. <u>View the programme here</u>

Call for abstracts / Young Investigator Travel Awards

The ICC abstract submission portal is now open!

All accepted abstracts will be published in ISAC's open access journal, the *Journal of Global Antimicrobial Resistance (JGAR)* (*impact factor* **1**. **4:035**).

The deadline to submit is **5 July 2022 - submit here**.

Young Investigators who submit an abstract are encouraged to apply for a Young Investigator Travel Award. The applicant must be the **2**. presenting author. A number of awards will be made with selection based on the quality of the abstract. Awardees will receive a grant towards the costs of their travel / accommodation as well as free registration.

There are two types of Young Investigator Travel Awards available:

ISAC Young Investigator Travel Awards (YITA) ISAC YITAs are available to applicants from ISAC Member Societies residing outside the Asia-Pacific region. Visit the website for more information on how to apply for an ISAC YITA.

ICC Young Investigator Travel Awards

ICC YITAs are available to all colleagues in the Asia-Pacific region.

Visit the $\underline{website}$ for more information on how to apply for a ICC YITA.

Hamao Umezawa Memorial Award (HUMA) Recipient

We are pleased to announce **Dr Robin Patel** as recipient of the Hamao Umezawa Memorial Award (HUMA), the most prestigious award given by the International Society of Antimicrobial Chemotherapy (ISAC) to recognise outstanding contributions to the field of antimicrobial chemotherapy.

Robin Patel is the Elizabeth P. and Robert E. Allen Professor of Individualized Medicine and the Director of the Infectious Diseases Research Laboratory, Co-Director of the Clinical Bacteriology Laboratory and Vice Chair of Education in the Department of Laboratory Medicine and Pathology.



Dr Patel will present the HUMA plenary lecture on **Microbial Theranostics – A Resistance Combatting Strategy** at the ICC in November 2022.



Photo credit: Tourism Western Australia

Top reasons to visit Perth

Kings Park & Botanical Garden

Kings Park is one of the world's largest and most beautiful inner-city parks, rich in Aboriginal and European history and contemporary culture.

Fremantle

The city of Fremantle boasts world-class attractions, microbreweries, waterside eateries, heritage pubs, cafés, markets and boutique shopping.

3. Beaches

Perth, the sunniest capital city in the world, has 19 beaches stretching 80km of coastline to explore.

4. Swan River cruises

Take a river cruise down Swan River to see some of Perth's top sights as it winds through the city.

5. Multicultural dining

Enjoy Perth's vibrant multicultural dining scene, world-famous wineries and craft breweries.

6. Rottnest Island

Sail to Rottnest Island to explore some of its 63 beaches and meet some quokkas, marsupials native to Western Australia.

ISAC is delighted to announce the launch of the <u>ISAC Academy</u> – a **free** e-learning resource which hosts educational content from ISAC, its Member Societies and organisations with common interests.

All ISAC webinars are available to watch on-demand via the ISAC Academy and you will also find details of upcoming events, publications, congress highlights and podcast.

In addition, ISAC is developing its first e-module on "Antimicrobial resistance and vaccination in pneumonia" with Dr David McIntosh as lead educator. Further, ISAC will deliver two freely available Massive Open Online Courses (MOOC) on Infection Prevention & Control in collaboration with the British Society of Antimicrobial Chemotherapy (BSAC).

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If you or your organisation has any relevant educational content to share on the ISAC Academy website, please email the Executive Office (secretariat@isac.world).

ISAC Academy

Similarly, if you have suggestions for collaborative activities (podcasts, webinars, e-learning modules etc), please send your proposals to the same address.

Future Webinars



While the whole world is focused on the COVID pandemic, antimicrobial resistance (AMR) takes no rest.

Join ISAC's next **free** webinar, organised by <u>The Alliance for the</u> <u>Prudent Use of Antibiotics (APUA</u>), where experts will provide updates on the current AMR situation worldwide and the efforts to fight it. <u>Register here for free.</u>

On demand webinars

MDR Gram-negative bacilli

In collaboration with the Japanese Society of Chemotherapy (JSC)

International experts presented up-to-date, informative talks on defining MDR in Gram-negative bacilli, mechanisms of resistance, rapid molecular diagnostics, current treatment options, basic research on novel antibiotics and ultraviolet disinfection for infection control. <u>Watch the recording here</u>.

Hot topics in skin, bone and joint infections

Organised by the Bone, Skin & Soft Tissue Working Group.

The webinar covered a variety of topics including mycobacterial peri-prosthetic joint infections, application of molecular assays in the diagnosis of septic arthritis, epidemiological data related to skin infections as well as timing for intravenous to oral switch in skin and soft tissue infections and antibiotic alternatives in some of these infections. <u>Watch the recording here.</u>

Working Group updates

In memoriam

Zoonoses Working Group

ISAC has appointed Prof. Georgios Pappas (Institute of Continuing Medical Education of Ioannina, Greece) as the new leader of ISAC's Zoonoses Working Group.

Prof. Pappas is developing a plan of activities to take the group forward and is in the process of recruiting new members. The aim of the Zoonoses Working Group is to provide an international platform for promoting and encouraging the exchange of information, raising awareness of the multiple aspects of zoonoses and developing activities in the field (of any etiology - bacterial, viral or parasitic).





All at ISAC were incredibly sad and shocked to hear of the passing of John McConnell, Editor-in-Chief of the Lancet Infectious Diseases. We enjoyed working with him as a key member of the Elsevier family and treasure time spent with him at numerous congresses and at the Elsevier office in London.

Our hearts go out to his family, friends colleagues at this sad time. This tribute was published by John's friends and colleagues at The Lancet.

ISAC Project Grants

ISAC is now accepting Project Grant applications to fund antimicrobial research in low- to middle- income countries (LMIC) from ISAC Member Society applicants

Applications are invited for grants between **£5,000** and **£10,000**.

Aim of Research Project

Applicants are required to demonstrate that ISAC funds will be utilised for a clearly defined piece of research, which will have an identifiable outcome on completion of the work. At least one country involved must be an LMIC country.

Research projects should address one of the three following areas:

- 1. What are feasible and effective prevention strategies to prevent transmission of (resistant) pathogens in low resource settings?
- 2. What basic laboratory support does a healthcare system minimally need to tackle infectious diseases?
- 3. How do we improve antimicrobial use worldwide to ensure it is delivered only to those who need it?

Deadline to apply: 1 September 2022

Member Society News

ISAC is delighted to welcome two new Member Societies, taking its number of affiliated societies to 95.

Is your society interested in joining ISAC? It's free and easy to apply—find out more here.

ISAC united infectious diseases societies around the world.

Senegalese Association of Microbiology The Senegalese Association of Microbiology (ASOSEMIC) was founded in 2020.

The current President is Dr Makhtar Camara.

The society's aims are:

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- To unite members motivated by the same ideals and to create bonds of understanding, solidarity and close collaboration.
- To promote the exchange of scientific information through the organisation of conferences, seminars or any other forms of communication.
- To contribute to the development of microbiology in all its aspects.
- To bring its expertise to the field of biotechnology.
- To bring its expertise to national and international institutions on issues related to microorganisms.

The activities of ASOSEMIC are grouped in four commissions:

1. Research, innovation, ethics; 2. Training, quality; 3. Cooperation and external relations; 4.Technical: biosafety, environment, biomedical waste management, risk management, biotechnologies.

Society registration is open to all health personnel (physicians, pharmacists, veterinarians, biologists, technicians, students), researchers and scientists. Find our more about ASOSEMIC on its website.

The Hong Kong Society for Infectious Diseases

The Hong Kong Society for Infectious Diseases (HKSID) was founded in 1995. The current President is Dr Ada Lim.

With a background in various emerging infectious diseases, the society gathered medical professionals together to serve these common goals:

- To promote the advancement of the study of infectious diseases.
- To keep the medical profession and the public well informed of the latest developments in the battle against infectious agents.

The society aims to achieve the above goals by organising different educational events and collaborating with other medical societies in Hong Kong. The society strives to facilitate knowledge sharing among medical professionals with different background. Find out more about HKSID on its website.

Grant Opportunity

Applications for ISAC Project Grants are now open

- Applications for £5,000 £10,000 are invited to support low-resource antimicrobial resistance
- research projects It's easy to apply
- Only principal applicant needs to be from an **ISAC Member Society**
- One country must be a low- to middle- income country

Visit the website for more information https://www.isac.world/funding/isac-project-grants

Deadline to submit 1 September 2022

For more information on eligibility and how to apply, visit the website.









About ISAC

ISAC was founded as a non-profit organisation in 1961 and, in response to the dynamic nature of the subject matter, has focused most recently on antimicrobial stewardship and antimicrobial resistance.

ISAC is a federation of affiliated **Member Societies** which aims to increase the knowledge of antimicrobial chemotherapy and combat antibiotic resistance around the world.

ISAC currently has a worldwide membership of 95 national and regional societies, which in turn have over 60,000 individual members. <u>Visit the website to see how your society can become an ISAC Member Society</u>.

ISAC has **22 Working Groups** on specialist subjects which are engaged in advancing scientific knowledge in antimicrobial chemotherapy, clinical microbiology and infectious diseases through various activities. To join an ISAC Working Group, please email Fee Johnstone, ISAC Executive Assistant (secretariat@ISAC.world) with a brief C.V. <u>Visit the website for more information</u> ISAC has two society **journals**:

- International Journal of Antimicrobial Agents (IJAA)
- Journal of Global Antimicrobial Resistance (JGAR) gold open access

ISAC's scientific congress, International Congress of Antimicrobial Chemotherapy (ICC), is held every two years and it is now in its 32nd year.

For more information on ISAC, visit www. ISAC.world

About APUA

Founded in 1981 by Prof. Stuart B. Levy as a global non-profit organisation, APUA's mission is to maximise the effectiveness of antimicrobial treatment by promoting appropriate antimicrobial use and containing drug resistance. It was the first organisation to address antibiotic preservation and continues to provide a strong voice in the field despite the subsequent emergence of many other organisations and groups addressing a topic which has become a specialty in its own right; that of "antibiotic stewardship".

APUA has affiliated Chapters in 19 countries. The APUA network facilitates the exchange of objective, up-to-date scientific and clinical information among scientists, healthcare providers, consumers and policy makers worldwide.

Prof. Levy's retirement was announced towards the end of 2018. This was an opportunity for the APUA Board to review its leadership and governance and it took the opportunity to seek a partner organisation with which to synergise. This led to the merger of APUA with the International Society of Antimicrobial Chemotherapy (ISAC), effective from February 2019.

The new international APUA Board meets regularly and aims to build on the work achieved by Prof. Levy and his excellent team of associates. <u>Visit the APUA website for more information</u>.

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*ISAC welcomes contributions. Please send us your article ideas. All content may be edited for style and length. Please email <u>secretariat@ISAC.world</u>

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