Anti-Microbial Resistance:
Setting the Social Science Agenda

Report of an ESRC Working Group: July 2014

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"The mechanisms which lead to antimicrobial resistance are biological. However the conditions promoting, or militating against, these biological mechanisms are profoundly social. How our farmers, vets, and regulatory systems manage livestock production for human consumption; how regulatory and fiscal frameworks incentivise or deter antimicrobial development, production and use; how the public and healthcare professionals understand, value and use antimicrobials; the context in which animals and humans interact; the ways in which particular groups of humans are exposed to particular microbial infections; all these are shaped by social, cultural, political and economic forces. Social science therefore has a key role to play in measuring, modelling, understanding, and where appropriate changing the social environment in relation to antimicrobial resistance."

Professor Dame Sally Macintyre

(Working Group Chair)

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BACKGROUND

Anti-Microbial Resistance (AMR) refers to the ability of microbes to become resistant to antimicrobial drugs. AMR, especially the development of bacterial resistance to antibiotics, is increasing rapidly around the world. The UK's five year Antimicrobial resistance strategy notes that '*If the number of hard to treat infections continues to grow, then it will become increasingly difficult to control infection in a range of routine medical care settings and it will be more difficult to maintain animal health and protect animal welfare*'.[1] Many medical advances we now take for granted, such as safe Caesarean sections, hip replacements, and chemotherapy for cancer involve prophylactic antibiotic treatment, with major health risks if such treatment were no longer effective. AMR not only poses a risk to routine care but also has major financial and welfare costs. For example, it is estimated that one child in the world dies every five minutes because of bacterial resistance to antibiotics.[2]

AMR clearly involves biological processes, but the context which determines the operation of these biological mechanisms is shaped by social, cultural, political, and economic processes. The most effective actions to reduce and control AMR will involve changes in social practices, including how farmers, vets, and regulatory systems manage livestock production for human consumption; how regulatory and fiscal frameworks incentivise or deter antimicrobial development, production and use; and how public and healthcare professionals behave in relation to infection and use antimicrobials. The most critical feature of AMR is that resistance to a new antimicrobial begins as soon as it is developed, and so development of new antimicrobials is not a panacea. Providing a mechanism for sustainable use of the valuable resource of antimicrobials will therefore necessitate considerable behavioural, cultural, political and economic change throughout the world, which needs a strategy to be developed in harmony with the scientific and professional agenda.

INTRODUCTION AND SUMMARY

The purpose of this report is to define the agenda for social science research in the UK. 'Social science research' covers a range of disciplines including economics, sociology, psychology, anthropology, geography, history, business studies, political science and policy analysis.

The ESRC convened a working group to investigate and advise on the priority areas relating to AMR which social science can address. This working group supplied a wide variety of background information which has informed this report.

Five agreed overarching key points were that:

1. Social science can contribute to the measurement, modelling and understanding of antimicrobial resistance and its geographical and social distribution, and to the development and evaluation of strategies to mitigate it.
2. Although resistance occurs to antivirals and antifungals, the most pressing welfare and social issues are posed by bacterial resistance to antibiotics, so these should be the primary focus of research.
3. It is important that social scientists work in close collaboration with other key sectors in the field (e.g. biologists, medical and veterinary scientists, industry and regulators).
4. To be effective, the social science contribution should range from large-scale macro-level (e.g. global trends and their drivers) to small-scale micro-level (eg social interaction between patients and doctors, or between vets and farmers or race horse trainers); and should include a wide range of social science disciplines.

[1] p7, UK Five year antimicrobial resistance strategy
[2] Zulfiquar Bhutta presentation at the ReAct conference September 2010

5. In addition to conducting new empirical and conceptual research, a major social science contribution should be to undertake systematic reviews of existing social science evidence (for example, on the relative effectiveness of different behavioural change strategies).

A summary of priorities agreed by the working group is listed below. This report takes each of these in turn and expands on the potential contribution social science can make in each area:

- Measuring, modelling, visualising and understanding AMR internationally
- Measuring, modelling, and understanding AMR in specific countries
- Measuring health burden and other socio-economic costs of AMR
- Understanding and developing business models to promote new antibiotics or alternatives to antibiotics
- Understanding community dynamics and interactions
- Understanding the realities of everyday antimicrobial use in humans
- Understanding realities of everyday antimicrobial use in animals
- The development and evaluation of behaviour change strategies

MEASURING, MODELLING AND UNDERSTANDING AMR INTERNATIONALLY

"Because globalisation increases the vulnerability of any country to diseases occurring in other countries, resistance presents a major threat to global public health. And no country acting on its own can adequately protect the health of its population against it".[3]

It is clear that AMR is a truly global problem. The World Health Organisation has been at the forefront of activity to co-ordinate stakeholders across nations on AMR and has recognised that without co-ordinated efforts the problem of resistance may be insurmountable.[4]

There is wide variation across the globe in patterns of use and resistance to antimicrobials and in the regulatory and health system frameworks which govern the use of antibiotics among animals and humans. There is a need for robust empirical social science research into areas such as: the geographical and social distribution of AMR; regulatory frameworks for antibiotic use in animals and humans in different countries; financial incentives and barriers for antibiotic prescribing and the development of new antibiotics; features of healthcare systems which promote or mitigate AMR; patterns of and changes in agronomy and animal husbandry; and other recent and likely future social drivers of AMR (eg patterns of global trade, pilgrimage and migration, changing demand for meat consumption). Providing a better understanding of the social and economic drivers of AMR and its mitigation internationally is likely to involve an explicitly comparative and historical perspective.

Case Study: Global Travel and Migration

It is estimated that 2 billion people move across large geographic distances each year, and that approximately half of these cross international borders. Working out what these statistics mean in terms of disease risk is challenging, not least because health and related surveillance systems tend inevitably to be domestic, rather than international, in focus (MacPherson, 2009). The mere fact that disease is seen to 'travel' between regions, apparently apportioning blame on particular 'origin' countries or groups carries political ramifications (as studies of pandemic flu have demonstrated – see e.g. Elbe, 2010), which can have a knock on effect on local responses, including willingness to engage in international collaboration regarding regulation and control.

[3] Smith & Coast, Bulletin of the World Health Organisation, 2002, 80 (2)
[4] For example, see 'Antimicrobial resistance: global report on surveillance 2014', published April 2014

What is needed?

- Better measurement of the social drivers associated with the distribution of AMR internationally
- Better understanding of how farming systems, healthcare systems, cultural and social norms, industry dynamics and regulatory frameworks vary across countries and regions, and how these variations might contribute to resistance
- Appreciation of how regulatory bodies and governance processes interact at a global level and can both enable or hinder innovation in antibiotics
- Studies of barriers to cross-sectoral and transnational action
- Modelling of the costs of and likely trends in AMR globally
- Measurement and modelling of international migration patterns and trade
- Analysis of the evolution of relevant policies in different political and economic contexts

MEASURING, MODELLING, AND UNDERSTANDING AMR IN SPECIFIC COUNTRIES

As well as contributing to an understanding of the global patterns of AMR, social scientists can contribute to better measurement, understanding and modelling of AMR within particular countries.

For example, this should involve quantification and enhanced understanding of the extent and distribution of prescribing of antibiotics to humans. Questions relating to this include; how many prescriptions are written, for what conditions, for which age and social groups, in what areas of the country, by which healthcare professionals? What proportion of prescriptions are collected, who pays for them, what proportion of courses are completed? What proportion of antibiotic use is over-the-counter? Similar questions can be addressed of antibiotic use in animals (for which species and types of animals are antibiotics prescribed, by whom, at what cost to owners or farmers, etc). Modelling exercises could be carried out to explore 'what if?' scenarios for both animals and humans.

Country-specific studies should also address locally important questions such as the role of pharmaceutical industries or other stakeholders in promoting antibiotic use, specific features of animal husbandry, patterns of human/animal interaction and of livestock trade and human migration flows, the cultural value attached to antibiotics in different settings, political and policy barriers and drivers, the role of poverty and social inequality, and alternative ways of dealing with infection.

Case Study: Tuberculosis in India

Anthropological research by Jeffery et al (e.g. Das and Jeffery, 2009) has demonstrated the difficulties in combatting TB in India, where 20 per cent of the global incidence of multi-drug-resistant TB (MDR-TB) is estimated to be found. Despite recent government attempts to tighten up monitoring of pharmacies, regulations are routinely ignored and so antimicrobial drugs are still readily available over the counter. Overuse of broad spectrum antibiotics is common. As much as 50 per cent of prescriptions for TB are thought to be inappropriate. These consumption patterns are affected by the global and national pharmaceutical market, and the ability of the government to change the status quo is limited. In addition, poverty plays a role: people with unstable incomes, poor living and working conditions, as well as lifestyle risk factors such as alcohol consumption, are likely to be missed by the government's anti-TB programme, and rarely take anti-TB medicines in the right combinations or durations for them to be successful. This contributes strongly to the growing prevalence of MDR-TB in India and globally.

What is needed?

- Robust empirical measurement and modelling of AMR in specific countries
- Robust empirical measurement and modelling of antimicrobial prescribing in animals and humans
- Context-specific information about drivers and trends in AMR and AMR risk factor

COMMUNITY DYNAMICS AND INTERACTIONS

Within communities, the prevalence of antimicrobial resistance varies widely, and the ways in which people and communities interact with each other affects this. It is crucial to surveillance and scenario-building to understand these dynamics better, not only in traditional health settings. For example, how do travel patterns, as well as behaviours when abroad and at home, affect the ways in which resistant strains circulate? How is antibiotic use and hygiene managed in care homes and to what effect? How do prisons and other settings manage drug use? How has multi-drug-resistant TB emerged, among which social groups, and with whom do MDR-TB patients interact? Is there the potential for politically motivated misuse of resistant strains of particular illnesses?

There is strong evidence to suggest that socio-economic factors, such as gender and poverty, will be key to understanding the effect of social interactions – for example, we know that access and use of health services is mediated by such factors both within the UK and internationally. Different groups and organisations have their own beliefs and expectations around antibiotic use which need to be better understood. Such social science research will both enhance understanding of who is at the greatest risk, and help ensure that policies and interventions take community dynamics into account.

Case Study: Measuring Social Mixing

Patterns of infection relate to patterns of social interaction. Any attempt to model the spread of resistant forms of infection, or to understand non-pharmaceutical measures to control spread, therefore needs a sound understanding of how individuals 'mix'. Work by Read et al (2012) studied the different methods that have been used to link infection to interaction, and found many methods typically used by social scientists (household analysis, time use diaries, video observation) were valuable. However studies that combine an understanding of social interaction and infection are rare and they suggest that improving understanding of social mixing patterns may significantly improve planned interventions.

What is needed?

- Understanding and modelling of patterns of interaction and associated infection, including incorporating evidence from earlier related studies
- Modelling of interaction patterns between different healthcare settings and the community
- Understanding of AMR impact on different social groups
- Work on risk pathways and microbial circulation, globally and within/between human and livestock and other animal populations.

HEALTH SYSTEM BURDEN AND OTHER COSTS

Health systems depend on antibiotics. As well as the familiar, direct use of antibiotics to treat common infectious diseases, the treatment of many illnesses and post-surgical standard practice also involves routine antibiotics use. In order to appreciate how health systems might function in a 'post-antibiotic' era, we need to fully understand the actual cost that use – and non-use – presents to current health systems. We need to quantify the true costs of antimicrobial resistance using a broad framework of social costs, since the cost of any actions to mitigate AMR must take into account the wider social costs of AMR. We then need to model different patterns of health care to create a more sustainable system in the presence of AMR and in

Case Study: Hip operations

Economists are able to model potential implications of declining antimicrobial effectiveness. For example, Smith and Coast (2013) investigated routine hip replacement surgery: "Currently prophylaxis is standard practise, and infection rates are about 0.5-2 per cent, so most patients recover without infection, and those who get an infection are successfully treated. We estimate that without antimicrobials, the rate of post-operative infection is 40-50 per cent, and about 30 per cent of those with an infection will die".

conjunction with various other proposed strategies and future scenarios they may present.

What is needed?

- Analysis of not only healthcare directly related to the antibiotic, but also care that is only enabled – or enabled at current levels of safety and efficacy – by antibiotics
- Analysis of financial and other costs of AMR
- Analysis of financial and other costs and benefits of AMR-mitigating actions (in both humans and animals)
- Interdisciplinary work between clinicians and social scientists to appreciate disease trajectories, associated costs and health system burden.

UNDERSTANDING AND DEVELOPING NEW BUSINESS MODELS FOR NEW ANTIBIOTICS OR ALTERNATIVES TO ANTIBIOTICS

The supply of antimicrobials is declining: only two new classes of antibiotics have been introduced into the market in the last three decades. Product innovation in the pharmaceutical industry is costly, risky and time-consuming. With decreased productivity, and research and development (R&D) costs representing a high proportion of the industry revenues, the pharmaceutical industry is facing unprecedented challenges to its R&D model. The industry's profitability and growth prospects are also under pressure as the finance of healthcare systems comes under increasing scrutiny. The very presence of widespread concern about AMR acts as a further disincentive in that antibiotic use is being discouraged, potentially reducing the market for new drugs. Essentially, the value of antimicrobials is low compared to other therapeutics, particularly because new, innovative drugs will not be prescribed until existing lines have developed resistance, so there is little incentive for Big Pharma companies to innovate. Both regulatory and reimbursement processes may need to be radically transformed to incentivise industry to develop new antimicrobial drugs and ensure they are used appropriately by health services.

Case Study: Business models

Typically, incentives for development of new drugs fall into two main types – push and pull mechanisms. Push mechanisms decrease cost and risk to the developer but are focussed on the beginning of the innovation process, and therefore don't reward further development such as completion of development projects. Pull mechanisms reward successful development of a final drug, but the challenge here is the risk faced by developers early on in the process, as well as rewarding appropriately later on in order to decrease likelihood of excessive waste. Health Policy analysts (e.g. Morel and Mossialos, 2010) have developed models that combine these two mechanisms, potentially enabling risk to be shared between developers and funders whilst at the same time incentivising development early on.

This scenario has led to the emergence of R&D initiatives with not-for-profit organisations leading the innovation process in these areas. These initiatives tend to be funded via combinations of public and philanthropic sponsorship, with variable success.

What is needed?

- Assessment of the performance of different business organisational models within the R&D process
- Development of new economic models that balance the appropriate use of drugs and the mitigation of AMR while appropriately rewarding innovation
- Exploration of effective regulatory models to encourage innovation. New technology, such as genome sequencing techniques to identify new targets and synthetic biology to synthesise complex biological molecules, could be better supported to tackle the antimicrobial crisis, but adaptive systems of regulation and governance will have an important role to play.

- Understanding of how different models affect incentives at the local level, in both livestock management and human health
- Develop key policy interventions for the commercial introduction of new antibiotics.

REALITIES OF EVERYDAY ANTIBIOTIC USE IN HUMANS

There is general agreement that antimicrobial use in humans, particularly antibiotic use, needs to be reduced and more carefully managed; and also that many current practices (e.g. prescribing, hygiene) will need to change as resistance increases. At a societal level, our expectations relating to antibiotics are complex – there might be an appreciation of the need to reduce their use, but when faced with specific personal circumstances patients often feel a desperate need for a prescription e.g. when their child is ill.

Before moving to develop interventions or regulations to change antibiotic prescribing behaviour and use, it is important to develop a robust understanding of how antibiotics are understood, valued, and used. What is the level of public understanding about the difference between viral, fungal and bacterial diseases, and the relative efficacy of antibiotics in dealing with these? What cultural values are embedded in antibiotic use? What is known about completion/non-completion of antibiotics treatment courses in humans and animals? What degree of regulation will the public and professionals be willing to tolerate in relation to controlling resistance? Do different levels of understanding about AMR exist among different groups of the public and professionals? To what extent do primary care physicians feel pressurised by patients to prescribe antibiotics to them or their children? How are hygiene practices (in homes, care homes, hospitals, schools etc), sexual behaviour and other activities related to different understandings of microbial infections and the efficacy of antibiotics? What can we learn from public and professional reactions to other public health issues such as vaccination, pandemic flu, food poisoning, TB, HIV/AIDS, smoking and cancer? What is the role of ritual in antibiotic use and hygiene practices? What is the role of financial incentives in the NHS in changing GPs' prescribing practices (perhaps learning from the existing use of financial incentives in the NHS)? All these questions would need to be sensitive to variations between cultural and socio-economic contexts.

Case Study: How people view medicines

People hold a range of deep-seated views about medicines. For example, research in Indonesia and Uganda has shown a preference for prescriptions involving injectable drugs due to the perception amongst the general public that these are swifter and more powerful than oral drugs (Van Staa and Hardon , 1996). In the UK, research investigating the effect of the 2009 influenza pandemic on the public's views showed that a fifth of respondents thought that Tamiflu was a vaccine (McNulty et al, 2012). These types of examples demonstrate the importance of unpicking how people understand antibiotics and their use.

What is needed?

- A context-specific understanding of norms, values, beliefs and practices about bacterial infections, antibiotic use, hygiene and AMR in different social groups
- Identifying the specific social norms, habits, cognitions and attitudes relating to antibiotics, in order to develop context-appropriate health strategies, from the perspective of both the patient and the prescriber
- Identifying the motivational, capability and opportunity factors that may support or undermine appropriate antibiotic use
- Enabling social scientists to work in interdisciplinary teams in order to develop interventions based on sound behavioural science principles.

REALITIES OF EVERYDAY ANTIBIOTIC USE IN ANIMALS

While human health-related behaviours often dominate discussions relating to AMR, it is important not to underplay the significance of the behaviours of humans in relation to animals.

The impact of human behaviour on AMR in relation to different categories of animals, including food animals, horses, and domestic companion animals, is not fully understood. In particular, pig and poultry farming have characteristics, including management systems that create particular challenges regarding the appropriate use of antimicrobials. There is a large trade in purchased and imported antibiotic use in the veterinary world, much of which is from poor quality sources.

Case Study: Danish pig farming practice

Intensive farming practices are linked with particularly high levels of prophylactic prescribing, and in many countries vets can make a significant profit from antibiotic sales. Evidence from Denmark suggests this prescribing is unnecessary and that clear and targeted state intervention can be beneficial. In 1995, Danish scientists pinpointed a bacterium that was resistant to one of the antibiotics being routinely used to promote growth in chickens and pigs, and this prompted the start of a process where the Danish government more tightly regulated the use of antibiotics in livestock and developed a surveillance system to target overuse. Pig and poultry production is not felt to have suffered as a result; Denmark remains the world's largest exporter of pork (Aarestrup, 2012).

Questions similar to those posed in relation to human health are highly relevant here. How do vets and farmers in different sectors understand and use antibiotics? What do they perceive as the costs and benefits of antibiotic use? To what extent are vets pressurised by pet owners or farmers into prescribing antibiotics? How do vets and farmers understand and respond to regulatory frameworks trying to reduce resistance? How do humans and animals interact, and how might their interaction promote or form a barrier to resistance? What cultural values shape our relationship with farm animals and pets in ways which might promote or militate against resistance? How our behaviour in relation to animals impacts the speed of mutation in ways that are detrimental to human health is also often overlooked, and requires thorough cross-disciplinary research that incorporates a clear understanding of the social and economic contexts of these behaviours.

What is needed?

- An understanding of prescribing practices and their socio/cultural/financial contexts, and the drivers for different categories of animals
- An understanding of the different economic conditions, including innovation and regulatory processes, associated with different categories of animals
- Multidisciplinary research involving social scientists and bioscientists, including microbiologists, to understand processes and risks relating to human-animal interactions.

BEHAVIOUR CHANGE STRATEGIES

A key role for social science is in the development and evaluation of strategies for behavioural change in this field**.** Attempts to change behaviour in relation, for example, to prescribing, antibiotic use, reduction of infection transmission and pharmaceutical innovation could be based on a number of approaches, ranging from relatively high-level regulatory, fiscal or penal approaches, through financial and other incentives or barriers, to educational or exhortatory approaches. These different approaches are likely to be acceptable to a varying degree by different stakeholders and jurisdictions, and also likely to be differentially effective.

It is very important that any attempts at behaviour change are based on sound behavioural science principles, adequate understanding of the specific socio/cultural/economic context targeted by behaviour change strategies, thorough development and piloting, and thorough evaluation of interventions.

What is needed?

- Synthesis of existing behavioural science research relevant to AMR
- Synthesis of best practice in behaviour change strategies likely to be relevant to AMR
- Collaboration between social scientists and policymakers in designing and evaluating any attempts to introduce behaviour change strategies
- Adequate consideration of the wider costs and benefits (and knock-on effects) of any behaviour change strategies.

Case Study: Hygiene behaviours

Researchers have started to unpick the complexity of motivations relating to behaviours. Integrating perspectives from psychology, ecology, epidemiology and cultural evolution, Curtis et al (2009) reviewed research on the motivations for hygiene behaviours across eleven countries. They demonstrated that a range of factors acted as key motivators, including disgust, nurture, comfort and affiliation. Fear of disease generally did not motivate hand-washing, and people's views were often affected by status, for example being seen to be clean or have a child with good manners were higher status attributes. They note that promotion programmes need to move away 'from the common assumption that imparting knowledge about germs and disease will change behaviour'.

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WORKING GROUP MEMBERSHIP

ESRC convened a working group to help advise them on this topic. Its membership was deliberately broad, to encompass a range of different disciplinary perspectives. Members are listed below.

- Professor Dame Sally Macintyre (Chair)
- Professor Ian Donald, Institute of Psychology Health and Society, University of Liverpool
- Professor Stephen Hinchliffe, College of Life and Environmental Sciences, University of Exeter
- Professor Roger Jeffery, School of Social and Political Science, University of Edinburgh
- Professor Susan Michie, Health Psychology Research Group, University College London
- Dr Marisa Miraldo, Business School, Imperial College London
- Dr James Mittra, Science, Technology and Innovation Studies, University of Edinburgh
- Professor Elias Mossialos, Dept of Social Policy, London School of Economics
- Dr Jonathan Read, Institute of Infection and Global Health,University of Liverpool
- Professor Richard Smith, Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine
- Professor Joyce Tait, Science, Technology and Innovation Studies, University of Edinburgh
- Dr Sally Theobald, Dept of International Public Health, Liverpool School of Tropical Medicine