

Regulating Resistance, Resisting Regulation: Project workshop

Population Health Sciences, Bristol Medical School, University of Bristol
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Room 4.02 (4th floor), School of Education, University of Bristol, 35 Berkeley Square,
Bristol BS8 1JA

Workshop Summary

Throughout 2018 and 2019, a team at the University of Bristol undertook a Wellcome Trust Seed funded project aimed at better understanding the regulatory challenges posed by antimicrobial resistance (AMR) and the consequences of novel regulations on antibiotic use. The team comprised Prof. Helen Lambert (PI), Dr. Adam Brisley (RA, social anthropologist) and Carla Rodrigues (RA, medical sociologist) and was supported by an international group of collaborators with backgrounds ranging from global health law and social policy, to health services research and primary care.

Toward the end of the project, the Bristol team organised a one-day workshop and networking event that would bring together a small group of researchers working on AMR and antibiotic use in diverse settings, in order to discuss our initial findings and potential frameworks for understanding the regulation of antibiotic resistance, share fieldwork insights and experiences, and consider potential research and collaboration opportunities. The following is a summary of that event.

Convenors' Introduction

Helen Lambert opened the workshop by explaining origins of the project in a Newton Fund study exploring the optimisation of antibiotic use in Anhui Province, China (MR/P007546/1, <http://www.bristol.ac.uk/amr/research/antibiotic-usage-and-behaviour-change-in-clinical-practice-and-livestock-production/identifying-key-determinants/>) and a Wellcome Trust Seed grant, 'Regulating resistance, resisting regulation: New regimes to tackle drug-resistant infections in European and Asian healthcare systems' (<https://wellcome.ac.uk/funding/people-and-projects/grants-awarded/regulating-resistance-resisting-regulation-new-regimes>), that was awarded in 2018. Her introduction described how the Seed Award project team conceives regulatory consequences as including the ways that changes in regulation can influence the secondary data which are then used to measure the putative effects of implementing regulatory actions. She illustrated this with an example from a study of electronic record completeness conducted in China, highlighting the relation between the accuracy of patient records (which can be used to monitor rates of antibiotic prescribing) and issues of access to and costs of medications that became visible when records were compared with direct observation in clinics. For example, some patients

used the names of family members to receive treatment when they have insufficient insurance cover, so that one patient may have multiple electronic records in different names and different records may have different diagnoses.

Project presentation: *'Dimensions of Regulation'*.

Carla Rodrigues presented the theoretical approach of the project regarding AMR regulation. She started by giving an overview of the global policy aims regarding antimicrobial resistance (AMR) and of the current global debates around the perceived need for harmonised regulatory frameworks. In order to explore a potential framework for studying AMR regulation, Carla discussed some of the main conceptual approaches to regulation in the literature in terms of its definitions, use, and dimensions. Using empirical examples from the case studies of this project (led by Adam for Spain and Meixuan for China) and from other studies, she critically discussed ideas about regulatory “challenges” and “failures” and emphasised the importance of attending to the ‘unintended consequences’ of regulatory policies in a more systematic way.

Session I: AMR in Europe

Session One opened with a presentation from **Christie Cabral**, who traced the journey of AMR from relative obscurity to priority for healthcare governance in UK primary care. Christie described how earlier high prescribing rates of broad-spectrum antibiotics for childhood cough and respiratory tract infections led to incentivising reductions in antibiotic prescribing. This has led to reduction in certain infections, e.g. from 50-30% in the case of *C.diff*. Yet, the most recent guidelines from the CCG are still unclear in advising on symptom-based prescribing. Regulatory activities have produced the image of the professionally virtuous clinician being a “low prescriber” among general practitioners but the continuing absence of clear clinical guidance on when to prescribe antibiotics leaves much to the judgement of individual clinicians and may compound health inequalities.

Alena Kamenshchikova presentation also covered issues of access and distribution. She explored the effects of prohibition on selling antibiotics without prescription (2017) in Russia and described how doctors, pharmacists and patient responded to these new regulations. Pharmacists in the region responded to the fear of “secret shoppers” and unexpected audits as mechanisms of enforcement by selling antibiotics only to people with whom they were familiar. This selective enforcement of regulation meant that access to antibiotics depended largely on the extent to which someone was embedded in local informal networks. Doctors welcome prohibition of OTC sales as this requires patients to seek medical treatment, but it leads to extra paperwork and increased caseloads often without immediate availability of bacterial cultures that are needed to support clinical decision-making.

Carsten Strøby Jensen raised the question of whether self-regulation should be seen as part of how regulations are implemented and developed, pointing to a very different effect of regulation, namely, the stigmatisation of pig farmers in Denmark that results from the discourse on “irresponsible” use of antibiotics in food production. Extensive

monitoring and the implementation of regulations in the last 5 years has changed the relationship between vets and farmers, so that vets are now managers of use rather than the farmers who they previously served. He also noted the discourse of ‘othering’ between the human and veterinary sectors in assigning blame for the AMR problem. EU regulations are interesting as these are cross-national and mainly comprise soft law initiatives. Whereas human health policy is primarily made at national level, the veterinary sector is regulated by cross-national initiatives as part of the economy.

Session One closed with a presentation from **Sibyl Anthierens**, who described the emergence of AMR regulation in Belgium, a country with high levels of antibiotics prescription. Belgium operates a fee for service system and the requirement to provide a sick note after one day off nursery or work (though now changing) encourages medical attendance and prescribing. New laws on regulation to reduce prescription by limiting reimbursement for antibiotics, a system for providing feedback to doctors every three years, and a decrease in the reimbursement that patients receive when using their prescriptions at pharmacies have been introduced. These measures have not produced reductions in antibiotic prescribing.

Project Presentation: *Crises of Care and the Circulation of Antibiotics in Barcelona*

Session One was concluded with a project presentation by **Adam Brisley** who, continuing with the theme of access, explored the unintended consequences of stricter regulation on the prescription in Barcelona. Adam suggested that in contexts defined by unstable employment and patchy access to formal healthcare, restricting access to antibiotics may provoke people to seek medication via the “black market”.

Session II: AMR in Asia

Session Two began with a presentation from **Papreen Nahar**, who spoke about the regulation of the pharmaceutical industry in Bangladesh. Direct-to-consumer advertising was banned by the government, but the industry has been able to create various “work arounds” – including the use of “pharmacy reps” – that ensure demand remains high. Her work with these reps suggests they have a high degree of access to health providers and could potentially act as mediators to encourage antibiotic stewardship.

Marco Haensszen described the continuing informal availability of antibiotics in Thailand, Lao PDR, and Viet Nam. A growing policy emphasis on AMR has led to various local initiatives but has produced confusion among clinicians, who are faced with ‘ethical dilemmas’ in whether to prescribe according to local expectations or restrict access to antibiotics. Monitoring antibiotic prescribing is also problematic as national statistics rely on e-records which fieldwork suggests are often inaccurate either through not being completed or through diseases being mis-classified. Marco also raised the question of what is being regulated and why AMR should be afforded so much attention in ODA countries as this reflects the priorities of more affluent nations. The problem of AMR is not only due to the consumption of medicines but is related to broader political and economic structures. Even if the “problem” of antibiotic supply and consumption

can be solved, precarity is an issue and similar problems with a host of other medicine will remain.

Sonia Lewycka and **Nam Nguyen Vinh** described some of the problems with implementing AMR policy and regulation in Vietnam and the dynamics of antibiotic use in different sectors – hospital (where most action has been taken so far), primary care, and farming. The national AMR network has 16 hospitals and there is a (2016) manual on antibiotic use in hospitals and associated stewardship actions. Problems include the increased (paper) work burden it creates for clinicians, which both limits implementation and has slowed down decision-making. There is mandatory monitoring through antibiotic use surveys, but a lack of technical and infrastructural support for this. So far, there is little action in primary care settings; doctors need to follow certain guidelines for insurance reimbursement, but can tailor their recording of a diagnosis to fit with this, resulting in inaccurate e-records. The main source of information comes from national insurance system. There is a new (2018) policy on antibiotic sales but this is not enforced and there are no monitoring mechanisms. Use of antibiotics for growth promotion in farming is now illegal but a lot of the focus is on therapeutic use. There are measures to monitor use but not on resistance and its spread.

Coll de Lima Hutchinson discussed how the national action plan in Myanmar was driven largely by the interests of non-nationals and how, more broadly, AMR had become a priority in LMICs because of its importance in high income countries. Coll drew parallels between this aspect of the global discourse on AMR and the historical rise of importance of smoking reduction in LMICs. Coll also highlighted the lack of critical engagement with pharmaceutical companies and the existence of advertisement carrying messages that promoted antibiotics as a means of “getting back to work quicker”.

Project Presentation: Antibiotics Regulation in China: Views of Rural Doctors

Session II ended with a project presentation delivered by **Meixuan Chen**, who summarised the emergence of various binding regulations in China such as the production of a national list of essential medicines, the requirement of doctors to purchase medicines only through official channels, and restrictions on the prescribing of IV antibiotics. Despite such measures, in the rural clinics studied, antibiotic prescription rates remain high. Patients continue to see antibiotics as effective and expedient way of dealing with minor illnesses. Doctors continue to be financially incentivised to prescribe IV antibiotics, probably due to the establishment of the ‘Zero mark-up policy’ on oral medicines, and to access medicines from the largely unregulated private sector, in order to fulfil perceived patient demand for swift treatment in a context where time equals productivity. There is little enforcement of regulations but financial punishment (where doctors exceed the 20% antibiotic prescribing cap) and public humiliation operate to discourage antibiotic prescribing.

Session III: Global AMR

Picking up on a theme raised earlier by Marco, *Mishal Khan* began by noting how policy documents written in high-income countries (HICs) may not be relevant in low- and middle-income countries (LMICs), where more urgent priorities such as human development and patients' interests are given precedence. Particularly when framed as a global health security risk to HICs, AMR may not be seen as salient in countries like Pakistan if not locally framed to make it a genuine political priority. Mishal discussed the accessibility of antibiotics in Cambodia, Pakistan and Indonesia, the policy focus on informal sellers of medicines, and the general reluctance to use harder measures against powerful actors such as pharmaceutical companies and doctors (there is a tension in Pakistan as to whether this results from a weak state or a lack of separation between those who work in regulation and those who own pharmacy chains). A consequence of this is the focus on 'awareness' instead as a politically safe alternative. Mishal finished by raising the question of whether regulation is appropriate in the absence of bioethical norms; if clinical practice is profit-driven and patient welfare isn't the issue, then can we really justify regulation?

The final presentation of the day came from *Anne Roemer-Mahler*. Her discussion of attempts to produce antibiotic prescription guidelines in a cancer hospital in Egypt again evoked the problem of applying global policy to local contexts. Anne described how the hospital's poor clinical hygiene (flies and rats contaminated surgical theatres) and particularly vulnerable population of patients meant using antibiotics prophylactically often seemed clinically rational, despite the hospital's extremely high resistance rates. Moreover, patients were seen as especially vulnerable, as immune-compromised. Whether guidelines have had any effect is unclear, even to those who created them, and there is ambivalence about the implementation and monitoring of new guidance. Those tasked with implementation of stewardship measures are the least powerful in the hospital hierarchy – IC nurses, pharmacists and microbiologists.

Resume of Presentations and Emerging Research Questions

In the next session, Helen Lambert commented on the presentations and summarised emergent common themes.

- 1) **Medical records and workarounds:** many presenters spoke of the ways in which monitoring of antibiotic use (if not antimicrobial resistance) depends on secondary data such as electronic patient records that are unreliable as reflections of actual usage patterns. This issue as far as it affects formal reporting of monitoring and surveillance is the 'elephant in the room' when it comes to national and international data on AMR trends. This links to bureaucracy and the burden of recording (5 below).
- 2) **Precarity and economic conditions:** several presenters pointed to the inability of local people to afford taking time of work to visit a doctor, thus rendering the consumption of OTC antibiotics entirely rational; but at the same time this form of 'self-care' is a commodified understanding of regaining health, reminiscent of notions of e.g. the 'pharmaceutical citizen'.

- 3) **Exclusions/inequalities** is another clearly emerging theme linked to the previous one; who gets access and who gets left out. We heard about kinship networks; migrants; travellers; the poor as those potentially excluded from access to antibiotics when these become more strictly regulated.
- 4) **Power/hierarchies** in health care institutions and among policy actors: at local level, these shape the ability of healthcare workers in hierarchical organisations and professions to institute antibiotic stewardship; at national level, affect the selection of AMR control measures when attempts to regulate might adversely affect more powerful interest groups; and at global scale, may result in the imposition of policies and regulatory actions that are not considered local priorities. It is worth noting that this is a politically sensitive issue when it threatens to reveal discrepancies between paper policies and their implementation in practice; in neither 'case study' country could the project get interviews with policy makers.
- 5) **Dilemmas of enforcement and the ethics of care:** Regulatory enforcement in many settings is seen by patient-facing clinical staff as going against their duties of care. Burdensome reporting requirements place burdens on nurses' time; junior/rural doctors must choose between 'good' care of patients that satisfies expectations or following prescribing guidelines. Related to this are questions about the object of regulation: Several presenters raised questions about what it is that is being regulated; regulations as enforceable rules, versus actions as education; which links to notions of 'self-responsibilisation'. Enforcement is also selective; hospitals have been the main focus so far and there is a north-south divide in implementation of actions in other sectors and among other publics.
- 6) **Agenda-setting:** Several types were raised by presenters. 'Global health security' emphasises contagion (e.g. emerging infectious diseases') across national boundaries and between LMICs and HICs, effectively prioritising this over (e.g.) provision of clean water. A behaviour-based approach to AMR versus a system-based approach constitutes another form of agenda-setting.

In the following discussion it was pointed out that new regulations are being instituted on the basis of old infrastructures that will inevitably limit their effectiveness, and that it is inappropriate to focus too much on AMR without looking at the wider system. Linked to the theme of hierarchy, the level of action is often too low for what needs to be done and it concentrates responsibility on the least powerful actors in the health care system.

We then considered how much of the issues discussed are part of a more generic 'medicine' problem as opposed to being specifically about antibiotics, and the need to consider what is different about antibiotics. It was pointed out that many of the issues surrounding action to control TB or improve nutrition have the same or similar drivers. Similarly, data constructs its own reality and reflects apparent successes when policies are created to effect change. It may be futile to expect this to change; but how do we research data better? Discussion also touched on the sensitivities in researching this

area and participants reflected on examples where research was seen as beneficial by showing what policies don't work in practice.

We also compared settings where specific population subgroups (refugee camp residents in Europe; travellers to Italy and farmworkers in Denmark) are being targeted for microbiological testing on the assumption that they are more likely to carry resistance. It may be worthwhile to highlight and compare such issues across settings where there are resource constraints but no commercial context, versus settings which are very commercially driven. Looking at different contexts helps to draw out distinctions created by health system differences when clinical uncertainty is the same.

Collaborative Opportunities and Future Research Pathways

In the final session, the group discussed possible routes forward. There was general consensus that the collaboration should continue, with the development of a network in the first instance together with a book proposal and chapter outlines for a potential edited volume. It was also agreed that the research team would produce a summary report of the workshop for circulation and that they would explore funding opportunities to support a collaborative network and the development of a platform for sharing materials.

Workshop Attendees

Adam Brisley	University of Bristol
Alena Kamenshchikova	Maastricht University
Ali Vedadhir	University of Tehran
Anne Roemer-Mahler	University of Sussex
Carla Rodrigues	University of Bristol
Carsten Strøby Jensen	University of Copenhagen
Christie Cabral	University of Bristol
Coll de Lima Hutchison	LSHTM
Helen Lambert	University of Bristol
Keith Syrett	University of Bristol
Marco Haenssger	Warwick University
Meixuan Chen	University of Bristol
Mishal Khan	LSHTM
Mustafa Al-Haboubi	LSHTM
Papreen Nahar	Brighton and Sussex Medical School
Sibyl Anthierens	University of Antwerp
Sonia Odette Lewycka	Oxford University