

THE GLOBAL ANTIBIOTIC RESISTANCE PARTNERSHIP

HELLEN GELBAND, CENTER FOR DISEASE DYNAMICS, ECONOMICS & POLICY, WASHINGTON, DC, USA



The Partnership operates to bring a set of new voices to the antibiotic resistance issue and to establish local capacity to develop and help to implement evidence-based policies in eight low- and middle-income countries in Africa and Asia. Awareness of antibiotic resistance and its potential to derail gains against infectious diseases was not on the global health agenda for low- and middle-income countries in 2008, when GARP began. Significant in-country progress supports expansion of the GARP model.

The Global Antibiotic Resistance Partnership (GARP)¹ began in 2008 with funding from the Bill & Melinda Gates Foundation. The aim has been to develop sustained local capacity to formulate and promote locally relevant policy related to antibiotic use and resistance in low- and middle-income countries (LMICs).

For several years prior, CDDEP (then a centre at Resources for the Future, an established United States think tank) had been examining the policy process and analyzing options for the United States in a project called Extending the Cure. That effort, which continues, gave CDDEP entrée into the global discussion about antibiotic resistance, mainly among the high-income countries. The absence of voices from LMICs led us to begin GARP.

Antibiotic resistance has gained prominence in recent years, but in 2008 it had a much lower profile – in LMICs it is not much of an exaggeration to say that it had no public profile, although some researchers everywhere had been active and interested. Importantly, it was not a high priority among the main bilateral health funders, such as the United States Agency for International Development (USAID) and the Department for International Development (DfID). AIDS, malaria and tuberculosis were – and remain – the highest priorities. An exception was the Swedish International Development Cooperation Agency (SIDA), which was active globally on antibiotic resistance, but with a different focus from that of GARP.

Yet it was clear that antibiotic use was growing in LMICs, the bacterial disease burden was high, and the loss of effective treatments for common infections could have even more dire consequences in LMICs than in high-income countries. In the United States, some people die from

antibiotic-resistant infections, but a major consequence is economic: later-generation antibiotics are significantly more expensive, and extended stays can double (or more) hospital bills. In low-income countries, however, those newer antibiotics are simply not available at all, and in middle-income countries, availability is limited.

An obvious question is whether the policy prescriptions from the United States and Europe, which focused almost entirely on reducing use, could simply be applied in LMICs. It was clear that the answer was no for at least two main reasons: first, because unlike high-income countries, lack of access is still a significant problem in LMICs. One million children die from pneumonia every year, nearly all of whom could be successfully treated with an inexpensive, simple antibiotic. Second, weak regulatory capacity in LMICs means that controlling access through laws and regulations – such as prescription-only laws – could not be relied upon. It was apparent that policy solutions would have a greater chance of success if local experts customized them to the local context.

The GARP concept was, therefore, to identify local experts in each country, assemble them into a working group, and provide them with the resources to meet, discuss, and analyze the national situation regarding antibiotic use and resistance, identify critical data gaps, and work toward developing locally relevant policy that could be adopted by government and private sector organizations, such as hospitals and professional societies.

GARP was established in 2009–2010 in four countries – Kenya, India, Vietnam and South Africa – chosen because they represented a range of conditions, particularly in type

¹ <http://cddep.org/projects/global-antibiotic-resistance-partnership>

of government, culture and income level. After promising starts and progress in those countries (phase 1), in 2011, a second grant was awarded, and programmes were established in four additional countries (phase 2): Mozambique, Tanzania, Nepal and Uganda.

CDDEP has provided support in each country for three to five years, after which countries are expected to raise the modest amounts needed to sustain the working group and any activities that it chooses to do.

GARP working groups

CDDEP found no models for the proposed approach, which was to create multidisciplinary, multisectoral groups and empower them to participate in a national policy process. The aim was that they would become trusted advisers to government, professional groups and the public (e.g. through the media). The working group members would be volunteers, but a paid staff person (the coordinator) was essential for the group to be productive.

CDDEP identified potential working group members in each country through literature searches and networking with professional contacts. Chairpersons were selected for their stature in the scientific and/or academic community and for affiliation with a prominent academic or scientific organization. In two cases (Vietnam and Uganda), the secretariat itself is the prominent organization and a principal investigator has assembled the working group, including the chairperson, in consultation with CDDEP.

From the beginning, GARP working groups included experts in both human and veterinary medicine, from the public and private sectors, and represented a range of scientific and health disciplines. Invariably, some group members were acquainted with or knew of other members, but no one knew everyone else; the mix of disciplines (especially animal and human sciences) was unusual – and is one of GARP's hallmarks. Moreover, in no country does the GARP working group duplicate another group, although interests may overlap (e.g. in Kenya, the Infection Prevention Network-Kenya [IPNET-Kenya], started by the GARP-Kenya vice chair, deals with infection and antibiotic use in hospitals). In some countries, the GARP working group is the only entity inside or outside government with the antibiotic resistance mandate.

GARP-Kenya and GARP-South Africa are offered as examples of successful programmes.

GARP-Kenya

Kenya was the first GARP project, beginning work in 2009 with a "situation analysis," which has become standard for

newly organized GARP projects. The situation analysis was not focused narrowly on studies of antibiotic resistance but looked at a range of factors impinging on antibiotic use and access in both humans and animals: the burden of infectious disease, which vaccines are in use and the coverage rates, the antibiotic supply chain, antibiotic use patterns and variation in these characteristics around the country. The situation analysis was the foundation document for the working group to define an evidence-based policy agenda for the coming years, including a research agenda aimed at filling important information gaps.

The situation analysis had additional value in Kenya, as elsewhere, as a means of building cohesiveness among the working group with a high-quality collaborative product that was recognized externally as authoritative and novel. It was a calling card that could be used to approach government and others and signaled seriousness of purpose.

Gap-filling research

CDDEP offered to fund small research projects (on the order of US\$ 10,000) that would produce information to fill important knowledge gaps identified in the situation analysis. In Kenya, two projects were funded.

1. Antibiotic use in food animals

This was a first-of-its-kind study of antibiotic resistance levels in bacteria cultured from carcasses (of cows, pigs and chickens) in slaughterhouses and in retail meat, coupled with interviews of farmers and herders in the same areas from which the slaughtered animals came. The bacterial sampling, culture and analysis were carried out by Dr Samuel Kariuki, chair of the GARP-Kenya working group, and Patrick Irungu, a young academic agricultural economist who has since become a member of the working group, conducted the fieldwork. The farmers and herders were asked about many things, including their practices related to antibiotics use.

This project was small and limited to the area around Nairobi, but it was used as a pilot to approach FAO for a larger project involving a nationwide sample, which has been completed.

Antibiotic use was widespread among all farmers and herders. Tetracyclines, sulfonamides, penicillins and streptomycins were the most frequently used. Most antibiotics were purchased directly at agro-vet stores, without the intervention of veterinarians (mainly because they are scarce and inaccessible for most animal husbandry men). Antibiotic resistance was equally prevalent in samples from all three types of animals: most bacteria cultured from beef were resistant to most of the commonly used

antibiotics, about half those cultured from chicken were resistant to some antibiotics and a smaller percentage of those cultured from pigs were resistant.

Other findings suggested effective interventions. One, in particular, was that nongovernmental organizations (NGOs) that provided support to farmers and herders often gave them free antibiotics. Not surprisingly, this increased antibiotic use (though it was not necessarily appropriate use). NGOs also provided other types of support – restocking, water provision and animal dips for parasites – that had no effect on antibiotic use.

This study (awaiting publication) provided a baseline and some interesting findings but also opened the conversation about antibiotic use in food animals.

2. Knowledge, attitude, perception and pricing of antibiotics in hospitals in two areas of Kenya

Another small study in and around Nairobi and in western Kenya in Nyanza province, was conducted by the Ecumenical Pharmaceutical Network, led by Donna Kusemererwa, then vice-chair of the working group and current vice-chair of the new GARP-Uganda working group. The study included public, private and mission hospitals in both regions. At least four individuals were interviewed at each hospital: a medical professional and one person each from pharmacy, laboratory and administration.

Not surprisingly, the large majority of professionals interviewed in the study were aware of the seriousness of antimicrobial resistance as a national problem, but many fewer found it a problem at their own hospital. The survey (awaiting publication) points to missing information (e.g. a survey of practices) and indicates what is and is not known by health professionals.

The associated study of antibiotic pricing (1) found that cash-flow problems force hospitals to engage in significant purchasing of small lots, even though large-quantity purchases result in lower costs per dose. It also found a wide range of markups – from 50% to 400% – for individual antibiotics, depending on where they were sold.

GARP-Kenya 2014

GARP-Kenya has matured into an independent group, incorporating in 2014 as an autonomous arm of IPNET-Kenya. A sampling of its recent activities includes the following:

- ▶ November 2013: two-day workshop on antimicrobial stewardship in Mombasa, with participation from around Africa (and Haiti), following an infection prevention and control meeting;

- ▶ November 2013: presentation on antimicrobial stewardship to the National Infection Prevention Control Committee at the invitation of the Infection Prevention and Control Unit of the Ministry of Health;
- ▶ February–March 2014: presentations on antimicrobial use, with the Ministry of Health, to the health executive members in each county (formerly states) on antimicrobial use in Kenya;
- ▶ November 2014: the second “antibiotic awareness week” in Kenya.

After several years of CDDEP nurturing, GARP-Kenya has become a trusted adviser to government and a recognized source of expertise for the country.

GARP-South Africa

Success in South Africa looks very different. An antimicrobial resistance summit was held in Johannesburg in October 2014, to introduce an “Antimicrobial Resistance National Strategy Framework for South Africa” and secure commitment of stakeholders to its implementation. The framework is the culmination of several years of work, which was set in motion by the publication of the GARP-SA situation analysis in the *South African Medical Journal* in 2011. GARP continues to support this work.

The GARP Network

The first four GARP country projects have evolved in somewhat different directions, but have all succeeded in creating a hub of antibiotic resistance expertise and activity. In Vietnam, for example, the secretariat is the Oxford University Clinical Research Unit (OUCRU) in Hanoi. The working group is chaired by Dr Nguyen Van Kinh, Director of the Infectious Disease Hospital (under the Ministry of Health) in which OUCRU is housed. GARP-Vietnam therefore has close ties to government. The GARP “brand” has been useful in setting policy research apart from purely scientific and clinical work, and gives voice to the policy implications of basic research.

GARP working groups in other countries – for example, Kenya and Nepal (where the secretariat is the Nepal Public Health Foundation) – have found value in being totally independent of their governments because of turnover and even new constitutions. While it is important for governments to take action on antibiotics, the value of authoritative groups outside government has obvious value.

GARP – Uganda is the last of the eight GARP projects started under the Gates Foundation grants; its inaugural meeting was held in February 2014. The secretariat is

lodged in the Uganda National Academy of Sciences, an organization whose main mission is to advise the government.

In addition to country-specific activities, GARP working group members are regular participants in global discussions on antibiotic resistance.

Moving forward

CDDEP is committed to maintaining GARP, expanding it and strengthening the partnership. CDDEP researchers continue to conduct innovative research on antibiotics and antibiotic resistance globally, for example, a study that quantified, for the first time since 1987, antibiotic consumption in 63 countries between 2000 and 2010 (2) and a call for global action in *The Lancet Infectious Diseases* (3).

In a move mirroring the development of GARP after work in the United States, CDDEP has also begun constructing a global version of Resistance Map (<http://cddep.org/projects/resistance-map>), an interactive tool to explore the evolution of antibiotic resistance in a set of pathogens over time in North America and Europe.

Conclusion

GARP has succeeded in bringing a set of new voices to the antibiotic resistance issue and to establishing local capacity to develop and help to implement evidence-based policies in eight LMICs. •

Acknowledgements

The author acknowledges support from the Graduate Institute of International and Development Studies (Geneva), the Royal Institute of International Affairs, the Institute of Chatham House (London), and the Center for Disease Dynamics, Economics & Policy.

Hellen Gelband is Associate Director for Policy at the Center for Disease Dynamics, Economics & Policy (CDDEP). Her work spans infectious disease, particularly malaria and antibiotic resistance, and non-communicable disease policy, mainly in low- and middle-income countries. Before joining CDDEP, then Resources for the Future, she conducted policy studies at the (former) Congressional Office of Technology Assessment, the Institute of Medicine of the United States National Academies, and a number of international organizations.

References

1. Kusemererwa D, Kariuki S, Winters C, Braykov N, Megiddo I, Plant S, & Wesangula E. (2013). Survey of antibiotic prices in public, private, and mission district-level hospitals in Kenya. *Pharmaceutical Journal of Kenya*, 21(3), 208.
2. Laxminarayan R, Duse A, Wattal C, Zaidi AKM, Wertheim HFL, Sumpradi N and Cars O. (2013). Antibiotic resistance—the need for global solutions. *The Lancet Infectious Diseases*, 13(12), 1057–98. doi:10.1016/S1473-3099(13)70318-9
3. Van Boeckel TP, Gandra S, Ashok A, Caudron Q, Grenfell BT, Levin SA, & Laxminarayan R. (2014). Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. *The Lancet Infectious Diseases*, 3099(14), 1–9. doi:10.1016/S1473-3099(14)70780-7