

SITUATION ANALYSIS AND RECOMMENDATIONS

Antibiotic Use and Resistance in Kenya

Executive Summary



The GARP-Kenya National Working Group

Dr. Samuel Kariuki, Chairman

August 2011

GARP-Kenya Working Group

- Sam Kariuki**, PhD, *Chairman*, Principal Researcher, Kenya Medical Research Institute (KEMRI)
- Moses Gichia**, BVM, MSc, Department of Veterinary Services, Ministry of Livestock Development
- Patrick Irungu**, PhD, Department of Agricultural Economics, University of Nairobi
- Rose Kakai**, PhD, School of Public Health and Community Development, Maseno University
- Donna Kusemererwa**, MPharm, MBA, Executive Director, Ecumenical Pharmaceutical Network
- William Macharia**, MBChB, MMed, MSc, Chair, Department of Pediatrics, Aga Khan University
- Tom Menge**, BPharm, MSc, Pharmaceutical Director, Kenyatta National Hospital
- Linus Ndegwa**, MPHE, HCS, PGD Ophth, Program Manager, Infection Control, Centers for Disease Control and Prevention
- Beatrice Olack**, MPHE, Surveillance Coordinator, International Emerging Infections Program, KEMRI/CDC
- Elizabeth Ominde-Ogaja**, MSc Pharm, Deputy Chief Pharmacist, Ministry of Medical Services; and Secretary to the Kenya National Medicines and Therapeutics Committee
- Jennifer Orwa**, PhD, MSc, BPharm, Kenya Medical Research Institute (KEMRI)
- Jayesh Pandit**, MPharm, Head, Department of Pharmacovigilance, Pharmacy and Poisons Board, Ministry of Medical Services
- Gunturu Revathi**, MD, Associate Professor, Division of Microbiology, Director of Pathology, Aga Khan University Hospital

GARP-Kenya staff

- Cara Winters**, GARP-Kenya Country Coordinator, Center for Disease Dynamics, Economics & Policy (until May 2011)
- Hellen Gelband**, Associate Director, Center for Disease Dynamics, Economics & Policy
- Ramanan Laxminarayan**, GARP Principal Investigator, Director, Center for Disease Dynamics, Economics & Policy

Recommended citation: Global Antibiotic Resistance Partnership—Kenya Working Group. 2011. *Situation Analysis and Recommendations: Antibiotic Use and Resistance in Kenya, Executive Summary*. Washington, DC and New Delhi: Center for Disease Dynamics, Economics & Policy.

Foreword

Since their discovery in the early 20th century, antibiotics and related medicinal drugs have substantially reduced the threat posed by infectious diseases. Over the years, these antimicrobials have saved the lives and eased the suffering of millions of people, especially in developing countries where infectious diseases remain a big challenge. Even in conditions of abject poverty and poor infrastructure and services, antibiotics have worked wonders. These gains are now seriously jeopardised by the emergence and spread of microbes that are resistant to most commonly available and effective ‘first-line’ drugs. For most of sub-Saharan Africa, the arsenal of antibiotics is already very limited. Any breach on the list leads to near-total loss of treatment choices for many severe infections.

In Kenya, the bacterial infections that contribute most to human disease are often those in which resistance is most evident. Examples are multidrug-resistant enteric bacterial pathogens such as typhoid, diarrhoeagenic *Escherichia coli* and invasive non-typhi salmonella, penicillin-resistant *Streptococcus pneumoniae*, vancomycin-resistant enterococci, methicillin-resistant *Staphylococcus aureus* and multidrug-resistant *Mycobacterium tuberculosis*. Resistance to medicines commonly used to treat malaria is of particular concern, as is the emerging resistance to anti-HIV drugs. Often, more expensive medicines are required to treat these infections, and this becomes a major challenge in resource-poor settings.

Although overuse and misuse of antimicrobials have contributed to the emergence and spread of resistance, paradoxically, underuse through lack of access, inadequate dosing, poor adherence, and substandard antimicrobials may play an equally important role. And of course, complete lack of access can mean death, especially for infants and children. A great hindrance to fixing these problems is the difficulty of implementing policies and guidelines, usually a result of inadequate regulatory authority and insufficient resources for enforcement. Loud whispers of ‘capsule! capsule!’ at busy and crowded bus stops are common as peddlers hawk drugs on the street. In many chemist shops across Kenya one easily purchases antibiotics (any proportion of actual dosage) over the counter, without prescription.

Even with the best intentions to implement guidelines for improving the use of antibiotics, we cannot. Local data on usage and resistance are inadequate to give a true reflection of the situation in Kenya, and the resources to do the job are not available. Only well-coordinated national surveillance will provide the necessary data for risk analysis and risk assessment. Our central reference laboratory will require personnel and funding support to take up this role. The situation analysis presented here gives a bird’s-eye view of the usage and resistance data currently available for Kenya, and the recommendations have been tailored to the situation as we understand it. Using this and information from other parts of Africa and the world, we can plot a course for the short term and beyond by thorough analysis of the policy options open to us. We must make the case that taking steps to control antibiotic resistance is worthwhile and that we can make a difference at reasonable cost. That is our challenge for the next year. We welcome ideas, comments and assistance from all quarters. I invite you to read, reflect and share your ideas with me and other members of the GARP Working Group–Kenya.

Samuel Kariuki

Director of the Centre for Microbiology Research, Kenya Medical Research Institute

Executive Summary

The past decade has been a period of positive change for the public health of Kenya. Looking ahead, the constitution adopted in August 2010 declares health a ‘basic human right’. According to results from the 2010 Demographic and Health Survey, poverty and child mortality have decreased, and a larger proportion of the population has access to healthcare—including life-saving antibiotics. Despite these improvements, the infectious disease burden in Kenya remains high. This combination of improved access to medication and demand for antibiotic treatment in fighting infections has brought with it an uninvited but not unexpected guest: antibiotic resistance.

As with other shared resources, antibiotics consumed by an individual—whether the individual benefits from the antibiotic or not—‘uses up’ a bit of the effectiveness of that drug. As antibiotics become less effective, Kenyan citizens and the government will be forced to either pay more for newer drugs to replace the inexpensive standards or forgo treatment because it is too costly. In some cases, antibiotic resistance rates are already high. The eventual loss of antibiotics that are now effective is inevitable, but it can happen years from now or decades from now, depending upon near-term actions. The growth of resistance rates can be slowed and even reversed as the health of the public is enhanced, by preventing many infections through vaccination; by better targeting antibiotic use for curable bacterial infections rather than viral, fungal, or parasitic illness; and by reducing non-therapeutic uses of antibiotics in livestock and poultry.

The Global Antibiotic Resistance Partnership (GARP), now completing its initial phase, aims to develop policy responses to manage antibiotic effectiveness through the actions and recommendations of multidisciplinary working groups representing both the public and private sectors, which consider the conditions and characteristics that determine what policy changes are feasible and likely to have an effect in the local context. In addition to Kenya, the three other founding GARP countries are India, South Africa and Vietnam. Each has gone through a similar process to assess the current situation and develop a menu of tailored policy options. In the next phase, the Working Groups in each country will finalize detailed recommendations (in a process described below) and new countries will join the Partnership.

Antibiotic Resistance

Around the world, bacterial pathogens are becoming ever more resistant to antibiotics. The ‘first generation’ of antibiotics is already of little use in many countries. Now some of the more expensive second- and third-generation antibiotics are losing effectiveness against infectious diseases common in low- and middle-income countries. The World Health Organization (WHO) has an ongoing initiative to develop interventions for reclaiming the effectiveness of antibiotics against global and local strains of resistant bacteria.

There can be no doubt that Kenya is already experiencing high levels of antibiotic resistance, and in most cases, it is worsening. Exactly how high the rates are currently or how quickly they are increasing is not known with any certainty, however, because antibiotic resistance surveillance is not systematically conducted in the country. Findings of high rates of resistance—for respiratory infections, for enteric infections and for infections acquired in healthcare facilities—indicate that many antibiotic regimens supplied by the government are unlikely to be effective against infections of wide concern.

Respiratory Infections

Streptococcus pneumoniae. Twenty-five percent of *S. pneumoniae* isolates in Nairobi were resistant to penicillin in the mid-1980s, and by 2003, 43 percent were resistant (Paul, Bates et al. 1996; Kariuki, Muyodi et al. 2003). Half were resistant to cotrimoxazole in 2002, and 7 percent were resistant to two or more first-line treatments (Mwangi, Berkley et al. 2002; Kariuki, Muyodi et al. 2003).

***Haemophilus influenzae* type B.** For children in Kilifi, the combination of amoxicillin plus chloramphenicol was effective against *H. influenzae* type B half the time in 2001 but only 32 percent in 2002 (Scott, Mwarumba et al. 2005). Up to 66 percent of isolates were resistant to cotrimoxazole in 2002 (Mwangi, Berkley et al. 2002; Kariuki, Muyodi et al. 2003).

Severe pneumonia. In 2005, half the children with severe pneumonia were infected with isolates that were resistant to penicillin in the laboratory (Berkley, Maitland et al. 2008).

Diarrheal Infections

Bacterial diarrhoea. In 2001, more than half the pathogens in the Western province were not susceptible to first-line antibiotics, and three-quarters were resistant to three or more agents (Shapiro, Kumar et al. 2001; du Prey, Ford et al. 2004).

Non-typhi *Salmonella* (mainly gastrointestinal infections). In the mid-1990s, more than 45 percent of isolates were resistant to ampicillin, cotrimoxazole or both. By 2005, resistance had risen to 94 percent for ampicillin and 67 percent for cotrimoxazole (Kariuki, Gilks et al. 1996; Kariuki, Revathi et al. 2005; Kariuki 2009). Reports of multi-drug resistant Non-typhi *Salmonella* in hospital and community settings are also cause for concern, rising from 31 percent in 1993 to 42 percent in 2003 (Kariuki, Revathi et al. 2005; Kariuki 2010). Isolates also demonstrate resistance to extended-spectrum cephalosporins and fluoroquinolones.

Dysentery (*Shigella* spp). As early as 2003, *Shigella* isolates were highly resistant to ampicillin (85 percent), cotrimoxazole (94 percent), chloramphenicol (91 percent) and tetracycline (100 percent) (Bartoloni and Gotuzzo 2010). Frequently, isolates are resistant to all of these antibiotics and to coamoxiclav (Kariuki, Gilks et al. 1996).

Typhoid fever (*Salmonella Typhi*). The spread and gradual replacement of drug-sensitive strains of *Salmonella Typhi* with multidrug-resistant strains threatens to reduce clinical options for treating typhoid fever (Kariuki 2010). Surveillance at Kenyatta National Hospital indicates that the prevalence of *S. Typhi* resistant to two or more antibiotics has been rising, from 50 percent in 1998 to 70 to 78 percent in 2004 (Kariuki, Revathi et al. 2004; Okeke and Ojo 2010). From 2000 to 2002 in Nairobi, Embu district and Thika, 82 percent of the strains were resistant to each of the five commonly used drugs—ampicillin, chloramphenicol, tetracycline, streptomycin and cotrimoxazole (Kariuki, Revathi et al. 2004).

Nonpathogenic 'commensal' bacteria. In young children, nonpathogenic *Escherichia coli* isolates are highly resistant to the second-line agent ciprofloxacin and common antibiotics like cotrimoxazole (68 percent), tetracycline (71 percent) and ampicillin (66 percent) (Bii, Taguchi et al. 2005; Kariuki 2009; Kariuki 2010). In Kilifi, *E. coli* exhibited resistance levels as high as 85 percent to cotrimoxazole, 78 percent to amoxicillin and 42 percent to chloramphenicol (Bejon, Mwangi et al. 2005).

Hospital-Acquired Infections

Hospital-acquired infections (HAIs) are a problem worldwide. HAIs increase the likelihood of death, prolong hospital stays, and can be very expensive to treat. And because antibiotics are so heavily used in hospitals, hospitals are perfect breeding grounds for antibiotic resistance. In Kenya, only a few studies have reported HAI rates. These suggest that up to 17 percent of neonatal patients and 40 to 50 percent of intensive-care unit (ICU) patients become infected. As in other countries, surgical site infections, infections of the urinary tract and pneumonias are the most common.

Factors Affecting Antibiotic Resistance Rates

Burden of Infectious Disease

The top five killers in Kenya are infectious diseases, but data documenting the portion caused by bacterial pathogens are not collected systematically. Most of what is known comes from site-specific, hospital-based studies. Yet the majority of illnesses and deaths occur outside the hospitals, where diagnostic facilities are few.

Acute respiratory infections (ARIs) are the second leading cause of death in all ages across the country, with pneumonia as the largest contributor to the burden of disease among children living in ‘urban informal settlements’ or slums. Diarrhoeal disease in Kenya ranks third as a cause of death, contributing to 16 percent of all mortality in children under five. Specific forms range from watery diarrhoea, treatable with oral rehydration therapy, to regular outbreaks of cholera, typhoid fever, shigella dysentery, and non-typhoidal salmonella. ARIs and diarrhoeal episodes are among the most frequent reason for antibiotic prescription and sales and are often diagnosed empirically. Their high incidence rate and the difficulty of determining their exact etiology remain critical challenges to rationalizing antibiotic use in Kenya.

HIV/AIDS, the country’s leading cause of death in all ages, and malnutrition predispose people to invasive bacterial disease and pneumonia. Antibiotics are increasingly used to prevent and treat opportunistic infections in people living with HIV. Many take cotrimoxazole daily as prophylaxis, raising concern over the emergence and spread of resistance to this cheap and well-tolerated drug.

Healthcare Environment and Behaviour

Antibiotics are also misused—their effectiveness wasted—in patients with conditions that cannot be cured by antibiotics. This practice is common not only among people who purchase antibiotics themselves, but also by doctors and other licensed prescribers. Studies from Kenya have uncovered an array of possible reasons for this behaviour that is similar to what has been found in other countries:

- lack of microbiology facilities and diagnostic capacity;
- fear of negative outcomes if antibiotics are withheld, particularly with malaria patients;
- limited access to formal healthcare services and the prevalence of self-medication; and
- insufficient knowledge about appropriate use of antibiotics.

Lack of diagnostics and fear of negative outcomes. Patients who make it to the hospital often arrive with serious infections, but in many places in Kenya, microbiology services are limited to nonexistent. In cases of life-threatening diseases, a culture result often takes longer to obtain than the time necessary to correctly treat the patient at risk of death. Frequently, the expense of laboratory services (often paid directly by the patient), where available, is beyond patients’ means, and they decline a culture test. The infecting organism (bacterium or not) cannot be identified in such contexts, nor can its antibiotic resistance profile be determined in the event of bacterial disease. Thus, broad-spectrum antibiotics are applied. Improved use and quality of diagnostics that match pathogens with narrow-spectrum antibiotics could avert some of the resulting loss in effectiveness and would certainly avoid the use of antibiotics for viral and other diseases.

Access and self-medication. Since independence, Kenya’s government has given high priority to improving the health status of citizens and has recognised health as a prerequisite to social and economic development. Health spending in Kenya has decreased, however, since reforms in 2002, from 9 percent to less than 6 percent of the government budget at present (Ministry of Health 2007; Ministry of Finance 2009). Of total health expenditures, the government share is low, 30 percent, compared with 75 percent in developed

countries. Households provide the largest share, 53 percent, through user fees (World Health Organization 2006; Wamai 2009). This means that currently, healthcare financing is dependent primarily on household out-of-pocket expenditures. Meanwhile, the 2009 Budget Strategy Report recommends a *decrease* in government health spending.

Inadequate access to formal healthcare and medicines leads to self-medication and fuels irrational use through underdosing and poor adherence. Access is difficult to define but plays an important role in people's healthcare decisions, including those concerning antibiotics. The high costs faced by patients in the formal healthcare system encourage them to bypass providers and purchase medicines without receiving a diagnosis. Around half of ill patients visiting the hospital previously seek care from informal drug sellers in rural, western Kenya and more than one-third of Nairobi residents use retail pharmacies as the first site for outpatient care (Kakai and Wamola 2002; Kwena, Sharma et al. 2008; Thoithi and Okalebo 2009; Bigogo, Audi et al. 2010; Karambu 2011). Legally, a prescription is required, yet consumers can purchase antibiotics over the counter at pharmacies and other shops. An estimated 70 percent of pharmacies dispense antibiotics without a doctor's prescription (Kakai and Wamola 2002; Kwena, Sharma et al. 2008; Thoithi and Okalebo 2009; Karambu 2011).

But while self-medication is very common, it is not very accurate. Staff at retail pharmacies, many of which are unlicensed and poorly managed, may recommend the wrong treatment or provide incorrect dosage levels. Patients with limited incomes may want to purchase only part of a recommended course and can more easily negotiate this practice at a local shop than in a formal healthcare facility. To stem the tide of antibiotic resistance, policymakers look for ways to limit antibiotic use—for example, by enforcing 'prescription only' laws for antibiotic sales. The situation is not simple, however. In Kenya, one is confronted with evidence of both overuse and underuse. The evidence for underuse—a lack of access to antibiotics—comes from the large proportion of deaths from pneumonia during infancy and childhood, which would not occur if those children were properly treated with antibiotics.

Although access is related to socioeconomic status, the reasons may not be directly financial; low education levels, lack of nearby facilities, and inconsistent presence of both medicines and healthcare workers also contribute. Would even more people go untreated and die if nonprescription access were cut off? In Kenya, we do not have the data to answer this question.

Lack of knowledge. Despite national treatment guidelines and other information, knowledge about antibiotic use is poor among healthcare workers. ARI and diarrhoea management often includes antibiotics, whether needed or not. When antibiotics are indicated, the type, dosage and duration of treatment prescribed by health workers are not necessarily consistent with the guidelines. For example, in district hospitals, nearly three-quarters of the antibiotics prescribed for pneumonia were for very severe cases even though only 16 percent of recorded admissions fell into this category (English, Esamai et al. 2004). In a survey of providers' knowledge about watery diarrhoea, 71 percent of clinicians cited antibiotics as among the most effective treatments (Ram 2008). Misinformation among health workers regarding the antiviral properties of common antibiotics was also frequent, with 73 percent of clinicians reporting that antibiotics kill viruses causing diarrhoea.

Antibiotic Use in Animals

Evidence on antibiotic use in farm animals indicates that these medicines are used primarily (90 percent) for therapeutic applications. Further investigation is warranted, however, since a survey of farmers found that the majority conflated treatment with prevention, effectively replacing hygiene and feeding practices as standard disease preventions with disease treatment (Kariuki, Gilks et al. 1997). Growth promotion does not appear to be an important source of antibiotic use in livestock production in Kenya.

More than half of the antibiotics used in livestock production are tetracyclines, popular for their broad-spectrum activity and relative affordability (Mitema, Kikui et al. 2001). Sulfonamides follow at around 21 percent, with aminoglycosides, beta-lactams, quinolones and macrolides constituting the rest. Poultry alone accounts for nearly one-fifth of mean consumption per year. The remaining consumption is shared among large animal—cattle, sheep, pigs and goats. Presently, antibiotic use in fisheries is unknown, but may become an important issue as the industry grows.

In Kenya, like most of the African continent, there is no formal system for surveillance of antibiotic resistance in agricultural bacterial isolates. The Department of Veterinary Services does, however, monitor antibiotic residue in agricultural products. A few studies indicate resistance to tetracycline and sulphonamides among chicken and swine bacterial isolates, possibly related to the crowded conditions in which the animals are housed and the greater potential for the spread of disease. An estimated 36 percent of salmonella isolates in pork tissue demonstrated resistance to ampicillin, tetracycline, streptomycin and chloramphenicol. Although ampicillin, tetracycline and streptomycin are easily available to farmers, chloramphenicol is not approved for use in food animals. Resistance, therefore, may indicate illegal use of the drug. Patterns of resistant *Staphylococcus aureus* in cattle imply a significant difference in resistance profiles of large- and small-scale farms, with smaller producers using nearly twice the amount of antibiotics per animal compared with larger producers (Shitandi and Sternesjö 2004). The prevalence of multidrug resistance, at 34 percent on small farms, was likewise almost double the rate found at large farms.

Although laws regulate the use of drugs in animal feed, enforcement and monitoring are inadequate. The Kenya Veterinary Association recently found that 78 percent of veterinary medicine outlets are operated by people not considered legally qualified for the position (Kenya Veterinary Association 2009). As with the human population, lack of access to professional diagnosis spurs self-medication, with farmers purchasing antibiotics from retail pharmacies in an environment of limited veterinary services. Reducing demand through improved sanitation and restricting use to when antibiotics are needed are policy options that deserve greater exploration.

Efforts to Address Antibiotic Resistance

Kenya has an array of policies that, while not directly aimed at containing antibiotic resistance, have proven effective at reducing the demand for and associated irrational use of antibiotics in other countries. They include adoption of the WHO-recommended *Haemophilus influenzae* type b (Hib) and 10-valent pneumococcal conjugate vaccines to prevent frequent causes of pneumonia; the launch of national hospital infection control guidelines; and support of surveillance of bacterial disease and resistance profiles in humans and antibiotic residues in livestock. Other facility-based measures, such as professional education and surgical checklists, are more site- and context-specific. Many of these interventions have yet to be thoroughly evaluated for their effectiveness in Kenya.

Surveillance. National surveillance for antibiotic resistance is a low government priority—lower than microbiology services for patient care. However, efforts exist within Kenya to provide quality surveillance on the resistance trends in clinically significant pathogens. These include facility-level reports on resistance patterns in HAIs (U.S. Centers for Disease Control and Prevention offices in Kenya [CDC-Kenya]), the number of episodes and drug susceptibility profiles of pneumonia (KEMRI - Wellcome Trust Research Programme), and tracking drug resistance, use and MRSA infections at Aga Kahn University Hospital in Nairobi. The Department of Veterinary Services monitors antibiotic residue in agricultural products for purposes of food safety, and the Kenya Medical Research Institute started a country-wide surveillance study on antibiotic resistance rates in poultry.

GARP–Kenya Research

One of the aims of GARP–Kenya is to fill information gaps by identifying the groups working on resistance issues nationally and supporting their research. Projects during the first phase of GARP included two areas not well studied in Kenya:

- **Survey on perceptions of antibiotic resistance and use in district hospitals**

Ecumenical Pharmaceutical Network, Donna Kusemererwa (PI)

Data on antibiotic prices, profitability to the supplier, and affordability to the patient or consumer were gathered, along with information on the volumes of antibiotics stocked at various district hospitals. Researchers also surveyed the knowledge and perceptions of health workers in hospitals to inform interventions focused on raising awareness and conducting education campaigns. The results from this study are found in Part IV (Antibiotic Use and Supply Chain).

- **Antibiotic resistance in livestock and associated follow-back survey on antibiotic use in livestock producers**

Kenya Medical Research Institute, Centre for Microbiology Research, Samuel Kariuki (PI), and University of Nairobi, Patrick Irungu (PI)

This pilot study lays the groundwork for ongoing surveillance of antimicrobial resistance and use in farm animals. It first determined patterns of resistance in *Salmonella* spp, *Campylobacter* spp, *Escherichia coli*, and *Enterococcus* spp isolates collected from healthy livestock and animal products found at retail meat outlets. Second, it assessed whether low or high resistance patterns were correlated with demographic and behavioural factors of animal husbandry, including the volumes and applications of antibiotics used in livestock production. Specific findings can be found in Parts III (Burden of Disease and Antibiotic Resistance) and IV (Antibiotic Use and Supply Chain).

Vaccines and prevention. Vaccines are among the best ways to prevent bacterial disease. In 2001, Kenya was among the first nine countries to introduce the Hib vaccine into routine immunisation services, dramatically cutting the annual incidence of Hib meningitis from 71 to 8 and Hib pneumonia from 296 to 34 per 100,000 children under five years (Sinha, Levine et al. 2007). Following the success of the Hib vaccine, the government introduced the 10-valent pneumococcal conjugate vaccine in February 2011. As coverage expands for these vaccines, mortality is expected to be cut by half in young children (English and Scott 2008).

Insurance and access. Who pays for healthcare—for antibiotics, for vaccines and for services in general—is important. Kenya’s current heavy reliance on out-of-pocket expenditure affects decisions about whether to seek formal healthcare, purchase a drug directly, or visit an informal provider. To improve the situation, Kenya is attempting to expand health insurance through the National Hospital Insurance Fund (NHIF). The NHIF board has proposed a progressive increase in statutory contributions, to enable the fund eventually to provide universal healthcare, including medicines. An estimated seven percent of the population is currently enrolled in health insurance through NHIF.

The drive for greater insurance coverage is not without controversy, however. NHIF’s chequered past includes fraud and mismanagement, causing concern that an increase in fees will not bring added benefits or expanded membership.

Infection control. The Ministries of Health launched national and site-specific policies and guidelines on infection control in December 2010. The policy calls prevention and control of infections ‘essential cornerstones’ in addressing the emergence of antibiotic resistant bacteria and notes resistance as a ‘major problem for patient safety’. It also states that the increase in antibiotic-resistant organisms ‘undermines progress made in the fight against infectious disease and poses a serious challenge to healthcare systems’.

As part of its vision, the policy intends to respond to resistance by providing guidance to healthcare workers on ensuring the safe management of infectious conditions. Although these guidelines are an important step towards national recognition of the issue, their ability to lower rates of hospital-acquired infections and reduce the development of antibiotic resistance is unknown.

Recommendations: Interventions against the Development and Spread of Resistance

Ideally, new policies would be designed to improve access to antibiotics where it is lacking and where the drugs might save lives, at the same time curtailing use where these drugs are unnecessary. Unfortunately, the evidence supporting interventions invariably comes primarily or exclusively from outside Kenya, and only a small amount from other low- and middle-income countries. As a result, the approaches that are emphasised generally do not concern improving access. With awareness of potential adverse effects on access, however, modifications could be made to avoid them.

- Three main approaches are applicable in Kenya:
- increased use of vaccines that reduce disease and, therefore, the demand for antibiotics;
- improved infection control, including procedures (e.g., hand hygiene, checklists) and information (e.g., guidelines, feedback), particularly in hospitals; and
- education and public awareness campaigns for providers and consumers.

The success of all approaches is dependent on better information from microbiology laboratories, in the form of surveillance. The specifics of developing an appropriate nationwide surveillance system and standardizing methods must be determined, but without knowing where we are with antibiotic use and resistance and a way to monitor changes over time and different between places, we will never know what is and is not working.

Three additional approaches deserve mention though they are not immediately implementable. They are:

- Increased use of (and improved) diagnostics, to better target antibiotic use,
- Fixing supply chain constraints and failures and
- Developing economic incentives (which may involve subsidies) to encourage better use of antibiotics

In March 2011, the Global Antibiotic Resistance Partnership (GARP)–Kenya Working Group, in collaboration with the Center for Disease Dynamics, Economics & Policy (CDDEP), convened a policy development workshop to identify ways stakeholders across diverse sectors and specialties could respond to the emergence of antibiotic resistance. The summary table (Table 1) outlines the policy actions discussed, their benefits and feasibility. Ongoing collaboration and discussion will be vital to determining implementation strategies for each recommendation. Facilitating consultations with stakeholders and updating recommendations as necessary will be an important aspect of the next phase of the GARP–Kenya agenda.

Focus Areas

In addition to producing necessary information on which to proceed, the recommendations are aimed at *reducing the need* for antibiotics and better *targeting* of antibiotics. Both approaches should lower overall demand. Five critical areas of disease management and access to effective treatment are targeted:

- surveillance and monitoring,
- training and education,
- vaccination,
- quality control and supply chain improvements and
- veterinary use of antibiotics.

Surveillance and Performance Monitoring. Although antibiotic resistance surveillance and performance monitoring do not themselves produce change, without knowing the levels or trends of antibiotic resistance or how key actors are performing, it is impossible to make rational recommendations or monitor the effectiveness of interventions. The prevalence of resistance, influenced by a host of local factors, varies within the country and between pathogens. This is particularly worrying in countries like Kenya, where the majority of infectious diseases are empirically diagnosed and patient management often depends on early, appropriate antibiotic administration.

Surveillance of antibiotic use (including indications) and of antibiotic resistance is recommended. Models that could be adapted for Kenya are available and should be considered.

Training and Education. Training and education can target healthcare staff at hospitals and dispensaries, clinicians and other prescribing health workers, and chemists and workers in private pharmacies, all of who can be sources of health advice and treatment. These groups receive varying amounts of information on antibiotic use and resistance.

Further, even though the development of standard treatment guidelines (STGs) and essential medicines lists (EMLs) in Kenya is cited as a model example, up-to-date guideline revisions are poorly communicated and the documents are hard to access within facilities. When coupled with educational interventions, however, guidelines can improve prescribing.

Vaccination. Every year, millions of children in Africa die before reaching their fifth birthday from treatable illnesses such as pneumonia and diarrhoea. The primary causes of most cases of these diseases—pneumococcus, *Haemophilus influenzae* type B (Hib) and rotavirus—are now preventable through vaccination. The health gains from these vaccines are unmatched by any other interventions. As a secondary benefit, vaccination can also decrease the use of antibiotics by reducing the need for them. In some cases, such as acute diarrhoea, vaccines may reduce unnecessary and inappropriate antibiotic use. A major constraint to introducing new vaccines or increasing coverage is financing, which will not be resolved in relation to antibiotic use or resistance.

Continued emphasis on adding vaccines and improving coverage are recommended. Strategies for this are well established, as are the challenges.

Quality Control and Supply Chain Improvements. The problem of antibiotic resistance cannot be addressed through interventions aimed solely at reducing antibiotic use. In countries where the burden of infectious diseases remains high and barriers to treatment are common, ensuring greater access to effective antibiotics is important. Most people who lack access to antibiotics are struggling with extreme poverty or living in remote areas and may face the highest burden of infectious disease.

The prevalence of substandard antibiotics in Kenya is unknown, yet the issue of poor-quality medicines is widely discussed in the media and inside government ministries. Poor-quality manufacturing, packaging, transportation and storage conditions, as well as counterfeiting can place substandard drugs in patients' hands.

Access to effective treatment also encompasses adequate financing and supply of essential antibiotics. Even if patients can afford medicines and reach a facility, a large number of 'vital' antibiotics listed on the Kenya essential drugs list are absent or in short supply in dispensaries and hospitals.

Each of these problems has been addressed successfully in other low-resource settings, and beginning this process is recommended for Kenya.

Reducing Veterinary Use of Antibiotics. Animals require antibiotics for treatment of infections, but antibiotics are widely used in low doses as growth promoters and for disease prophylaxis. In Europe, it has been demonstrated that much of this use can be avoided without harming animal or human health. The particular actions have been to outlaw the use of antibiotics for growth promotion, to prohibit the use in animals of antibiotics of particular importance to human health and to limit antibiotic residues permitted in food. Since 2010, the Kenyan government has prohibited the use of chloramphenicol and nitrofurans in food-producing animals, including for use in growth promotion but little is known about how effective this ban has been.

As with human, increased adoption and coverage with appropriate animal vaccines is also important and a strategy welcomed by Kenyan farmers.

Finally, education and training about the use of antibiotics and ways to reduce that use for the range of stakeholders may also be of benefit.

Additional Strategies. Three additional strategies would support the four critical areas described above—monitoring and surveillance, training and education, vaccination, and quality control and supply chain improvements—but require further development and detail before being recommended. All may be addressed in the next phase of GARP.

- improved microbiology services and rapid diagnostic testing;
- chemist accreditation; and
- stronger medicine and therapeutic committees in hospitals.

Summary Table of Policy Options

Addressing antibiotic resistance requires action by hospitals, the community, livestock producers, health workers and the government. The table below presents the major action items recommended by the GARP–Kenya Working Group and additional stakeholders. These will be taken up in the next phase of GARP, when 'critical paths' will be developed for those policies with the highest likely impact and feasibility.

Action area	Intervention, policy	Notes	Feasibility
Hospital Infection Control			
Surveillance and monitoring	Conduct HAI surveillance, with public reporting. Document rates of HAIs and, where possible, consequences (mortality, extended hospital stay, attributable cost, resistance).	Useful where HAI rates are mistakenly perceived as low and ICP is presumed good. Studies in other countries show improved infection control practices following outcome surveillance. Could discourage patient transfers and referrals.	Hospitals lack ability to determine HAIs. Referral system makes it difficult to determine origin of infections.
Education and training	<p>Incorporate ICP into all curricula.</p> <p>Base curricula on national ICP guidelines and include activities and projects in hospitals to increase learning.</p> <p>Rely on professional associations to provide schools and trainings. Support IPC curricular development and coordinate across schools and training opportunities through MoH.</p>	Doctors and other clinical staff may not consider themselves part of hospital ICP system. Inadequately trained members of ICCs may lack knowledge or motivation. No studies show long-term improvement in practice from education interventions alone.	Not expensive, but difficult to maintain over time. Members of ICCs and professional associations generally express interest in ongoing education. Requires administrative support to develop curriculum and ensure use in educational settings.
Hospital Antibiotic Use			
Surveillance and monitoring	Conduct resistance and antibiotic use surveillance, with public reporting and STGs based on regional susceptibility data. Document and report resistance rates and, where possible, the consequences (mortality, extended hospital stay, attributable cost). Include antibiotic use rates by department.	Useful where HAI rates are mistakenly perceived as low or without consequence. Potential to address appropriate medicine use, as well as capture emergence and spread of resistance.	Hospitals lack human resource capacity, infrastructure and financial means to perform resistance surveillance. Labs are underutilized.
Education and training	Educate and train all providers on STGs and antibiotic use. For prescribers, focus on new (2010) STGs and antibiotic use and resistance. Conduct audits on prescribing patterns to monitor intervention effect. Include feedback from handouts, group discussions and peer review, or from refresher courses.	Helpful where STGs exist and standards are known but not followed. Studies show that training on STGs plus audits, feedback and peer review reduce antibiotic use. Training alone has little effect; audits and feedback are critical.	At hospital level, not expensive to implement. May be difficult to implement monitoring and feedback at regional or national scale. Hospital administrators must be motivated to adopt practice. Collecting prescribing data is challenging in district-level hospitals.

Community Use

Vaccination

Improve long-term financing for vaccines against bacterial pneumonia (Hib and PCV-10). Build capacity of local manufacturers to produce vaccines for domestic market at reduced prices through technology transfers and private-public partnership.

Can decrease antibiotic use by reducing the need to treat bacterial disease. Long-term financing concerns for national immunization program could be eased by producing vaccines locally at lower cost.

Strategy is relatively untested. Good strategy and implementation models do not exist.

Education and training

Train staff at private pharmacies and provide certification for training. Use one-on-one sessions to train chemist shop owners in antibiotic use, resistance and STGs and laws on prescribing. Follow with small-group training for counter attendants. If possible, collect feedback or conduct sales audits for private pharmacies and chemists.

Study found that one-on-one meetings with pharmacists, followed by small-group training sessions with attendants, improved use of oral rehydration therapy and antibiotics in short term. Long-term effects and generalizability to other health conditions (e.g., acute respiratory infections) are uncertain. No studies show long-term improvement in practice after workshops.

Not expensive to implement. Organizations capable of providing training are available. Unlicensed chemist shops concerned about being discovered and shut down may be reluctant to participate. Turnover of trained staff would undermine effectiveness.

Education and training

Conduct broad public awareness campaign about antibiotic use, coupled with small-group training for mothers about medicines; involve community advocacy groups. Use popular media (radio, TV, newspapers) and gatherings (village market days, mamas groups, community leader meetings) to disseminate messages about antibiotic use, antibiotic substitutes (e.g., oral rehydration therapy), and dangers of self-medication. Consider use of package inserts in literate communities.

Broad media campaign launched with package inserts was effective in Indonesia with small groups of mothers taught to review inserts.

Not difficult to plan or implement. Can replicate models used for other public health campaigns in region.

<p>Insurance</p>	<p>Review expansion of NHIF by committee within PPB or MOMS pharmaceutical division. Consider how NHIF expansion can help or hinder community access to clinical diagnosis and full courses of appropriate antibiotics.</p>	<p>High out-of-pocket costs drive sales of small doses of antibiotics and sharing and hoarding of drugs; insurance may offset this.</p>	<p>NHIF expansion must reach those most in need. Unclear whether mandate will cover those who now buy small doses of antibiotics OTC.</p>
<p>Livestock Use</p>			
<p>Surveillance</p>	<p>Establish national surveillance system for antibiotic resistance and use in livestock production.</p>		
<p>Education and training</p>	<p>Train farmers in alternative methods of disease prevention (e.g., herd and flock hygiene). Consider demonstration booths or lecture sessions on market days, village demonstrations on agricultural hygiene and sanitation, and small-group training sessions with agricultural cooperatives at district or village level.</p>	<p>Education interventions have not had sustainable effect on practice in human medicine. Effect on animal husbandry is unknown.</p>	<p>Unclear who should conduct training for farmers. Cost is unknown: inputs are not expensive, but reaching farmers in rural areas may be costly. Farmers may require demonstration of economic benefit.</p>
<p>Supply chain and vaccines</p>	<p>Review current recommendations for vaccines and rates of vaccination for poultry, cattle and hogs. If necessary, update recommendations to include vaccines that prevent diseases commonly treated with antibiotics. Review and improve coverage of vaccines.</p>	<p>Animal vaccination may reduce therapeutic use of antibiotics by reducing incidence of disease.</p>	<p>DVS policy on vaccinations is unclear. Farmers' access to vaccines is unknown, as is cost of vaccination compared with antibiotic prophylaxis and treatment. Field assessments show that demand for vaccines is high and farmers want to learn more.</p>

Government Regulation and National Health System

<p>Quality control</p> <p>Enhance anticounterfeit and medicine quality control efforts. Consider education for judiciary, improved reporting channels, public information campaigns, routine surveys of medicine quality, blister packaging, and mPedigree platform.</p>	<p>Options listed have shown some effectiveness in case studies. Legal measures have not proven significant.</p> <p>Can be used as advocacy tool with government and as assessment tool at facility level. Guidelines have shown little effectiveness without training and education.</p>	<p>Enforcing regulations would be difficult. Such interventions lack funding support from donors and international agencies.</p> <p>Feasible and relatively simple to produce but will take time to develop.</p>
<p>Education</p> <p>Create national antibiotic guidelines ('guideline of guidelines for antibiotics') listing clinical situations in which antibiotics can be used and describing economic and health costs of resistance. Provide training for health workers on using guidelines.</p>		
<p>Supply chain improvement</p> <p>Place price or mark-up controls on antibiotics to increase access. Legislate a maximum retail price on essential antibiotics, based on constitutional right to have access to essential medicines. Institute measures to improve prescribing and dispensing of antibiotics in formal and informal health sectors.</p>		<p>Possible EAC implications and backlash from retailers and hospital administrations.</p>

Abbreviations: DVS = Department of Veterinary Services; EAC = East African Community; HAI = Hospital-Acquired Infection; ICC = Infection Control Committee; ICP = Infection Control Practice; MoH = Ministry of Health; MOMS = Ministry of Medical Services; NHIF = National Health Insurance Fund; OTC = over-the-counter; PPB = Poisons and Pharmacy Board; STG = standard treatment guideline

References

- Bartoloni, A. and E. Gotuzzo. 2010. Bacterial-Resistant Infections in Resource-Limited Countries. *Antimicrobial Resistance in Developing Countries*. A. Sosa, D. K. Byarugaba, C. F. Amabile-Cuevas et al, Springer.
- Bejon, P., I. Mwangi, et al. 2005. Invasive Gram-negative bacilli are frequently resistant to standard antibiotics for children admitted to hospital in Kilifi, Kenya. *Journal of Antimicrobial Chemotherapy*. DOI: 10.1093/jac/dki145.
- Berkley, J. A., K. Maitland, et al. 2008. Use of clinical syndromes to target antibiotic prescribing in seriously ill children in malaria endemic area: observational study. *BMJ*. DOI: 10.1136/bmj.38408.471991.8F.
- Bigogo, G., A. Audi, et al. 2010. Health-seeking patterns among participants of population-based morbidity surveillance in rural western Kenya: implications for calculating disease rates. *International Journal of Infectious Diseases* **14**(11): e967-973.
- Bii, C. C., H. Taguchi, et al. 2005. Detection of virulence-related genes by multiplex PCR in multidrug-resistant diarrhoeagenic *Escherichia coli* isolates from Kenya and Japan. *Epidemiology and Infection* **133**(4): 627-633.
- du Prey, B., B. D. Ford, et al. 2004. Antimicrobial recommendation by health care providers in Kenya. *American Journal of Health-System Pharmacy* **61**(Feb 1): 302-303.
- English, M., F. Esamai, et al. 2004. Assessment of inpatient paediatric care in first referral level hospitals in 13 districts in Kenya. *The Lancet* **363**: 1948-1953.
- English, M. and A. G. Scott. 2008. What Is the Future for Global Case Management Guidelines for Common Childhood Diseases? *PLoS Medicine* **5**, e241 DOI: 10.1371/journal.pmed.0050241.
- Kakai, R. and I. A. Wamola. 2002. Minimising Antibiotic Resistance to *Staphylococcus Aureus* in Developing Countries. *East African Medical Journal* **79**(11): 574-579.
- Karambu, I. 2011. Abuse of 'prescription only' drugs on the rise. *Corporate News*. Accessed 29 July 2011 from <http://www.businessdailyafrica.com/Corporate+News/-/539550/1116580/-/rifi4x/-/index.html>.
- Kariuki, S. 2009. Antimicrobial Resistance in Kenya: What Surveillance Tells Us. Global Antibiotic Resistance Partnership Inaugural Meeting, Nairobi, Kenya. Unpublished conference proceedings. Resources for the Future, Washington DC, 2009. Powerpoint.
- Kariuki, S. 2010. Antimicrobial Resistance in Enteric Pathogens in Developing Countries. *Antimicrobial Resistance in Developing Countries*. A. Sosa, D. K. Byarugaba, C. F. Amabile-Cuevas et al, Springer.
- Kariuki, S., C. Gilks, et al. 1996. Multi-drug resistant non-typhi salmonellae in Kenya. *Journal of Antimicrobial Chemotherapy* **38**: 425-434.
- Kariuki, S., C. Gilks, et al. 1997. Plasmid diversity of multidrug resistant *Escherichia coli* isolated from children with diarrhoea in a poultry-farming area in Kenya. *Annals of Tropical Medicine and Parasitology* **91**: 87-94.
- Kariuki, S., J. Muyodi, et al. 2003. Antimicrobial Susceptibility in Community-Acquired Bacterial Pneumonia in Adults. *East African Medical Journal* **80**(4): 213-217.
- Kariuki, S., G. Revathi, et al. 2005. Increasing prevalence of multidrug-resistant non-typhoidal salmonellae, Kenya, 1994-2003. *International Journal of Antimicrobial Agents* **25**(2005): 38-43.
- Kariuki, S., G. Revathi, et al. 2004. Characterization of Multidrug-Resistant Typhoid Outbreaks in Kenya. *Journal of Clinical Microbiology* **42**(4): 1477-1482.

- Kenya Veterinary Association. 2009. Policy Position Paper on Regulation of Veterinary Medicines in Kenya. Nairobi, Kenya Veterinary Association (KVA).
- Kwena, Z., A. Sharma, et al. 2008. Provider Characteristics Among Staff Providing Care to Sexually Transmitted Infection Self-Medicating Patients in Retail Pharmacies in Kibera Slum, Nairobi, Kenya. *Sexually Transmitted Diseases* **35**(5): 480-483.
- Ministry of Finance. 2009. The Medium Term Budget Strategy Paper 2009/10-2011/12. Nairobi, Ministry of Finance (Government of Kenya).
- Ministry of Health. 2007. Reversing the trends: NHSSP-II of Kenya - Annual Operational Plan (AOP) 3 2007/08. Nairobi, Ministry of Health (Government of Kenya) with the Sector Planning and Monitoring Department.
- Mitema, E. S., G. M. Kikui, et al. 2001. An assessment of antimicrobial consumption in food producing animals in Kenya. *Journal of Veterinary Pharmacology and Therapeutics* **24**: 385-390.
- Mwangi, I., J. A. Berkley, et al. 2002. Acute bacterial meningitis in children admitted to a rural Kenyan hospital: increasing antibiotic resistance and outcome. *Journal of Pediatric Infectious Diseases* **21**(11): 1042-1048.
- Okeke, I. N. and K. K. Ojo. 2010. Antimicrobial Use and Resistance in Africa. *Antimicrobial Resistance in Developing Countries*. A. Sosa, D. K. Byarugaba, C. F. Amabile-Cuevas et al, Springer.
- Paul, J., J. Bates, et al. 1996. Serotypes and Antibiotic Susceptibilities of *Streptococcus pneumoniae* in Nairobi, Kenya. *Journal of Infection* **32**: 139-142.
- Ram, P. K. 2008. Community case management of childhood diarrhoea in Asembo and Kibera, Kenya, 2007. University at Buffalo, Centers for Disease Control and Prevention, the Ministry of Health of the Republic of Kenya, and U.S. Agency for International Development.
- Scott, A. G., S. Mwarumba, et al. 2005. Progressive Increase in Antimicrobial Resistance among Invasive Isolates of *Haemophilus influenzae* Obtained from Children Admitted to a Hospital in Kilifi, Kenya, from 1994 to 2002. *Antimicrobial Agents and Chemotherapy* **49**(7): 3021-3024.
- Shapiro, R. L., L. Kumar, et al. 2001. Antimicrobial-Resistant Bacterial Diarrhea in Rural Western Kenya. *Journal of Infectious Diseases* **183**(1 June): 1701-1704.
- Shitandi, A. and A. Sternesjö. 2004. Prevalence of Multidrug Resistant *Staphylococcus aureus* in Milk from Large- and Small-Scale Producers in Kenya. *Journal of Dairy Science* **87**: 4145-4149.
- Sinha, A., O. S. Levine, et al. 2007. Cost-effectiveness of pneumococcal conjugate vaccination in the prevention of child mortality: an international economic analysis. *The Lancet* **369**: 389-396.
- Thoithi, G. N. and F. A. Okalebo. 2009. Country case study: Kenya. 2009 FIP Global Pharmacy Workforce Report. International Pharmaceutical Federation.
- Wamai, R. G. 2009. The Kenya Health System - Analysis of the situation and enduring challenges. *Japan Medical Association Journal* **52**(2): 134-140.
- World Health Organization. 2006. Kenya: Country Health System Fact Sheet 2006. *World Health Organization*.

ABOUT CDDEP

The Center for Disease Dynamics, Economics & Policy (CDDEP) was founded with the objective of using research to support better decision-making in health policy. The CDDEP team employs a range of expertise—including economics, epidemiology, disease modeling, risk analysis, and statistics—to produce actionable, policy-oriented studies on malaria, antibiotic resistance, disease control priorities, environmental health, alcohol and tobacco, and various other diseases.

Many CDDEP projects are global in scope, spanning Africa, Asia, and North America. The strength of CDDEP derives from its researchers' experience in addressing country and region-specific health problems, as well as truly global challenges, while recognizing the circumstances in which the answers must fit. The outcomes of individual projects go beyond the usual models to inspire new strategies for analysis, and innovative approaches are shared through publications and presentations focusing specifically on methodology.

Founded in 2009 as a center of Resources for the Future, CDDEP is an independent non-profit organization. With headquarters in Washington D.C. and New Delhi, CDDEP currently employs full-time staff members in India, Kenya, and the United States, and relies on a distinguished team of academics and policy analysts around the world.

**The full report and Executive Summary are available at
www.resistancestrategies.org**

cover photo credits: Flickr: computerwhiz417, Here Be Dragons, CIMMYT