Integrated AMR surveillance for foodborne bacteria in Africa: Guidance from AGISAR

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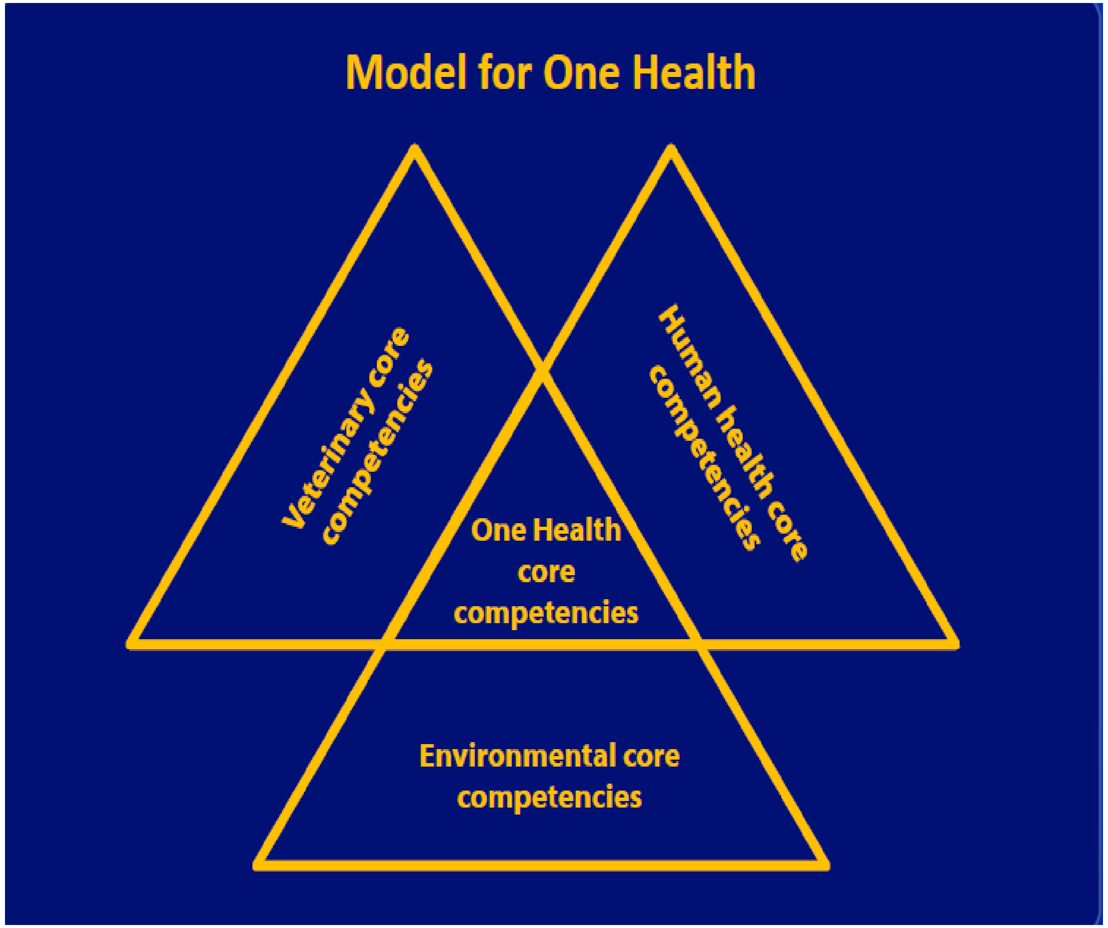
Defining One health

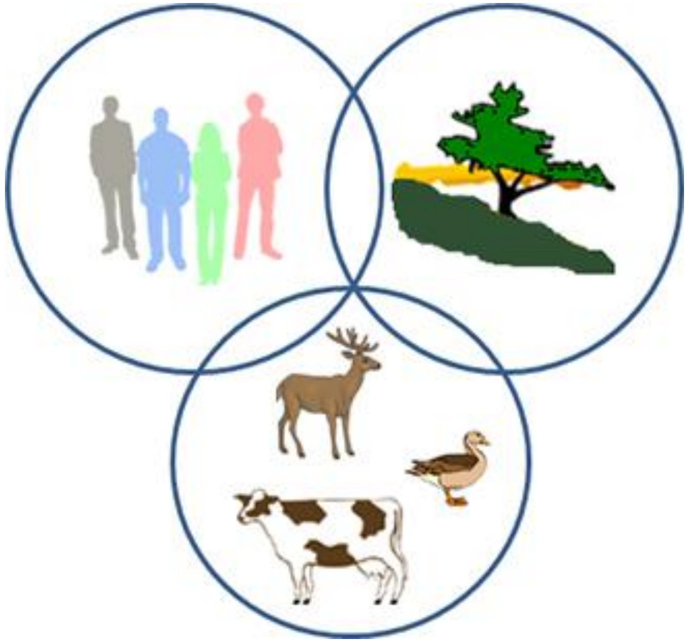
- A collaborative, multisectoral, and trans-disciplinary approach working at the local, regional, national, and global levels.
- Goal: achieving optimal health outcomes recognizing the interconnection between humans (public health), animals (vets and others), plants (plant health), and their shared environment (ecologists and others)



Overview of One Health concept

One Health aims at providing holistic, multidisciplinary prevention and treatment of human and animal diseases.

Takes into consideration the interconnections among these ecosystems that influence the epidemiology of zoonotic diseases.



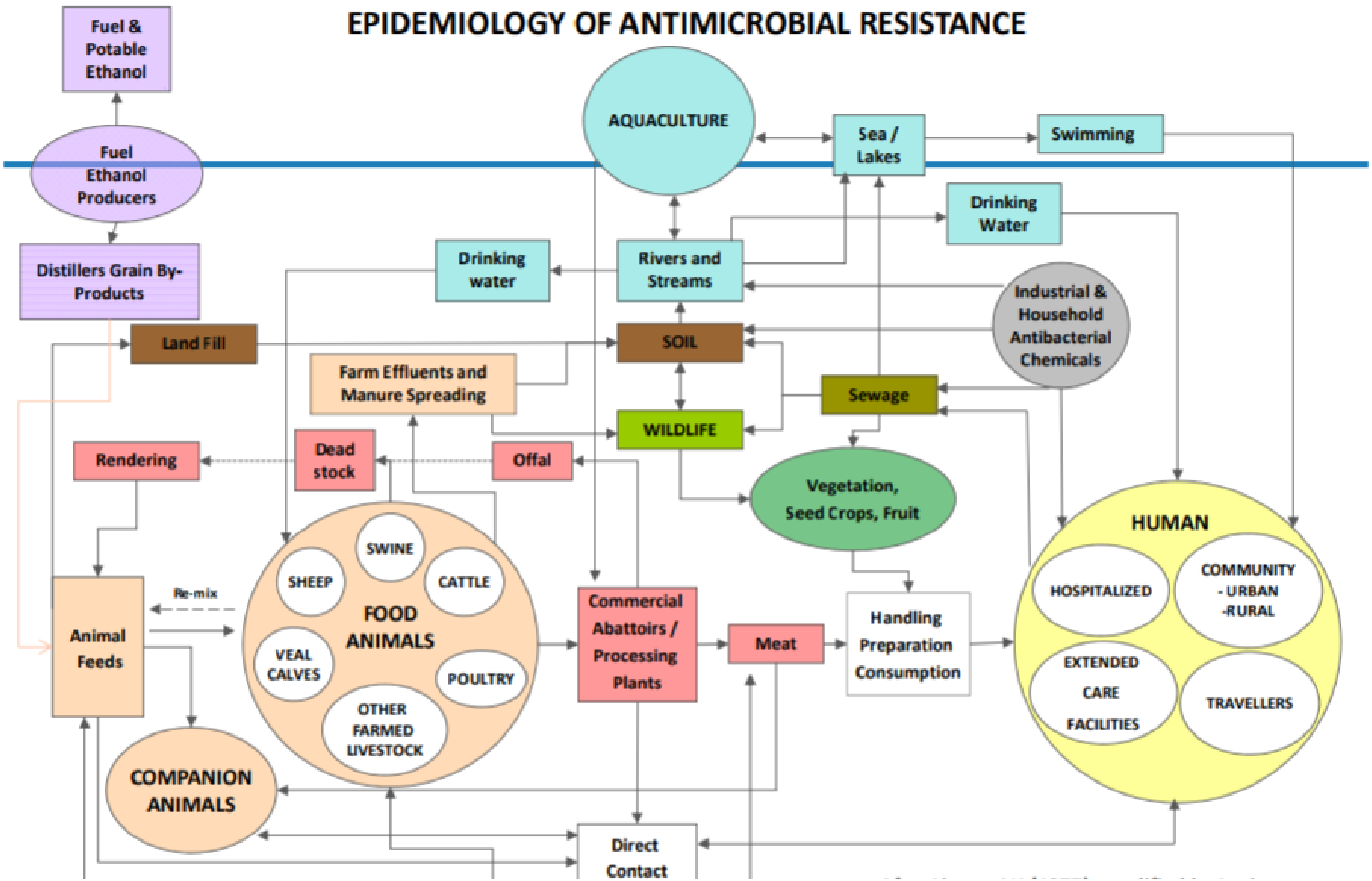
Unfortunately, multidisciplinary collaboration has crucial barriers to overcome - ‘single discipline’ established structures.

Why a "One Health "Approach?

- Antimicrobial Resistance TRULY Global
- Antibiotics are used in many settings

– Clinical medicine, communities, animal husbandry / aquaculture, horticulture

- Same classes of antimicrobial agents are used in
- different sectors
- Any use will select for resistance
- Resistant bacteria and resistant genes do not recognize
- geographic or ecologic borders


EPIDEMIOLOGY OF ANTIMICROBIAL RESISTANCE
Fuel & Potable Ethanol
Fuel Ethanol Producers
Distillers Grain By-Products
AQUACULTURE
Sea / Lakes
Swimming
Drinking Water
Drinking water
Rivers and Streams
Industrial & Household Antibacterial Chemicals
Land Fill
SOIL
Farm Effluents and Manure Spreading
Sewage
WILDLIFE
Rendering
Dead stock
Offal
Vegetation, Seed Crops, Fruit
HUMAN
HOSPITALIZED
COMMUNITY - URBAN -RURAL
EXTENDED CARE FACILITIES
TRAVELLERS
Re-mix
Animal Feeds
FOOD ANIMALS
SWINE
SHEEP
CATTLE
VEAL CALVES
POULTRY
OTHER FARMED LIVESTOCK
Commercial Abattoirs / Processing Plants
Meat
Handling Preparation Consumption
COMPANION ANIMALS
Direct Contact

What comprises integrated surveillance of AMR in foodborne bacteria?

Integrated surveillance of antimicrobial resistance in foodborne bacteria is the collection, validation, analyses and reporting of relevant microbiological and epidemiological data on antimicrobial resistance in foodborne bacteria from humans, animals, and food, and on relevant antimicrobial use in human and animals.

WHO Advisory Group on Integrated Surveillance on Antimicrobial Resistance (AGISAR)

WHO AGISAR was established in December 2008 to support WHO's effort to minimize the public health impact of antimicrobial resistance associated with the use of antimicrobials in food animals. The Group comprises over 30 internationally renowned experts in a broad range of disciplines relevant to antimicrobial resistance

The terms of reference for AGISAR

1. Develop harmonized schemes for monitoring antimicrobial resistance in zoonotic and enteric bacteria,
2. Support WHO capacity-building activities in Member States for antimicrobial resistance and antimicrobial usage monitoring.

Integrated surveillance a key element of AGISAR- AMR Containment strategy

- *- Documentation of the situation*
- *- Identification of trends*
- *- input data for:*
  - *Establishing associations antimicrobial usage and antimicrobial resistance*
  - *risk assessment*
  - *evaluation of effectiveness of interventions*
- *- identify need for interventions*
- *- Basis for focused and targeted research"*
- *- Basis for communication*

How these objectives are achieved

- Development of guidance for integrated AMR surveillance
- National capacity building projects, including Pilot and National focused projects
- Review and maintaining the WHO List of Critically Important Antimicrobials for Human Medicine.

Small/pilot Projects and Country Projects

An integrated AMR surveillance system for bacteria commonly transmitted by food should provide data that can be used to:

- document the levels of AMR in different reservoirs;
- identify AMR trends over time and from place to place;
- describe the spread of resistant bacterial strains and genetic determinants of resistance;
- study the association between AMR and use of antimicrobial agents;
- generate hypotheses about sources and reservoirs of resistant bacteria;
- identify, and evaluate the effectiveness of interventions to contain the emergence and spread of resistant bacteria;
- develop targeted epidemiological and microbiological research for source attribution studies, identify risk factors and clinical outcomes of infections caused by resistant bacteria;
- inform risk analysis of foodborne antimicrobial resistance hazards;
- guide evidence-based policies and guidelines to control antimicrobial use in hospitals, communities, agriculture, aquaculture, and veterinary medicine (ONE-HEALTH)
- support awareness efforts aimed at mitigating current and emerging hazards.

Training Courses

Microbiology training

- Global/Region-specific pathogens
  (e.g. *Salmonella*, *Campylobacter*, *E. coli, V. cholera*).
- Quality assurance
- Biosafety
- Antimicrobial Susceptibility Testing

Epidemiology training

- Outbreak detection and response
- Evaluation of surveillance systems
- Study design
- Source attribution
- Burden of disease

Joint Epidemiology and Laboratory

- Joint case studies
- Integrated surveillance
- Risk assessment
- Country Plans of Action
- Advocacy and communication
- Information sharing networks

Funding available

1. Small grants for focused projects (USD 15-30,000)

- These projects should include characterization of foodborne pathogens in at least two of the following sectors; human, food and animal. Characterization should include antimicrobial susceptibility testing. The duration of the project is one year and the total amount requested from WHO should not exceed 15,000 USD.

2. Country pilot projects (USD 75,000)

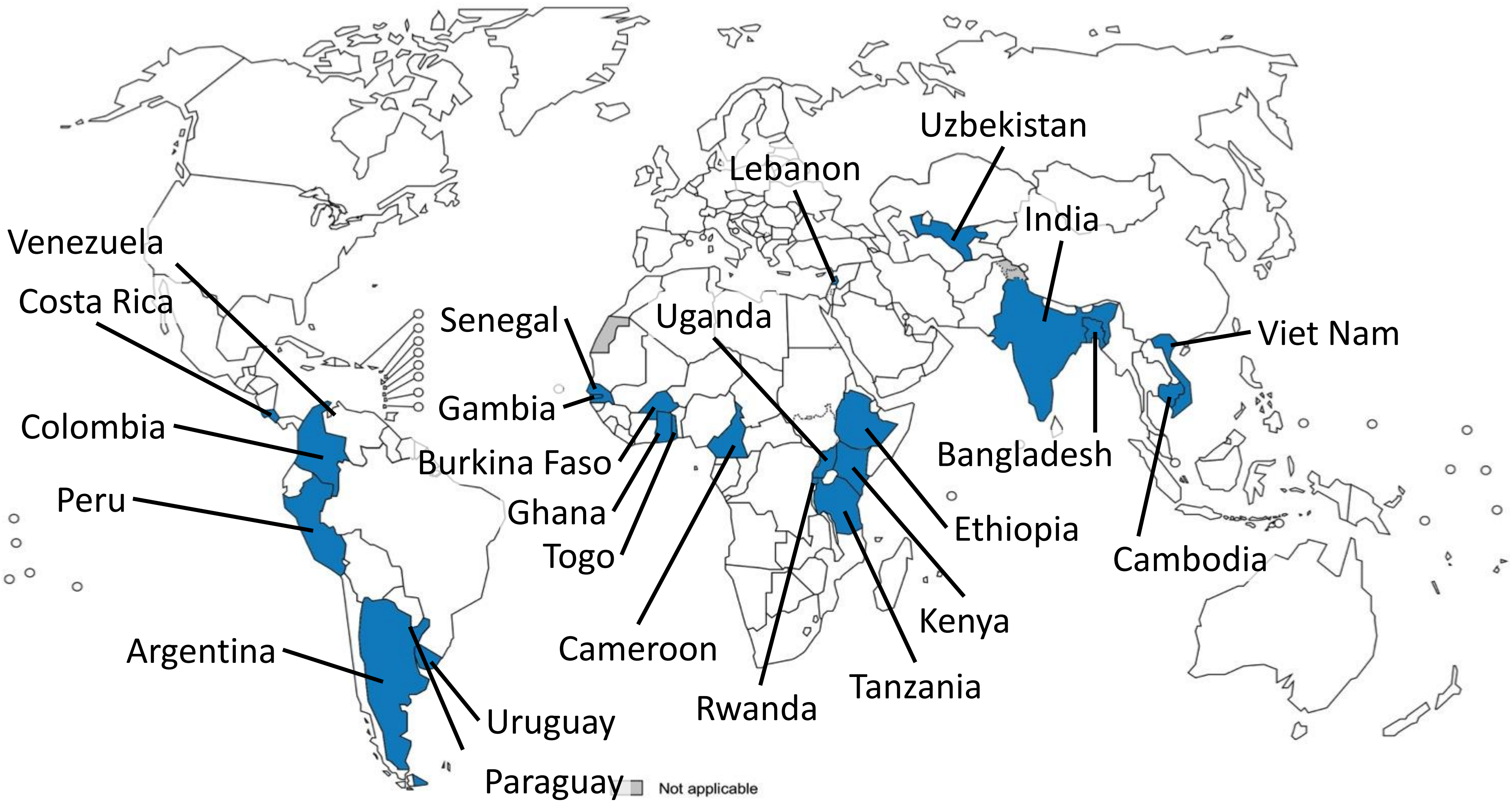
These projects implemented at country level should include:

- Sampling and characterization of foodborne pathogens (*Salmonella spp* and *Campylobacter* as a minimum) in human, food and animal sectors.
- Antimicrobial susceptibility testing should be performed in pathogens and indicator bacteria (*E. coli, Enterococcus*).
- Monitoring of antimicrobial usage in animals and in humans.
- An inclusion of an attribution component will be an asset.

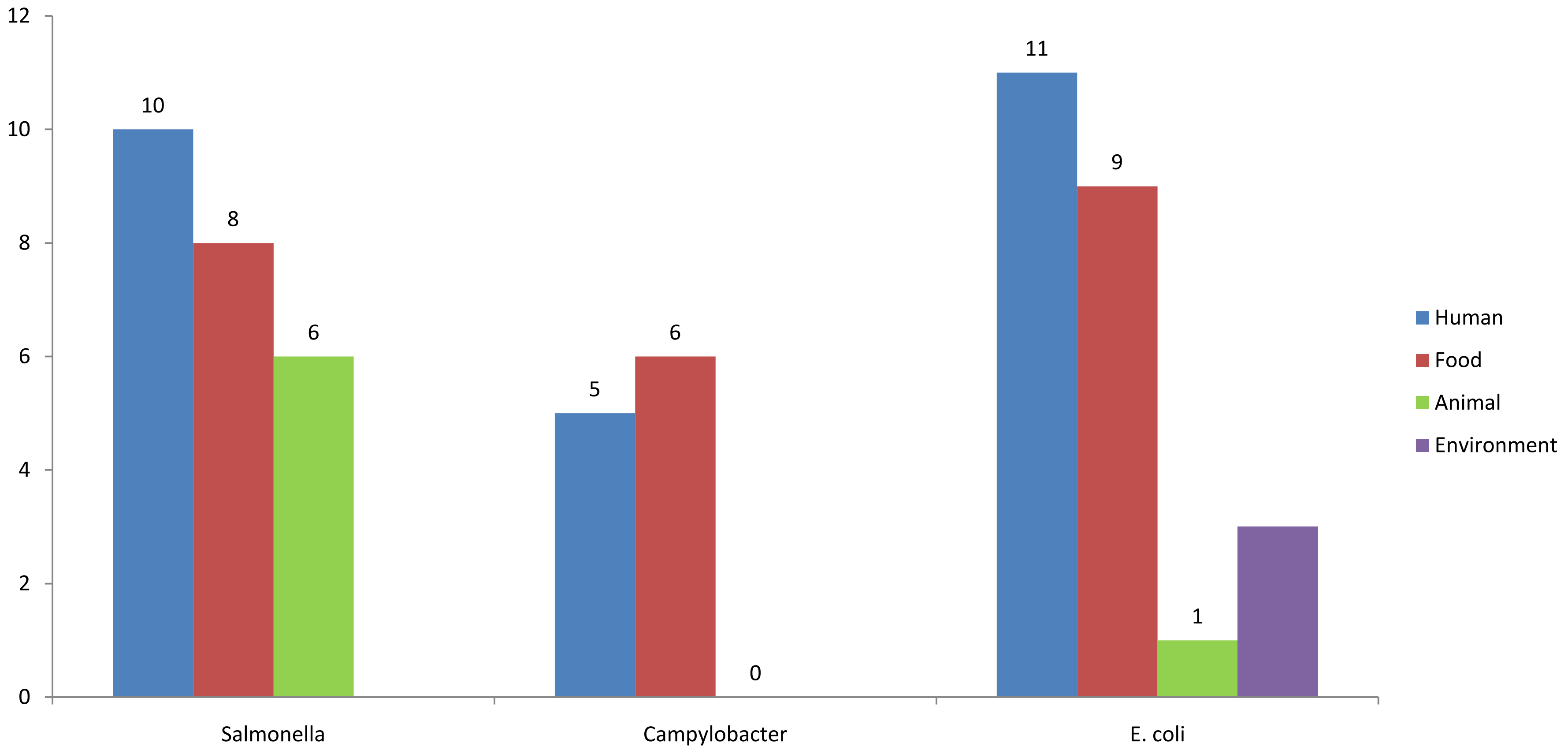
Resources and calls for applications

- WHO | WHO Advisory Group on Integrated Surveillance of ...
- www.who.int/foodsafety/areas_work/antimicrobial-resistance/agisar/en/

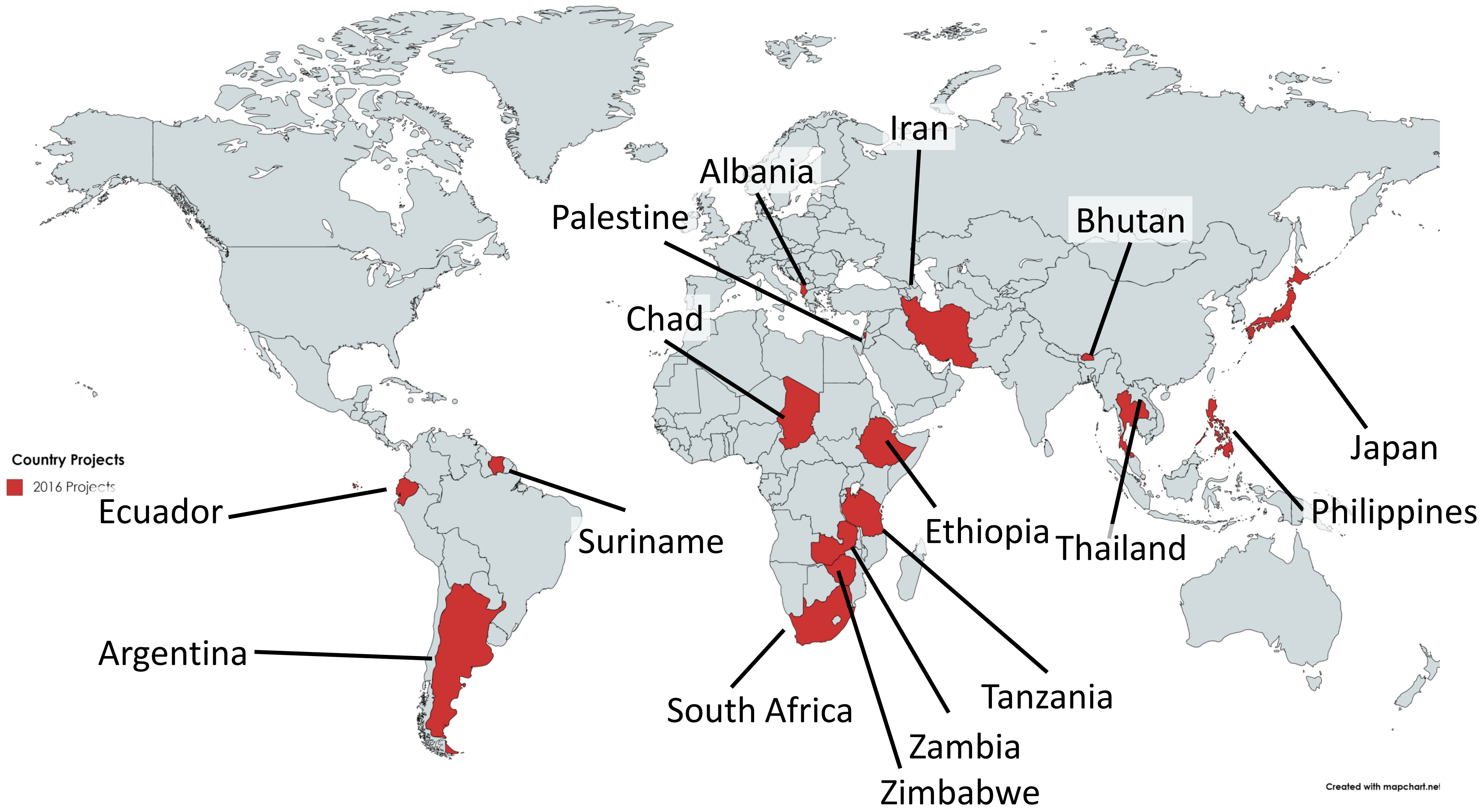
Pilot projects spread out globally



Pilot Project 2010-2016



Awards for – 2017/18



Some Sentinel integrated surveillance data

An integrated surveillance of antimicrobial resistance in *Salmonella* spp, *Campylobacter* spp *Escherichia coli* and *Enterococcus* spp from gut of healthy food animals and retail meat outlets as well as from human clinical specimens in selected regions in Kenya

World Health Organization

KENYA MEDICAL RESEARCH INSTITUTE
KEMRI

Food and Agriculture Organization of the United Nations
for a world without hunger

MDR Invasive NTS in Africa: A Killer in Slums and Poor Rural Children.

Epidemiology and Genomics of Invasive Nontyphoidal *Salmonella* Infections in Kenya

Samuel Kariuki and Robert S. Onsare
Centre for Microbiology Research, Kenya Medical Research Institute, Nairobi

Background. In Kenya, invasive nontyphoidal *Salmonella* (iNTS) disease causes severe bacteremic illness among adults with human immunodeficiency virus (HIV) and especially among children <5 years of age coinfected with HIV or malaria, or who are compromised by sickle cell disease or severe malnutrition. The incidence of iNTS disease in children ranges from 166 to 568 cases per 1

Journal of Medical Microbiology (2006), 55, 585–591 DOI 10.1099/jmm.0.46375-0

Invasive multidrug-resistant non-typhoidal *Salmonella* infections in Africa: zoonotic or anthroponotic transmission?

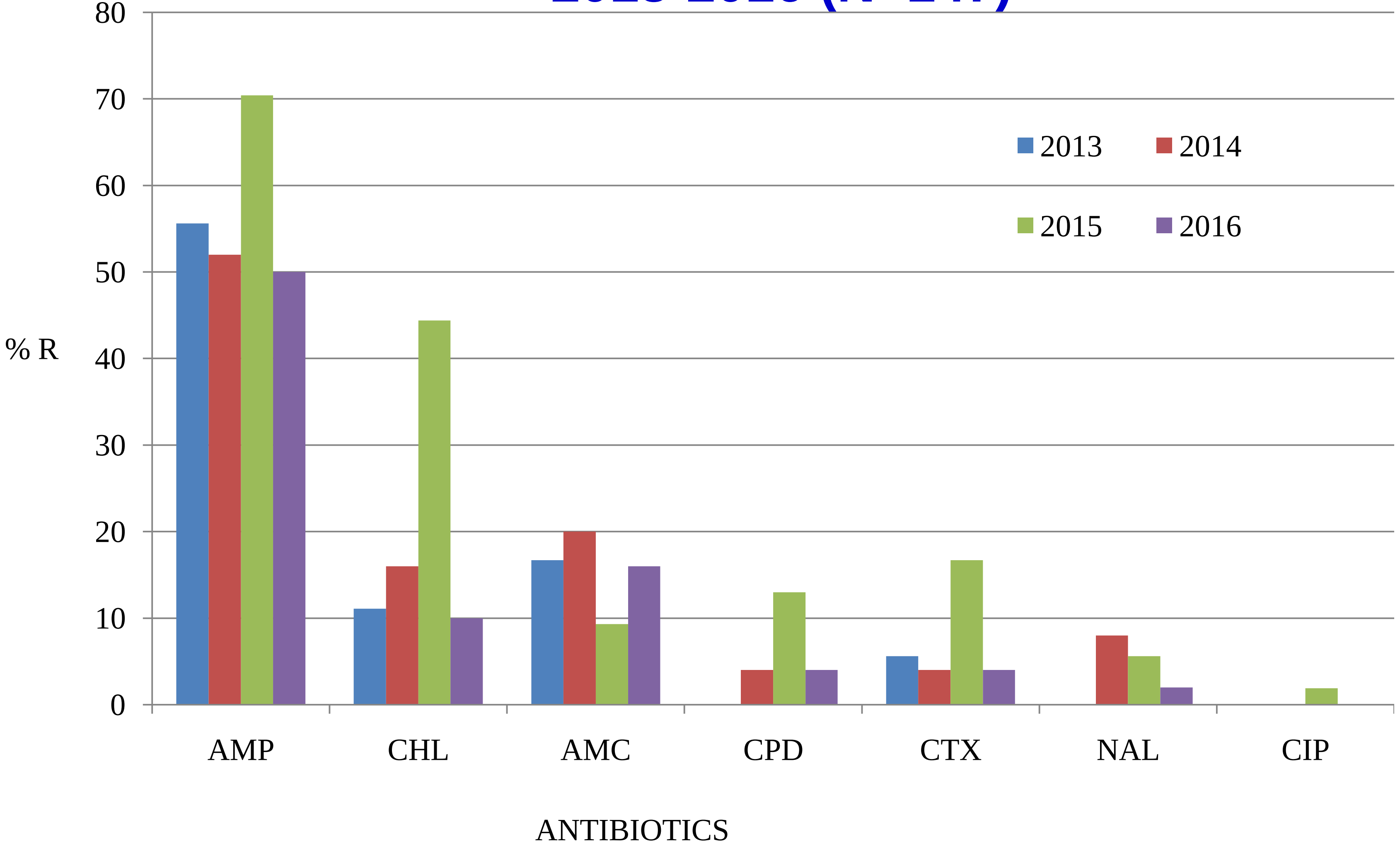
Samuel Kariuki,[1,2] Gunturu Revathi,[3] Nyambura Kariuki,[3] John Kiiru,[1] Joyce Mwituria,[1] Jane Muyodi,[1] Jane W. Githinji,[4] Dorothy Kagendo,[1] Agnes Munyalo[1] and C. Anthony Hart[2]

Published in final edited form as:
Vaccine. 2015 June 19; 33(0 3): C21–C29. doi:10.1016/j.vaccine.2015.03.102.

Antimicrobial resistance and management of invasive *Salmonella* disease

Samuel Kariuki[1,2], Melita A. Gordon[3,4], Nicholas Feasey[4,5], and Christopher M Parry[6,7]
[1]Centre for Microbiology Research, Kenya Medical Research Institute, PO Box 43640-00100, Nairobi

S. Typhimurium Resistance Trends from 2013-2016 (N=147)



MAPPING HOTSPOTS

EMERGENCE OF ESBL PRODUCING NTS

- 15 patients treated at AGUH 1 year apart.
- 12 S. Typhimurium isolates from blood.
- Sensitive to – Chloramphenicol, Ciproxin and Cefoxitin.
- Resistant to Nalidixic acid, Cotrim, Ampicillin, Ceftriaxone and Aztreonam. MIC Ceftriaxone >256 ; MIC Ciprofloxacin=0.12.
- Resistance to β-lactams, including to ceftriaxone, was associated with carriage of a combination of *bla*CTX-M-15, *bla*OXA-1, and *bla*TEM-1 genes on 304 kb plasmid.

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Ceftriaxone-Resistant *Salmonella enterica* Serotype Typhimurium Sequence Type 313 from Kenyan Patients Is Associated with the *bla*$_{CTX-M-15}$ Gene on a Novel IncHI2 Plasmid

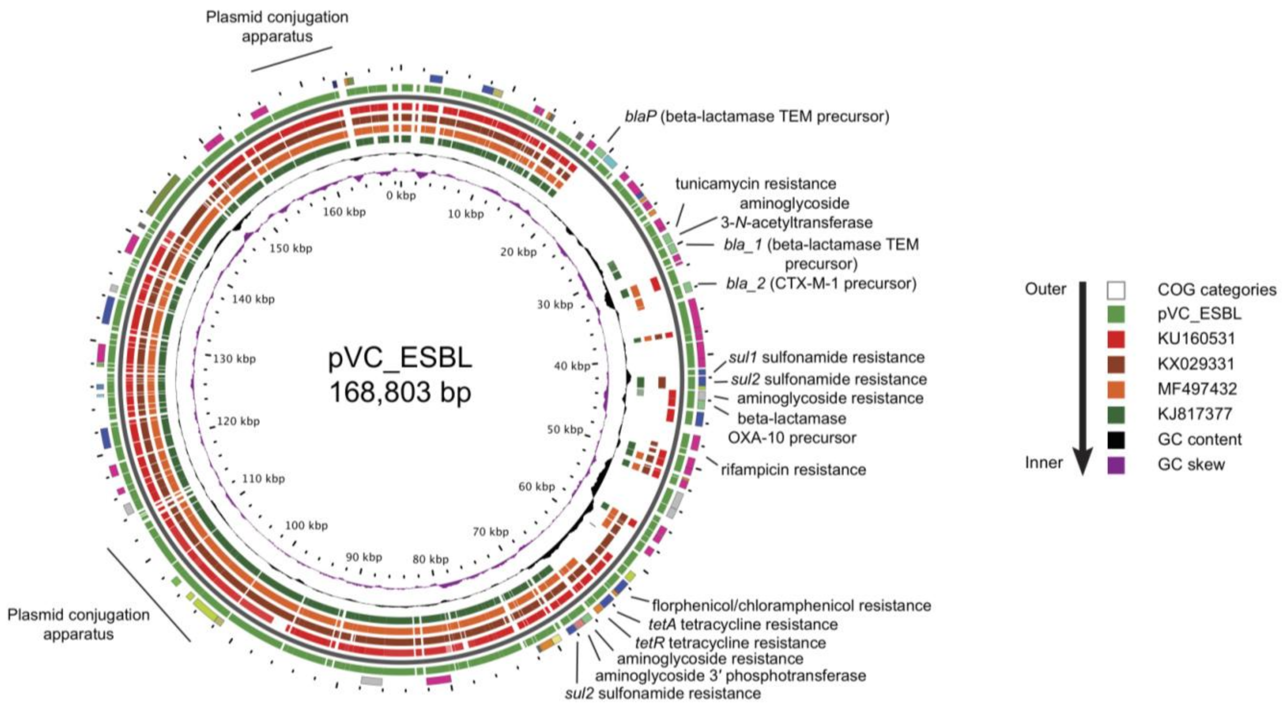
Samuel Kariuki[a,c], Chinyere Okoro[c], John Kiiru[a], Samuel Njoroge[a], Geoffrey Omuse[b], Gemma Langridge[c], Robert A. Kingsley[c], Gordon Dougan[c] and Gunturu Revathi[b]

The Kenyan Cholera outbreak route

Emergence of ESBL-producing *Vibrio cholerae* in 2012

Isolate Number	ESBL enzymes present
38/2012	CTX-M, TEM
39/2012	none- negative control
57/2012	CTX-M, TEM
52/2012	CTX-M
54/2012	CTX-M, TEM
58/2012	CTX-M, TEM
64/2012	CTX-M, TEM
68/2012	CTX-M, TEM
56/2012	CTX-M, TEM
43/2012	CTX-M
74/2012	CTX-M, TEM
73/2012	CTX-M, TEM
78/2012	CTX-M, TEM
75/2012	CTX-M, TEM
76/2012	CTX-M, TEM
44/2012	TEM
41/2012	CTX-M, TEM
45/2012	CTX-M, TEM
42/2012	CTX-M, TEM

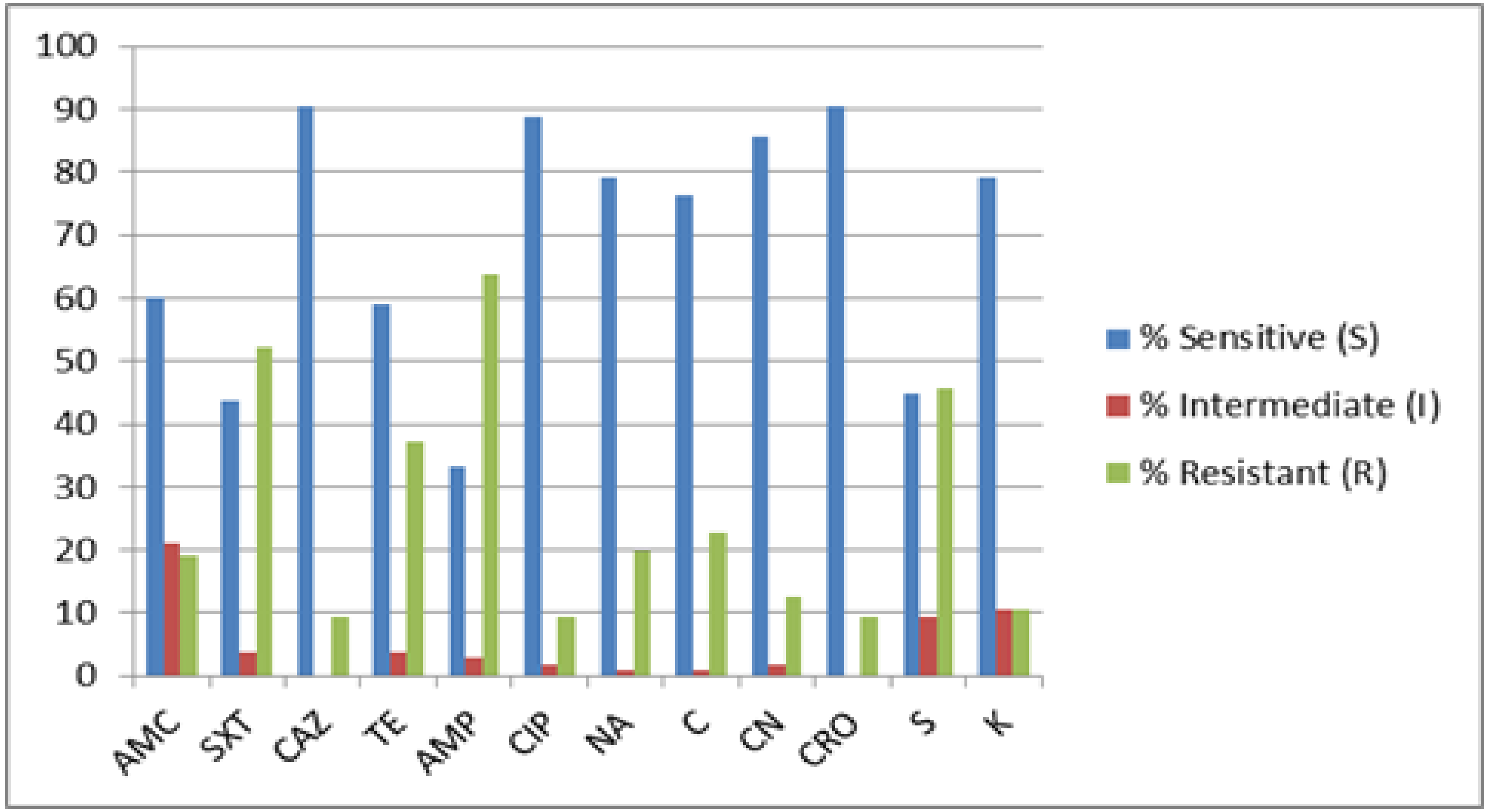
WGS shows 3 main regions on the pVC_ESBL



1. SXT R319 carrying the *flo*R-*dhfr*A1-*str*A-*Str*B-*sul*2 genes.
2. class 1 integron carrying *aadB-arr2-bla*$_{\text{TEM1B}}$-*cmlA-bla*$_{\text{OXA-10}}$-*arr*-2-*aadA1* cassettes and with *sul1* and a truncated *qacEΔ*1 gene at the 3' conserved end.
3. Resistance genes inserted into the plasmid backbone encoding resistance to third generation cephalosporins (*bla*$_{\text{CTX-M-15}}$), *aac(3)-IIc* that confer resistance to Streptomycin, kanamycin and tobramycin and a putative gene for tunicamycin resistance

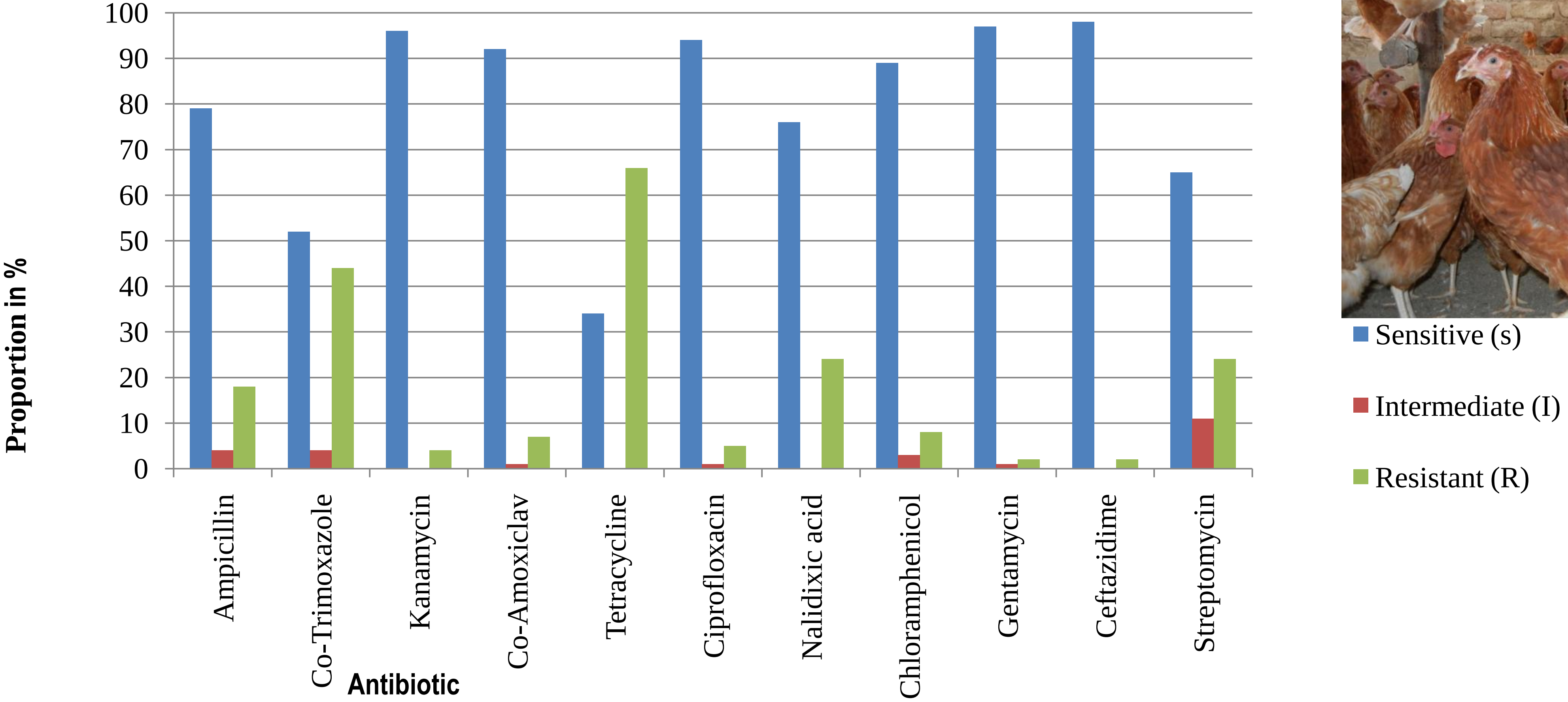
Escherichia coli as a marker of contamination and AMR transmission along meat value chain

Susceptibility for *E. coli* from children treated at District Hospital 2010-2013, (n=325)



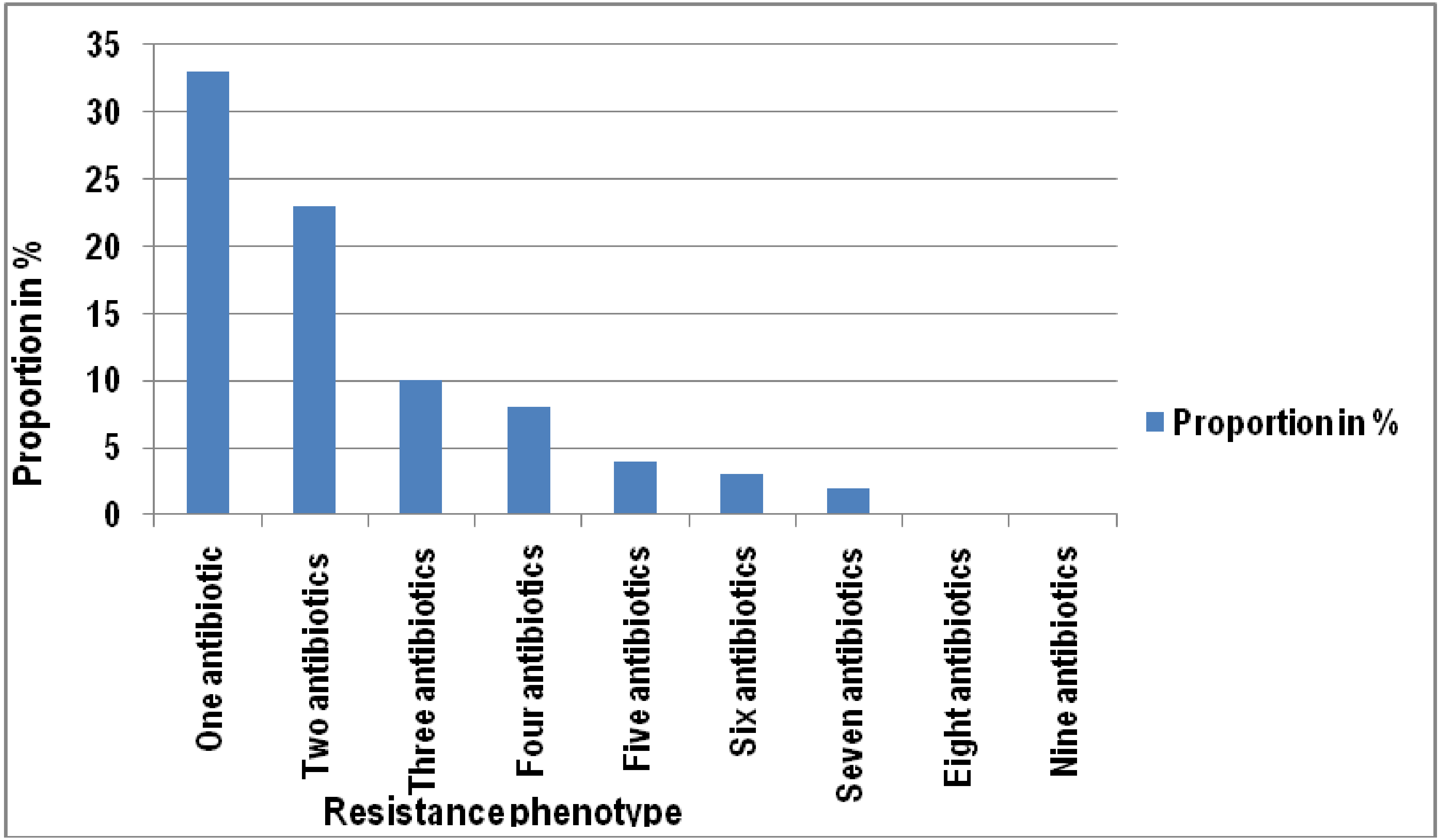
Highest prevalence of resistance was observed for commonly used antimicrobials including ampicillin, co-trimoxazole, streptomycin and amoxillin-clavulanic acid

Antibiotic susceptibility patterns for E. coli isolated from poultry in small scale farms in Thika, n=350

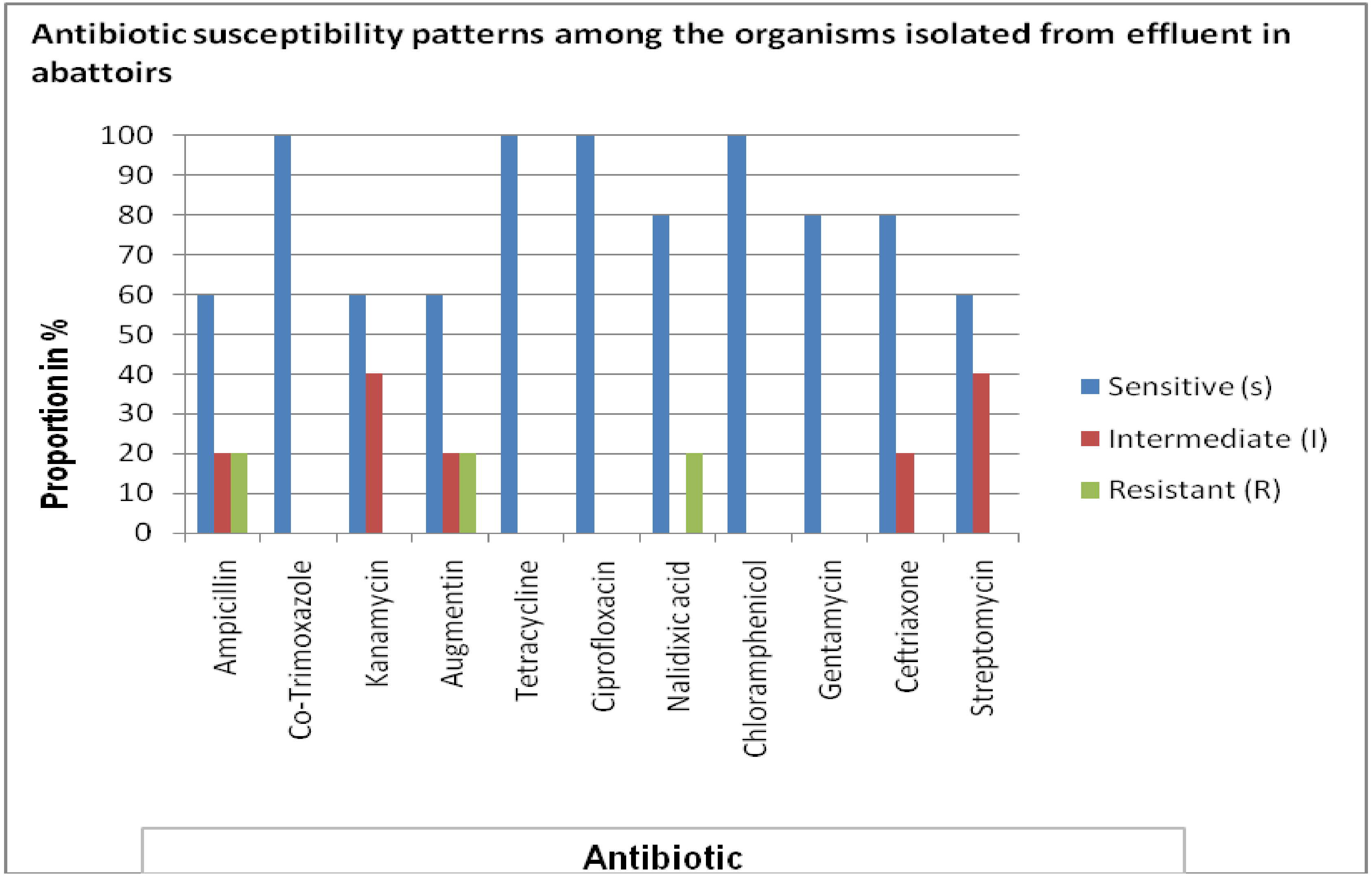


Note small (4%) resistance to ceftazidime, co-amoxiclav (7%), ciprofloxacin (4%)

Resistance phenotypes *E. coli* from poultry in small scale farms in Thika town and Thika chicken slaughter house; N=300



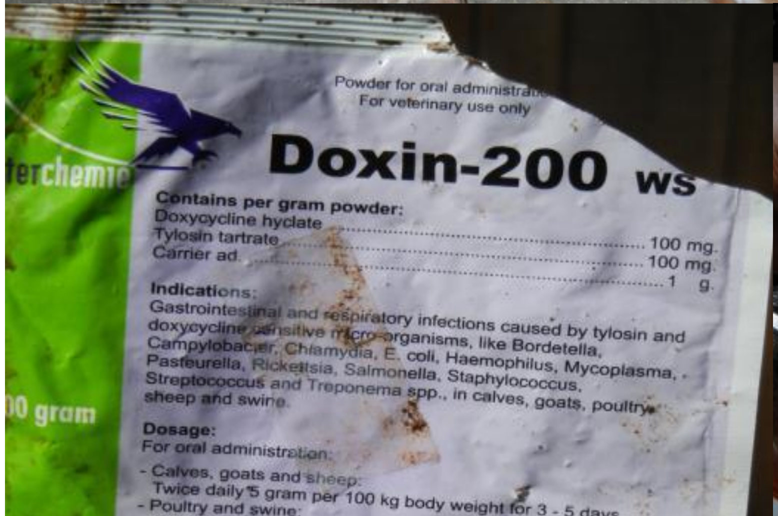
Antibiotic susceptibility patterns for *E. coli* isolated from effluent in abattoirs and their proportions in percentage; N=55



Summary of antibiotic/drug use among the farmers

District	Village	No. of Households/ questionnaires covered	Type and total No. of animals reared	Most common antibiotic/drug used for treatment/prophylaxis/ growth promotion
Thika west	Kiganjo	5	3100 chicken	Fluquin (Enrofloxacin); Biosol (Trimethoprim sulphamethoxazole); Hipralona Entos (Enrofloxacin); Fosbac; Molar plus multivitamins
	Landless	6	6524 chicken	Hipralona Entos (Enrofloxacin);Agdoxythyl; Keplox 2.5%; Colive; Alamycin, Levacide; Neoxy-vitamin WSP; OTC plus (Oxytetracycline)
	Muthaiga	4	3896 chicken	Neoty-VCA WSP; Aliseryl WS; Biosol (Trimethoprim sulphamethoxazole); Fosbac
	Munyu	5	5060 chicken	Kepcox; Coacidiostat; Bremalan; Levacide poultry; Bedgen-40 liquid; Medicated liquid paraffin; Alamyci n
	Athena	1	1000 chicken	Amoxyvet; Fosbac; Levacide
Gatundu North	Kairi	13	7760 chicken	Aciracox; Levacide; Poltricin; Vita poultry (multivitamin); Oxytetracycline; Doxyvet- SOS, Neoxy vitamin; Oxyfurazole; Limoxin; Amitotal; Egg boost
	Gatono	4	4780 chicken	Trimovet; Alamycin; Amidiostat
	Kihingo	1	500 chicken	Multiflox (multivitamin)
	Gaisugi	2	500 chicken	OTC plus (oxytetracycline); Alamycin
	Nguna	1	13,000 chicken	Bedgen O liquid; Limoxin
Nyando	Ko'bango	1	650 chicken	Oxytetracycline
Kisumu East	KARI	2	127 chicken	Biotrim- vet plus; Aliseryl WS
Kisauni		2	100,000 Chicken; 10,00 Cows	Fosbac; Aidamycin
Kwale		4	4300 Chicken; 11 cows	Biotrin; Esb3 30%; veriben

For antibiotic use at small holder settings, evidence abounds everywhere!



Veterinary Antimicrobials Imported into Kenya through the Single Window system (July 2016-January 2017)

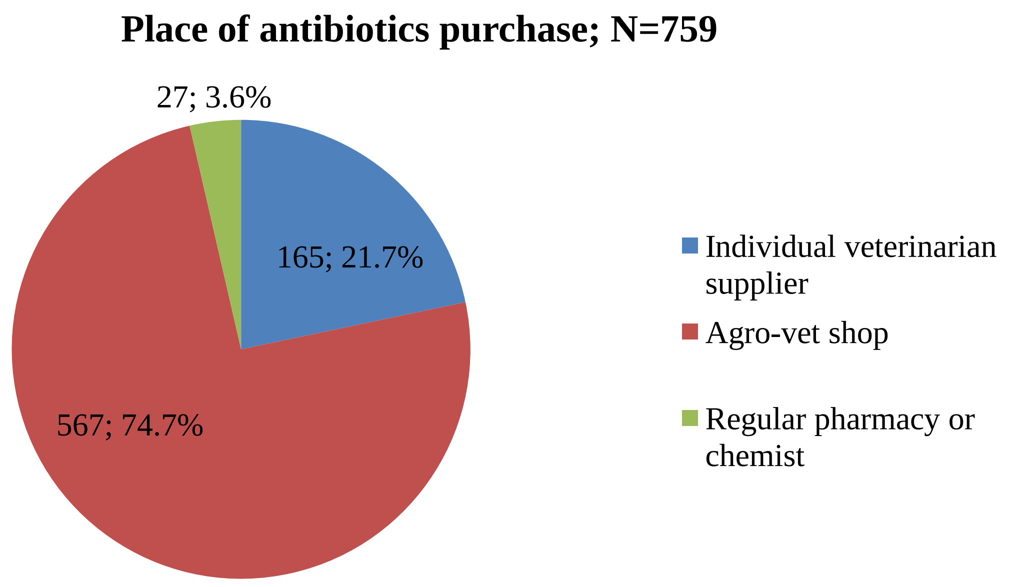
Antibiotic	Quantity (Kg)
Oxytetracycline Hydrochloride	2,560,861
Tylocin	1,026,000
Penicillin + Streptomycin	830,004
Amprolium	443,877
Chlorotetracycline	234,879
Penicillin	64,654
Ampicillin	21,652
Gentamycin	16,200
Sodium sulphadimidine	11,245
Sulfamethoxaxole + Trimethoprim	3,322
Ampicillin	2,346
Cloxacillin	2,149
Sulfamethoxazole	1,536
Ampicillin + Cloxacillin	856
Doxycycline	321

AMU in Livestock production – crucial insights from KAP study

Commonly used antimicrobials

- The most commonly used antibiotics in livestock production are:
  - **Treatment**-Penicillin +Streptomycin combo for cattle and pigs and Biotrim for chicken
  - **Prophylaxis**-Penicillin G for cattle, Alamycin (Oxytetracycline) for chicken and Tetracycline for pigs
  - **Growth promotion**- Neoxy Vitamins (Oxytetracycline +Neomycin) for cattle, Alamycin (Oxytetracycline) for chicken and oxytetracycline for pigs. Others used for growth promotion include Penicillin G for cattle and Neoxy Vitamins (Oxytetracycline +Neomycin) for chicken
- Majority of farmers were aware of antimicrobial resistance, but fear of losses from disease led to more use.
- Biosecurity was widely practiced, if improved could reduce the need for antibiotic use

Agrovet shops most frequent outlets for antibiotics



Individual vet. supplier, Agro-vet shop and regular pharmacy/chemist were the common sources of antibiotics to farmers with **Individual vet. supplier** (75%) being the most common supplier of antibiotics to farmers

Major findings among food animals

- Meat products contaminated with *E. coli*, *Salmonella*, *Campylobacter*; highest contamination rates in retail meats at lower end markets
- Contamination rates higher in chicken at retail markets compared to the commercial abattoir higher for *E. coli*, *Salmonella* and *Campylobacter* in comparison to beef.
- Antimicrobial resistance highest among isolates from poultry, then pigs and cattle
- Poor hygiene at local settings major risk factor for contamination and AMR

Major findings among food animals

- Oxytetracycline most commonly used antibiotic, especially among poultry small scale farmers.
- In addition farmers often used fluoroquinolones (including norfloxacin and enrofloxacin), erythromycin, variety of sulphonamides and co-trimoxazole in both poultry and cattle rearing.
- Antimicrobials easily obtainable from shops barely 10-15 min walking distance.
- Most stockists could give information on usage but generally farmers gave different doses of antibiotics and multivitamins to their flocks.
- Less than 20% of farmers understood the dangers of misuse of antibiotics

The GARP-MoH-MoALF One-Health Team