Antimicrobial Resistance in Key Foodborne Bacterial Pathogens in Kenya

Sam Kariuki

Outline

- Background of AMR situation in Kenya.
- Some key sentinel surveillance data on AMR in foodborne bacteria.
- The roadmap to implementation of NAP.
- Conclusions.

Situation in Kenya

- Although no systematic national surveillance is in place, sentinel studies indicate that problem of antimicrobial resistance is a major public health concern.

- Antibiotic use in domestic animals not well documented, but massive use in intensive small holder and commercial farming systems.

- There is antibiotic overuse in some settings, yet little or no access in others, especially rural and remote places.

ANTIMICROBIAL USE

Veterinary Antimicrobials Imported into Kenya through the Single Window system (July 2015-January 2016)

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

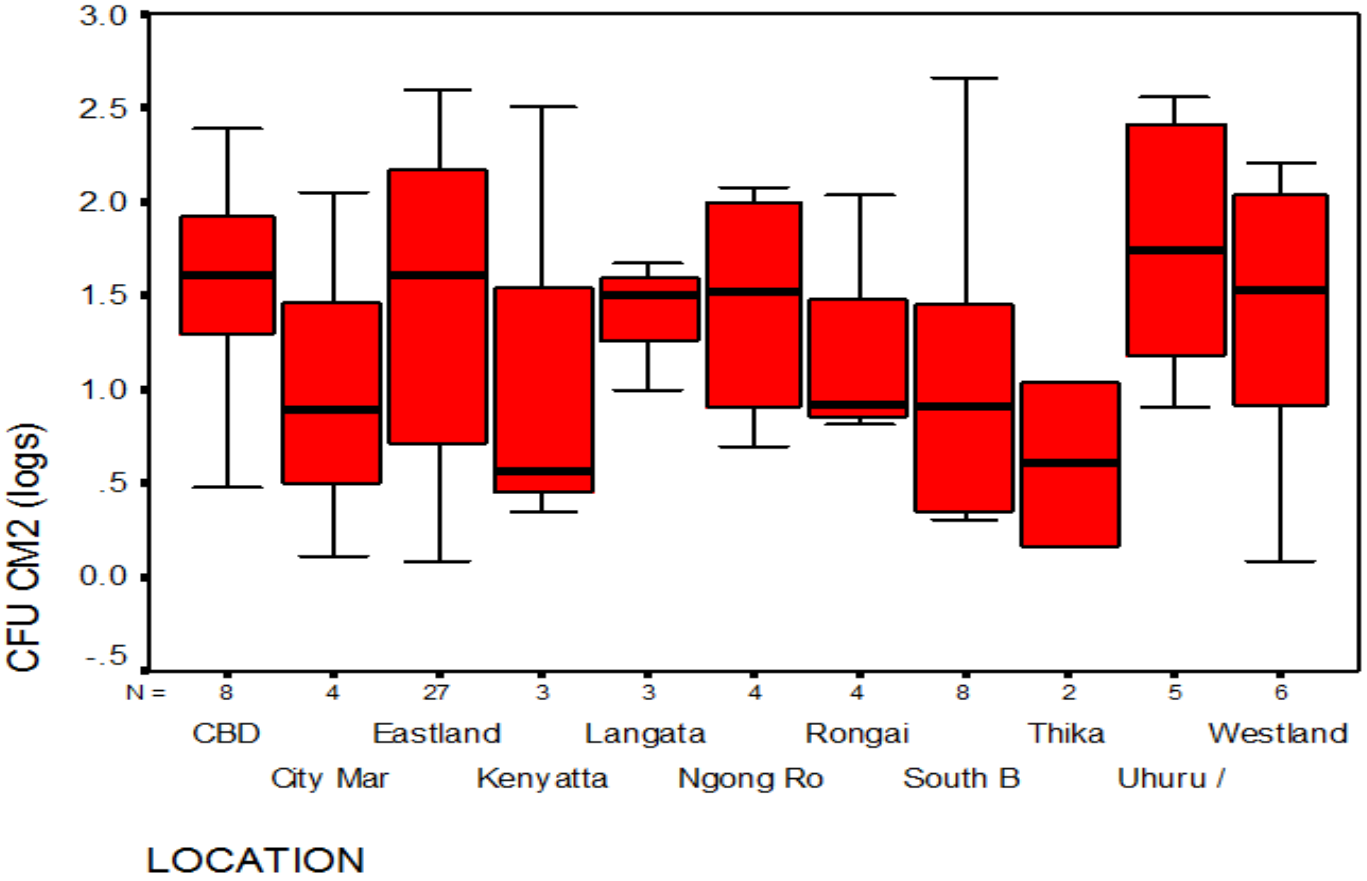
Summary of Antimicrobial use Patterns among Small-holder Farmers

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

Antimicrobial use even in remote pastoralist Marsabit County

Type of farming practice	Total No. animals reared in 20 farms visited	Main purpose of using antibiotics	Antibiotic most commonly used and purpose	Main source of antibiotic
Cattle (local)	120	Treatment	Oxytetracycline 10% (all for treatment)	Agro-vet
Cattle (grade)	52	Treatment	Oxytetracycline 10% Penstrep (all for treatment)	Agro-vet
Goats (local)	200	Treatment	Oxytetracycline Penstrep (all for treatment)	Agro-vet
Goats (grade)	8	Treatment	Oxytetracycline Penstrep (all for treatment)	Agro-vet
Camels	280	Treatment	Oxytetracycline Penstrep	Agro-vet

Contamination Levels for Poultry Meat from Retail Outlets in Nairobi Region



78% (145/186) of samples *E. coli*/coliforms detected, range log -0.09 to 2.38 cfu/mL of Rinsate. Other contaminants; *Campylobacter* spp (52%) and *Salmonella* spp (4%).

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.

- Poor hygiene at local settings major risk factor for contamination and AMR.

Major Findings Among Food Animals

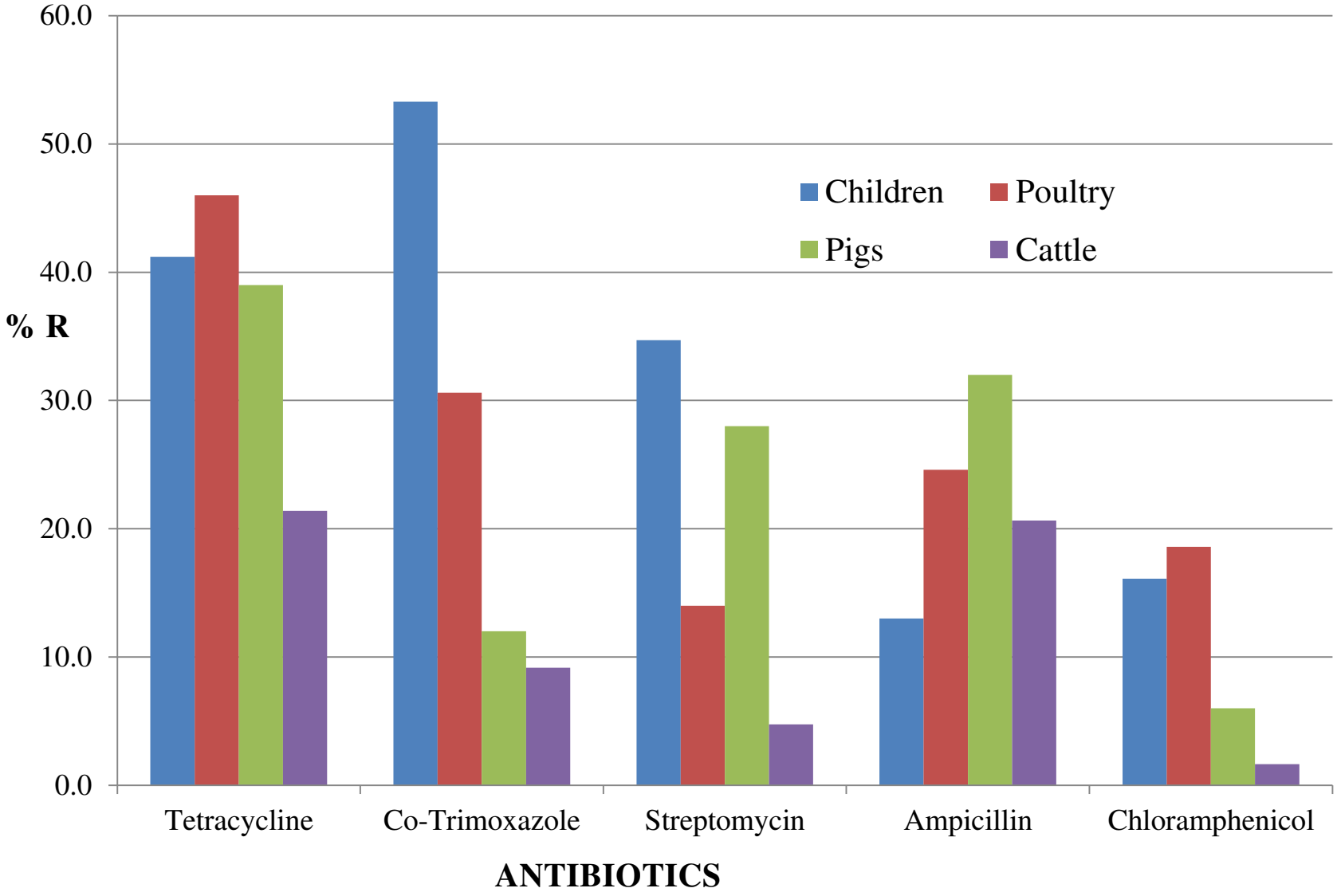
- **Oxytetracycline** most commonly used antibiotic, especially among poultry small scale farmers.
- In addition farmers often used **fluoroquinolones** (including norfloxacin and enrofloxacin especially in calves and also in feed), **erythromycin**, variety of **sulphonamides** and **co-trimoxazole** 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

Antimicrobial Resistance: Meat Value Chains

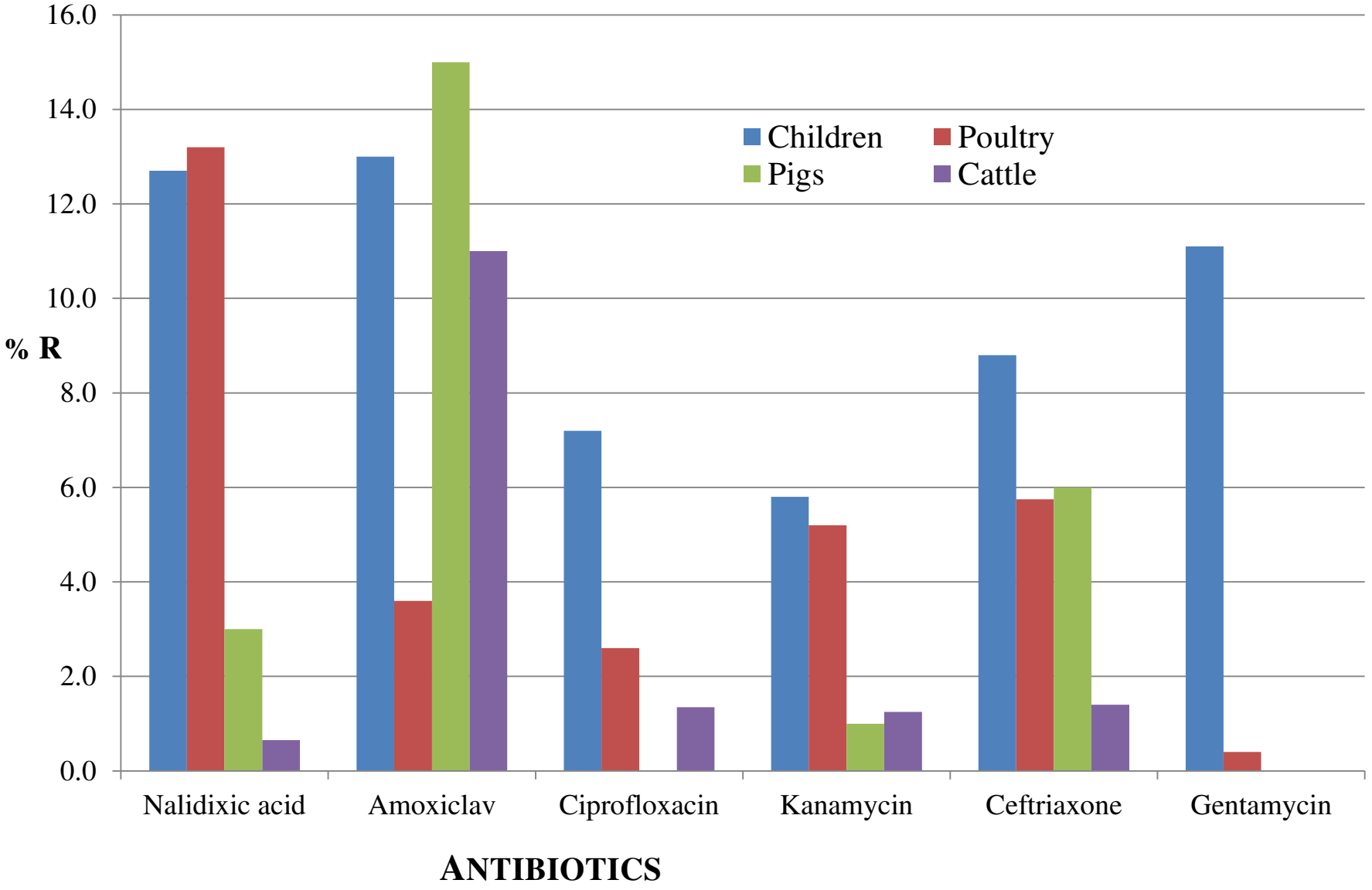
E. coli, coliforms and other Enterics.



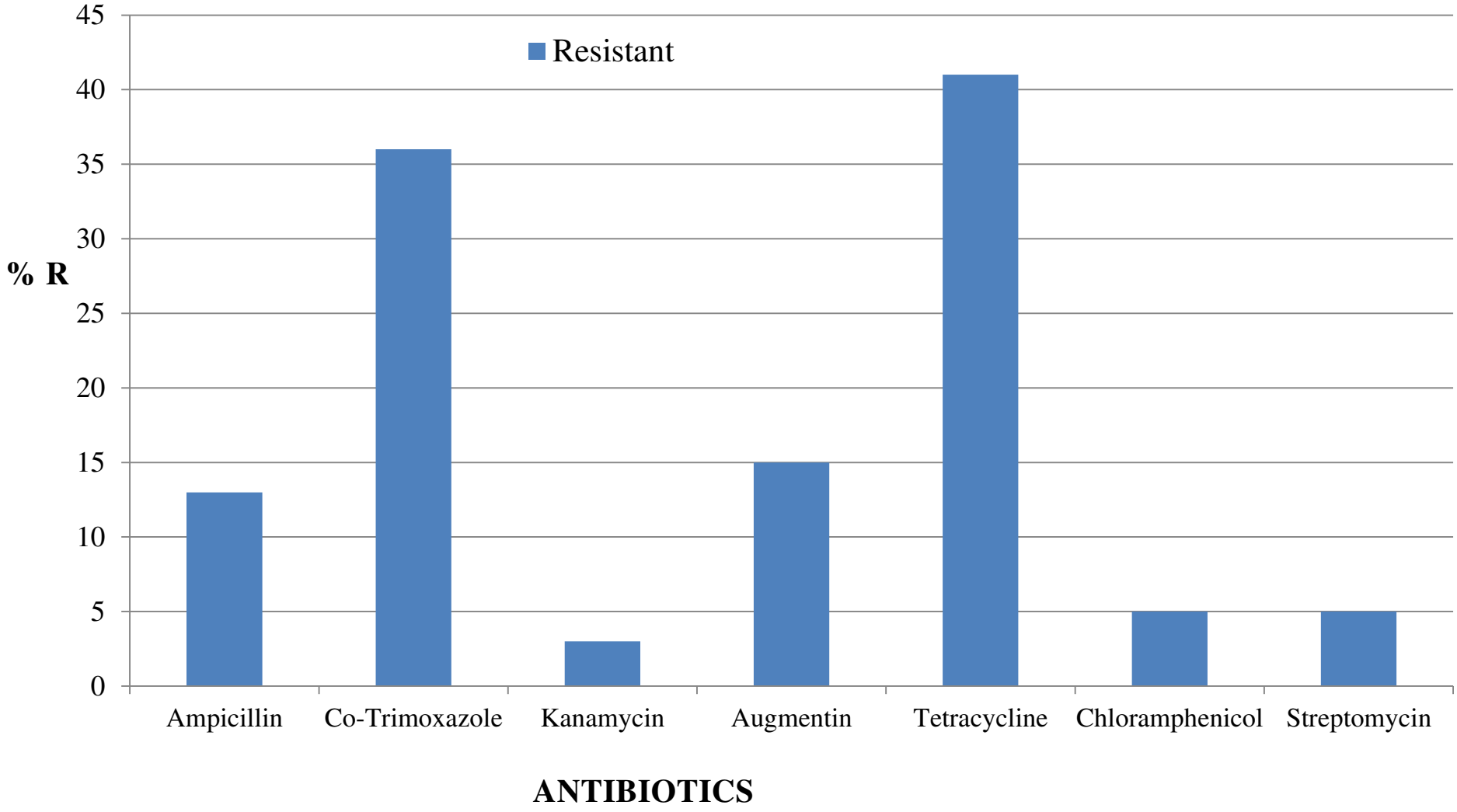
Resistance in *E. coli* Isolated from Children, Poultry, Pigs and Cattle



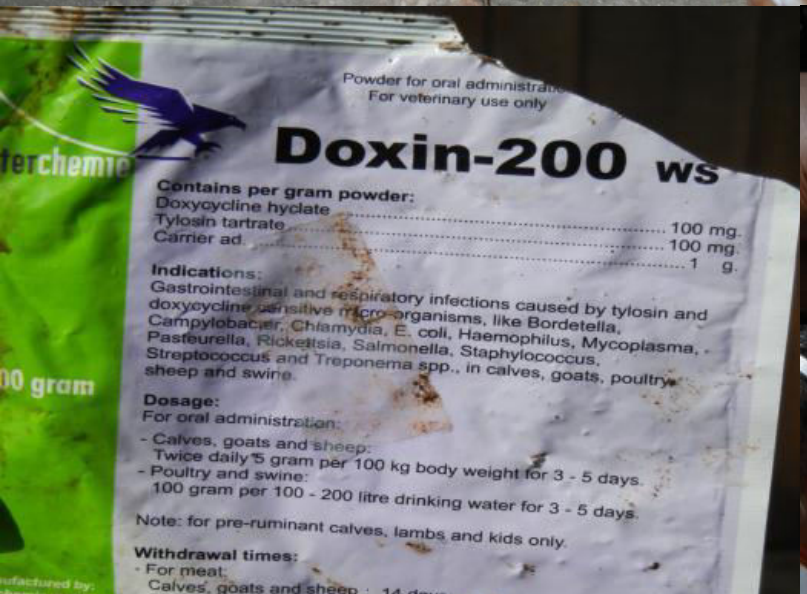
Resistance In *E.coli* From Children, Poultry, Pigs And Cattle

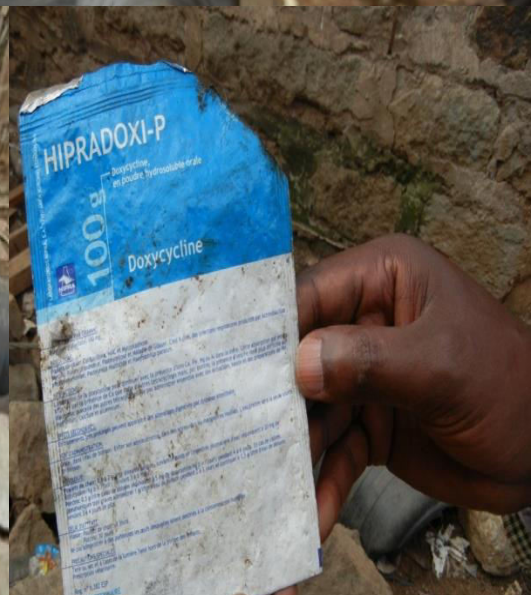


AMR in Salmonella spp from Poultry, Cattle and Pigs.



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





Chicken Farming and Markets.

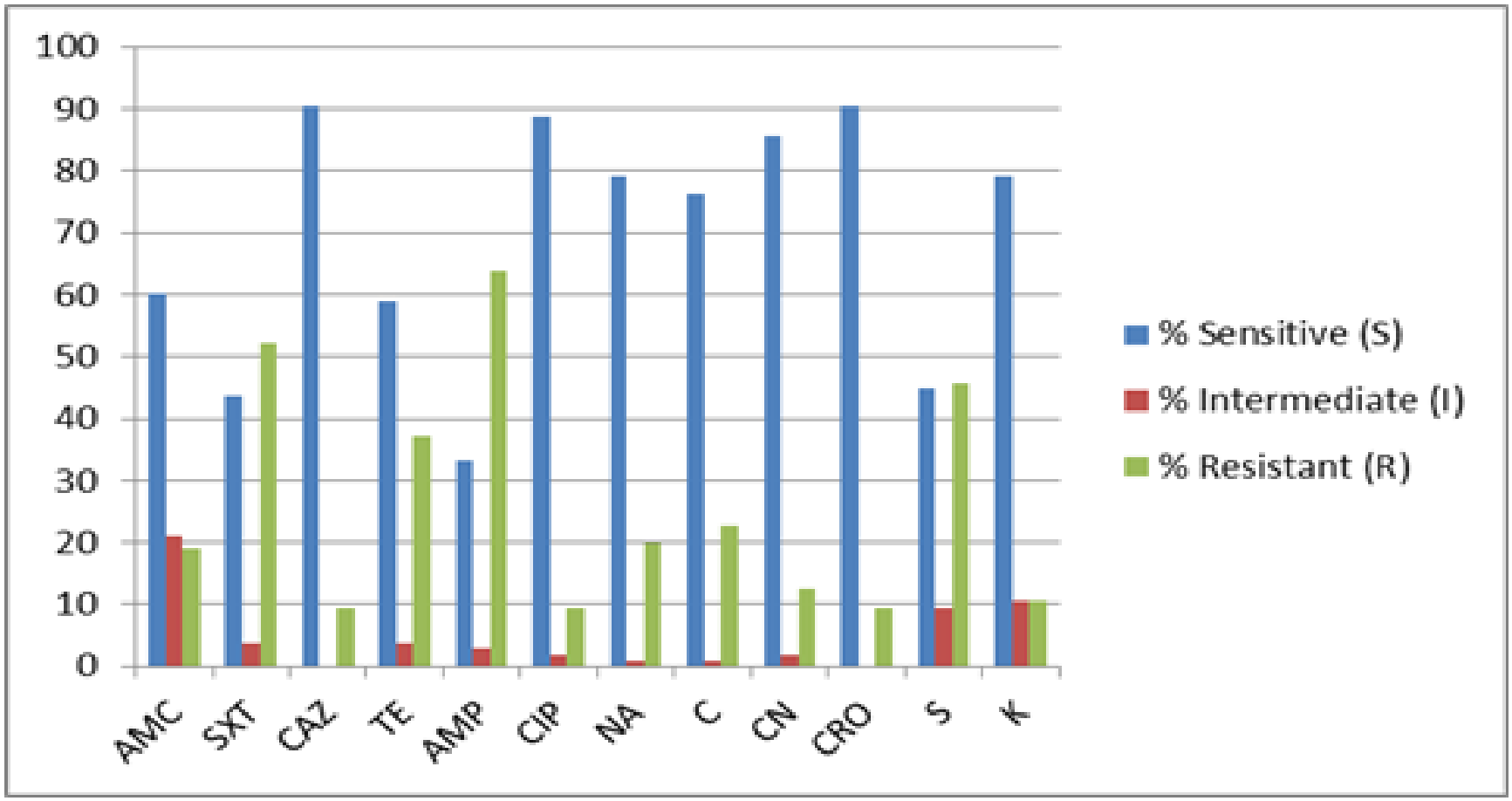
AMR Impact on Human Health

- Most AMR in zoonotic enteric pathogen borne on mobile genetic elements, so transmission happens across species.

- Commonly used products in animal production are similar to those used in humans, some are in the of Critically Important Antibiotics for human use.

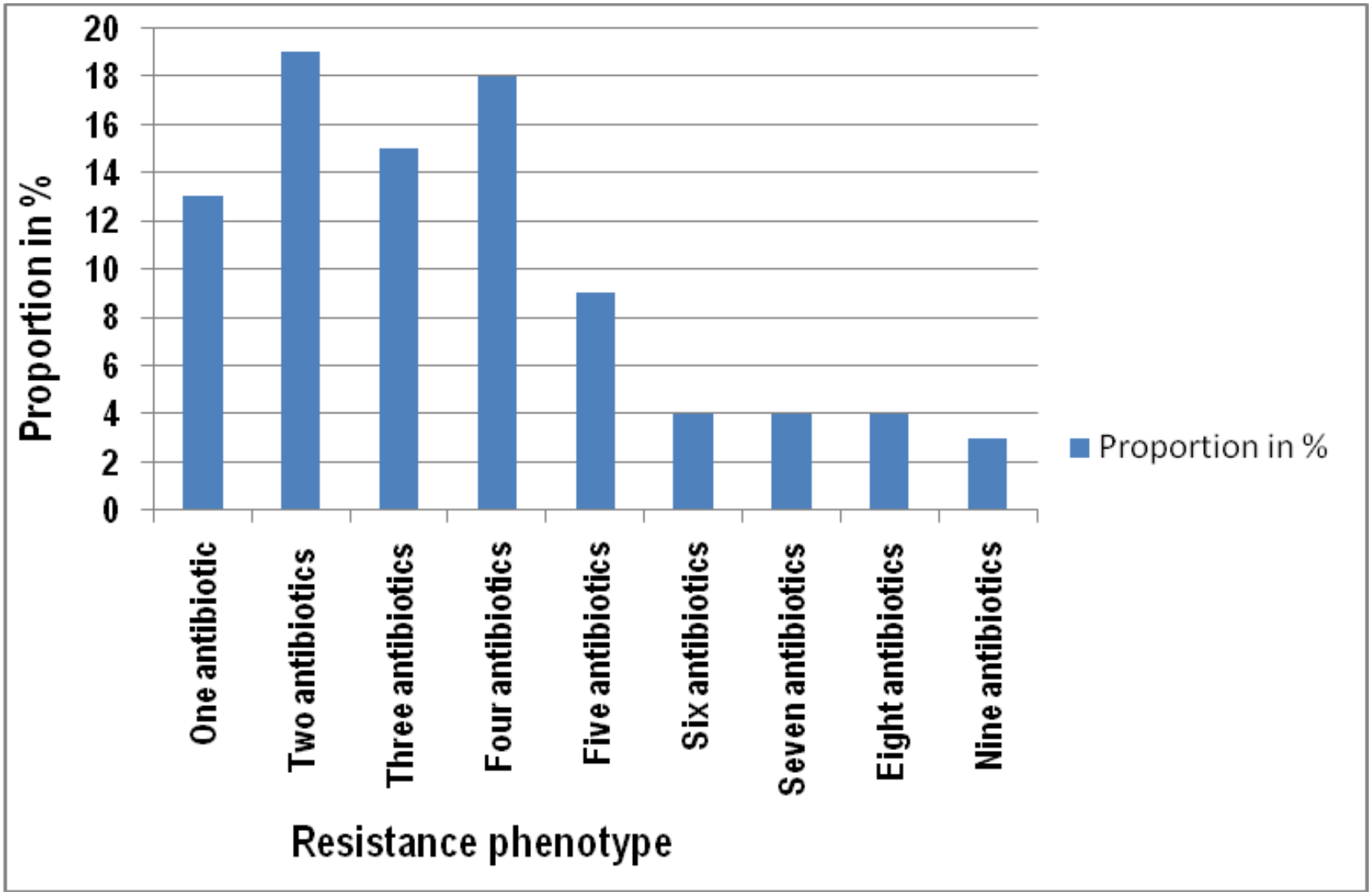
- Effects on severity of infections, prolonged hospitalization, increased costs of treatment and even higher mortality from difficult to treat infections

Susceptibility for *E. coli* From Children Treated at MDH 2010-2013, (N=325)



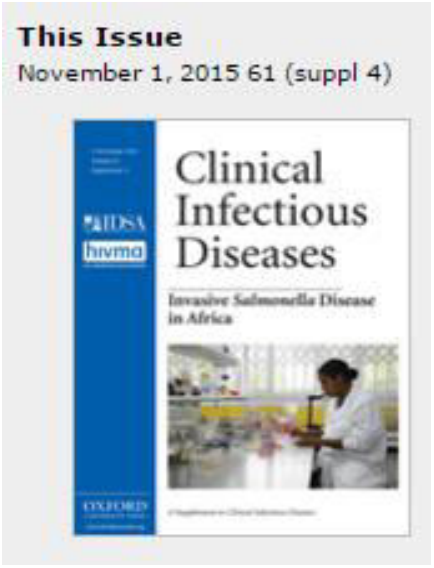
Highest prevalence of resistance was observed for commonly used antimicrobials including Ampicillin, Co-trimoxazole, Streptomycin and Amoxillin-clavulanic acid.

Resistance Phenotypes of *E. coli* Isolated From Stool Specimen of Patients Attending Mbagathi Hospital.



SALMONELLA BACTEREMIA STUDIES

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



Clin Infect Dis. 2015 Nov 1;61 Suppl 4:S317-24. doi: 10.1093/cid/civ711.

Epidemiology and Genomics of Invasive Nontyphoidal Salmonella Infections in Kenya.

Kariuki S[1], Onsare RS[1].

⊕ Author information

Abstract

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 100,000 persons per year.

Clin Infect Dis. 2015 Nov 1;61 Suppl 4:S290-301. doi: 10.1093/cid/civ737.

Invasive Salmonellosis in Kilifi, Kenya.

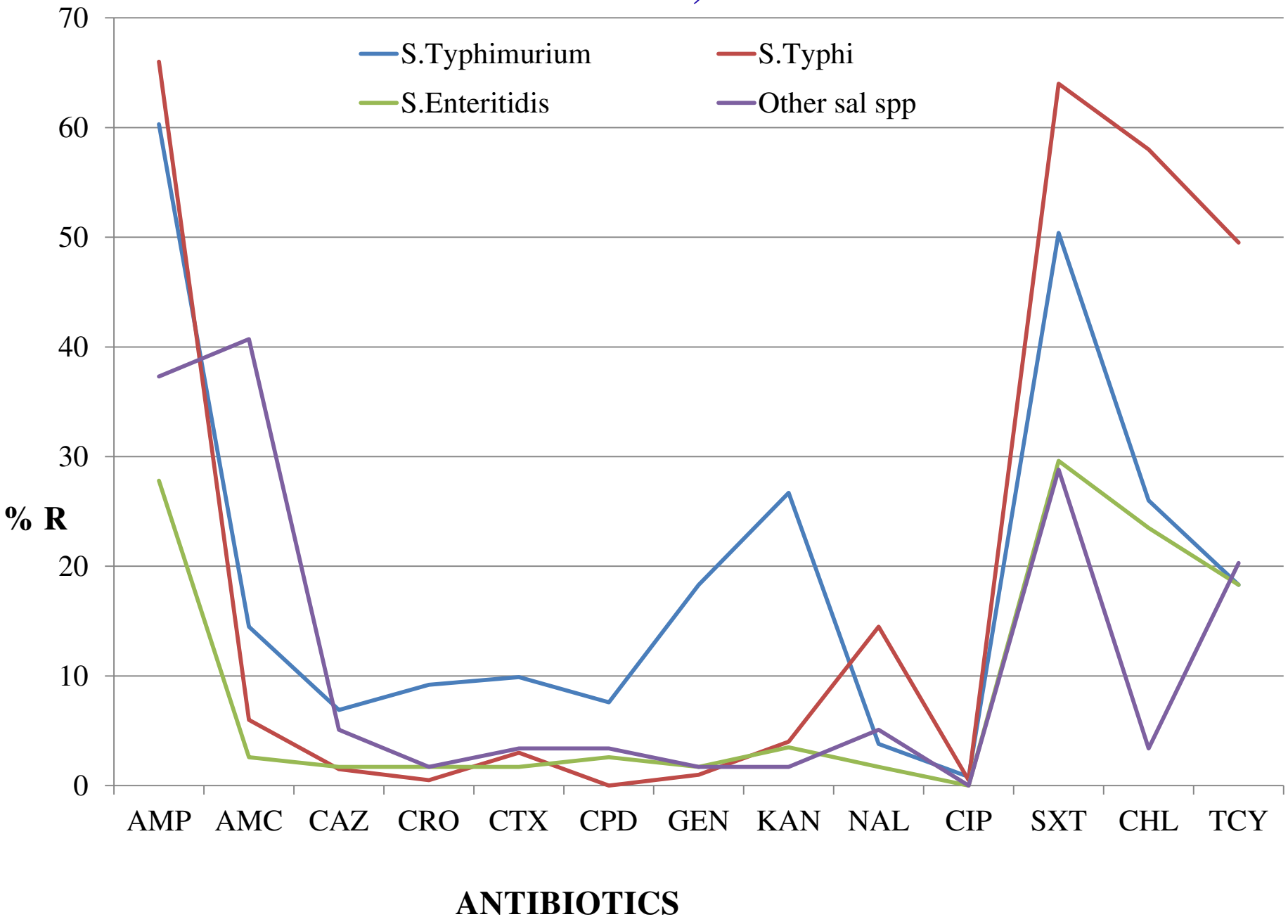
Muthumbi E[1], Morpeth SC[2], Ooko M[1], Mwanzu A[1], Mwarumba S[1], Mturi N[1], Etyang AO[2], Berkley JA[3], Williams TN[3], Kariuki S[4], Scott JA[2].

⊕ Author information

Abstract

BACKGROUND: Invasive salmonelloses are a major cause of morbidity and mortality in Africa, but the incidence and case fatality of each disease vary markedly by region. We aimed to describe the incidence, clinical characteristics, and antimicrobial susceptibility patterns of invasive salmonelloses among children and adults in Kilifi, Kenya.

% Resistance; n=545



MDR Invasive S. Typhimurium Hospitalised Children, 2010-2014 (N=325)

Antimicrobial Agent	MIC (µg/ml) Range	Mode	MIC50	MIC90	% R
Ampicillin	0.25->256	>256	82	64	48
Co-amoxyclav	0.75->256	4	1	16	8
Cefuroxime	2->256	>256	8	32	30
Ceftriaxone	0.094-16	0.064	0.5	2	0
Gentamicin	0.06->256	4	1	8	16
Co-trimoxazole	0.064->32	>32	8	32	46
Chloramphenicol	0.19->256	>256	4	32	26
Tetracycline	0.064->256	3	16	128	49
Nalidixic acid	1.5->256	3	3	3	12
Ciprofloxacin	0.064-4	0.16	0.06	0.125	0

Kariuki et al. Vaccine. 2015 Apr 23. pii: S0264-410(15)441-7; Tabu et al. Plos ONE 2012

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Journals.ASM.org

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] Gunturu Revathi[b]

Centre for Microbiology Research, Kenya Medical Research Institute, Nairobi, Kenya[a]; Aga Khan University Hospital, Nairobi, Kenya[b]; The Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, United Kingdom[c]

- 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.

Typhoid Fever

Emerging Fluoroquinolone Resistance Reduced Susceptibility to 3rd Gen Cephalosporins.

MDR Typhi Emerging Major Problem

- Only 18% are fully susceptible to commonly available drugs.
- The majority (71%) multiply-resistant - Ampicillin, Chloramphenicol, Tetracycline (MICs > 256µg/ml) and Co-trimoxazole (MIC > 32µg/ml).
- 25% Nalidixic resistance and 5-10% resistance to Ciprofloxacin susceptibility common.

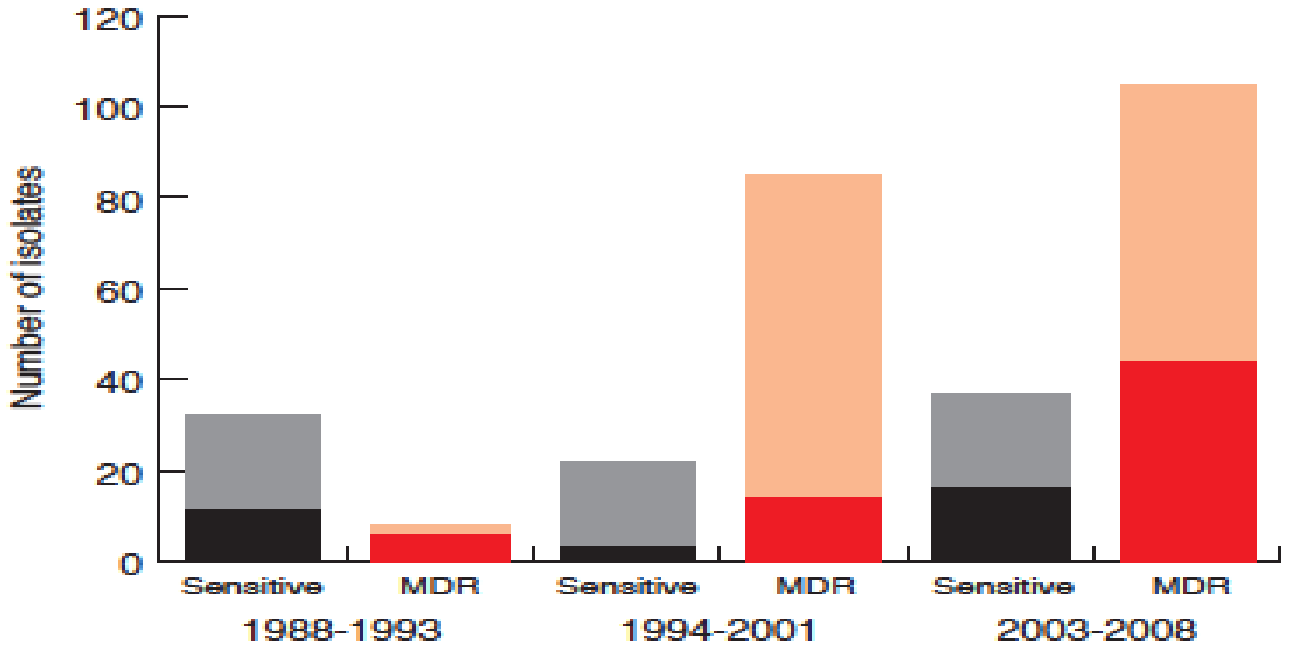
JOURNAL OF CLINICAL MICROBIOLOGY, June 2010, p. 2171–2176 Vol. 48, No. 6
0095-1137/10/$12.00 doi:10.1128/JCM.01983-09

Typhoid in Kenya Is Associated with a Dominant Multidrug-Resistant *Salmonella enterica* Serovar Typhi Haplotype That Is Also Widespread in Southeast Asia▽†

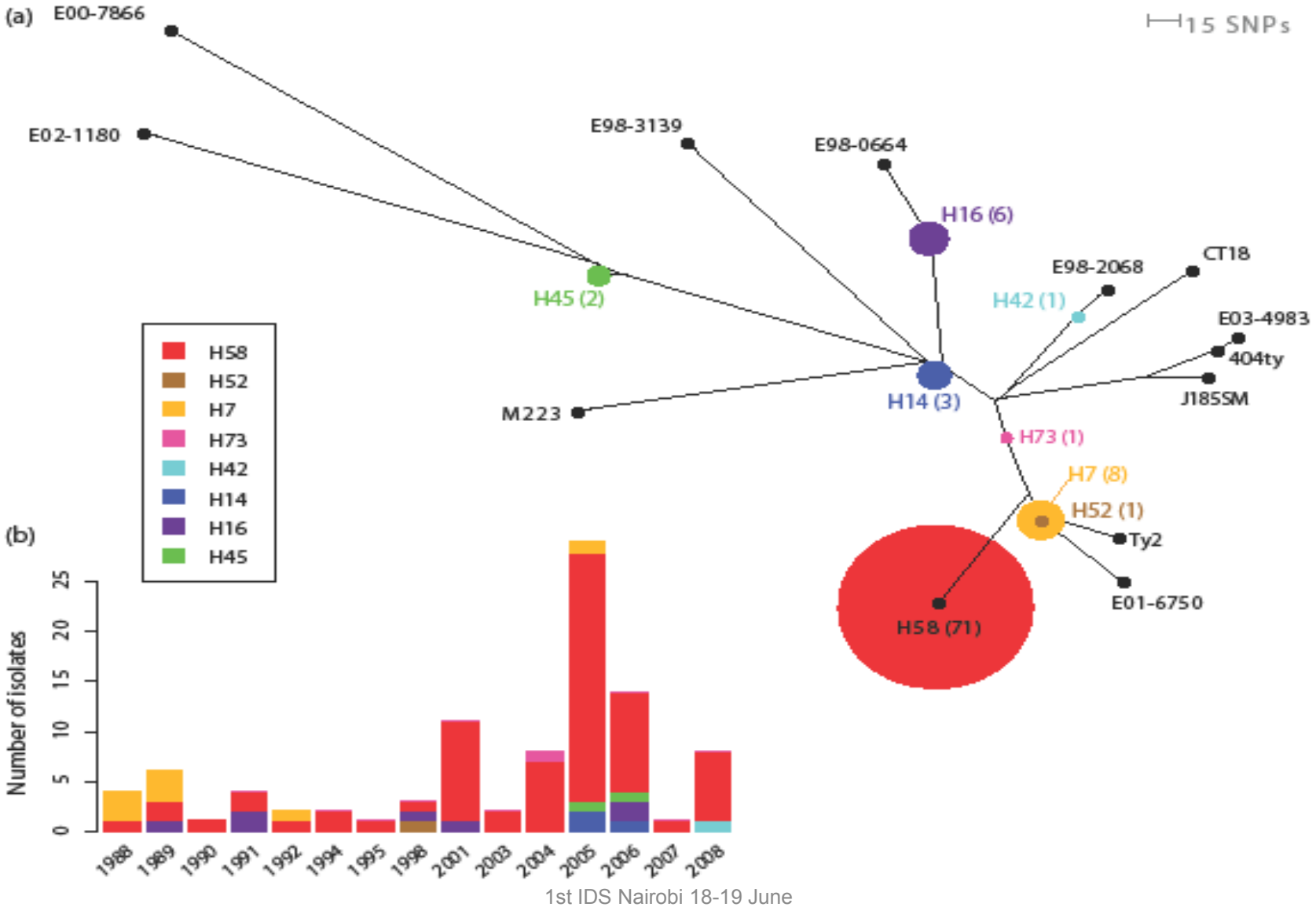
Samuel Kariuki,[1,4]* Gunturu Revathi,[2] John Kiiru,[1] Doris M. Mengo,[1] Joyce Mwituria,[1] Jane Muyodi,[1] Agnes Munyalo,[1] Yik Y. Teo,[3] Kathryn E. Holt,[4] Robert A. Kingsley,[4] and Gordon Dougan[4]

Centre for Microbiology Research, Kenya Medical Research Institute, P.O. Box 43640, Nairobi, Kenya[1]; Aga Khan University Hospital, Nairobi, Kenya[2]; The Wellcome Trust Centre for Human Genetics, University of Oxford, Roosevelt Drive, Oxford OX3 7BN, United Kingdom[3]; and The Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, CB10 1SA, United Kingdom[4]

Received 7 October 2009/Returned for modification 23 March 2010/Accepted 2 April 2010



MDR Haplotype H58 Now Well Established in the Region



Emergence of ESBL Producing *Vibrio cholerae* in Kenya

Curent ESBL Genotypes

Isolate Number	ESBL Enzymes Present	Intergron	Insertion Sequence	Plasmid
38/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
39/2012	Negative control			
37/2012	CTX-M, TEM	Int2	IS26	IncA/C
52/2012	CTX-M	Int2	IS26, ISCEp1	IncA/C
54/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
58/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
64/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
68/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
56/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
43/2012	CTX-M	Int2	IS26, ISCEp1	IncA/C
74/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
73/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
78/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
75/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
76/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
44/2012	TEM	Int2		
41/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
45/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C
42/2012	CTX-M, TEM	Int2	IS26, ISCEp1	IncA/C

Note

Isolates were negative for OXA-1, OXA-2, INT class 1, aac-(6′)-1b-cr, INT class 3, CMY

Isolates from Haiti in year 2012 had IncA/C2 plasmid with CTX-M-1 or 2, INT-2, CMY among others.

What Are We Doing About AMR in Kenya?

Roadmap to implementing the NAP

Global Antibiotic Resistance Partnership

KENYA MEDICAL RESEARCH INSTITUTE KEMRI

SITUATION ANALYSIS AND RECOMMENDATIONS

Antibiotic Use and Resistance in Kenya

http://www.cddep.org/publications/situation_analysis_and_recommendations_antibiotic_use_and_resistance_kenya

THE NATIONAL POLICY FOR PREVENTION AND CONTAINMENT OF AMR
OCTOBER, 2016

Scope of the Policy

- Introduction to awareness on antimicrobial resistance, policy and legislative focus, situational analysis, rationale, goals and objectives.

- The policy proposes interventions that will help reduce misuse and minimize emergence of AMR.

- Provides for a National Action Plan that will guide all the stakeholders in playing their respective roles.

Policy Implementation Framework

National Action Plan

- A comprehensive **National Action Plan (NAP)** has been developed in line with the Global Action Plan (GAP) on AMR to effectively implement the AMR policy.

Financing

- The National and County Governments in collaboration with development partners will ensure that **adequate funding** is available to enable the implementation of sustainable AMR interventions identified in the policy and National Action Plan.
- The budget for AMR activities will be across multi-agency and directly aligned to the National Action plan, operational plans and Monitoring and Evaluation plan.

Policy Implementation Framework

Monitoring and Evaluation(M&E)

- The objective of Monitoring and Evaluation will be to ensure prudent AMU and reduction of AMR against set targets and document useful lessons for planning purposes.

Communication Strategy

- A communication strategy is essential for creating awareness, influencing behavior change and controlling AMR.

Summary

- AMU in public health and livestock sectors not well documented, but abuse is commonly observed in both sectors.
- AMR huge issue in enteric bugs as they acquire MGE with ESBL and other key R-genes.
- For some life-threatening illnesses, we are gradually running out of treatment options.
- A NAP encompassing all sectors will be crucial to stem AMR.

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Veterinary Public Health

Ministry of Agriculture, Livestock and Fisheries