Antimicrobial Resistance, the sure and ongoing pandemic

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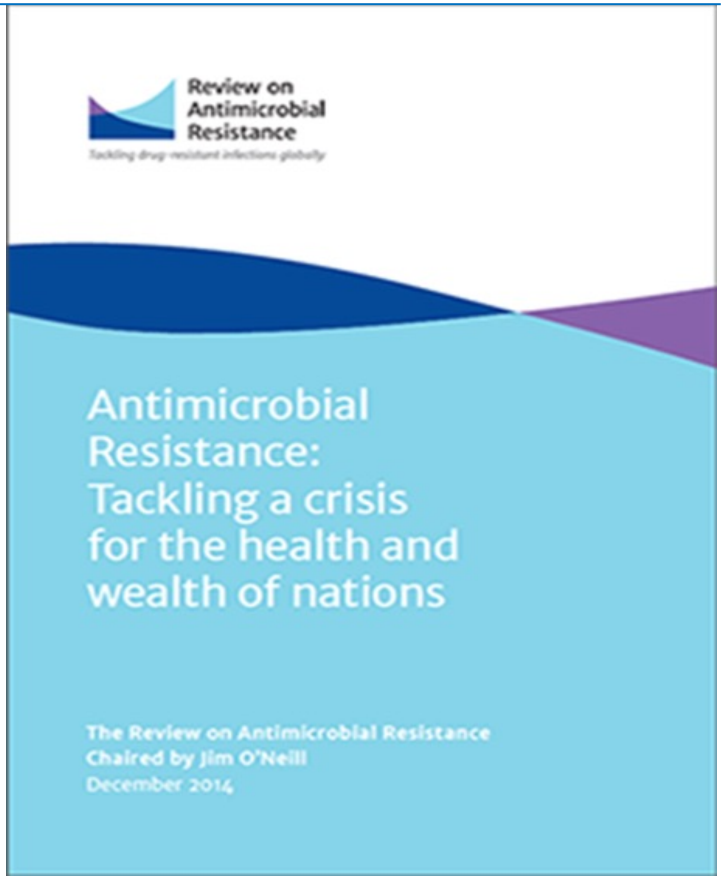
AMR IN GLOBAL CONTEXT: Why the Concern now?

- AMR is increasingly serious global public health threat:
  - Untreatable infections, prolonged hospital care
  - Desperation over "dry Ab pipeline“
  - Africa will suffer most being most disease endemic, economies unable to afford effective antimicrobials, nearly 4.15m deaths by 2050.
- Economic burden
  - In 2050 costing the world up to $100 trillion
- Growing awareness and commitment
  - Political, professional, public



In Search of Better Health

"Drug resistance follows the drug like a faithful shadow."

- Paul Erhlich 1854-1915

In Search of Better Health

Millions are dying from drug-resistant infections, global report says

5 hours ago

BBC News 21 January, 2022

THE LANCET

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PDF [3 MB]

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

Antimicrobial Resistance Collaborators † • Show footnotes

Open Access • Published: January 19, 2022 • DOI: https://doi.org/10.1016/S0140-6736(21)02724-0 •

Check for updates

Summary

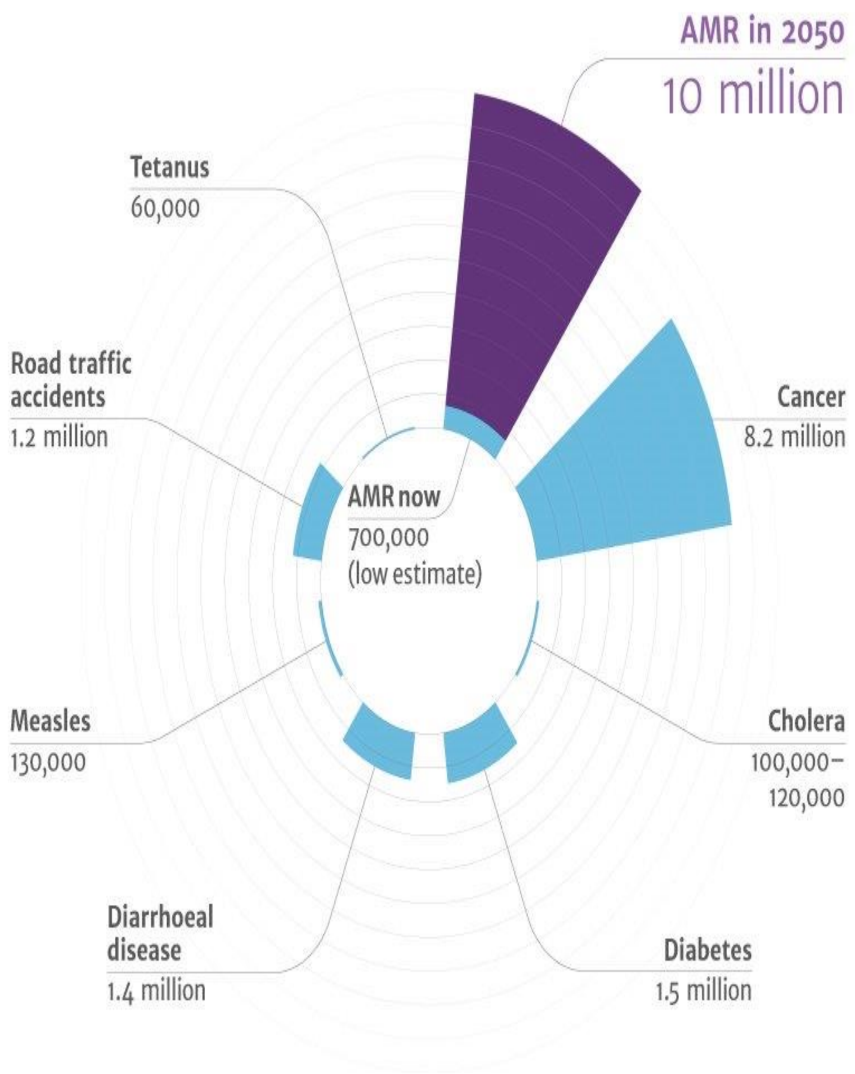
Background

Antimicrobial resistance (AMR) poses a major threat to human health around the world. Previous publications have estimated the effect of AMR on incidence, deaths, hospital length of stay, and health-care costs for specific pathogen–drug combinations in select locations. To our knowledge, this study presents the most comprehensive estimates of AMR burden to date.

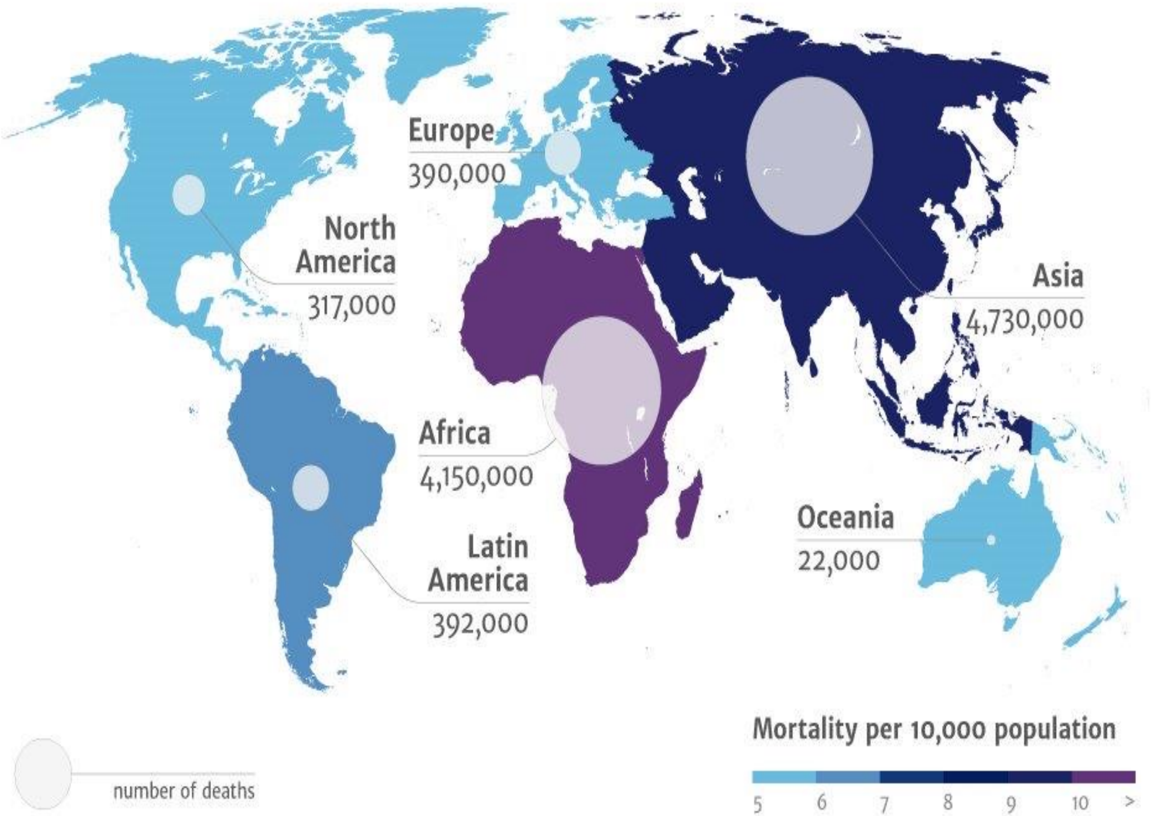
The AMR Health Crisis

- To put this health crisis in perspective, **let's compare the global impact of COVID-19 to that of AMR**:
- In 2021 COVID-19 caused **3.55 million deaths worldwide**
- In 2019 bacterial AMR was associated with **4.95 million deaths** globally* and that death toll is expected to be 10 million by 2050

Cumulative deaths due to AMR by 2050



Distribution of AMR deaths by Region



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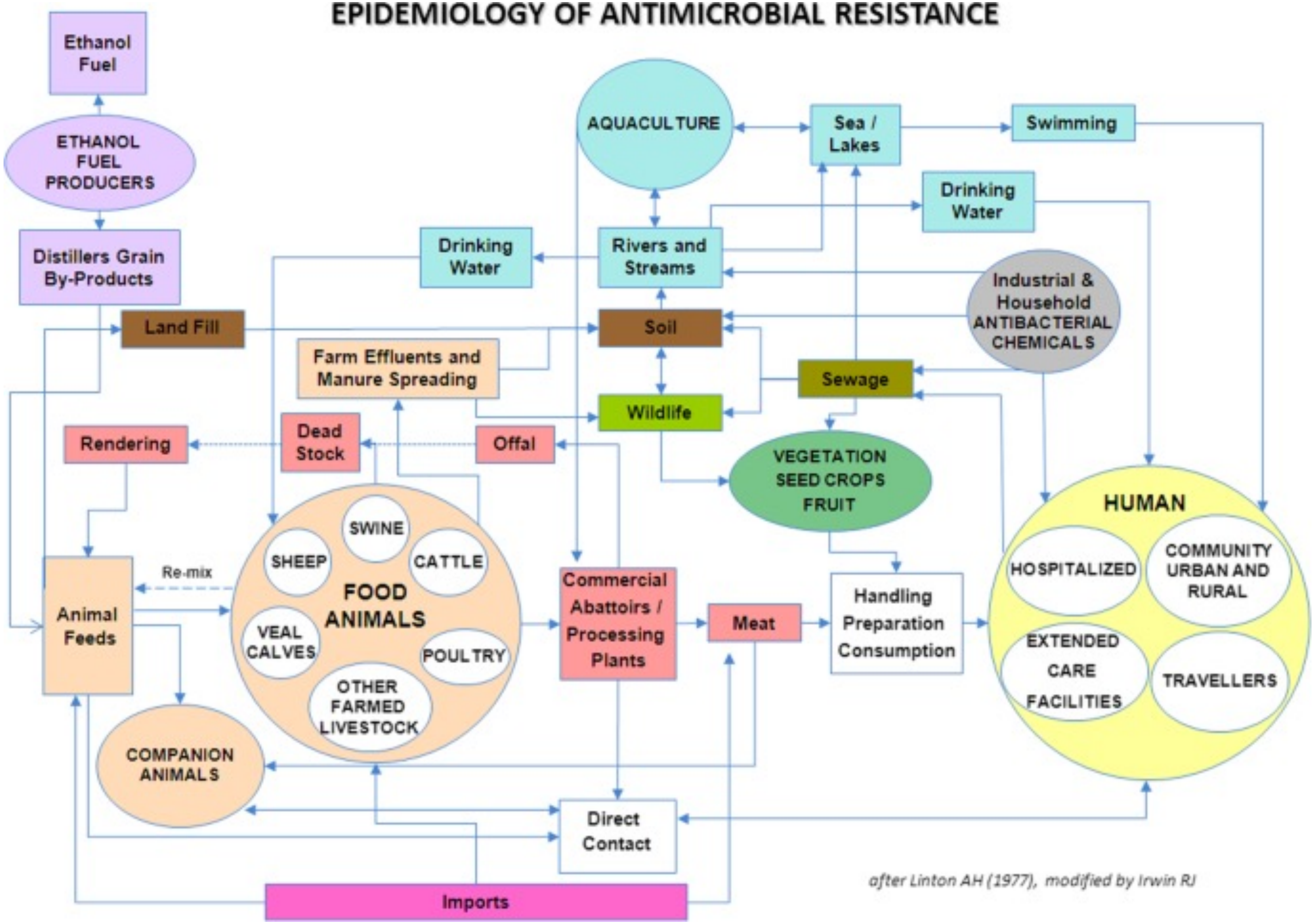
Why a "One Health "Approach in AMR?

- 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 resistance genes do not recognize geographic or ecologic borders

EPIDEMIOLOGY OF ANTIMICROBIAL RESISTANCE



Examples of AMR in One Health

Cholera

- The **first ESBL strains** were recovered from Daadab refugee camps close to the Somali border in early **2012**.
- Such strains later **emerged in urban slums** including Kibera and Mukuru.
- The **first major outbreak of cholera with the MDR phenotype** started in Tana river delta 250 km East of Nairobi in **2015**.
- Since then ESBL producing *Vibrio cholerae* have persisted in disease outbreaks in Kenya.
- Analysis of our strains showed similarity with strains from the Yemeni major epidemic

Weill, FX et al. Genomic insights into the 2016–2017 cholera epidemic in Yemen. Nature 2019, Jan;565(7738):230-233.

The Headlines!

DAILY NATION | NEWS | BUSINESS | COUNTIES | SPORTS | BLOGS & OPINION | LIFE & STYLE | VIDEOS | PHOTO

Families at risk as cholera becomes deadlier

ALERT

Nairobi county issues warning on cholera outbreak

DAILY NATION | NEWS | BUSINESS | COUNTIES | SPORTS | BLOGS & OPINION | LIFE & S

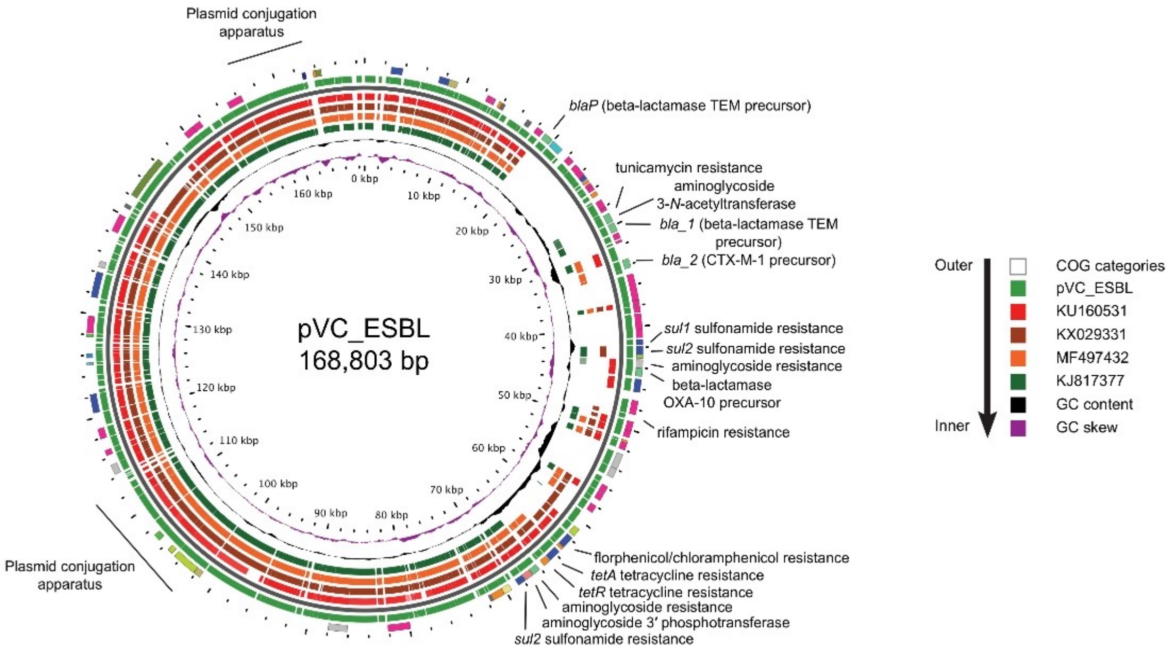
Nairobi Hospital cholera cases hit 58

SATURDAY APRIL 20 2019

Cholera death toll hits 33, as 11 regions suffer

Graham Kajilwa And Anyango Otieno 27th Sep 2019 00:00:00 GMT +0300

Kenyan strains show 3 main AMR 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*$_{TEM1B}$-*cmlA-bla*$_{OXA-10}$-*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 *bla*$_{CTX-M-15)}$, *aac(3)-IIc* that confer resistance to streptomycin, kanamycin and tobramycin and a putative gene for tunicamycin resistance

Novel Multidrug resistant NTS strains, recently emerged

PLOS NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

High relatedness of invasive multi-drug resistant non-typhoidal *Salmonella* genotypes among patients and asymptomatic carriers in endemic informal settlements in Kenya

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Abstract

Invasive Non-typhoidal *Salmonella* (iNTS) disease is a major public health challenge, especially in Sub-Saharan Africa (SSA). In Kenya, mortality rates are high (20–25%) unless prompt treatment is instituted. The most common serotypes are *Salmonella enterica* serotype Typhimurium (*S.* Typhimurium) and *Salmonella enterica* serotype Enteritidis (S. Enteritidis). In a 5 year case-control study in children residing in the Mukuru informal settlement in Nairobi, Kenya, a total of 4201 blood cultures from suspected iNTS cases and 6326 fecal samples from age-matched controls were studied. From the laboratory cultures we obtained a total of 133 *S.* Typhimurium isolates of which 83(62.4%) came from cases (53 blood and 30 fecal) and 50(37.6%) from controls (fecal). A total of 120 *S.* Enteritidis consisted of 70 (58.3%) from cases (43 blood and 27 fecal) and 50(41.7%) from controls (fecal).

The *S.* Typhimurium population fell into two distinct ST19 lineages constituting 36.1%, as well as ST313 lineage I (27.8%) and ST313 lineage II (36.1%) isolates. The *S.* Enteritidis isolates fell into the global epidemic lineage (46.6%), the Central/Eastern African lineage (30.5%), a novel Kenyan-specific lineage (12.2%) and a phylogenetically outlier lineage (10.7%). Detailed phylogenetic analysis revealed a high level of relatedness between NTS from blood and stool originating from cases and controls, indicating a common source pool. Multidrug resistance was common throughout, with 8.5% of such isolates resistant to extended spectrum beta lactams. The high rate of asymptomatic carriage in the population is a concern for transmission to vulnerable individuals and this group could be targeted for vaccination if an iNTS vaccine becomes available.

Data from Sentinel Surveillance on Antimicrobial Resistance in Health Facilities

- Cases: <16 years of age, at least 3 days of fever and fever, at least 37.5°C or they present with a history of fever
- Three or more loose stools in the 24 hours before presentation,
- Controls: Age matched children from same clinic coming for routine vaccination

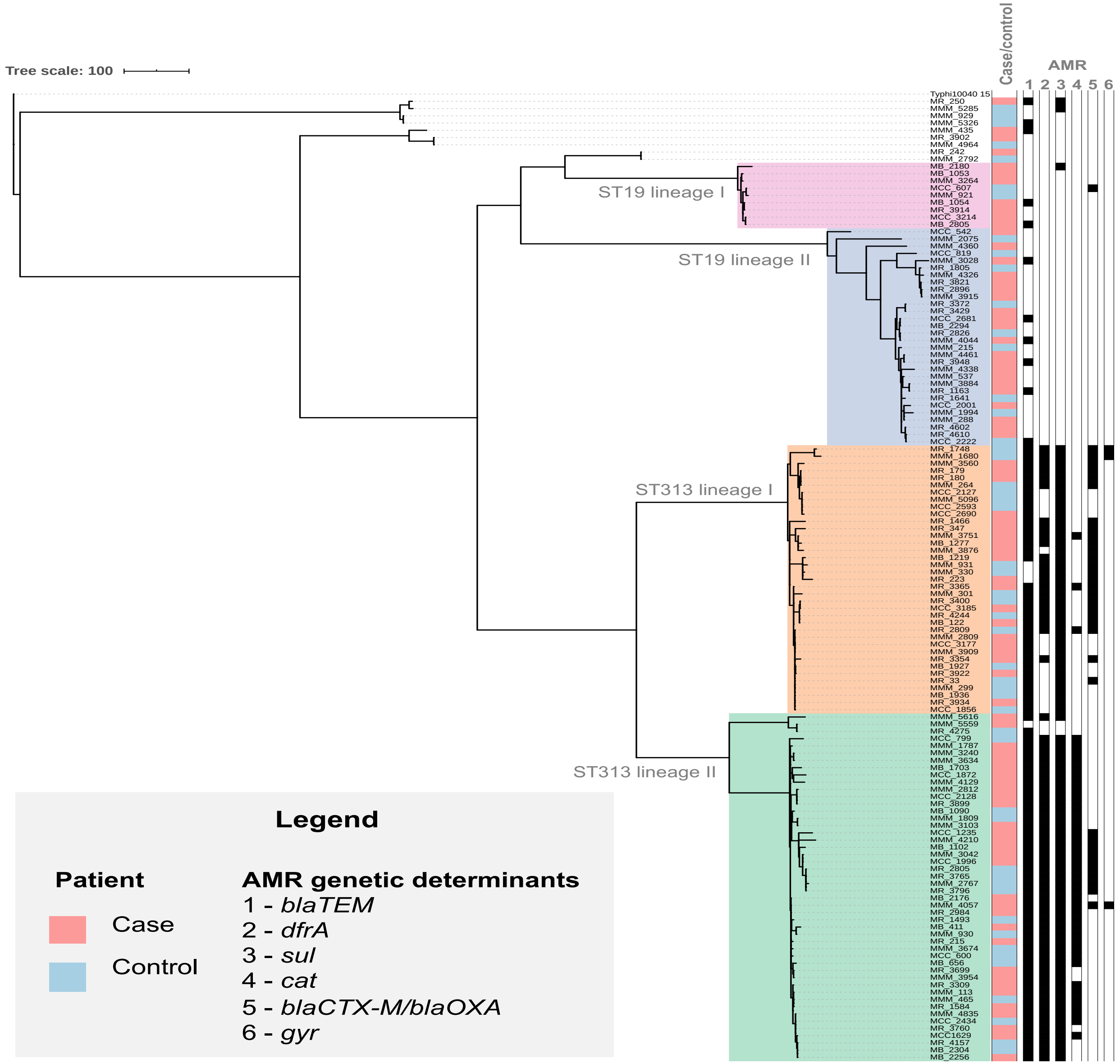
Table 1: Age distribution of patients, both cases and controls

	Case	Control
Age category	No. (%)	No. (%)
0-12 months	811 (19.3)	846 (13.4)
13-24 months	1096 (26.1)	1812 (28.6)
25-36 months	875 (20.8)	1412 (22.3)
37-48 months	828 (19.7)	1304 (20.6)
49-60 months	591 (14.1)	952 (15.1)
Total	**4201 (100)**	**6326 (100)**

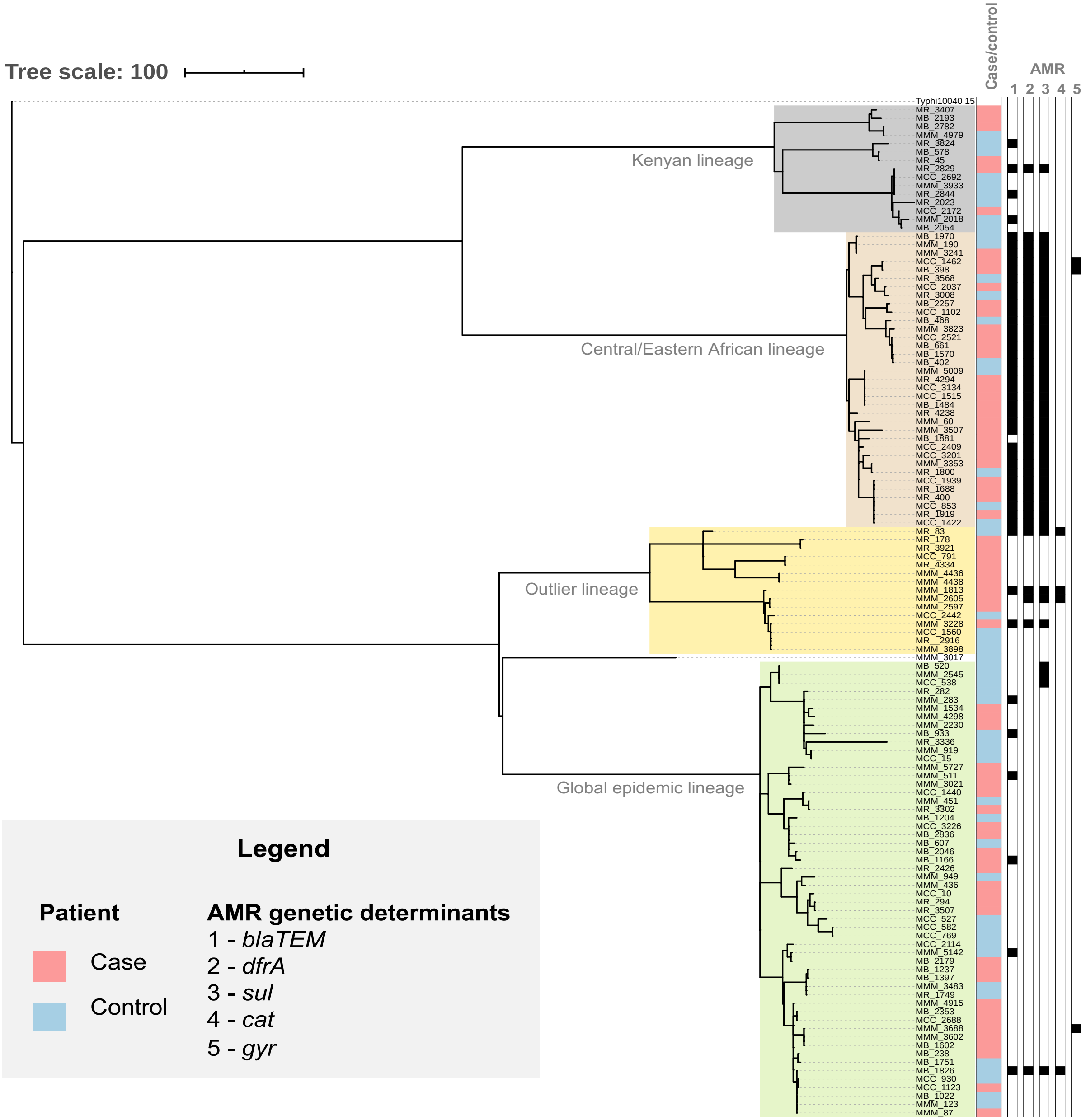
Epidemiology of iNTS Infections in Kenya

- Invasive NTS (iNTS) is a major cause of morbidity and mortality especially in children below 5 years of age
- Incidence rates range from 166 to 568/100,000 cases pyo.
- ***iNTS bacteraemia in young febrile children has poor outcome***
  - *Upto 28-35% may die within 48h*
- *Although no zoonotic source identified so far, transmission is enhanced in rainy season, poor sanitation and contaminated water source*

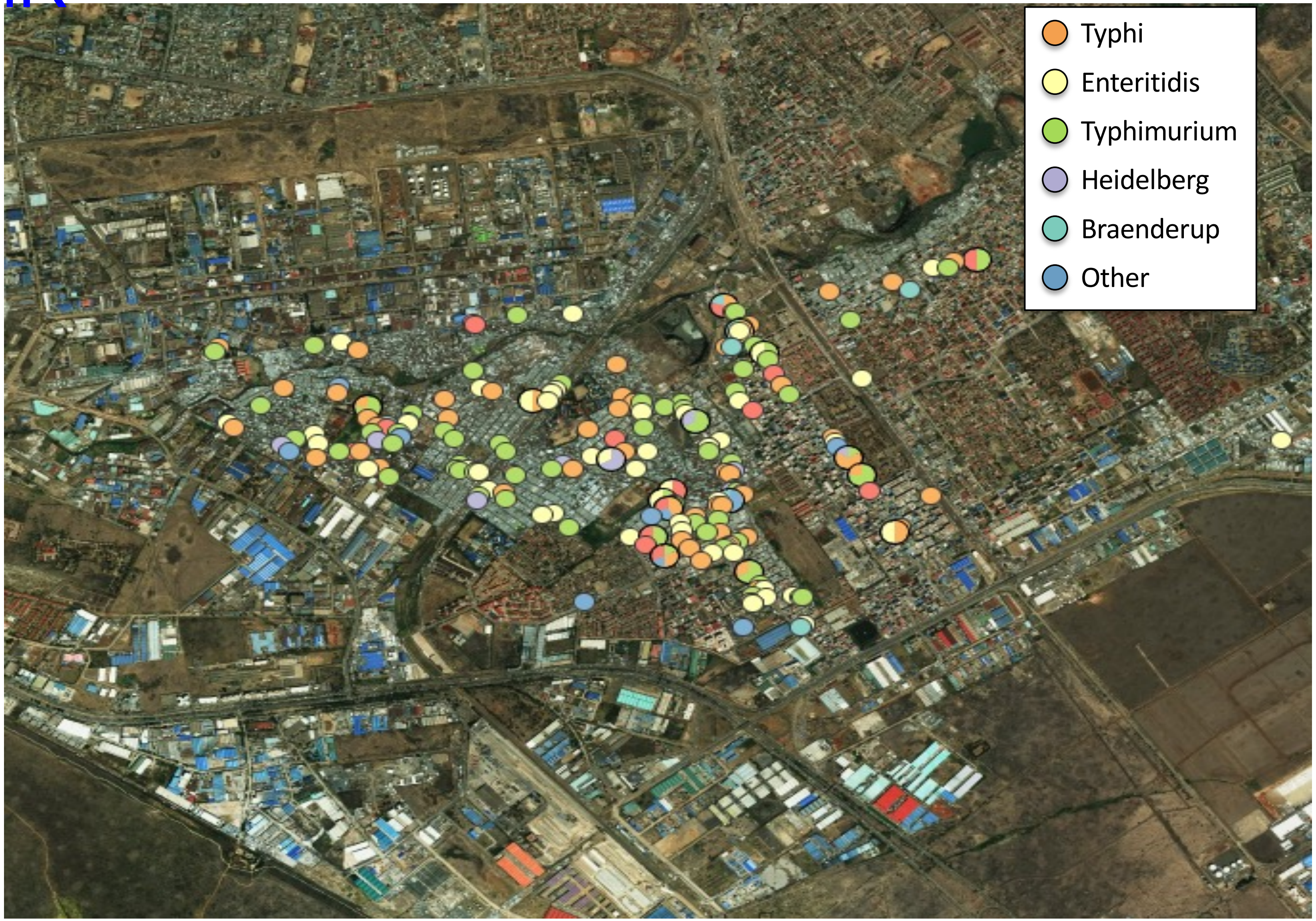
AMR – *S.* Typhimurium



AMR – *S.* Enteritidis



Mapping hotspots of *Salmonella* disease and AMR



Antibiotic use and Resistance in Livestock in Kenya

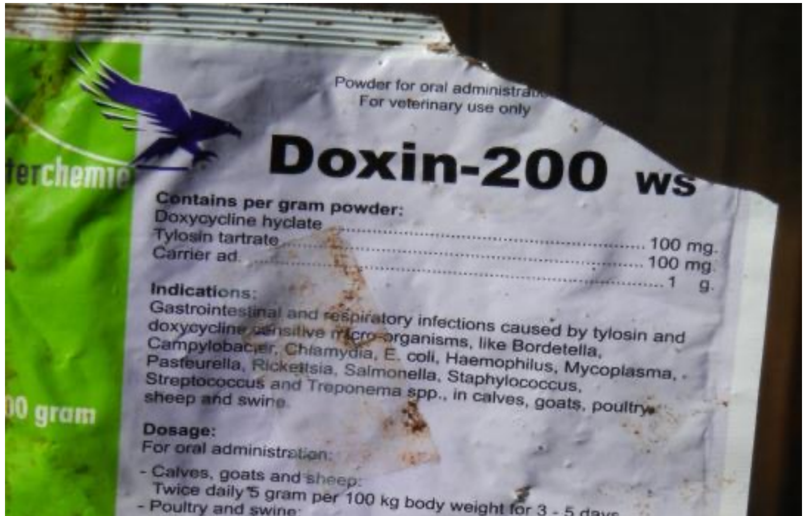
Veterinary Antimicrobials Imported into Kenya through the Single Window system (July 2017-January 2018)

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

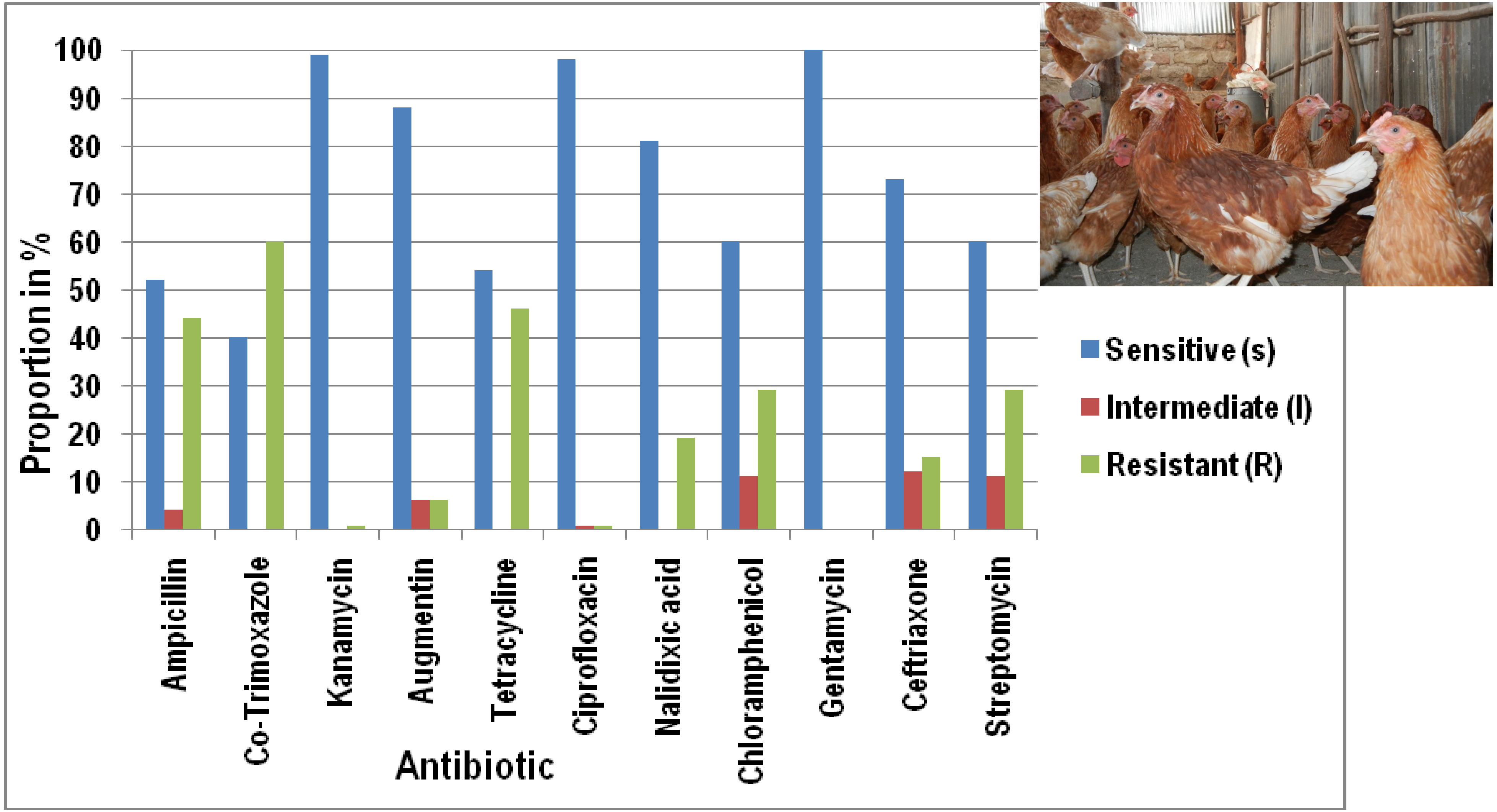
Most commonly used antimicrobials used in livestock same as in humans

County/Sub-County	Total No. of poultry reared	Most common antibiotics used for treatment/prophylaxis/ growth promotion
Thika west	3100	Enrofloxacin; Trimethoprim-Sulphamethoxazole, Fosfomycin
	6524	Enrofloxacin, Oxytetracycline
	1000	Amoxicillin, Fosfomycin
Gatundu North	7760	Oxytetracycline, Furadolidone
	4780	Trimethoprim, Oxytetracycline
Kisumu East	127	Trimethoprim
Kisauni	90,000	Oxytetracycline, Fosfomycin
Kwale	4300	Oxytetracycline

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

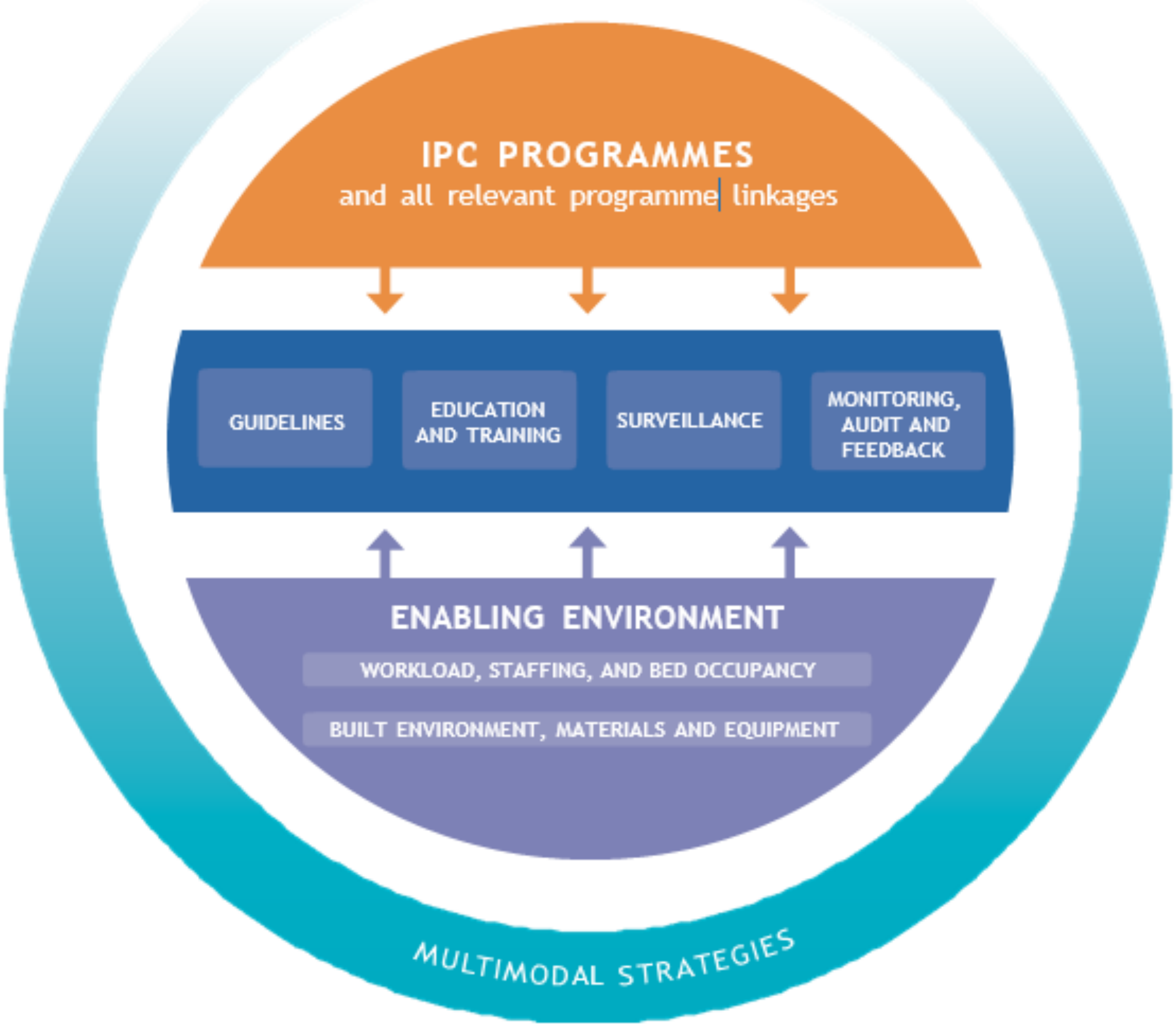


Antibiotic susceptibility patterns for E. coli isolated from Chicken processing factory



The role of IPC in combating AMR; Core strategies

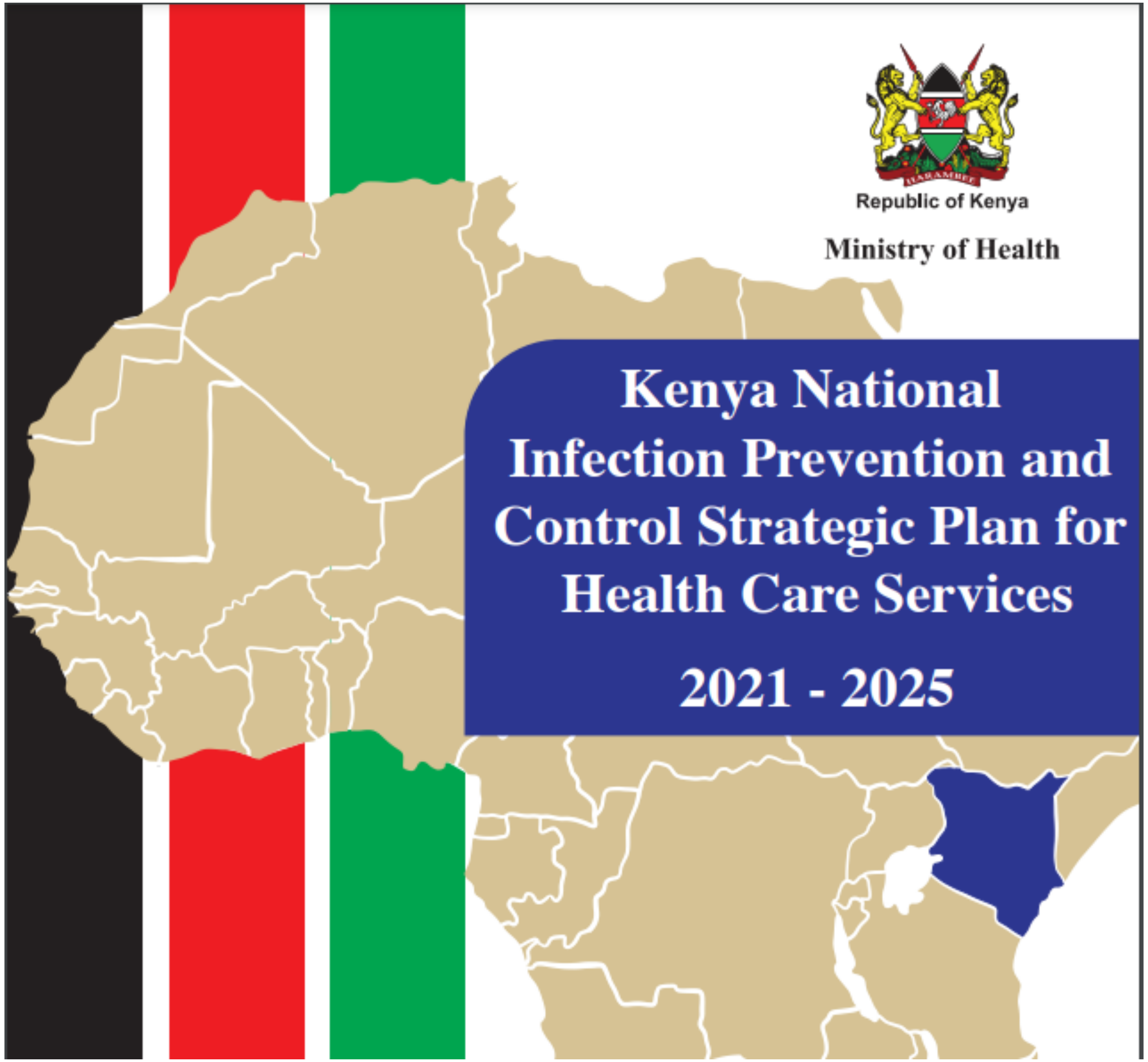
Core IPC strategies in combating AMR



Infection prevention and control guidelines

- Technical guidelines provide clear directions on IPC priorities and evidence-based standards.

- If effectively linked to education and training when implemented and monitored, guidelines can lead to desired IPC outcomes



Education and training

- Support of IPC education and training is a key function of IPC programmes with the ultimate aim of developing a skilled and knowledgeable health workforce. This includes;
  - Training of those with basic IPC competencies.
  - Providing continuous education for IPC specialists

Surveillance of Health care-associated infection

Surveillance provide critical information on the incidence and prevalence of HAIs and AMR

These are the most common HAIs causing organisms are;

- **Commensal bacteria-** E.coli ,Coagulase Negative *Staphylococcus*
- **Pathogenic bacteria-** *Staphylococcus aureus*, Enterobacteriacae (e.g. *Escherichia coli, Proteus, Klebsiella, Enterobacter, Serratia marcescens)* and *Pseudomonas* spp

Monitoring/audit of IPC practices and feedback and control activities

Recommended processes and indicators to be monitored.

- Hand hygiene compliance
- Transmission-based precautions implementation for resistant organisms and highly transmissible infectious diseases
- Disinfection and sterilization of medical equipment/instruments
- Consumption/use of alcohol-based handrub or soap
- Consumption/use of antimicrobial agents

Return on Investment: Effective IPC saves money!

When IPC and hand hygiene are implemented in combination with antibiotic stewardship programmes

2/3
Reduction
IN FREQUENCY OF AMR INFECTIONS

27,000
Deaths avoided
IN EUROPE

85%
Reduction
IN HEALTH BURDEN

3€
Per capita
SAVED EVERY YEAR

Emerging issues

- With increasing informal settlements with little or no WaSH infrastructure, we will continue to experience outbreaks, we have to prepare!
- Accurate diagnosis a major challenge in our settings – simple, affordable, rapid kits that can be deployed under field conditions.
- Burden of disease data and economic implications important to policy makers as these mobilize action!
- We have options for vaccine introduction in the short-term…

The Data and advocacy Gaps

- Do we really have data on AMU? NO.
- What are key social-economic drivers of AMU and AMR?
- Stewardship programs in healthcare facilities require scaling up
- Socio-anthropological approach (Behaviour change) on AMU: Huge task
- IPC doing a great job so far – advocacy must be scaled up too
- Approaching AMU and stewardship from One-Health paradigm slow in our setting

Some points to ponder to address our challenges

- Consider a **comprehensive "programmatic approach"** to tackling AMR in the human health sector that puts the patient at the center
- Comprehensive and **graded AMR Assessment Tool** to help countries in revision of their AMR NAPs, and identify current capacity levels
- Development of **guidance on an "Essential package of interventions"** to move countries forward along their capacity levels
- **Guidance on other technical tools** useful and effective to strengthen AMR NAP implementation

Some points to ponder to address our challenges ctn'd

- **Engage external stakeholders** and strengthen coordination

- Identify **a minimum list of indicators for success** that are achievable by all – this can be linked to the minimum essential package based on prioritization of interventions.

  STAG AMR Consideration from STAG for the Global Regulators' Summit on Antibiotic Use in Humans and Animals

- Need for the **AMR response to be sustainable and equitable**, link to existing plans, programmes and budgets e.g. health systems strengthening and UHC.

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HARAMBEE

MINISTRY OF HEALTH

Study site clinicians

Field workers