



UNIVERSITY OF <sup>TM</sup>  
**KWAZULU-NATAL**  
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**YAKWAZULU-NATALI**

# Antibiotic Resistance and One Health

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**South African Research Chair in Antibiotic Resistance and One Health**

**Antimicrobial Research Unit, University of KwaZulu-Natal**



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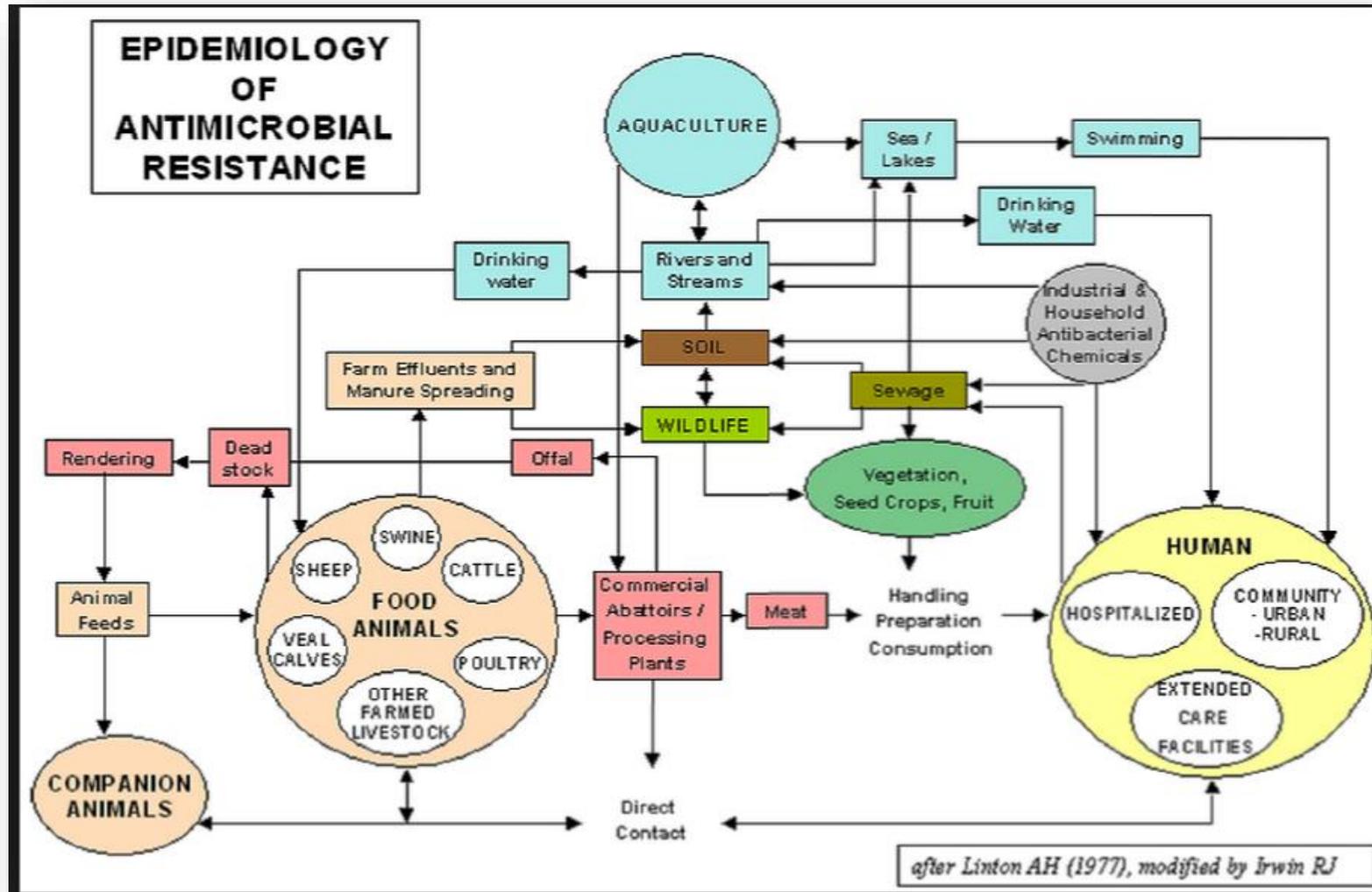
UKZN INSPIRING GREATNESS

# Overview

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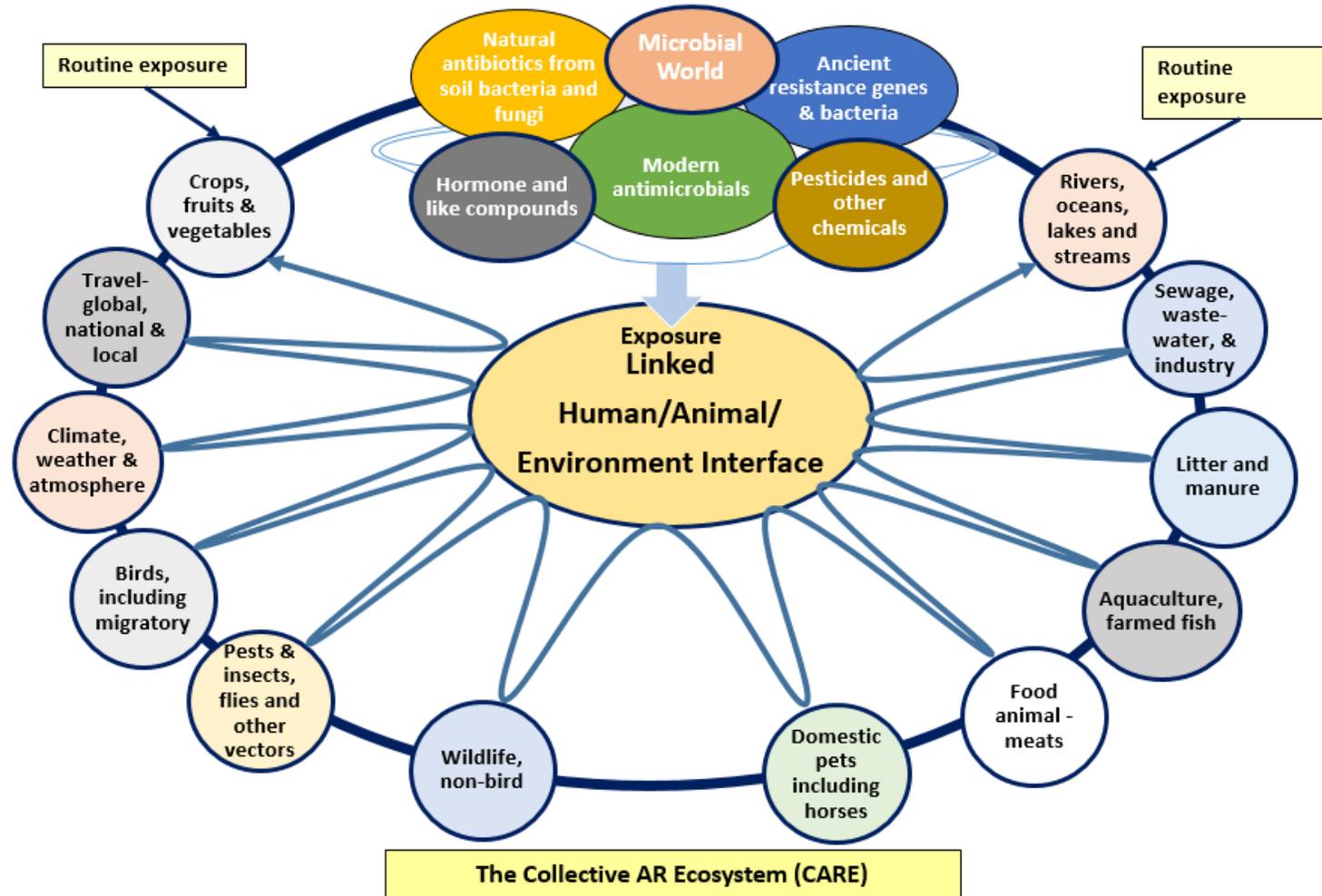
- One Health
- National Imperative
- Conceptual Framework
- Aim and Work Packages
- Study Site & Study Design
- Progress to Date
- Envisaged Output

# One Health



[http://www.phac-aspc.gc.ca/cipars-picra/gfx/2b\\_e.gif](http://www.phac-aspc.gc.ca/cipars-picra/gfx/2b_e.gif)

# One Health (2)

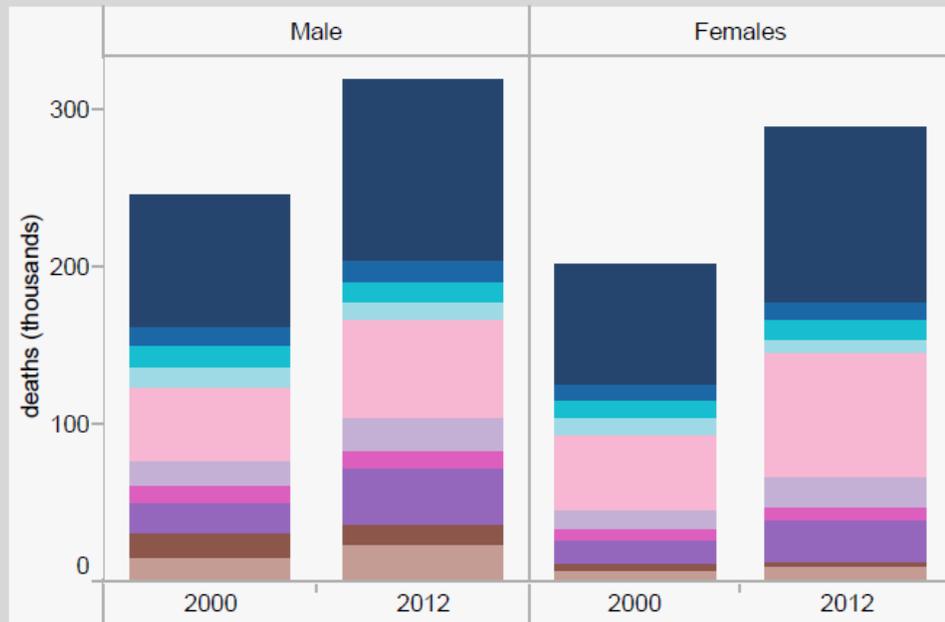


Courtesy of Paula Cray

**NC STATE** Veterinary Medicine

# National Imperative

Deaths by broad cause group



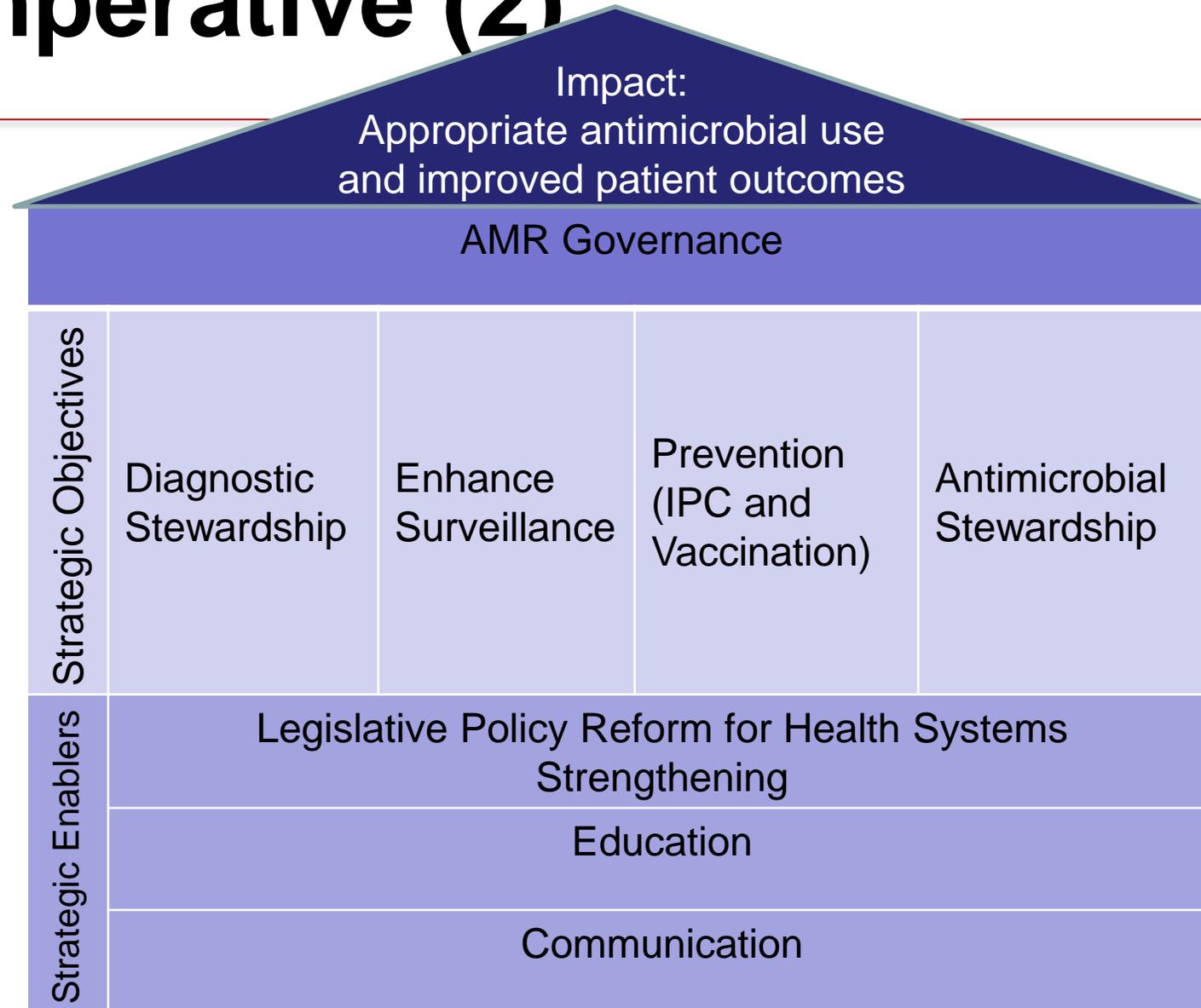
- 2/3 of the 1 538 433 kg of antimicrobials sold for animal use between 2002-4 were used in growth promotion.
- Included antibiotics banned as AGPs in the EU.
- SA amongst the 5 countries responsible for 76% of the 36% overall increase in antibiotic use in 71 countries over the period 2000-10 .

<http://www.who.int/gho/countries/zaf.pdf>

Van Boeckel TP et al., [Lancet Infect Dis.](#) 2014 14:742-750

Antimicrobial Resistance National Strategy Framework: A One Health Approach 2017-2024 Department of Health, Pretoria, South Africa. 2017

# National Imperative (2)



Antimicrobial Resistance National Strategy Framework: A One Health Approach 2017-2024 Department of Health, Pretoria, South Africa. 2017

# Aim & Work Packages

## Aim

To comprehensively delineate the molecular epidemiology, nature and extent of ABR in human, animal and environmental health in the “One Health” context to inform evidence-based strategies for its monitoring, prevention and containment

## Work Packages

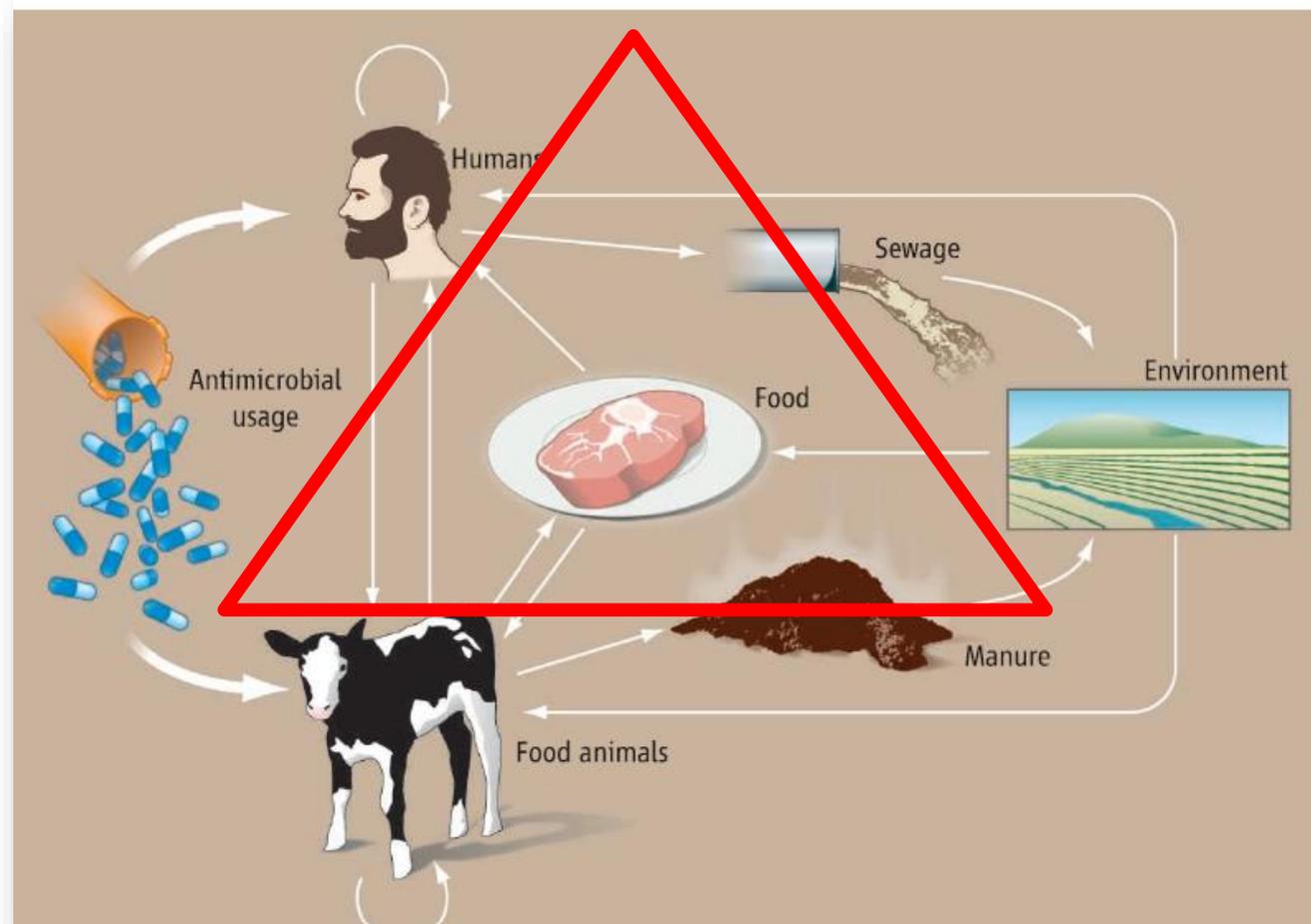
- WP1: Surveillance
- WP2: Resistance Mechanisms
- WP3: Resistance Dissemination
- WP4: Virulence
- WP5: Policy Briefs

# Aim (2): Mapping

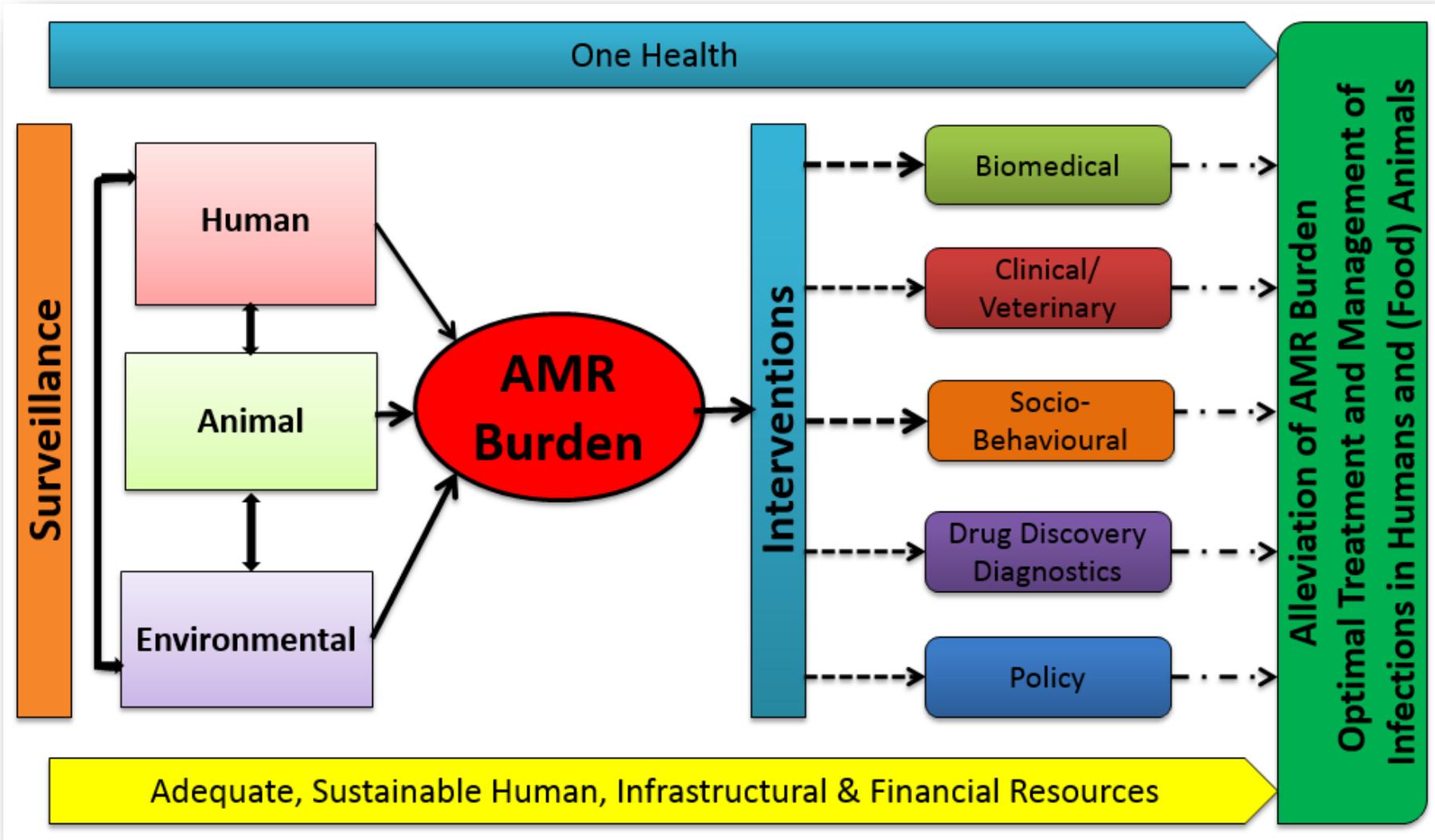
Map the fluidity of

- antibiotic-resistant bacterial clones,
- antibiotic resistance genes, and
- associated mobile genetic elements

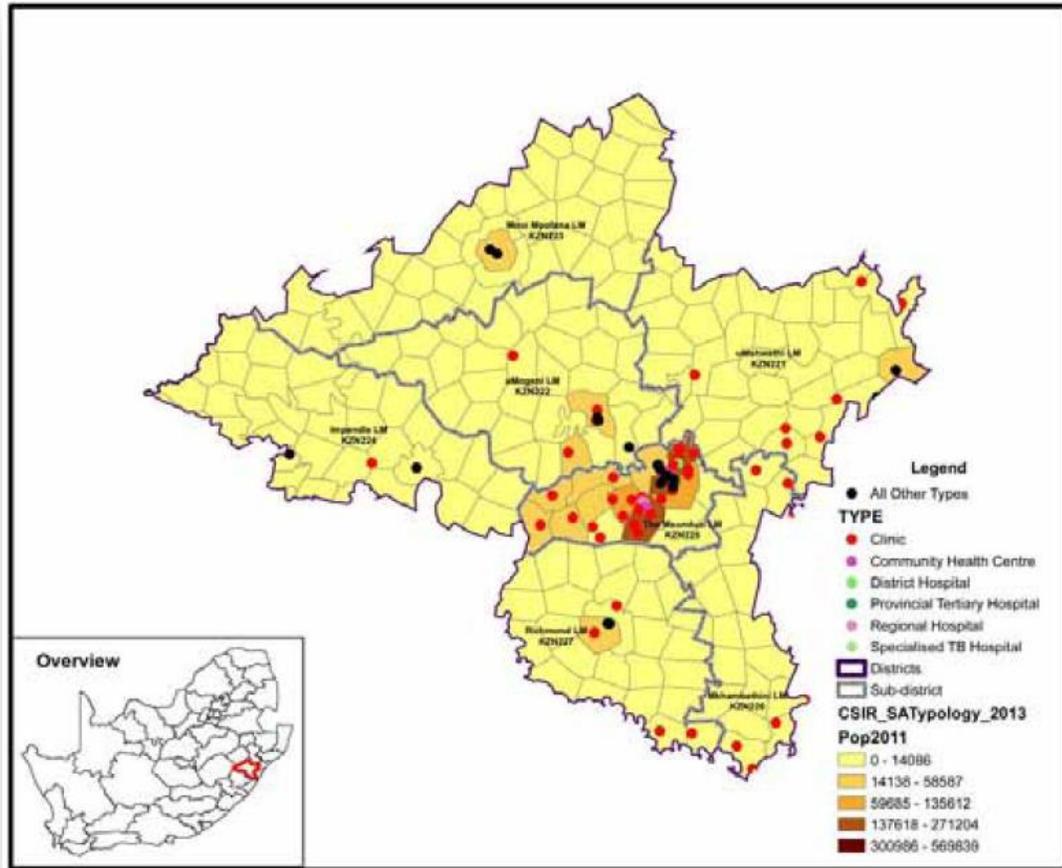
within and between the human, animal, and environmental health sectors



# Conceptual Framework



# Study Site: uMgungundlovu District



- PHC centres, district, regional & tertiary hospitals.
- Urban & rural case mix.
- Intensive poultry & pig livestock production.
- Pig & poultry litter used to fertilize agricultural soil.
- 6 waste water treatment plants.

# Study Design: Ethical Considerations

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- Ethical clearance from the:
  - UKZN Animal Research Ethics Committee (AREC)
  - UKZN Biomedical Research Ethics Committee (BREC)
  - Provincial Health Research Ethics Committee (PHREC)
  - Department of Agriculture, Forestry and Fisheries (DAFF)
- Confidentiality Agreements signed with producers, farmers and abattoirs.
- Voluntary, informed consent obtained for samples taken for research purposes.
- Anonymity & confidentiality assured at all times.

# Study Design: One Health Surveillance



Human Health: Hospital & Community Levels



Animal Health: Intensive Pig & Poultry Farms



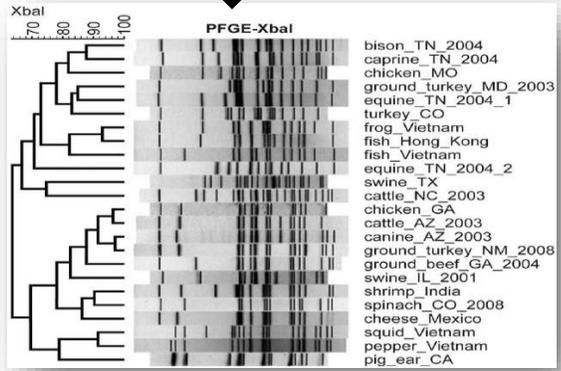
Environmental Health: Water & Soil

One Health Surveillance Programme

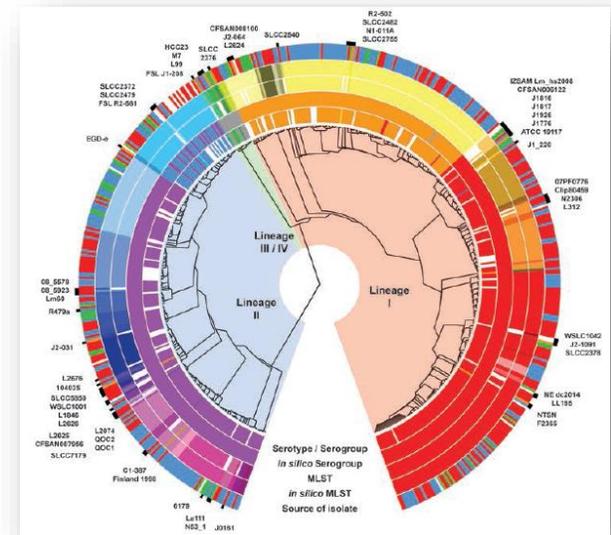
Resistance pattern*	Resistance type	No. of isolates (%)
Amp	I	5 (15.6)
Amp, Cip	II	2 (6.25)
Amp, R	III	1 (3.12)
Amp, Ery, Cli, Cip	IV	7 (21.88)
Amp, Ery, Cli, Cip, SXT	V	7 (21.88)
Amp, Ery, Cli, Gent, R, STX	VI	6 (18.75)
Amp, Ery, Cli, Gent, Ak, STX	VII	4 (12.5)

\*Amp, Ampicillin; Cip, Ciprofloxacin; R, Rifampin; Ery, Erythromycin; Cli, Clindamycin; SXT, Trimethoprim/sulfamethoxazole; Gent, Gentamicin; Ak, Amikacin.

Phenotyping:  
ASTs, screening, antibiograms

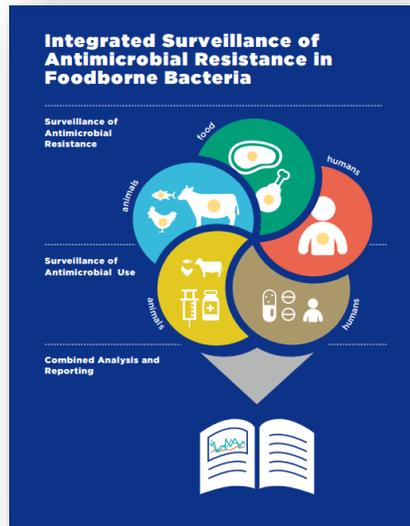
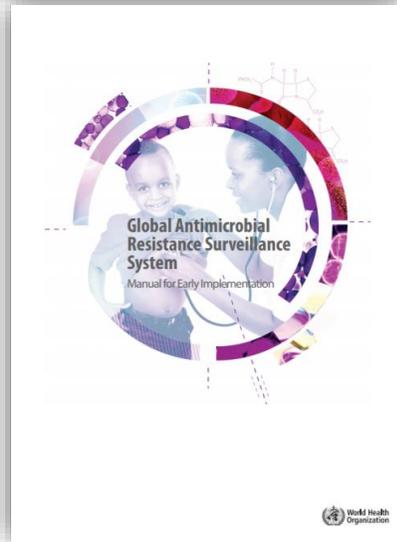


Genotyping:  
PFGE/ERIC-PCR/REP-PCR



WGS

# Progress to Date



- Implemented surveillance in human, food animal & environmental health, i.e. :
  - Passive laboratory, active sentinel surveillance & active comprehensive surveillance in human health at community health centre & hospital levels,
  - Surveillance from farm to fork in intensive poultry & pig production system,
  - Surveillance in water (influent and effluent of WWTPs + upstream & downstream surface water),
  - Surveillance in soil fertilized by chicken litter.
- eAMR App
  - Sample collected & patient details captured at bedside prior to antibiotic administration

# Outputs: Human Health

African Journal of Laboratory Medicine  
ISSN: (Online) 2225-2010, (Print) 2225-2002



Page 1 of 8 Original Research

## Antibiotic resistance trends of ESKAPE pathogens in Kwazulu-Natal, South Africa: A five-year retrospective analysis

Founou et al. *Antimicrobial Resistance and Infection Control* (2018) 7:134  
<https://doi.org/10.1186/s13756-018-0423-0>

Antimicrobial Resistance and Infection Control

RESEARCH

Open Access



Extended spectrum beta-lactamase mediated resistance in carriage and clinical gram-negative ESKAPE bacteria: a comparative study between a district and tertiary hospital in South Africa

Raspail Carrel Founou<sup>1,2\*</sup>, Luria Leslie Founou<sup>1,3</sup> and Sabiha Yusuf Essack<sup>1</sup>



RESEARCH ARTICLE

Clinical and economic impact of antibiotic resistance in developing countries: A systematic review and meta-analysis

Raspail Carrel Founou<sup>1,2\*</sup>, Luria Leslie Founou<sup>1,3</sup>, Sabiha Yusuf Essack<sup>1</sup>

## SCIENTIFIC REPORTS

OPEN

Whole Genome Sequencing of Extended Spectrum  $\beta$ -lactamase (ESBL)-producing *Klebsiella pneumoniae* Isolated from Hospitalized Patients in KwaZulu-Natal, South Africa

Raspail Carrel Founou<sup>1,2</sup>, Luria Leslie Founou<sup>1,3</sup>, Mushal Allam<sup>4</sup>, Arshad Ismail<sup>4</sup> & Sabiha Yusuf Essack<sup>1</sup>

25 June 2018  
2 April 2019  
18 April 2019



Microbiology  
Resource Announcements

GENOME SEQUENCES



Genome Sequence of a Novel *Enterococcus faecalis* Sequence Type 922 Strain Isolated from a Door Handle in the Intensive Care Unit of a District Hospital in Durban, South Africa

Christiana O. Shobo<sup>a,b,c</sup>, Daniel G. Amoako<sup>a,d</sup>, Mushal Allam<sup>e</sup>, Arshad Ismail<sup>e</sup>, Sabiha Y. Essack<sup>a</sup>, Linda A. Bester<sup>b,c</sup>



Microbiology  
Resource Announcements

Whole-Genome Sequence of a Novel Sequence Type 3136 Carbapenem-Resistant *Klebsiella pneumoniae* Strain Isolated from a Hospitalized Patient in Durban, South Africa

Yogandree Ramsamy<sup>a,b</sup>, Koleka P. Mlisana<sup>a,b</sup>, Mushal Allam<sup>c</sup>, Arshad Ismail<sup>c</sup>, Ravesh Singh<sup>a,b</sup>, Daniel G. Amoako<sup>d</sup>, Sabiha Y. Essack<sup>d</sup>

# Outputs: Animal Health

MICROBIAL DRUG RESISTANCE  
Volume 00, Number 00, 2018  
© Mary Ann Liebert, Inc.  
DOI: 10.1089/mdr.2017.0383

EPIDEMIOLOGY

## Antibiotic Resistance in Food Animals in Africa: A Systematic Review and Meta-Analysis

Luria Leslie Founou,<sup>1,2</sup> Daniel Gyamfi Amoako,<sup>1</sup>  
Raspail Carrel Founou,<sup>1,3</sup> and Sabiha Yusuf Essack<sup>1</sup>

frontiers  
in Microbiology

REVIEW  
published: 23 November 2016  
doi: 10.3389/fmicb.2016.01181

## Antibiotic Resistance in the Food Chain: A Developing Country-Perspective

Luria Leslie Founou<sup>1\*</sup>, Raspail Carrel Founou<sup>1,2</sup> and Sabiha Yusuf Essack<sup>1</sup>



Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: [www.elsevier.com/locate/scitotenv](http://www.elsevier.com/locate/scitotenv)

Genomic analysis of methicillin-resistant *Staphylococcus aureus* isolated from poultry and occupational farm workers in Umgungundlovu District, South Africa

Daniel Gyamfi Amoako<sup>a,b,\*</sup>, Anou Moise Somboro<sup>a,b</sup>, Akebe Luther King Abia<sup>a</sup>, Mushal Allam<sup>c</sup>, Arshad Ismail<sup>c</sup>, Linda Bester<sup>b</sup>, Sabiha Yusuf Essack<sup>a,\*\*</sup>



Contents lists available at ScienceDirect

Journal of Global Antimicrobial Resistance

journal homepage: [www.elsevier.com/locate/jgar](http://www.elsevier.com/locate/jgar)

Genome Note

Draft genome sequences of extended-spectrum  $\beta$ -lactamase-producing *Enterobacter aerogenes* isolated from swine and human

Luria Leslie Founou<sup>a,b,\*</sup>, Raspail Carrel Founou<sup>a,c</sup>, Mushal Allam<sup>d</sup>, Arshad Ismail<sup>d</sup>, Sabiha Yusuf Essack<sup>a</sup>



Contents lists available at ScienceDirect

International Journal of Food Microbiology

journal homepage: [www.elsevier.com/locate/ijfoodmicro](http://www.elsevier.com/locate/ijfoodmicro)

Mannitol-fermenting methicillin-resistant staphylococci (MRS) in pig abattoirs in Cameroon and South Africa: A serious food safety threat

Luria Leslie Founou<sup>a,b</sup>, Raspail Carrel Founou<sup>a,c</sup>, Sabiha Yusuf Essack<sup>a</sup>, Cyrille Finyom Djoko<sup>d,e,\*</sup>

pathogens

Article

## Genome Mining and Comparative Pathogenomic Analysis of An Endemic Methicillin-Resistant *Staphylococcus Aureus* (MRSA) Clone, ST612-CC8-t1257-SCCmec\_IVd(2B), Isolated in South Africa

Daniel Gyamfi Amoako<sup>1,2,\*</sup>, Anou M. Somboro<sup>2,3</sup>, Akebe Luther King Abia<sup>3</sup>, Mushal Allam<sup>4</sup>, Arshad Ismail<sup>4</sup>, Linda A. Bester<sup>2</sup> and Sabiha Y. Essack<sup>3</sup>

pathogens

Article

## Emergence and Spread of Extended Spectrum $\beta$ -Lactamase Producing Enterobacteriaceae (ESBL-PE) in Pigs and Exposed Workers: A Multicentre Comparative Study between Cameroon and South Africa

Luria Leslie Founou<sup>1,2,\*</sup>, Raspail Carrel Founou<sup>1,3</sup>, Noyise Ntshobeni<sup>4</sup>, Usha Govinden<sup>1</sup>, Linda Antoinette Bester<sup>5</sup>, Hafizah Yousuf Chenia<sup>4</sup>, Cyrille Finyom Djoko<sup>6,7</sup> and Sabiha Yusuf Essack<sup>1</sup>

# Outputs: Environmental Health

**NC STATE UNIVERSITY**  
AES-1041  
23.06.2019

**Hospital effluent in South Africa as a source for antibiotic resistant carbapenemase-producing *Klebsiella* species**

T. L. King<sup>1,2</sup>, S. Schmidt<sup>1</sup>, S. Thakur<sup>1</sup>, P. Fedorka-Cray<sup>1</sup>, S. Keelara<sup>1</sup>, L. Harden<sup>1</sup>, S. Y. Essack<sup>1</sup>

<sup>1</sup>Discipline of Microbiology, University of KwaZulu-Natal, Pietermaritzburg, South Africa, <sup>2</sup>Centre for Veterinary Medicine, North Carolina State Univ., Raleigh, NC, <sup>3</sup>Antimicrobial Research Unit, University of KwaZulu-Natal, Durban, South Africa

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**ABSTRACT**

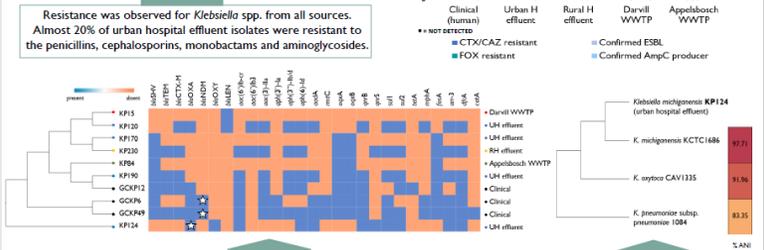
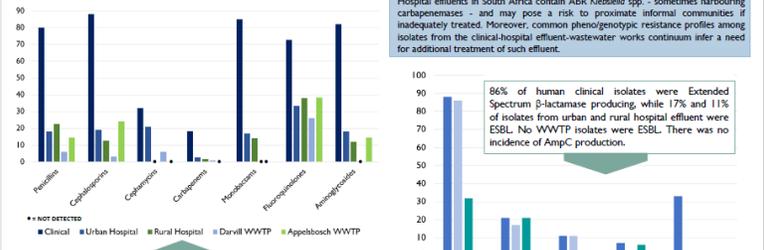
**Introduction and scope**  
Hospital effluents are crucial hotspots for the dissemination of antibiotic resistant microorganisms and may threaten public health if incorrectly handled and disposed. This study analysed hospital and proximate effluents for the presence of antibiotic resistant *Klebsiella* spp.

**Methods**  
Effluent samples were obtained twice over a three-month period from two hospitals (urban tertiary and rural district) and two wastewater works (WWTPs). Membrane filtration and chromogenic agar was used to enumerate and isolate presumptive *Klebsiella* spp., and confirmation was achieved via AP20E. Clinical *Klebsiella* spp. isolates were provided by the urban hospital for comparison. The antibiotic resistance profiles were established according to EUCAST, and ESBL and carbapenemase production was elucidated. Representative isolates were chosen for whole genome sequencing.

**Results**  
A combination of *K. pneumoniae* and *K. oxytoca* were obtained as per APL. A higher proportion of *Klebsiella* spp. from urban tertiary hospital effluent was MDR (23%) compared to rural district hospital effluent (9%). Widespread resistance to  $\beta$ -lactams, fluoroquinolone and aminoglycoside antibiotics was observed, and ESBLs were observed from both the clinic and hospital effluents. *Klebsiella* spp. from clinical sources (and a small proportion of effluent) presented carbapenem resistance. Fifteen *Klebsiella* spp. isolates were phenotypically carbapenemase positive: 14 clinical and 1 from urban hospital effluent.

**Conclusions**  
Antibiotic resistance genes detected via WGS included the bla<sub>KOXA-181</sub> carbapenemase in *K. oxytoca* from urban hospital effluent, bla<sub>KOXA-181</sub> carbapenemase in a clinical isolate from the same hospital, and a variety of aminoglycoside (aac, aph, aad) and quinolone resistance genes (qnr, qnr). Sequence type 872 was common among urban and rural hospital effluent isolates, and one clinical and one urban hospital effluent isolate were ST-307.

**Conclusions**  
Hospital effluents in South Africa contain ABR *Klebsiella* spp., sometimes harbouring carbapenemases – and may pose a risk to proximate informal communities if inadequately treated. Moreover, common phenotypic resistance profiles among isolates from the clinical-hospital effluent-wastewater works continuum infer a need for additional treatment of such effluent.



**ETHICS, ACKNOWLEDGEMENTS & DISCLOSURES**  
Ethical approval (22) Biomedical Research Ethics Committee, NCAAM416 All hospital, WWTPs and NHLS sampling permission Hospital owner were here confirmed as part of the MCOU between the ARU and the hospital. The authors thank the various hospitals and WWTP facility staff for assistance with sample collection. The National Research Foundation, South Africa and DAAD is acknowledged for financial support. Professor Essack is Chairperson of the Global Respiratory Infection Partnership sponsored by an unrestricted educational grant from Baxter & Becton.

**AMERICAN SOCIETY FOR MICROBIOLOGY**

**Microbiology**  
Resource Announcements

GENOME SEQUENCES

Check for updates

## Draft Genome Sequence of *Providencia rettgeri* APW139\_S1, an NDM-18-Producing Clinical Strain Originating from Hospital Effluent in South Africa

Noiyse B. Ntshobeni,<sup>a</sup> Mushal Allam,<sup>b</sup> Arshad Ismail,<sup>b</sup> Daniel G. Amoako,<sup>c</sup> Sabiha Y. Essack,<sup>c</sup> Hafizah Y. Chenia<sup>a</sup>

**Science of The Total Environment**

Available online 18 November 2019, 135550

In Press, Journal Pre-proof

ELSEVIER

## Antibiotic resistant *Klebsiella* spp. from hospital, hospital effluents and wastewater treatment plants in the uMgungundlovu District, KwaZulu-Natal, South Africa

Tracy L.B. King<sup>a, b</sup>, Stefan Schmidt<sup>a</sup>, Sabiha Y. Essack<sup>b</sup>

**NC STATE UNIVERSITY**  
AES-1038  
23.06.2019

**Surveillance and Whole Genome Sequencing of Antibiotic Resistant *Enterococcus* spp. from South African Hospital Effluents**

T. L. King<sup>1,2</sup>, S. Schmidt<sup>1</sup>, S. Thakur<sup>1</sup>, P. Fedorka-Cray<sup>1</sup>, S. Keelara<sup>1</sup>, L. Harden<sup>1</sup>, S. Y. Essack<sup>1</sup>

<sup>1</sup>Discipline of Microbiology, University of KwaZulu-Natal, Pietermaritzburg, South Africa, <sup>2</sup>Centre for Veterinary Medicine, North Carolina State Univ., Raleigh, NC, <sup>3</sup>Antimicrobial Research Unit, University of KwaZulu-Natal, Durban, South Africa

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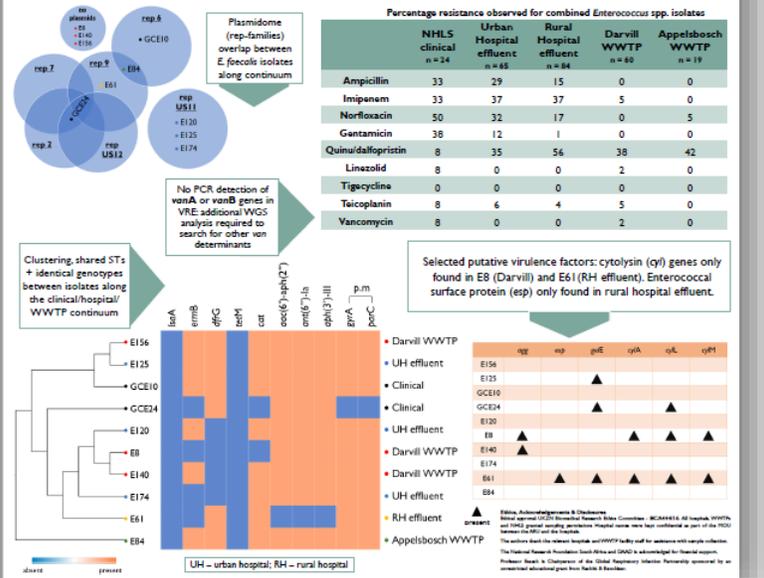
**ABSTRACT**

**Introduction and scope**  
Inadequately treated municipal wastewater and effluent originating from hospital environments are critical sites for the dissemination of antibiotic resistant bacteria. Ineffective handling and compromised sewage infrastructure may pose a threat to public health. This study analysed *Enterococcus* spp. from hospital and proximate wastewater effluents in KwaZulu-Natal and assessed antibiotic resistance profiles and clonality along the hospital-municipal effluent continuum.

**Methods**  
Water samples were obtained twice over a three-month period from two hospitals (urban tertiary and rural district) and two wastewater works (WWTPs). *Enterococcus* spp. were isolated and quantified (ISO7899-2) and confirmed (AP202Strap), while clinical *Enterococcus* isolates were provided by the hospitals. API identification confirmed a total of 149 *Enterococcus* spp. isolates from both hospitals, 80 from both WWTPs and 24 clinical isolates. The antibiotic resistance profiles were established for all isolates (EUCAST disk diffusion), and a sub-set of representative isolates was selected for further whole genome Illumina sequencing.

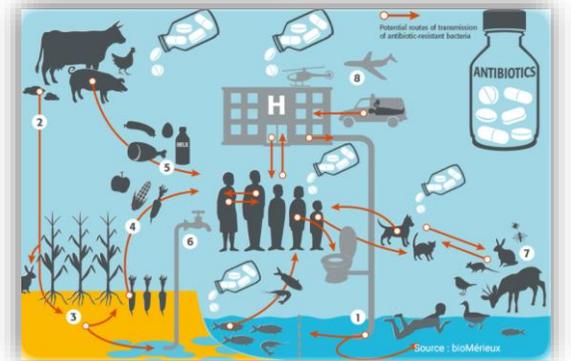
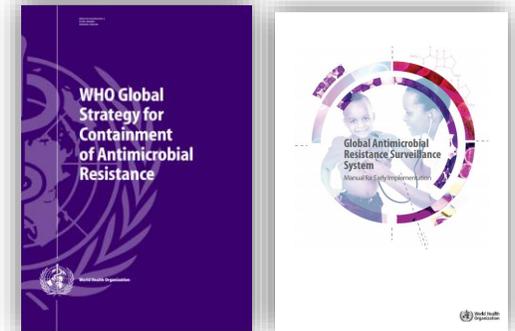
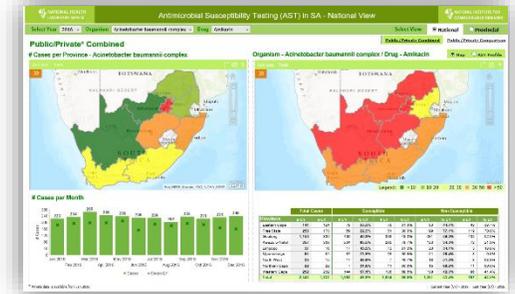
**Results & Discussion**  
Effluent from the urban hospital presented a higher degree of multidrug resistant (MDR) *Enterococcus* isolates (12%) compared to the rural hospital (4%). The rural and urban wastewater treatment samples did not contain any MDR isolates. There was no incidence of vancomycin resistant *Enterococcus* (VRE) from hospital effluents or Appelsbosch WWTP; however one isolate from Darvill WWTP was VRE 875 (2/24) of clinical strains were VRE. In addition, analysis of WGS data from ten randomly selected *E. faecalis* isolates revealed genes conferring resistance to the tetracyclines (tetM), aminoglycosides (aac(6), omt(6'), oph(3')), macrolides (ermB, lsaA), phenicol (cat) and trimethoprim (dhfr) classes. Four *E. faecalis* isolates from urban hospital and urban WWTP samples belonged to sequence type (ST) 16, while two isolates from each source shared ST 19, as well as identical genotypic resistance profiles.

**Conclusions**  
The surveillance carried out in this work confirmed that effluents from hospital, municipal sewage in South Africa contain ABR *Enterococcus*. Additionally, a large proportion of MDR strains was observed in the tertiary, urban hospital compared to the district rural hospital. Moreover, any interruptions or breaks along the sewage line may cause dissemination of such strains into public and recreational waters – posing a potential threat to public health.



# Envisaged Output

- Create an electronic platform that will triangulate, in real time trends in antibiotic use & resistance from robust, representative One Health surveillance programmes.
- Compare surveillance systems in terms of technical feasibility & cost effective delineation of robust, representative surveillance data.
- Explore a proxy surveillance system for antibiotic resistance in humans and food animals.
- Unambiguously give credence to the One Health approach for the containment of antibiotic resistance.



[https://www.antimicrobial-resistance.biomerieux.com/wp-content/uploads/2015/10/Illustration\\_Chap1-1e.png](https://www.antimicrobial-resistance.biomerieux.com/wp-content/uploads/2015/10/Illustration_Chap1-1e.png)

# References (Graphical Abstracts)

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1. <https://www.indiamart.com/proddetail/effluent-treatment-plant-2838980388.html>
2. <https://extension.unh.edu/resource/guidelines-using-animal-manures-and-manure-based-composts-garden-fact-sheet>
3. Al Laham N. 1AJAA 2015.5 (4): 2
4. Cao G, Meng J. Strain E et al PLoS ONE 2013 8(2):e55687
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7. <https://theecologist.org/2014/jan/14/tax-farm-antibiotics-fight-superbugs>
8. [https://www.anti-microbial-resistance.biomerieux.com/wp-content/uploads/2015/10/Illustration\\_Chap1-1e.png](https://www.anti-microbial-resistance.biomerieux.com/wp-content/uploads/2015/10/Illustration_Chap1-1e.png)
9. Lanza VF, de Toro M, Garcillaín-Barcia MP et al. PloS Generics 2014.10 (12): e1004766

# Acknowledgements



THANK YOU  
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