

What genomic surveillance offers Nigeria, your institution, and your lab.

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Faculty of Pharmacy

University of Ibadan

PHA4GE virtual training opening

Day 1: Monday – 16.08.2021

30 min



UNIVERSITY
OF IBADAN



Global action plan on antimicrobial resistance

Draft resolution with amendments resulting from informal consultations

The Sixty-eighth World Health Assembly,

PP1 Having considered the summary report on progress made in implementing resolution WHA67.25 on antimicrobial resistance and the report on the draft global action plan on antimicrobial resistance;¹

May 2015

(OP2) URGES Member States:¹

- (1) to implement the proposed actions for Member States in the global action plan on antimicrobial resistance, adapted to national priorities and specific contexts;
- (2) to mobilize human and financial resources through domestic, bilateral and multilateral channels in order to implement plans and strategies in line with the global action plan;
- (3) to have in place, by the Seventieth World Health Assembly, national action plans on antimicrobial resistance that are aligned with the global action plan on antimicrobial resistance and with standards and guidelines established by relevant intergovernmental bodies;

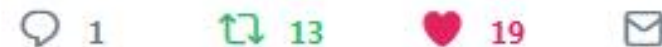


ChikweNCDC @Chikwe_I · 18h

In less than a year, the Team had developed a National Situation Analysis & Action Plan on #AMR for Nigeria, signed by 3 Ministers in the #OneHealth approach & presented by HMH @IsaacFAdewole at the World Health Assembly in 2017. Available on ncdc.gov.ng



Prof. Isaac Adewole, John Nkengasong, Dipo Aboderin and 6 others

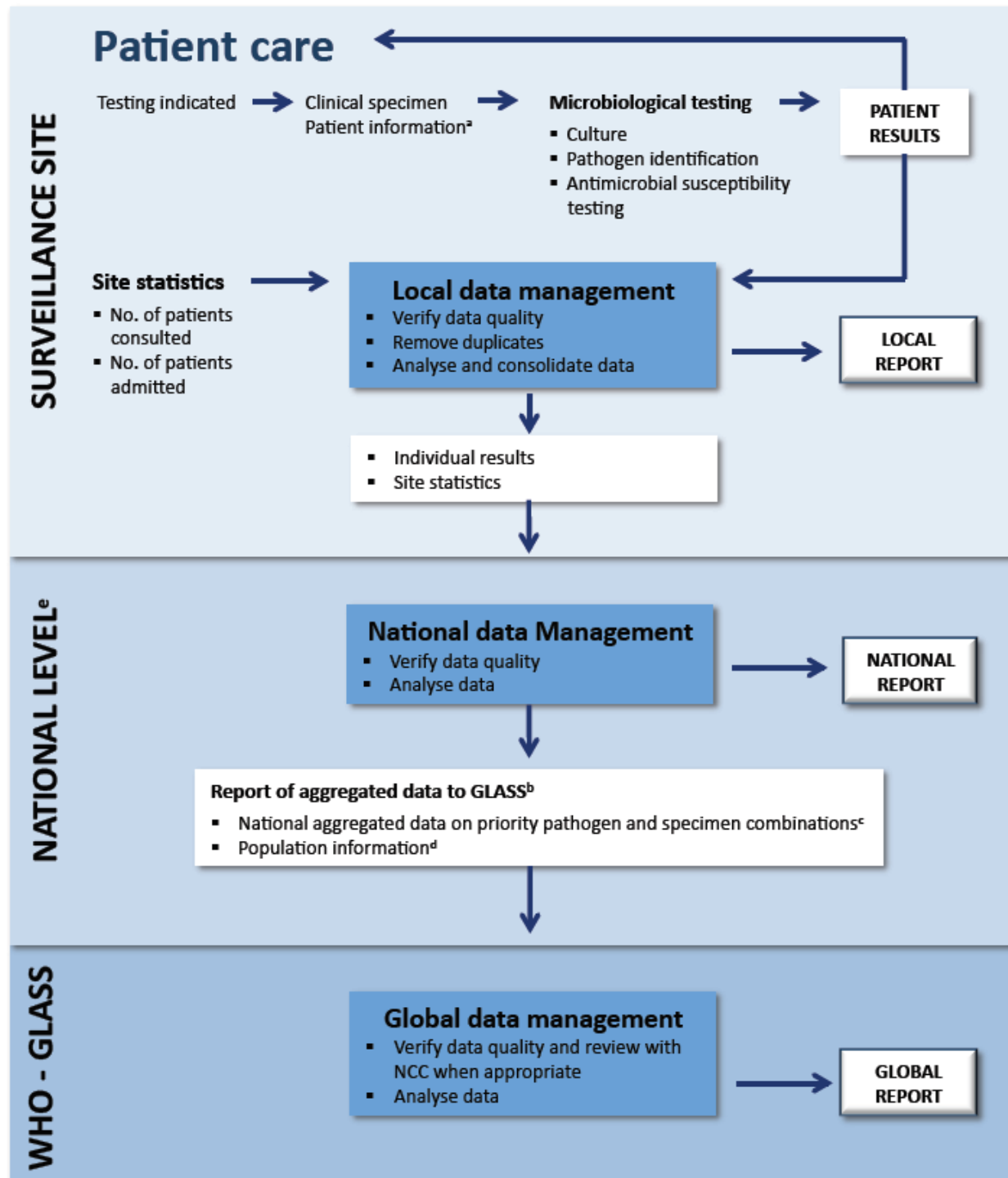


World Health Organization



Nigeria's 'instant' Antimicrobial Resistance National Action Plan

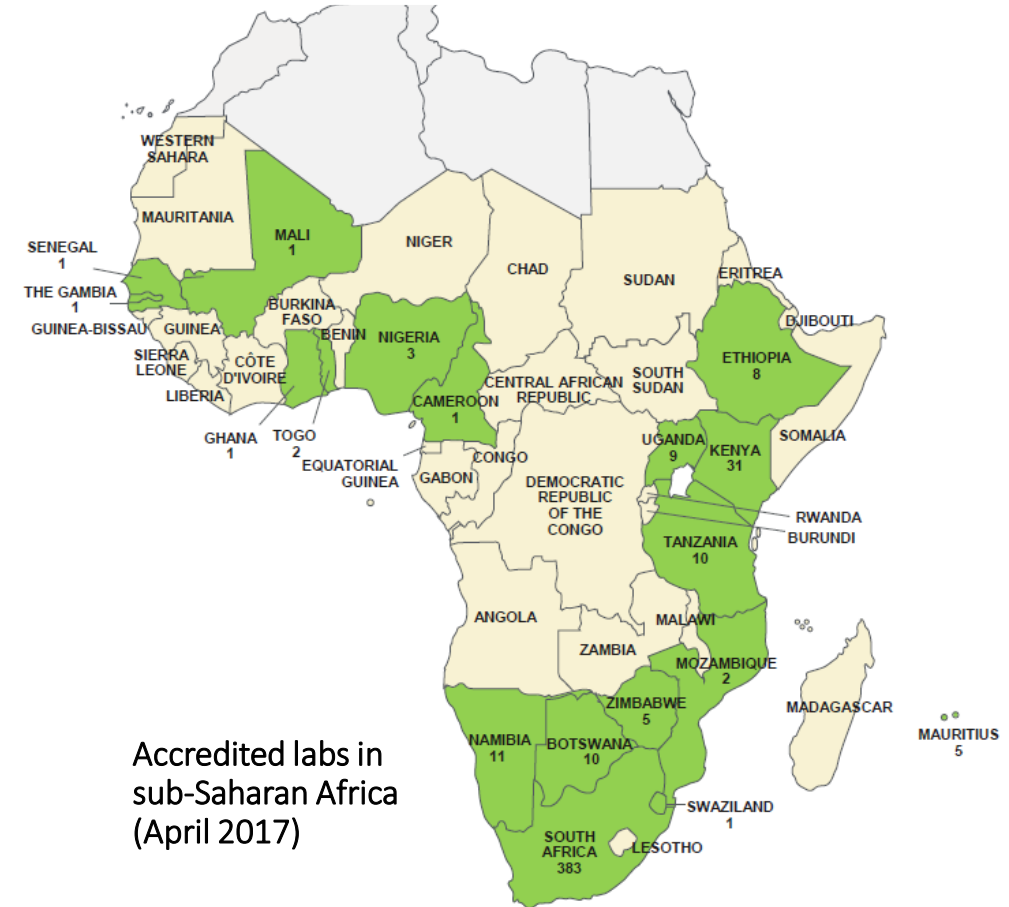
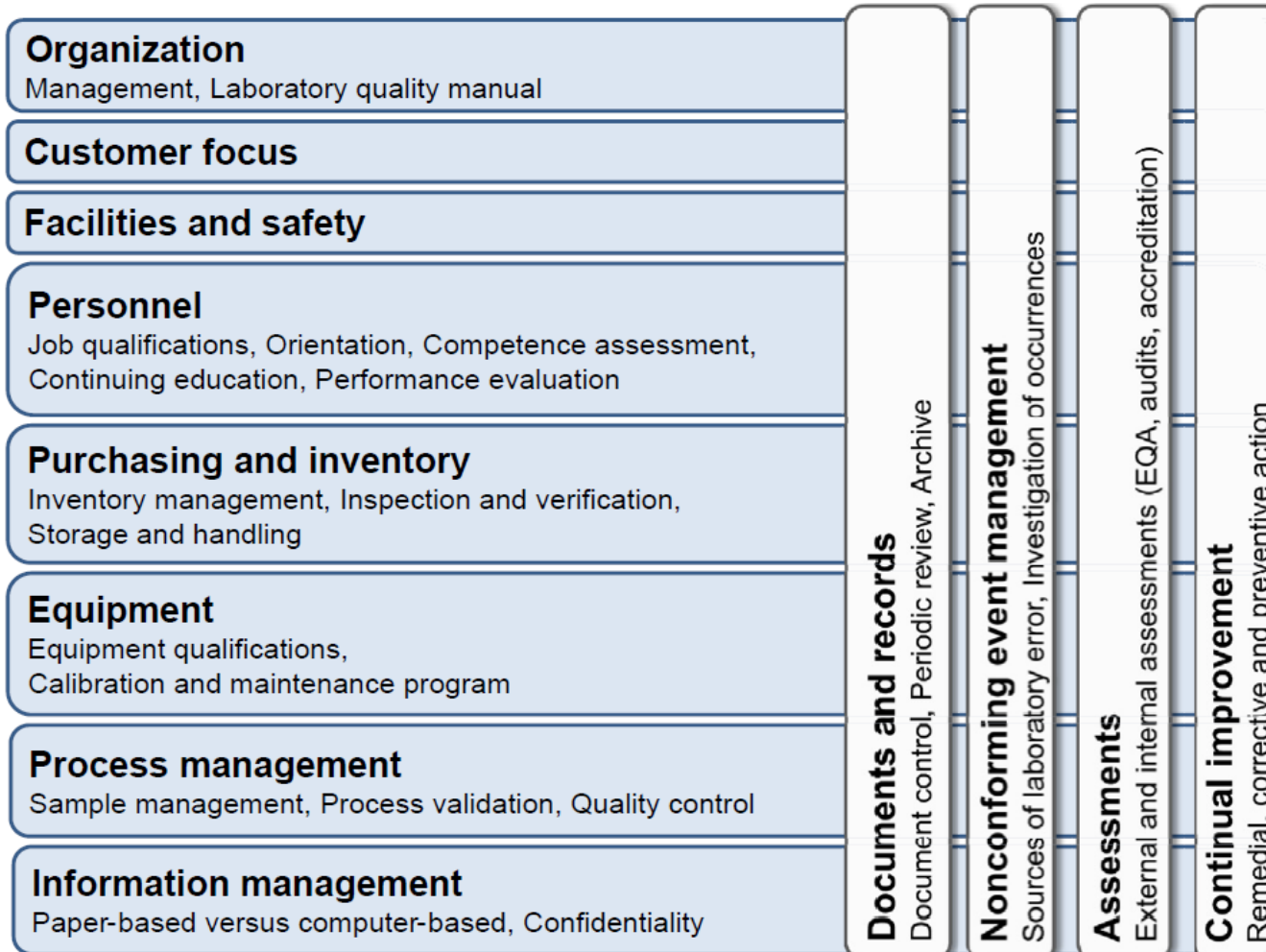
- High reputational stakes
- Local expertise, local action
- Access to essential resources
- Motivated leadership
- Cooperative engagement
- Exploited existing networks, resources and connections
- Great expectations



[GLASS Manual for
Early
Implementation](#)

Implementation of quality management for clinical bacteriology in low-resource settings

Barbé B, Yansouni CP, Affolabi D, Jacobs J. Clin Microbiol Infect. 2017 Jul;23(7):426-433.





Why genomic surveillance for Nigeria?

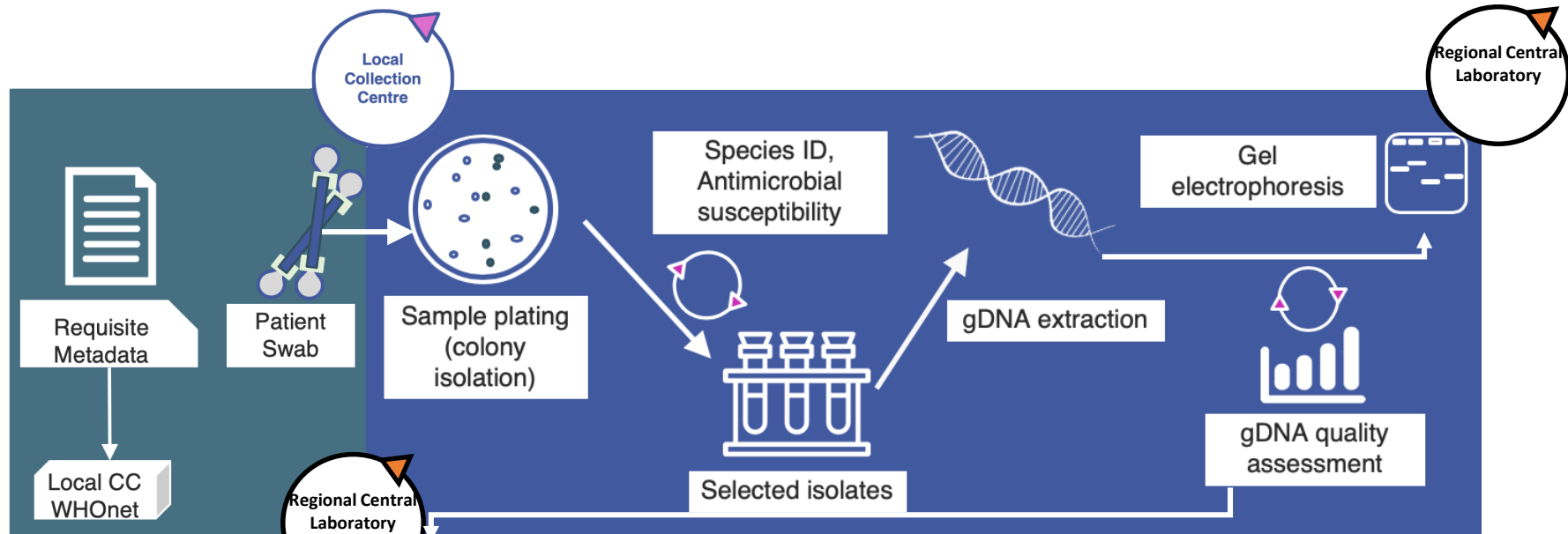
- Leapfrog us over some of resistance surveillance roadblocks
- Provide reference laboratory services for the Nigeria Centre for Disease Control's (NCDC's) fledgling AMR surveillance system
- Build a resistance surveillance program that is useful to the NCDC in other ways e.g. outbreak support
- Help to connect what we find in Nigeria with data from elsewhere in the region and the world
- Answer the why/how questions that arise in the course of surveillance



“There is no need for us to go through all the long and complicated stages of the development of science which other countries have gone through in the past. We are, as it were, jumping the centuries, using knowledge and experience already available to us. What others have taken hundreds of years to do, we must achieve in a generation”

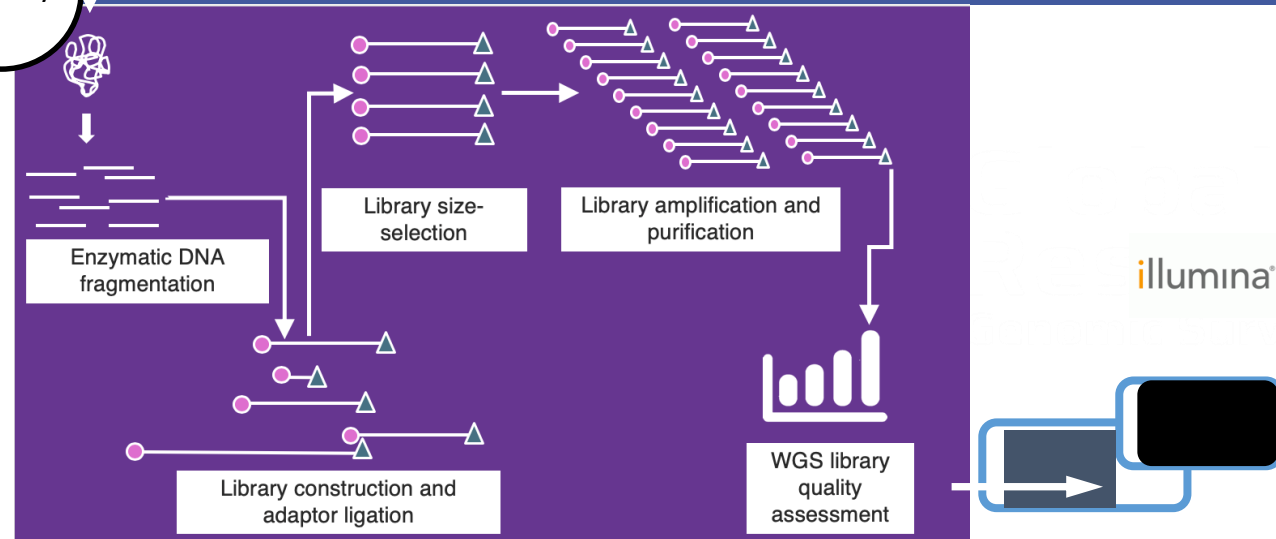
Kwame Nkrumah
(1909-1972)

Implementing genomics lab set up



CHALLENGES

- Laboratory set-up
- Equipment set-up
- Staff training in genomics
- Laboratory information management
- Procurement and financial management



Sample areas where genomic surveillance is valuable and likely highly cost-effective

- Replacing reference lab services such as sub-species level typing
- Investigating hospital outbreaks of resistant bacteria
- Community outbreaks of cholera and bacillary dysentery
- Invasive typhoid epidemiology
- Pneumococcal surveillance

Sample areas where genomic surveillance is valuable and likely highly cost-effective

- **Replacing reference lab services such as sub-species level typing**
- Investigating hospital outbreaks of resistant bacteria
- Cholera, Shigellosis and Invasive typhoid epidemiology
- Pneumococcal surveillance
- Providing ancillary surveillance information at no additional cost

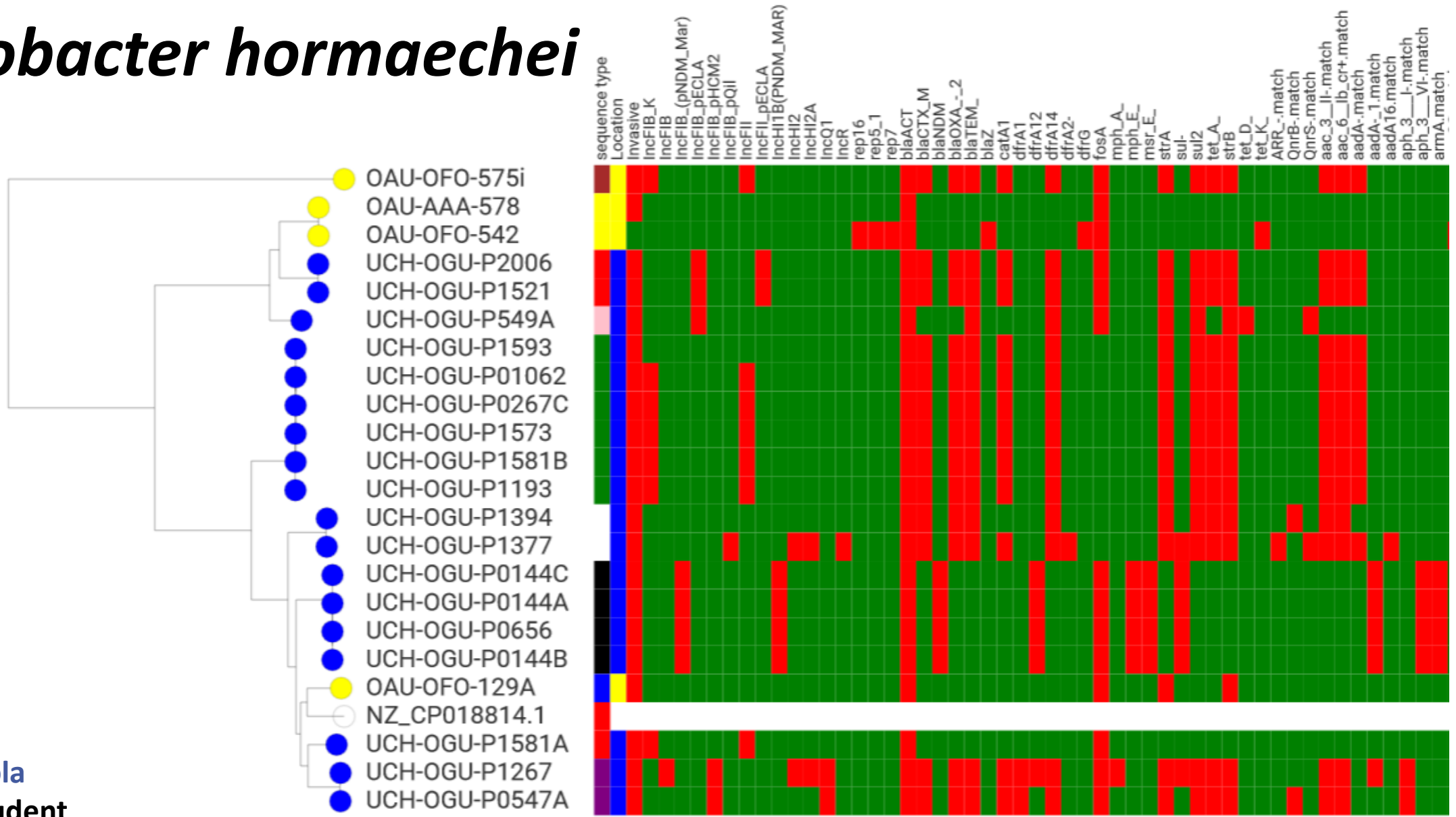
Enterobacter hormachei: Important, unseen

<u>sample id</u>	<u>Sentinel initial ID</u>	<u>VITEK Species</u>	<u>sequence</u> <u>type</u>	
OAU-OFO-575i	Enterobacteriaceae	Ent.cloacae complex	78	
UCH-OGU-P0144B	<i>Acin. baumani</i>	Aci. Baumannii	109	
UCH-OGU-P0144C	<i>Acin. baumani</i>	Aci. Baumannii	109	
UCH-OGU-P0144A	Enterobacteriaceae	Ent.cloacae complex	109	
UCH-OGU-P0656	Enterobacteriaceae	Ent.cloacae complex	109	
UCH-OGU-P0547A	Enterobacteriaceae	Ent.cloacae complex	121	
UCH-OGU-P1267	<i>Ent. cloacae</i>	Ent.cloacae	121	
UCH-OGU-P01062	Enterobacteriaceae	Ent.cloacae complex	148	
UCH-OGU-P0267C	Enterobacteriaceae	Ent.cloacae complex	148	
UCH-OGU-P1581B	Enterobacteriaceae	Ent.cloacae complex	148	
UCH-OGU-P1193	<i>Ent. cloacae</i>	Ent.cloacae	148	
UCH-OGU-P1593	<i>P. aeruginosa</i>	Esch. coli	148	
UCH-OGU-P1573	<i>P. aeruginosa</i>	Ps. aeruginosa	148	
UCH-OGU-P1377	<i>Ent. cloacae</i>	Ent.cloacae	270	
UCH-OGU-P1394	<i>Ent. cloacae</i>	Ent.cloacae	270	
UCH-OGU-P549A	Enterobacteriaceae	Ent.cloacae complex	306	
OAU-AAA-578	<i>E. cloacae</i> cplx	Ent.cloacae complex	346	
OAU-OFO-542	<i>E. coli</i>	K. pneumoniae	346	
OAU-OFO-129A	Enterobacteriaceae	Ent.cloacae complex	1053	
UCH-OGU-P1581A	Enterobacteriaceae	Ent.cloacae complex	unknown	
UCH-OGU-P2006	<i>Ent. cloacae</i>	Ent.cloacae complex	unknown	
UCH-OGU-P1521	<i>K. pneumoniae</i>	K. pneumoniae	unknown	

Enterobacter hormaechei



Faith Popoola
Master's student



Sample areas where genomic surveillance is valuable and likely highly cost-effective

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- **Investigating hospital outbreaks of resistant bacteria**
- Cholera, Shigellosis and Invasive typhoid epidemiology
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Sequence-based phylogenies – the pluses

- Reproducible and portable: Gets rid of “YATMs”

YATM \yat' em, *Brit.* ya' tem\ *n* acronym for *Yet Another Typing Method*

TATBSTM \tate' bee stem, *Brit.* tat' bistem\ *n* acronym for *Tried And True But Stodgy Typing Method*

TBCA \tib' see ay, *Brit.* tib' ka\ *n* acronym for *Totally Boring Clonal Analysis*

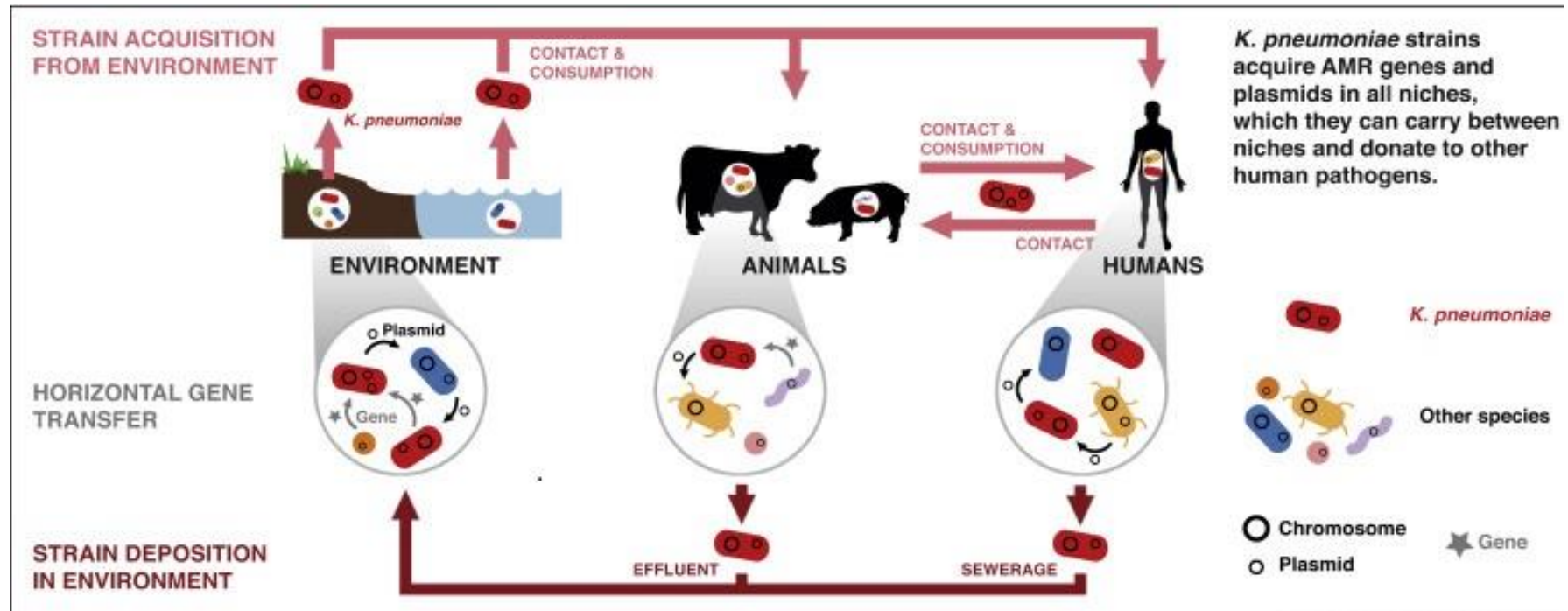
The increasingly distressed Mark Achtman, JCM 1996

- Sequence-based phylogenies have shown good correlation with the most reliable phenotype- and gel-based methods.
- Curated publicly available genetic, genomic and multilocus sequence typing databases for many species

Sequence based phylogenies – the pitfalls

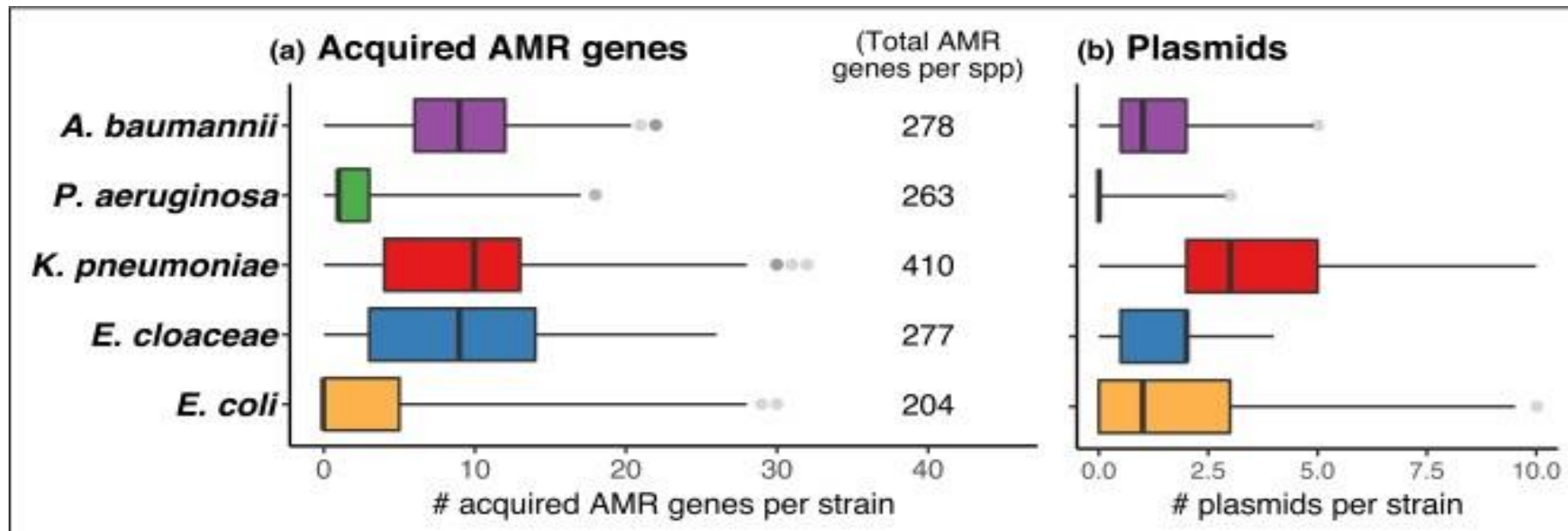
- Expensive
- Inferring phylogenetic relationships of strains that are not obviously clonal is not as simple as it may seem

Klebsiella: niche exploiter



Wyres KL, Holt KE. *Klebsiella pneumoniae* as a key trafficker of drug resistance genes from environmental to clinically important bacteria. *Curr Opin Microbiol.* 2018;45:131-139

Klebsiella: resistance gene trafficker?

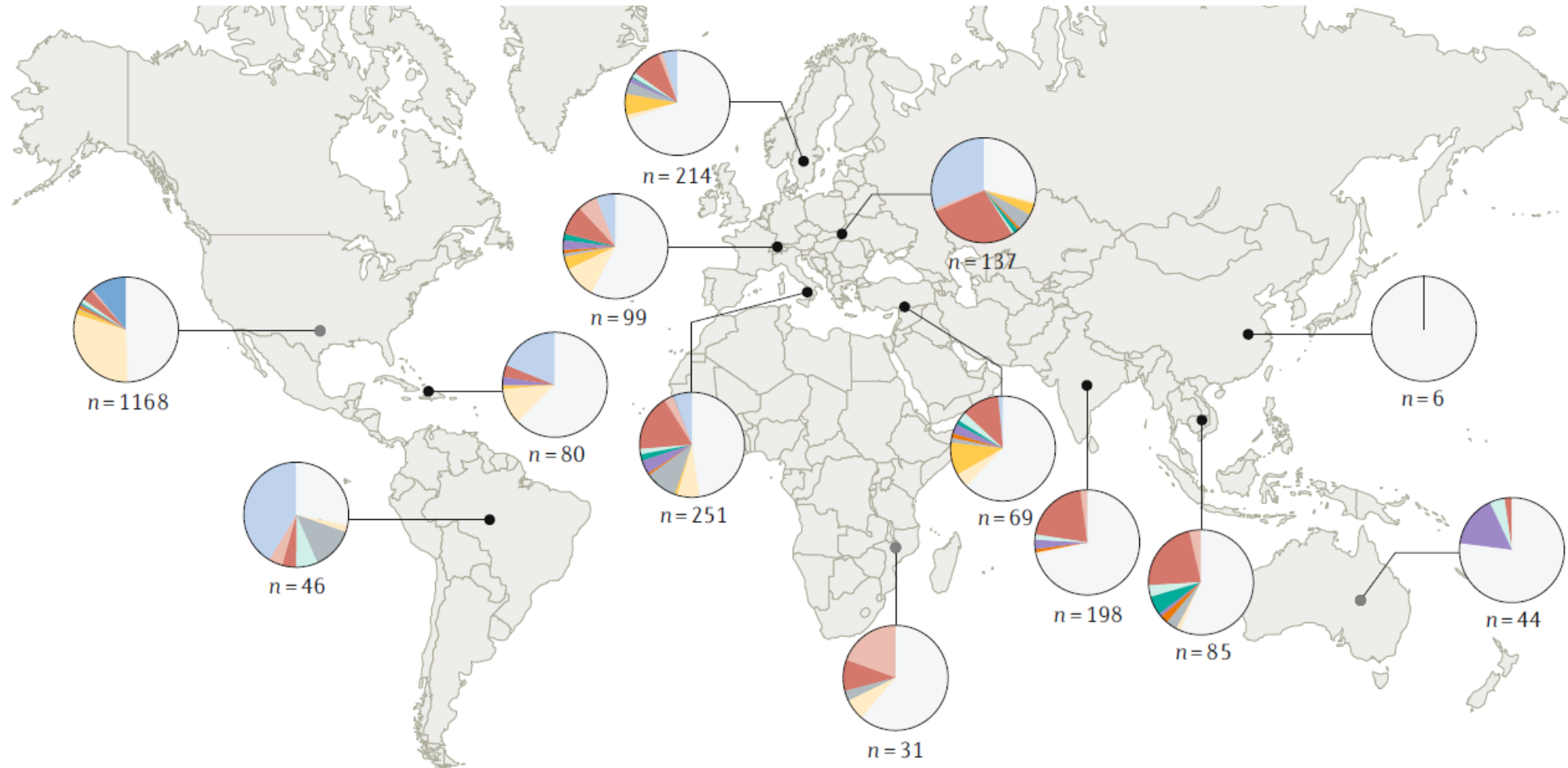


Wyres KL, Holt KE. *Klebsiella pneumoniae* as a key trafficker of drug resistance genes from environmental to clinically important bacteria. *Curr Opin Microbiol.* 2018;45:131-139

STs of 3rd-gen cephalosporin-resistant, carbapenem-susceptible *K. pneumoniae*

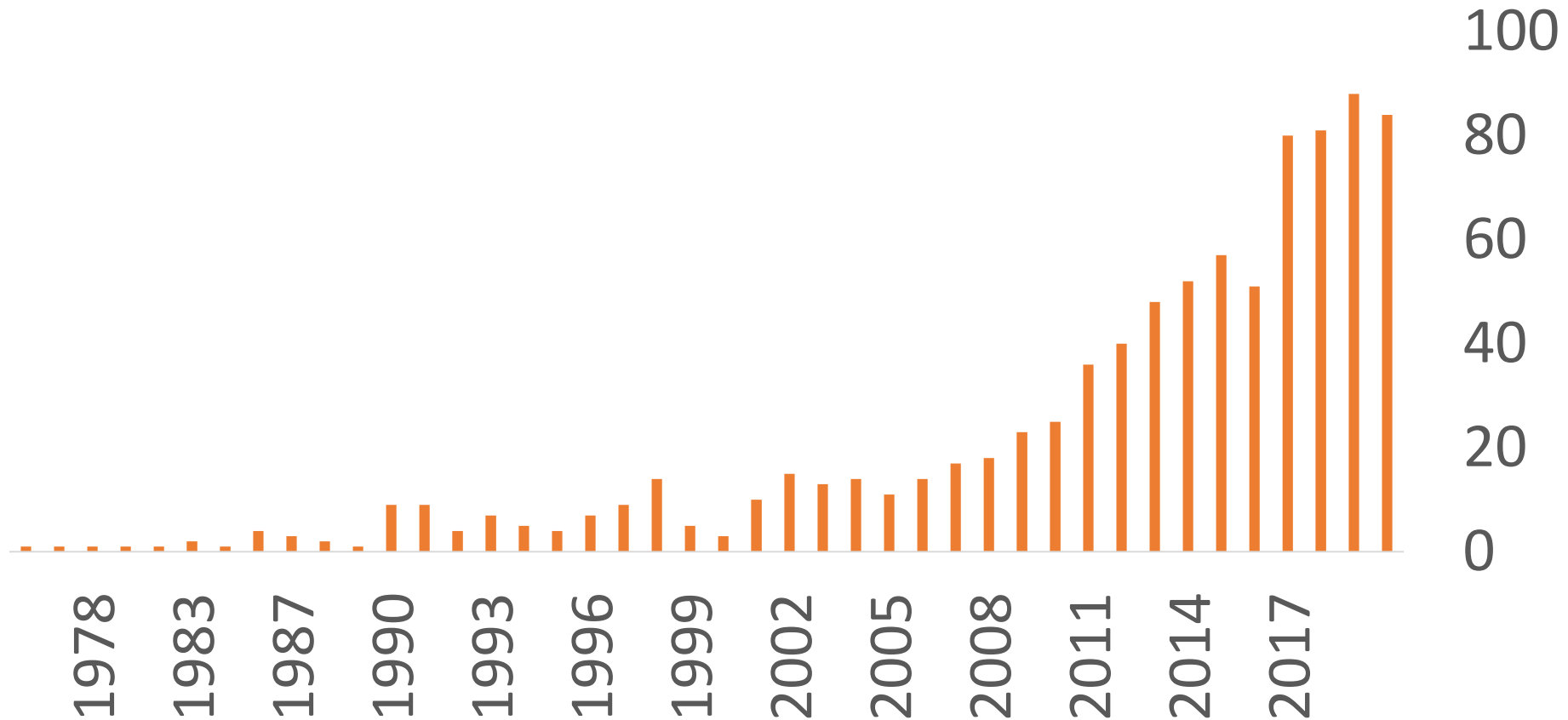
Wyres KL, Lam MMC, Holt KE. Population genomics of *Klebsiella pneumoniae*.

Nat Rev Microbiol. 2020 Jun;18(6):344-359.



Increasing number of reports of resistant bloodstream *Klebsiella* from Africa

Search query (PubMed): klebsiella resistant africa



**Nigerian
patients and
health system
cannot afford
the costs of
resistance**

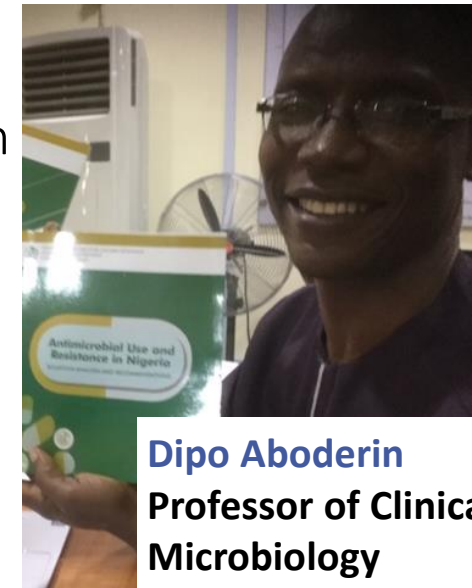
Case: 8-year old girl with systemic infection caused by ESBL-producing *Klebsiella pneumoniae*.

Time to diagnosis: Over 6 weeks

Admission and nursing costs: N20,400 (\$132.36)

Laboratory investigations costs: N14,000 (\$19.42)

Treatment costs: N89,900 (\$583.77)



Dipo Aboderin
**Professor of Clinical
Microbiology**

Period	Treatment	Cost	
		NGN	USD
First week	I/V ciprofloxacin & I/M gentamicin	3780.00	24.55
Second week	I/V ceftazidime & I/M gentamicin	10 920.00	70.91
Third/Fourth week	I/V ceftriaxone & I/M gentamicin	8500.00	55.19
Fifth week	I/V amoxicillin/clavulanate & I/M gentamicin	6800.00	44.16
Sixth week	I/V imipenem/cilastatin	50 400.00	327.27
-	Blood transfusions	9500.00	61.69
Total cost		89900.00	583.77

•Aboderin, AO, Adefehinti, O, Odetoyin, BW, Olotu, AA, Okeke IN and Adeodu, OO (2012) *African Journal of Laboratory Medicine*. 1(1), Art. #16, 4 pp.

**Ladoke Akintola Univ
Teaching Hospital (LAUTECH)**



**Obafemi Awolowo University
Teaching Hospitals Complex**

University College Hospital, Ibadan



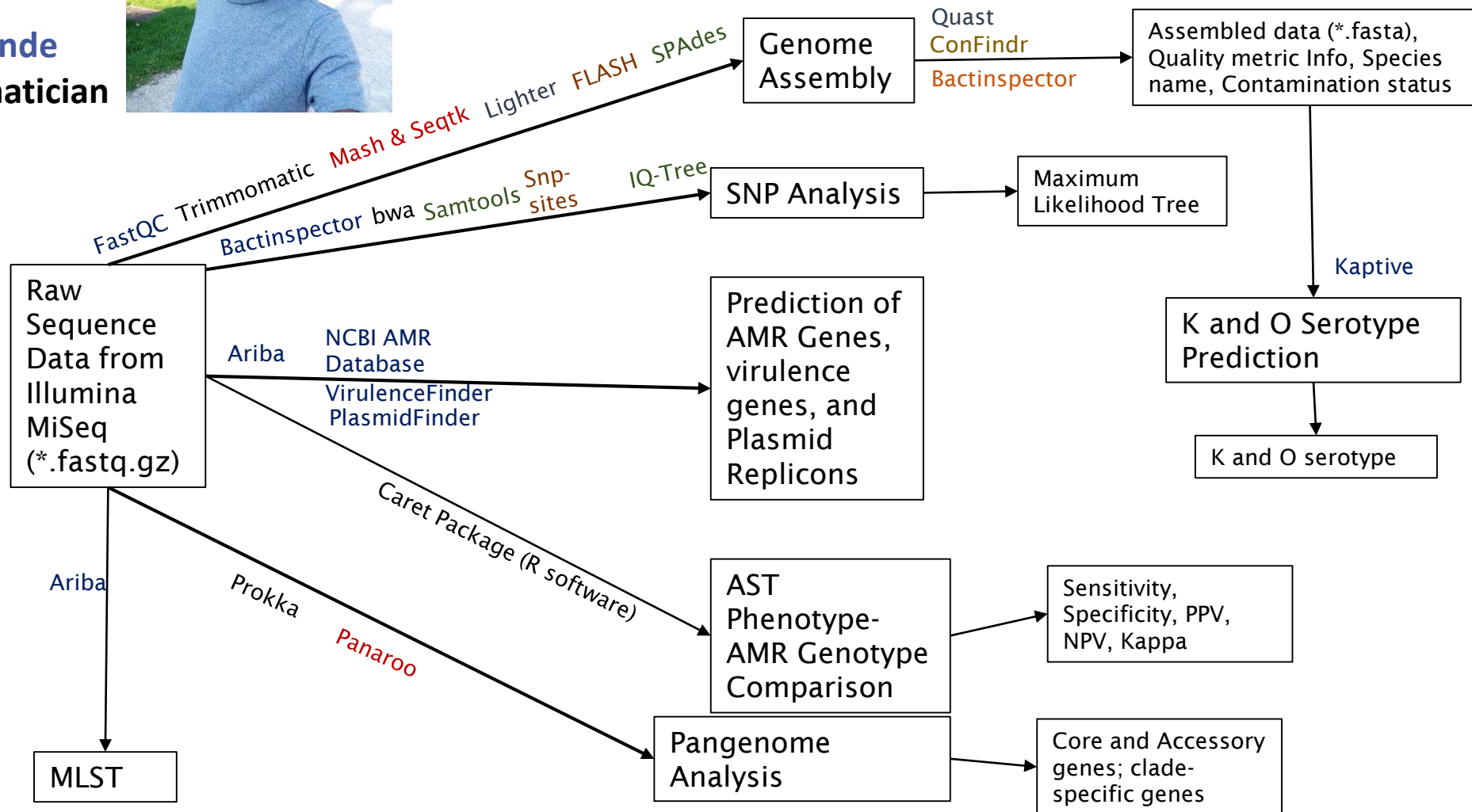
Microbiology and sequencing

Anderson Oaikhena
Lab scientist &
Doctoral student

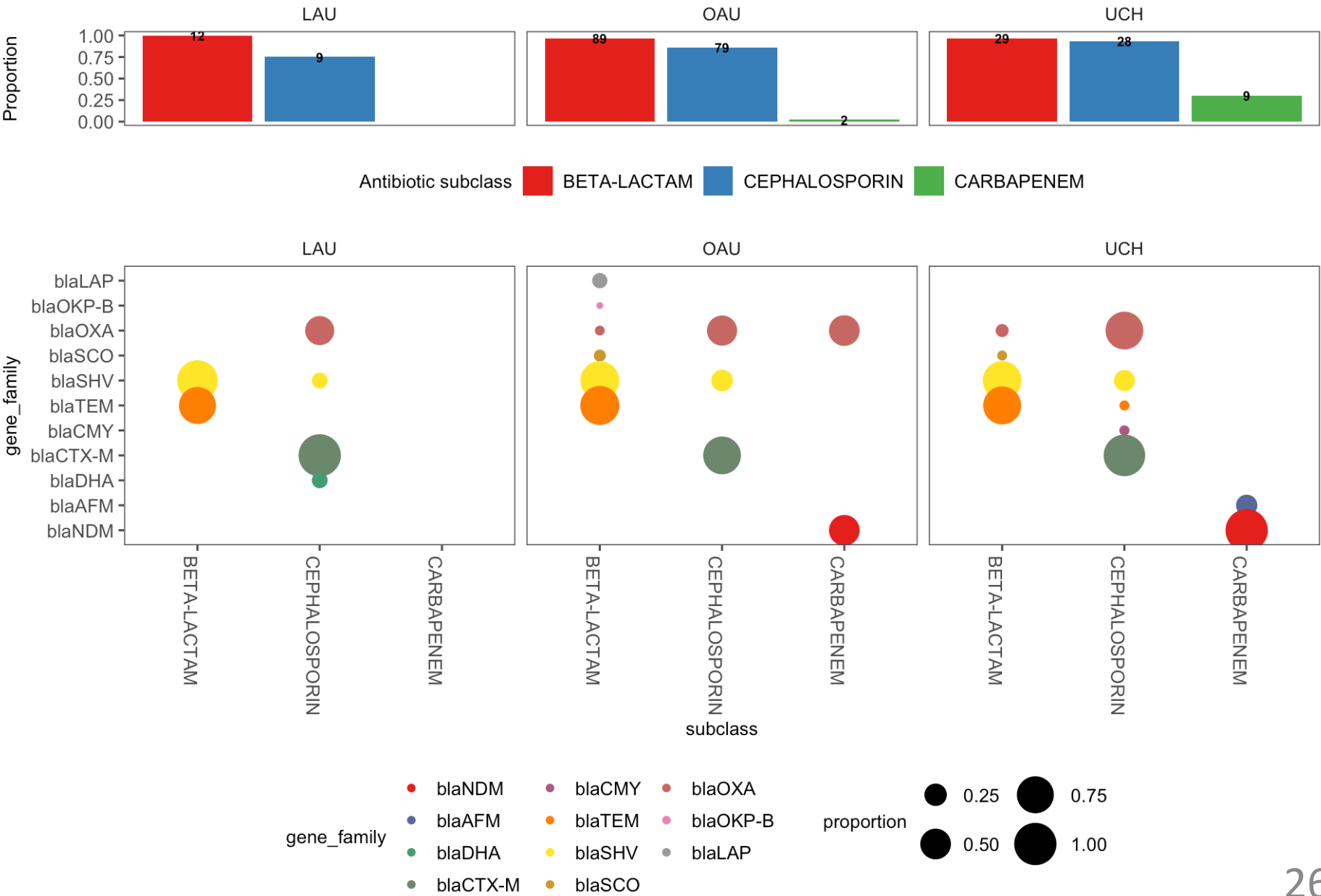


- Checked purity on selective-diagnostic media
- ID and AST on VITEK
- DNA extraction: Promega Wizard Kit, Concentration on Qubit
- Illumina-sequenced @Wellcome Trust Sanger Institute (Centre for Pathogen Surveill)

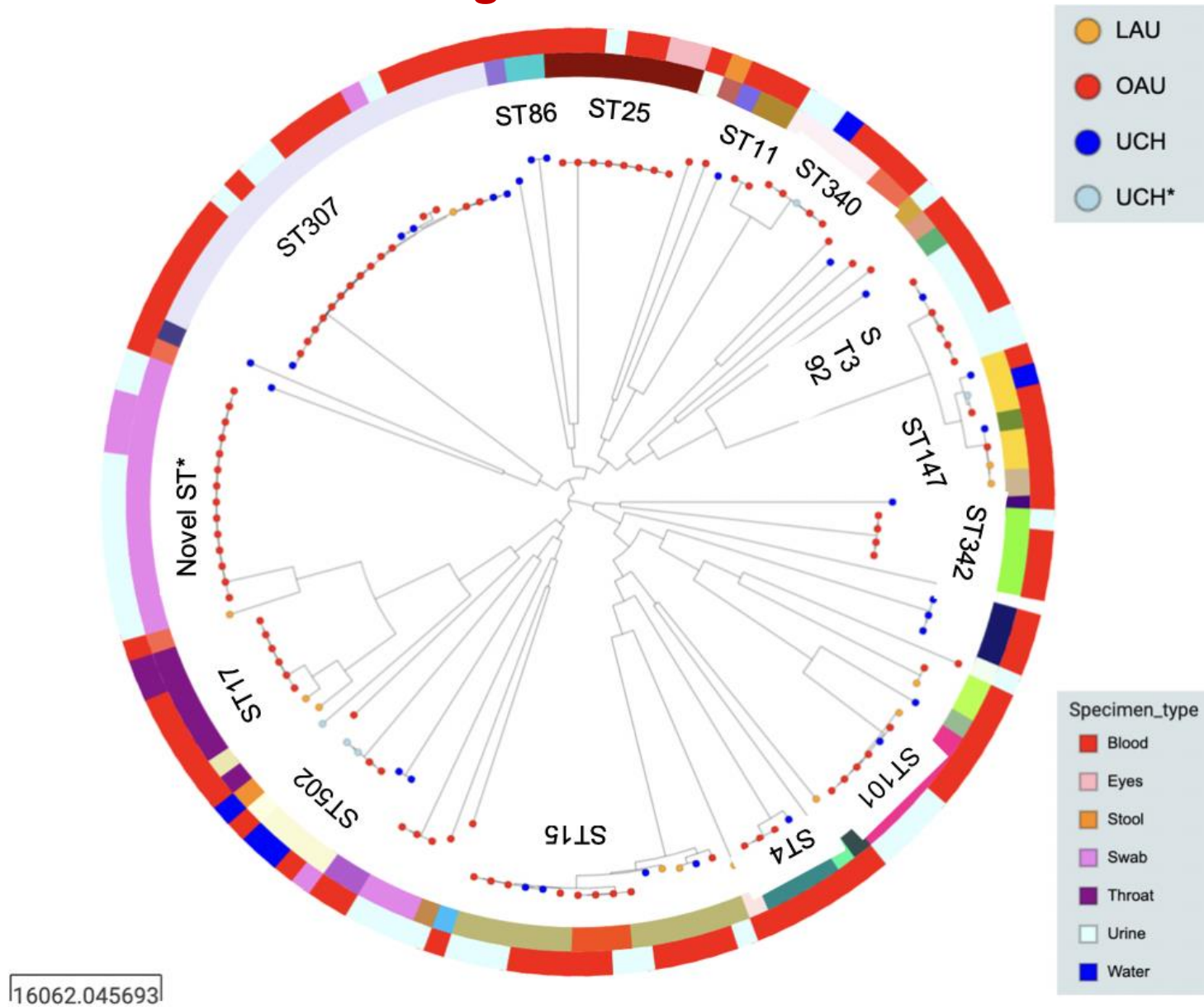
Ayo Ayorinde
Bioinformatician



Beta lactam resistance

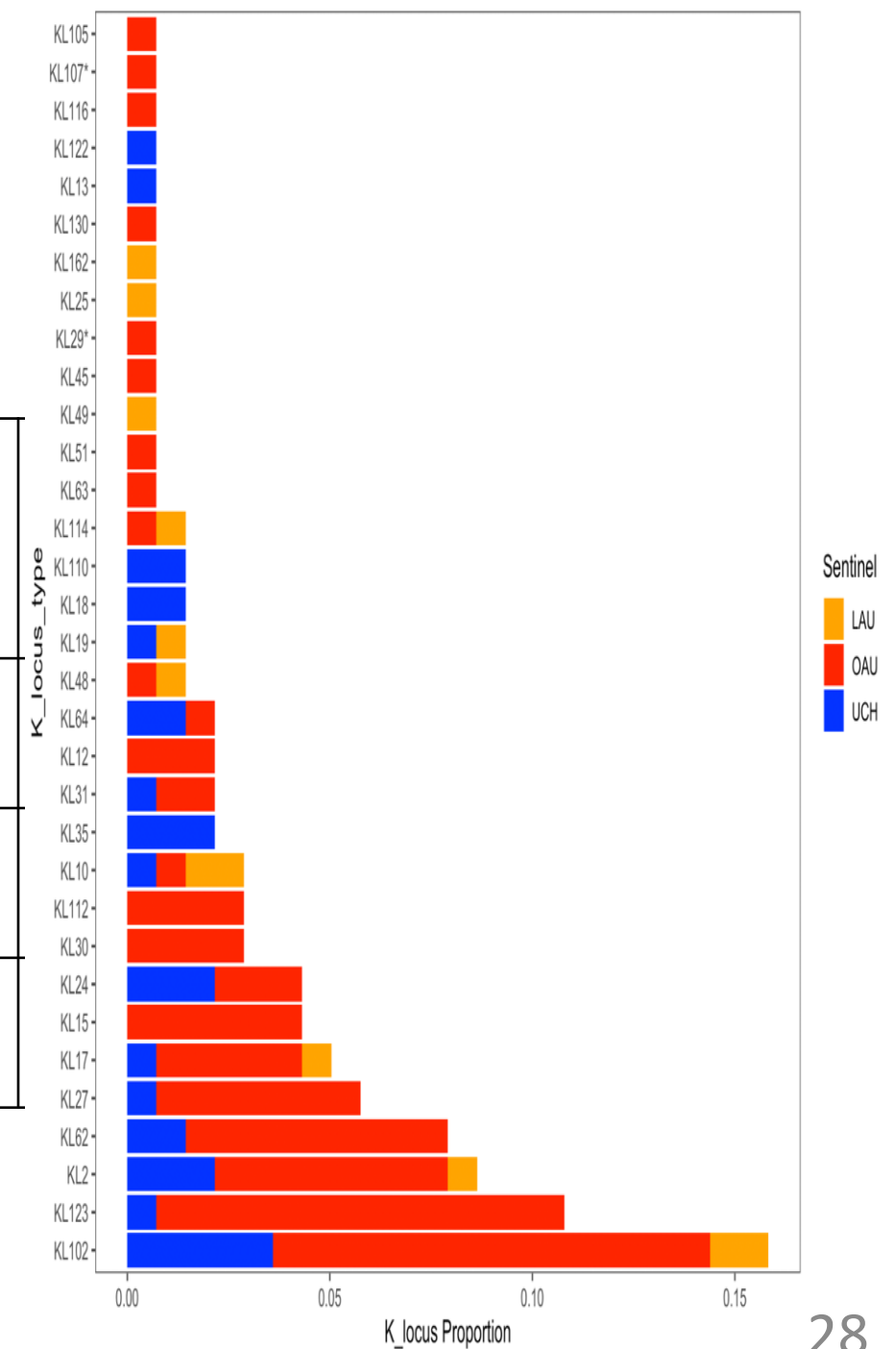


Phylogenetic analysis of *K. pneumoniae* genomes from three southwestern Nigeria sentinel sites

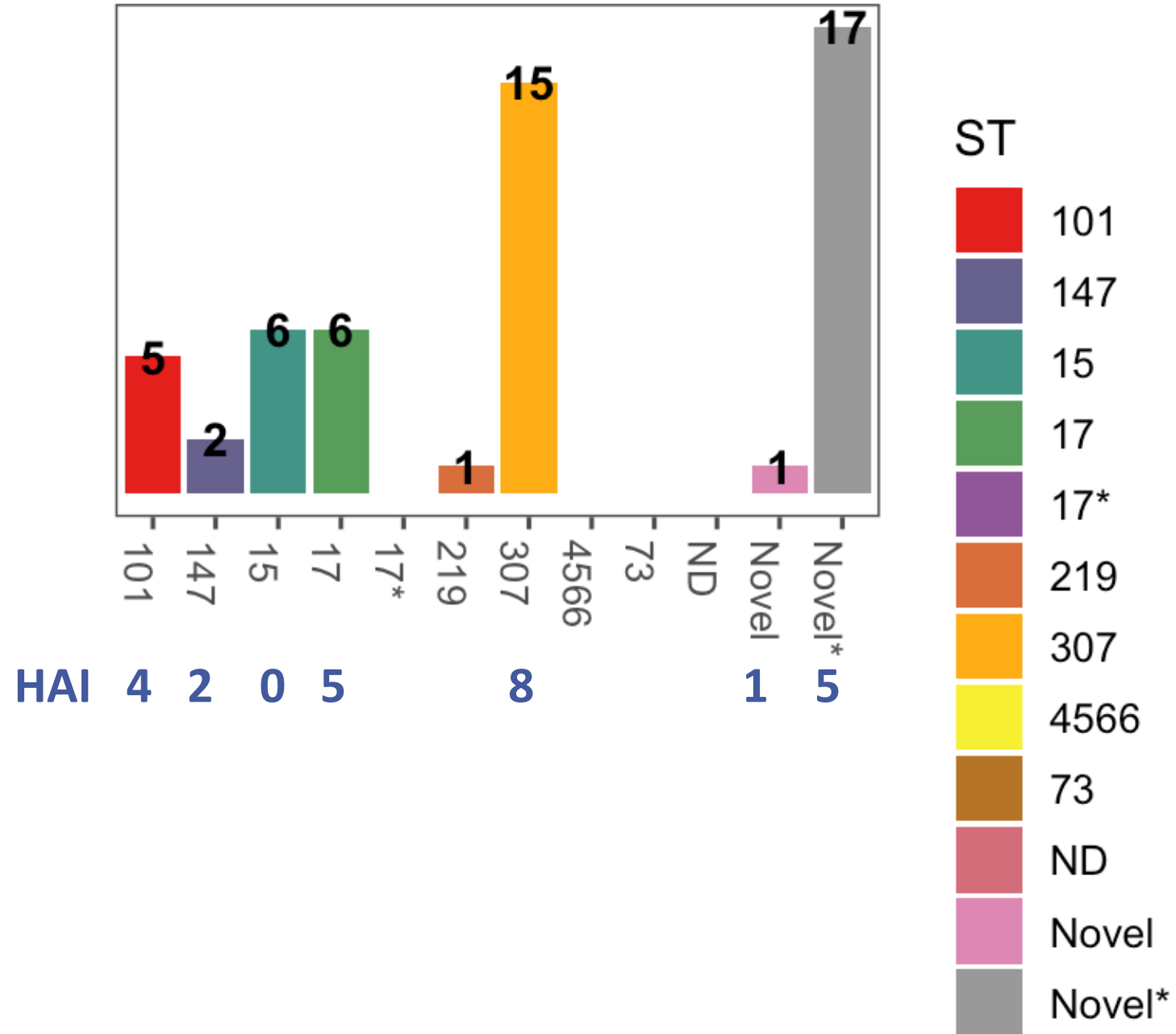


Diminished diversity at OAUTHC and UCH

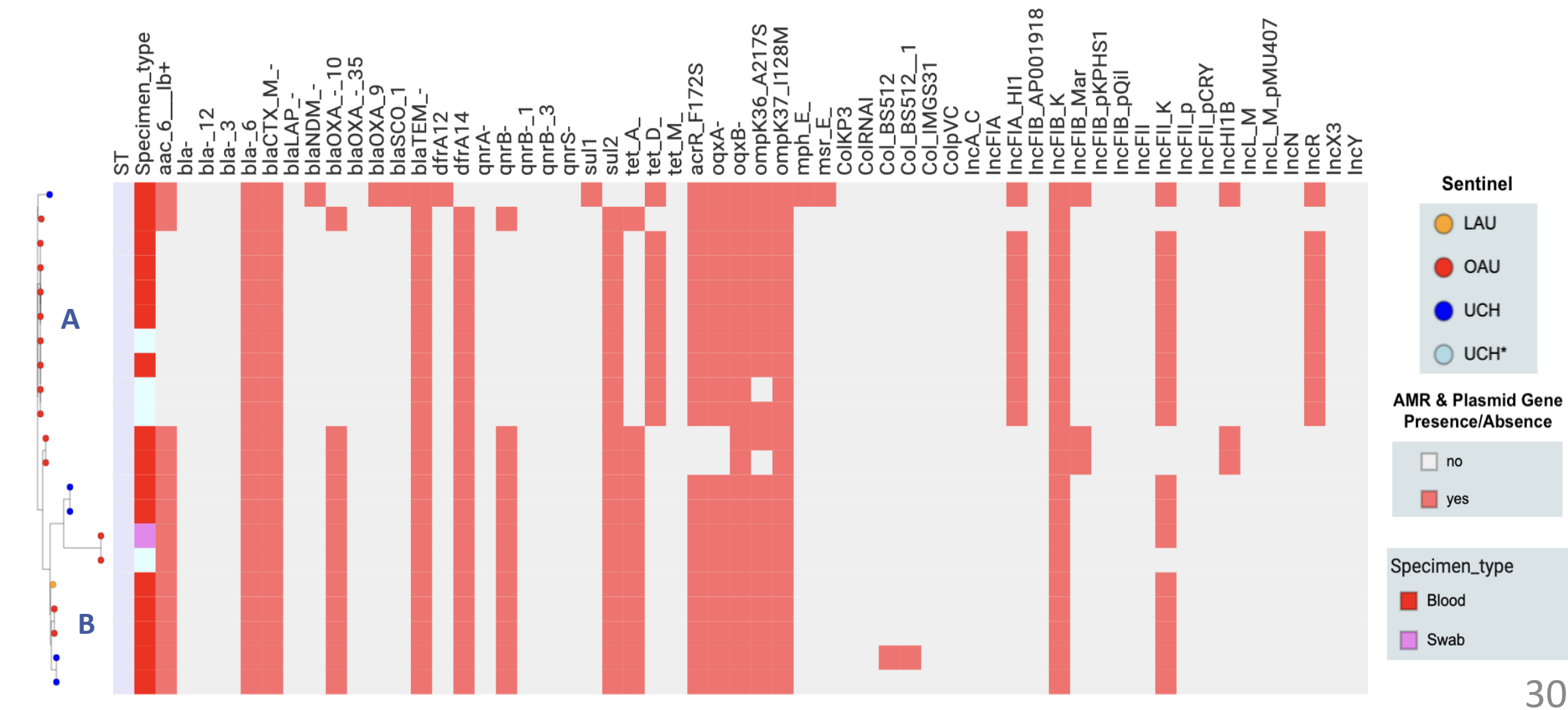
	Total #	K-types	Strains per K-type	O-types	Strains per O-type
OAUTHC	92	21	4.4	10	9.2
UCH	30	16	1.9	7	4.3
LAUTECH	12	10	1.2	7	1.7



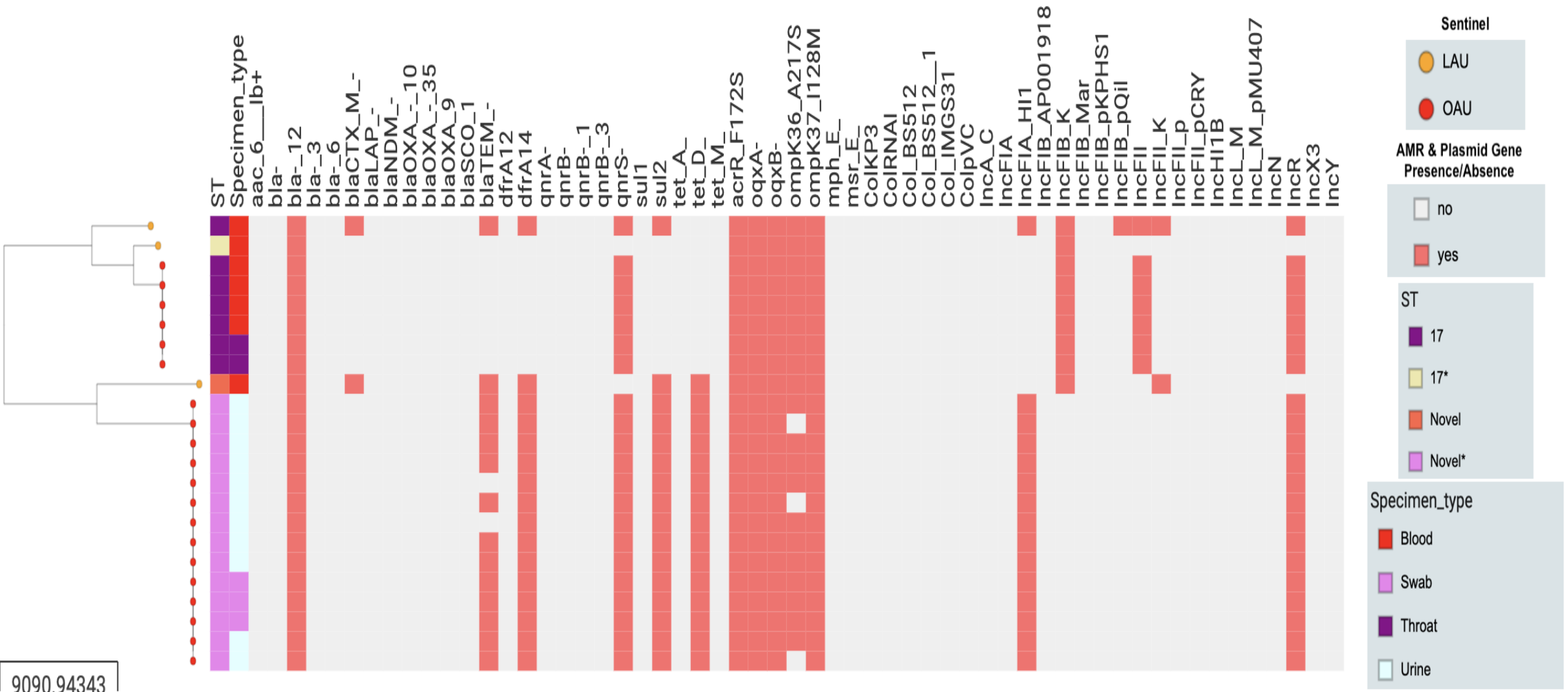
OAU



ST307



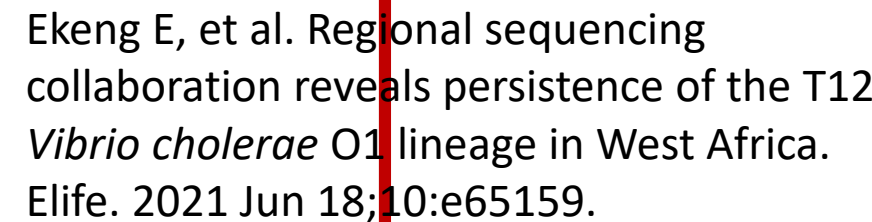
ST17 complex:
ST17 (7), ST17* (1), STNovel (1). NovelST* (14)



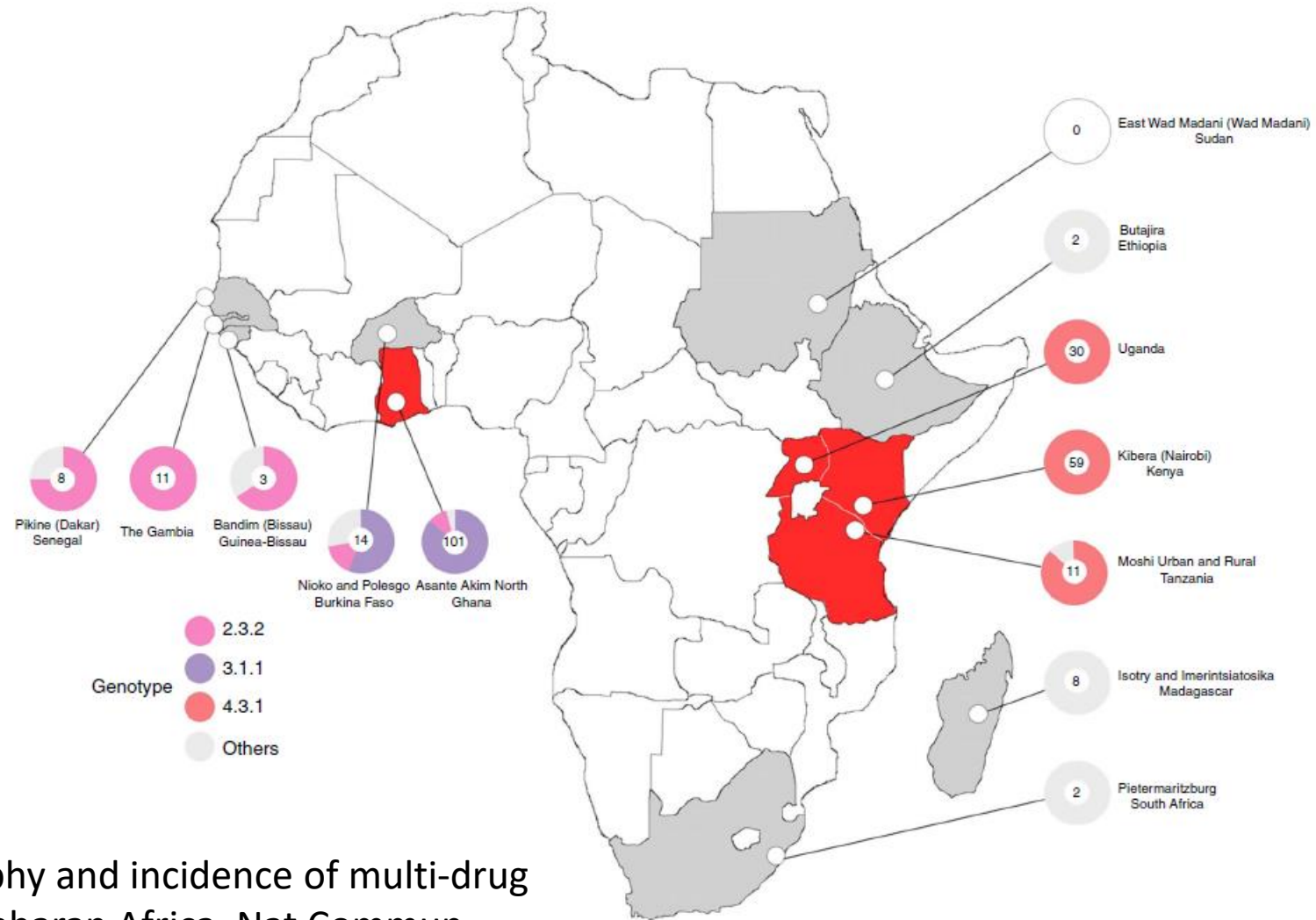
9090.94343

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Multidrug resistant *Salmonella* Typhi epidemiology in Africa



Park SE, et al. The phylogeography and incidence of multi-drug resistant typhoid fever in sub-Saharan Africa. Nat Commun. 2018 Nov 30;9(1):5094.

Reference laboratory services available to the AMR surveillance network via GHRU

- ID verification (VITEK/ WGS)
- Susceptibility pattern verification/ MIC on demand (VITEK)
- Susceptibility pattern extension/ Resistance mechanism (VITEK/ WGS)
- Ruling in or out outbreaks
- Feedback on performance and resistance information
- Trouble-shooting / training



Pathogen coverage

- WHO priority organisms from blood or CSF, except *Helicobacter*, *Campylobacter*
- *Vibrio cholerae*
- *Neisseria* and *Haemophilus spp* – consult first
- Outbreaks by other bacteria – consult first
- *Candida* – consult first (no WGS – VITEK only)
- No other mycology, virology or parasitology



A problem shared is a problem smashed...



Iruka Okeke
PI



Ayo Ayorinde
Bioinformatician



Erkison Odih
Bioinformatician



Jolaade Ajiboye
Program Officer



Ifeoluwa Akintayo
Lab & sequencing
scientist



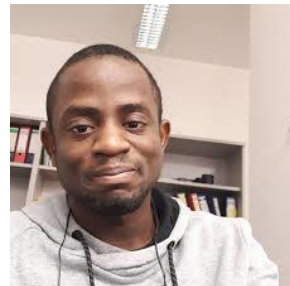
Anderson Oaikhena
Lab & sequencing
scientist lead



Rotimi Dada
Bioinformatician



Faith Popoola
Sequencing
scientist



Odion Ikhimiukor
Bioinformatician



Kesiana Akpede
Finance Officer



David Kwasi
Lab manager



**G. Temitope
Sunmonu**
Lab scientist



Olabisi Akinlabi
Lab & sequencing
scientist

Acknowledgements



- PHA4GE: University of the Western Cape
- Global Health Research Unit for Genomic Surveillance of Antimicrobial Resistance supported by the National Institute for Health Research
 - David Aanensen, Ravi Kumar, Pilar Donado-Godoy, Celia Carlos
 - Nigeria GHRU: Ayorinde Afoloayan, Anderson Oaikhena, Jolaade Ajiboye
- SEQAFRICA
 - Rene Hendricksen, Pernille Nilsson, Christina Odgaard, Blandina Mmbaga, Marco van Zwetselaar, Anthony Smith, Beverly Egyir
- Nigeria Centre for Disease Control
 - Chikwe Ihekweazu, Joshua Obasanya, Abiodun Egwenu, Tochi Okwor
- CDDEP, ReACT, WHO, WHO-Africa, WHO Nigeria
- Nigeria's Technical Working Group for Antimicrobial Resistance
 - Oladipo Aboderin, 'Onyi' Estelle Mbadiwe, Debola Olayinka
- Public Health England
 - Marie Chattaway, Colin Brown, Bee Afshar
- Wellcome Trust Sanger Institute
 - Nicholas Thomson, David Aanensen, Anthony Underwood, Mihir Kekre, Silvia Arigomon



Vaccine
REGULATORS HUMAN
PROVIDE
MUTUALLY
BENEFICIAL
FEEDBACK

BACTERIA BECOMES RESISTANT by CHANGING DNA

SELECTIVE
ADVANTAGE
TO THE ONE
WHO ARE

RESISTANT

IT IS CRITICAL TO
HOW WE CONTROL
INFECTIOUS DISEASES
NOW AND IN THE
FUTURE!

**DON'T WASTE ANTI-
BIOTICS, EVADE CURE,
FUEL RESISTANCE.
AVOID INFECTIONS
DISEASE CRISIS**

WE NEED SURVEILLANCE
DIAGNOSTIC TESTS

Smart
ANTIMICROBIAL RESISTANCE
SURVEILLANCE
to MEET AFRICA
NEEDS

WITH ANTIBIOTICS WE KILL SENSITIVE BACTERIA

Africa

WHO IS AT RISK?
WHAT CAUSES ILLNESS?
WHAT'S THE CURE?

DATA

GENOMIC SEQUENCING

ACCESS to KNOWLEDGE & RESOURCES



KNOWLEDGE BRINGS ASSURANCE,
DECISIVENESS AND POWER