Invasive Salmonellosis in Central Nigeria

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9th International Conference on Typhoid and Invasive NTS Disease, 2015

Objectives

- Background
- Bacteremia surveillance of young children
- Preliminary results
- Gaps in knowledge
- Way forward

Child Mortality in Nigeria-General Facts

- About 5.3 million children are born yearly in Nigeria~ 11,000 everyday
  - 1 million of these children die before the age of 5 years
- Nigeria's newborn death rate (NMR)-528 per day- is one of the highest in the world
  - About 9 of ten of newborn deaths are preventable

Lack of Etiologic Data for Bacteremic Syndromes

Limitations of previous studies

- Sub optimal laboratory Methods
- Culture media
- Agar preparation- suboptimal blood agar source
- Identification of isolates- misidentification
- Incomplete characterization

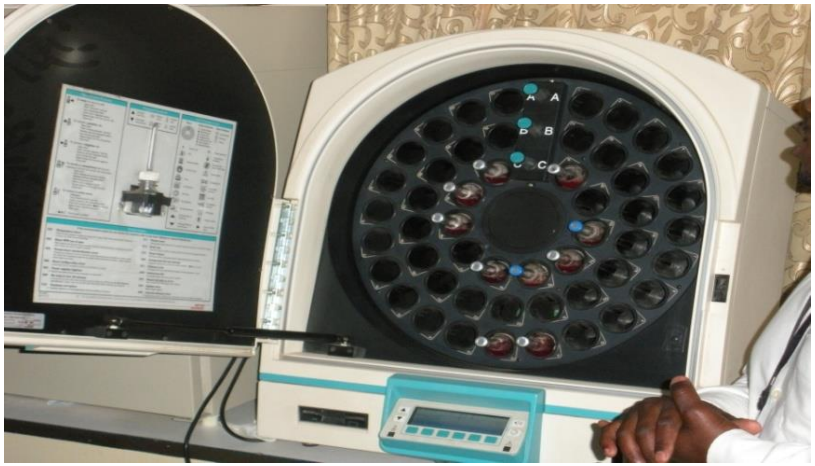
Community **A**cquired **B**acteremic **S**yndrome in **Y**oung **N**igerian **C**hildren (CABSYNC)

A COLLABORATIVE STUDY
National Hospital Abuja
Zankli Medical Center
MRC Laboratories, The Gambia
Michigan State University
CDC, ATLANTA

Objectives

- To introduce automated blood culture system to pediatric clinical care
- Pilot study of the etiologic agents of bacteremia in young children in central Nigeria

Equipping the Laboratory



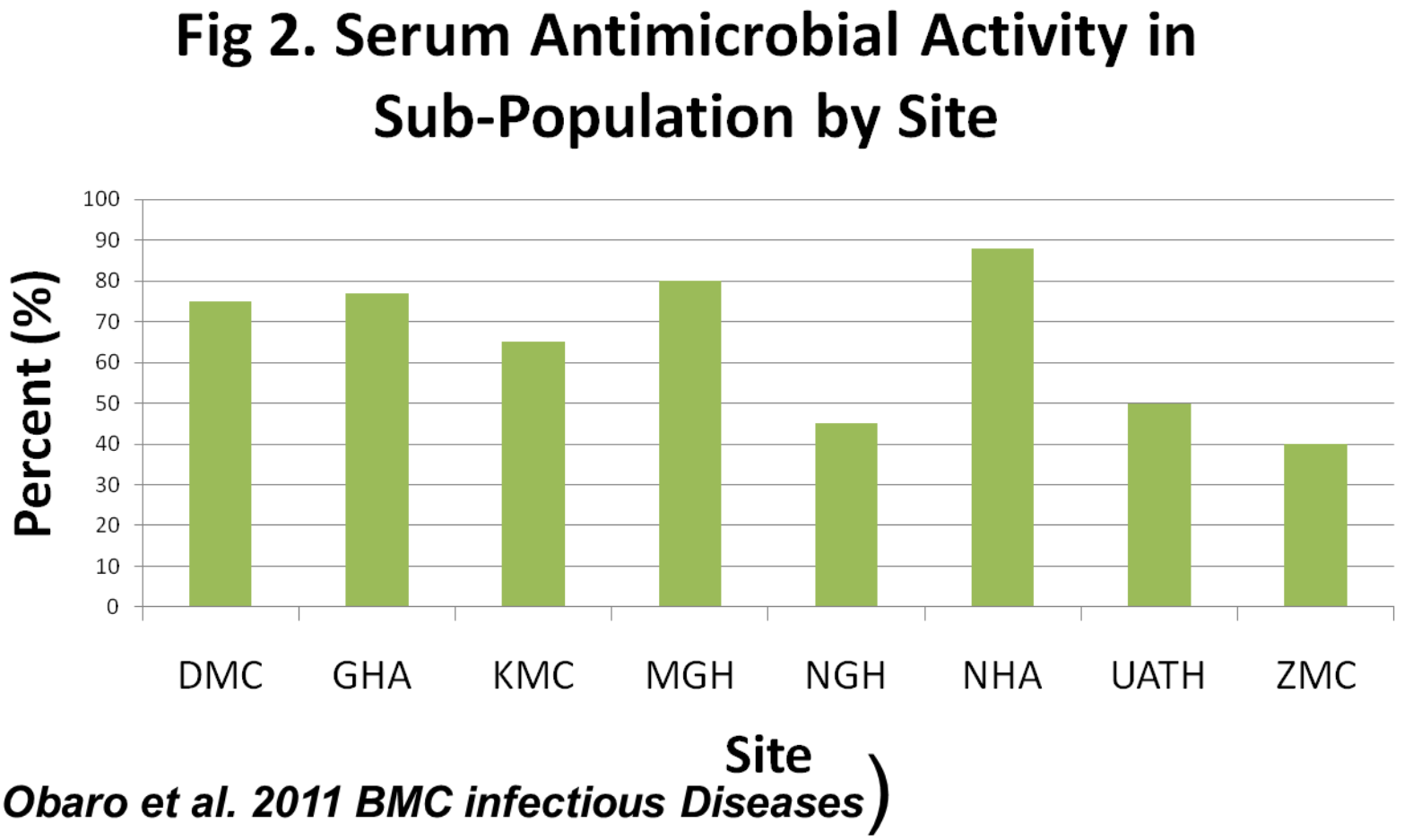
Surveillance

- Enrolment from Sept 2008-
- All children aged 2months-5years
- Fever or hypothermia (temp greater or equal to 38.5^{o}C or less than 34.5^{o}C **plus** prostration, respiratory distress, convulsion or diarrhea
- Informed consent

Methods II

- Blood drawn aseptically into culture bottle with other clinically indicated tests
- Culture bottles incubated for 5 days (max)
- Positive cultures Gram stained and sub cultured on appropriate agar plates
- Identification by standard biochemical method (API)

Pre-Consultation Antibiotic Exposure in FCT



(*Obaro et al. 2011 BMC infectious Diseases*)

Childhood Bacteremia in FCT, Central Nigeria

- 969 children aged 2months-5years. Mean age was 21 ± 15.2 months.
- Salmonella spp were the leading cause of bacteremia -28.5% with *S.typhi* accounting for 20.9% and non-typhi salmonella -7.6%)
- *S. aureus* -20.2%
- *S.pneumoniae* -11.9%
- Acinetobacter -11%.

Obaro et al. BMC Infect Dis 2011

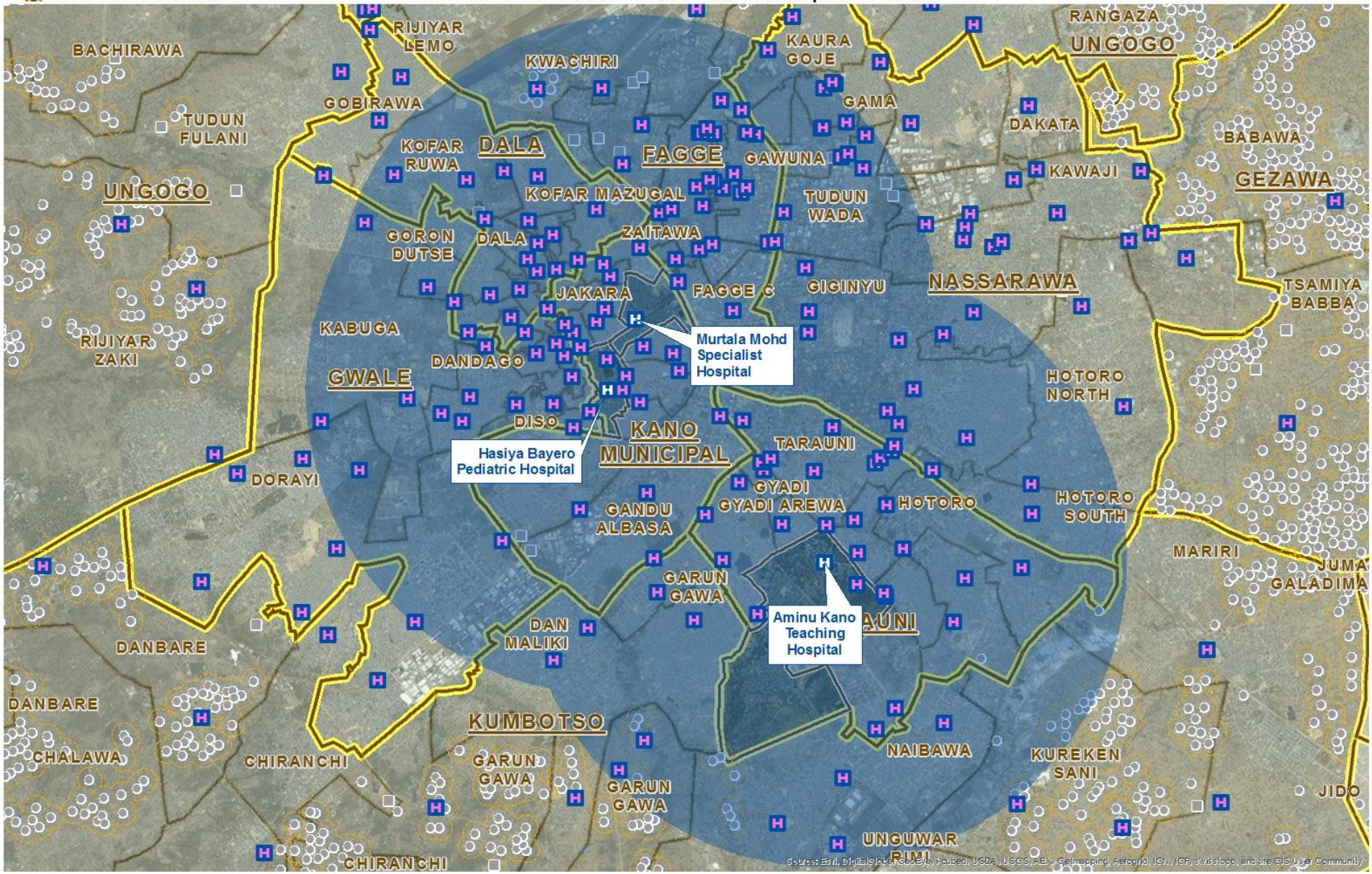
Nigeria-Culturally Diverse

Bacteremia Surveillance in Young Children

Surveillance Sites in Kano

Kano State Government

5km buffer of Selected Health Facilities in Respective Wards



Legend

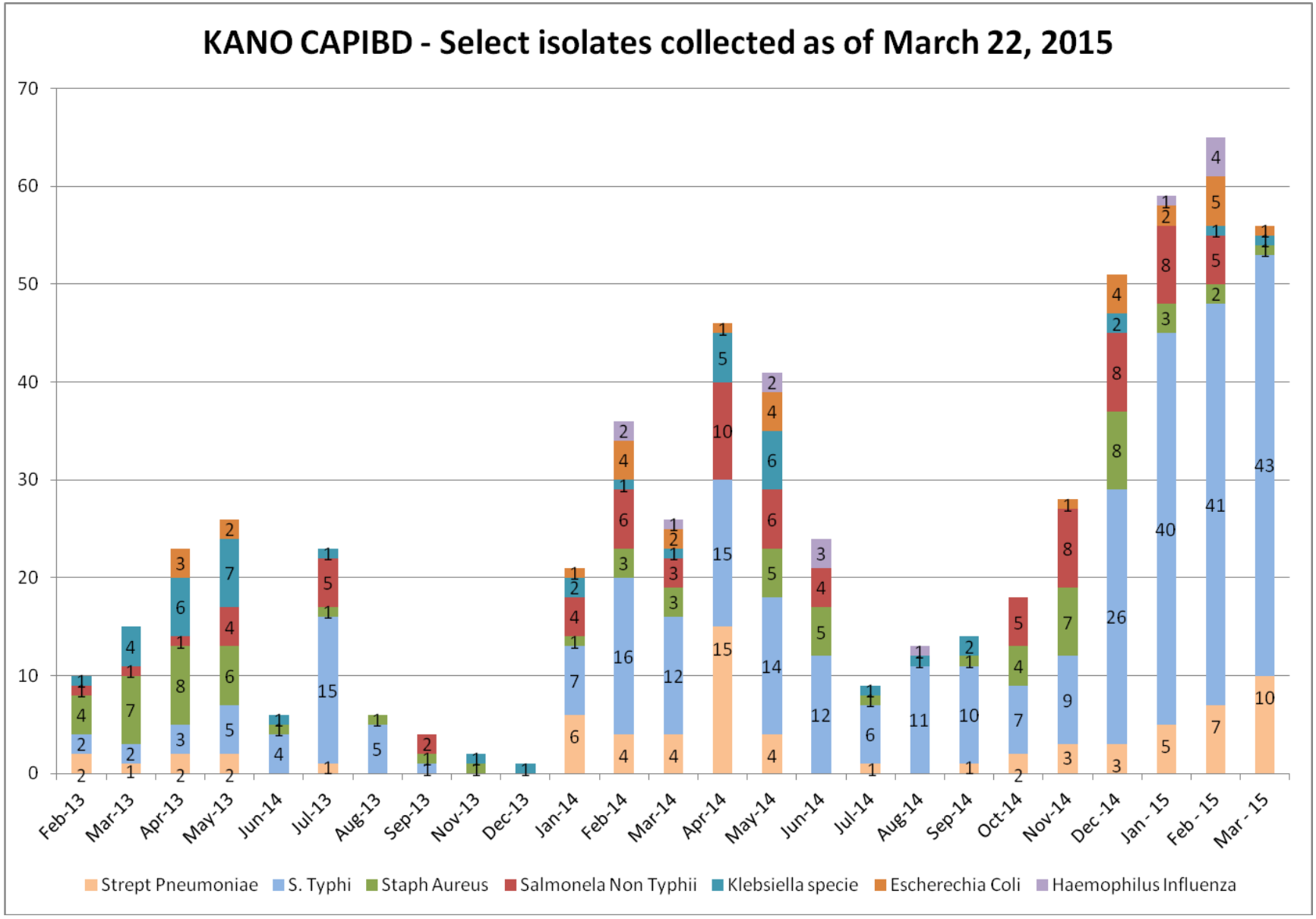
LGA · Ward · Hamlet area · Hamlet · Small Settlement · Health facility · Health Facilities_Out · HF_5km_Buffer · Waterway_North · Waterbody_North

1 centimeter equals 560 meters

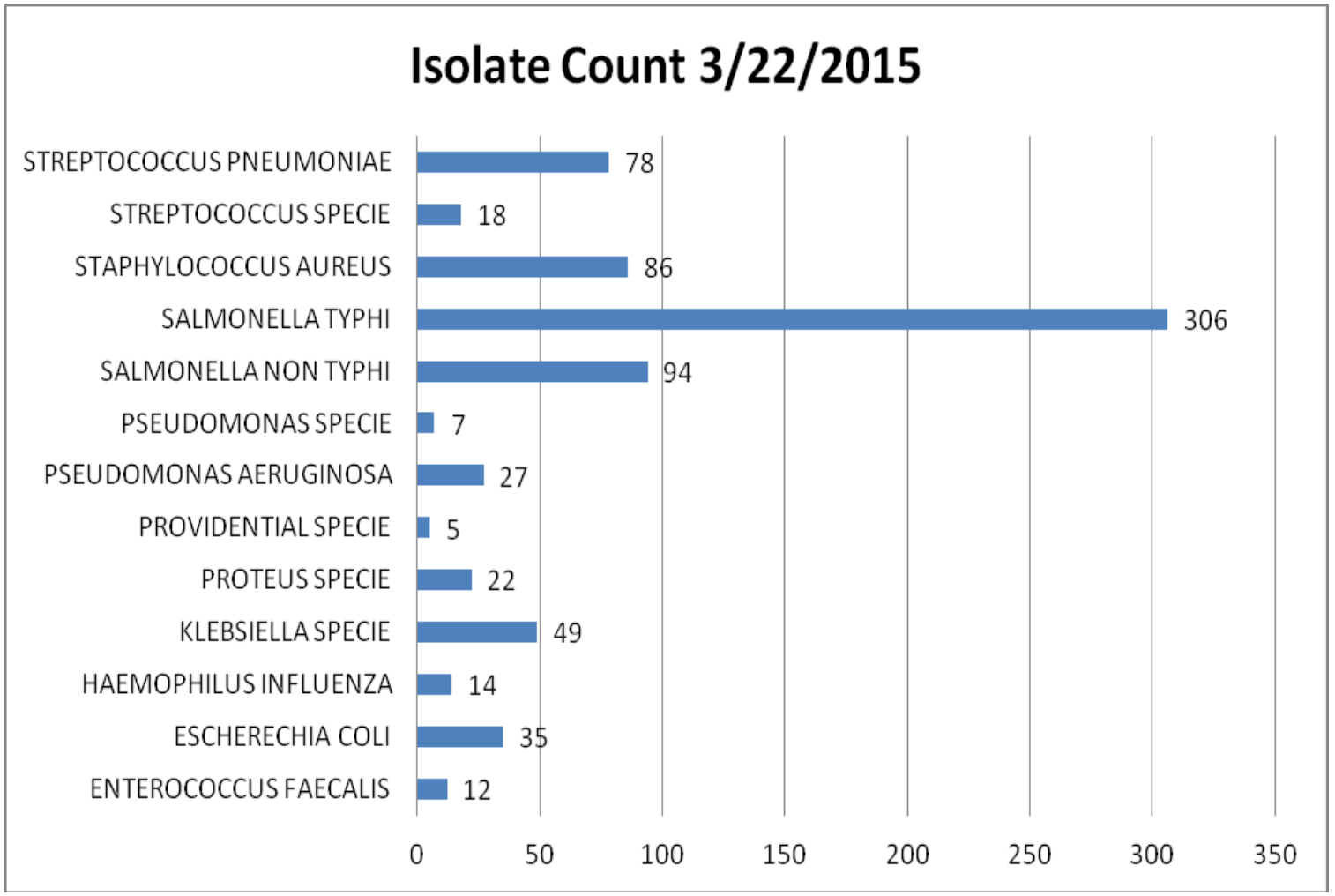
This special use-map was produced to support Nigerian Polio Immunization Programme field operation planning. It was designed specifically for vaccination team assignment planning and is not intended to be a topographic map. The content was compiled from commercial satellite sources and includes settlement names and points of interest from field data collection. Boundaries and Names are for reference purposes and should not be considered authoritative.

Production Date: 4/23/2015

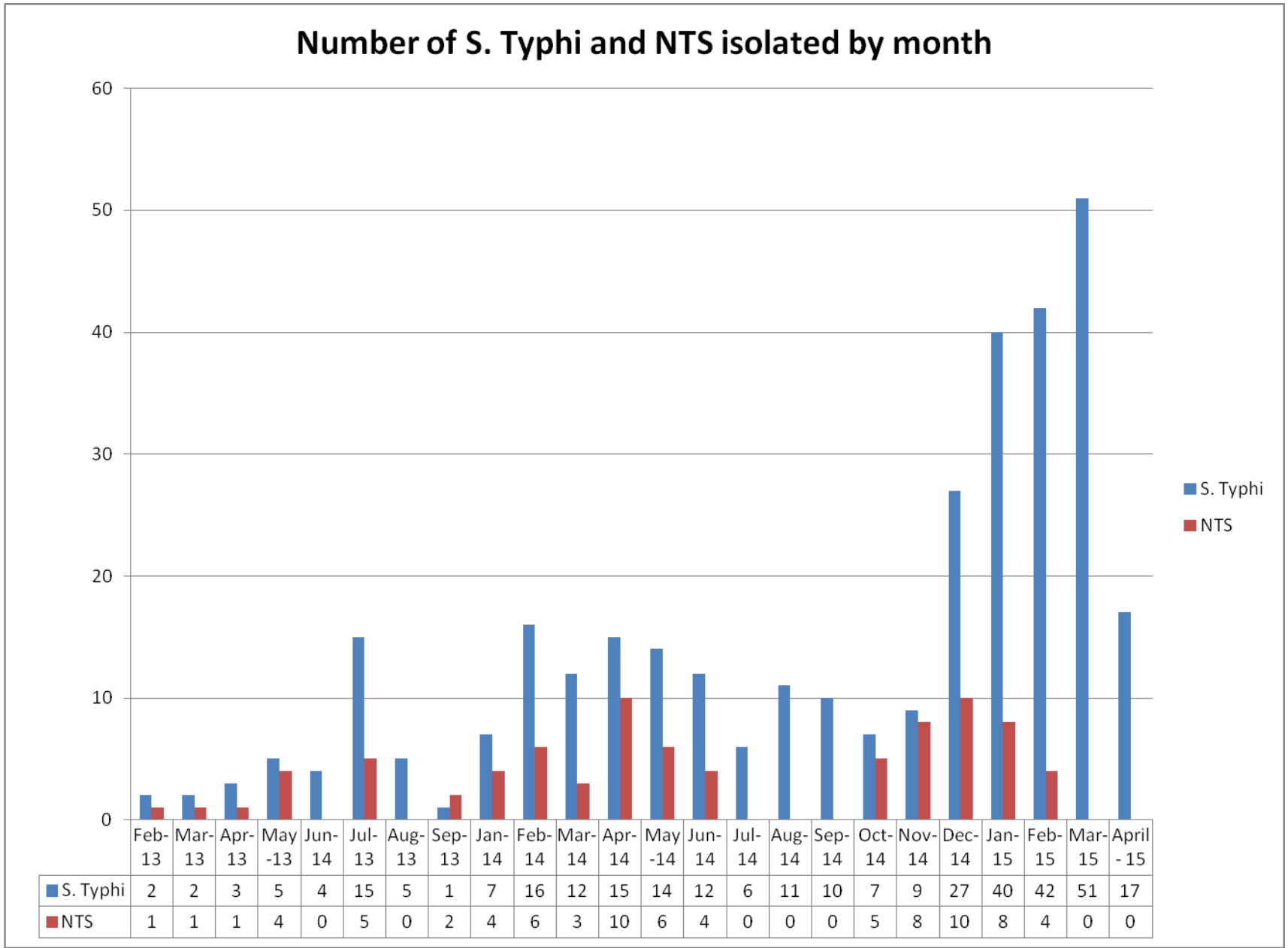
Facilities in Kano


KANO CAPIBD - Select isolates collected as of March 22, 2015
70
60
50
40
30
20
10
0
Feb-13
Mar-13
Apr-13
May-13
Jun-14
Jul-13
Aug-13
Sep-13
Nov-13
Dec-13
Jan-14
Feb-14
Mar-14
Apr-14
May-14
Jun-14
Jul-14
Aug-14
Sep-14
Oct-14
Nov-14
Dec-14
Jan - 15
Feb - 15
Mar - 15
Strept Pneumoniae
S. Typhi
Staph Aureus
Salmonela Non Typhii
Klebsiella specie
Escherechia Coli
Haemophilus Influenza

Etiologic Agents of Childhood Bacteremia in North Central Nigeria



Seasonal Trend of Invasive Salmonellosis



	Feb-13	Mar-13	Apr-13	May-13	Jun-14	Jul-13	Aug-13	Sep-13	Jan-14	Feb-14	Mar-14	Apr-14	May-14	Jun-14	Jul-14	Aug-14	Sep-14	Oct-14	Nov-14	Dec-14	Jan-15	Feb-15	Mar-15	April-15
S. Typhi	2	2	3	5	4	15	5	1	7	16	12	15	14	12	6	11	10	7	9	27	40	42	51	17
NTS	1	1	1	4	0	5	0	2	4	6	3	10	6	4	0	0	0	5	8	10	8	4	0	0

Age Distribution of Bacteremic Children

	Mean Age (Months)	**Median**	**N**
S.Typhi	32.5	31.5	260
NTS	24.3	22	73
Other bacteria spp	13.7	9	333
			686

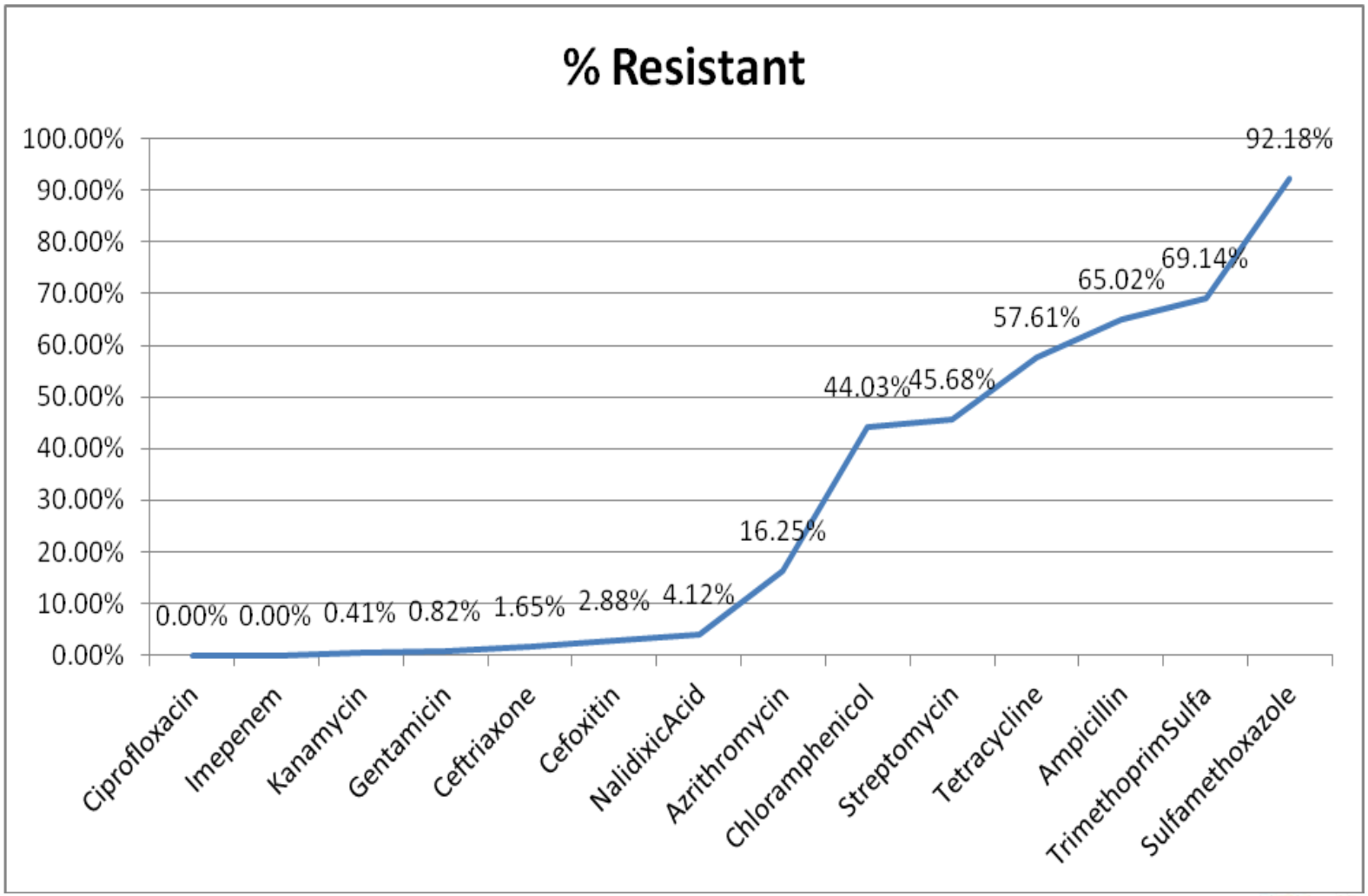
Isolates from Neonates

Isolates from Infants< 1 month	Frequency	Percent
ALKALIGENS SPECIE	1	1.1%
Aeromonas Hydrophila	1	1.1%
HAEMOLYTIC STREPTOCOCCUS SPECIES	3	3.2%
Candida specie	5	5.4%
ENTEROCOCCUS FAECALIS	4	4.3%
ESCHERECHIA COLI	9	9.7%
KLEBSIELLA PNEUMONIAE	14	15.1%
MORGANELLA MORGANII	1	1.1%
NON HAEMOLYTIC STREPTPTOCOCCUS SPECIE	2	2.2%
PROTEUS MIRABILIS	2	2.2%
PROTEUS SPECIE	5	5.4%
PROVIDENTIAL SPECIE	1	1.1%
PSEUDOMONAS AERUGINOSA	9	9.7%
SALMONELLA TYPHI	2	2.2%
SERRATIA SPECIE	1	1.1%
STAPHYLOCOCCUS AUREUS	28	30.1%
STREPTOCOCCUS PNEUMONIAE	5	5.4%
Total	93	

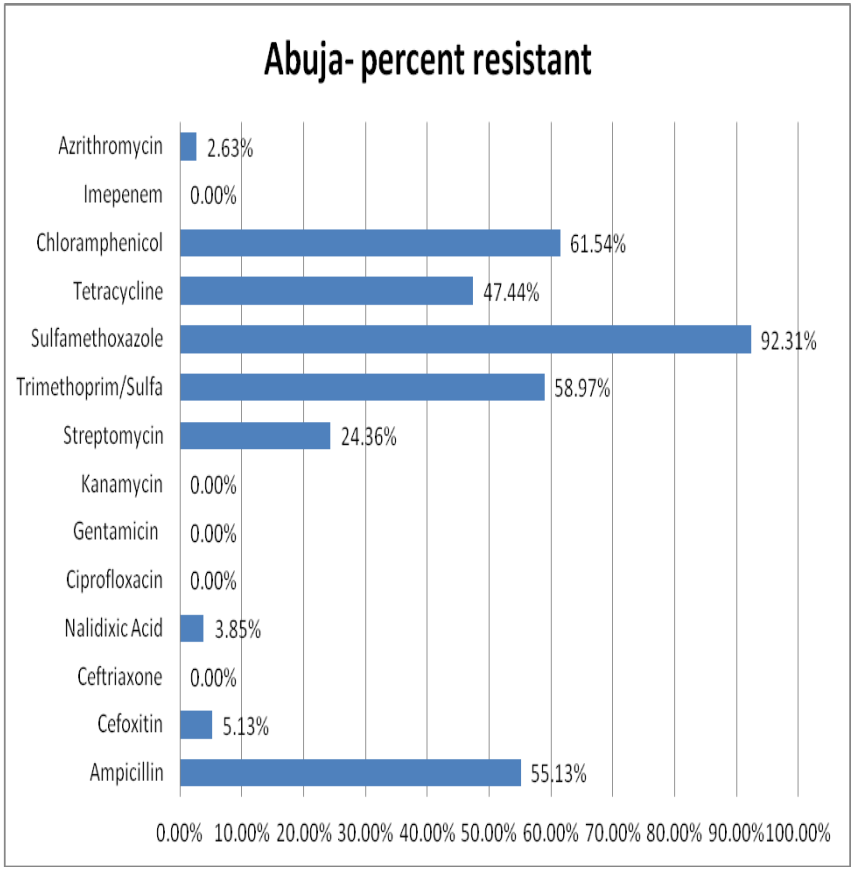
NTS Serovars

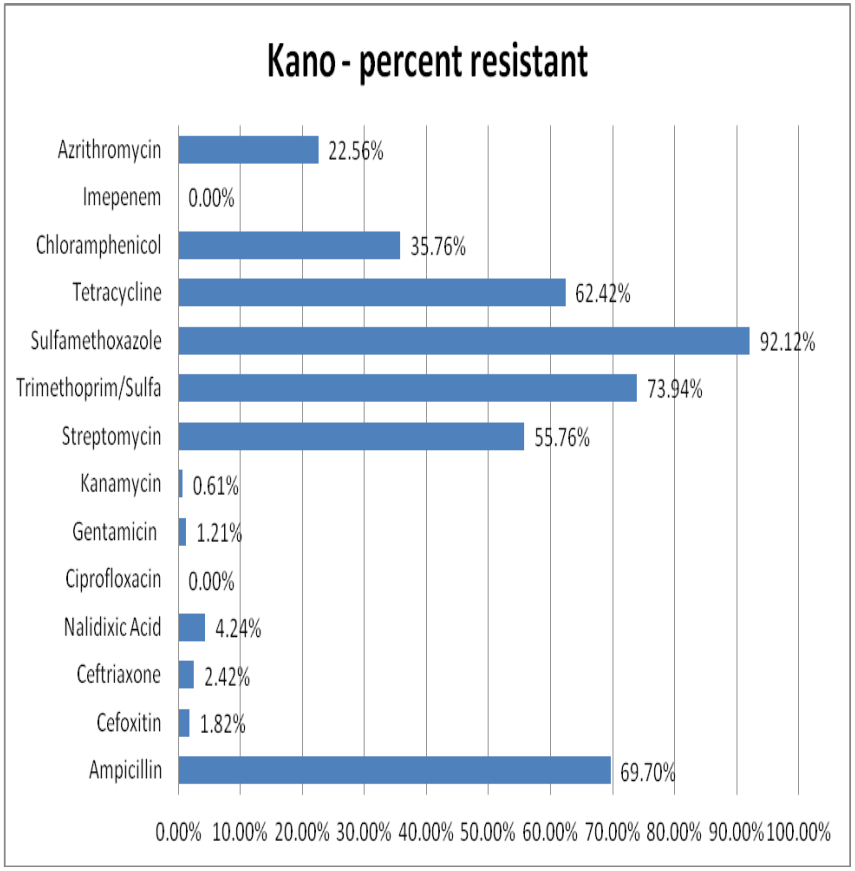
Salmonellae	N
Salmonella brendeney	1
Salmonella dublin	2
Salmonella durban	1
Salmonella enteritidis	34
Salmonella Galiema	1
Salmonella group B	12
Salmonella Group C	2
Salmonella group D	2
Salmonella Paratyphi C	1
Salmonella Pasing	1
Salmonella poona	3
Salmonella ser. Pullorum Grp D	1
Salmonella spp	9
Salmonella typhimurium	30
Total	100

Resistance Pattern of Invasive *S.typhi* Isolates



Regional Differences in S.Typhi

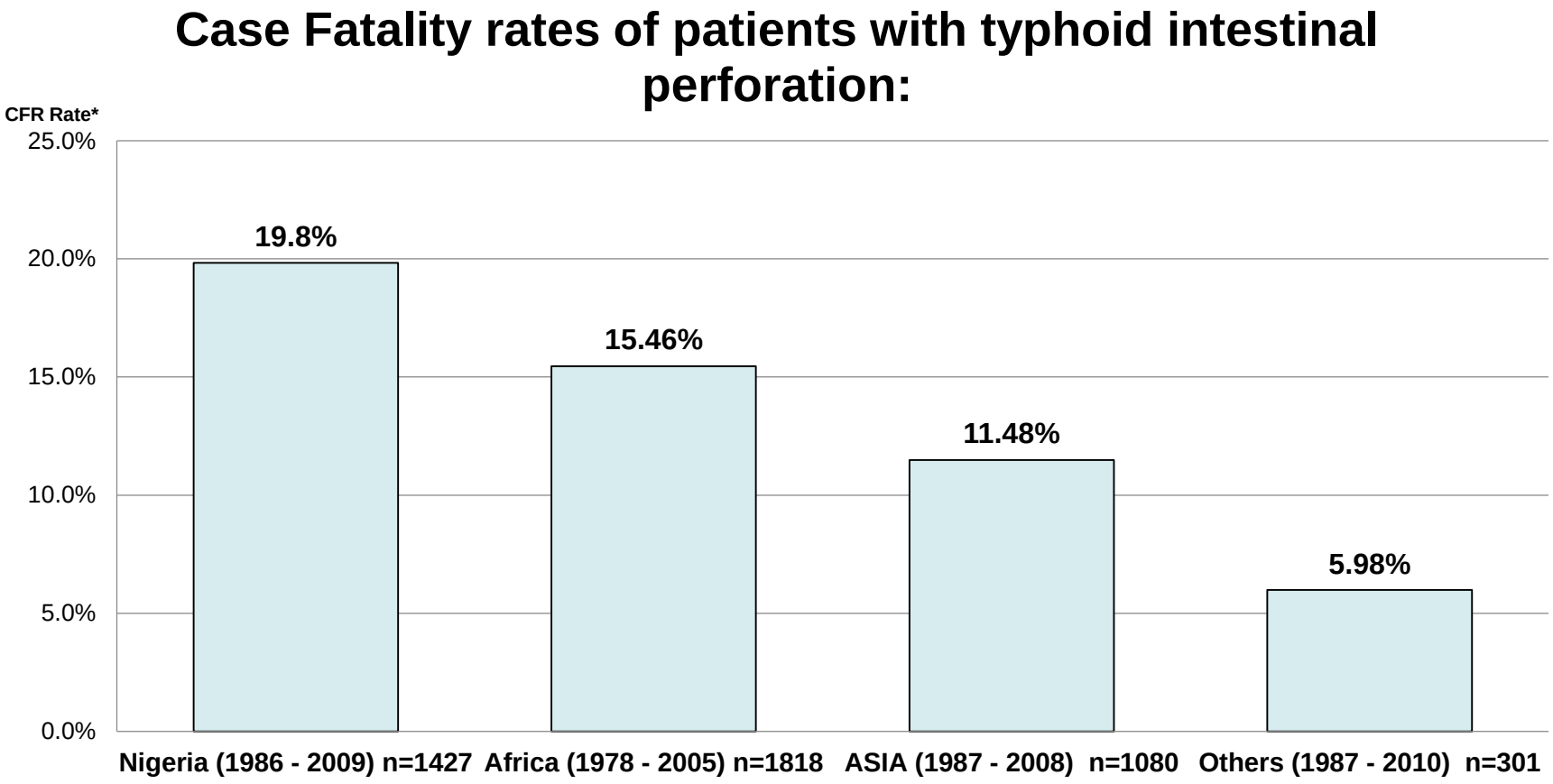




Terminal Ileal Perforation (TIP)

- **Mortality** : Dickson et al (Br. J Surg 1964) 58%
- Adesunkanmi et al (Ann Coll Surg Hong Kong 2003) 28%
- Ugochukwu et al (Int J Surg 2013) 19%

Typhoid Perforation-CFR



*unweighted

Source: Mogasale V, Desai SN, Mogasale VV, Park JK, Ochiai RL, et al. (2014) Case Fatality Rate and Length of Hospital Stay among Patients with Typhoid Intestinal Perforation in Developing Countries: A Systematic Literature Review

TIP

- A complication of treatment?
- An unusual manifestation of TF?
- Host genetic and/or bacterial virulence?

Need for improved understanding of TIP

Sickle Cell Disease

- 300x more likely to develop bacterial meningitis
- 600x more likely to develop pneumococcal meningitis
- 116x more likely to develop *H.influenzae* meningitis
- 25x more likely to develop NTS sepsis than non-SCD children from same community

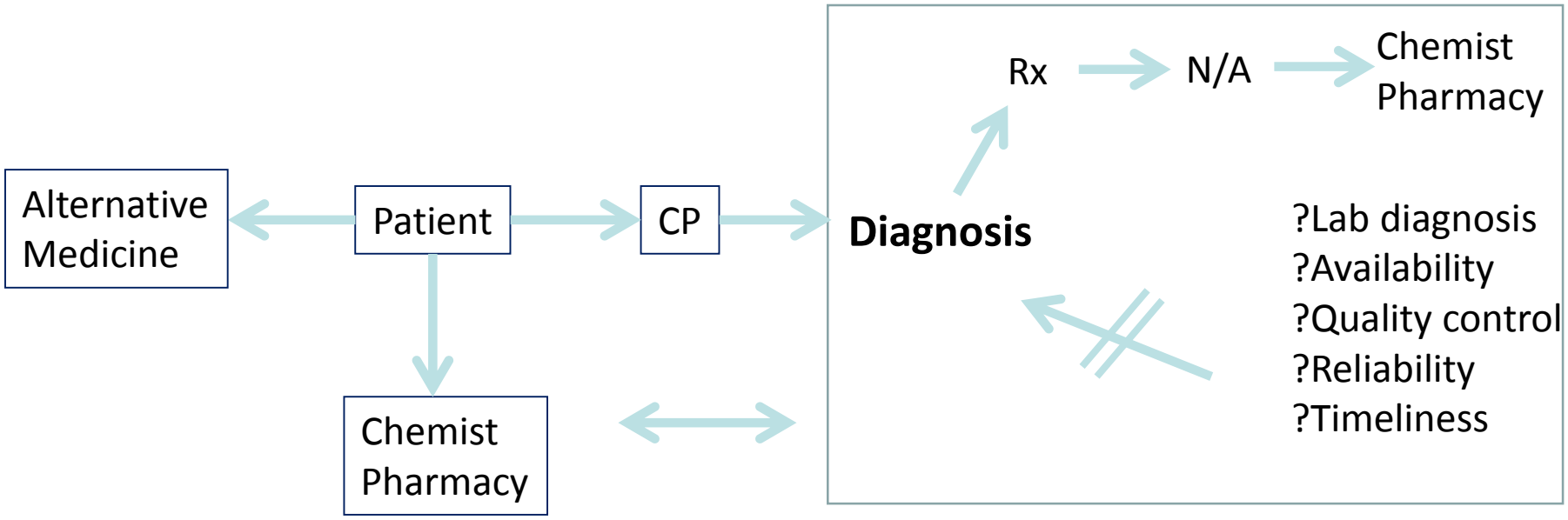
1.Barret-Connor- Bacterial infection in sickle cell disease Medicine 1971:50:97-112

2. Booth, Inusa, Obaro IJID 2011

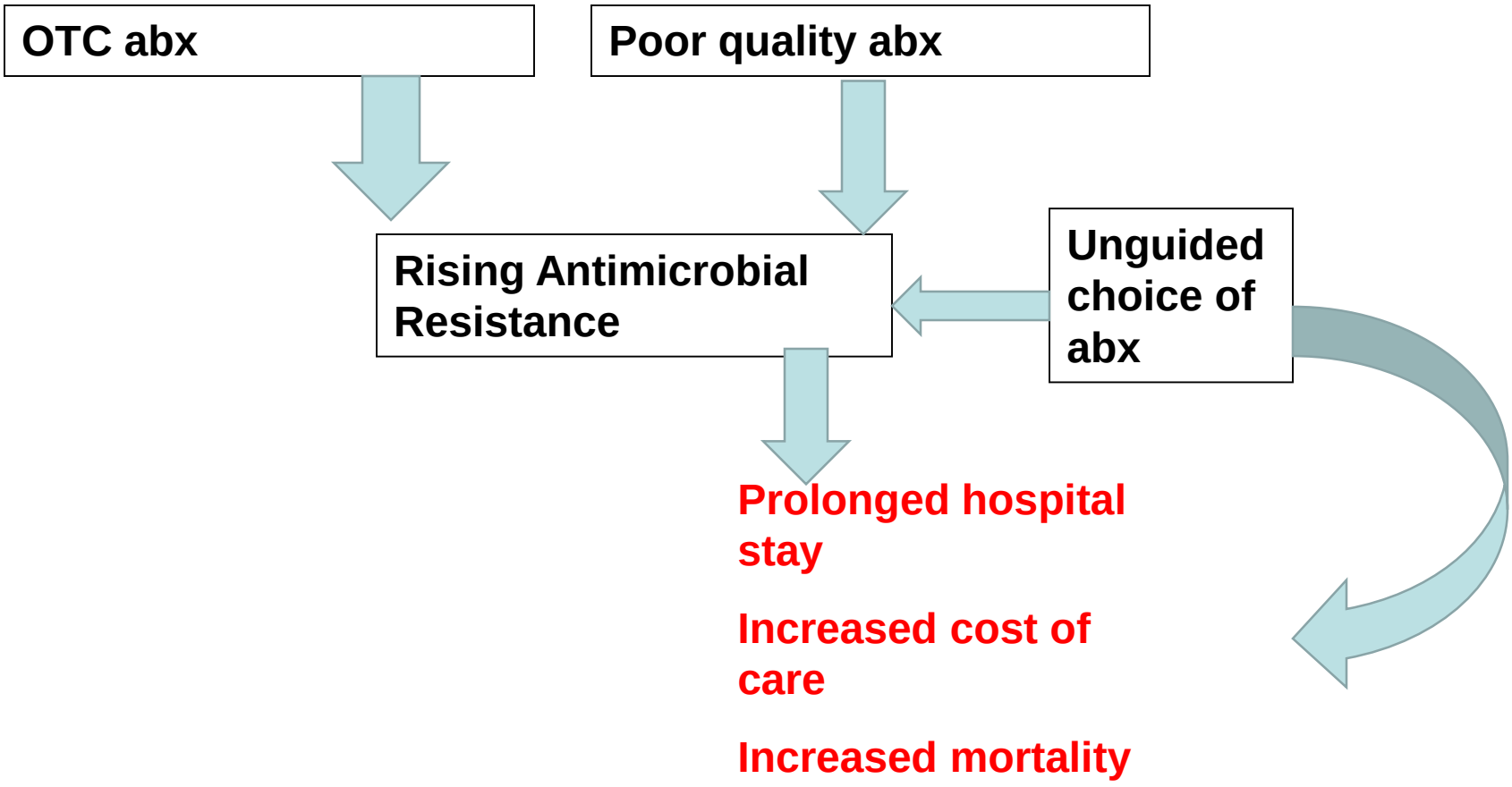
Public Water Supply

Public Water Supply

Health Care Seeking Behavior



Rising Abx Resistance



Conclusions

- High prevalence of S. typhi over NTS
- Overall high prevalence of MDR (NTS>Typhi)
- High prevalence of infant disease, including neonates
- Significant regional difference in the epidemiology of invasive salmonellosis
- High prevalence of TIP
- Rare disease by Paratyphi
- Surveillance
  - population-based surveillance
  - Multi-disciplinary research teams

“The microbe that felled one child in a distant continent yesterday can reach yours today and seed a global pandemic tomorrow”

Nobel Laureate
Dr. Joshua Lederberg

Acknowledgement

- Funding- BMGF
  - NIAID (NIH)
  - UNMC
- Local Logistics- Zankli Medical Center, Abuja
  - NHA
  - AKTH
  - HSMB
- Laboratories- MRC, Gambia
- CDC, Atlanta
- Wellcome Trust Sanger Institute

Thank you!