NATIONAL HEALTH LABORATORY SERVICE

Global Antibiotic Resistance Partnership

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

Reflections from GARP Phase 1

South Africa

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The Republic of South Africa

Economic Development and Health Indicators:

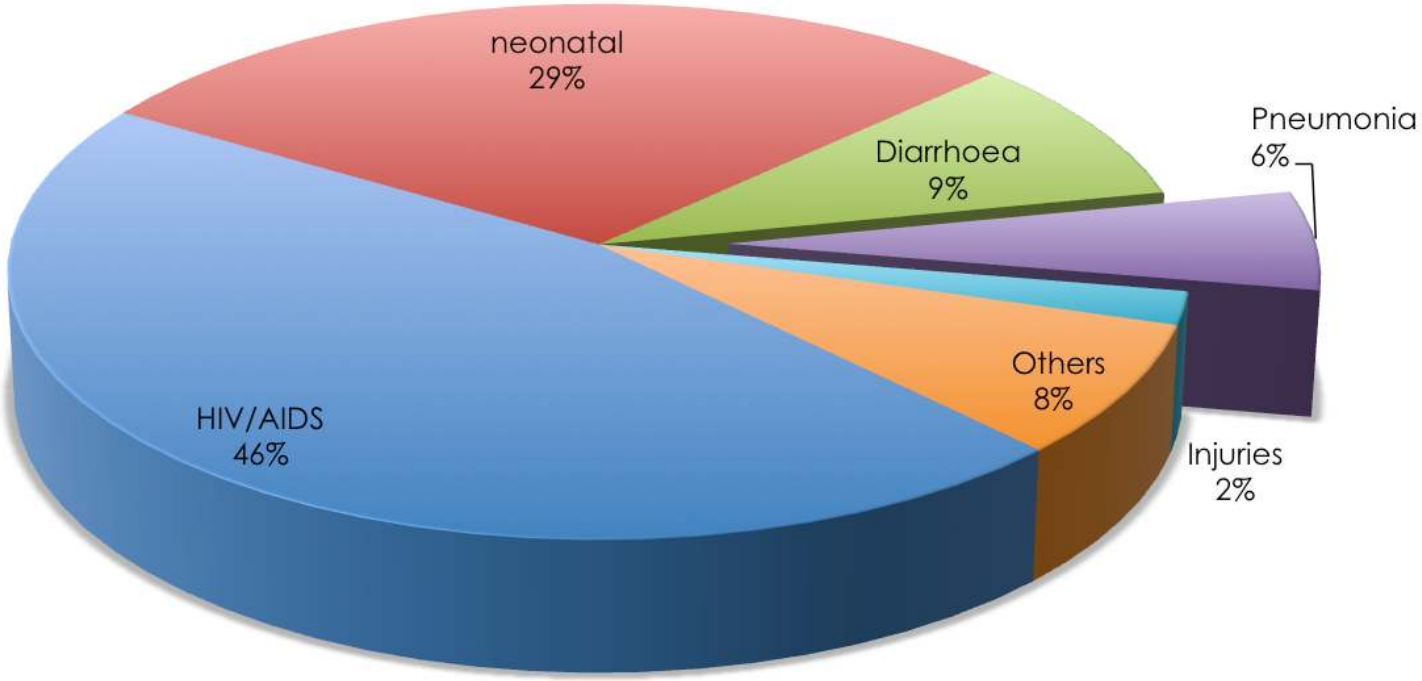
Population (2010)	49991470
Population growth rate (2009)	1.06%
Life expectancy (2009)	53y ♂, 55y ♀
Gross national income per capita (2009)	US$5.79
Child (<5y) mortality rate (2009)	104/1 000
Maternal (15-49y) mortality rate (2007)	625/100 000
Population living in poverty (<US$1 per day) (2006)	5%
Population with access to clean water (2009)	89%
Adult (15+) literacy rate (2007/8)	82.5%

World Bank, Country Brief; South Africa. September 2010

Background:

- Current challenges: 'quadruple' burden of disease:
  - Infections:
    - ~ 29% HIV-infected. HIV accounts for 26% of deaths (single most common cause)
    - TB accounts for 28% of the global burden TB related to HIV
  - Other infectious diseases: meningeal and respiratory infections, diarrhea, STIs etc.
  - Trauma & injuries
  - Non-communicable diseases

Leading Causes of Mortality in Children Under 5, South Africa, 2008:



Source: 2010 South African Health Review

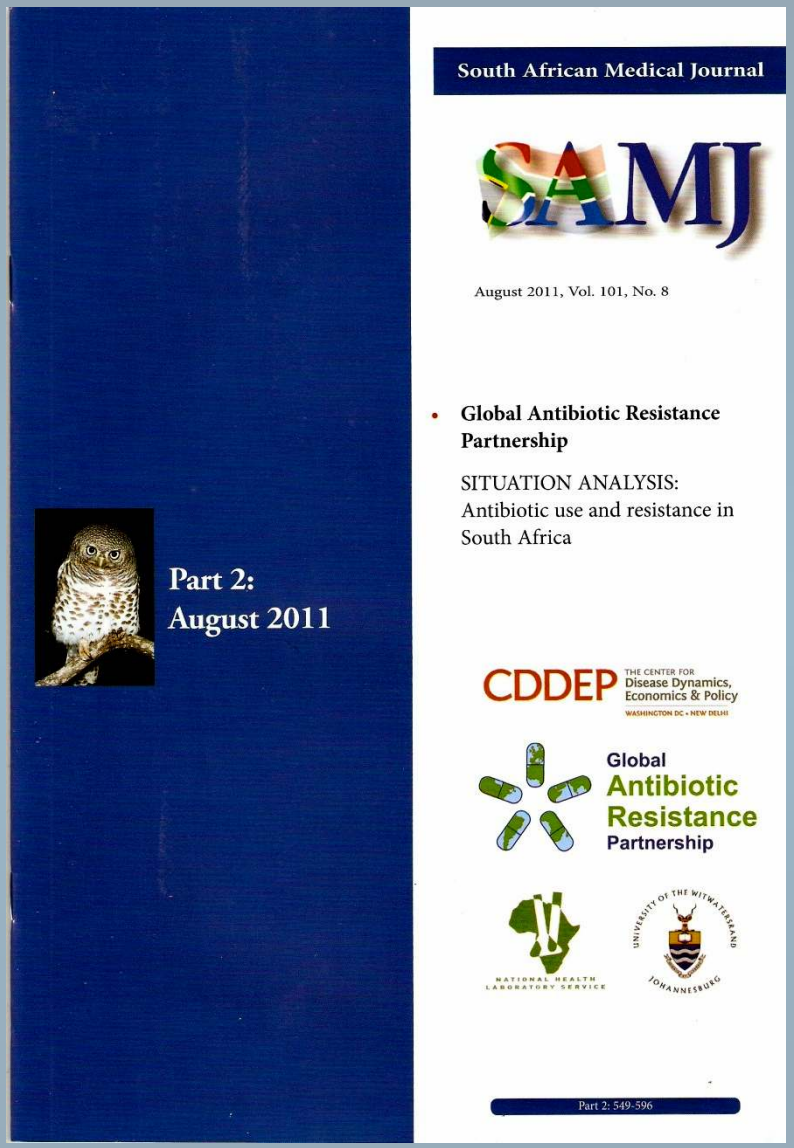
Paradoxes:

- Profound changes in social & governmental structures since 1994 have not yet resulted in improvement of health indicators for the majority of South Africans

- Despite being relatively well-resourced, and having a wealth of available expertise nationally, SA has yet:
  - To adequately manage the HIV & TB co-epidemics
  - To clearly identify the extent and driving factors of AMR
  - To implement nationally standardized hospital infection and AMR surveillance systems
  - To fully translate available AMR surveillance data into policy
  - To implement nationally standardized and effective infection prevention and control training and programs countrywide

GARP and the South African Situational Analysis:

- GARP-SA launched 8-9 February 2010
- 40 experts: clinical, veterinary, policy, research, & pharmaceutical spheres
- Issues identified in this meeting:
  - Establishment of a multi-disciplinary GARP-SA National Task Team
  - Urgent need for a situational analysis to consolidate all available information pertaining to antibiotic resistance (ABR)
  - To reflect on our strengths and weaknesses, and identify gaps, in our approach to the challenges posed by ABR
  - To draw on expertise from CDDEP & all GARP collaborating partners in this venture for the translation of all aspects of ABR into policy



Aspects of ABR in South Africa

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Strengths:

- Respiratory and Meningeal Pathogens Research Unit
- Group for Enteric Respiratory & Meningeal Surveillance in South Africa (GERMS-SA)
- STI Reference Centre (STIRC)

Respiratory & Meningeal Pathogens Unit (RMPRU)

- Initial focus: pneumococcal disease
- Mandate broadened to perform research and evaluate:
  - Antimicrobial resistance in respiratory pathogens
  - Research and development of pneumococcal and protein conjugate vaccines
  - Impact of HIV-1 on respiratory & invasive infections
  - Respiratory viruses and their interaction with bacteria in RTIs
- More recently: vaccine-preventable research dimension & prevention strategies other than vaccination

RMPRU Pivotal Study:

- 'A trial of a 9-valent pneumococcal conjugate vaccine (PCV) in children with and those without HIV infection' *NEJM 2003;349:1341-5*
  - PVC-9 reduced vaccine serotype-specific invasive pneumococcal disease (IPD) by 83% in HIV+ve children and by 65% in fully vaccinated HIV-ve children
  - Despite lower efficacy in the HIV-infected, who contributed to 75% of all the IPD in the study population (Soweto, Johannesburg) , vaccination was associated with an 18-fold reduction in absolute burden of IPD being prevented in HIV+ve compared with HIV-ve children
- Impact: Incorporation of PCV into EPI schedules of developing countries
  - August 2008: 26 introduced PCV into EPI
  - April 2009: PCV introduced into RSA EPI (first in Africa)
  - January 2010: total of 43 with PCV into EPI

GERMS-SA: Impact

- Extensive database relating to communicable diseases (in South Africa that informs public health decision-making
- Interesting work being done to e.g. measure impact of PCV introduction in 2009

Is this the impact of PCV-7?

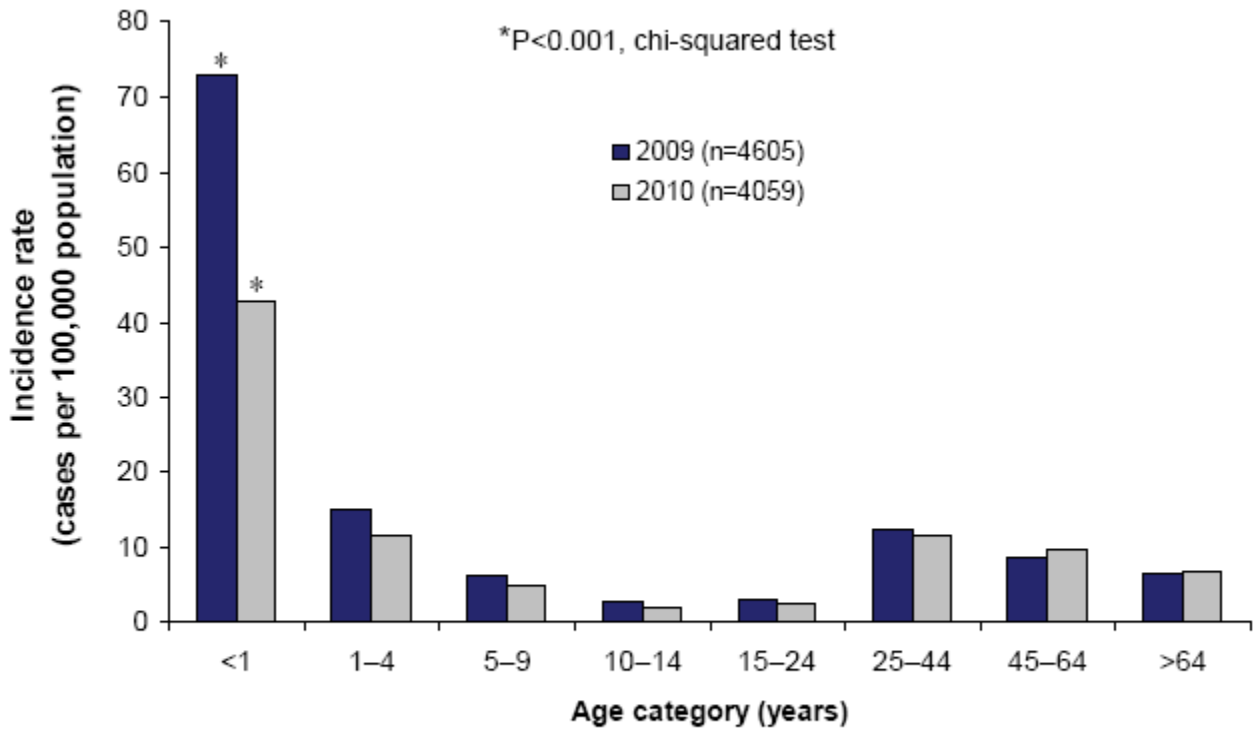
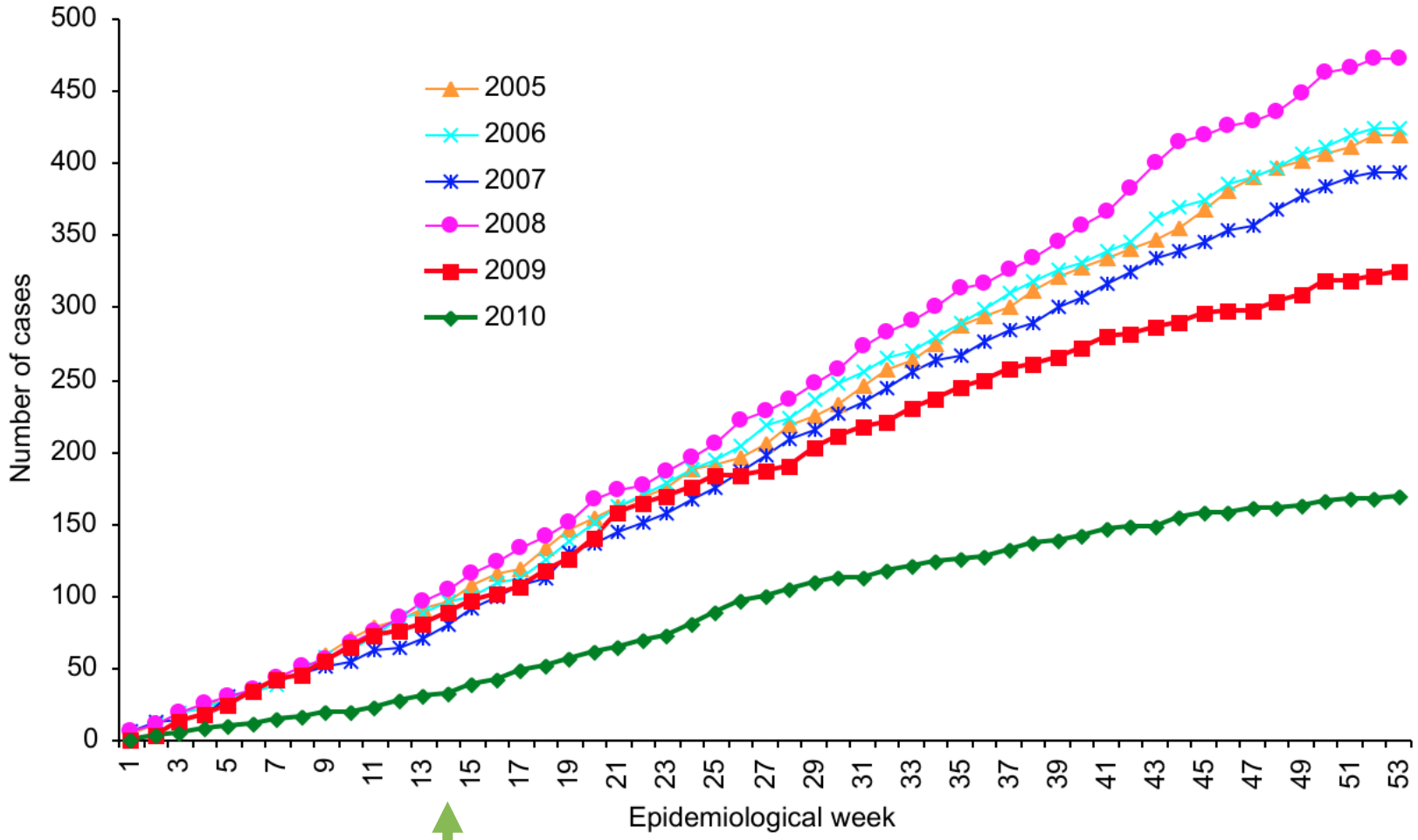


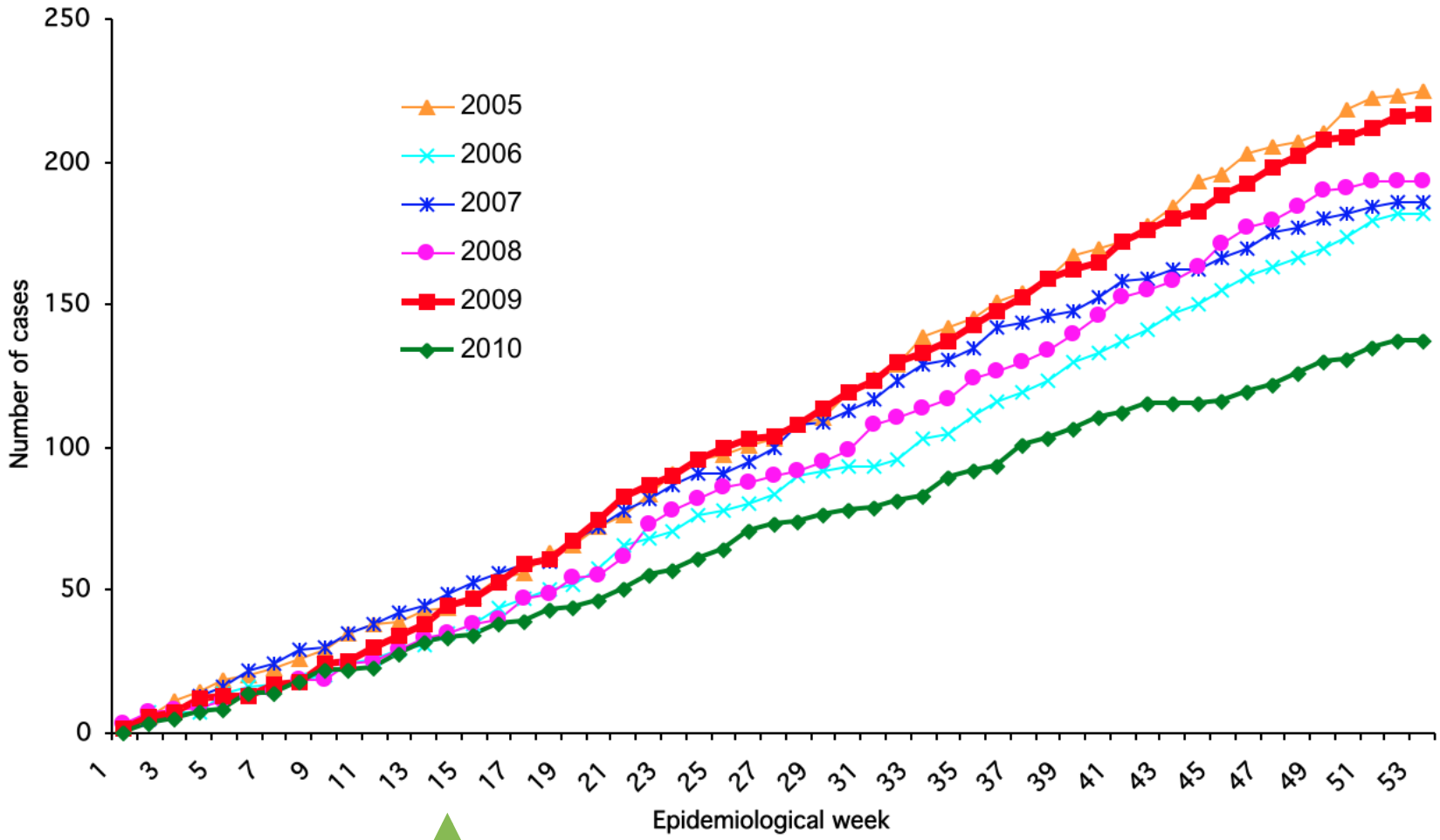
Figure 13: Age-specific incidence rates for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2009 and 2010 (2008: n=4769; age unknown for n=164; 2009: n=4206; age unknown for n=147).

Cumulative weekly numbers of cases of invasive pneumococcal disease due to any of the seven serotypes in PCV7 (plus serotype 6A): children <1 year, South Africa



Slide courtesy of Dr Anne von Gottberg – NICD

Cumulative weekly numbers of cases of invasive pneumococcal disease due to any of the serotypes NOT in PCV7: children <1 years, South Africa



Slide courtesy of Dr Anne von Gottberg – NICD

The STIRC Unit: NICD, NHLS

- Resource of knowledge and expertise in STI surveillance, research, training and teaching to South African, Southern African Development Community countries & the African continent
- Collaborating with WHO in establishing a gonococcal antimicrobial surveillance program (GASP) network across Africa

Protocol training - Zimbabwe

Laboratory training - Tanzania

Clinical training - Madagascar

Meeting to review Afro-GASP - Zimbabwe

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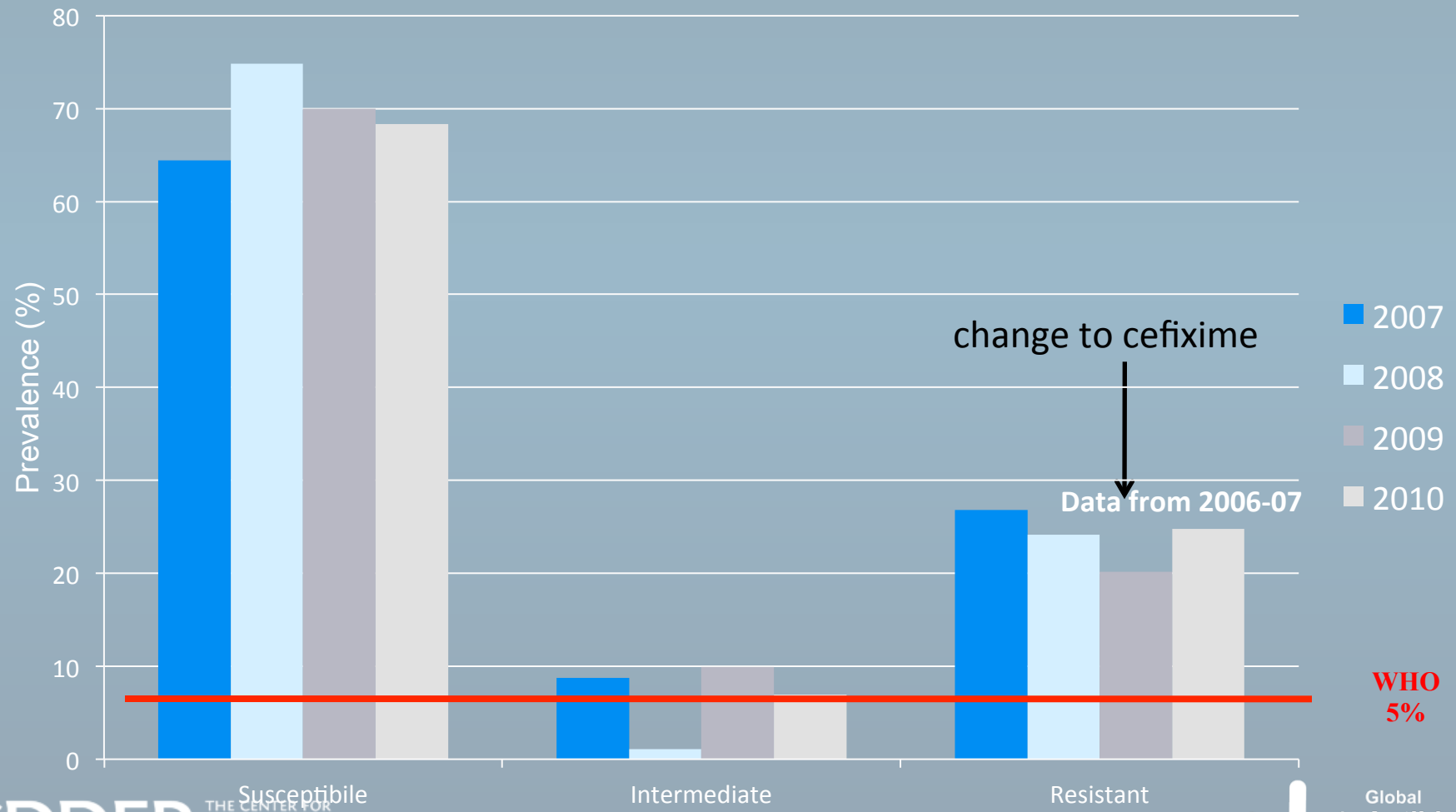
Ciprofloxacin Resistance in South Africa (2007-2010)



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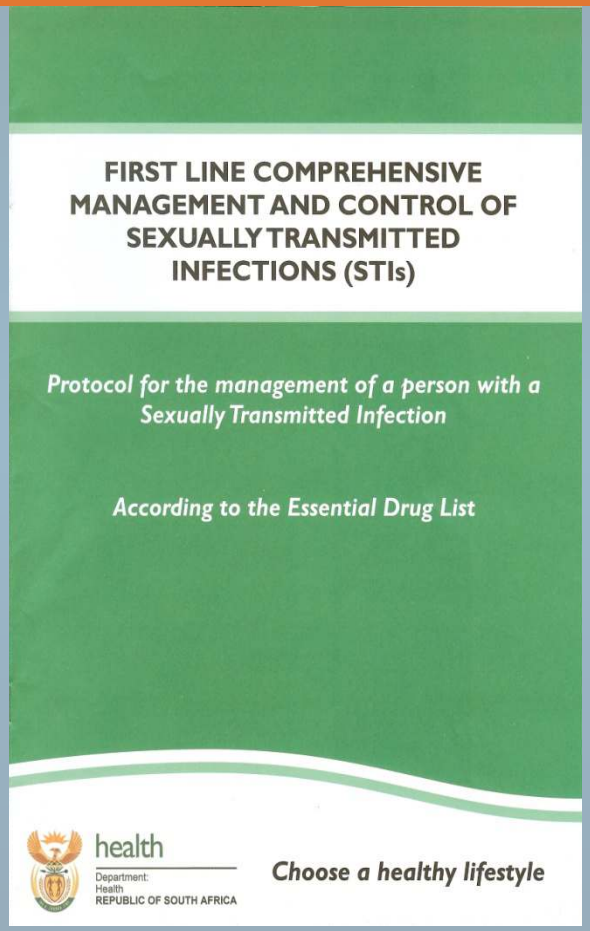
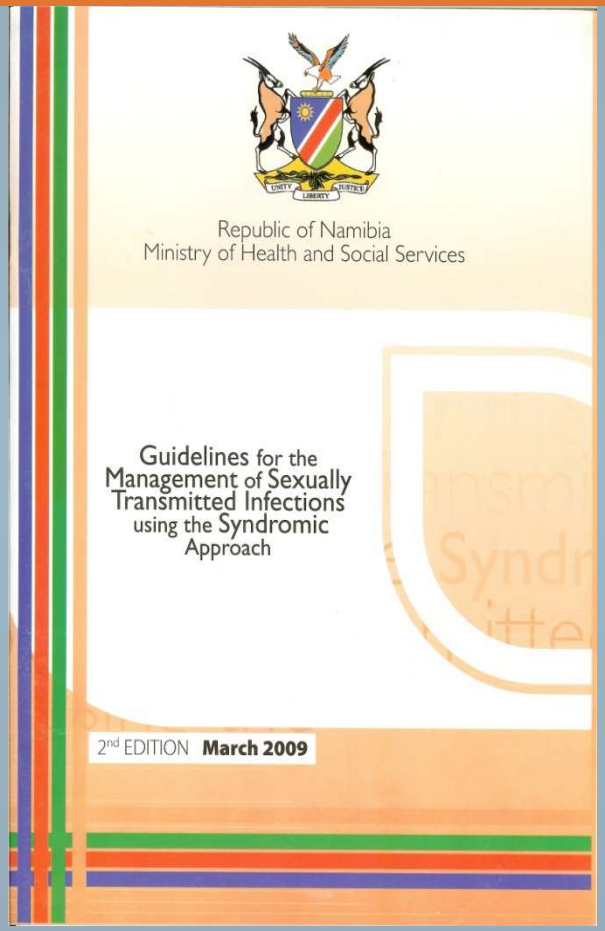
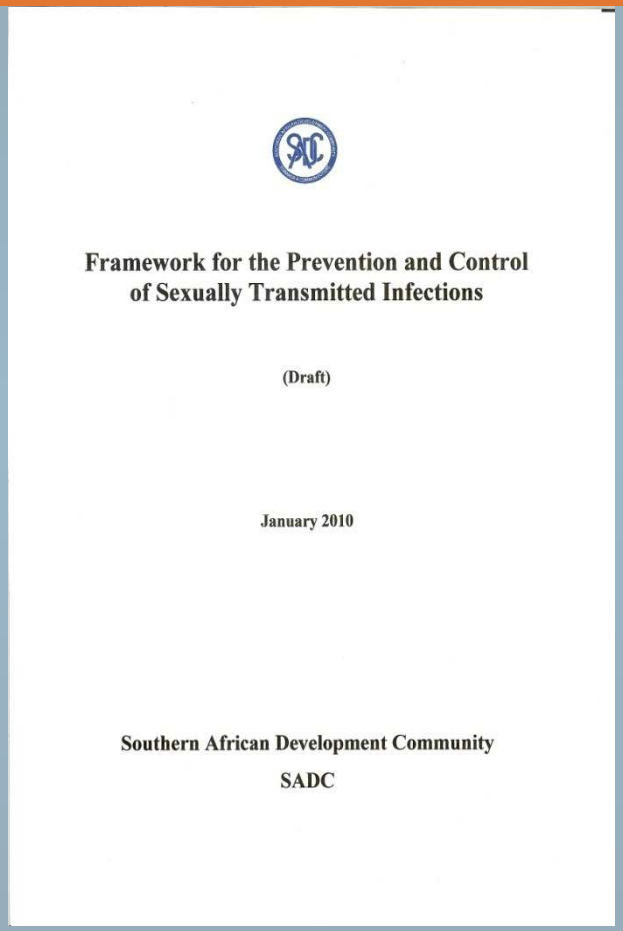
New Surveillance-Driven Guidelines



South Africa

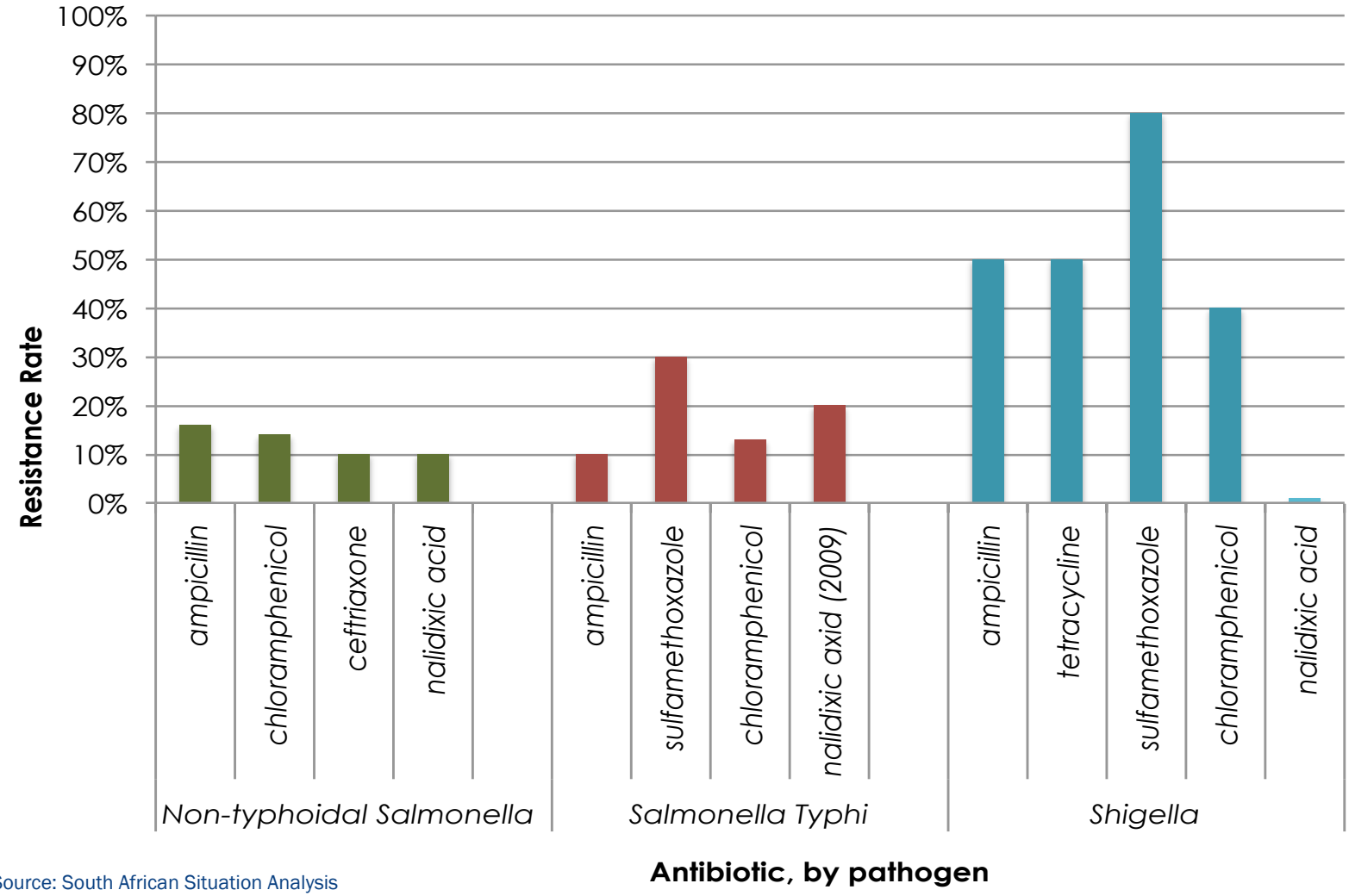


Namibia



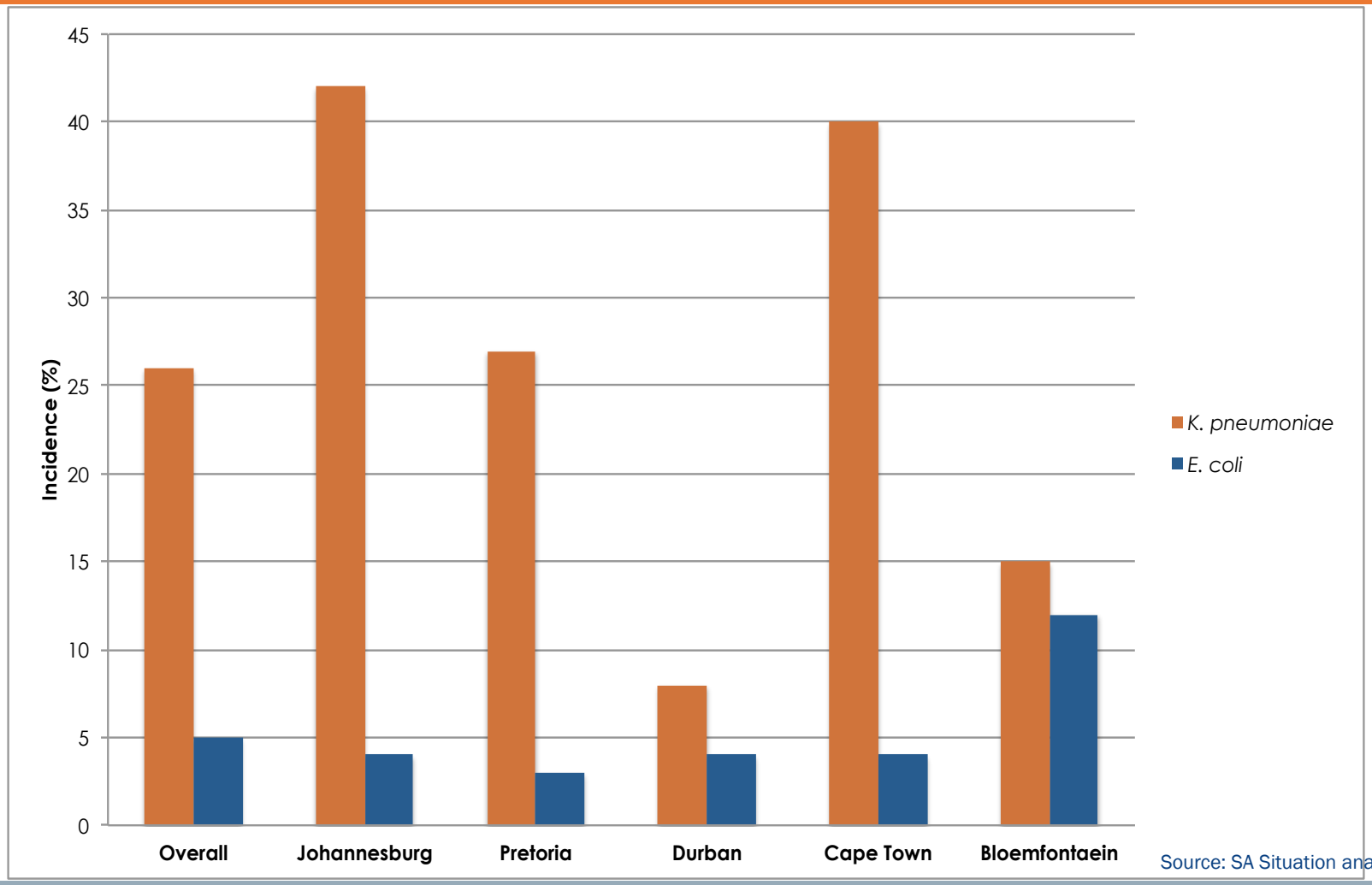
SADC Region

Resistance in pathogens responsible for common diarrhoeal infections in the community (2010)



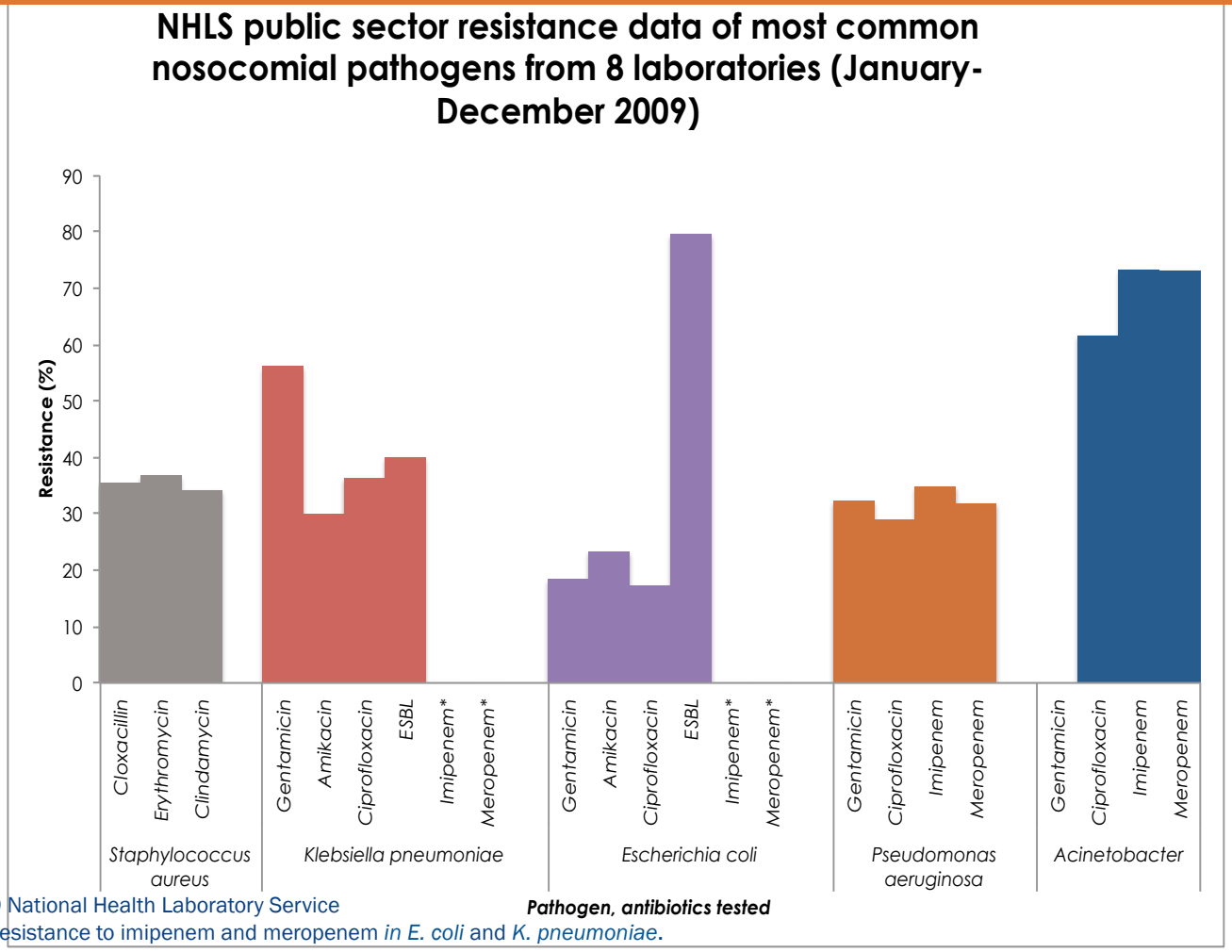
Source: South African Situation Analysis

Incidence (%) ESBL production (number of isolates) in *K. pneumoniae* and *E. coli* in private practice in South Africa, (January - June 2006)



Source: SA Situation analysis

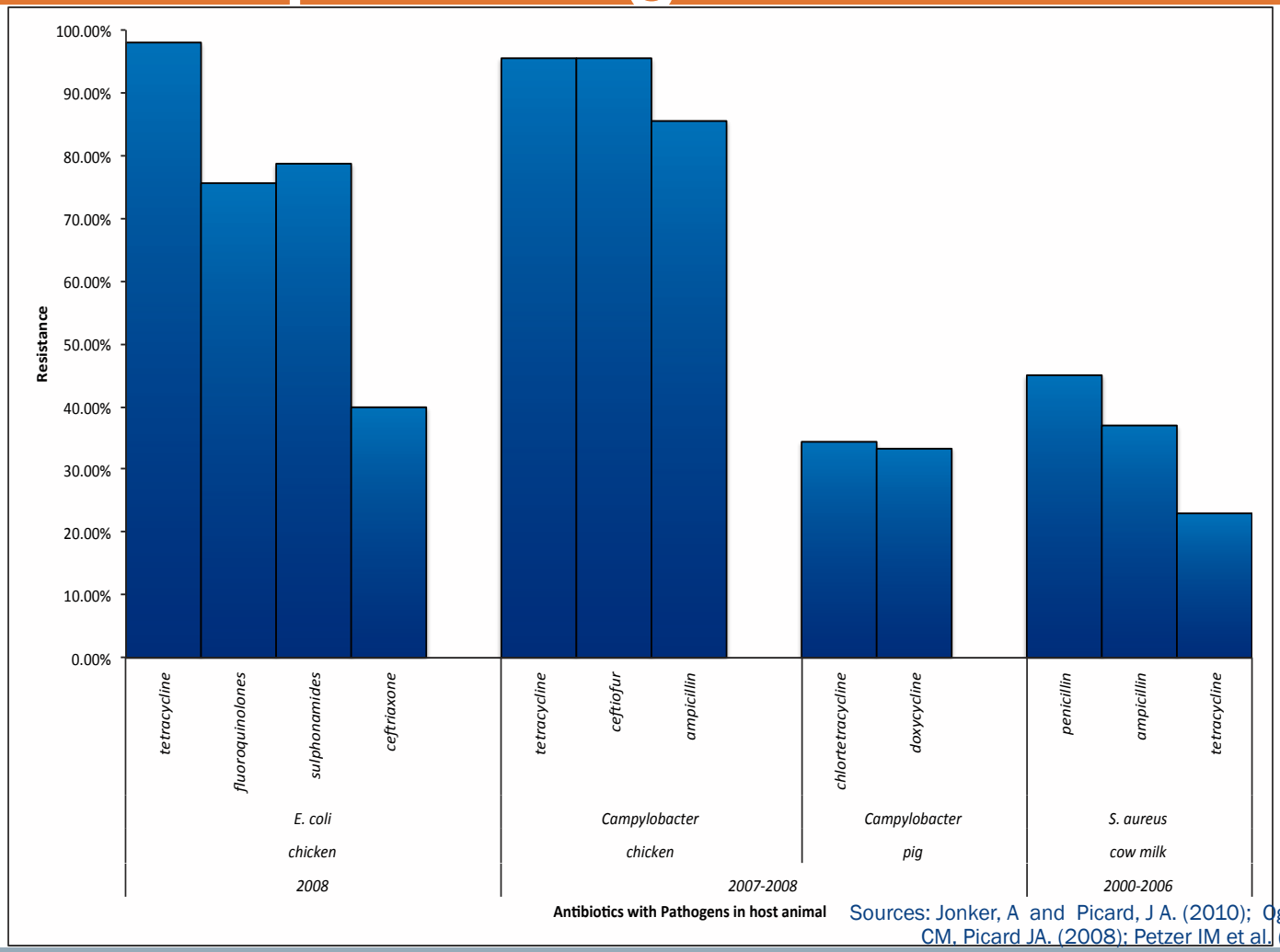
There is a high rate of resistance observed in the most common nosocomial pathogens



Source: 2009 National Health Laboratory Service

Notes: * 0% resistance to imipenem and meropenem *in E. coli* and *K. pneumoniae*.

Antibiotic resistance in food producing animals



Sources: Jonker, A and Picard, J A. (2010); Oguttu JW, Veary CM, Picard JA. (2008); Petzer IM et al. (2007).

GERMS-SA, NICD/NHLS & collaborating partners:

- Active laboratory-based surveillance program for bacterial and fungal pathogens of public health importance
- Clinical isolates/specimens received from a nationwide network of laboratories (private & public sector)
- Enhanced surveillance at 16 sentinel sites
- 4 areas of interest: vaccine-preventable diseases, epidemic-prone diseases, opportunistic infections in AIDS & nosocomial infections

Weaknesses /opportunities:

- What don't we know?
- What can we improve?
- Challenges / opportunities

1. Future Directions for GARP-SA Phase2:

- Filling the gaps – what don't we know?
  - Accurate quantification of antibiotic consumption in both public and private sectors
  - Analysis of appropriateness of antibiotic-prescribing patterns
  - Determination of the economic impact of antibiotic use and misuse
  - Knowledge of health impact & economic burden of ABR infections

2. Future Directions for GARP-SA Phase2:

- Filling the gaps – what can we improve?
  - Address weaknesses of current national private/public sector ABR surveillance networks
    - Additionally, perform site-specific enhanced surveillance
  - Alignment of the essential drug list & standard treatment guidelines with relevant ABR data
  - Foster ABR-related collaborative research between clinicians and veterinarians
  - Take the opportunity to enhance infection prevention and control (IPC) programs as IPC is among the top 5 priorities of the Minister of Health's agenda – more about this in IPC lecture

3. Challenges for GARP-SA:

- Paucity of available health economists
  - Solution: CDDEP/GARP collaboration
- Mining ABR data from the public sector
  - Solution: focus on private sector initially
- Expertise in disease modeling for antimicrobial resistance
  - Solution: CDDEP/GARP collaboration
- Ensuring that GARP-SA activities will impact on health policy
  - Solution: Identification of & engagement with a 'champion' for antibiotic stewardship at a high-level within the DoH & draw on CDDEP/GARP expertise in health policy