Reflections from GARP Phase 1
South Africa
Adriano G Duse, Chair: GARP RSA
<table>
<thead>
<tr>
<th>Indicator</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (2010)</td>
<td>49991470</td>
</tr>
<tr>
<td>Population growth rate (2009)</td>
<td>1.06%</td>
</tr>
<tr>
<td>Life expectancy (2009)</td>
<td>53y ♂, 55y ♀</td>
</tr>
<tr>
<td>Gross national income per capita (2009)</td>
<td>US$5.79</td>
</tr>
<tr>
<td>Child (&lt;5y) mortality rate (2009)</td>
<td>104/1 000</td>
</tr>
<tr>
<td>Maternal (15-49y) mortality rate (2007)</td>
<td>625/100 000</td>
</tr>
<tr>
<td>Population living in poverty (&lt;US$1 per day) (2006)</td>
<td>5%</td>
</tr>
<tr>
<td>Population with access to clean water (2009)</td>
<td>89%</td>
</tr>
<tr>
<td>Adult (15+) literacy rate (2007/8)</td>
<td>82.5%</td>
</tr>
</tbody>
</table>

World Bank, Country Brief; South Africa. September 2010
• 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:

- HIV/AIDS: 46%
- Neonatal: 29%
- Diarrhoea: 9%
- Pneumonia: 6%
- Others: 8%
- Injuries: 2%

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

Data from 2006-07 change to cefixime

WHO 5%

Prevalence (%)
New Surveillance-Driven Guidelines

South Africa

Namibia

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

- **Non-typhoidal Salmonella**
  - Ampicillin: 10%
  - Chloramphenicol: 10%
  - Ceftriaxone: 10%
  - Nalidixic acid: 10%

- **Salmonella Typhi**
  - Ampicillin: 30%
  - Chloramphenicol: 30%
  - Nalidixic acid: 30%

- **Shigella**
  - Ampicillin: 80%
  - Tetracycline: 80%
  - Sulfamethoxazole: 80%
  - Chloramphenicol: 80%
  - Nalidixic acid: 80%

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.

NHLS public sector resistance data of most common nosocomial pathogens from 8 laboratories (January-December 2009)

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

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