A SOUTH AFRICAN PERSPECTIVE ON THE ANTIMICROBIAL RESISTANCE CHALLENGE

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### SA Economic Development and Health Indicators

<table>
<thead>
<tr>
<th></th>
<th>South Africa</th>
<th>Sub-Saharan Africa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (2012), millions</td>
<td>52.3</td>
<td>911</td>
</tr>
<tr>
<td>Average annual population growth rate (2006-12), %</td>
<td>1.3</td>
<td>2.7</td>
</tr>
<tr>
<td>Life expectancy, at birth (2012), years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>61.3</td>
<td>56</td>
</tr>
<tr>
<td>Female</td>
<td>58.5</td>
<td></td>
</tr>
<tr>
<td>64.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gross national income per capita (2012), US$</td>
<td>7,460</td>
<td>1,350</td>
</tr>
<tr>
<td>Child (under 5 yr) mortality rate per 1,000 live births (2012)</td>
<td>41</td>
<td>-</td>
</tr>
<tr>
<td>Neonatal mortality rate1 (&lt;28 days) per 1,000 live births (2012)</td>
<td>12</td>
<td>-</td>
</tr>
<tr>
<td>Population living in poverty (&lt;US$1 per day) (2006), %</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>Population with access to clean water (2012), % of population</td>
<td>95</td>
<td>64</td>
</tr>
<tr>
<td>Adult (15+) literacy rate (2012), % of population</td>
<td>93</td>
<td>60</td>
</tr>
</tbody>
</table>
## SA’s burden of disease

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Deaths</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV/AIDS</td>
<td>180,870</td>
<td>29.4</td>
</tr>
<tr>
<td>Hypertensive heart disease</td>
<td>39,272</td>
<td>6.4</td>
</tr>
<tr>
<td>Lower respiratory infections</td>
<td>38,576</td>
<td>6.3</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>37,913</td>
<td>6.2</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>37,519</td>
<td>6.1</td>
</tr>
<tr>
<td>Diarrhoeal diseases</td>
<td>26,564</td>
<td>4.3</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>24,510</td>
<td>4.0</td>
</tr>
<tr>
<td>Interpersonal violence</td>
<td>20,155</td>
<td>3.3</td>
</tr>
<tr>
<td>Road injuries</td>
<td>18,166</td>
<td>3.0</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>13,667</td>
<td>2.2</td>
</tr>
<tr>
<td>COPD</td>
<td>11,458</td>
<td>1.9</td>
</tr>
<tr>
<td>Nephritis/nephrosis</td>
<td>9,130</td>
<td>1.5</td>
</tr>
<tr>
<td>Top 12 causes</td>
<td>457,800</td>
<td>74.3</td>
</tr>
<tr>
<td>Total</td>
<td>615,788</td>
<td>100.0</td>
</tr>
</tbody>
</table>

The quadruple burden of disease in South Africa: A cocktail of four colliding epidemics

- **Maternal, newborn & child health**
  - <1% of global burden
  - 2-3 times > average for comparable countries

- **HIV/AIDS and TB**
  - 17% of HIV burden
  - 23 times > global average
  - 5% of TB burden
  - 7 times > global average

- **Non-communicable diseases**
  - <1% of global burden
  - 2-3 times > average developing countries

- **Violence and injury**
  - 1.3% global burden of injuries
  - 2 times global average for injuries
  - 5 times global average for homicide

Source: Lancet Series
HIV

• South Africa has the highest number of infected individuals
• In 2012, it is estimated that 12.2% of population (~6.4 million) were HIV positive
• Increase of 1.2 million over 2008 (10.6% or 5.2 million)
• South Africa has also the largest antiretroviral (ART) programme with > 2 million patients.
• Approximately 75% individuals in need of ART received it.
HIV (2012 estimates)

Figure 1: Overall HIV prevalence by province, South Africa 2012

HIV (2012 estimates)

Figure II: HIV prevalence by sex and age, South Africa 2012

- **Males**
  - 0-14: 2.324
  - 15-19: 5.6
  - 20-24: 5.1
  - 25-29: 28.4
  - 30-34: 25.6
  - 35-39: 36.0
  - 40-44: 28.8
  - 45-49: 28.0
  - 50-54: 19.7
  - 55-59: 15.5
  - 60+: 5.5

- **Females**
  - 0-14: 0.7
  - 15-19: 5.1
  - 20-24: 17.4
  - 25-29: 17.3
  - 30-34: 28.4
  - 35-39: 31.6
  - 40-44: 15.8
  - 45-49: 13.4
  - 50-54: 15.7
  - 55-59: 9.7
  - 60+: 4.6
Figure III: HIV prevalence in females (a) and males (b) by age, South Africa 2008 and 2012

a

Females

Age group

HIV prevalence (%)

2008

2012

b

Males

Age group

HIV prevalence (%)

2008

2012
Elimination of HIV infection in infants?

- South Africa progresses to elimination of HIV infection in children!
- Prevention of mother to child transmission (PMTCT) prog. with antiretroviral (ART) had reduced the infection rate from 25% (2004) to less than 2% (2013).
ART roll-out leading to major gains in life expectancy

- Adult life expectancy (Years)
- Year

Public sector ART roll-out

- 60.6 years in 2011
- 52.4 years in 2003

Bor et al. Science 2013
ART impact on drug resistance

Increase on transmitted resistance:

• 0% (0/72) in 2010
• 5.4% (13/372) 2011
• 8.2% (5/61) 2012
• ART reduces incidence in adult and children, decrease mortality, increases life expectancy, employment rates and quality of life.

• However, attention should now shift to quality of care, sustaining treatment adherence and managing co-morbidities, in particular TB.

• The clinical management of drug resistance will be major challenges in the next decade as well the cost of universal and life-long ART programme.
TB

- **Worldwide:**
  - ~450,000 prevalent cases of MDR-TB in 2012

- **South Africa:**
  - 2012 - 14,419 MDR-TB cases (culture-confirmed)
  - 2011 - 10,085 cases

- Only 6,500 started on treatment in 2012

- ~10% were culture confirmed XDR-TB

NHLS communicable diseases survey bulletin; vol 9; August 2011
Suspending treatment and community care

These patients often reside in single roomed dwellings and informal housing often with children

Is discharging such patients into impoverished communities (often living in single roomed dwellings) justified?
What is the Cost of Diagnosis and Management of Drug Resistant Tuberculosis in South Africa?

Anil Pooran, Elize Pieterson, Malika Davids, Grant Theron, Keertan Dheda*

Lung Infection and Immunity Unit, Division of Pulmonology and UCT Lung Institute, Department of Medicine, University of Cape Town, Cape Town, South Africa
Antibiotic resistance in SA

- Factors that drive antibiotic resistance:
  - Inappropriate use (clinical indication, choice, administration and dosing)
  - The regulatory environment
  - Knowledge of health care workers (lack of continuous education)
  - Impoverished living conditions of patients – malnutrition, limited access to clean water and sanitation, HIV/TB epidemic
  - Insufficient supply of antibiotics to the public sector
  - Poor quality antimicrobials and use of degraded and expired medicines
  - Unreliable access to diagnostic facilities and clinicians
Antibiotic resistance in SA

- Respiratory and meningeal pathogens
  - *Streptococcus pneumoniae*
    - In 2004, 1/3 of pneumococcal isolates displayed multidrug resistance
    - Resistance levels have increased annually – dependent on the site of collection, age of patient and location within the country
  - *Haemophilus influenzae*
    - Resistance to penicillin is high with prevalence rates >45% reported in some settings

SAMJ, August 2011, Vol. 101, No. 8
Antibiotic resistance in SA

• Enteric pathogens
  – *Salmonella* Typhi
    • Resistance to ampicilin has fluctuated from 10% of isolates in 2003 to 40% in 2006
    • At end of 2010 the rate was back to 10%
  – *Shigella*
    • Resistance to older antibiotics has been constant from 2003 to 2010

SAMJ, August 2011, Vol. 101, No. 8
Antibiotic resistance in SA

- Sexually transmitted infections (STIs)
  - Resistance has been rising in several centres eg. Durban (24% in 2004, 42% in 2005), Cape Town (75 in 2004, 27% in 2007) and Johannesburg (11% in 2004, 32% in 2007)

SAMJ, August 2011, Vol. 101, No. 8
Antibiotic resistance in SA

• Hospital-acquired infections (HAIs)
  – Several groups collect data, they include:
    • SA Society Clinical Microbiology
    • Antimicrobial Resistance Reference Unit of the National Institute of Communicable Diseases
    • Division of Hospital Epidemiology and infection Control of the National Health Laboratory Service
    • Private sector AMR data collaborators
  – In both public and private sector hospitals resistance rates among the most common Gram-negative bacteria are very high.
  – The extent of the problem of HAIs in all categories of SA health care facilities remains to be determined.
Antibiotic resistance in SA

• Surveillance for antibiotic resistance
  – SA has the most active antibiotic surveillance of any country in Africa
  – In the public sector there are two main groups that are active ie. the Group for Enteric Respiratory and Meningeal disease Surveillance in SA (GERMS-SA) and the National Antibiotic Surveillance Forum (NASF)/SA Society for Clinical Microbiology (SASCM)
  – Private sector AMR data are generated through a collaborative effort involving private pathology laboratories that use a common lab system, Meditech. It enables all participants to use a standarised and reproducible means of data extraction for generation of AMR reports
The regulatory environment and drug supply

- SA National Drug Policy – “adequate and reliable supply of safe, cost-effective drugs of acceptable quality to all citizens of SA and the rational use of drugs by prescribers, dispensers and consumers”
- Medicines Control Council (MCC)
- Essential drugs list (EDL) and standard treatment guidelines (STGs) address use of antibiotics in the public sector
- Prevalence of resistance not considered in EDL and STG
- Antibiotics only available on prescription
Addressing antibiotic resistance

• Surveillance – monitoring the extent of the problem and trends
  – Inform key policy makers and opinion leaders

• Vaccination strategies – reduce burden of infectious diseases in susceptible populations
  – SA Expanded Programme on Immunization

• Infection prevention and control (IPC) – aimed at containing AMR, thus preventing spread of resistance
  – Listed as top 4 priorities by DoH
  – Overcrowding and understaffing of health care facilities fuel HAI outbreaks
  – Courses being offered
  – More research required on extent and cost of HAIs.
Specific challenges

• Determine the true economic impact of antibiotic use and misuse and AMR on the population – requires global collaboration on methods and local data

• Conduct a careful analysis of the appropriateness of antibiotic prescribing patterns in various health care delivery settings

• Calculate the costs and benefits of vaccination vs antibiotics for infectious disease prevention

• Strengthen the current AMR surveillance systems and fix identified weaknesses

• Pay greater attention to hospital-acquired infections, firstly determining the national prevalence and secondly, tracking the incidence of these infections

• Updates of STG and EDL with relevant AMR data
AMR research and funding

• Several research groups are active – many collaborating with national and international partners

• Most studies supported by the National Health Laboratory Service (NHLS), in particular, the National Institute of Communicable Diseases (NICD)

• The SAMRC is providing funding through its Self-initiated Research granting mechanism, intramural and extramural research programmes

• Other national funders include: Dept of Science and Technology (DST)/National Research Foundation (NRF) – Research Chair initiative
AMR research and funding

International funders include:

- EU Delegation to South Africa (SANTE 2007) - €3.45 m over 5 years
- EU : FP7
- EDCTP (European and Developing Countries Clinical Trial Partnership)
- Wellcome Trust
- Global Alliance for TB Drug Development
- UK MRC
- CDC (Centers for Disease Control and Prevention)
- NIH (National Institutes of Health)
- WHO
- USAID’s Antimicrobial Resistance Initiative
- Netherlands Ministry of Foreign Affairs
- Gates Malaria Partnership
- Pharma
How much funding for AMR research in SA?

- ??
- Estimates R100m (€7m) – R200 (€14m)
Conclusion

• AMR is an important public health concern in SA. It is also a global concern.

• SA has world-class scientists and research infrastructure

• Research findings will undoubtedly be of interest and relevance to other countries

• Favourable exchange rate – higher research productivity!

• Collaboration with the Global Antibiotic Resistance Partnership (GARP).
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