

## Part VII: Interventions

*Principal authors:* A Visser, D P Moore, A Whitelaw, W Lowman, G Kantor

*Co-authors:* A Hoosen, S Madhi, A Brink, D van den Bergh, L Devenish, P Moodley, T Apalata, A G Duse, H Gelband

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Antimicrobial resistance (AMR) surveillance activities in South Africa have been described in Part V of this report. Surveillance – knowing the levels of resistance and the trends around the country and in different types of institutions – is essential, but is only useful to the extent that the data influence practice. That link is not made automatically, nor is it always easy. Choices must be made among the available interventions based on what will work best in a given situation, and taking into consideration feasibility, cost, likely impact, acceptability to patients and providers, political will, etc.

Clearly, surveillance and recent studies can inform revisions of the essential drugs list (EDL) and standard treatment guidelines (STGs). What is more difficult but still possible is that these data can influence and change antibiotic prescribing practices and result in policy formulation geared to limit inappropriate antibiotic use and, consequently, AMR and its spread. However, so far the efficacy and clinical outcomes of both EDLs and STGs have, since their implementation, not been adequately evaluated.

Reducing the burden of infectious diseases also reduces the need for antibiotics but, primarily, prevents illness. Vaccination and infection prevention and control in hospitals and other health care facilities are the two critical interventions in this category.

In this section, the status and challenges of all these interventions in South Africa are reviewed.

### Prescribing practices and available treatment guidelines

When considering the problem of AMR and how to address the issue, it is important to look at it from two perspectives. Both laboratory and clinical practice play an important role and each will be addressed separately, although the two are not mutually exclusive.

From a laboratory perspective a critical deficiency in the South African setting is the adaptation of laboratory testing in the provision of relevant results. It is common practice in South Africa to adapt practice according to reports in the literature from abroad, without first assessing the situation locally. Unfortunately the state of AMR is not universally applicable and it is imperative that local data are made available, which may then either corroborate or refute the problems of resistance experienced elsewhere in the world.

A concerted effort to investigate the problem of resistance in nosocomial pathogens in a systematic and periodic manner is critical. Research funding needs to be invested in this endeavour, and the results of such investigations must be disseminated locally in such a way that will influence clinical practice.

Correct choice of antibiotic and adequate dosing is important in curbing the development of resistance, and the application of pharmacological principles, including pharmacokinetic and pharmacodynamic parameters, is critical in determining what the optimal drug and dose should be. Unfortunately, these criteria are seldom applied and the choice of antibiotic is often based on a laboratory report and familiarity with a particular agent. The reality is that the medical practitioner of today often does not have the time to read around the issues of antibiotic pharmacodynamics, and consequently inappropriate prescribing practices are common.

Specialist staff, including clinical microbiologists, clinical pharmacologists, hospital pharmacists and infectious disease sub-specialists, need to be part of a management team, especially for managing critically ill patients requiring antimicrobial therapy. Staff constraints are a serious hindrance to this approach, which will require not only the training of more specialists but also a change in mindset. The concept of a team approach and seeking of advice from others needs to be engendered, with broader consultation and acknowledgement of the consequences of inappropriate prescribing.

Great scope exists to improve overall antibiotic management in South Africa. The overuse of antibiotics extends to both the public and private sectors, and to all types of health care facilities (including physician offices). Not only are antibiotics prescribed for cases that do not require them (e.g. for viral illnesses, which do not respond to antibiotics), but also for prolonged duration, and two or more together inappropriately; there is a virtual absence of de-escalation. A recent nationwide survey in academic, public and private institutions (Prevalence of Infection in Intensive Care in South Africa study (PISA) – unpublished) revealed that all of these practices were rife.

What is needed is a formal, strategic programme of sustained reduction in consumption of all classes of antibiotics over the long term, and the strategies may be different in public and private hospitals because of differences in their organisation and governance. In this regard the results of the survey of antibiotic consumption practices in several private hospitals identified as pilot sites in the recently launched ‘Best Care ... Always!’ (BCA) campaign (<http://www.bestcare.co.za> – see below) are eagerly awaited.

In private institutions in South Africa, it appears that the antibiotic prescribing fraternity has not yet accepted stewardship of the emerging problem of multidrug and extensive drug-resistant Gram-negative bacilli (refer to Part IV of this report). Currently, doctors in private institutions can decide, without consulting guidelines or other policies, whichever antibiotic they wish to prescribe, at whatever dose and for how long. In this regard, clinical pharmacists have now been employed in some private institutions in Johannesburg. The aim, in conjunction with clinical microbiologists (or in future, infectious disease sub-specialists), is to actively intervene in cases of inappropriate antibiotic selection, dose and duration as an integral aspect of an ‘antibiotic care bundle’ as opposed to adoption of antibiotic restriction policies. Unfortunately, this is not policy everywhere and structures to enforce such changes are still being tested.

### Vaccination and its impact on infectious diseases – the South African experience

Vaccination has not only significantly reduced morbidity and mortality of a range of infectious diseases – its primary benefit and a great achievement – but the absolute reduction in infection rates secondary to widespread vaccination coverage also reduces the necessity for antimicrobial therapy. Less antibiotic use means slowing the spread of antibiotic-resistant bacteria. Vaccination is an integral part of reducing global trends in progressive AMR, and the consideration of whether to employ new vaccines should take this into account, as well as their primary benefits.

## Historical overview

Edward Jenner heralded the start of the vaccine era in 1792 through demonstration of protective immunity to smallpox by active immunisation. Less than 200 years later, smallpox was the first (and still singular) communicable disease to be declared eradicated by the World Health Organization (WHO).<sup>1</sup> Since then, the repertoire of vaccine-preventable diseases has increased considerably.

Six vaccine-preventable diseases (diphtheria, measles, pertussis, poliomyelitis, tetanus and tuberculosis (TB)) are significant contributors to infant and child mortality. Before 1974, fewer than 5% of children worldwide had access to these vaccines.<sup>2</sup> This led to the launch of the WHO's Expanded Programme on Immunization (EPI), in collaboration with various organisations including UNICEF, with the aim of supplying vaccines targeting these six diseases to every child by 1990. By 1990, approximately 80% of children were reached (i.e. had received at least the third dose of diphtheria-tetanus-pertussis (DTP3) vaccine), preventing an estimated 3 million deaths annually. By 2007, 82% of children were being vaccinated. In the USA, the Centers for Disease Control and Prevention (CDC) reported in 1999 that cases of nine vaccine-preventable diseases had been reduced by at least 95% (Table I).<sup>3</sup> Vaccines work. Despite this demonstration of success (repeated in Europe and in a few other countries), vaccination rates vary significantly around the world. For example, DTP3 coverage rates for industrialised countries are estimated at 96%, but in sub-Saharan Africa and South Asia, rates are much lower.<sup>4</sup>

In 2000, the Global Alliance for Vaccines and Immunization (GAVI) was formed to facilitate a broader availability and administration of vaccines in developing countries.<sup>5</sup> South Africa is classified as a middle-income country and so does not qualify for financial support from GAVI and similar associations.<sup>6</sup> In addition to supplying low-income countries with vaccines, GAVI has assisted in accelerating the development and deployment of new (rotavirus, pneumococcal conjugate and human papillomavirus) vaccines and underused (hepatitis B and *Haemophilus influenzae* type B (Hib) vaccines).<sup>4</sup>

## South African Expanded Programme on Immunisation (EPI)

The EPI was initiated in South Africa in 1995, which included vaccines against the six major vaccine-preventable diseases mentioned above.<sup>7</sup> Hepatitis B vaccine was promptly included within the first year of EPI initiation, followed by Hib vaccine in 1999. Bacillus Calmette-Guérin (BCG) vaccination was converted from the percutaneous route of administration to intradermal in 2000. South Africa was declared free of polio in 2006, with the last case reported in 1989.

The South African EPI has greatly impacted on childhood morbidity and mortality, significantly reducing the incidence of a variety of childhood diseases (Table II).

The South African EPI was significantly restructured in 2009, with the addition of 7-valent pneumococcal conjugate vaccine (PCV-7), rotavirus vaccine (Rotarix) and the pentavalent combination vaccine Pentaxim (which includes acellular pertussis and parenteral poliomyelitis components).<sup>1</sup> Furthermore, a pneumococcal booster dose at 9 months and Hib booster dose at 18 months were introduced.<sup>1</sup> The new EPI aims to contribute to reaching the fourth Millennium Development Goal by reducing mortality among children under the age of 5 by 66% for the period 1990 - 2015.

## Production, distribution and cost

The worldwide demand for vaccines has been increasing exponentially, almost doubling in the past 5 years.<sup>9</sup> Manufacturers typically attempt to anticipate market demands 5 years in advance. Despite this, short-term needs remain unpredictable and are particularly problematic if manufacturing timelines are considered. Production is tightly governed in South Africa through the Medicines and Related Substance Act (Act 101 of 1965) and regulated by the Medicines Control Council as the statutory body.<sup>10</sup>

The South African governmental budget for vaccination in 2010 exceeded R1 billion.<sup>11</sup> Vaccines are procured from various multinational companies (Sanofi-Pasteur, Statens Serum Institute, Pfizer, GlaxoSmithKline, Herberbiovac and Novartis) under the auspices of the Biovac Institute, a private-public partnership situated in Cape Town. From this point, vaccines are either directly distributed by Biovac (Western Cape and areas of Gauteng) or to medical depots of the National Department of Health (NDoH). The Biovac Institute carries the contract for supply and distribution of vaccines in South Africa up to December 2016.<sup>11,12</sup>

**Table II. Impact of EPI vaccination on childhood diseases in South Africa, 1980 - 2006<sup>8</sup>**

	Cases reported to NDoH per year			
	1980	1990	2000	2006
Measles	19 193	10 624	1 459	86
Neonatal tetanus	166	58	11	6
Poliomyelitis	112	5	0	0
Diphtheria	57	34	2	1

NDoH = National Department of Health.

**Table I. Decrease in cases of vaccine-preventable disease in the USA through 1998 as reported by the US Centers for Disease Control and Prevention<sup>3</sup>**

Disease	Cases at baseline	Cases in 1998	Reduction (%)
Smallpox	48 164	0	100
Diphtheria	175 885	0	100
Pertussis	147 271	7 405	95
Tetanus	1 314	41	97.9
Paralytic polio	1 316	0	100
Measles	503 282	100	100
Mumps	152 209	666	99.6
Rubella	47 745	364	99.3
<i>Haemophilus influenzae</i> type b	20 000	63	99.7

The previous EPI vaccines were procured at a cost of approximately R 81.90 per child.<sup>8</sup> One of the major hurdles to introduction of new vaccines was the cost (remembering that South Africa is not a GAVI-supported country). Despite this, the new EPI was introduced and incorporated a range of new and underutilised vaccines. The revised 2009 EPI schedule costs R 1 338.00 per child in the public sector (based on government tender prices) and R 4 103.00 per child in the private sector, where the consumer pays in most cases through medical aid schemes.<sup>6</sup> Although this is a significant cost, vaccines in general are considered a highly cost-effective method of reduction of mortality, second only to supply of clean water.<sup>2</sup>

### Coverage and mass vaccination campaigns

According to Health Systems Trust Statistics, DTP3 vaccination coverage in South Africa for 2009 was estimated at 101.7% ranging from 78.5% in the Free State to 121.5% in Gauteng (Table III).<sup>13</sup> Rates in excess of 100% reflect vaccinations over and above routine administrations, typically as part of mass vaccination campaigns. Individuals therefore received more than the routine amount of vaccine administrations.

**Table III. Statistics from the Health Systems Trust depicting DTP3 and Fully Immunized Child (FIC) data for 2009**

	DTP3	FIC (<1 year)
Eastern Cape	87.8	90.7
Free State	78.5	86.6
Gauteng	121.5	115.4
KwaZulu-Natal	95.3	84.9
Limpopo	118.6	99.2
Mpumalanga	107.7	92.2
Northern Cape	111.7	92.3
North West Province	92.4	86.2
Western Cape	95.7	102.5
South Africa	101.7	95.5

Current data from the WHO paint a slightly less optimistic picture with countrywide DTP3 rates estimated at 91%, translating to just under 900 000 infants out of a population of 985 000 receiving full DTP3 coverage,<sup>11</sup> but these figures must be considered very encouraging.

In 2010, the South African government embarked on mass vaccination campaigns focusing on three major pathogens – measles, poliomyelitis and influenza. The measles campaign was launched in response to the recent outbreak, predominantly in the Gauteng area. The epidemiology of this outbreak showed an age distribution different to that typically seen. In the Tshwane area, adolescents were most severely affected, while Johannesburg seemed to have the majority of cases reported among infants younger than 1 year of age (4 220 infants within total of 12 499 total reported cases). Polio was targeted in view of cases of wild-type polio in Angola and Nigeria.<sup>14</sup> Despite current vaccination practices, South Africa has not yet reached coverage for measles or oral polio vaccine (OPV) exceeding 90%. Furthermore, pockets exist with significantly lower coverage and data obtained from certain areas are very unreliable.<sup>14</sup>

The influenza campaign was the first of its kind in South Africa. The main rationale for this intervention was the already significant disease burden associated with annual infections, as well as the H1N1

outbreak since 2009, which caused 93 confirmed deaths. Despite the obvious advantages to making trivalent influenza vaccine widely available, only 1.3 million doses could be procured for an estimated high-risk population group of 6.6 million persons.<sup>15</sup>

These mass immunisation programmes are generally conducted every 3 - 5 years as a supplement to routine EPI activities. The main aim remains to reduce the number of susceptible hosts from crossing the epidemic threshold, and thereby reducing the possibility of outbreaks occurring.<sup>14</sup> The reduction in antibiotic demand is a secondary, though important, benefit.

### Vaccines targeting bacterial disease

**Pertussis.** Despite the availability of an effective vaccine, 16 million cases of pertussis are still reported annually. The majority of these are found in developing countries, leading to almost 200 000 child deaths. The biggest impact on disease control has been through establishing vaccination campaigns. The so-called cocoon strategy was first proposed by the CDC in 2006 in an attempt to curb spread that was not covered with routine immunisation strategies. This involves giving a preschool booster dose and immunisation of adolescents,<sup>16</sup> coupled with vaccination of child minders, health care workers and contacts of newborns.<sup>17</sup> However, this practice is not currently advocated by the WHO.<sup>11</sup>

***Streptococcus pneumoniae.*** The pneumococcus is a major pathogen of childhood worldwide,<sup>1</sup> and has been estimated to cause infection in 349 per 100 000 children annually in South Africa.<sup>18,19</sup> It is well established that the incidence of invasive pneumococcal disease has declined significantly with the introduction and use of pneumococcal conjugate vaccine (PCV) in children. The protective effect of childhood vaccination has been proven to extend to adults, reflecting the effects of herd immunity.<sup>20,21</sup> Although vaccine efficacy seems to be lower among HIV-1-infected children, impact may still be sufficient to significantly reduce the incidence of invasive disease and thereby the need for antimicrobial therapy.<sup>22,23</sup>

**Tetanus.** Neonatal tetanus still caused a staggering 59 000 deaths worldwide in 2008, with the majority of cases reported from Africa and southern and eastern Asia. The biggest impact on this disease has been through maternal vaccination, as treatment once infection has been established is exceedingly difficult, with mortality often approaching 100%.<sup>4,24</sup>

***Haemophilus influenzae* type B.** South Africa was the first African country to introduce Hib vaccine into its national EPI in 1999.<sup>25,26</sup> Since its introduction, rates of invasive infection have declined significantly. The most recent 2009 EPI schedule includes an additional booster dose at 18 months<sup>1</sup> in an attempt to further reduce rates of breakthrough invasive disease occurring after infancy.

### Soweto as a setting for research into global infectious diseases priorities

Sociopolitical forces have played a major role in shaping the state of health and burden of disease in South Africa, and the township of Soweto is no exception to this rule. Soweto, a peri-urban township near Johannesburg, was established in the 1930s as a consequence of policies that sought to segregate the population on the basis of race. The population of Soweto is currently estimated to be 1.3 million predominantly black South Africans (although some estimates propose a figure of 3.5 million).<sup>27,28</sup> The far-reaching consequences of apartheid policy provided a platform for socio-economic instability that is still felt, despite South Africa's transition to democracy in April 1994; an estimated

28% of households earn less than R800 per month and 40% of household heads are unemployed.<sup>27</sup> Most Sowetans do not have access to private health care facilities, and an estimated 90% of children in Soweto use the local public health facilities.<sup>29</sup>

The under-5 mortality rate in South Africa was estimated to be 63 per 1 000 in 1995, and rose to 79 per 1 000 in 2005,<sup>30</sup> the increase being attributed to the HIV epidemic.<sup>31</sup> The strongly criticised inertia of the South African government to face the realities of the HIV/AIDS catastrophe until April 2004, when the national roll-out of antiretroviral therapy (ART) commenced, only served to increase the toll of HIV-related morbidity and mortality in this community.<sup>32</sup>

HIV prevalence among children admitted to Chris Hani Baragwanath Academic Hospital (CHBAH), the only secondary/tertiary public hospital serving Soweto, rose from 3% to 20% between 1992 and 1995,<sup>33</sup> with a 21% increase in in-hospital child mortality during the same period.<sup>34</sup> HIV prevalence among children admitted to the paediatric wards at CHBAH remained at 30% between 2000 and 2008.<sup>35-37</sup> It is now estimated that 54% of HIV-infected children in need of ART have access to this therapy in South Africa,<sup>38</sup> with 74% of Sowetan HIV-infected children in need of ART accessing appropriate care in the public health sector in the township.<sup>39</sup>

Because of the unique social and health care status and high HIV-1 prevalence in Soweto, CHBAH and Soweto serve as a pertinent, geographically defined area from which important research to evaluate the local burden of infectious diseases and possible strategies for infectious disease prevention has emanated over the past 15 years.

The Respiratory and Meningeal Pathogens Research Unit (RMPRU), formerly known as the Pneumococcal Diseases Research Unit, was established in 1995. The RMPRU, which was initially focused on researching pneumococcal disease, is now mandated to perform research aimed to evaluate: (i) antimicrobial resistance in respiratory pathogens; (ii) research and development of pneumococcal conjugate and common protein-antigen vaccines; (iii) the impact of the local HIV-1 epidemic on respiratory and invasive diseases, e.g. otitis media, sinusitis, pneumonia and meningitis; and (iv) respiratory viruses and their interaction with bacteria in respiratory infections.

Childhood pneumonia aetiology studies conducted in Soweto in the 1990s indicate that *Streptococcus pneumoniae* is the commonest bacterial cause of community-acquired pneumonia in HIV-infected and uninfected children under 5 years of age in Soweto.<sup>40</sup> Similarly, *S. pneumoniae* was observed to be the most important aetiological agent in HIV-infected children admitted to CHBAH with bacterial meningitis.<sup>41</sup>

In 1998, RMPRU embarked upon a pivotal double-blind placebo-controlled study of 9-valent pneumococcal conjugate vaccine (PCV) in Soweto, in which 39 000 infants were enrolled with the aim of describing the efficacy of the vaccine in a setting with high HIV prevalence. This study demonstrated a highly significant 85% reduction in invasive disease caused by vaccine-serotype pneumococcal strains, and for the first time demonstrated the safety and efficacy of PCV in HIV-infected children.<sup>29</sup> The findings of the Soweto PCV study, and a similar study conducted in The Gambia in 2000 to 2003,<sup>42</sup> provided compelling evidence for the incorporation of PCV into the

EPI schedules of developing countries, despite initial concerns regarding the cost of the vaccine.<sup>43</sup> In August 2008, 26 countries offered PCV vaccination as part of their EPI<sup>44</sup> which increased to 43 countries by January 2010.<sup>45</sup> PCV was included in the South African EPI in April 2009.

Additional vaccine probe studies arising from the PCV trial have implicated the pneumococcus as being a significant co-pathogen in children presenting with radiographically confirmed pneumonia, viral pneumonia, and culture-confirmed TB at the study site.<sup>46-54</sup>

The CHBAH-based research unit has since focused more closely on other vaccine-preventable diseases, and now includes a vaccine-preventable diseases research dimension. Madhi and colleagues have published widely on the differences in vaccine response between HIV-infected and uninfected children to PCV,<sup>29,53,55-60</sup> Hib conjugate vaccine,<sup>61-64</sup> rotavirus vaccine,<sup>65,66</sup> parainfluenza virus type 3 live-attenuated vaccine,<sup>67</sup> and novel vaccine preparations<sup>68</sup> through studies conducted at the site. Vaccination strategies in adults have also been explored in studies conducted by the unit, and efficacy and safety data of trivalent inactivated influenza vaccination in HIV-infected adults has recently been described.<sup>69</sup> Influenza vaccination studies in pregnant women are in progress, and plans are under way to conduct an *S. agalactiae* vaccination study in pregnant women attending antenatal clinics in Soweto.

Prevention strategies other than vaccination have also been explored in studies conducted by the RMPRU. The use of chlorhexidine vaginal wipes to prevent early-onset neonatal sepsis in infants born to mothers giving birth at CHBAH was recently explored by Cutland and colleagues,<sup>70</sup> who demonstrate that chlorhexidine has no advantage over water wipes of the external external genitalia before delivery. A further prevention strategy, that of providing primary isoniazid preventive therapy (IPT) to HIV-1 infected children with access to ART in order to prevent them from developing active TB, was evaluated as part of a multicentre study; the results of this trial failed to demonstrate an advantage of IPT over placebo in protecting against the primary outcome of TB disease-free survival in the intervention group.<sup>71</sup>

A significant future direction for research planned by the unit includes involvement in a multinational case-control study to determine the aetiology of childhood pneumonia in the era of HIV-1 infection, access to ART, urbanisation, and current vaccination policy.

Soweto is beset by overwhelming challenges, including the high burden of disease. A wealth of research activity aimed at delineating the major infectious diseases affecting children has been conducted in this setting. This research has impacted positively not only the individuals residing there, but has had a major impact on the health status of children and adults in South Africa, Africa and the developing world.

### Summary: Vaccination as a means of limiting AMR

Vaccination has not only significantly reduced morbidity and mortality of a range of infectious diseases, but the absolute reduction in infection rates also reduces the necessity for antimicrobial therapy. Its role in reducing global trends in progressive AMR should be recognised formally, as a secondary but important benefit.



## The current status of infection prevention and control in South Africa

Infection prevention and control (IPC) is a neglected field of medicine in South Africa that is now gaining new prominence. This area has been identified by the national Minister of Health, Dr Aaron Motsoaledi, as one of the priorities in health care in South Africa. The country faces increasing demands on its health care services, driven at least in part by the HIV-1 and TB epidemics. Antibiotic resistance is a major concern,<sup>72,73</sup> and with the lack of new antimicrobials on the market, IPC becomes even more important as a strategy to combat the threat and expense of antibiotic-resistant organisms.

Infection prevention relates to practice targeted at decreasing health care-associated infections while infection control refers to the management of nosocomial outbreaks. This document outlines the currently available resources for IPC and highlights current activities in the field. Areas of emphasis are:

- staffing
- policies
- training
- additional resources
- current problems
- potential solutions.

There is a dearth of information in the public domain regarding many of the above, and much of the information cited here has been sourced from personal contacts, as well as first- and second-hand experience. Where possible, original sources have been acknowledged.

South Africa has a public and private health care structure. Public health care serves approximately 85% of the population, so much of this document deals with infection prevention and control in the public sector. However, the private sector faces similar challenges; where possible, information from the private sector is included.

### Numbers of IPC practitioners

According to draft legislation,<sup>74</sup> the currently recommended staffing levels for IPC practitioners (IPCPs) is 1 per 200 beds. There is some debate about the validity of this ratio,<sup>75</sup> as some feel that it should be revised to take into account the nature of the hospital and its bed allocation (the complexity of the cases admitted), with higher level hospitals possibly requiring more IPCPs. The NDoH recently completed a survey of IPCP numbers throughout the country (T Apalata – personal communication). Of the hospitals responding (Western Cape data were missing at the time of writing), 253 IPCPs were identified; no facility surveyed had the required number of trained IPCPs based on the recommended ratio. A survey in the Western Cape in 2005<sup>76</sup> found that in tertiary hospitals, the ratio of IPC nurses to acute beds was 1:400, while it ranged from 1:250 to 1:300 in smaller hospitals. No official figures were obtained from the private sector, but every hospital has a designated person tasked with the IPC function. In most hospitals, this person has a combined post, usually with occupational health and safety (OHS). While the IPCPs certainly add value to managing key OHS risks to staff, the additional functions detract from the time available for traditional IPC activities. In hospitals with more than 300 beds, there is a full-time equivalent (FTE) dedicated IPCP post. The IPCP manpower is further supplemented by the designation of an IPC link nurse in all units.

In the recent NDoH survey, 116 of the 253 IPC staff were not employed primarily as IPCPs at all and were performing their infection prevention function either 'on the side' or out of interest. There is a lack of a clearly defined career path for formally employed IPCPs, resulting in IPCPs moving to other areas of nursing (e.g.

theatre management), a situation that will probably continue unless this issue is addressed.

Even among staff employed formally as IPCPs, there is a common feeling in both the private and public sector that IPCPs are regularly assigned duties that intrude on the time available to perform IPC functions. These extra duties include acting as unit managers, OHS officers, practitioners and theatre scrub nurses. It is also worth bearing in mind that many international recommendations regarding the ratio of IPCPs to bed numbers assume the presence of an epidemiologist and/or microbiologist in the infection control team. In South Africa, many hospitals do not have microbiologists or epidemiological support on site, and the IPCP therefore has additional responsibilities (for which they are not specifically trained) related to infection control.

### Dedicated infection control units

There are three academic centres in South Africa with dedicated infection control units: Stellenbosch University, the University of the Witwatersrand and the University of KwaZulu-Natal (UKZN). These are involved in infection prevention activities as well as outbreak control. In addition, the University of Cape Town and National Health Laboratory Service (NHLS) have started a satellite National Institute for Communicable Diseases (NICD) epidemiology unit that will offer laboratory and clinical epidemiological services to assist with outbreak investigations in Cape Town (and potentially further afield). Whether the presence of these units provides sufficient resources for the entire country is difficult to assess; a detailed analysis of what resources are required, and what resources are offered by the units, is necessary.

### Training in infection control

There are currently three academic centres offering postgraduate training in infection control:

- University of the Witwatersrand (IPC certificate and postgraduate diploma)
- Stellenbosch University (IPC certificate and postgraduate diploma)
- UKZN (IPC certificate and BSc Hons degree).

In addition, a number of centres offer IPC certificates, including the Netcare, Life Healthcare and MediClinic private hospital groups and the University of Limpopo (previously known as Medunsa). At present these courses are not recognised by the South African Nursing Council for career development purposes, although efforts are being made to change this. The content of the courses is also not standardised nationally.

In many provinces formal training in IPC is not a prerequisite for appointment to the post of IPCP, either in the public or private sector. Of the 253 IPCPs identified by the NDoH survey, 149 (58.9%) had no formal training in infection control. Of those that did, 78 had a certificate in IPC, 14 an IPC diploma and 12 a BSc Hons in IPC.

In a survey conducted in the Western Cape<sup>76</sup> provision of infection control training to general staff was also poor, with only 10% of staff in hospitals with <200 beds having received any formal IPC training in the preceding 4 years. In hospitals with >400 beds, 40% of staff had received this training. These figures are consistent with those described in a national survey performed by the Human Sciences Research Council looking at HIV/AIDS in the workplace. They found that just over 35% of staff had received training in standard (universal) precautions.<sup>77</sup> Although many IPCPs may have no formal training in the field, it is likely that many have accumulated a number of years' worth of experience. It is unclear whether this experience would be sufficient to include a 'grandfather' clause should recognised formal IPC training become a prerequisite for appointment as an IPCP.

A compromise may be to offer experienced, but untrained, IPCPs priority and funded places in training programmes.

### Management and oversight

In the public sector, IPC falls under either the quality assurance directorate or directly under nursing management. In the private sector, IPCPs mostly report directly to nursing management. The reporting therefore varies from hospital to hospital, which causes confusion. There are plans within the NDoH to discuss these arrangements. Clearly, a standardised management and reporting structure implemented nationally would be ideal.

Each province should have a provincial infection control committee with the mandate to ensure adherence to national and provincial policies, review such policies, review surveillance data, evaluate infection control needs, etc. It is not known how well these committees are functioning.

Each hospital should have an infection control advisory committee. The audit performed by the NDoH showed that the membership of these committees consisted primarily of nursing staff, medical officers and pharmacists, followed by microbiologists and environmental health staff. An important point noted by this audit was the poor representation by hospital administration and management. Without adequate representation by hospital management on infection control committees, recommendations made by these committees are unlikely to be implemented.

At present there is draft legislation governing communicable diseases (which includes infection control).<sup>74</sup> There are also a number of national and provincial policies related to infection control, published by the NDoH as well as by various academic centres. These include policies related to prevention of nosocomial transmission of TB, prevention of health-care-acquired infections, requirement for infection control, an IPC manual (in press), guidelines for prevention of ventilator-associated pneumonia (VAP), guidelines for prevention of nosocomial infections, etc. On the face of it there is therefore adequate information available regarding IPC. The only concern is that there may be too many guidelines, sometimes giving conflicting messages. Standardisation of these guidelines is therefore required.

Many facilities in the public sector draft their own infection control policies, based on national and/or provincial guidelines. This is an appropriate approach in order to ensure that policies are relevant to each facility. However, it is not clear whether these policies adhere to the principles in the national guidelines, how often policies are updated or how accessible the policies are to staff in the facilities. To the best of our knowledge, there have been very few well-conducted surveys to evaluate these issues.

### Other IP resources/structures

#### Infection Control Society of Southern Africa (ICSSA)

ICSSA's mandate is to promote infection control throughout the country, mainly through the formation and support of local 'chapters'. However, sustaining these local chapters is proving difficult. At present, there are three established local infection control societies: Western Cape, Gauteng and Pretoria. The corresponding society in the Free State communicates with members electronically, but no longer holds meetings that individuals can attend. The KwaZulu-Natal chapter has undergone a setback since the IPCP tasked with re-forming the chapter moved to theatre management. This confirms the problem related to lack of career paths for IPCPs.

The local chapters function primarily by holding seminars and other educational activities and provide a forum for IPCPs to discuss policy and practice. More recently, members of the Western Cape

Infection Control Society have been represented in the Provincial Infection Control Committee of the Western Cape. The KwaZulu-Natal Provincial Committee has recently been placed under the IPC unit at the UKZN. To date, members of the Gauteng and Pretoria infection control societies have not been included in their provincial committees.

### Surveillance

There is no formal, standardised reporting scheme for nosocomial infections in the public sector in South Africa. Ongoing active surveillance cannot be managed, given the shortage of IPCPs in the majority of facilities. Point prevalence surveys have been conducted occasionally, but again, without these being performed regularly, it is difficult to measure trends or to use the data effectively.

Few surveys of IPC practices are available in the public domain. One conducted in the Western Cape<sup>76</sup> found a number of breaches of what would be considered standard practice. These included needles left in multidose vials in 10% of the wards surveyed, overfull sharps containers in 12% of the wards, and blood splatters around sharps containers in 20% of the wards. Encouragingly, 95% of the wards had provision for hand disinfection – however, the study did not examine compliance with hand hygiene.

A study conducted at Red Cross War Memorial Children's Hospital found hand hygiene compliance rates to be approximately 60%, and that hand hygiene compliance was better after patient contact than before.<sup>78</sup> A survey of disinfection of nasopharyngoscopes found that more than half of respondents did not follow published guidelines for disinfection of these instruments.<sup>79</sup> This again points to the disconnection between knowledge and practice. A survey of infection control in dental practices found that, despite adequate provision of knowledge, there was poor compliance with recommendations, particularly with respect to hand hygiene, use of eye protection, and cleaning and disinfection of dental equipment.<sup>80</sup>

Other evidence of shortfalls in infection control practice can be gleaned from the various reports of outbreaks of nosocomial infection from South Africa hospitals. However, this is a poor surrogate, as it provides a snapshot of practices when a problem occurs, which may not necessarily reflect what is being done routinely. However, it could be argued that if infection control processes were being followed properly and consistently, the outbreaks would have been less likely to occur.

A common breakdown in IPC that has been identified during outbreak investigations is that of contamination of parenterally administered fluids or solutions by multiple use of single-dose parenteral supplements.<sup>81-83</sup> The Western Cape has recently issued guidelines about the use of multidose vials, as has at least one of the private health care groups, but as with all policies or guidelines, the degree to which they are enforced is not clear.

Movement of patients and staff between hospitals has been implicated in transmission of resistant organisms in more than one study.<sup>84,85</sup> This practice, while certainly likely to contribute towards transmission of organisms, may be very difficult to prevent, as movement from one facility to another is often essential for effective clinical management of patients, but it does mean that resistance problems may be shared in the community, and thus provide a rationale for community action.

Overcrowding has been described in many published outbreak investigations,<sup>82,86</sup> as well as in a report on an outbreak of *Klebsiella* sepsis and necrotising enterocolitis at a Gauteng Hospital (2010). While it is not always possible to prove that overcrowding is the sole reason for an outbreak, it is hard to argue against the likelihood of overcrowding resulting in a breakdown in IPC practices.

Some strategies for optimising IPC in hospital settings are working. The BCA campaign, which links the public and private sectors and facilitates communication across the sectors, is thought to be having an impact.

### Best Care...Always! (BCA) as a model for optimising IPC practice

Health-care-associated infections (HAIs) are among the most common and serious adverse events in hospitals globally, occurring in about 1 in 10 admissions overall. A recent meta-analysis provides evidence that the problem of HAIs is much bigger in the hospitals of developing countries than in the industrialised world.<sup>87</sup> The prevalence of HAIs is 15.5 per 100 patients, at least double the overall rate in Europe, and the incidence of HAIs acquired in intensive care units (ICU) is 34.2 per 1 000 patient-days, triple the rate in the USA. Regardless of the setting, infections such as surgical site infections (SSIs), VAP, catheter-associated urinary tract infection (CAUTI), and central-line-associated bloodstream infection (CLABSI) cause considerable morbidity and mortality, waste precious resources and can clearly be reduced if not entirely eliminated. Prevention of HAIs therefore deserves high priority in all health systems.

Although HAI prevention targets are quantitative, the institutional culture in health care facilities is harder to quantify than are infection rates. However, improvement of safety is facilitated by improvement of the safety culture, which can be measured. A standardised safety culture survey can be used to assess the attitudes and beliefs of frontline teams about the environment in which we expect high performance but less often achieve it.<sup>88</sup> Another important element at the heart of improvement science is the use of carefully designed checklists, which can, as Atul Gawande, lead researcher in WHO's safer surgery programme puts it, 'get the dumb stuff out of the way'.<sup>89</sup> That safety can be dramatically enhanced by the appropriate use of checklists has been demonstrated in recent landmark surgical studies.<sup>90,91</sup> However, sustained effort over time is required, not to 'tick the boxes' but to make sure that the correct steps occur in key clinical processes, every time. Most hospitals that achieve success take 1 - 2 years to get to the desired level of performance.

For these reasons it was mandatory for South Africa to implement a campaign with urgency.

#### Aims of the BCA campaign in South Africa

Launched at the 3rd joint Federation of Infectious Diseases Societies of Southern Africa (FIDSSA) Congress in Sun City (20 - 23 August 2009), the BCA campaign is a uniquely collaborative effort among health care organisations, clinical teams and supporting stakeholders and organisations across South Africa including funders, vendors and professional societies, including FIDSSA. It advocates a non-punitive, 'just culture' approach and emphasises measurement (not only to establish a baseline but more importantly to monitor the effects of interventions), shared learning and continued iterative improvement through the implementation of a relatively small number of simple, evidence-based tasks aggregated in 'bundles' that should be performed every time on every eligible patient.

There are four BCA infection prevention interventions (CAUTI, CLABSI, SSI and VAP, mentioned above) that collectively represent the majority of HAIs for which local versions of

internationally developed care bundles have been endorsed by the BCA task force and expert panel. Measurement tools have also been developed, adopted or adapted. These tools do not require a sophisticated data infrastructure. Bundle implementation coupled with a programme to improve safety culture produces results. For example, in Michigan, USA, central-line infection rates have been driven to zero in many of the 100 or so ICU members of the Keystone initiative.<sup>92</sup> Importantly, low infection rates can be sustained through continued effort. Such programmes have a high return on investment, in both lives and money saved.

Another aim of BCA in the future is to introduce antibiotic stewardship programmes as an integrated component of the campaign. One goal is the development of an 'antibiotic use bundle' to reduce inappropriate antibiotic prescribing in an attempt to promote appropriate choice, dosing and duration of antibiotic therapy. The ultimate aim is to optimise microbiological and clinical outcomes while simultaneously minimising the development of antibiotic resistance.

The BCA approach does not dispense with individual accountability or with education, but recognises that education and the diligent effort of solitary individuals cannot by themselves effect sustained improvement in practice or outcomes. What is needed instead is to redesign clinical processes for greater reliability.

#### Progress with implementing the BCA campaign in South Africa

In the private sector, hospital groups that have implemented all or some of the BCA bundles include the Life Healthcare, Netcare, Medi-Clinic and National Hospital Network (NHN) groups of hospitals. In the public sector, 14 Gauteng hospitals, several in the Free State and 9 in the Western Cape have joined the campaign, making a total of 192 BCA-affiliated hospitals in South Africa. Over 600 active infection prevention interventions have been introduced in these hospitals as follows: VAP (74%,  $N=143$ ), SSIs (78%,  $N=150$ ), CLABSI (75%,  $N=144$ ), CAUTI (80%,  $N=154$ ). Furthermore, at least 7 hospitals in the private sector have launched antibiotic stewardship programmes involving clinical pharmacologists who, in conjunction with clinical microbiologists, prospectively audit antimicrobial use with intervention and feedback.

Within the BCA network, many of the early adoption hospitals have provided mentorship to those who started later. A website (<http://www.bestcare.org.za>) has been established as a vehicle for learning and obtaining implementation material, to share best practices and as a discussion forum for staff in participating hospitals. Monitoring and evaluation has obviously been a strong focus for the campaign, with almost all participating hospitals now measuring at least one intervention on an ongoing basis. There is an ongoing journey towards improvement involved in establishing reliable best practice. Participating hospitals are learning the science of monitoring and evaluation for improvement, which uses different statistical tools and concepts than traditional measurement for research.

Selecting and defining measures within the constraints of the public sector has been a critical focus of provincial government in South Africa. Successfully implementing measures for CLABSIs and VAP, based on 'incidence per 1 000 intervention days', has been a serious challenge because of the difficulty of collecting

device-day denominator data. Hence hospital teams in Gauteng have developed their own outcome measures for each of the bundles. One example is the measurement of days between CLABSIs in the neurosurgical ICU of the Steve Biko Academic Hospital in Pretoria (Fig. 1).

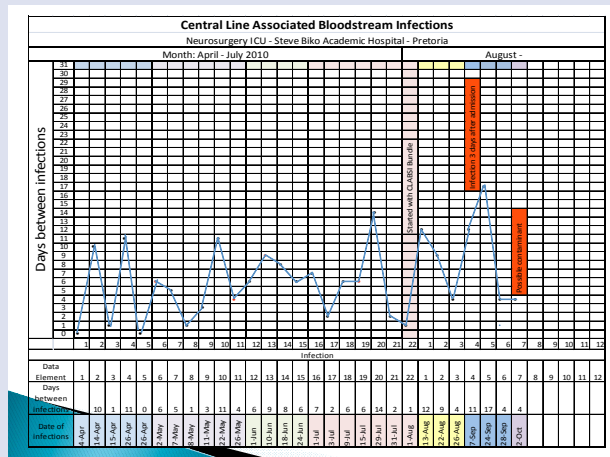


Fig. 1. CLABSI infection rates depicted as 'days between infections' (courtesy of EM de Bruin, Operational Manager, Neurosurgery ICU, Steve Biko Academic Hospital, Pretoria).

The aim is to develop a process that will ultimately result in viable measures for tracking the impact of the BCA bundles on the incidence of HAIs in public hospitals. Lessons learnt may also be applicable to the private sector, especially in making the data more accessible to front-line staff.

Many organisations worldwide have implemented strategies, campaigns and programmes in hospitals to improve patient safety and to support 'best practice; obtaining results is difficult. Knowledge and guidelines are widely disseminated but are at best inconsistently applied, and it often takes years before routine incorporation into practice and improved clinical results occur. For example, in developed countries patients receive 'recommended (evidence-based) care' only about half of the time.<sup>93</sup> During hospital admissions 10 - 17% of patients suffer an adverse event, and around half are considered preventable. The changes needed in organisational, team and individual clinical practice for real, sustained improvement are a challenge for all health care systems.

BCA is potentially a significant contributor to the development of widespread clinical systems improvement capacity in both private and public hospitals, and for a future health care system in which public and private care divisions may be less clear and the unifying focus is on quality of care.

**Summary: IPC as a means of limiting HAI**

It seems clear that infection prevention and control is not being practised adequately in South Africa. The key reasons for this are most probably a lack of IPCPs, as well as a lack of training among a significant number of IPCPs. Underlying reasons for the lack of training are probably multifactorial, including poor job descriptions, a lack of training opportunities (particularly in the past), no perceived need among management for such training, and lack of time to receive training. The solution to these problems sounds easy – employ more well-trained IPC staff. However, for this to happen prior training in IPC should ideally be a prerequisite for employment (taking

prior experience into account), and clearly thought out and well-communicated career paths should be implemented. Furthermore, employing extra IPC staff will require additional funding, and it is not known whether this is available. Creative approaches should be sought, and there may be a need to move away from the paradigm of dedicated IPCPs and involve more staff employed in other sectors in infection control responsibilities. Ideally, there needs to be a comprehensive review of the systems involved in infection control to inform new thinking on infection prevention systems, structures and roles, which is beyond the scope of this document.

There is a need for more data related to the incidence of nosocomial infections. Ideally, there should be a national strategy to collect data in a standardised, systematic fashion, and the means of doing this using current resources needs to be discussed. Given current staffing concerns, active surveillance is unlikely to be sustainable in the long term, and better use of existing infrastructure, such as the hospital and laboratory information technology systems, may be more realistic. Existing infection control units and societies should take the lead in this, and, in conjunction with the NDoH, as well as other interested organisations, discuss and make recommendations for surveillance that is cost-effective, reliable and of clinical value.

**Conclusion**

In this paper, we have sought to describe the barriers which exist to curtailing the problem of AMR in public and private health care facilities in South Africa. It is likely that, if current practices of indiscriminate antibiotic prescribing, suboptimal IPC practice, and reluctance to involve nursing and medical staff with higher degree training in infectious disease management in patient care are not dealt with in the next few years, patient outcomes may well be severely impacted upon. Promising primary preventive interventions that will assist in halting the spread of AMR organisms do exist, however. A concerted public/private partnership, with strong leadership by the NDoH, has the potential to have a lasting and positive impact on the issue of emerging AMR. The expertise base exists in South Africa, and needs to be broadened through up-training of nurses and doctors with special interest in the management of infectious diseases. The time to act is now.

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