

Promoting the Rational Use of Medicines through Pharmaceutical and Therapeutics Committees in South Africa: Results, Challenges, and Way Forward

SPS South Africa

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Strengthening Pharmaceutical Systems
Center for Pharmaceutical
Management
Management Sciences for Health
4301 N. Fairfax Drive, Suite 400
Arlington, VA 22203 USA
Phone: 703.524.6575
Fax: 703.524.7898
E-mail: sps@msh.org

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About SPS

The Strengthening Pharmaceutical Systems (SPS) Programme strives to build capacity within developing countries to effectively manage all aspects of pharmaceutical systems and services. SPS focuses on improving governance in the pharmaceutical sector, strengthening pharmaceutical management systems and financing mechanisms, containing antimicrobial resistance, and enhancing access to and appropriate use of medicines.

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ACRONYMS AND ABBREVIATIONS

ADR	adverse drug reaction
AMR	antimicrobial resistance
ARV	antiretroviral
BPharm	Bachelor of Pharmacy
CHC	community health centre
CRC	Clinical Resource Centre
DoH	Department of Health
EDL	essential drugs list
EML	essential medicines list
GPPTC	Gauteng Provincial PTC
MSH	Management Sciences for Health
MUE	medicine use evaluation
NCS	National Core Standards
NDoH	National Department of Health
NDP	National Drug Policy
NEMLC	National Essential Medicines List Committee
NMMU	Nelson Mandela Metropolitan University
PCC	Provincial Coding Committee
PharmD	Doctor of Pharmacy
PHC	primary health care
PQII	Pharmacy Quality Improvement Initiative
PTC	Pharmaceutical and Therapeutics Committee
RPM Plus	Rational Pharmaceutical Management Plus
SIAPS	Systems for Improved Access to Pharmaceuticals and Services
SPS	Strengthening Pharmaceutical Systems
SOP	Standard Operating Procedure
STG	standard treatment guideline
TORs	terms of reference
USAID	US Agency for International Development
WHO	World Health Organization

EXECUTIVE SUMMARY

The purpose of this report is to examine how South Africa uses Pharmaceutical and Therapeutics Committees (PTCs) to promote rational medicine use in the public health care system.

The experience gained during the Strengthening Pharmaceutical Systems (SPS) Programme is used to illustrate the role played by PTCs in ensuring quality of therapeutic care within the South African context.

Examples are chosen from all levels of the health care system: national, provincial, district, and institutional. The examples are presented according to the World Health Organization (WHO) framework showing the on-going process necessary for a sustainable promotion of rational medicine use.

The major findings are as follows—

- The majority of PTCs are active in establishing standards and conducting regular assessments but are quite weak in investigating reported problems and correcting them.
- The high variability in terms of the functions performed, functionality, and communication strategy and available skills from one PTC to another may be linked to non-standardisation of the terms of reference (TORs).
- The establishment of sub-committees enhances the number of PTC functions performed simultaneously.
- The development of operational plans promotes active and effective involvement of PTC members.
- The involvement of top management to initialise and support the establishment or revitalisation of PTCs is a key success factor.
- Few PTCs have an operational budget. This may limit the interventions and support visits to institutions.
- Only a few students from pharmacy school benefit from pre-service training on PTCs; no modules on PTCs are offered to medical students.

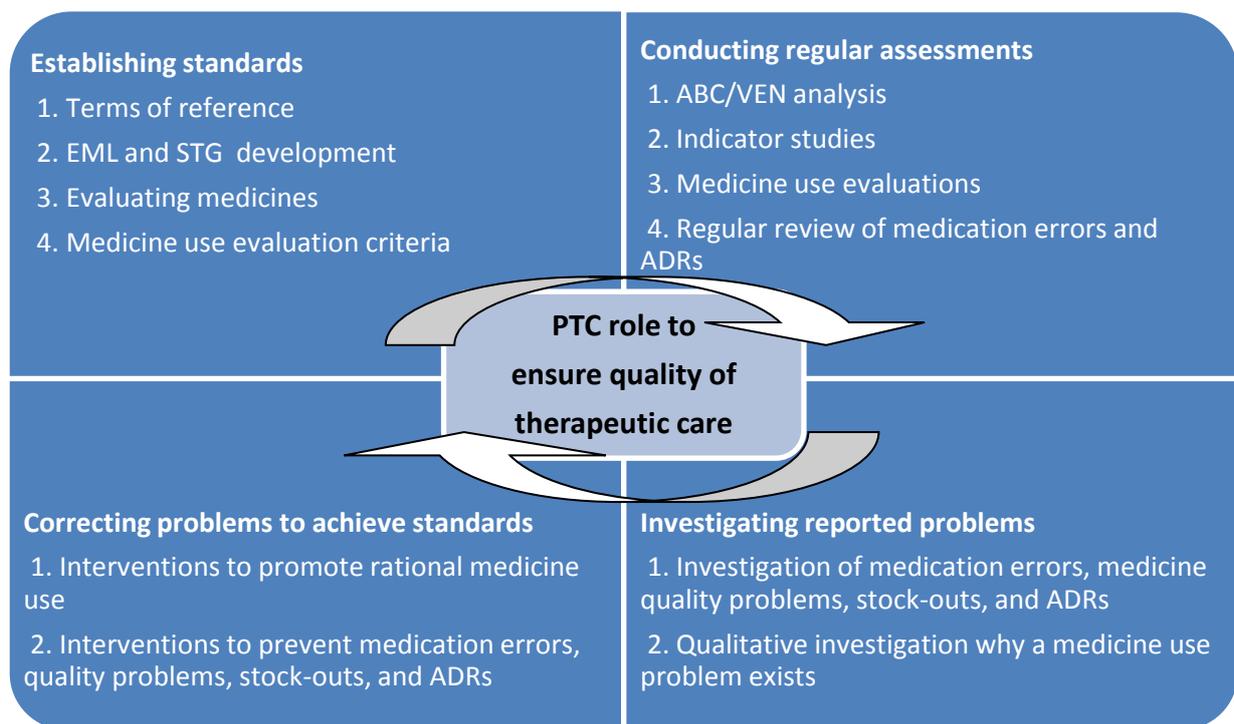
The principal recommendations are—

- Develop a national policy on PTCs to harmonise the functions of the PTCs through generic TORs per level and governance tools
- Make provision for the establishment of sub-committees using generic TORs
- Use generic TORs and governance tools in provincial Standard Operating Procedures (SOPs) for PTCs
- Design a capacity-building model for PTCs around a centre of excellence
- Include results from PTC activities in the performance appraisal criteria of top management

- Assign an operational budget for provincial PTCs from the overall provincial health budget and for district PTCs from the overall district health budget
- Develop a platform to share useful information generated by PTCs
- Advocate for inclusion of PTC and rational medicine use modules in pharmacy and medical school pre-service training

INTRODUCTION

The establishment of pharmaceutical and therapeutics committees (PTCs) has been advocated by the World Health Organization (WHO) as one of the 12 key interventions¹ to promote rational medicine use. PTCs are committees designated to ensure the safe and effective use of medicines in health facilities. Their functions include establishing standards, conducting regular assessments, investigating the problems reported, and correcting the identified problems to achieve the established standards. Key PTC responsibilities are outlined in figure 1, which illustrates the on-going process necessary for sustainable promotion of rational medicine use.



Adapted from Terry Green, John Chalker, Kathleen Holloway, and RPM Plus-WHO. Promoting Drug and Therapeutics committees in the Developing World, oral presentation at the 2nd International Conference on Use of Medicines, Chiang Mai, Thailand, March 2004.

Note: ADR = adverse drug reaction; EML = essential medicines list; STG = standard treatment guideline.

Figure 1: Responsibilities of a PTC

The 1985 Conference of Experts on the Rational Use of Drugs, convened by the WHO in Nairobi, defined rational medicine use as follows: “the rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own clinical requirements for an adequate period of time and at the lowest cost to them and their community.” Rational medicine use integrates two major principles: (a) the use of medicines according to scientific information on efficacy, safety, and adherence, and (b) the cost-effective use of medicines within the constraints of a health system. Unnecessary and irrational use of medicines is a serious problem affecting treatment costs and public health in

¹ WHO, Medicines, The Pursuit of Responsible Use of Medicines: Sharing and Learning from Country Experiences, http://www.who.int/medicines/areas/rational_use/en/ (accessed 17 July 2012).

many countries. In many countries, objective information on medicines is scarce. Moreover, health workers receive limited basic training or continuing education on medicines. Inappropriate use of medicines is widespread and can be found at various functional levels, such as prescribing, dispensing, administration, and patient use. Inappropriate use of medicines has far-reaching consequences both from a health system perspective with a waste of resources as well as from a public health perspective with an increase in anti-microbial resistance and poor patient outcomes caused by increased adverse drug reactions (ADRs). Figure 2 illustrates the consequences of inappropriate use of medicines.

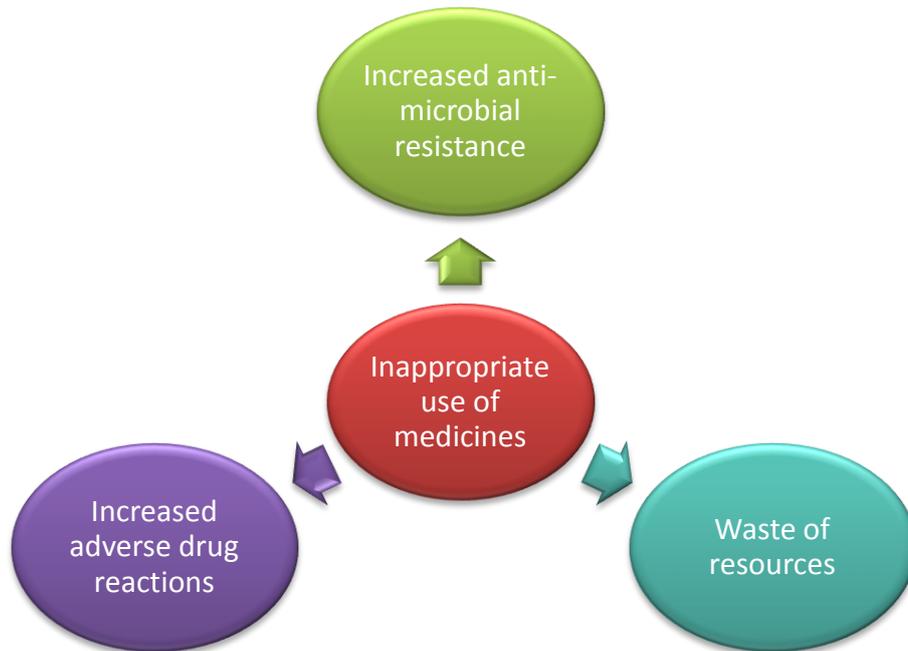


Figure 2: Consequences of inappropriate use of medicines

Although all countries are affected, the impact of inappropriate medicine use is greatest in developing countries because of financial, technical, and management challenges involved in responding to such a complex problem.

As multidisciplinary committees, PTCs have the expertise within themselves to target the various threats to rational medicine use. At the 60th World Health Assembly, the WHO reported progress in rational use of medicines and continued to advocate for the role of PTCs to improve the use of medicines in districts and hospitals.² PTCs have been shown to be effective in promoting rational medicine use in developing countries, even though the use of such committees has been minimal. Since 2001, the Strengthening Pharmaceutical Systems (SPS) Programme, funded by the US Agency for International Development (USAID), and its predecessor, the Rational Pharmaceutical Management (RPM) Plus Programme, have collaborated with the WHO, ministries of health, and other in-country organizations to conduct PTC training courses and supported the establishment and implementation of PTCs through the presence of country-level programmes in various countries including South

² Progress in the rational use of medicines. World Health Assembly Report A60/24, 22 March 2007. http://apps.who.int/gb/ebwha/pdf_files/WHA60/A60_24-en.pdf.

Africa.^{3,4} *MDS-3: Managing Access to Medicines and Other Health Technologies and Drug and Therapeutics Committees: A Practical Guide*^{5,6} are books freely accessible to health professionals that provide background information for an understanding of the role of PTCs in promoting the rational use of medicines.

³ Special achievements of DTC alumni, Management Sciences for Health Drug and Therapeutics Committee Learning Center. <http://erc.msh.org/mainpage.cfm?file=9.9.htm&module=dtc&language=English>.

⁴ Rational Pharmaceutical Management Plus. Drug and Therapeutic Committees and Training of Trainers, <http://www.msh.org/projects/rpmpplus/WhatWeDo/Antimicrobial-Resistance/DTC-Committees.cfm>.

⁵ Management Sciences for Health. 2012. *MDS-3: Managing Access to Medicines and Health Technologies*. Arlington, VA: Management Sciences for Health. <http://www.msh.org/resource-center/mds-3-digital-edition.cfm>.

⁶ Kathleen Holloway (ed.) and Terry Green 2003. *Drug and Therapeutics Committees: A Practical Guide*. Geneva: World Health Organization and Management Sciences for Health. <http://apps.who.int/medicinedocs/en/d/Js4882e/4.1.html>.

PURPOSE

The purpose of this report is twofold—

- First, to identify the determinants of effective promotion of rational use of medicines by PTCs through lessons learned during South Africa's SPS country programme support to the objective of the National Department of Health (NDoH) of promoting the rational use of medicines
- Second, to propose mechanisms for the replication of PTCs and expansion of their coverage and influence over rational medicine use

The report is organized in four sections plus annexes. First, it offers a brief overview about how rational medicine use is promoted in the country through the South African national policies and legislative context. The report then presents the support and interventions implemented at the three levels of government (national, provincial, and district or facility) as well as collaborations with institutions of higher learning. The next section is devoted to presentation of examples of particular interventions to enhance the role of PTCs in ensuring quality therapeutic care in South Africa. Last, a proposed way forward to strengthen PTCs and overall rational medicine use in the country at national, provincial, and facility levels is presented.

In May 2012, to identify potential case studies to illustrate the role and functions of PTCs, the SPS Programme met with pharmacists and doctors who had been trained and mentored on PTCs by SPS, in several provinces and hospitals across the country. The meetings yielded information on how these provinces or hospitals were able to establish or maintain functional PTCs as well as perform specific activities on rational medicine use.

THE SOUTH AFRICAN NATIONAL POLICY AND LEGISLATIVE CONTEXT

In South Africa, the provision of pharmaceutical services is guided by the National Drug Policy (NDP), which was adopted in 1996. The NDP requires hospital PTCs to be established and strengthened in “all hospitals in South Africa (both public and private sector) in order to ensure the rational, efficient and cost-effective supply and use of drugs.”⁷ A PTC is a multidisciplinary forum established to promote the safe, efficacious, and cost-effective use of medicines. Functional PTCs at provincial, district, and facility levels are a cornerstone of the South African NDP. At each of these levels, evidence-based selection of medicines for the development and maintenance of essential medicines lists (EMLs) or formularies, promotion of rational medicine use, and performance of medicine use evaluations (MUEs) fall within the responsibility of the PTC. The NDP further identifies appropriate training to prescribe and dispense medicines, the provision of information to professionals and the public, the establishment of hospital PTCs, enhancing the role of pharmacists, and the control of inappropriate marketing as the appropriate strategies to promote rational medicine use. However, a need still exists to strengthen the role of provincial PTCs. A major achievement of the 1996 South African NDP was the compilation of an essentials drugs list (EDL) with a set of standard treatment guidelines (STGs). The STGs were designed to address different levels of care, such as primary health care (PHC) and hospitals, as well as specialized populations of interest. The Paediatric Guidelines were visionary and have set an international example.

The most important pieces of legislation that give effect to the NDP are the Pharmacy Act (53 of 1974, as amended) and the Medicines and Related Substances Act (101 of 1965, as amended). The Good Pharmacy Practice Regulations published in terms of Section 35A of the Pharmacy Act, 1974, and which are legally binding, require pharmacists in institutional (hospital) pharmacies to be involved in all appropriate hospital committees, including the PTC (see 4.3.1 and 4.3.2 of the Good Pharmacy Practice Regulations). The rules also provide guidelines for the purpose and functioning of these committees.

Other legislation that affects the control of medicines in South Africa includes the National Health Act (61 of 2003), which is the overarching piece of legislation; the Health Professions Act (56 of 1974), which regulates medical practitioners, dentists, and other health care professionals; and the Nursing Act (33 of 2005), which gives some nurses the right to prescribe and dispense medicines.

In the South African context, PTCs have a crucial role to play in actively promoting the use of the EML, STGs, antibiotic supply chain management, prescribing, dispensing, infection control, and so on, as acknowledged by the Global Antibiotic Resistance Partnership in its inaugural report involving both global and national South African experts. This report further declared anti-microbial resistance (AMR) containment a priority in the national health agenda.⁸

In October 2010, the Minister of Health, Dr. P.A. Motsoaledi, stated that both public and private health sectors were engaging in very destructive, unsustainable, and expensive

⁷ National Department of Health. 1966. *National Drug Policy for South Africa*, section 7.5.

⁸ The Global Antibiotic Resistance Partnership. 2011. Situational Analysis: Antibiotic Use and Resistance in South Africa. *South African Medical Journal* 101(8):552.
<http://www.samj.org.za/index.php/samj/issue/view/116/showToc>.

curative health care systems.⁹ The government has since embarked on several initiatives aimed at strengthening the health systems and to monitor and improve the quality of service delivery at all levels. One of these initiatives is the implementation of the *National Core Standards for Health Establishments in South Africa*. The National Core Standards (NCS) provide a benchmark describing the quality of care that patients should receive when visiting a health care facility at any level of the health care system. Compliance with the standards, which are applicable in both the public and private sectors, will translate into improved health outcomes. The NCS are divided into the following seven domains—

1. Patient rights
2. Patient safety—clinical governance and care
3. Clinical support services
4. Public health
5. Leadership and corporate governance
6. Operational management
7. Facilities and infrastructure

Pharmaceutical services fall into domain 3. Within the NCS, the Minister of Health identified six priority areas for fast-track improvement: staff values and attitudes, waiting times, cleanliness, patient safety, infection prevention and control, and availability of medicines and supplies. The NDoH has further identified three fast-track priorities that relate to pharmaceutical services with the expectation that managers oversee compliance for these critical areas. They are—

- Patient safety and security
- Infection prevention and control
- Availability of basic medicines and supplies

Standard 3.1.4 of the NCS¹⁰ specifies that medicines must be prescribed according to treatment guidelines. Each hospital or community health centre (CHS) must have a functional PTC, or in the case of PHC clinics, one in the district, with the mandate of ensuring the quality use of medicines. The standards, criteria, and measures relating to PTCs in the NCS and Pharmacy Quality Improvement Initiative (PQII) are compiled in Annex A.

The NCS are part of the development of a regulatory framework that will ensure the quality of care provided in health care establishments. An external body, the Office of Standards Compliance, will undertake external audits to assess the level of compliance, issue certificates, and take appropriate measures to enforce compliance. Audit findings will be used to implement quality improvement initiatives.

Attention is also being given to the re-engineering of PHC services, which focuses on strengthening the district health system. The approach is based on the Brazilian model and places much greater emphasis on population-based health outcomes. The model includes the creation of specialist teams in each health district, the introduction of a school health programme, and ward-based PHC services with at least 10 community health workers

⁹ Report of National Consultation on Quality of Health Services, 6 October 2010. <http://www.sarrahsouthafrica.org/LinkClick.aspx?fileticket=Ua2TaEvof0s%3D&tabid=2327> (accessed 25 July 2011).

¹⁰ National Department of Health. 2011. *National Core Standards for Health Establishments in South Africa*, (Tshwane: Department of Health, Republic of South Africa), Domain 3: Clinical Support Services, page 26.

operating in each ward. The new approach to PHC will require new models for the supply of medicines and the delivery of pharmaceutical services that include ensuring rational medicine use.

The implementation of a National Health Insurance system is another mammoth task that the government is currently undertaking. Although the time frame for its implementation is still unclear, there is no doubt that it requires strong supporting health systems and that the provision of health care will not be “business as usual.”

SUMMARY OF THE SPS PROGRAMME'S SUPPORT TO IMPROVE RATIONAL MEDICINE USE IN SOUTH AFRICA

Since 2007, the SPS Programme in South Africa, in partnership with the national and provincial Departments of Health (DOHs), has provided support to promote rational medicine use by working at various levels, using simple intervention approaches, while strengthening the PTC role to ensure quality of therapeutic care. The proposed intervention approaches used¹¹ have proven to be effective in some settings to monitor medicine use. They include development and review of STGs, development of EMLs or formularies, implementation of PTCs, problem-based basic professional training, and targeted in-service training of health workers.

Selected case studies are presented in the next section to illustrate the support provided towards the promotion of rational medicine use in South Africa over the five-year duration of the SPS Programme.

National Level: Standard Treatment Guidelines and Essential Medicines List

In 2007 SPS, in consultation with the EDL Secretariat, conducted a strategic analysis of the preceding nine years of implementation. Of the various options that were identified, improved governance and consideration of the cost of medicines during selection were identified as key targets. In collaboration with the NDoH Affordable Medicines Directorate, SPS provided technical support in developing TORs, methodology for the review of the STGs, training of reviewers, and governance systems.

In 2009, at the request of the NDoH's Quality Assurance Directorate and Affordable Medicines Directorate, assessment tools were developed to assess the quality of pharmaceutical services. This project, called the Pharmacy Quality Improvement Initiative, formed part of an initiative by the NDoH to improve the quality of care in 1,000 facilities. One of the tools developed was used to assess the functionality of PTCs (see Annexes B and C). The forms were field-tested in all provinces and subsequently applied in some facilities. The focus of the NDoH then changed from concentrating only on selected facilities in the quest to improve the quality of care, to a broader approach with the introduction of a uniform set of standards for the quality of care provided in all health facilities in the country. In 2010, SPS was invited to be a member of the national reference group that was appointed to revise the NCS. These standards are aimed at setting the benchmark for quality of care against which the delivery of services is monitored. SPS participated in the work of the reference group, which worked on the design of the standards, criteria, measures, and checklists as well as the field-testing of the tools at health care facilities in Gauteng Province. The final documents were published in April 2011. The NDoH acknowledged SPS's contribution in the development of the NCS and the assessment tools.

Following a decision of the Heads of Pharmaceutical Services, the data elements included in the PQII tools were integrated into the NCS. An extended pharmacy audit was created, which allows more in-depth assessment of aspects of pharmaceutical services, including PTCs (see

¹¹ R. O. Laing, H. V. Hogerzeil, D. Ross-Degnan. 2001. Ten recommendations to improve use of medicines in developing countries. *Health Policy and Planning* 16(1):13–20.

Annexes A, B, C, and, D). The intention of this approach is to allow pharmacists to do a more in-depth assessment of the quality of pharmaceutical services. The pharmacy measures, including the PQII assessment, have been incorporated into the National Database and constitute a module of the District Health Information System.

Workshops to orientate pharmacy personnel on the NCS as well as to advocate their use were subsequently facilitated by SPS in all nine provinces, and follow-up technical assistance was provided. Work was subsequently done with the NDoH Affordable Medicines Directorate of on suggested amendments. A guidance document for application of the NCS tools was developed. The data elements in the tools were integrated into the routine monitoring of pharmaceutical services.

SPS provided considerable support in the development and implementation of the NCS. One of the results of this approach has been the institutionalization of the existence of functional PTCs at every facility because it is a requirement of the NCS.

Provincial, District, and Facility Levels: PTCs, In-Service Training of Health Workers

Technical support was provided for the establishment, revitalization, and maintenance of functional PTCs in the South African health care system. This was undertaken within the SPS approach to capacity building, using the capacity-building framework presented in figure 3, which takes a systems perspective in addressing a hierarchy of needs to be considered if investments are to pay sustainable dividends.

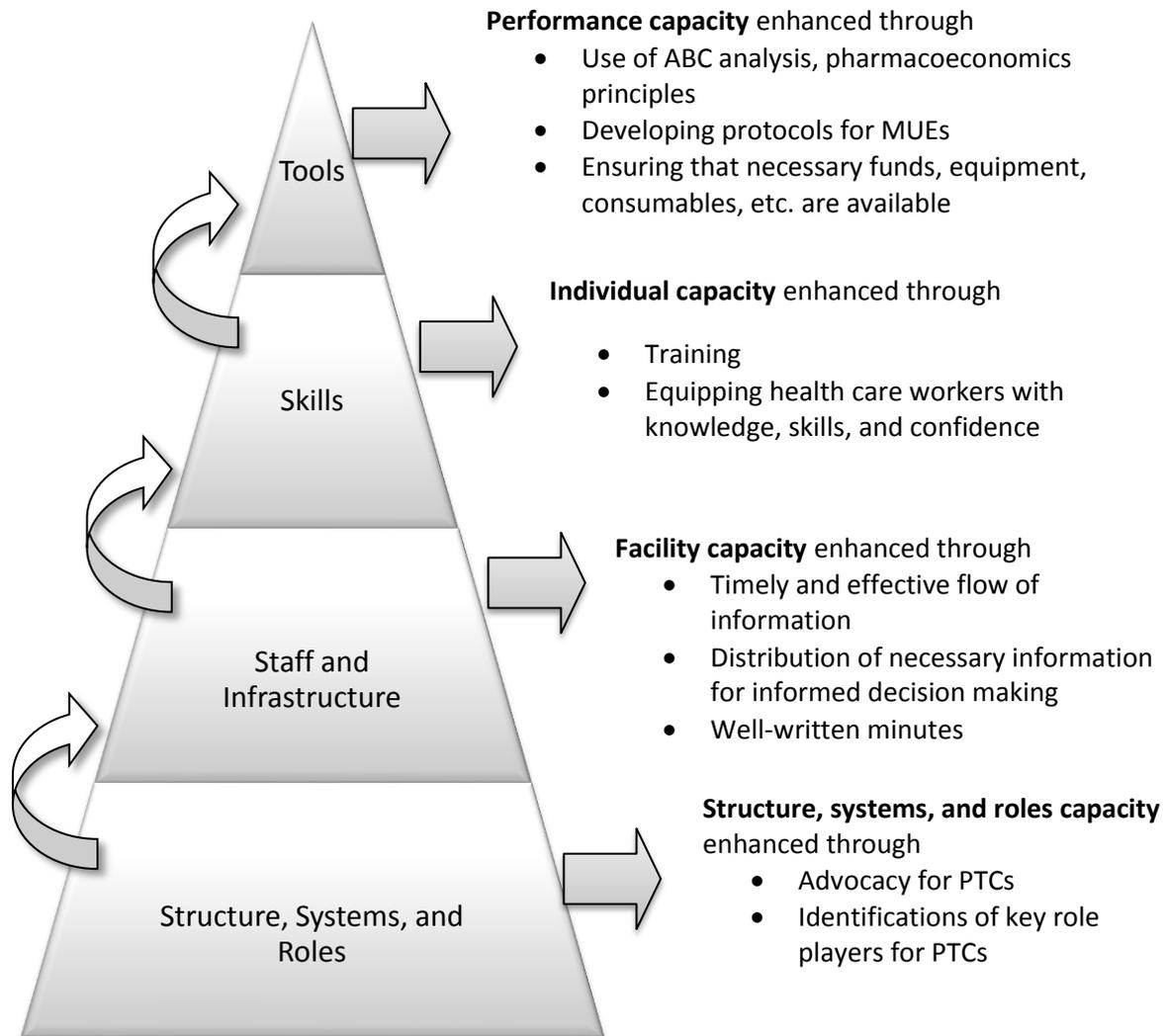
The process involves differentiating separate but interdependent components that ultimately are part of a unitary concept of capacity building. In strengthening PTC functions, SPS supported targeted system structures and roles, staff and infrastructure, and skills and tools, to different degrees, depending on the gaps and priorities identified. In their report on capacity building measurement, Lianne Brown et al. emphasized the central role played by capacity building in USAID health sector assistance strategies: “Capacity is critical to sustaining health outcomes and reducing reliance on external assistance.”¹²

Although the Pharmacy Act makes involvement in their institution’s PTC a legally binding requirement for institutional pharmacists, this is not always a sufficient condition for the establishment of a functional PTC. Health care workers need training and mentorship to strengthen their skills on PTCs.

A three-day PTC training course was implemented based on the PTC training material developed by Management Sciences for Health (MSH) under RPM Plus. The accreditation of the PTC training course by the South African Pharmacy Council gave more legitimacy and weight to the course. The standards set by the council are a guaranty of quality for the professionals who attend the course. Accreditation is a long and tedious process; to fulfil the requirement of competency assessment, a carefully designed compulsory take-home assignment had to be completed by the participants. The accredited course was implemented

¹² Lianne Brown, Anne LaFond, and Kate Macintyre. 2001. *Measuring Capacity Building*, MEASURE Evaluation, Carolina Population Center, University of North Carolina at Chapel Hill, p. iii. http://pdf.usaid.gov/pdf_docs/PNACM119.pdf (accessed 7 November 2012).

over a number of years to address the skill and knowledge gaps amongst pharmacists, nurses, and doctors.



Adapted from C. Potter and R. Brough. 2004. Systemic capacity building: A hierarchy of needs. *Health Policy and Planning* 19(5):336–45.

Figure 3: Capacity-building framework

The course covered 10 sessions and consisted of interactive lectures, class activities, and a take-home assignment. Because the course is modular, it can be adapted and shortened to address the needs of particular PTCs. The course covers the role, structure, and organization of the PTC and its core functions. Participants are also provided with the necessary tools and skills to make evidence-based decisions and carry out methodological operational research, including ABC analysis and VEN analysis and a checklist to monitor the PTC's functionality. The practical assignment aimed to encourage the systematic and routine use and application of the skills and tools learnt during the training. For example, the participants were requested to assess the functionality of their own PTC and to develop an improvement plan based on the identified weaknesses. They also had to identify a medicine use issue based on the ABC analysis at their facility and develop an MUE data collection tool to further investigate the problem identified. The course covered the following topics—

1. The role, functions, and structure of PTCs and their importance in promoting rational medicine use and management of AMR
2. Formulary concepts and medicines selection
3. Principles of medicine safety
4. Evaluating evidence for safety and efficacy through review and interpretation of medical literature
5. Evaluating the costs of pharmaceuticals using pharmacoeconomic principles
6. Quantitative methods to identify medicine use problems
7. Qualitative methods to understand reasons for medicine use problems
8. Strategies to improve medicine use and educational, managerial, and regulatory interventions in promoting rational medicine use
9. STGs
10. MUEs

SPS supported PTC trainings in eight of South Africa's nine provinces between January 2007 and July 2011. Health workers such as doctors, pharmacists, and nurses were trained. Table 1 summarizes the health workers, broken down by category and province, who underwent the three-day PTC training or the one-day follow-up workshop supported by SPS. A total of 32 training workshops were conducted. In Limpopo Province, where PTC performance is part of the annual performance review for the hospital clinical manager position, the number and proportion of doctors trained was relatively higher, at 31 per cent, than in other provinces. In the Northern Cape, the participation of doctors in the training was high because of a directive from the Kimberley Hospital Complex Clinical Manager, making attendance of the PTC training mandatory. These figures illustrate the importance of hospital management support to achieve better involvement of doctors in the PTC. In KwaZulu Natal no requests were made for PTC training over the period, because under RPM Plus, many previous trainings were conducted there by MSH, and KwaZulu Natal had a very proactive provincial PTC advocate.

The South Africa SPS programme acknowledges that training plays a role in capacity building, provided an adequate pre-training needs assessment is made and post-training evaluation is used to determine whether capacity was built. Training is only one step in the capacity-building process. Capacity building may need coaching, mentoring, direction, idea generation, and encouragement. The requirements and time needed for a PTC to function as intended vary considerably, depending on the level of care, the province, the support provided by management, and individuals' motivation. The SPS Programme, through placement of one staff member in each of the nine South African provinces, provided targeted follow-up technical support to selected sites but was not able to meet the demand because of time and resource constraints.

Table 1: Workshops Held and Health Care Workers Trained on PTCs in South Africa between January 2007 and July 2011

Province	Number of workshops held	Distribution of health care workers trained on PTCs				Total
		Pharmacists	Doctors	Nurses	Other	
Limpopo	6	55 (51%)	33 (31%)	11 (10%)	8 (8%)	107
Mpumalanga	5	44 (45%)	12 (13%)	32 (33%)	9 (9%)	97
Free State	6	47 (53%)	17 (19%)	18 (20%)	7 (8%)	89
Northern Cape	7	23 (29%)	17 (22%)	16 (21%)	22 (28%)	78
Gauteng	3	22 (29%)	9 (12%)	23 (31%)	21 (28%)	75
Western Cape	3	50 (88%)	7 (12%)	0 (%)	0 (%)	57
North West	1	15 (71%)	6 (29%)	0 (0%)	0 (0%)	21
Eastern Cape	1	16 (100%)	0 (0%)	0 (0%)	0 (0%)	16
KwaZulu Natal	0	0	0	0	0	0
Total	32	272 (50%)	101 (19%)	100 (19%)	67 (12%)	540

Collaboration with Institutions of Higher Learning: Problem-Based Professional Training

Traditional medical, nursing, and pharmacy curricula have been highly science based and have not adequately addressed practical aspects such as medicine management in the real world, rational medicine use, and AMR. In recent years, global stakeholders including the WHO have consistently advocated for educational and practice-based interventions in health care settings. Institutes of higher learning such as colleges and universities are excellent avenues for enriching existing curricula or introducing new topics for rational medicine use. As part of the overall SPS South Africa country programme strategy to involve institutions of higher learning, SPS has striven to find opportunities to involve university personnel during various PTC trainings and meetings. An example is the support for pre-service training provided to the Nelson Mandela Metropolitan University (NMMU) to incorporate the role of a PTC in promoting the rational use of medicines in its curriculum with a field practical. Another example is the technical support provided to Rhodes University for the implementation of a Doctor of Pharmacy (PharmD) programme. (See next section for more details.)

PRE-SERVICE EDUCATION ON RATIONAL USE OF MEDICINES

Experience from Nelson Mandela Metropolitan University, Port Elizabeth

The WHO'S global strategy on AMR specifies, among priority interventions, "Maximize and maintain the effectiveness of the EDL and STGs by conducting appropriate undergraduate and postgraduate education programmes of health care professionals on the importance of appropriate antimicrobial use and containment of antimicrobial resistance."¹³ The WHO strategy also declared that PTCs are a key intervention in containing AMR. The Department of Pharmacy in the Faculty of Health Sciences at NMMU already had an enabling environment in critically reviewing the relevance of its Bachelor of Pharmacy (BPharm) curriculum in light of the reality of today's pharmacy practice in South Africa.

Initially in 2008, an elective research module (ZPE401) on pharmacovigilance was first offered to final-year BPharm students as one of four possible elective modules that could be selected. This option was made possible through collaboration with the SPS Programme and by using SPS's training materials on pharmacovigilance. Fifteen final-year BPharm students were involved in this elective. The elective was repeated in 2009, with eight students participating. One of these students, subsequently registered for her master's degree in 2010, is currently working with SPS in evaluating the medicine safety reporting systems in the public sector in South Africa, using the SPS-developed Indicator-Based Pharmacovigilance Assessment Tool (IPAT). In 2010, the Department of Pharmacy updated its final-year curriculum to include a lecture on pharmacovigilance to ensure all final year BPharm students were aware of the need for pharmacovigilance and the reporting systems in place in South Africa and globally. Another six students completed the pharmacovigilance ZPE401 elective in 2011.

Two faculty members from NMMU's School of Pharmacy participated in the three-day training on PTCs conducted by SPS for NMMU in 2010. They recognized the value of educating pharmacy students regarding the role of PTCs in promoting rational use of medicines. As a result of this training, the Department of Pharmacy then successfully included an elective module on PTCs among five choices of electives for final-year pharmacy students as a formal part of their curriculum in 2011. Four students participated in the first PTC elective in 2011, and this elective has been repeated in 2012, with a further nine students participating.

The SPS-developed PowerPoint slides were used for the introductory two-hour lectures for the PTC elective to create an awareness of "What is a PTC?"; "How do you select a medicine for a formulary?"; "Identifying medicine usage problems and approaches to resolving these problems." The design of this elective not only provides hands-on knowledge to students on the role and functions of PTCs but also equips them with skills needed for medicine use evaluations.

In March 2012, the Department of Pharmacy sought collaboration with the Port Elizabeth Hospital Complex's PTC in having students participate as observers in at least one PTC meeting. With the permission of the chairman and PTC members, five of the students

¹³ Intervention 5.11 in World Health Organization. 2001. *WHO Global Strategy for Containment of Antimicrobial Resistance*. WHO/CDS/CSR/DRS/2001.2. Geneva: WHO.

attended a PTC meeting on May 14, 2012. The students will now perform a retrospective review of the minutes of PTC meetings that have occurred in the last two years (2010, 2011) to evaluate the functioning of this PTC in light of the PTC roles and functions they have learnt about. This process permits the students to identify the nature of the decisions made by the PTC and to reflect on the PTC functions. From these minutes, the students are expected to follow up on the decisions made on specific medicines for inclusion, deletion, or restriction in the hospital formulary. This process will involve working with the relevant pharmacy managers to look at the cost implications over the past two years, usage patterns (named patient, restricted or general use), and current stock holding and may even require interview-based discussions with the relevant prescribers to identify the extent to which the decisions made by the PTC have been implemented. This research process allows interaction between students and PTC members for mutual support and learning.

This experience enabled the students to recognize the reality of the real-world practice settings and the barriers facing implementation of treatment guidelines. Because this was an elective research module, students were trained on data analysis, report writing, and abstract development and encouraged to prepare their research report as an article for publication in peer-reviewed journals (an example of research is presented in the MUE section of this report and the draft article is attached as Annex F).

Experience from Rhodes University, Eastern Cape

In 2004, RPM Plus provided technical support to Rhodes University in adapting the US PharmD approach to one suitable for implementation in the South African resource-constrained environment. The objective of the programme was to train advanced practitioners in the field of clinical pharmacy of which the main scope is promotion of the rational use of medicines. This was a three-year post-graduate pharmacy programme where students are resident in public sector health facilities in the Eastern Cape.

From 2007 to 2012 SPS provided on-going support to Rhodes University that included annual review of the academic module; assessment tools and outcomes; a preceptor for various rotations, which included mentorship and assessment; and a supervisor for rational medicine use-related research activities.

The MSH PTC training materials form a key component of the foundation management module with PTC outcomes being assessed in 3 of the 12 rotations. In addition, selected chapters from *Managing Drug Supply* are used during the management rotation.

Relevant outcomes for PTCs and rational medicines use include—

- **Medicine use reviews:**
Each student must complete three medicine use reviews during the course of the degree and present results to the PTC.
- **Evidence-based medicine:**
Each student must apply evidence-based medicine principles in assessing submissions for PTC formulary inclusion and the provision of medicine information in the rational medicine use and pharmaceutical care interventions.
- **Pharmacoeconomics:**

Students are exposed to the four methodologies used in pharmaco-economics and need to provide evidence of application of two models in their support to the PTC.

- ABC, VEN (vital, essential, non-essential), and ATC (Anatomical-Therapeutic-Chemical) analysis:
On a monthly basis an ABC analysis of the allocated ward needs to be presented and the application of VEN and ATC analysis demonstrated through a report to management in at least one rotation.
- Monitoring and evaluation:
Each student provides a monthly report evaluating service delivery in the preceding month. This provides each candidate with the skills to evaluate rational medicine use-oriented services rather than the traditional product-focused pharmacy approach.
- Pharmacovigilance:
Medication errors are routinely collected by students; each student submits a report three times during the course of the degree. In addition, ADR trends are analysed and reported to the PTC on a quarterly basis.
- Pharmaceutical care:
A problem-based learning model for key EDL conditions is carried out through the provision of pharmaceutical care using the STGs as standard of care.

In conclusion, PTC activities are a fundamental component of each student's outcomes, which have been supported directly and indirectly by SPS.

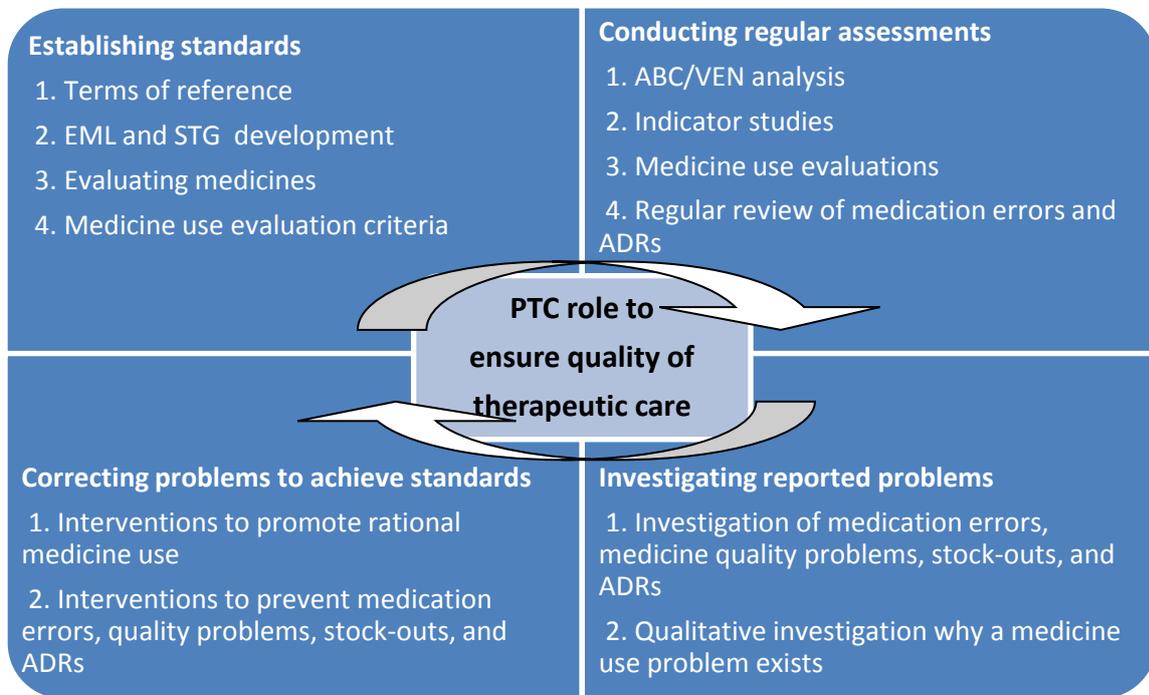
To date five students have graduated, and four of them remain in the public sector. One graduate is employed by the NDoH as a senior policy analyst with the key responsibility for supporting the EML process and promotion of rational medicine use. The most recent graduate was appointed to the National EML Secretariat during her final year and has served on both the Adult Hospital level and Primary Health Care Expert Committees under the mentorship of an SPS senior programme associate. The first graduate in collaboration with SPS implemented a medication error surveillance programme and has subsequently been appointed to the Pharmacovigilance Committee of the Medicines Control Council. Finally, the last graduate has assumed a leadership role in the Eastern Cape's Provincial PTC. Each of these graduates was mentored by an SPS senior programme associate both in the pre-service and in-service environments.

These trends of graduates assuming high-level positions within the public health sector contribute to the sustainability of the PTC activities.

PTC ROLE TO ENSURE QUALITY OF THERAPEUTIC CARE: ILLUSTRATIVE EXAMPLES FROM SOUTH AFRICA

As mentioned in the previous section, the PTCs at different levels have different needs in terms of support and assistance. In some institutions the PTCs are non-existent, and the institutions will need assistance in establishing a PTC; others are not functional, in which case the support will aim at revitalising them; and finally, some are already functional but need assistance to go the extra mile. The WHO framework, representing the role of the PTC, highlights the different stages in the functions of a PTC.

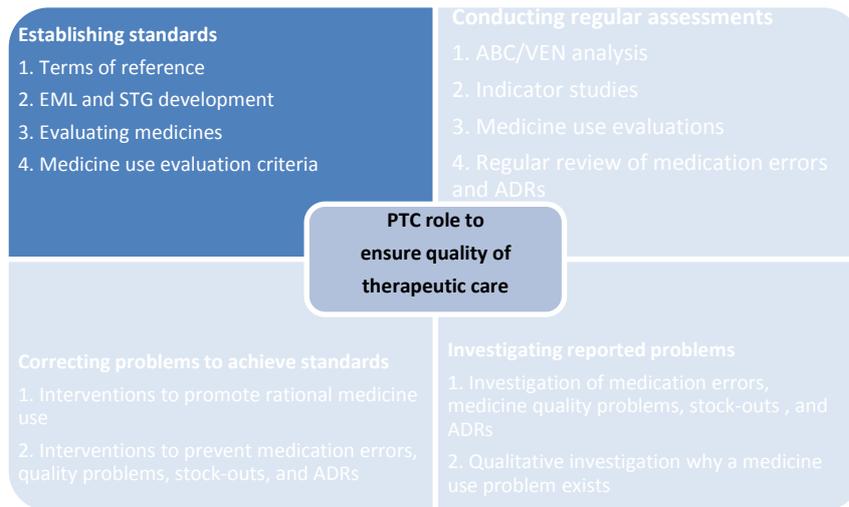
This section presents examples of how some South African PTCs, supported by SPS, fulfilled their role as described by the WHO framework below. The examples are arranged by quadrant and by activity within a quadrant. An institution may be represented in more than one quadrant.



Adapted from Terry Green, John Chalker, Kathleen Holloway, and RPM Plus-WHO. Promoting Drug and Therapeutics committees in the Developing World, oral presentation at the 2nd International Conference on Use of Medicines, Chiang Mai, Thailand, March 2004.

The first two quadrants, related to *establishing standards* and *conducting regular assessments*, are process based whereas the other two, *investigating reported problems* and *correcting problems to achieve standards*, are outcome based. Most of the examples are in the first two quadrants of the framework, highlighting the relative immaturity of a majority of PTCs at the time of the review. One consequence of the majority of the support being provided within the first two quadrants is the difficulty in showing results or outcomes. As the PTCs move toward the third and fourth quadrants as they mature, the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) programme will support them in achieving outcomes and showing results.

Establishing Standards



Terms of Reference/Governance Tools

The TORs describe the purpose and structure of a committee. They are essential at all levels because they provide a documented basis for making future decisions as well as developing a common understanding of the objective among members and stakeholders. SPS acknowledged the development of sound TORs as the essential foundation for PTCs. From national to provincial, district, and institutional levels, technical assistance was provided in revising or developing TORs for the committees.

To ensure an ethical approach, further support was provided to promote the use of good governance tools, such as conflict of interest and confidentiality declaration forms. The following examples highlight the positive effect of having sound TORs on the functionality of the committees through all levels of the health system.

National Level

To better plan, implement, and document National Essential Medicines List Committee (NEMLC) meetings while clarifying roles of members, the SPS Programme supported the development of the TORs. The TORs describe the role of the chairperson, the secretariat, and various categories of members so that all members are clear about each one's responsibilities. In addition to the objectives and functions of the committee, the TORs emphasise the stakeholder consultation process as part of any EML publication review process.

To protect the integrity of decision-making processes through disclosure and transparency, the NEMLC issued a Conflict of Interest Policy. NEMLC members are asked to complete a Declaration Form with details of relevant financial relationship with any entity and also sign a Confidentiality Declaration form acknowledging the code of conduct. As a result, important deliberations and key decisions by the NEMLC are expected to be protected from any untoward influence by commercial interests.

Provincial Level

Prior to 2007, the Free State Provincial PTC was dysfunctional, had no proper TORs, and held irregular meetings. Members were appointed informally, they did not know their responsibilities, and commitment was poor with only a few active members doing most of the work. SPS organized PTC training in September 2008 for Free State provincial stakeholders, which triggered a wave of prompt action by the Pharmaceutical Services department of the Free State provincial DoH. The presence of a full-time SPS senior program associate based in the province promoted effective technical collaboration. Support was provided for the revision of the TORs using information from the PTC manual. Guidance from the National EML Secretariat helped strengthen the TORs, and the first draft was produced in 2008 by the Pharmaceutical Services department of the Free State provincial DoH.

In the past, the PTC never had a time-limited membership period. The PTC members are now appointed on an annual basis through nomination by their peers or supervisors. The then acting chairperson of the Free State Provincial PTC provided leadership and facilitated management support received from other unit heads. This process had not been implemented previously and led to ownership by key stakeholders involved. The district pharmacists, who were admitted as members, were informed that they were representing all provincial district pharmacists and so a greater level of commitment was expected.

Following the new process of nomination and approval of members on an annual basis as well as steady improvement in the quality of PTC meetings, the membership increased from 15 representatives in 2008 to 37 members in 2012. The PTC now meets every quarter as scheduled. The provincial PTC attempts to monitor functions of institutional and district PTCs in the province, as budget and time allow. A landmark decision was made in May 2009 with an official circular that the establishment and convening of the PTC is part of the key responsibilities of the Chief Medical Officers' Performance Development and Management Systems.

The Provincial Coding Committee (PCC) of the Western Cape had been in existence since the 1970s. The prime function of the committee was the selection of medicine for use by different categories of prescribers in the province. Although the committee had been functioning for a number of years and training was provided, various areas where improvements could be made were identified. In 2007, the members of the Western Cape PCC were invited to attend a workshop aimed at optimising the functioning of the PCC. Discussions were facilitated under RPM Plus, the predecessor of SPS.

The workshop emphasised the other functions and roles of the committee besides coding. The subsequent change of the name of the committee to the Provincial Pharmaceutical and Therapeutics Committee and the revision of its TORs highlights the commitment of the committee to undertake activities related to rational use of medicines in addition to selection. As a result, the committee was reconstituted and for the first time all members were officially appointed by the Head of Health of the province for a two-year period. To improve the functionality and build capacity in the newly appointed committee, a planning and orientation workshop was held in March 2007. An assessment tool adapted from an international reference was developed to measure the past performance and functioning of the committee. The 33-item assessment tool (Annex G) covered the areas of structure, function, policies and processes, and other general items such as accomplishments, drawbacks, and options for improvement. During the two-day workshop, numerous challenges were identified and an

action plan developed to address them. One of the key results of the workshop was a clear understanding and awareness in the province of the role of this important committee.

SPS then collaborated with the Western Cape Provincial PTC in reviewing the provincial policy and procedure regarding product quality problems, revising the policy regarding interaction with pharmaceutical representatives, reviewing the conflict of interest policy and procedure, and developing indicators to monitor and evaluate the performance of provincial, regional, or institutional PTC committees.¹⁴ In that regard SPS support was valued because it assisted the Provincial PTC secretariat in presenting the relevant documents and bringing the information together as well as in sharing experiences from other provinces. The Western Cape Department of Health has made provision for an operational budget for the Provincial PTC, strengthening its institutionalization within the provincial department of health.

In 2010, a technical task team, called the Interim Formulary Task Team, was appointed by the chairman of the Gauteng Provincial PTC. The team's brief was to review the provincial TORs and rationalize the provincial formulary. SPS was part of the task team. SPS also supported the review of the TORs. Examples of TORs and guidelines from other provinces in South Africa as well as generic TORs from MSH were provided. The first draft of the new TORs was produced by the Pharmaceutical Services in collaboration with SPS. The TORs for the provincial PTC were reviewed as well as the ones for institutional and district PTCs. The governance tools, including confidentiality and conflict of interest forms, were also reviewed.

Following the finalization of the TORs and governance tools, there was a call for nominations in August 2011. A task team reviewed the responses received and scored them against a checklist based on the needs expressed in the TORs. Recommendations were made and submitted to the Head of Department and Member of the Executive Council for appointment of the provincial PTC members.

The Gauteng Provincial PTC (GPPTC) TORs provide for the establishment of four sub-committees, namely Procurement sub-committee, Formulary sub-committee, Safety and Quality sub-committee, and Rational Medicine Utilization sub-committee. Each sub-committee has its own TORs that make explicit its functions, role, and responsibilities. According to their expertise, each member of the GPPTC was assigned to one of the sub-committees during the first meeting of the revitalised GPPTC held in March 2012. The GPPTC holds quarterly meetings; the sub-committees meet monthly. Each sub-committee developed its operational plan for the first year and presented it to the GPPTC during the second meeting. The GPPTC meeting's agenda has standing items by sub-committee. Each sub-committee reports quarterly to the main GPPTC about its progress and current and planned interventions.

The TORs define the communication strategy within the province between the different levels of PTCs. District and institutional PTCs report directly to the GPPTC Secretariat for inclusion of a specific item in the agenda. However, some urgent matters cannot wait until the next GPPTC meeting. The TORs provide for the appointment of an Executive committee, the function of which is to attend to urgent matters that are then ratified at the full provincial PTC at the next available meeting. The Executive committee is constituted of four members plus the chairperson of the provincial PTC. The provincial PTC members have appointed the

¹⁴ Y. Johnson, S. J. Putter, M. E. Sclanders, and G. Steel. 2008. Building capacity in a provincial PTC—the Western Cape experience. Poster presented at the 22nd Annual Conference of the South African Association of Hospital and Institutional Pharmacists, 6–9 March, Drakensburg, South Africa.

chairpersons of the four sub-committees as members of the Executive committee. “Urgent matters” as defined by the TORs are “when public health will be compromised if an item is not approved; resistance to an antimicrobial agent listed on the formulary; matters regarding the non-approval of an item at a lower level where the patient’s life is in danger; out of stock of non-substitutable vital or essential item.” The Executive sub-committee is able to co-opt experts when needed.

One SPS staff member is an ex officio member as a representative of the NEMLC and is part of the Formulary sub-committee; another SPS staff member has been co-opted to the Rational Medicine Utilization sub-committee.

The preceding examples illustrate that revitalising a provincial PTC can be a lengthy process. Because the provincial PTCs have such a strong potential impact on pharmaceutical expenditure in the province, high-level authorisations and consultations are needed along the way to ensure that good governance principles are respected.

District Level

The Western Cape Provincial PTC, in collaboration with SPS, worked on strengthening the capacity of regional and institutional PTCs in the province.

Since early 2000, the West Coast district in the Western Cape had a Clinical Pharmacological Committee. The district PTC was properly constituted in 2009. The SPS training programme on PTC management stimulated new thinking on good governance in PTCs with the provincial office giving the lead. Technical assistance was provided for drafting the TORs, which were subsequently authorized by the District Manager.

Institutional Level

Boitumelo Regional Hospital is located in the town of Kroonstad, Free State, and is the only regional hospital within Fezile Dabi District. Boitumelo functions as both a district and a regional hospital and provides care to both level 1 and level 2 patients. Its mission is to provide quality health care services to the Fezile Dabi community through knowledgeable and skilled personnel with optimal use of modern technology.

The PTC at Boitumelo Regional Hospital was established in 2002. Its functionality fluctuated over the years. Some of the challenges that affected the PTC’s functionality included lack of sufficient doctors to participate in PTC meetings and poor commitment with last-minute cancellation of scheduled meetings. The PTC also lacked top management support. However, all this changed in 2008 when one hospital staff pharmacist attended an SPS-organized PTC training. Insights gained from the PTC training helped build some structure in PTC meetings, which are now scheduled on the last Tuesday of every month. The Boitumelo Regional Hospital PTC makes efforts to stimulate the interest of the members during the PTC meetings by discussing and reviewing practical issues, such as clinical guidelines for antibiotics, guidelines for cost-saving measures, and “information notes” to assist prescribing. Decisions made by the PTC are shared with all relevant persons through documented minutes.

A representative from the Oudtshoorn Hospital in Western Cape participated in the SPS-organized PTC training programme in 2008. Subsequently, the institutional PTC in Oudtshoorn Hospital developed its TORs and improved its functionality through various

activities, as described below. Before the training, the PTC's meetings were irregular and the mandate was not clear to its members. The clinicians had difficulty in seeing the PTC as a key element to promote rational use of medicines in the hospital. The PTC is chaired by a senior physician, and membership has wide representation from the hospital. Over time, PTC meetings progressively occurred on a monthly basis. Key decisions are serially communicated to weekly physicians meetings, monthly nurses meetings, and other relevant side meetings that take place in practice to ensure clarity. This ensures that information flow is not only seamless but also reinforced to prescribers. According to the Chief Pharmacist, staff enthusiasm allowed for collaborative work in an enabling environment.

EML and STG Development and Maintenance

*MDS-3*¹⁵ defines treatment guidelines as disease oriented whereas the EML or formulary manuals are medicine oriented. They can both be developed at various levels of care. Together they are powerful tools in promoting the rational use of medicines. However, “to maintain the credibility of the information, a system for regular updates and for incorporation of accepted amendments into the next edition is essential for both formularies [EML] and treatment guidelines.”

In South Africa, the national EML is developed concurrently with STGs at the national level by the NEMLC. The provinces then develop their own formulary based on their needs. The NEMLC recommends that the provincial formulary contain a maximum of 20 per cent of non-EML items. This allows for the delay during the revision of the national EML and for named patients' medicines.

The following examples illustrate the systems in place in South Africa for the sound development of the EML and STGs and the processes followed to update and maintain the EML, STGs, and formularies at all levels of the health system.

National Level

The National EML Secretariat successfully implemented a peer review process by institutional and provincial PTCs for EMLs and STGs through five stages. First, a lead reviewer ensures that the right people are assigned for the peer review process. Second, the submissions undergo peer review by the identified Expert Committee. Third, external peer review is conducted by selected PTCs, educational facilities, and clinical societies. Fourth, the Expert Committee conducts the final peer review process before finally sending the document for editorial processing. Before 2008, provincial PTCs were sending their motivation forms for new items directly to their procurement entity, resulting in the introduction of non-EML items in the country. Now, the motivation forms are sent to the NEMLC for review. Recent analysis indicates that an average of 101 comments from peer reviewers were incorporated into decision making while the number of approved medicines declined by 16 per cent.¹⁶ Moreover, this methodological approach ensured that the selection of essential medicines is aligned with the STGs.

¹⁵ Management Sciences for Health. 2011. *MDS-3: Managing Access to Medicines and Other Health Technologies* (Arlington, VA: Management Sciences for Health), chapter 17: Treatment Guidelines and Formulary Manuals.

¹⁶ G. Steel, K. Jamaloodien, T. Pillay, A. Parris, and B. Maharaj. 2012. The South African Methodological Approach to Developing the Essential Medicines List and Standard Treatment Guidelines. Poster presented at the Asia Pacific Conference on National Medicines Policies, 26 May, Sydney, Australia.

Because of the growth in the use of the EML in South Africa's public health system, the Pharmaceutical Care Management Association sought training on its use. The Board of Healthcare Funders Southern Africa requested that SPS make a presentation on the systematic EML selection process and its advantages to the Council for Medicines Scheme. In addition, Innovative Medicines South Africa (IMSA, a representative association of multinational pharmaceutical manufacturers) wanted to know how to interact with the EML process, given the envisaged National Health Insurance scheme. As a result, SPS facilitated dialogue with key stakeholders on policy and practice concerning access to medicines in the private sector.

According to the WHO,¹⁷ “essential medicines are medicines that satisfy the priority health care needs of a population. They are selected with regard to disease prevalence, safety, efficacy, and comparative cost-effectiveness.” The EML and STGs developed by the NEMLC are the foundation of rational medicine use. The PTCs at all levels have the responsibility to promote the use of medicines in line with the EML and the STGs.

Provincial Level

Following the training on pharmacoeconomic methods conducted by SPS, the Free State Provincial PTC and the Pharmacology Department of the University of Free State forged a fruitful working relationship. The university's pharmacologist was appointed as a member of the provincial PTC, hence enabling the PTC to access peer-reviewed literature for better evidence-based decision making.

SPS further advocated for the use of pharmacoeconomic principles in the analysis of the motivation forms for new items submitted to the provincial PTC. SPS highlighted the need for the PTC members to be allocated enough time, at least two weeks, to analyse the motivations prior to the PTC meeting. As a result, the provincial PTC made a policy decision that all facilities are required to submit motivations for changes in the formulary list one month in advance of the scheduled provincial PTC meetings. The provincial PTC Secretariat would then review and assess the evidence provided, conduct pharmaco-economic analyses (using methods such as cost-effectiveness analysis, cost-minimization analysis, numbers needed to treat, and the like). Finally, two weeks before the scheduled PTC meeting, the secretariat would send prepared packages of analysis to all provincial PTC members. This process helped facilitate a robust discussion and allowed all PTC members to meaningfully contribute during decision making. Over a three-year period, this refined working process improved the capacity of the provincial PTC to handle volumes of applications on a timely basis (table 2).

¹⁷ WHO, Medicines: Essential medicines, Fact sheet N°325, revised June 2010.

Table 2: Free State Provincial PTC Motivations for New Items, 2009–2011

Description	2009	2010	2011
Applications	5	13	17
Approved	4	9	15
Not approved	1	4 ^a	2

a. Three of the four items were withdrawn or stood over to the next meeting but also ultimately withdrawn.

SPS collaborated with the Western Cape Provincial PTC in updating the Provincial Code List to a more user-friendly format. The provincial PTC has been successful in raising awareness on the importance of the code list, and the expenditure for pharmaceuticals in the province is always within its budget. Within the Provincial Code List, restrictions in the form of prescriber level were introduced to improve rational prescribing. Circular H3/2009 specified the “Process for applying for amendment of coding status, addition or deletion of pharmaceuticals to the provincial code list.” District PTCs and institutional PTCs submit their motivations to the provincial PTC secretariat six weeks before PTC meetings. The motivations are then compiled by the secretariat and distributed to the PTC members for review one month prior to the meeting.

The importance of rational medicine use was emphasised during a presentation made by SPS at the Gauteng Pharmacy Conference in 2010. The presentation entitled “Rational Medicines Use, a Policy Perspective” (Annex H) was well received, and the Gauteng Head of Pharmaceutical Services acknowledged that “it will go a long way towards preparing us at Gauteng to clean our formulary.” Within the Gauteng Interim Formulary Task Team, technical support was provided by SPS in identifying medicines in the formulary that are not part of the EML. The prescriber levels, prices, and therapeutic classes of medicines were then added to the electronic version of the Gauteng formulary. One of the Formulary sub-committee’s roles is to ensure alignment of the Gauteng provincial formulary with the EMLs, including the tertiary EML. The targeted percentage of non-EML medicines in the provincial formulary is 20 per cent, in accordance with the National EML recommendation.

In the Northern Cape Province, Kimberley Hospital plays a central role in the province and provides essential support to the provincial PTC on clinical issues. The use of evidence-based information for PTC decision making is strongly advocated by SPS. However, health care workers do not always have access to peer-reviewed literature and quality evidence. The idea for the establishment of the Clinical Resource Centre (CRC) at Kimberley Hospital was put forward by the provincial DoH, through the management of the Kimberley Hospital Complex. The CRC was developed to serve the needs of the entire province and health care workers from all its five districts. Health care workers would be able to access evidence-based information, receive updates on all health-related matters to make critical decisions regarding patient care, and assist in research activities and clinical trials. Through this, it was envisaged that PTC activities would be enhanced. The first step was the establishment of a functional provincial PTC. In June 2006, a five-day PTC workshop was held in Kimberley for clinicians and pharmacists to provide the basis for establishing the provincial PTC before implementation of the CRC. Following a number of preparatory activities, the PTC convened its first meeting in November 2006.

In April 2007, an assessment showed that the provincial PTC was functional. The Kimberly Hospital Complex management then provided suitable space for the CRC. Thereafter, SPS worked in partnership with the provincial DoH to determine requirements for establishing the

centre as well as the most suitable approach, which would ensure effectiveness and sustainability of the venture. Information on best practices and minimum requirements was obtained from the Medicine Information Centre at the University of Cape Town. Members of staff who would be working in the CRC were identified. SPS arranged for three doctors and seven pharmacists from the Kimberly Hospital Complex to receive training from the manager of the Medicine Information Centre in Cape Town in February 2010.

SPS supported the strengthening of institutional capacity, including infrastructure support by providing office furniture, computers, textbooks, and start-up support for subscriptions to peer-reviewed journals both in print and online. SPS further provided support service capacity through the development of SOPs and tools for addressing queries and tracking and communicating usage statistics. Guidance was provided in the development of the job description for the pharmacist who would run the centre. At present the centre has 10 computers with Internet access, as well as a comprehensive stock of textbooks addressing most health care areas.

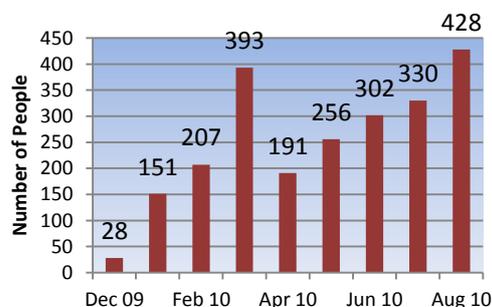


Figure 4: CRC use, December 2009–August 2010

The establishment of the CRC has been well received by health professionals. The centre was also hailed as a “significant milestone in the improvement of quality health services as well as the creation of a vehicle enabling us to access life saving and much needed information in the field of health and medicine,” as stated by the Honourable MEC for Health, Mxolisi Sokatsha, during the opening ceremony, 24 May 2010.¹⁸ Since the facility began operating in December 2009, the number of people using it has increased steadily. By August 2010, the average number of CRC users per month was 428 (figure 4). The majority of users were from the surgical (24 per cent), clinical support services (20 per cent), and medical (16 per cent) departments. The centre also plays a vital role in disseminating decisions made by the PTC to management, clinicians, and pharmaceutical personnel, thus enhancing the effectiveness of the committee.

An administration clerk and the pharmacist involved with both the centre and the PTC provide information on usage statistics through the CRC’s quarterly newsletter. Data on type of queries highlight the range of queries received (table 3).

¹⁸ Opening of the newly refurbished Clinical Resource Centre, Province of the Northern Cape, Republic of South Africa website. http://www.northern-cape.gov.za/index.php?option=com_content&view=article&id=269&Itemid=54 (accessed 9 July 2012).

Table 3: Number and Type of Queries Received

Month	Therapy	Pharmacokinetics	Availability/supply	Other
September 2011	35	2	1	2
October 2011	20	1	1	1
November 2011	35	0	5	4
January 2012	40	5	6	0
February 2012	24	2	9	0
March 2012	29	6	0	9
April 2012	40	1	2	5
May 2012	33	1	2	4
June 2012	39	5	4	0

A number of items have been added to the Northern Cape formulary, and substitutions of items on the formulary have been made following evidence-based information from sources in the CRC. The centre also helped in sourcing information for the dressings/wound care protocol. This information allowed cost-benefit analyses to be done on different dressings in different classes, and one dressing from each class was selected and approved for the hospital's formulary (e.g., silver-releasing topical antiseptic dressings, non-silver-releasing topical antiseptic dressings, moisture-retention dressings, impregnated hydrogels). A separate surgical sundries formulary was developed using the CRC and the surgical sundries sub-committee of the provincial PTC.

District Level

The Metro District PTC in Western Cape was established following the SPS-organized PTC training in 2008. The first PTC meeting was held in 2009. Currently, PTC meetings are held on a quarterly basis. Representatives from the district hospitals and sub-districts are members of the district PTC. The head of the PTC is a medical doctor. Two-way communication between the district PTC and the provincial PTC is functioning. The submissions for additions to the Provincial Code List or for changes to the prescriber level of an item within the Provincial Code List start at the institutions and proceed through the district PTC to the provincial PTC. The submissions are reviewed by the relevant prescribers in the district's facilities. During the review of the STG chapters and the EML, the National EML Secretariat sends them for comments to the provincial PTCs. The Metro District PTC receives those chapters via the Western Cape provincial PTC. The chapters are then reviewed and commented upon among the district PTC members. The chapter comments are submitted back to the provincial PTC, which consolidates the comments received from the different district PTCs. This model could be used in other provinces as an example of effective coordination through different PTC levels for the call for comments during the STG and EML review process.

The West Coast district in Western Cape covers a large area. In some locations, outlying hospitals procure the service of the town's general practitioners for a few hours. The minutes of the district PTC meeting are e-mailed to those doctors. To aid the implementation of PTC decisions, the secretariat undertakes academic detailing. An observation during one of these visits, to a remote town, revealed that one of these general practitioners had adopted the Provincial Code List by downloading it to his personal computer to guide his day-to-day

prescribing. This model may provide evidence for the implementation of formularies for national health insurance.

Institutional Level

Formulary management is one of the Kimberley Hospital PTC's strengths. It is a standing item on all PTC agendas. All motivations for addition to the formulary have to provide sufficient evidence on safety, efficacy, and cost as well as the reasons why new items should be coded.

In the four-year period since 2008, approximately one of every three applications for inclusion of a new medicine onto the Provincial Code List by the Oudtshoorn Hospital PTC was approved. This is a relatively high rate of successful applications for a district-level hospital. Involvement of doctors and specialists was critical to achieve this success. Decisions are based on a review of an adequate number of studies from peer-reviewed literature. The hospital PTC then communicated its decision to George District PTC, which was then communicated to the Western Cape Provincial PTC.

Evaluating Medicines

In the draft Guidelines for Pharmacoeconomic Submissions,¹⁹ the NDoH asked, "There is no doubt that new medicines have the potential to greatly improve health outcomes but at what cost?" and stated that "in order to conduct clinical decision-making with credibility a transparent, consistent and formal process of cost-effectiveness evaluation is required." The following are examples that show how SPS supported the NEMLC in answering that call.

National Level

New approaches to EML reviews were introduced at varying stages. Prior to 2007, prices were used to evaluate the cost of medicines to justify any addition or deletion of medicines from the EML. However, using data from medicine prices alone can be misleading. Over the last five years, the SPS Programme introduced new approaches to pricing analysis, namely, comparison of tender price to single exit price, impact of new medicine cost relative to hospital costs, transportation costs, and potential for price migration. These methods are now routinely applied by the NEMLC. A recent instance is the savings of R 27 million through review of an application to introduce a conjugated anti-meningococcal vaccine during an outbreak of meningitis. Such methodology was also applied for comparison of products in oncology treatment.²⁰

Decisions on medicine selection are made based on quality, safety, effectiveness, and cost. The National EML Secretariat now has a systematic process in place for making decisions concerning new medicines. Provinces are asked to submit formal written requests. The conditions are reviewed against available ABC analysis. After a review of the relevant STGs,

¹⁹ Republic of South Africa. Department of Health. 2010. Medicines and Related Substances Act No. 101 of 1965, Regulations, Transparent Pricing System for Medicines and Scheduled Substances, Guidelines for Pharmacoeconomic Submissions, Draft. Regulation Gazettes, No. 33914 of 31 December 2010.

²⁰ G. Steel, P. Ruff, and L. Dreosti. 2011. Improving Access to Oncology Treatments in a Resource Constrained Setting Using Pharmacoeconomic Analysis. Poster presented at the Third International Conference for Improving the Use of Medicines, Antalya, Turkey, November.
<http://www.inrud.org/ICIUM/ConferenceMaterials/1076-steel- a.pdf>

a new medicine report is compiled. Chapters of the EML are sent out to provinces for comment before finalization of the STGs and editing of the EML book.

Before 2006, pharmacoeconomic evaluation methods (cost-benefit analysis, cost-minimization analysis, etc.) were rarely used. In the course of the last five years, pharmacoeconomic methods have been used routinely, and such skills were transferred to the National EML Secretariat. Cost analysis of pharmacotherapeutic options in managing rheumatoid arthritis, hypertension, cardiac failure, diabetes mellitus type II, asthma, gastroesophageal reflux disease, schizophrenia, depression, Parkinson's disease, and several other areas was performed to better inform EML decisions. SPS recently supported the development of a pharmacoeconomic model that boosted the NDoH's ability to persuade a pharmaceutical company to reduce the price of an expensive oncology medication, rituximab, by nearly 50 per cent R 14,500 in 2006 compared with the 2012 price of R 7,950 for a 50-millilitre vial). As a result, the negotiated price is on a two-year tender and permits provinces to significantly increase access to this life-saving medication for various childhood cancers.²¹ SPS supported the NDoH in handling media enquiries about this important medicine selection decision to better inform the public.²²

The Minister of Health raised concerns about the high prices of antiretrovirals (ARVs) in relation to programme sustainability. SPS assisted the Ministerial Task Team on Medicines Procurement in conducting a comparison of national prices of ARVs with international prices. As a result of the international benchmarking exercise, price reductions of up to 65 per cent were obtained for four key ARVs.²³ The price savings in the 2010 South African ARV tender were multifactorial; economies of scale and stimulation of competition through the introduction of reference pricing appear to have played a role.²⁴

Medicine Use Evaluation Criteria

The American Society of Health-System Pharmacists²⁵ defines medicine use evaluation as a performance method that focuses on evaluating and improving medicine use for optimal patient outcomes. MUE is a proactive, criteria-based process that should be designed and managed by a multidisciplinary team and carried out in a systematic manner. The value and usefulness of the MUE rests on the relevance of the criteria and thresholds, as illustrated by the following example.

²¹ Supply and Delivery of Oncology and Immunological Agents to the Department of Health for the Period 1 April 2012 to 31 March 2014. Contract Number: HP04-2012ONC. Republic of South Africa.

²² State patients to benefit as Roche is persuaded to cut price of cancer drug, *Business Day*, 20 June 2012. <http://www.businessday.co.za/articles/Content.aspx?id=174530>

²³ B. Pharasi, G. Steel, and JP Sallet. 2011. Application of an International Reference Price List to National Medicines Procurement Tenders. Poster presented at the Third International Conference for Improving the Use of Medicines, Antalya, Turkey, November. <http://www.inrud.org/ICIUM/ConferenceMaterials/1159-steele-c.pdf>

²⁴ G. Steel, B. Pharasi, JP Sallet. and C. Van der Walt. 2012. Analyzing savings from the 2010 South Africa antiretroviral tender: Did increased volumes or reference pricing play a role? Poster presented at the 19th International AIDS Conference, Washington, DC, July.

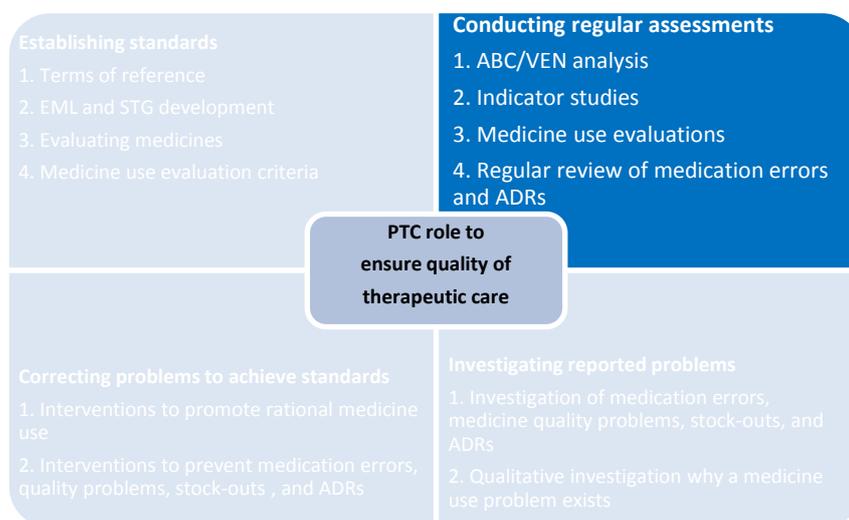
²⁵ American Society of Health-System Pharmacists. 1996. Guidelines on Medicine-Use Evaluation, *Formulary Management—Guidelines*, 163–65.

Provincial Level

SPS, in collaboration with the Eastern Cape DoH, planned the launch of the 2008 PHC edition of the EDL as an intervention to promote rational medicine use. Based on the prevailing cost at the time, one aspect of the new STGs was the restriction of tenofovir for patients who met specified criteria. One of the PharmD students from NMMU, under the supervision of an SPS senior programme associate, designed an MUE tool to assess the rational prescribing of tenofovir and used this tool to evaluate the outcomes of the EDL launch and an associated managerial intervention on the use of tenofovir. Ten sites were selected in the Amatole District, and data were collected on 556 patients enrolled in the tenofovir access programme during the study observation period. One of the findings was poor compliance with adherence assessment when initiating patients on tenofovir and the monitoring of renal functions.

This study offers one of the few examples of a technically sound MUE tool. Many local efforts omit the consultation of prescribers in setting the thresholds, and the findings are not deemed to be clinically significant. As judged by the MUE tool, the introduction of the intervention led to an average increase of 21.5 per cent in percentage compliance with the STGs. The study highlighted the need for a focus on adherence support measures and the development of a medicine safety culture in antiretroviral therapy programmes.

Conducting Regular Assessments



ABC/VEN Analysis

ABC analysis is a powerful tool by which items are compared according to their use over a set period of time and which allows for the identification of class A items (10 to 20 per cent of items that account for 70 to 80 per cent of funds spent). Knowing the value of such a tool, SPS strongly promotes the systematic use of ABC analysis as a means to detect the potential inappropriate use of medicines.

This section presents examples of PTCs that performed ABC analyses. As explained earlier, investigations and corrective interventions following findings from ABC analysis illustrate the third and fourth quadrant sections.

Provincial Level

The value of ABC analysis was demonstrated as part of the PTC training package. Subsequently, the Free State Provincial PTC required the Medical Depot (provincial medical stores) to provide results from the ABC analysis prior to every quarterly provincial PTC meeting. This information empowered the provincial PTC to monitor pharmaceutical expenditure and observe any significant variations from the norm. Thus, talking points with evidence are prepared prior to the meeting, and findings are routinely shared with PTC members to allow for ease in informed decision making.

Examples of use of ABC analysis for decision making by the Free State Provincial PTC include the following—

- The 2008 edition of the PHC Standard Treatment Guidelines and Essential Drug List specify that amlodipine is the preferred choice in the treatment for hypertension. High volumes of nifedipine 30 mg slow-release tablets were consumed despite issuance of the national guidelines. In the period May–July 2009, analysis showed that nifedipine 30 mg slow-release tablets consumed 3.6 per cent of total pharmaceuticals procured by the Free State Medical Depot. This signal prompted the PTC to request an annual ABC analysis for the period September 2008–August 2009. This analysis revealed that nifedipine was the second-most consumed item (214,394 items), valued at R 3,299,523.
- In August 2009, the 2008 STG for hypertension was brought to the attention of all health facilities. In April 2010, the provincial PTC decided to reinforce the message regarding the use of amlodipine, re-circulating the STGs for treatment of hypertension. Over time, amlodipine use steadily increased whereas the consumption of nifedipine 30 mg declined (table 4) because of improved compliance with the 2008 STGs for hypertension.

Table 4: Extracted Data from ABC Analysis on Nifedipine and Amlodipine Consumption

Financial year analysis		2007/2008 (12 months' data)	2009/2010 (12 months' data)	2010/2011 (12 months' data)	2011/2012 (3 months' data)
Nifedipine	Average monthly consumption	17,900	23,700	15,000	7,600
	Rank in top 100 items	2nd	12th	24th	43rd
Amlodipine	Average monthly consumption	Data not available	Data not available	13,000	36,750
	Rank in top 100 items	Not in top 100 ^a	Not in top 100 ^a	81st	24th

a. Provincial ABC analysis report allows only top 100 items; Medical Stock Administration System reporting system shortcoming.

ABC analysis is a standing item for the Rational Medicine Utilization sub-committee report on the GPPTC agenda. One of SPS staff presented an ABC analysis for each of the six larger hospitals in the province during the first meeting of the GPPTC. Subsequently, ABC analysis was performed for the items delivered directly to those six institutions because they are usually more costly. At a later stage, an ABC analysis was performed of use of anti-microbial agents in the province. An analysis by level of care followed the provincial one and assisted in designing targeted investigations.

Institutional Level

Dihlabeng Regional Hospital is a provincial general hospital based in Bethlehem, Thabo Mofutsanyane, and a Ministerial Priority District. It serves as a specialized referral facility for five district hospitals and renders basic clinic specialty services except psychiatry. The SPS predecessor project, RPM Plus, organized PTC training in early 2005. The Chief Pharmacist participated in this training and subsequently, in June 2005, the hospital established its PTC. In the first year, the PTC held its meetings on a quarterly basis. An ABC analysis was conducted to identify the main cost drivers for pharmaceuticals. Soon after, the benefits of the PTC became clear, and the management became interested in participating in PTC meetings. ABC analysis was used as evidence on which motivations for changes and improvement in practices could be based.

Further, to complement the on-going efforts on rational use of medicines through PTCs, the Rx Solution software was piloted in 2006. Rx Solution provided the necessary data and various reports on pharmaceutical management. The software was subsequently approved by provincial authorities in 2007 as the pharmaceutical data management software for the province. Rx Solution facilitates the routine performance of ABC analysis to inform decision making.

Examples of ABC analysis results at Dihlabeng Regional Hospital—

- Ciprofloxacin 100 ml IV appeared among the top 10 items in the ABC analysis. Because ciprofloxacin IV is not a hospital EDL item, this triggered a meaningful discussion among doctors on the rational use of this IV antimicrobial, leading to consensus on the correct use of ciprofloxacin IV.
- In early 2011, during a routine ABC analysis, the PTC found that the top three items consumed 11.2 per cent of the pharmaceutical budget, while the top six items cumulatively consumed nearly 18 per cent over a period of 12 months. Two expensive antimicrobials from the carbapenem group were found among the top six products.

Table 5: ABC Analysis: Top Six Items

Item (generic names)	Percentage of total expenditure
Total parenteral nutrition solution	4.27
Dipeptiven 20%, 100 ml	3.51
Ertapenem	3.50
Immunoglobulin IV (lyophilized powder for IV infusion)	2.73
Pantoprazole IV 40 mg	1.98
Imipenem/cilastatin 500 mg	1.98

At Kimberley Hospital, ABC analyses have been reported to all PTC meetings since 2008. A quarterly report on the expenditure on pharmaceuticals and oncolytics is presented at PTC meetings. This gives a good indication of measuring expenditure against budget.

Indicator Studies

In some instances, usage data are not easily accessible, making an ABC analysis difficult to conduct. The following examples illustrate how the PTC resorts to the study of different types of indicators to assess the rational use of medicines.

District Level

The Metro District PTC does not have access to consumption data. To identify potential inappropriate use of medicines, the PTC reviews procurement trends and uses the information to plan interventions. During one such routine review, the PTC discovered a high use of tramadol.

Institutional Level

During its monthly meetings, the Oudtshoorn Hospital PTC reviews the top 40 items, ranked by expenditure. High use of budesonide inhalers and high use of sodium valproate are two examples of problems identified through this review of the top 40 items. The average monthly use of medicines is also used as an indicator to detect items needing attention. In December 2010, the average monthly consumption of ceftriaxone was 300 packs, which is considered high in this hospital. Early in 2011 cefuroxime usage was also identified as high, with an average of 200 packs per month.

Medicine Use Evaluations

Although no doubt exists about the value of MUEs to improve rational medicine use, this time-consuming activity is not conducted routinely in the institutions because of the workload of the health care workers at facility level.

Provincial Level

After conducting an ABC analysis for the direct delivery items, the Rational Medicine Utilization sub-committee of the GPPTC identified the top six cost drivers among the EML items. An open-ended questionnaire was then sent to the hospitals to clarify the indications

for use of the six medicines in the institutions. Feedback from the hospitals showed an irrational use for five of the medicines. It was then agreed that quantitative data were needed to measure the extent of the problem. Medicine use evaluation tools have to be developed. The tool for the evaluation of use of polyvalent human immunoglobulin has been developed and was presented during the GPPTC third meeting.

The aim of the sub-committee is to build a system to promote rational medicine use within the Gauteng Province through systematic review of medicine use at local level. One way to achieve this goal is to provide the local PTCs with MUE tools developed by the sub-committee and assist them in implementing the evaluation. This process should build confidence and expertise at the local level.

District Level

In the West Coast district, institutional reports regarding irrational medicine use or any other issue are fed through the system to the district PTC. This feedback from professionals in the institutions allowed the district PTC to identify areas for intervention. Following the report of overuse of co-amoxiclav (a specialist restricted item) in some of the district's hospitals, the West Coast District PTC decided to conduct an MUE. To support this initiative, SPS conducted a workshop on MUEs in Citrusdal and trained pharmacists and doctors on how to conduct an MUE. The report of the MUE was compiled with SPS support. The results showing an overall irrational use of co-amoxiclav were discussed at the PTC during a follow-up meeting.

Institutional Level

At Oudtshoorn Hospital pharmacy, the increased volume of co-amoxiclav orders triggered the systematic review of prescriptions containing co-amoxiclav over a month. The dosage and indication from prescriptions containing co-amoxiclav were analysed for the month of June 2011. The use of co-amoxiclav was found to be irrational in 60 per cent of prescriptions. This analysis not only was presented in a PTC meeting but also was addressed in physicians' meetings, resulting in the issuance of guidelines for co-amoxiclav use.

According to the 2010 South African ARV guidelines, adult patients should be initiated on tenofovir and switched from stavudine to tenofovir unless stavudine is well tolerated. In Eastern Cape Province, the PTC of the Nelson Mandela Metropole²⁶ identified the implementation of this aspect of the guidelines as potentially problematic. Four students from the PTC elective course at NMMU undertook to assess the extent to which this switch was successfully made according to the 2010 South African guidelines. Using a purpose-designed data collection tool, they collected data from 165 adult patients' medical records in a municipal PHC clinic. The results showed that the guidelines were followed correctly in only 27 per cent of the sample (n = 165). The recommendations were that the underlying reasons for failure of the staff to follow the guidelines should be investigated and the appropriate measures taken to solve the situation (see Annex F).

²⁶ Sibabini Khatsha, Kushantha Govender, Sara Mustafa, Shabeerah Ramkhalawon, S-A. Boschmans, and J. McCartney. 2011. 2010 SA Antiretroviral Guidelines in a primary healthcare setting: Switching from stavudine to tenofovir (draft); research conducted for the course work elective entitled "Role and Functions of the Pharmaceuticals and Therapeutics Committee" at NMMU.

Regular Review of Medication Errors and ADRs

Medicine safety encompasses medication errors, ADRs, and poor medicine quality.

The PTC has responsibility for reviewing all medication errors to address individual incidents and look for patterns and trends to address health systems and managerial and environmental problems that may be encouraging such errors.²⁷

In practice, the ADRs are more commonly reported than the medication errors. The misunderstanding of the basis for medication error reporting might be one of the reasons. Of the examples below, only one illustrates the review of medication errors.

Provincial Level

Review of ADR reporting is a standing item on the GPPTC agenda and is presented by the Safety and Quality sub-committee. During the third meeting of the GPPTC, the Safety and Quality sub-committee reported the review of 25 ADRs. The sub-committee developed draft guidelines for ADR and quality reporting that were submitted for review to the full PTC. Once approved, the guidelines will assist the province in strengthening its reporting system while improving the quality of reporting.

In the Northern Cape, the CRC serves as a hub for the collation of reports of ADRs completed by clinicians in the hospital and surrounding facilities. All ADR forms received are captured into the CRC's pharmacovigilance database and then forwarded to the National Adverse Drug Event Monitoring Centre in Cape Town. A dedicated pharmacist who works at the centre prepares reports on the ADRs. These reports, together with relevant information from literature reviews, are submitted to the PTC for further review and action as needed.

District Level

To promote medicine safety, the Metro District PTC in the Western Cape has a policy to facilitate and report on ADRs. However, reporting on ADRs remains low. Individual reports are received, analysed, and compiled in a database. A need has been identified to assimilate the information from the database to the provincial and national pharmacovigilance system. This finding highlights the need for ADR reporting forms in each and every room and ward to facilitate reporting. The health care workers also need to be sensitized.

Institutional Level

The Dihlabeng Hospital's PTC showed its commitment to patient safety by implementing a medication error tracking tool consisting of 14 indicators for prescription errors, 5 indicators for dispensing errors, and 8 indicators for administration errors. One pharmacist was responsible for managing the medication error reporting activity. The activity was implemented in seven hospital wards. Once a month, the pharmacist would randomly select about five in-patient folders from each ward to audit them for medication errors and record them in a database. A prepared report was then presented during the PTC meeting. Initial findings on the major medication errors over a 12-month period are summarized in table 6.

²⁷ Kathleen Holloway (ed.) and Terry Green 2003. *Drug and Therapeutics Committees: A Practical Guide*. Geneva: World Health Organization and Management Sciences for Health.
<http://apps.who.int/medicinedocs/en/d/Js4882e/4.1.html>.

Table 6: Medication Error Findings over 12 Months

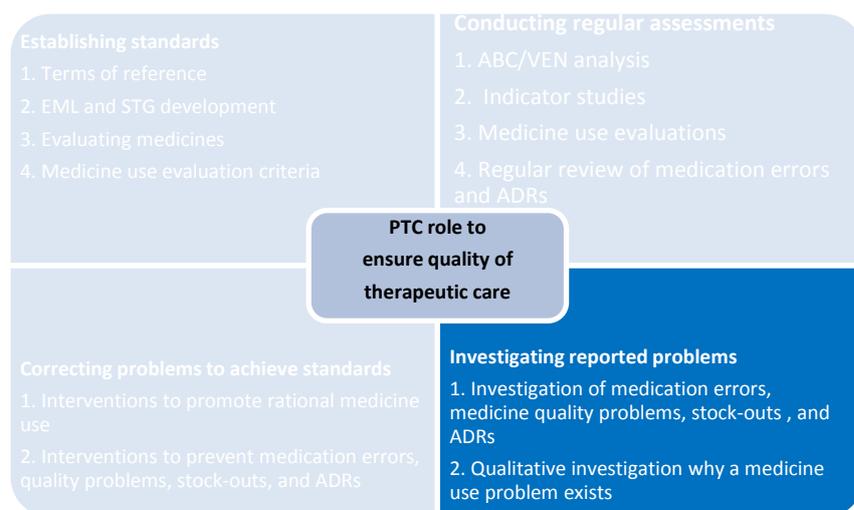
Prescription errors	Maximum dose exceeded Prescriptions not according to set regulation (Act) Incorrect dose prescribed
Dispensing errors	Failure to dispense prescribed drugs
Administration errors	Omission Administration schedule not according to prescription

The Free State Provincial PTC secretary and an SPS representative visited the Boitumelo Hospital in February 2011, in an attempt to improve the fluctuating functionality of its PTC with senior management. Orientation was provided on how to set the agenda and establish priorities such as medication error tracking and reporting.

At Oudtshoorn Hospital, after initial plans in November 2008, no ADR reports were received by the PTC in the period 2008–2009. ADR reporting started in December 2010 after physicians were carefully engaged with concomitant educational support by SPS. The processes and structures for ADR reporting were endorsed by the district PTC and the hospital PTC. Although only a few reports are received on a monthly basis, all personnel are kept informed and encouraged to complete the ADR forms and to submit them. Significant effort is required to orient, educate, advocate, and inspire staff to detect and report ADRs. For example, data on ADRs associated with enalapril along with proposed interventions to address them were communicated to authorities in George.

Hospital staff routinely observes any medicinal product deficiencies, such as badly sealed packages, bad taste, and fizz in paediatric cough syrups. Feedback from patients on acceptability of key medicines is also solicited, which resulted in an increase in product complaint forms completed and submitted to the district PTC every month.

Investigating Reported Problems



Once a problem has been detected and reported, the PTCs will support investigation on the cause and extent of the problem. The examples illustrate the need at this stage of the process for careful and sensitive planning, ensuring full collaboration from all health care workers involved.

Investigation of Medication Errors, Drug Quality Problems, Stock-Outs, and ADRs

Institutional Level

The information on the medication errors report was fed back to Dihlabeng Hospital's health care workers in the wards. They responded positively to the reports and improved their prescribing, dispensing, and administration practices. As a result of this exercise, it was identified that nurses employed through nursing agencies and who were not permanent staff complied poorly with policies and STGs, highlighting challenges faced as a result of high staff turnover.

Qualitative Investigation Why a Medicine Use Problem Exists

District Level

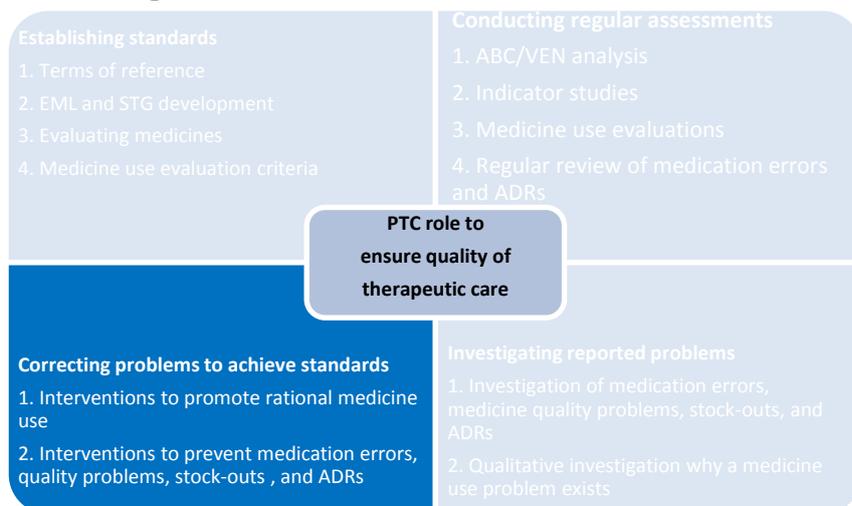
After investigation, it was discovered that the identified dosing medication error in paediatric dosing of anti-helminthic agents in some facilities of the West Coast district was linked to confusing guidance in the 2008 PHC EDL book.

Institutional Level

The pharmacist at Boitumelo Hospital attended the SPS-organized Pharmacy Leadership Development Program in 2011. Together with three pharmacists from four other hospitals in the Free State, they identified the "non-adherence to STGs and incorrect administration of antibiotics in the wards" as a problem. Using the challenge model, they listed their priority actions to address their challenge. The baseline assessment showed that less than 50 per cent of prescriptions comply with STGs.

The Oudtshoorn Hospital PTC decided to examine the prescribing patterns of sodium valproate to understand why this specialist initiated (except for HIV patients) and expensive item was systematically part of the top 40 items. There are no plans to restrict usage of sodium valproate; the main focus is on ensuring rational and safe use of the medicine.

Correcting Problems to Achieve Standards



Once the reason for the inappropriate or unsafe medicine use has been identified, the members of the PTC have to design and implement a corrective intervention. Then, at a later stage, they need to re-evaluate their standards before conducting the assessment. This is the fourth stage of an on-going process. The following examples illustrate the strategies implemented by the PTCs to correct their problems. Guidelines, policies, and SOPs seem to be at the heart of each intervention. This finding highlights the reluctance of some prescribers to willingly change their prescribing habits, leading to the need for a more formal intervention.

Interventions to Promote Rational Medicine Use

Provincial Level

In the Northern Cape, the CRC assisted the PTC in developing interventions to promote rational medicine use, such as the development of information charts for clinicians and patients (e.g., renal/hepatic dosing chart), the formulation of patient information or instruction sheets (e.g., correct use of steroid creams and ointments), and the development of protocols for antibiotics.

District Level

To improve the rational use of tramadol, the Metro District PTC introduced a guideline and restriction policy. Some prescribers, especially clinicians, are reluctant to comply with these measures. Similarly, guidelines for the rational use of H₂-antagonists were also issued.

The results of the MUE conducted by the West Coast District PTC showing an overall irrational use of co-amoxiclav were discussed during a follow-up meeting, and the district PTC introduced a restriction tool (motivation form) for co-amoxiclav as a management intervention to correct this trend.

Institutional Level

Following the identification of irrational medicine use, the Dihlabeng Regional Hospital PTC held an iterative series of five PTC meetings between May 2011 and March 2012 to discuss how to correct the problems. Corrective interventions were designed to target each problem and then implemented. The policy for total parenteral nutrition was changed in November 2011 so that only the Medical Officers can prescribe it and not the interns. In June 2011, a new policy was implemented that restricts the usage of pantoprazole. And finally, in October 2011, use of ertapenem, immunoglobulin IV, and imipenem/cilastatin were made subject to specialist approval.

Measuring a meaningful effect of any intervention takes time. The Dihlabeng PTC documented initial findings as shown in table 7.

Table 7: Decrease in Use of Ertapenem following Intervention

Item	Average monthly use (before interventions)	Average monthly use (after interventions)
Ertapenem 1 g	84	38 (less 54%)

Note: At the time of analysis, no significant improvement could be noted for other products.

An SOP for the prescription and administration of antibiotics was identified by the Boitumelo Hospital PTC as a tool to improve rational prescribing and administration of antibiotics. The SOP was drafted by the team members in collaboration with PTC members and other hospital staff. The SOP was approved by Boitumelo Hospital CEO in November 2011. In-service training on the new SOP was provided to doctors, nurses, and pharmacists and helped sensitize them on rational prescribing and administration of antibiotics in their wards. Raising awareness on the irrational prescribing and administration of antibiotics paved the way for implementation of corrective interventions. Rational prescribing and administration of antibiotics has been closely monitored over a 12-month period. The high staff turnover appears to be a brake on continuous improvement of rational prescribing and administration because the newly appointed staff are not systematically trained on the SOP. During a support visit, SPS took the opportunity to orientate the newly appointed head of department of internal medicine on the value of PTCs and the SOP for rational prescribing and administration of antibiotics.

The Oudtshoorn Hospital PTC introduced asthma peak-flow meters in consulting rooms to assist in the correct differential diagnosis between asthma and COPD (chronic obstructive pulmonary disease). Furthermore, continued education is provided to medical staff regarding asthma and COPD. These interventions improved the rational use of budesonide inhaler, thereby decreasing its use. The value of budesonide inhalers purchased was reduced by 41 per cent over a six-month period.

To correct the high use of cefuroxime and ceftriaxone, the PTC issued a circular reminding staff of the correct indications and use of ceftriaxone and cefuroxime. Subsequently, use of these important antimicrobials gradually reduced. For ceftriaxone, this represented approximately a 44 per cent reduction in use. Similar results are observed for cefuroxime, but reinforcement of correct indications through meetings with opinion leaders is necessary.

Doctors doing community service in the hospitals have a relatively high turnover rate. The new doctors were not aware of the antibiotics available at this level of care, resulting in the prescription of antibiotics reserved for level 2 or 3 hospitals. To assist the new staff members, the Oudtshoorn Hospital PTC compiled a three-page list of the antibiotics listed for level 1 hospital in the Western Cape Code List. This list of antibiotics available for level 1 hospitals was formally vetted through a PTC meeting along with consensus in the doctors' meeting. Periodic education was provided through telephonic support. As a result, physicians provided tremendous support to the rational use of antibiotics.

Interventions to Prevent Medication Errors, Quality Problems, Stock-Outs, and ADRs

Provincial Level

Information about a dosing medication error in paediatric dosing of anti-helminthic agents was reported to the West Coast District PTC. This error was ascribed to confusing guidance in the EDL STGs. The matter was reported to the Western Cape Provincial PTC, which developed and issued a more practical dosage protocol.

Institutional Level

Since 2008, pharmacovigilance is a standing item on the agenda of the Kimberley Hospital PTC as a means to promote medicine safety. Subsequently, a database of ADRs has been established and maintained by pharmacy personnel.

Findings from the medication error reports were used by Dihlabeng Regional Hospital to design interventions for medicine safety, including the development of policies and guidelines for the safe administration of medicines in the wards to make it easier for the nurses and doctors. Medication error reports will also now be presented at the Adverse Events Meetings of the facility. Because of the success in implementing the medication error tracking tool in Dihlabeng Regional Hospital, the Free State Provincial PTC approved the use of the tool by all health facilities.

To promote ADR reporting, the Oudtshoorn Hospital PTC bound the ADR forms with the Code List and placed them in strategic areas.

The role of pharmacists as part of the health care team in ward rounds is a new concept in the hospital and aimed at preventing medication errors. Pharmacists have the potential to review medication charts, check for accuracy of dose, assess potential side effects, monitor for potential drug-drug interactions, and so on. In addition, a documentation system was introduced to record products about to expire or at risk of stock-outs in wards; such information is transmitted to the main pharmacy, which can then act upon it. The Chief Pharmacist felt it is important to increase visibility of pharmacists and their role in provision of pharmaceutical care. With a surge in chronic cases, such as hypertension and diabetes, pharmacists can contribute to patients' quality of care. Significant effort was required to get buy-in from other hospital staff on the value of pharmacists as part of the health care team.

LESSONS LEARNED AND WAY FORWARD

According to international literature, the essential role of the PTC in promoting rational medicine use is uncontested. The examples gathered during the SPS programme as well as the lessons learned highlighted that further strengthening of the PTCs' responsibilities is necessary for a sustainable promotion of rational medicine use in the South African context.

Despite constraints such as staff turnover, workload, and absence of a dedicated budget to support PTCs, health care workers show their willingness to work toward implementing a patient-centred approach and ensuring quality of therapeutic care in the public sector. On the basis of its understanding of the PTC situation in the country and the lessons learned from health professionals, the SIAPS programme supports the following recommendations, because it firmly believes they could be the next step toward improving rational use of medicines in South Africa. Because rational use of medicines needs a concerted effort, each level of the health system has to be focused on. Each level of PTC has not only its own objectives and role within the health system, but also its own challenges. Hence this section presents the lessons learned, identifies the determinants for effective pharmaceutical management through PTCs, and proposes way forward by level.

Although this report strives to be a valuable tool for all health care workers in promoting rational medicine use, the following recommendations are intended for decision makers at each level.

National Level

Lessons Learned

The framework in figure 5 illustrates how use of medicines is at the heart of the health system. PTCs play a pivotal and vital role in promoting and ensuring rational medicine use. The provisions for this role are laid out in various policy documents and pieces of legislation in South Africa, including the National Drug Policy, the Public Finance Management Act, and the Pharmacy Act. Furthermore, the South African constitution provides “access to health care services” as a right for citizens. The National Core Standards, as part of the revamping and quality of health services provided, now make provision for the existence of PTCs to ensure rational medicine use.

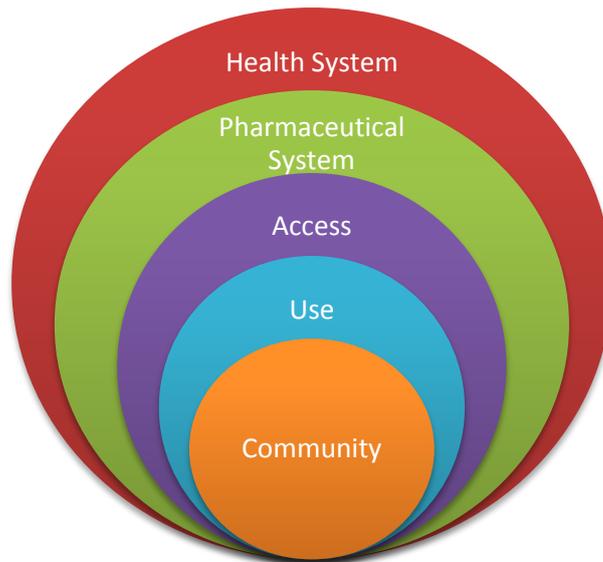


Figure 5. Health system framework adapted from MSH CPM-SPS framework, *The Pharmaceutical (Sub) System*

However, the overall picture of PTCs in the country shows that the currently available legislation is a necessary condition but is not sufficient. Although all PTCs should play their role in ensuring the quality of therapeutic care, as illustrated by the WHO framework, the examples presented in the previous sections highlight the gaps among the various PTCs. A high variability exists in terms of the functions performed, functionality, and communication strategy between the three levels of PTCs.

The TORs differ from one province to another, from one district to another, and from one hospital to another, which leads to great variations in the objectives and functions of PTCs. Variability also exists with regard to the position of the PTC Chairperson at provincial, district, and institutional PTCs. Chairing the PTC is linked more to a person's skills than to his or her position. This might be because the qualification of clinical executives varies from one institution to another. It could be in nursing, medicine, or physiotherapy. The commonality is, however, found with the Secretariat position, which is consistently held by a pharmacist. The involvement of top management to initialise and support the establishment or revitalisation of PTCs has proven to be a key success factor across the levels—for example, the Head of Department for the provincial PTC, the District Chief Directors for district PTCs, and hospital CEOs for institutional PTCs.

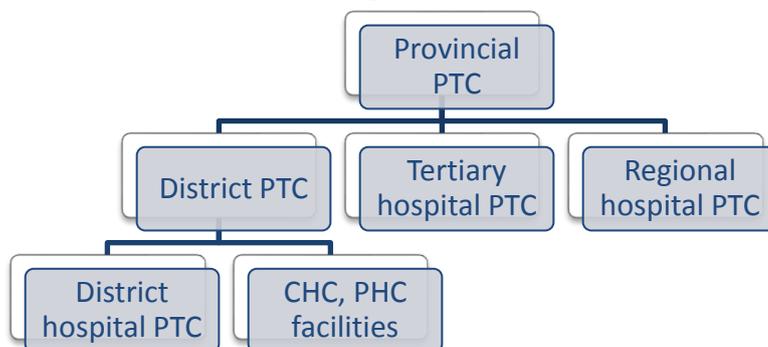
South Africa has three levels of PTCs: provincial, district, and institutional. The institutional PTCs refer to district, regional, and tertiary hospital PTCs. Although all three levels of PTCs can be found in the nine provinces, the communication strategy between the various levels differs from one province to another.

The common point is that the provincial PTC communicates directly with NEMLC and the PHC facilities communicate with district PTCs. However, the mechanism behind the link is not clear. Some CHCs and PHC facilities have a representative on the district PTC. Others have district pharmacists who are on the district PTC and assigned to be the link between the clinic and the PTC. The pharmacists report on PTC activities through outreach. Both mechanisms have advantages and pitfalls. Further clarification is needed on the links as well as how effective and monitored they are.

Four different models of communication were found across the country. The main variation between the models is the place of the district PTC in the communication strategy.

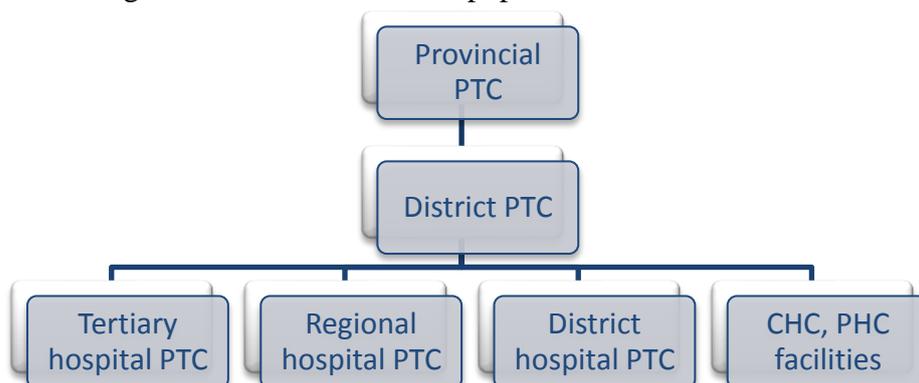
Two-Tiered Structures

The district PTC is at the same level as tertiary and district hospital PTCs. This type of structure is found in the Western Cape Province.



The district PTC plays a pivotal role between the provincial PTC and the institutional PTCs.

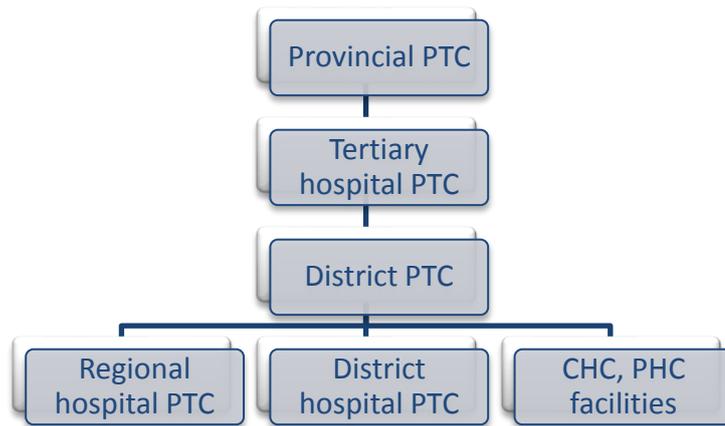
The following structure is found in Limpopo and North West Provinces.



The district PTC's functionality varies greatly from one district to another even within the same province. In the two-tiered structure, there is a greater risk of having a weak link in the communication strategy because of a poorly functional district PTC.

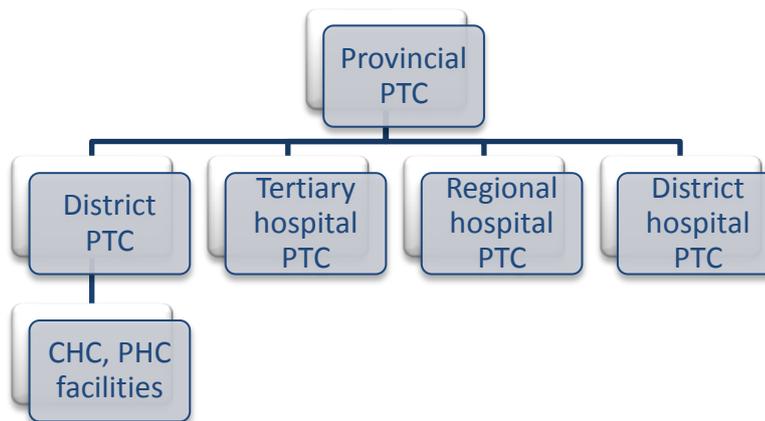
Three-Tiered Structure

In the Northern Cape Province, the tertiary hospital, which also serves as the main provincial hospital, plays a vital link because of its expertise.



“Flat” Structure

In Gauteng Province, the institutional PTCs and district PTCs report directly to the provincial PTC. This structure has been chosen because of the weakness of some of the district PTCs in the province. However, members of the district hospital PTCs sit at district PTC meetings. This structure has the advantage of minimising the responsibilities of the district PTCs within the overall communication strategy, hence minimising the risk of having a weak link in the structure.



Way Forward and Recommendations

To overcome the gaps and differences between the various PTCs, the functions, functionality, and communication strategy needs to be unified and standardised across the provinces. The current legislation available does not give clear indications on what functions the PTCs should perform at each level, how to measure functionality based on results, and what the best communication strategy is.

The development of a national policy on PTCs would provide the basis to answer those needs. Such a policy would provide the basis for embedding the responsibility for rational medicine use throughout the health system, using generic TORs to define the objectives and functions of the PTC at each level. This would harmonise functions, roles, and objectives for all PTCs at different levels based on the template TORs provided by the policy. It would assist in establishing a clear and coherent two-way reporting system between the National

EML Secretariat, provincial PTCs, institutional PTCs, and district PTCs. It would also elaborate the NDoH's role and commitment to support rational medicine through PTCs at the different levels in the health system.

Within the national policy on PTCs, it is recommended that an outcome-based definition of PTC functionality be developed.

The criteria on PTCs in the NCS and the PQII support a more process-based definition of functionality (e.g., the presence of a documented strategic plan, review of the formulary or code list, review of ABC analysis, medicine expenditure in the institution, and so on), making it difficult to link with results. The PTCs need to be more accountable. An outcome-based definition of functionality would be the starting point for the PTCs to develop their operational plans. It would also ensure that PTCs across levels and location work towards contributing to the same ultimate goal. The inclusion of the results of PTCs in the performance appraisal for the Head of Department at the provincial DoH will strengthen the support from top management for the establishment or revitalisation of PTCs; the same should apply for the district's chief directors. The provincial PTC could report on the implementation of its operational plan on a quarterly basis, using on specific indicators previously agreed on with the NEMLC.

Provincial Level

Lessons Learned

The revitalised GPPTC illustrates how the establishment of sub-committees can promote effectiveness. This structure can assist in tackling different areas of interventions simultaneously. The expertise of provincial PTC members is used in an optimum way. Each sub-committee develops its own action plan, which contributes to the overall provincial PTC operational plan, thereby re-enforcing the responsibility and accountability of each member towards the common goal. Furthermore, the frequent meetings of the sub-committee encourage active involvement from the members.

Very few provincial PTCs have an operational budget allocated by the provincial DoH. Some provincial PTCs rely on partners for catering, printing, access to reputable peer review journals, and sometimes also the travelling costs of their members. This can be a threat to sustainability.

The different provincial PTCs are unequal in terms of the skills represented; however, they are often faced with the same issues at different points in time. There is currently no systematic sharing of information between the provincial PTCs. The work conducted by the provincial PTCs across the provinces such as formulary, pharmacoeconomic evaluations, or MUE tools could be shared, building the capacity of other provincial PTCs' members.

Way Forward and Recommendations

The development of the recommended national policy on PTCs might be a relatively lengthy process. Meanwhile, the provincial PTCs can develop provincial SOPs for PTCs, including generic TORs that provide for the establishment of sub-committees as well as good governance tools. This will ensure alignment of functions and roles from the provincial to the

local (district and institutional) PTCs. The SOP will also provide guidance regarding the communication strategy between the different levels of PTCs in the province.

The provincial DoH should allocate an operational budget to the provincial PTC, in the same way that the NEMLC has an operational budget. This will not only promote sustainability but also institutionalise the provincial PTC in the provincial organogram.

Until the communication strategy is standardised through a national policy, a “flat” type of structure is recommended, unless all the districts in the province have strong PTCs. The disadvantage of the flat structure is the increase in responsibilities for provincial PTC members. They would have to support the local PTCs to ensure that their work contributes to implementation of the provincial PTC operational plan. This could be achieved by guidance provided to those PTCs for developing an operational plan in line with that of the provincial PTC. Guidance should also be provided on decision-making tools and operational research, such as MUEs to promote effective contribution of the district and institutional PTCs toward rational medicine use. In addition, the provincial PTC members should regularly conduct support visits to the district and institutional PTCs to ensure cohesion and avoid duplication of effort in the province. The district and institutional PTCs would report to the provincial PTC on a quarterly basis on indicators previously agreed upon.

The allocated budget for the operational activities of the provincial PTC should then take into consideration the field trips to hospitals and districts, besides the stationery, catering, and logistical fees involved with the provincial PTC meetings and interventions. It is also recommended that access fees to a reputable literature database be provided as part of the operational budget. Access to clinically relevant, up-to-date, user-specific, independent, objective, and unbiased evidence is a basic essential requirement for evidence-based decision making. Identifying and accessing sources of information on medicines is an important activity for a health system.

The development of a platform where the provincial PTCs can share useful information is recommended. Through the platform, the provincial PTCs could access, among other information, peer-reviewed literature used as evidence, pharmacoeconomic analysis, and MUE criteria from other provinces. This will strengthen the transparency of the decision-making process while leveraging time and effort. Such a platform could be accessible through the National EML Web page on the NDoH website.

The development of a capacity-building model around a “Centre of Excellence” could drive the process of strengthening effective pharmaceutical management through the PTC. The Centre of Excellence would be a chosen provincial PTC, serving as a reference point for other provincial PTCs in the country who could learn from it. This model would address the sustainability challenge and give South Africa ownership of the replication and diffusion of the best practices from the Centre of Excellence. A similar approach could be used for lower levels of PTCs. It could be arranged for SIAPS to support the establishment of such a model.

Local Level: District and Institutional Levels

Lessons Learned

The functions and roles of the local PTCs varied greatly from province to province, district to district, and hospital to hospital. Motivation of the pharmacist and support from top management at local level seem to be the winning combination.

The involvement of doctors in PTC activities at institutional level can be challenging if such activities are not strongly supported by the CEO of the hospital. Most of the examples show that PTC interventions have been initiated by hospital pharmacists. The focus of PTC training has been more on pharmacists, both at institutional and district levels, whereas a strong need exists to emphasise the benefits of PTCs among medical practitioners. Establishing or revitalising an institutional PTC needs more than a motivated trained pharmacist. Pharmaceutical services have an essential role to play in promoting the implementation of the SOPs on PTCs with generic TORs and good governance tools.

The institutional PTCs should support and/or conduct operational research to improve the rational use of medicines in the hospital. Investigating the reported problems is the first step toward correcting them and improving the situation.

A strong system for reporting ADRs is essential; information on medicine safety should play a key role in the maintenance of the hospital formulary. The establishment of sub-committees for rational medicine use, medicine safety, and infection prevention and control could be a means to strengthen the role of the PTC in these priority areas.

SIAPS acknowledges the need for customised workshops with PTC members, addressing the specific challenges of the PTC. Follow-up assistance has proven to be essential and will be of primary importance in support provided to PTCs. Inclusion of PTC and rational medicine use modules as part of pre-service training, for not only pharmacy but also medical students, will go a long way in embedding rational medicine use culture within the health system.

To institutionalize the district PTC within the district health system, the establishment of an operational budget is recommended because it will allow implementation of the operational plan. In the case where the district pharmacist is the link between facilities and the district PTC, the operational budget needs to take into account the travel costs for the district pharmacist to visit the facilities and be able to report the information back to the district PTC. To counter-act the high turnover of staff in the hospitals, it is recommended that the PTC be part of the institution's organogram.

ANNEXES

Annex A PTC-Related Standard, Criteria, and Measures in National Core Standards and Pharmacy Quality Improvement Initiative Questionnaires

Standard	Criteria	Measure (NCS and PQII)
<p>3.1.4 Medicines are prescribed according to treatment guidelines, and patients are educated to understand how to take their medicine.</p>	<p>3.1.4.1 There is functional PTC in the health establishment (hospital community health centre) or district (PHC clinics) that ensures quality use of medicine.</p>	<p>3.1.4.1.1 A document is available which details the membership and terms of reference of the multi-disciplinary PTC to optimize quality use of medicine in the health establishment.</p>
		<p>3.1.4.1.2 The minutes of the PTC demonstrate that actions have been taken to optimize the quality use of medicine.</p>
		<p>3.1.4.1.3 The PTC has a documented strategic plan.</p>
		<p>3.1.4.1.4 The decisions taken at the PTC are communicated to all stakeholders through various media.</p>
		<p>3.1.4.1.5 The PTC has guidelines on the information required in submissions for additions to the national/ or provincial formulary.</p>
		<p>3.1.4.1.6 The formulary code list has been critically reviewed by the PTC in the last 24 months.</p>
		<p>3.1.4.1.7 The PTC reviews cases of mortality thought to have been caused by preventable adverse drug reactions.</p>
		<p>3.1.4.1.8 The PTC has reviewed the ABC analysis of the institution or district (as applicable) in the last 12 months.</p>
		<p>3.1.4.1.9 Checklist evaluation of PTC statistics</p>
		<p>3.1.4.1.10 The PTC conducts audits of prescriptions to ensure accordance with Standard Treatment Guidelines every 12 months and communicates these outcomes to the health professionals of the establishment.</p>

Annex B PQII Assessment Questionnaire



Assessment Questionnaire (PQI)

Facility: Month:

PQI Pharmacy

Type Score Notes

Domain 1 Patients Rights: 1.5.1.2 Waiting times are monitored and improvement plans are implemented

1.5.1.2.3 CHECKLIST - Monitoring of patient waiting times for medicines	OBS		
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Domain 3 Clinical support services: 3.1.3.1 Medicines are stored and managed in compliance with the Pharmacy Act 53 of 1974 / Medicines and Related Substances Act 101 of 1965 / relevant rules and regulations

3.1.3.1.4 There is sufficient space in the refrigerator/cold room to store medication and provide adequate flow of cool air	OBS		
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Domain 3 Clinical support services: 3.1.3.5 There is an up-dated computerised or manual (stock cards) inventory management system for medical supplies in place

3.1.3.5.4 There is an up-to-date records of dispensing - either computerised or manual	DA		
3.1.3.5.5 There is record of the number of stock outs per day kept	DA		
3.1.3.5.6 There is record of the patients who have left the pharmacy without their medication due to stock outs with contact details so their can be followed up once stock arrives	DA		
3.1.3.5.7 CHECKLIST Management and records of stock outs	stats		

Domain 3 Clinical support services: 3.1.4.1 There is a functional Pharmacy and Therapeutics committee in the health establishment (hospital / CHC) or in the district (PHC clinics) that ensures quality use of medicines

3.1.4.1.3 The PTC committee has a documented strategic plan	DR		
3.1.4.1.4 The decisions taken at the PTC are communicated to all stakeholders through various media	DR		
3.1.4.1.5 The PTC has guidelines on the information required in submissions for additions to the national/provincial formulary	DR		
3.1.4.1.6 The formulary/code list has been critically reviewed by the PTC (institutional/district/provincial) in the last 24 months	DR		
3.1.4.1.7 The PTC reviews cases of mortality thought to be due to preventable adverse drug reactions and/or medication errors	DR		
3.1.4.1.8 The PTC has reviewed the ABC analysis of the institution/district/province (as applicable) in the last 12 months	DR		
3.1.4.1.9 CHECKLIST evaluation of the PTC statistics	Stats		
3.1.4.1.10 The PTC conducts audits of prescriptions to ensure accordance with standards treatment guidelines every 12 months and communicates these outcomes to the health professionals in the establishment	DA		

Domain 3 Clinical support services: 3.1.4.3 Patients are counselled appropriately to ensure adherence to therapy

Facility: **Month:**

3.1.4.3.2 CHECKLIST Patient satisfaction with services and access to services	PI		
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Domain 3 Clinical support services: 3.1.4.4 Prescribing is done in accordance with applicable guidelines and policies

3.1.4.4.2 CHECKLIST The pharmacy/clinic has copies of or electronic access to standards treatment guidelines and formularies	DR		
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3.1.4.4.3 CHECKLIST Audit of compliance of patient records to standards treatment guidelines	DA		
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Domain 3 Clinical support services: 3.1.5.1 There is a clear system for the management of adverse drug reactions

3.1.5.1.3 The establishment can show records of the number of medication errors reported in the last 12 months	DA		
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3.1.5.1.4 The establishment can show records of the number of adverse drug reactions reported in the last 12 months	DA		
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Annex C PQII PTC Checklist

3.1 Pharmaceutical services

The prescribing and dispensing of medicines comply with relevant regulations and protocols and promote the quality use of medicine

Number of checklist	Criterion	Checklist reference	Measure	
3.1.4.1.9 Integrated audit	There is a functional Pharmacy and Therapeutics committee in the health establishment that ensures quality use of medicines	Pharmaceutical and therapeutics committee	CHEKLIST evaluation of the PTC statistics	
Number of questions	Planned number of responses	Unit where assessed	Type of assessment	
9	1	CD4 CC04 CX04	OBS	
Instructions: Through the documentation of the pharmaceutical and therapeutics committee gather the following information and statistics.				
No.	Question / Aspect	No.	Description	Comments
1	No of meetings of PTC held during the last calendar year as evidenced by minutes			
2	No of meetings of PTC which were quorate			
3	No of PTC members who attended at least 75% of meetings during the last calendar year			
4	Total number of members of the PTC in the last calendar year			
5	Methods of communication used to communicate decisions of the PTC to stakeholders			
6	Number of submissions for addition to the formulary considered by the PTC in the last calendar year			
7	Number of submissions for addition to the formulary approved by the PTC in the last calendar year			
8	Number of copies of adverse drug reaction (ADR) reports forwarded to the national data base in the last calendar year			
9	No of drug utilisation reviews (DURs) done per annum			
10	Number of complaints relating to the quality of products considered by the PTC in the last calendar year			
11	Medicine expenditure of the institution/district/province (as applicable) in the last financial year		R	
12	No of patients served by the institution/ district/province (as applicable) during the last financial year			
13	Expenditure on motivation items in the institution/district/province (as applicable) in the last financial year (TO BE DEFINED)		R	
14	Percentage of prescriptions in accordance with standard treatment guidelines (as per survey conducted in the last 12 months)			
Actual Score (Sum of positive responses)				
Maximum possible score (Sum of all questions minus the not applicable responses)				

Annex D NCS Pharmacy Assessment Questionnaire (Hospital)



health

Department
of Health
REPUBLIC OF SOUTH AFRICA

Assessment Questionnaire (Hospital)

Facility: Month:

C04 Pharmacy

Type Score

Notes

Domain 1 Patients Rights: 1.5.1.1 Procedures are followed to ensure queues are kept short

1.5.1.1.1 A queue manager or marshal or triage officer is available to assist patients in the queue where to sit

OBS

E

1.5.1.1.2 A queue marshal informs the patient approximately how long he or she will wait OR the current waiting time is displayed on a board

OBS

E

Domain 1 Patients Rights: 1.5.1.3 Patients obtain their medicines from the pharmacy on the day of their scheduled visit

1.5.1.3.1 CHECKLIST - 10 random selected scripts in pharmacy are correlated with medication dispensed to ensure that all medication was received as prescribed

PI

V

Domain 1 Patients Rights: 1.5.1.4 Patients are sorted / classified and attended to according to the severity and nature of their health condition or problem

1.5.1.4.3 Observe whether special queues are designated for specific groups of patients

OBS

E

Domain 1 Patients Rights: 1.5.1.5 An efficient filing system is in place

1.5.1.5.1 Trends in waiting times for files show an improvement over time

DA

E

Domain 2 Patient Safety / clinical governance / clinical care: 2.3.1.2 There is a formal supervision programme for healthcare professionals

2.3.1.2.2 Healthcare professionals specifically pharmacists and radiographers indicate that they have access to adequate supervision

SI

E

Domain 2 Patient Safety / clinical governance / clinical care: 2.4.3.4 The safety of patients receiving medication is assured

2.4.3.4.1 A protocol regarding the safe administration of medicines to patients is available including a protocol for the safe administration of medicines to children

DR

V

Domain 3 Clinical support services: 3.1.1.1 Pharmacy has been licensed by the Director General of the National Department of Health

3.1.1.1.1 There is a copy of the licence issued by the Director-General of the National Department of Health (hospitals and CHCs)

DR

D

Domain 3 Clinical support services: 3.1.1.2 Pharmacy is recorded with the South African Pharmacy Council

3.1.1.2.1 There is a copy of the current certificate of recording of the pharmacy with the South African Pharmacy Council (hospitals and CHCs)

DR

D

Domain 3 Clinical support services: 3.1.1.3 A responsible pharmacist is designated and registered as such with the South African Pharmacy Council

3.1.1.3.1 There is a copy of the current registration certificate of the responsible pharmacist with the South African Pharmacy Council (hospitals and CHCs)

DR

D

Domain 3 Clinical support services: 3.1.2.1 Medicines required for care of patients accessing the health establishment are in stock (in accordance with applicable Essential Drugs List or formulary)

Facility: Month:

3.1.2.1.1 CHECKLIST - Tracer medicines as per applicable Essential Drugs List or formulary are available in the pharmacy/medicine room	OBS	
	V	

Domain 3 Clinical support services: 3.1.2.2 Medical supplies required for care of patients accessing the health establishment are in stock

3.1.2.2.1 CHECKLIST - Tracer medical supplies are available in the area where medical supplies are stored	OBS	
	E	

Domain 3 Clinical support services: 3.1.2.3 Designated supplier(s) and delivery systems for medicines adhere to contractual obligations for the supply and delivery of medicines

3.1.2.3.1 A document outlining the terms of agreement for the supply of medicine is available and there is evidence that compliance with the agreement is being monitored and appropriate action taken as necessary also look for medicine stock	DA	
	E	

3.1.2.3.2 A document outlining the delivery schedule for medicine is available	DR	
	E	

Domain 3 Clinical support services: 3.1.2.4 Designated supplier(s) and delivery system for medical supplies adhere to contractual obligations for the supply and delivery of medical supplies

3.1.2.4.1 A document outlining the terms of agreement for the supply of medical supplies is available and there is evidence that compliance with the agreement is being monitored and appropriate action taken as necessary (check stock-outs)	DA	
	E	

3.1.2.4.2 A document outlining the delivery schedule for medical supplies is available	DR	
	E	

Domain 3 Clinical support services: 3.1.2.5 Access to medicines is ensured during operating hours of the health establishment

3.1.2.5.1 Duty rosters indicate that at least one pharmacist in pharmacies or pharmacist's assistant or professional nurse in clinics is on duty and available to dispense medicine as required during opening hours	DR	
	E	

Domain 3 Clinical support services: 3.1.2.6 Health care professionals have access to medicines required urgently by patients after hours

3.1.2.6.1 A standard operating procedure is available which indicates how health care professionals can access medicines when the pharmacy is closed	DR	
	E	

3.1.2.6.2 The name and contact details of the pharmacist on duty for the provision of services after hours is available	OBS	
	E	

3.1.2.6.3 There is a locked emergency cupboard for the supply of medicines needed after hours	OBS	
	E	

Domain 3 Clinical support services: 3.1.3.1 Medicines are stored and managed in compliance with the Pharmacy Act 53 of 1974 / Medicines and Related Substances Act 101 of 1965 / relevant rules and regulations

3.1.3.1.1 CHECKLIST - Medicine is stored correctly as per Good Pharmacy Practice	OBS	
	E	

3.1.3.1.2 CHECKLIST - Procedures relating to the management of medicine as required by Good Pharmacy Practice are followed in the pharmacy	OBS	
	E	

Domain 3 Clinical support services: 3.1.3.2 There is an up-dated computerised or manual (stock cards) inventory management system for medicines in place

3.1.3.2.1 The stock control system stock cards or computerised system shows minimum and maximum or re-order levels for medicines	OBS	
	E	

3.1.3.2.2 CHECKLIST - Physical stock corresponds to stock on the inventory management system as per checklist 31211	OBS	
	E	

3.1.3.2.3 There is evidence that a stock take was done in the last 12 months for medicines	DR	
	E	

Facility: Month:

Domain 3 Clinical support services: 3.1.3.3 Schedule 5 and 6 medicines are controlled and distributed in accordance with the Medicines and Related Substances Act 101 of 1965 and Good Pharmacy Practice guidelines

3.1.3.3.1 A standard operating procedure is available which indicates how schedule 5 and 6 medicines are stored / controlled / distributed in accordance with the Medicines and Related Substances Act 101 of 1965	DR E		
3.1.3.3.3 The entries in the schedule 6 drug register are complete and correct Check that physical stock of one S6 medicine corresponds to the quantity in the register	OBS E		

Domain 3 Clinical support services: 3.1.3.4 Medical supplies are stored and managed in compliance with medicine supply chain management principles

3.1.3.4.1 There is a procedure relating to the management of medical supplies	DR E		
3.1.3.4.2 CHECKLIST - Medical supplies are stored correctly	OBS E		

Domain 3 Clinical support services: 3.1.3.5 There is an up-dated computerised or manual (stock cards) inventory management system for medical supplies in place

3.1.3.5.1 The stock control system stock cards or computerised system shows minimum and maximum or re-order levels for medical supplies	OBS E		
3.1.3.5.2 CHECKLIST - Physical stock corresponds to stock on the inventory management system as per Checklist 31221	OBS E		
3.1.3.5.3 There is evidence that a stock take was done in at least the last 12 months	DR E		

Domain 3 Clinical support services: 3.1.4.1 There is a functional Pharmacy and Therapeutics committee in the health establishment (hospital / CHC) or in the district (PHC clinics) that ensures quality use of medicines

3.1.4.1.1 A document is available which details the membership and terms of reference of the multidisciplinary Pharmacy and Therapeutics committee (PTC) to optimise quality use of medicine in the health establishment	DA D		
3.1.4.1.2 The minutes of the Pharmacy and Therapeutics committee demonstrate that actions have been taken to optimise the quality use of medicine	DR E		

Domain 3 Clinical support services: 3.1.4.2 Practices for dispensing medicines comply with the Pharmacy Act 53 of 1974 / Medicines and Related Substances Act 101 of 1965 / relevant regulations

3.1.4.2.1 A standard operating procedure is available which outlines the dispensing of medicines according to the Pharmacy Act 53 of 1974 and Medicines and Related Substances Act 101 of 1974	DR E		
3.1.4.2.2 A standard operating procedure is available for the compounding of medicines including extemporaneous compounds / cytotoxics and TPN as applicable	DR E		
3.1.4.2.3 CHECKLIST - Dispensing is done in accordance with applicable policies and legislation including labelling	OBS V		
3.1.4.2.4 CHECKLIST - The labels of medicines dispensed for patients comply with legislative requirements as per Checklist 31423	OBS V		

Domain 3 Clinical support services: 3.1.4.3 Patients are counselled appropriately to ensure adherence to therapy

3.1.4.3.1 CHECKLIST - A random selection of 10 patients receiving medicine indicate that they have a clear understanding of how and when to take their medication and any other relevant information - Generic outpatient checklist	PI V		
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Domain 3 Clinical support services: 3.1.4.4 Prescribing is done in accordance with applicable guidelines and policies

3.1.4.4.1 CHECKLIST - A random selection of 10 prescriptions audited shows that prescribing is done to facilitate rational use of medicine and in accordance with prescribing guidelines and policies	PRA V		
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Facility: **Month:**

Domain 3 Clinical support services: 3.1.5.1 There is a clear system for the management of adverse drug reactions

3.1.5.1.1 There are standard operating procedures for the monitoring of adverse drug reactions

DR		
E		
DA		
V		

3.1.5.1.2 The minutes of the committee which deals with adverse drug reactions demonstrates that actions have been taken to report / analyse and take appropriate action regarding adverse drug reactions

Domain 4 Public Health: 4.4.1.3 Disposal procedures ensure that toxic chemicals / radioactive waste / expired drugs are safely disposed of

4.4.1.3.1 The establishment has a service level agreement for the safe disposal of toxic chemicals / radioactive waste and expired drugs with an accredited service provider and the service levels are monitored for compliance

DA		
D		

Domain 7 Facilities and Infrastructure: 7.1.3.1 Waiting areas are appropriately located and adequate for the number of patients using them

7.1.3.1.1 The waiting area has adequate space / heating / number of chairs to accommodate all patients in the area

OBS		
E		

7.1.3.1.2 Waiting areas are located in the areas where the service takes place

OBS		
E		

Annex E NCS Rational Prescribing Checklist

3.1 Pharmaceutical services

The prescribing and dispensing of medicines comply with relevant regulations and protocols and promote the quality use of medicine

Number of checklist	Criterion	Checklist reference	Measure			
3.1.4.4.3	Practices for dispensing medicines comply with the Pharmacy Act 53 of 1974, Medicines and Related Substances Act 101	Standard treatment guidelines audit of patient records	CHECKLIST An audit of patient records shows compliance with standard treatment guidelines			
Number of questions	Planned number of responses	Unit where assessed	Type of assessment			
9	1	C04 C04 CX04	DR			
Instructions: Check if the patients have received medication in line with approved standard treatment guidelines. Mark Y for Yes if they are compliant and in N for No if not compliant.						
Patient file	Diagnosis or symptom (write it exactly as stated on the prescription)	Item (write it exactly as stated on the prescription)	Dispensed by pharmacist/ pharmacist's assistant/ nurse/dr	Qty or regimen indicated (write it exactly as stated in the STG)	Item on EDL or Provincial/ Institutional Formulary? (Yes/No)	Treatment complies with approved STGs? (Yes/No)
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						
16						
17						
18						
19						
20						
Actual Score (Sum of positive responses)						
Maximum possible score (Sum of all questions minus the not applicable responses)						20

Annex F 2010 South African Antiretroviral Guidelines in a Primary Care Setting: Switching from Stavudine to Tenofovir (draft)

Abstract

The revision of the South African antiretroviral (ARV) guidelines in April 2010 incorporated a change in the first-line treatment regimen by replacing stavudine with tenofovir according to international recommendations. Insufficient local research has been undertaken to assess the level of implementation of the 2010 ARV guidelines in the public sector. However, because of the challenges posed by highly active antiretroviral therapy (HAART), the Pharmaceuticals and Therapeutics Committee (PTC) of the Nelson Mandela Metropole identified implementation of the switch from stavudine to tenofovir as potentially problematic. This study aims to assess the extent to which this switch was successfully made according to the 2010 guidelines. The study was conducted at a primary health care clinic identified by the PTC. The study population consisted of 165 adult patients who had been on ARVs for at least six months. A quantitative, retrospective review of the antiretroviral therapy regimens prescribed at the municipal clinic was performed. Data were collected from the clinic-held patient records over two weeks during July and August 2011. The information was gathered using a purpose-designed data collection tool, standardised prior to the data collection process. Statistical analysis revealed that only 17 per cent of the population sample (n = 165) was correctly switched to tenofovir from stavudine and a further 10 per cent of the sample (n = 165) was correctly initiated on tenofovir after the 2010 revision. This means that in only 27 per cent of the sample (n = 165) the guidelines were followed correctly. Tenofovir should have been prescribed in a higher percentage of patients in the year following the introduction of the 2010 guidelines. A second significant finding of the study was that the adherence rate was less than 83 per cent in 70 per cent of the population (n = 165). The research indicates a need not only for training of clinic personnel but also for education of patients concerning the importance of adherence to antiretroviral therapy.

Introduction

Background and Rationale

HIV/AIDS has become a worldwide pandemic warranting urgent attention (Jurgens 2007). South Africa was classified as the country with the highest prevalence of HIV in 2009, with an estimated population of 5.6 million people infected with HIV (UNAIDS 2010). Statistics depicting HIV/AIDS prevalence vary in the different provinces with Mpumalanga and Kwazulu Natal having the highest prevalence and the Western and Northern Cape having the lowest (Nicolay 2008). The Eastern Cape had the third largest population with HIV with an estimate of 729,000 people infected with HIV in 2008 (Nicolay 2008). The negative impact of HIV/AIDS in the country is reflected, among other items, by increased mortality caused by the disease: an estimated 310,000 people in 2009 (UNAIDS 2010).

Because of these alarming statistics, South Africa has one of the largest ARV treatment programmes in the world (WHO/UNAIDS/UNICEF 2010). In an effort to address the HIV scourge, the South African government has put stringent policies in place for the management of ARV treatment (International NGO Training and Research Centre 2008). However, the high demand for ARVs outstrips treatment delivery: of the total number of people eligible for therapy, only an estimated 37 per cent were actually receiving treatment at the end of 2009 (WHO/UNAIDS/UNICEF 2010). Statistics show a “treatment

gap” between the number of people who are in need of antiretroviral therapy and the patients who are actually receiving treatment. Provinces with the largest treatment gap were Kwazulu Natal and Gauteng, followed by the Eastern Cape (Nicolay 2008). The Eastern Cape provided treatment for only 44 per cent of the HIV-infected population eligible for therapy in 2008. The treatment gap contributes to the rising numbers of people with HIV and ultimately results in a higher mortality rate (Nicolay 2008). Numerous debates have been initiated since 2009 in South Africa concerning earlier initiation of ARV treatment; that is, when patients have a CD₄ count of fewer than 350 cells/mm³ instead of the threshold of 200 cells/mm³ at which treatment was previously initiated. However, the concern was that South Africa had not been able to meet the current demand for antiretroviral therapy with a treatment threshold of 200 cells/mm³. The country still seriously lags in terms of treatment delivery. Therefore the emphasis was to get more people on effective treatment rather than to initiate treatment at an earlier stage of the disease (Alcorn 2009).

Accordingly, the national ARV guidelines are under continuous review in South Africa to apply the latest available evidence-based practice in line with international recommendations (Department of Health 2006). Following the World Health Organization (WHO) recommendations made in 2005, relating to the management of HIV/AIDS, the South African National Department of Health implemented a change in April 2010 to the recommended first-line ARV regimen. The first-line regimen before the 2010 guidelines consisted of a combination of stavudine, lamivudine, and efavirenz. The change that was introduced was the replacement of stavudine with tenofovir. Tenofovir was to be used in combination with lamivudine and efavirenz. However, despite its more tolerated side effect profile, tenofovir carries the risk of long-term toxicity, and the switch needs to be applied in relation to patients’ individual needs. In addition, several potential problems arise from the challenges posed by the use of HAART that makes the implementation of the revised guidelines complex. Potential problems had been identified by the Nelson Mandela Metropole PTC. These included the competence of the clinic personnel to implement the switch from stavudine to tenofovir; the availability of tenofovir in the primary clinics, and the consumption of the remaining stavudine stock.

Problem Statement

Clearly, the above-mentioned problems would significantly hinder the smooth implementation of the 2010 ARV guidelines. It is essential therefore to assess whether the guidelines are being strictly implemented and followed in the public sector. Since the change in the guidelines was published in April 2010, little local research has been done to assess this adherence.

Research Objectives

In an attempt to address this information gap, the primary aim of the study is to evaluate the implementation of the switch from stavudine to tenofovir according to the 2010 Clinical Guidelines for the management of HIV and AIDS in adults and adolescents in a primary health care setting. A secondary aim of the study is to assess patient compliance with antiretroviral therapy.

Contribution to the Field

The study is a retrospective review of the use of ARVs in patients with HIV/AIDS at a municipal clinic. The findings of the research indicate that the implementation of the switch from stavudine to tenofovir

has been inadequate. The recommendations will assist in improving the provision of ARV treatment. The findings and recommendations were made available to the PTC of the relevant Metro. In addition, the outcomes of the research could trigger further studies in other regions of South Africa to assess whether a similar trend exists.

Literature Review

Challenges Posed by the Use of HAART

The use of HAART enables chronic management of HIV. The markers used to assess the clinical efficacy of the therapy include an increase in CD₄ count and a reduction in plasma viral load to undetectable levels. However, the challenge posed by the use of HAART remains the advent of side effects in the long term (Gallant et al. 2004).

Studies investigating the long-term effects of the nucleoside reverse transcriptase inhibitor (NRTI) stavudine have reported common toxicity results. Stavudine causes mitochondrial toxicity through its metabolism from a pro-drug to the active form (WHO 2009). More specifically, stavudine, a thymidine analog, inhibits the polymerase enzyme in mitochondria in adipocytes. The adipocyte tissue found in the nerves, liver, and pancreas is most affected (WHO 2009). Thus stavudine use may lead to peripheral neuropathy, lactic acidosis, pancreatitis, and lipodystrophy, which are the more severe adverse effects associated with stavudine use (WHO 2009).

Because of the relatively low cost involved, stavudine has been widely used in the public sector in South Africa and has long formed an important part of the first-line regimen for HAART (WHO 2009). However, this advantage is now outweighed by stavudine's toxic effects. With respect to evidence-based practice, the 2010 South African ARV Guidelines state that the side effects for which patients on stavudine should be monitored include peripheral neuropathy, or paraesthesia; lipodystrophy; lactic acidosis, or hyperlactataemia; hepatic steatosis, or fatty liver; and pancreatitis. If these effects are severe or life threatening, therapy should be discontinued immediately and the patient treated symptomatically (NDoH 2010). The seriousness of these side effects has warranted the switch to another NRTI, specifically tenofovir (Conradie, Ive, and Sanne 2005).

Thus, patients who are on stavudine need to be assessed for these adverse effects, and if they present, treatment must be switched from stavudine to tenofovir. Certain contraindications to the use of stavudine also require the use of tenofovir instead of stavudine. These contraindications are body mass index (BMI) greater than 28 units, symptoms of peripheral neuropathy, and a history of severe toxicity with the use of stavudine. Both these drugs have a similar mechanism of action with comparable efficacy (Gallant et al. 2004). Tenofovir, however, has a better tolerated side effect profile than stavudine (Gallant et al. 2004).

Although the recommendations of the WHO to switch from stavudine to tenofovir were published in 2005, South Africa incorporated the change only in 2010. The reason behind this delay is that tenofovir disoproxil fumarate was not registered in South Africa in 2005 (Conradie, Ive, and Sanne 2005). Since the amendment to the ARV regimens in April 2010, tenofovir has been included as part of the first-line regimen in combination therapy with lamivudine and efavirenz in the public sector in South Africa (NDoH 2010). A concern has been raised regarding the high cost of tenofovir as compared to stavudine.

However, a pharmacoeconomic study that investigated this issue was presented at the 4th International Workshop on HIV Treatment, Pathogenesis and Prevention Research in Resource-Poor Settings and concluded that tenofovir was cost-effective in the long term in South Africa (Marais et al. 2010).

The revised 2010 WHO ARV Guidelines stressed that countries still using stavudine should reduce its use in their first-line regimen because of related toxicities (WHO 2010). Nlooto (2010) investigated the recommended dosage reduction of stavudine from 40 mg twice daily to 30 mg two times a day between August 2004 and January 2006. The stavudine dose decrease resulted in a reduction in the occurrence of severe side effects (Nlooto 2010). Patients were more stable on their therapy, and mortality from complications of lactic acidosis was reduced. It could be deduced that the toxicity of stavudine is therefore dose related (Nlooto 2010). However, the 2010 ARV Guidelines did not advise a lowering of the dose of stavudine in patients experiencing side effects. Instead, the 2010 South African ARV Guidelines recommended that a switch from stavudine to tenofovir be made if stavudine side effects were severe and did not resolve within a short time. The offending drug (stavudine) should then be replaced with a drug within the same class that does not have the same adverse reaction; in this case tenofovir was selected (NDoH 2010). South Africa made the switch to tenofovir from stavudine in April 2010.

Tenofovir has a relatively more tolerable side effect profile than stavudine (Schooley et al. 2002). However, tenofovir may cause renal toxicity within five weeks of initiation of therapy (Roussow et al. 2010). Thus, as stated in the 2010 guidelines, only patients with a creatinine clearance greater than 50 ml/minute are eligible to start tenofovir (NDoH 2010). Creatinine clearance is a better marker than plasma/serum creatinine level for assessing renal function because in elderly patients and those with low body weight, the serum creatinine could be in the normal range whilst kidney functionality is reduced (NDoH 2010). Following implementation of therapy with tenofovir, renal function should be assessed on a regular basis.

According to various guidelines, regular check-ups need to be made after a three-month and a six-month period on ARVs (Roussow et al. 2010). However, renal toxicity can occur after a minimum of five weeks of therapy; thus earlier kidney tests are recommended (Roussow et al. 2010). Risk factors such as an underlying kidney problem; age older than 40 years; certain co-morbid conditions, for example, diabetes mellitus and hypertension; concurrent use of nephrotoxic drugs; and BMI less than 18.5 kg/m² predispose patients to renal dysfunction (WHO 2010). An important aspect that is not included in the South African 2010 ARV Guidelines is the recommendation for electrolyte monitoring because of the possible development of Fanconi Syndrome in immune-compromised patients with the use of tenofovir (Mathew and Knaus 2006).

Thus although stringent guidelines have been implemented to support the switch from stavudine to tenofovir in the South African public sector, no studies have yet confirmed the correct implementation in a primary health care setting. The updated 2010 South African ARV guidelines recommended that stavudine be replaced with tenofovir if there are no contraindications to tenofovir use. Because of the renal toxicity caused by tenofovir, creatinine clearance must be assessed prior to tenofovir implementation. If the patient is not eligible for tenofovir or no side effects are experienced with stavudine, then treatment with stavudine is continued (NDoH 2010).

In fact, the cornerstone for treatment efficacy remains adherence to antiretroviral therapy (Frank and Duncan 2009, 1). Adherence to therapy can be defined as the extent to which a patient follows the medicine regimen correctly (Chung et al. 2002, 310). Importantly, whether stavudine or tenofovir is used, a large part of the efficacy of these drugs depends on the patient adhering to therapy. Nonadherence to therapy may be associated with treatment regime complexity or may be caused by presentation of adverse effects that are not tolerated by the patients (Miller and Hays 2000). This parameter was also considered during the study. Patient adherence to antiretroviral therapy is reflected by the CD₄ count increasing and the viral load decreasing.

Research Method and Design

Design

A retrospective review of clinic charts of patients with HIV who were receiving HAART was undertaken. A cross-sectional population-based approach was used to extract information from the patient files; that is, the data collection was carried out at only a single point in time (Smith 2005, 30). The study was quantitative in nature. The objective was to determine the number of patients who were correctly switched from stavudine to tenofovir and those who were correctly initiated on tenofovir according to the South African 2010 Adult ARV Guidelines. This research could be considered a pilot study for the PTC of the relevant metro to lay the foundation for further studies within the metro and the country at large.

Sample and Study Site

The study was conducted at a primary health care clinic in the Nelson Mandela Metropole in the Eastern Cape Province of South Africa. The clinic addressed the ARV needs of patients living in the vicinity who were attending the clinic for their ARV treatment. The study sample consisted of adult patients with HIV who had been on HAART for a period of at least six months. The inclusion criteria for patients were as follows—

- Diagnosed with HIV/ AIDS
- At least 18 years old
- Received treatment for a period of at least six months
- Attended the clinic for their ARV medication

Patients who defaulted on their treatment were not excluded from the study, and the reason for non-adherence to therapy as noted in the patient file was recorded. Exclusion criteria were patients with HIV who were younger than 18 years of age and female patients who were pregnant. These patients follow the National ARV Paediatric Guidelines (2010) and Prevention of Mother to Child Transmission Guidelines, respectively. Patients who had passed away were also excluded.

To avoid introducing any element of selection bias (Gow 2009), the study applied the principle of randomised selection when choosing patient files. In this way, each file had an equal chance of being selected. From the electronic database of patient files, a list of patients who fitted the inclusion criteria was drawn up. Patient file numbers were used to maintain confidentiality of patients during the study and to avoid prejudice during selection. The numbers were then shuffled, and each fifth file number was

then chosen from the list. However, when matching the file number to the actual file on the shelf, some of the files could not be found. Upon enquiry with the staff, some of the files were determined to be either missing or under processing in the data-capturing room. Thus random file numbers from the list were then matched to those available on the shelf and included in the study. A total of 165 clinic files were taken in the study.

Data Collection Method

Data were collected over a two-week period during the months of July and August 2011. The information was gathered using a purpose-designed data collection tool that was standardised prior to the start of the data collection process. The data collection tool was in the form of an electronic spreadsheet into which data were directly captured and saved. The tool had been designed using a sample of the clinic chart for ARV patients entitled “Adult Clinical Record- Eastern Cape Department of Health Comprehensive HIV/AIDS Care and Treatment Programme.” The headings used in the spreadsheet were designed to follow the clinic chart’s order so that the process of data capture would be more effective and less time consuming. The information entered was cross checked by the researchers to ensure accuracy and to avoid any errors, which would make the results more precise, reliable, and reproducible. Some of the challenges encountered during the data collection process included limited work space and lack of help from the staff, who were very busy. It was also found that the order of information as laid out in the older clinic cards differed from that in the newer sample card provided to the researchers. Because of the missing files, time was spent in searching for these files, thus making the process less effective and more time consuming.

The information was gathered under the main headings of patient demographics, medication history, chronic conditions, and disease state details. The demographic details that were gathered were patient number, file number, date of birth, sex, height, weight, and BMI.

Details of the chronic conditions that patients were diagnosed with at the time of treatment were also included, that is, details of whether patients had been diagnosed with chronic conditions such as diabetes mellitus, hypertension, asthma/chronic obstructive pulmonary disorder (COPD), epilepsy, psychiatric conditions, and other chronic conditions.

Information pertaining to the disease state under review was collected as follows: HIV status according to the WHO staging classification, date of diagnosis of HIV, initial CD₄ count and date, most recent CD₄ count and date, initial viral load and date, most recent viral load and date, and TB history including prophylaxis and treatment. Information pertaining to the medication history was also captured. Information concerning the ARV medication and relevant TB medication was collected as follows: months on ARV; drugs prescribed including dates started and stopped together with reason for stopping as listed in the patient file; serum creatinine levels; alanine transferase (ALT) liver enzyme levels, and haemoglobin (Hb) levels. It should be noted that tenofovir had already been introduced at the study site, in limited volumes, around April 2008 when treatment with tenofovir was initiated.

The symptom screening recorded in the charts was also captured. The symptoms that the health care providers identified included paraesthesia (peripheral neuropathy), lipodystrophy, lactic acidosis, jaundice, abdominal pain, skin rash, central nervous system (CNS) symptoms, sexually transmitted infection (STI) symptoms, anaemia, and lymphadenopathy. Another important parameter directly

influencing drug therapy is adherence. Relevant data relating to adherence to antiretroviral therapy was also recorded. A parameter used to measure the patients' adherence to antiretroviral therapy was the number of times patients came to collect their repeat treatments from the clinic. Patients eligible for antiretroviral therapy were first given a month's supply of medication and then given a date every month on which to collect their repeats for their antiretroviral medication. The date on which the patients came to the clinic to collect their ARVs was recorded and signed by the nurses in the patients' antiretroviral chart. This gave an indication of whether the patients were compliant with the therapy or not. The number of times the patients had come to collect their ARV repeats within the last six months (from February/March 2011) until the start of the study (July/August 2011) was recorded. Patients who had not come to collect their medication over these six months were given a zero rating (0/6) for adherence.

Data Analysis

Analysis of the results was performed using a Microsoft Excel spreadsheet. Descriptive statistics were used to analyse the raw data in order to draw meaningful conclusions.

Ethical Considerations

Ethics approval was obtained in writing from the Faculty Research and Technology Innovative and Research Ethics Committee–Humans of the Nelson Mandela Metropolitan University (NMMU) prior to the start of the research. Permission to conduct the study at the premises of the identified municipal clinic was sought and granted by the acting Head of Primary Health Care Directorate of Nelson Mandela Bay Municipality. Patient confidentiality and anonymity were maintained at all times by using only patient file numbers and not linking patient names to the data.

Results

The results obtained from the 165 patient files screened and important findings of the research were summarised according to demographic data and clinical data, ARV prescribing patterns, and adherence to ARV treatment.

Demographic and Clinical Data

The demographic and clinical data obtained are summarised in table 1.

Table 1: Overview of Demographic and Clinical Data of the Population Sample

Age (years)	Nuber of patients (% of patients) (n = 165)
18-29	24 (15%)
30-39	68 (41%)
40-49	53 (32%)
50-59	16 (10%)
60+	4 (2%)
Mean: 40 ±9 years (min = 18 years; max = 74 years)	
Sex	
<i>Female</i>	115 (70%)
<i>Male</i>	50 (30%)
WHO HIV staging	
<i>Stage 1</i>	52 (32%)
<i>Stage 2</i>	31 (19%)
<i>Stage 3</i>	74 (45%)
<i>Stage 4</i>	8 (4%)
CD₄ count (initial)	
Mean: 185 ±70 cells/mm ³ (min=2 cells/mm ³ ; max = 1023 cells/mm ³)	
Viral load (initial) [Measured in only 21% of patients]	
Mean: 131 862 ± 253 448 copies/ml (min = 25 copies/ml; max = 1 100 000 copies/ml)	
Duration on ARV (months)	
0–11	29 (18%)
12–23	45 (27%)
24–35	33 (20%)
36–47	28 (17%)
48–59	17 (10%)
60–72	6 (4%)
73–84	7 (4%)
Mean: 30 ±2.4 months(min: 0 month ; max: 84 months)	

In terms of age distribution (table 1), the largest number of patients was from the category 30–39 years of age (41 per cent). This category consists mostly of the working population, which negatively affects the economy. Patients in this age group are also in the reproductive age, which would contribute to the high rate of babies infected with HIV. The high percentage of female patients (table 1) could be a result of a higher incidence of HIV in young women and those of child-bearing age than in men as concluded in a study published in 2007 (Rehle et al. 2007). The WHO HIV staging was recorded in all the patients and is important for tracking and monitoring the patients with regard to disease progression and clinical management. It also serves to gauge the patients' eligibility for antiretroviral therapy, to monitor their response to treatment, and to assess whether fast-tracking is required (NDoH 2010).

An initial CD₄ count was measured in all 165 patients before initiation of ARV, and the average was 185 ±70 cells/mm³. This low CD₄ count is expected, as according to the South African 2010 ARV Guidelines, patients with a CD₄ count of fewer than 200 cells/mm³ should be put on ARV treatment.

The high maximum initial viral load (1,023 cells/mm³) is probably caused by a patient having been transferred from another clinic where ARVs had previously been initiated and who was already on treatment before coming to the study clinic site. Viral load was measured in only 21 per cent of patients. The 2010 guidelines recommend routine monitoring of viral load after the first six months on ARV, then after the first year, and thereafter every 12 months on ARV (NDoH 2010). Thus a higher percentage of patients should have had their viral load tested because most patients (92 per cent) were on ARV for longer than six months. After a six-month period on ARV, the viral load should be under 400 copies/ml if adherence to therapy is maintained (NDoH 2010). The high mean (131,862 ± 253 448 copies/ml) could indicate poor adherence to antiretroviral therapy, or if patient is compliant, it indicates poor response to ARVs. Further tests are warranted to assess ARV adherence or response.

When considering the duration on ARVs (table 1) and the fact that one of the inclusion criteria was that patients should have been on ARVs for at least six months, in the current study 0–6 months on ARV means the first few weeks or months after re-initiation of ARV after a patient had previously defaulted on treatment. The possible reasons for non-adherence were listed in the file as being appearance of side effects, pregnancy, poor adherence (poor adherence to the specific therapy warranting change to another therapy probably due to complexity of therapy or intolerable side effects), medicines out of stock, no reason, or other reason not specified.

At the time of initiation on antiretroviral therapy, 3.9 per cent (n = 165) of the patients were suffering from co-morbid conditions, namely diabetes mellitus, hypertension, asthma, and psychiatric disorders. In South Africa there is a high incidence of TB in people co-infected with HIV (WHO 2011, 11). In this study (n = 165), 41 per cent of the patients had received TB treatment and 14 per cent had received prophylaxis for TB.

Table 2: Antiretroviral Regimen Patterns Prescribed at the Municipal Clinic before and after Implementation of the 2010 South African ARV Guidelines

Before April 2010		After April 2010	
Regimen 1A (Therapy I)	Stavudine 30 mg bd Lamivudine 150 mg bd Efavirenz 600 mg nocte	First-line regimen (Therapy IV)	Tenofovir 300 mg od OR Stavudine 30 mg bd OR Zidovudine 300 mg bd) PLUS Lamivudine 150 mg bd + Efavirenz 600 mg nocte OR Nevirapine 200 mg bd
Regimen 1B (Therapy II)	Stavudine 30 mg bd Lamivudine 150 mg bd Nevirapine 200 mg bd		
Regimen 2 (Therapy III)	Zidovudine 300 mg bd Didanosine 400 mg od Lopinavir/Ritonavir 400/100 mg bd	Second-line regimen (Therapy V)	Tenofovir 300 mg od (OR Zidovudine 300 mg bd) + Lamivudine 150 mg bd + Lopinavir/Ritonavir 400/100 mg bd

ARV Prescribing Patterns

Half (52 per cent) of the population sample (n = 165) was currently on *Therapy I* (table 2). Fifteen patients (9 per cent) were on *Therapy II* (Table 2). Seventeen patients were originally on *Therapy I* then switched to *Therapy II* during a previous pregnancy. It should be noted that one of the exclusion criteria was patients who were pregnant. Thus none of the patients included in the population sample were pregnant at the time when the study was carried out. Of the 17 patients who were previously on *Therapy II*, only 8 patients were correctly switched back from nevirapine to efavirenz according to the 2010 national ARV guidelines (NDoH 2010). The remaining 9 patients were continued on nevirapine. Eighteen patients were started on nevirapine at the time of initiation of ARVs, possibly because of pregnancy, but never changed to efavirenz after the delivery and breast-feeding period. Insufficient information was available to assess why these patients were still on nevirapine.

Thirty-eight per cent (n = 64) of the patients were on *Therapy IV* (table 2). Of these 64 patients, 48 were on tenofovir as part of the triple regimen. Twenty-eight patients (58 per cent of patients receiving tenofovir) had been correctly switched from stavudine to tenofovir. Twelve patients had been switched from stavudine to zidovudine, that is, they were changed from *Therapy I* to *Therapy IV* (table 2). The reasons for the switch in the patients were presentation of stavudine-associated side effects (11; 39 per cent); poor adherence (4; 14 per cent); pregnancy (5; 18 per cent); treatment failure (4; 14 per cent); and reason not specified (5; 18 per cent).

Amongst the 165 patients in the study, the side effects reported with the highest incidence were skin rash (24 per cent), followed by peripheral neuropathy (10 per cent) and gastro-intestinal disturbances (5 per cent). For most of the patients (60 per cent), no side effects were recorded. The fact that 60 per cent of the patients did not report any side effects could be because they either could not identify the symptoms or assumed they were associated with the disease state and not with the medication, or that the health care provider did not enquire and/or document the presence of side effects.

The remaining 20 patients (42 per cent of patients on tenofovir) had been initiated on tenofovir therapy as part of *Therapy IV* (table 2) at the time of initiation of ARVs. Of these 20 patients, 17 (85 per cent) were started with tenofovir after the implementation of the 2010 South African ARV Guidelines in April. The other 15 per cent had been started on tenofovir before April 2010. A total of 40 patients (24 per cent of the population sample) had been discontinued on stavudine. Out of these 40 patients, only 28 patients (76 per cent) were switched to tenofovir. The other 12 patients (24 per cent) were changed to zidovudine (7 per cent of the population). In one patient, all ARVs were stopped owing to the remarkable increase in CD₄ count and undetectable viral load. Eight patients (5 per cent of the population) were still started with stavudine after the implementation of the 2010 South African ARV Guidelines in April. Insufficient information was available to assess whether or not tenofovir was contraindicated in these patients. Two of these patients were then later switched to tenofovir because of stavudine-associated side effects.

Table 3: Adherence Rate to Antiretroviral Therapy by the Population Sample

Adherence ARV collection over a six-month period (%)	Patients (%) (n = 165)
0/6 (0%)	15
1/6 (17%)	5
2/6 (33%)	8
3/6 (50%)	15
4/6 (66%)	27
5/6 (83%)	25
6/6 (100%)	6

Adherence was measured by determining the number of times patients had collected their monthly repeat medication during the previous six months. Only 6 per cent of patients were adherent to their ARV treatment in that they had collected their repeat medication for six of the previous months (table 3). Forty-two patients (70 per cent of the population sample) had adherence levels of less than 83 per cent. A study measuring the levels of adherence rate to antiretroviral therapy required for virologic suppression deduced that a minimum of 80 per cent adherence rate is required for effective (80 per cent) virologic suppression (Kobin and Sheth 2011). Thus the findings are of concern because the lower the adherence rate, the higher the possibility of treatment failure, which has serious implications in terms of development of viral resistance to the drugs, possibility of re-infection, higher risk of developing opportunistic infections, and higher mortality.

Limitations of the Study

The study was conducted at only one clinic in the Eastern Cape Province, and the results of the research cannot be extrapolated to other clinics in the region or to other provinces in the country. The study included only adult patients with HIV and excluded pregnant women and children because they follow the Prevention of Mother to Child Transmission and Paediatric ARV Guidelines, respectively. The situation in these special groups of the population could not be assessed.

Conclusion and Recommendations

The principal aim of the study was to assess whether the switch from stavudine to tenofovir in a primary health care clinic had been implemented according to the 2010 South African ARV Guidelines. Only a low percentage of patients (17 per cent) were correctly switched to tenofovir from stavudine of the 85 patients (52 per cent) who were on stavudine as part of the first-line regimen. A further 10 per cent of patients were correctly initiated on tenofovir after these guidelines had been implemented. This means that in only 27 per cent of the sample (n = 165) were the guidelines followed correctly. Tenofovir should have been prescribed in a higher percentage of patients in the year following the introduction of the 2010 guidelines. A small number of patients were still being initiated on stavudine after the 2010 ARV guidelines were put in place. Insufficient information was available to determine if the use of tenofovir was contraindicated in these patients, information which should have been documented in the patient's file. Factors that could have negatively affected adherence to the 2010 ARV guidelines that could be inferred from the study include the incompetency of the clinic staff to follow these guidelines. This could indicate a need to train the clinic personnel and educate them about the significance of complying with national ARV guidelines. Another setback that could have hampered the correct implementation of

the guidelines could have been the stavudine stock on hand that needed to be exhausted or the low levels or poor supply of tenofovir to the clinic.

Sixty per cent of the patients did not report any side effects either because they could not identify the symptoms or assumed they were associated with the disease state and not with the medication or because the health care provider did not enquire and/or document the presence of side effects. A possible reason could also be the lack of proficiency of the clinic staff to identify and record the side effects described by patients. A more thorough investigation into the side effects experienced by patients could be carried out to clarify this point. This finding also suggests the need for staff training in the primary health care clinics.

The underlying reasons for failure of the staff to follow the guidelines should be investigated and the appropriate measures taken to improve the situation. Further research in other clinics in the Eastern Cape Province and throughout the country should be undertaken to assess whether they show a similar trend. A larger population sample would increase the reliability of the results and give a better overview of the response of health care professionals to the recommendation for a switch from stavudine to tenofovir and the correct implementation of the 2010 South African ARV Guidelines.

A significant second finding of the study is the adherence rate, which was less than 83 per cent for 70 per cent of the population. Even if the medications were prescribed according to guidelines and the switch from stavudine to tenofovir was made correctly, the medications would not have been effective if the patients were not compliant with therapy. This is of concern because the lower the adherence rate (< 80 per cent), the higher the possibility of treatment failure, which has serious implications in terms of development of viral resistance to the drugs, possibility of re-infection, higher risk of developing opportunistic infections, and higher mortality. A rigorous campaign to emphasize the consequences of adherence to antiretroviral therapy and patient education is critical.

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Authors' Contributions

S.R., S.K., S.M., and K.G were responsible for the data collection. S.A.B. and J.M. were the project supervisors.

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Annex G Questionnaire to Assess the Functioning of a Pharmaceutical and Therapeutics Committee

Question	Answer	Comments
Structure		
Does the committee have an established place in the organisational structure of the province with clear authority and accountability?		
Does the committee have the necessary subcommittees/task teams (e.g., antimicrobials, infection control, etc.)?		
What professional staff members are represented on the committee? How many typically attend meetings?		
Are the roles and responsibilities of the chairperson, members of the committee, and the secretariat clearly defined?		
What is the relationship between the committee and regional/institutional PTCs?		
Functions		
What are the major functions of the committee?		
What topics/standing items are covered in the regular meetings of the committee?		

Question	Answer	Comments
Does the committee routinely evaluate requests for inclusion of medicines on the code list?		
What criteria are used to select medicines for the code list?		
What sources of information are used to evaluate medicines for inclusion on the code list?		
Does the committee regularly review the code list to ensure availability of the most effective, safe, and cost-effective medicines?		
Does the committee play a role in the detection and reporting of ADRs and medication errors?		
Does the committee have established criteria to ensure product quality? If so, what are they?		
Do established mechanisms exist for reporting product defects to the committee?		
What role does the committee play in evaluating medicine expenditure in the province?		

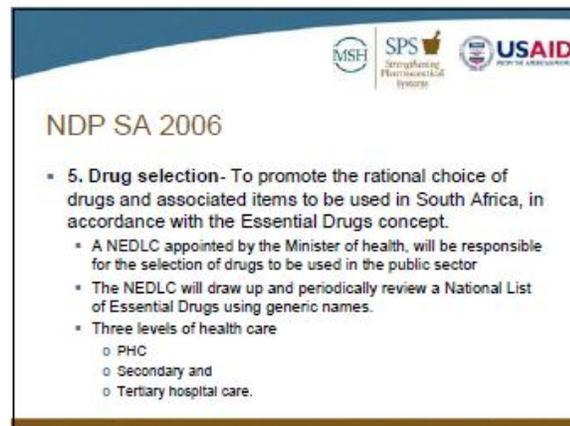
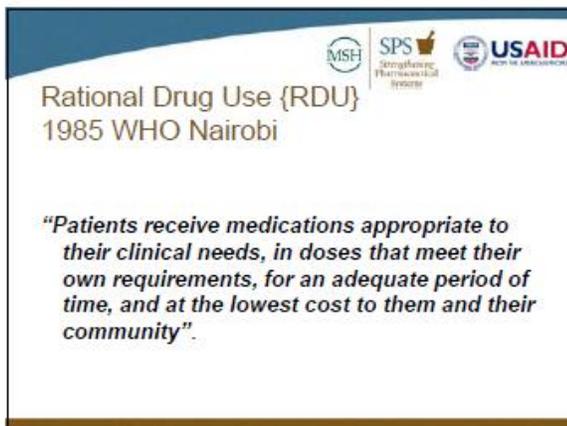
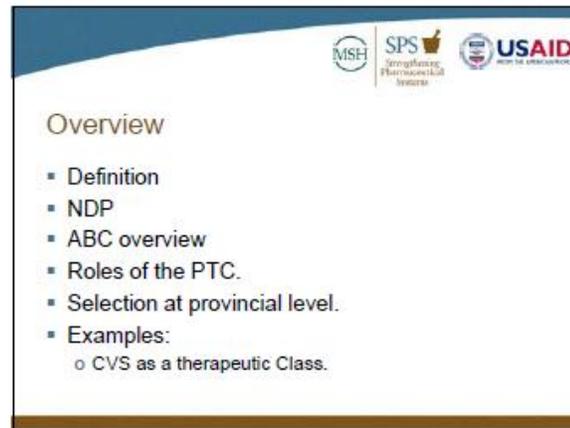
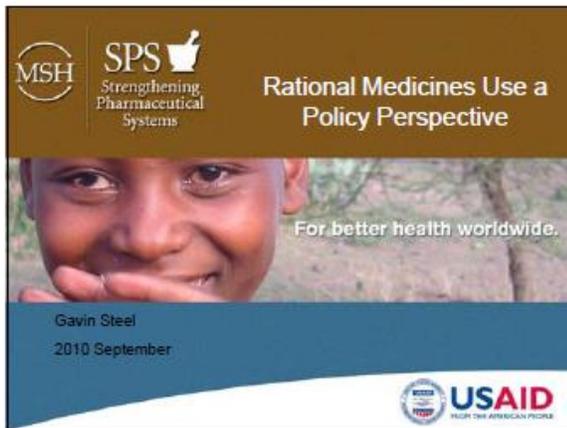
Question	Answer	Comments
Does the committee have established methods for periodically evaluating the use of medicines in the province? If yes, what methods are used?		
Has the committee detected any problems in the use of medicines? If yes, please describe the problems.		
Does the committee have programmes to address medicine use problems? What are these programmes?		
What is the function of the committee in regulating the provision of information on medicines and the promotion of medicine by the pharmaceutical industry in the province?		
What role does the committee play in the provision of written material to health workers, detailing of information to prescribers, lectures/workshops on therapeutics?		
Policies and processes		
Does the committee have terms of reference and a strategic plan?		
What policies and procedures does the committee have that regulate the functioning of the committee?		
Are policies and procedures in place to address conflict of interest?		
Is the rationale for decisions taken documented and made available to stakeholders?		

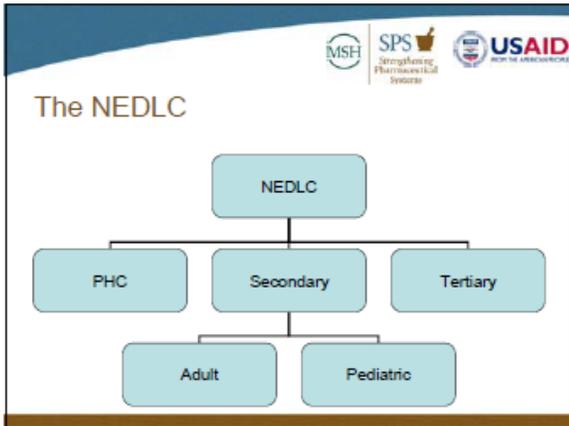
Question	Answer	Comments
What mechanism is in place for appeals against decisions of the committee?		
Are resources allocated to the functioning of the committee?		
Is a system in place to monitor and evaluate the activities of the committee?		
What mechanisms are in place to provide feedback to stakeholders?		
General		
What are some major accomplishments of the committee?		
What are major drawbacks?		
How can the image and standing of the committee be improved?		
What steps can be used to build capacity in the committee?		
What would you like to see accomplished by the committee?		

Annex H Rational Medicine Use: A Policy Perspective

Ethics in provision of HIVAIDS

Module 2, Session 7





- ### Technical committee composition
- A chairperson and vice chairperson
 - Members of the NEDLC.
 - Chair person would have served at least one term.
 - Members with a sound working knowledge in the following areas:
 - Practice at the hospital level within the public sector.
 - Pharmacology.
 - General internal medicine.
 - Rational Prescribing.
 - Health economics & or Pharmacoeconomics
 - Evidence based medicine.
 - Public health.
 - The functioning of PTCs

- ### EDL Selection - Process
- Call up notice.
 - Conditions.
 - Chapters
 - 1st draft lead reviewer
 - 2nd draft committee consensus
 - 3rd draft comments from stake holders.
 - 4th draft final technical document.
 - EDL secretariat
 - Editing

- ### EDL Selection – Medicine technical report
- Executive summary
 - Background
 - Discussion regarding the quality of available evidence and a statement regarding scope of any literature survey performed.
 - A statement regarding.
 - Efficacy.
 - Safety.
 - Cost and or practice considerations.
 - Recommendation to the sub committee.

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EFAVIRENZ TABLET 600MG;30'S
PNEUMOCOCCAL VACCINE CONJUGATED
LAMIVUDINE TABLETS 150MG; 60'S
LOPINAVIR AND RITONAVIR TABLETS 200MG
VACCINE PENTAXIM;0,5ML
ROTAVIRUS ORAL VACCINE SINGLE DOSE
ZIDOVUDINE TABLETS 300MG;60'S
VACCINE: MEASLES,LIVE ATTENUATED VIRUS;
NIFEDIPINE TABLETS 30MG;CONTROLLED RELEASE
PERINDOPRIL TERBUTYLAMINE TABLETS 4MG;28'S
TENOFOVIR DISOPROXIL FUMARATE TABLETS
STAVUDINE CAPSULES 30MG 60'S
RISPERIDONE TABLETS 2MG;30'S
INSULIN INJECTION HUMAN;BIOSYNTHETIC
RISPERIDONE TABLETS 3MG;30'S
PIPERACILLIN 4G AND TAZOBACTAM 500MG
TEST STRIPS
NORETHISTERONE ENANTHATE INJECTION
NEVIRAPINE TABLETS 200MG;60'S
LOPINAVIR AND RITONAVIR ORAL SOLUTION

ABC GP

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PNEUMOCOCCAL VACCINE CONJUGATED;SUSPENSION
VACCINE PENTAXIM;0,5ML
RETAVIRUS ORAL VACCINE SINGLE DOSE
FACTABLE FOR INJECTION CONCENTRATE FOR INFUSION;100MG
FACTOR VII COMPLEX INJECTION 500 UNITS PER VIAL 2 VIALS
VACCINE: MEASLES,LIVE ATTENUATED VIRUS, W/O SLENT; 20 DOSES/VIAL
SEVOFLURANE LIQUID; 250ML
FACTOR IX COMPLEX INJECTION 2000 UNITS/VIAL (INNOVING) 1000; 1'S
ACTIVATED RECOMBINANT COAGULATION FACTOR VIII FOR INJECTION(SKE)
VACCINE HEPATITIS B;INTRAMUSCULAR/PNEUMATIC
VACCINE POLIOIMPETEL TRIVALENT ORAL; 20 DOSES/VIAL
FACTOR VII COMPLEX INJECTION 500 UNITS/VIAL (INR); 1'S
ERYTHROPOIETIN RECOMBINANT HUMAN
METFORMIN HYDROCHLORIDE TABLETS PATENT READY PACK
MYCOPHENOLATE MOFETIL CAPSULES 250MG;180'S
AMOXICILIN TRIHYDRATE CAPSULES PATENT READY PACK
EFAVIRENZ TABLET 600MG;30'S
GLUCAGON TABLETS PATENT READY PACK;300MG; 30'S
TACROLIMUS CAPSULES 1MG;180'S
GOOSEBURN INJECTION 100MG;100PCT

ABC DDVs

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PTC Functions - WHO

- Advising medical, administrative, and pharmacy departments on medicines-related issues
- Developing medicine policies and procedures
- Evaluating and selecting drugs for the formulary and providing for its periodic revision
- Assessing medicine use to identify problems
- Promoting effective interventions to improve drug use (including educational, managerial, and regulatory methods)
- Managing adverse drug reactions and medication errors

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PTC Functions – Selection Province

- Compilation of formulary and procurement catalogues.
 - EDL
 - Therapeutic Class.
 - Pack sizes.
 - Re packaging.
 - Up to 20% non EDL medicines – bridges reviews.
- Named patient access.
- Recommendations to the NEDLC.



PTC Functions – *Selection Province* (2)

- **Users' Guides to the Medical Literature: XIX. Applying Clinical Trial Results; B. Guidelines for Determining Whether a Drug Is Exerting (More Than) a Class Effect.**
- Finlay A. McAlister; Andreas Laupacis; George A. Wells; et al.
- *JAMA*. 1999;282(14):1371-1377 (doi:10.1001/jama.282.14.1371)



PTC Functions – *Selection Province* (3)

- PHC 2008
 - Antifungal lozenges (troches), e.g. amphotericin B.
 - HMGCoA reductase inhibitors (statins) that lower LDL by at least 25%, e.g. Simvastatin, oral, 10 mg daily.
 - Nitrates, short acting e.g. Isosorbide dinitrate, sublingual, 5 mg
 - Calcium channel blocker e.g. Amlodipine, oral, 5 mg daily or Nifedipine, oral, slow release 30 mg daily
 - ACE inhibitor, e.g. Enalapril up to maximum of 10 mg twice daily
 - Beta-adrenergic blocking agent e.g. atenolol
 - Imidazole cream, e.g. clotrimazole 2%
 - Potent topical corticosteroids, e.g. betamethasone 0.1% ointment
 - NSAID, e.g. ibuprofen
 - Beta2 agonists, e.g. salbutamol (short acting)
 - Inhaled corticosteroids, e.g. budesonide and beclomethasone
 - Corticosteroid, e.g. beclomethasone, aqueous nasal solution
 - weak opioid e.g. tramadol



PTC Functions – *Selection Province* (3)

- **Why therapeutic class.**
 - Clinically equivalent so similar outcomes.
 - Improves economies of scale by pooling.
 - Allows for competition where there is no or limited generic competition.
 - Originators often have in house generics.
 - Prior to expiration of the patent.
 - Addresses ever greening techniques.
 - Pharmaceutical market is imperfect and distorted.



PTC Functions – *Selection Province* (4)

- **Therapeutic-Class Wars - Drug Promotion in a Competitive Marketplace**
David A. Kessler, Janet L. Rose, Robert J. Temple, Renie Schapiro, and Joseph P. Griffin - NEJM Vol 331:1350-1353 November 17, 1994 Number 20
- Beware of “opinion leaders”.
- Need strong protection from conflict of interest.
- Because of competition we need regular review of ATCs

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Therapeutic Class

- CVS Therapeutic Class

	Cost per mnth	Cost pa
1st line	R 2.15	R 28.03
2nd line ACEI	R 5.57	R 72.61
2nd line Ca	R 6.80	R 88.74
3rd line	R 10.23	R 133.32
4th line	R 12.21	R 159.13

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Therapeutic Class (2)

	Cost per day	Cost per mnth	Cost pa
Hydrochlorothizide	R 0.08	R 2.15	R 28.03
Enalapril	R 0.12	R 3.42	R 44.58
Enalapril	R 0.24	R 6.84	R 89.16
Perindopril	R 0.44	R 12.30	R 160.34
Ramipril	R 0.30	R 8.50	R 110.80
Ramipril	R 0.36	R 10.00	R 130.36
Quinapril	R 0.90	R 25.08	R 326.94
Lisinopril	R 0.28	R 7.89	R 102.85
Losartan	R 0.61	R 17.10	R 222.91
Amlodipine	R 0.17	R 4.66	R 60.71
Nifedapine	R 0.39	R 10.83	R 141.18
Atenolol	R 0.07	R 1.98	R 25.81
Carvedilol	R 0.87	R 24.48	R 319.13
Spirolactone	R 0.28	R 7.96	R 103.76
Verapamil	R 1.70	R 47.70	R 621.80
Furosemide	R 0.06	R 1.60	R 20.86

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Re Packaging – The phenytoin case

- Capsules

Tablets	Pack size	Cost per year
	5000	R 361.87
	300	R 348.43
	34	R 361.87

Note – excludes labor, packaging and label

