Consolidating SIAPS' Five-Year Support to the Ministry of Health and Social Services for Strengthening Pharmacovigilance in Namibia

October 2016

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SIAPS
Systems for Improved Access to Pharmaceuticals and Services

Consolidating SIAPS' Five-Year Support to the Ministry of Health and Social Services for Strengthening Pharmacovigilance in Namibia

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October 2016

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About SIAPS

The goal of the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program is to assure the availability of quality pharmaceutical products and effective pharmaceutical services to achieve desired health outcomes. Toward this end, the SIAPS result areas include improving governance, building capacity for pharmaceutical management and services, addressing information needed for decision-making in the pharmaceutical sector, strengthening financing strategies and mechanisms to improve access to medicines, and increasing quality pharmaceutical services.

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Key Words

Pharmacovigilance, Namibia, SIAPS

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CONTENTS

ACRONYMS AND ABBREVIATIONS

ADR	adverse drug reaction
AE	adverse event
AIDS	acquired immunodeficiency syndrome
AMR	antimicrobial resistance
ART	antiretroviral therapy
ARV	antiretroviral
DOTS	directly observed treatment, short course
HAART	highly active antiretroviral therapy
ICASA	International Conference on AIDS and STIs in Africa
IR	intermediate result
I-TECH	International Training and Education Centre on HIV/AIDS
MI	medicines information
MOHSS	Ministry of Health and Social Services
MSH	Management Sciences for Health
NAAR	Namibians Against Antibiotic Resistance
NGO	nongovernmental organization
NIP	Namibia Institute of Pathology
PMTCT	prevention of mother-to-child transmission
PV	pharmacovigilance
SIAPS	Systems for Improved Access to Pharmaceuticals and Services
SPS	Strengthening Pharmaceutical Services
TIPC	Therapeutics Information and Pharmacovigilance Centre
TOT	training of trainers
UNAM-SoP	University of Namibia School of Pharmacy
USAID	US Agency for International Development
WHO	World Health Organization

ACKNOWLEDGMENTS

SIAPS Namibia acknowledges the productive collaboration by the Therapeutics Information and Pharmacovigilance Centre (TIPC) of the Ministry of Health and Social Services (MOHSS), the University of Washington, University of Namibia School of Pharmacy, and Project HOPE, with whom interventions mentioned in the report were accomplished and without whose cooperation and inputs the milestones in the report may not have been reached.

EXECUTIVE SUMMARY

Namibia is among the countries with the highest prevalence of HIV. In 2013, an estimated 13.1% of the adult population was living with HIV.[1] As of March 2016, more than 140,000 patients were receiving antiretroviral therapy (ART).[2] Namibia also faces a high tuberculosis (TB) burden, with a case notification rate of 529/100,000, and the TB/HIV co-infection rate at 47% in 2012.[3]

The goal of the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program in Namibia was to improve the quality and safety of pharmaceutical services to achieve sustained HIV epidemic control. Since 2012, SIAPS focused on interventions that increased the availability of quality antiretrovirals (ARVs), other essential medicines, and services to sustain more than 80% ART coverage of patients in need. SIAPS activities also contributed to ensuring patient safety through pharmacovigilance (PV) activities.

In Namibia, there is a body that functions to monitor PV and therapeutics activities, called the Therapeutics Information and Pharmacovigilance Centre (TIPC). With support from SIAPS, the TIPC implemented these interventions: monitoring medicine use to assure patient safety and achieve desired health outcomes, formulating policies and regulations to improve pharmaceutical care, and disseminating information and educational materials to promote public health. Other related support was given to activities to improve rational medicine use and advocate for antimicrobial resistance (AMR) prevention and containment.

In pursuit of these goals, the TIPC was able to set up a system for PV in Namibia that included community and health facility PV. There was increased awareness of the importance of seeking out and reporting adverse drug reactions (ADRs) by health facility staff, and the TIPC analyzed ADR reported data generated from spontaneous reports of patients on ART in Namibia from 2011 to 2013. In addition, 60 Project HOPE TB field promoters in Kavango region were trained to improve reporting of adverse reactions to TB/HIV medicines.

SIAPS collaborated with the University of Washington in providing technical guidance to the TIPC of the MOHSS to determine the projected health, cost, and economic outcomes of an active surveillance system for all HIV patients placed on ART in public HIV clinics in Namibia. These findings provided key inputs in informing the potential national expansion of an active surveillance PV program.

A number of technical reports, abstracts, and manuscripts related to strengthening PV in Namibia were developed during the five years of SIAPS in Namibia. These will act as reference materials for subsequent PV activities in Namibia.

There was a decline in the number of ADR reports since 2011, which was attributed to reporting fatigue among practitioners in health care facilities. To improve ADR reporting, SIAPS supported the TIPC in increasing PV knowledge and awareness among health professionals, which was achieved through numerous trainings conducted as well as PV awareness campaigns to create awareness among health care workers on PV and ADR reporting to the TIPC for management.

These achievements need to be consolidated by supporting the TIPC to roll out the active surveillance plan to more health facilities. In addition, the TIPC will need to increase PV awareness campaigns among health professionals to achieve an improvement in ADR reporting levels.

INTRODUCTION

About Namibia's Public Health System and SIAPS Support

Namibia's MOHSS manages approximately 350 public health facilities in 14 regions. Fifty of the facilities are designated main sites for ART; these main sites provide outreach and support services to more than 200 primary health care facilities. Namibia is among the countries with the highest prevalence of HIV. In 2013, an estimated 13.1% of the adult population was living with HIV.[1] As of March 2016, more than 140,000 patients were receiving ART.[2] Namibia also faces a high TB burden, with case a notification rate of 529/100,000 and a TB/HIV co-infection rate of 47% in 2012.[3]

Beginning September 2011, the SIAPS Program, supported by the US Agency for International Development (USAID), took over the technical assistance activities initiated by the USAID-supported Strengthening Pharmaceutical Systems (SPS) Program, which was also implemented by Management Sciences for Health (MSH) in Namibia. The SIAPS goal in Namibia was to improve the quality and safety of pharmaceutical services to achieve sustained HIV epidemic control. Since 2012, SIAPS focused on interventions that increased the availability of quality ARVs, other essential medicines, and services to sustain more than 80% ART coverage of patients in need. SIAPS activities also contributed to ensuring patient safety through PV activities.

Overview of PV

The science and activities relating to the detection, evaluation, understanding, and prevention of adverse events (AEs) associated with medicine use is known as pharmacovigilance (PV).[4] PV aids in the inevitable tradeoff between benefits and potential harm from medicine use through the detection and analysis of AEs and communication to an audience that has the knowledge to interpret the information to minimize harm.[4] If an AE is detected early, a clinician can alter treatment to minimize negative effects on patient quality of life, improve medication adherence, and/or slow disease progression.[5]

Linking and coordinating national PV activities with in-country public health programs supports overall system strengthening and can help achieve better program outcomes. Public health systems traditionally use spontaneous reporting or passive surveillance PV systems to identify AEs.[6] In a spontaneous reporting system, physicians, other health care providers, and/or patients report a suspected AE to a public health or governmental organization typically via a phone or mail system. Spontaneous reporting systems, though useful for safety signal generation, lack a well-defined population denominator and, therefore, lack the ability to calculate incidence. Moreover, significant underreporting of AEs is a well-documented limitation of spontaneous reporting systems for AEs.[7,8]

On the other hand, active surveillance is a type of PV whereby active measures are taken to detect the presence or absence of AEs on an ongoing basis among a defined group of people. Many in the field of PV have cited the importance of active surveillance as a systematic approach to medicine safety assessment and pharmaceutical systems strengthening.[6,9] Active PV systems better estimate the true burden of AEs and can allow for more effective and efficient use of resources to reduce burden of disease on the national level.[10,11]

Despite potential population health improvements and society's willingness to pay for regulation and to avoid AEs,[12-16] active surveillance systems have yet to be implemented on a large scale in low- and middle-income countries, largely because they can be complex and costly to implement and maintain. Data have yet to be presented on the health benefits and medical costs of an active PV program at a national level.

BACKGROUND OF PHARMACOVIGILANCE IN NAMIBIA

A formal medicines information (MI) center and systems for monitoring and reporting ADRs had not existed in Namibia as of 2002. A pre-assessment of the pharmaceutical management system in 2003 highlighted this deficiency as a serious impediment to the rational use of medicines in the country.[17]

The need for a MI center to provide unbiased and up-to-date information to health professionals in the country had long been established, as the National Drug Policy (NDP) of 1998 had actually recommended the establishment of a medicines information center and ADR monitoring unit linked to the Medicines Control Council to coordinate adverse reaction reporting and to manage data collection, analysis and dissemination.[18] In addition, the Namibia Medicines and Related Substances Control Act, 2003 (Act. No. 13 of 2003), required the reporting of ADRs by health professionals. Thus, the establishment of a center to handle MI and ADR monitoring as proposed by the NDP became necessary to facilitate ADR reporting as stipulated by the act.

To address this gap, a working group was formed under the leadership of the MOHSS and charged with the responsibility of developing and carrying out an implementation plan for the establishment of a center combining the twin functions of medicines information and PV. Members of this team were drawn from the MOHSS Directorate of Special Programs, Tertiary Health Care and Clinical Support Services, and various development partners, including MSH, Medicos del Mundo, and the International Training and Education Centre on HIV/AIDS (I-TECH). The working group developed an implementation plan that detailed the office setup plans, proposed functions, staff, and a work plan for the center.[19] Subsequently, an office was set up at the Windhoek Central Hospital with an MI pharmacist engaged as coordinator to run the center.

The key objectives of the center were (1) to provide both proactive and query-response therapeutics information to health professionals in Namibia, and (2) to become a reference unit on PV by collecting and monitoring ADRs.

STATUS OF PHARMACOVIGILANCE AT INCEPTION OF SIAPS IN NAMIBIA

At inception of SIAPS in 2011, the following had been achieved by SIAPS' predecessor project, SPS:

- SPS had helped establish the TIPC, and had four project-supported staff (two pharmacists, one medical doctor, and a librarian).
- The project had also provided books, a database on medication interactions and side effects, and subscription to journals.
- SPS had supported training activities of the TIPC staff on awareness activities and the implementation of the ART literacy package in order to promote medicine safety activities by TIPC staff.
- A total of 154 participants, including health workers (124) and community health workers (30), had been provided with skills in monitoring of medicine safety during the period 2007 to 2010.
- The TIPC had collected and analyzed information on AEs through the use of AE reports and therapeutic queries.[20]
- During the period October–September 2009, a total of 258 ADR reports were received from different regions. During the same period, 62 therapeutics queries were received. A total of 126 therapeutics queries had been received by TIPC by March 2010.[21]
- SPS had supported cost-benefit analysis of active surveillance activities in Namibia.

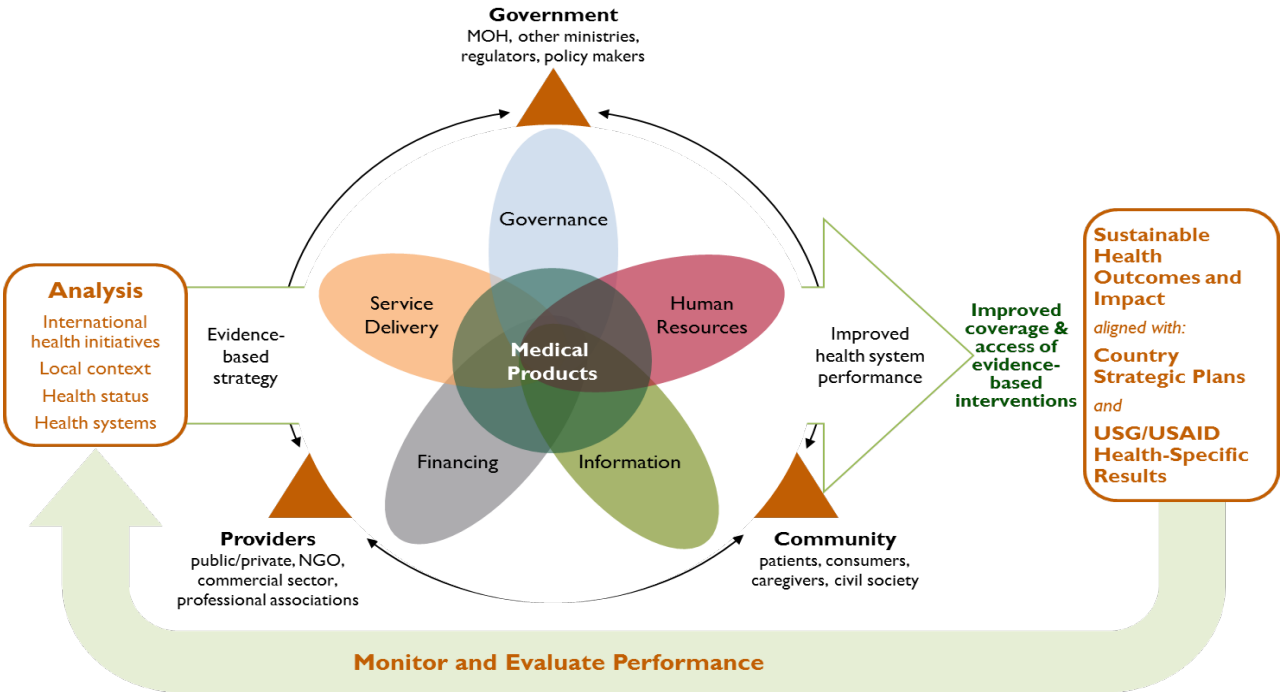
SIAPS NAMIBIA FIVE-YEAR SUPPORT IN STRENGTHENING PHARMCOVIGILANCE

SIAPS Namibia

The goal of the USAID-funded SIAPS Program is to contribute to the achievement of health outcomes by assisting Namibia in improving access to quality pharmaceutical products and the delivery of effective pharmaceutical services. The SIAPS pharmaceutical systems strengthening approach included engaging stakeholders (government, health providers, and community) and encouraging country ownership; building the capacity of local governments and organizations; and improving metrics and monitoring and evaluation to meet disease-specific needs set out in country strategic plans, while strengthening the overall pharmaceutical system.

SIAPS Approach

SIAPS framework and result areas (figure 1) reflect the dynamic relationships among five health systems building blocks: governance, human resources, information, financing, and service delivery, with a pharmaceutical product overlay that guides the technical content.



Source **http://siapsprogram.org/wp-content/uploads/2013/09/SIAPS-Fact-Sheet_2013.pdf**

Figure 1. SIAPS pharmaceutical system strengthening approach.

The SIAPS goal in Namibia was to improve the quality and safety of pharmaceutical services to achieve sustained HIV epidemic control. To achieve its goal, the program intended to strengthen the pharmaceutical services by attaining the following five objectives, or intermediate results (IRs):

- IR1: Quality and safety of ARVs and medicines for treatment and prevention of opportunistic infections assured

- IR2: Human resource capacity in pharmaceutical management and service delivery strengthened for improved HIV and AIDS treatment outcomes

- IR3: Availability and use of pharmaceutical service data for improved quality of ART services enhanced

- IR4: Financing mechanisms strengthened to improve access to medicines

- IR5: Quality, efficiency, and accessibility of pharmaceutical services strengthened to attain 90% treatment coverage and 90% viral suppression

Strengthening Pharmacovigilance

Building on the achievements of its predecessor project, SPS, SIAPS in Namibia—under IR5: Quality, efficiency, and accessibility of pharmaceutical services strengthened to attain 90% treatment coverage and 90% viral suppression—set out to further strengthen PV in Namibia.

Under this results area, SIAPS in Namibia set out to improve pharmaceutical services by supporting activities that pharmaceutical staff carry out to support patient care and treatment. Pharmaceutical services supported by the project included monitoring medicine use to assure patient safety and achieve desired health outcomes, formulating policies and regulations to improve pharmaceutical care, and disseminating information and educational materials to promote public health. Other related activities supported included activities to promote rational medicine use and advocate for AMR prevention and containment. Figure 2 illustrates the key PV strengthening activities carried out by SIAPS Namibia.

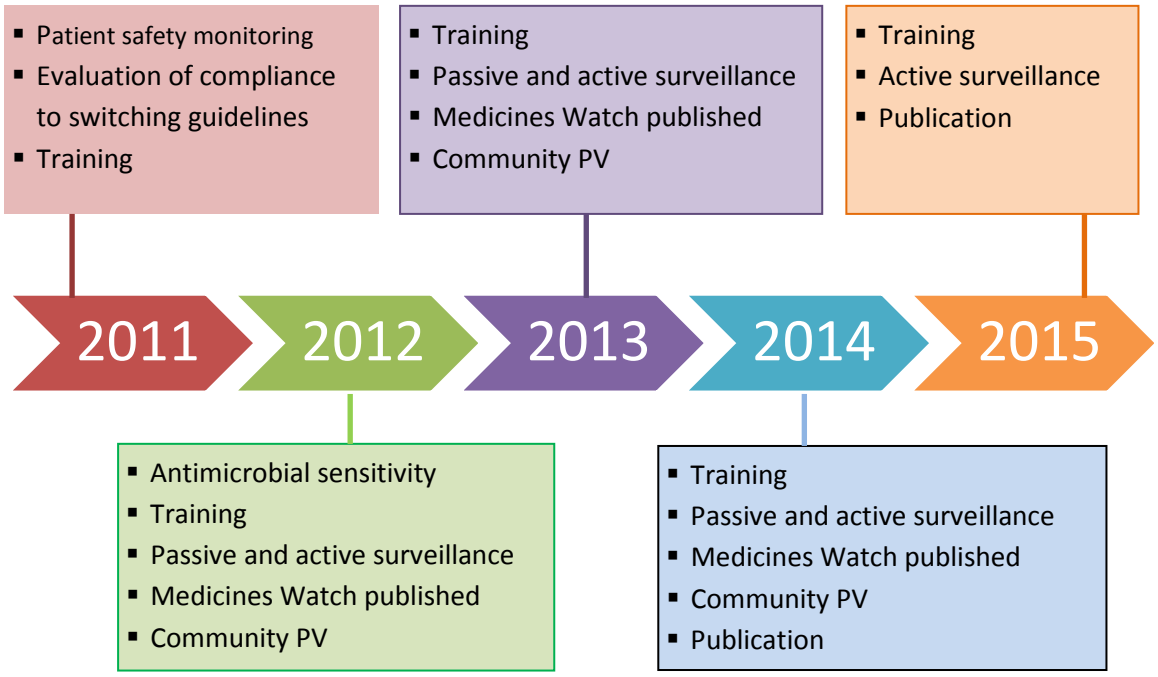


Figure 2: Key PV strengthening activities

During project year 1, SIAPS provided support to the TIPC in Namibia to carry out patient safety monitoring activities. A total of 250 ADR reports were received, reviewed, and analyzed by the TIPC with technical assistance from SIAPS. Additional support included investigation of the risk of nevirapine-associated skin and liver reactions, and the risk of renal failure associated with tenofovir.[22]

During project year 2,[23] SIAPS supported the MOHSS in the analysis and use of AMR data from the Namibia Institute of Pathology (NIP). Under this activity, SIAPS provided technical assistance to the MOHSS to analyze and disseminate antimicrobial sensitivity/resistance patterns of common pathogens based on NIP data. To this end, the TIPC obtained data from the NIP on culture and sensitivity patterns of pathogens to different antimicrobials. SIAPS provided technical assistance to the TIPC on the methodological approach to be used in the analysis of the data as well as in the interpretation of the findings. This technical assistance was continued into project year 3,[24] and TIPC subsequently compiled and shared with the NIP a draft report of the findings for their comments and input, before finalizing it for dissemination. SIAPS also provided further technical assistance to the TIPC in reviewing and refining a manuscript based on the report of the analysis of the NIP antimicrobial sensitivity data, which were subsequently submitted to the *Southern Medical Review* for consideration for publication.

During project year 2, SIAPS provided technical support to Windhoek Central Hospital to establish an antimicrobial stewardship committee with terms of reference. SIAPS provided advocacy and support to the committee to enable it execute its mandate. SIAPS held meetings with the head of the Windhoek Central Hospital's antimicrobial stewardship committee to identify potential areas of collaboration. Subsequently, SIAPS provided technical input in the review of the Windhoek Central Hospital's draft antibiotic use guidelines, which was aimed at promoting rational antibiotic use to reduce risk of generating antibiotic resistance. These guidelines were later adopted by the Namibians Against Antibiotic Resistance (NAAR). The

NAAR, a multidisciplinary coalition jointly formed in 2012 by Windhoek Central and Katurura Hospitals, was composed of both private and public health practitioners (doctors, pharmacists, and nurses). SIAPS provided technical support in data analysis, reporting, and advocacy on measures to mitigate the emergence and spread of AMR in Namibia.

SIAPS, in collaboration with the University of Namibia School of Pharmacy (UNAM-SoP) and MOHSS, conducted a two-day workshop and a one-day stakeholders' forum on AMR and promoting rational use of ARVs, anti-TB, and other medicines in Namibia. SIAPS developed and customized the training materials and co-facilitated the training workshop and forum. Overall, 66 participants attended, including academics and students from UNAM and a wide spectrum of health care professionals from public and private hospitals, the Pharmaceutical Society, and the Health Professions Council of Namibia. The workshop, hosted by UNAM-SoP in Windhoek in July 2013, aimed to raise awareness on the problem of AMR and engaging stakeholders in promoting the rational use of antimicrobial medicines as a strategy for containing the emergence of AMR.

SIAPS provided technical materials to assist the NAAR in organizing and coalition building and also linking with the University of Namibia for technical input in conducting AMR-related operational research. SIAPS also developed and sent a FAQ (frequently asked questions) document on AMR for use on various media channels, in response to a request from NAAR.

During project year 2, SIAPS continued to support the TIPC to strengthen PV and therapeutics information activities. SIAPS provided technical assistance and advocated for the full transition of TIPC activities to MOHSS. SIAPS provided technical assistance to analyze PV data generated from passive surveillance, review published medicine safety reports, produce patient safety-related information, and improve completeness of PV reports. SIAPS provided technical assistance in the review of nevirapine safety data collected by the TIPC and a nevirapine safety report was compiled. Findings of this analysis were presented to the HIV Treatment Advisory Committee (TAC) of the MOHSS on February 14, 2013. The TAC provided useful recommendations that guided patient treatment strategies using nevirapine-containing ART to minimize potential adverse reactions.

The rollout of the MOHSS treatment literacy approach was started during project year 2. SIAPS provided technical assistance in the review of technical specification for the reproduction of the videos and flipcharts for the rollout of the MOHSS ART literacy approach.

During project year 2, SIAPS provided technical assistance in the review of the October 2012–March 2013 issue of the *Namibia Medicines Watch*. This was subsequently forwarded to MOHSS for final review, approval, and dissemination. The *Namibia Medicines Watch* was a specialized publication that provided comparative information on medicines and communicated all local and international efforts that contributed to the ready availability of information to improve medicines safety and rational use. This activity was continued into project years 3 and 4 with the review and printing of subsequent copies of TIPC's *Namibia Medicines Watch*, and SIAPS supported the development of the issue covering the period October–December 2014 (figure 3).[25]

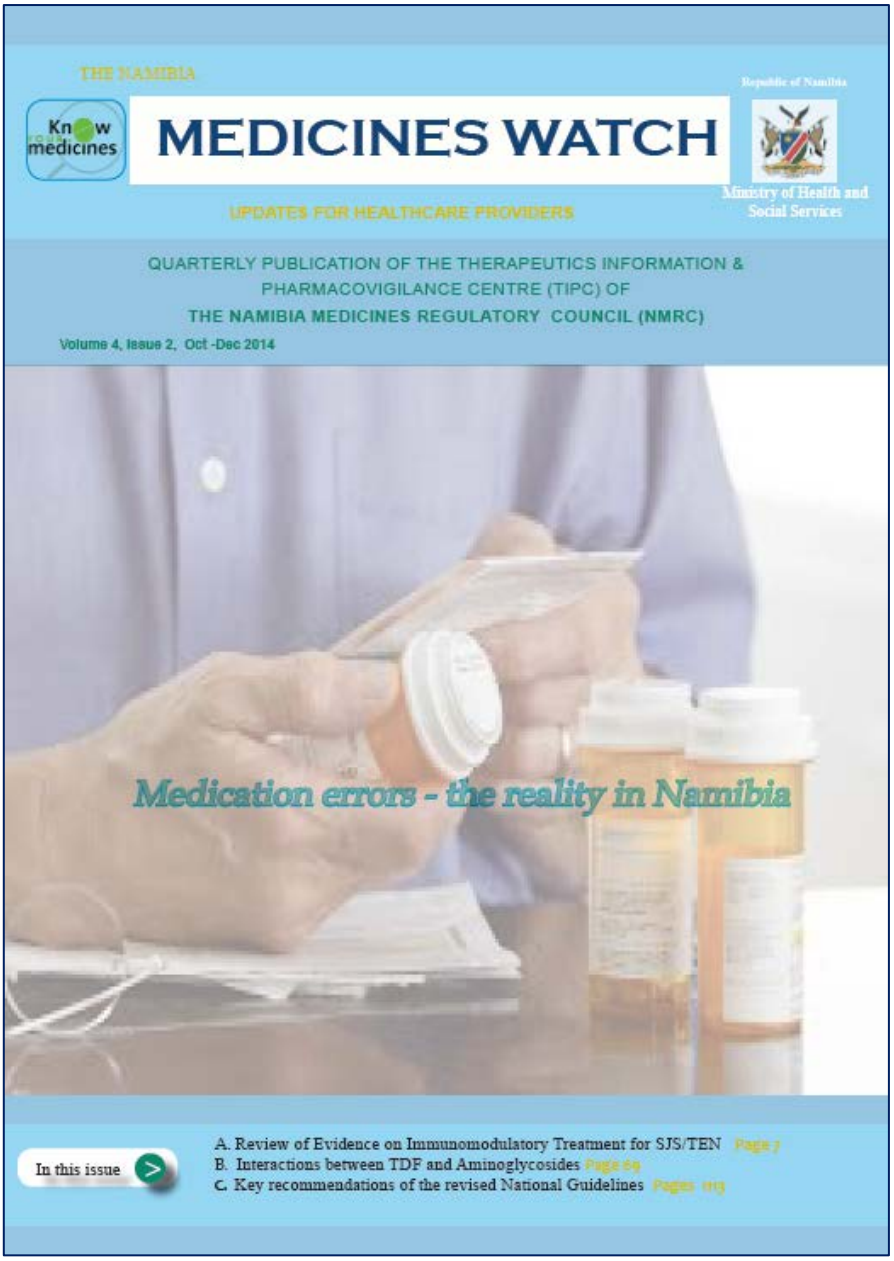


Figure 3. *Namibia Medicines Watch* for the period October–December 2014

In project year 2, SIAPS supported the TIPC in initiating active surveillance on the safety of patients on ART at two sentinel sites in Windhoek (Windhoek Central and Katutura State Hospitals), with a patient enrollment period of six months and patient follow-up of 12 months. In collaboration with the University of Washington (Seattle, WA, USA) and TIPC, SIAPS developed and deployed the data entry tool that was used for analyzing the cohort data of 470 patients enrolled in the active surveillance of safety of first-line ARVs at the two sentinel sites.[26] Detailed activities included the following:

- Providing technical assistance to MOHSS to implement the active surveillance plan for PV

- Developing and deploying a data entry tool for an active surveillance system being implemented in two sentinel ARV sites and in assisting TIPC with activity monitoring and data entry

- Conducting analysis of data from the active surveillance system being implemented in the two sentinel ARV sites

- Disseminating findings from the active surveillance system, including organizing a dissemination meeting in Windhoek and preparing a final report, abstracts, and manuscripts

- Assisting TIPC with planning for expansion of the active surveillance system into additional ARV clinic sites as well as prevention of mother-to-child (PMTCT) and TB clinic sites

- Assisting TIPC with records-linkage PV to assess emerging safety signals

With the successful completion of these activities, an ARV safety active surveillance program of the MOHSS/TIPC to assess the safety of commonly used first line ARV medicines in the public sector in Namibia was established.

This activity was continued into project year 3, with SIAPS staff participating in advocacy for PV through a presentation made to health care workers in Ohangwena region during the monthly seminar for capacity building; 27 health workers (medical officers and nurses) attended the meeting.

SIAPS facilitated the collaboration between TIPC and Project HOPE, a PEPFAR-funded community-based nongovernmental organization (NGO), to improve community-based ART and TB-PV and ADR reporting. SIAPS supported the strengthening, identification, and reporting of ADRs. This included training 60 Project HOPE's TB field promoters and district TB coordinators in medication safety monitoring and basic education/counseling of patients regarding their therapy.

The first TB and HIV medication safety trainings were conducted on November 15–16, 2014 in Ongwediva, where 34 field-based TB DOTS promoters were trained. Participants were trained in basic PV techniques, data collection, and reporting of ADRs experienced by the patients whom they care for at community level. This activity was continued into to project year 3, with trainings also conducted in Rundu (Kavango region) for an additional 26 TB field promoters. The training equipped the field promoters with knowledge and skills to improve reporting of adverse reactions to TB/HIV medicines.[27]

Ms. Thelma Davids of Project HOPE, one of SIAPS' project collaborators on community PV, co-facilitates a session on reporting ADRs of ARVs and anti-TB medicines during training for health workers conducted July 1, 2014, in Oshana, Namibia. Photo credit: SIAPS Namibia

SIAPS staff conducted a support visit to Project HOPE's office in Ongwediva and trained the clerk on how to enter data in the ADR spreadsheet. During this period, SIAPS collaborated with Project HOPE to improve community-based PV, focusing on anti-TB and ARVs.

Two abstracts were submitted for presentation during the International Conference on AIDS and STIs in Africa (ICASA) that was held in 2013: "Effect of Change in CD4 Count Threshold for Initiation of Antiretroviral Therapy on Rates of Substitution from Nevirapine to a Protease Inhibitor in Namibia" and "Increase in Reports of Nevirapine-Associated Serious Adverse Events in Namibia: Is This Cause for Concern?"

SIAPS worked with the TIPC and University of Washington to conclude the sentinel-based active surveillance activity. A technical report on the sentinel-site active safety surveillance of first-line ARVs carried out at the Katutura Intermediate and Windhoek Central Hospitals was completed in December 2014. The active surveillance activity prospectively determined the incidence and severity of and risk factors for AEs in persons receiving first-line, highly active ART (HAART) at two sentinel sites. The report indicated that 66 (16%) of the 413 patients experienced at least one adverse event, none of which was fatal or life-threatening. The incidence rate of experiencing at least one adverse event was 33/100 person-years. Based on this report, SIAPS worked with TIPC and University of Washington to write an abstract and a manuscript on the sentinel surveillance results. The abstract was presented at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) conference held in November 2015.

In collaboration with the University of Washington, SIAPS provided technical guidance to the MOHSS Division of Pharmacy Services to conduct a pharmacoeconomics analysis of the health benefits, potential costs, and cost-effectiveness of a national active surveillance program, compared to the existing spontaneous ADR reporting system. The draft report is under review by the MOHSS. The MOHSS-TIPC, which SIAPS has supported in previous years, was able to review all 55 ADR reports received in January–March 2015 without help from SIAPS

SIAPS provided support to the TIPC to plan and adapt a curriculum and materials for the Second Medicine Safety Surveillance Training of Trainers (TOT), which was conducted on March 4–6, 2015.

Medicine Safety Surveillance for TB and HIV TOT, held in Ondangwa, Oshana region, October 1–3, 2014, Photo credit: *SIAPS*

The training drew a total of 13 participants, who were pharmacists and medical doctors from district hospitals and regional offices from the southern, central, eastern, and western regions of Namibia.

RESULTS

Systems Established for Pharmacovigilance

Community Pharmacovigilance

- SIAPS facilitated discussions between TIPC and Project HOPE aimed at improving the detection and reporting of adverse reactions to antiretroviral and anti-TB medicines and supporting adherence to treatment, especially among TB/HIV co-infected patients, by Project HOPE's field promoters.

- SAIPS supported the training of 60 of Project HOPE's TB field promoters in Kavango region to improve reporting of adverse reactions to anti-TB medicines and ARVs.

- SIAPS staff conducted a support visit to Project HOPE's office in Ongwediva and trained the clerk on how to enter data in the ADR spreadsheet.

- SIAPS staff participated in advocacy for PV through a presentation made to health care workers in Ohangwena region.

Health Facility Pharmacovigilance

SIAPS supported health facility PV by providing technical assistance on issues of passive surveillance and active surveillance.

With regard to passive surveillance, SIAPS supported the TIPC to achieve the following results:

- Increased awareness of the importance of seeking out and reporting ADR by health facility staff

- Increased capacity of TIPC to analyze ADR-reported data generated from spontaneous reports of patients on ART in Namibia from 2011 to 2013

In collaboration with the University of Washington, SIAPS provided technical assistance to the TIPC in implementing the active surveillance plan by achieving the following results:

- Developed and deployed a data entry tool for active surveillance system being conducted in two sentinel ARV sites (Windhoek Central Hospital and Katutura State Hospitals) and assisted TIPC with activity monitoring and data entry

- Conducted analysis of data from active surveillance system being conducted in two sentinel ARV sites

- Disseminated findings from active surveillance system conducted in two sentinel ARV sites, including organizing a dissemination meeting in Windhoek, and preparation of final report, abstracts, and manuscripts

- Assisted TIPC with planning for expansion of active surveillance system into additional ARV clinic sites as well as PMTCT and TB clinic sites

- Assisted TIPC with records-linkage PV to assess emerging safety signals

Active versus Spontaneous Surveillance—Cost-Benefit Analysis

Health outcomes, potential costs, and cost-effectiveness of a national active surveillance program, compared to those of the existing spontaneous AE reporting system, were projected. SIAPS collaborated with the University of Washington in providing technical guidance to the TIPC to determine the projected health, cost, and economic outcomes of an active surveillance system for all HIV patients placed on ART in public HIV clinics in Namibia. The cost-effectiveness report findings provided key inputs in informing the potential national expansion of an active surveillance PV program.

Development of Technical Reports, Abstracts, and Manuscripts

The following technical reports, abstracts, and manuscripts related to strengthening PV in Namibia were developed during the five years:

- *National Guidelines for Medicines Safety Surveillance,* November 2011

- Technical report: *Signal of Increased Frequency of Severe and Life-Threatening Reactions to Nevirapine: Pharmacovigilance in Namibia, May 2012*

- *Namibian Antibiotic Guidelines,* 2012 edition (published by NAAR)

- *Projected Cost-Effectiveness of Active Surveillance Pharmacovigilance of First-Line Antiretroviral Medicines Compared to Spontaneous Reporting Pharmacovigilance in Namibia,* May 2015

- TIPC report on the analysis of ART spontaneous adverse event report, March 2014

- Technical report on ADR reporting to TIPC in Namibia, October 2014

- Abstract titled "Review of Spontaneously Reported Adverse Event Data in Namibia's Vigibase® Database: Assessing the Safety of Antiretroviral Medicines"

- Manuscript titled: "Sentinel Site Active Surveillance of Safety of First-Line Antiretroviral Medicines in Namibia," accepted for the journal *Pharmacoepidemiology and Drug Safety* in 2016, published online in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/pds.4022

- An article titled "Antimicrobial Sensitivity Patterns of Cerebrospinal Fluid (CSF) Isolates in Namibia: Implications for Empirical Antibiotic Treatment of Meningitis," published in *Journal of Pharmaceutical Policy and Practice* 2013 (volume 6)

- Two abstracts submitted for presentation at ICASA 2013: "Effect of Change in CD4 Count Threshold for Initiation of Antiretroviral Therapy on Rates of Substitution from Nevirapine to a Protease Inhibitor in Namibia" and "Increase in Reports of Nevirapine-Associated Serious Adverse Events in Namibia: Is This Cause for Concern?"

Trainings Conducted

Table 1 summarizes SIAPS-led trainings in PV.

Table 1: PV Trainings Provided by SIAPS

Title	Date
TB Field Promoters and Health Workers Training in Namibia 2012	November 15-16, 2012
TB Field Promoters' Training on Community PV Kavango	June 25-26, 2013
Training of Therapeutics Committees in Kunene Region	September 16-18, 2014
PV/Medicine Safety Surveillance for HIV and TB-Training of Trainers in Namibia	October 1-3, 2014
Medicine Safety Surveillance Training of Trainers, Namibia	March 4-6, 2015

PV Awareness Campaigns Supported by SIAPS

The following PV awareness campaigns were supported by SIAPS:

- The pharmaceutical symposium at UNAM-SoP for the dissemination of results from the analysis of NIP data conducted by TIPC. The symposium was held at UNAM on June 22, 2013.

- Medical Doctors and Dentists Forum 2014, held in Ondangwa in August 2014

Trend of ADR Reporting in Namibia

Since 2007, when the TIPC was created, there was a steady increase in ADR reporting up through 2011, and thereafter there was a sharp decline in the number of reports received by the TIPC from health care workers. This is illustrated in figure 4.

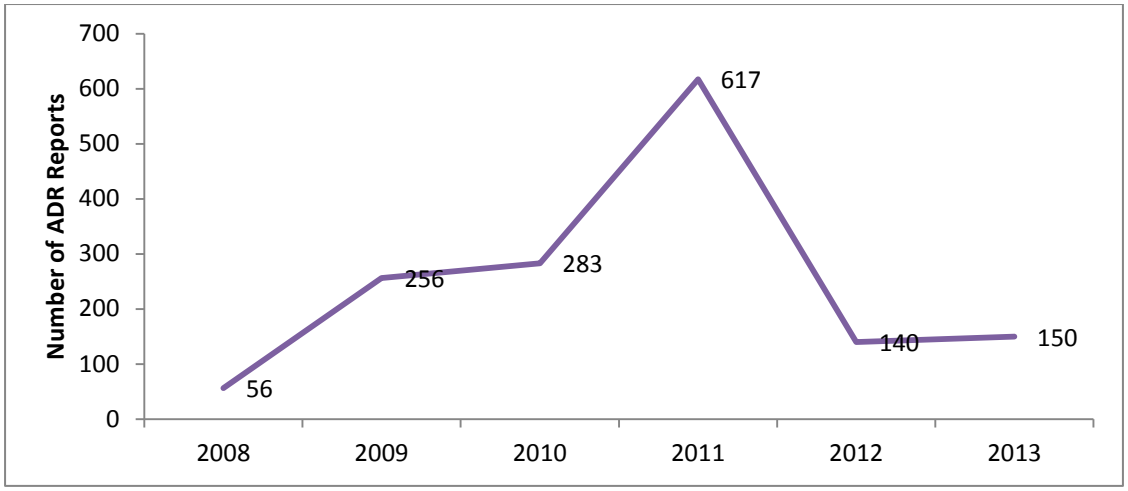


Figure 4. ADR reports received by TIPC, 2008–2013

SIAPS has provided technical assistance to the TIPC to create awareness among health care workers on PV and ADR reporting to TIPC for management. SIAPS also supported the TIPC to train TB field promoters on community PV and ADR reporting to TIPC. In fiscal year 2014, SIAPS also provided support to the TIPC to analyze ADR-reported data for the period 2011 to 2013. That review revealed that the highest frequencies of ADRs reported in 2011–2013were associated with skin disorders, and in particular, Stevens-Johnson syndrome accounted for the highest number (94 reports out of 218). With regard to ADRs associated with blood disorders, anemia 96/97 (99%) was associated with AZT. In addition, most reactions reported were serious in nature.

CONCLUSION

PV data are crucial for ensuring safety and effectiveness of medicines after they have been granted marketing approval. In 2007, the MOHSS with funding from USAID and assistance through the SPS Program implemented by MSH, created the TIPC. The TIPC serves as the ministry's official center for PV and therapeutics information, with a clear mandate to provide both proactive and query-response therapeutic information to health care workers as well as serve as a reference unit on PV by collecting and monitoring ADR reports spontaneously generated from facilities.

Since 2011, the USAID-funded SIAPS project implemented by MSH has been providing technical assistance to the TIPC to strengthen PV systems.

Adverse reactions continued to be reported to the TIPC although, since 2011, the rate of reporting slumped. This has been attributed to reporting fatigue among practitioners in health care facilities. To strengthen passive PV, SIAPS created awareness among health care workers on PV and ADR reporting to TIPC for management. SIAPS also supported the TIPC in training TB field promoters on community PV and ADR reporting to TIPC. From the analysis of ADR data from 2011–2013, it is clear that most of the reactions reported are serious in nature, therefore requiring targeted efforts by programs to identify strategies to reduce medicine harm to patients.

In collaboration with the University of Washington, SIAPS provided technical assistance to the TIPC to set up an active surveillance PV system pilot program for first-line ARVs, which was implemented at two sentinel ART sites (Windhoek Central and the Katutura Intermediate Hospitals). The incidence and severity of, and risk factors for, AEs in persons receiving first-line HAART at the two sentinel sites were determined. This, together with the findings of the cost-effectiveness analysis, provided key inputs in informing the potential national expansion of an active surveillance PV program.

These achievements need to be consolidated and advanced by supporting the TIPC to continue to roll out the active surveillance plan to more health facilities. In addition, TIPC will need to increase PV awareness campaigns among health professionals to improve ADR reporting.

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