Addressing the under-reporting of adverse drug reactions in public health programs
controlling HIV/AIDS, Tuberculosis and Malaria: A Prospective Cohort Study

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Abstract

**Background:**

Adverse Drug Reactions (ADRs) are a major clinical and public health problem world-wide. The prompt reporting of suspected ADRs to regulatory authorities to activate drug safety surveillance and regulation appears to be the most pragmatic measure for addressing the problem. This paper evaluated a pharmacovigilance (PV) training model that was designed to improve the reporting of ADRs in public health programs treating the Human Immunodeficiency Virus (HIV), Tuberculosis (TB) and Malaria.

**Methods:**

A Structured Pharmacovigilance and Training Initiative (SPHAR-TI) model based on the World Health Organization accredited Structured Operational Research and Training Initiative (SOR-IT) model was designed and implemented over a period of 12 months. A prospective cohort design was deployed to evaluate the outcomes of the model. The primary outcomes were knowledge gained and Individual Case Safety Reports (ICSR) (completed adverse drug reactions monitoring forms) submitted, while the secondary outcomes were facility-based Pharmacovigilance Committees activated and health facility healthcare workers trained by the participants.

**Results:**

Fifty-five (98%) participants were trained and followed up for 12 months. More than three quarter of the participants have never received training on pharmacovigilance prior to the course. Yet, a significant gain in knowledge was observed after the participants completed a comprehensive training for six days. In only seven months, 3000 ICSRs (with 100% completeness) were submitted, 2,937 facility-based healthcare workers trained, and 46 Pharmacovigilance Committees activated by the participants. Overall, a 273% increase in ICSRs submission to the National Agency for Food and Drug Administration and Control (NAFDAC) was observed.

**Conclusion:**

Participants gained knowledge, which tended to increase the reporting of ADRs. The SPHAR-TI model could be an option for strengthening the continuous reporting of ADRs in public health programs in resource limited settings.

1. **Background**
Adverse Drug Reactions (ADR) have emerged as a major clinical and public health problem accounting for approximately 5 to 35% of hospital admissions in both developed and developing countries [1-7]. In the United States and Europe, ADRs are also the leading causes of mortality [4, 8, 9 and 10]. In African countries, the introduction of ART has led to an upsurge in the cardio-metabolic disorders such as type 2 diabetes mellitus and hypertension. Some authors have provided evidence linking the use of the ARVs to the cardio-metabolic disorders [11, 12]. Similarly, treatment of drug resistant tuberculosis is contributing to the incidences of mental illnesses (psychosis), loss of hearing (ototoxicity) and kidney damage – all associated with the ADRs of second line anti-tuberculosis drugs [13].

Under-reporting of ADRs is a major challenge even in developed countries with adequate human and material resources to tackle the problem [4, 8, 9 and 10]. A systematic review of 37 studies by Hazell and Shakir found a median under-reporting rate of 94% [14]. There are many factors associated with the under-reporting of ADRs [15]. The commonest factors frequently cited in most of the studies are healthcare workers’ lack of knowledge and poor attitude [16-29]. In a very recent study by Terblanche et al [30] found that 53.8% of the participants gave not “knowing how to report” ADR as the reason discouraging the reporting. Interestingly, some studies have shown that training could address the lack of knowledge and increase the accuracy and rate of reporting of ADRs to regulatory bodies [14, 31].

Prompt reporting of ADRs to regulatory bodies to activate drug safety surveillance and regulation is the most pragmatic and cost-effective public health approach to addressing the risks of ADRs and ensuring public health [32]. The delay in reporting ADRs can be catastrophic. For example, almost seven million patients took Fenfluramine before its association with Valvular Heart Disease (VHD) was reported and the drug withdrawn from the market [33]. Similarly, over 10,000 children
in Germany in the early sixties had suffered Phocomelia before Thalidomide – the causative agent, was identified and withdrawn from clinical practice [34].

In the public health programs, especially the HIV, Tuberculosis and Malaria programs, millions of people are treated with a wide range of drugs, some of which have serious/life threatening adverse reactions [35-38]. In the western countries where anti-retroviral drugs (ARVs) have been used for many years, cases of rising obesity, weight gain and cardio-metabolic diseases are persistently being reported in association with the use of ARVs [39-40]. Drug safety is therefore a serious concern, especially in the public health programs treating large populations of people with potentially life-threatening drugs.

1.2. The pharmacovigilance system in Nigeria

Pharmacovigilance systems (PVS) refer to schemes that are established to facilitate the reporting of suspected ADRs to national or international body responsible for the monitoring of drug safety and regulations. Countries participating in the international drug monitoring scheme are required to collect and submit their reports to the International Drug Monitoring Center in Geneva.

Nigeria joined the International Drug Monitoring Scheme in 2004 and became the 74th member country. The National Agency for Food and Drug Administration and Control (NAFDAC) – the body responsible for drug safety and regulation, thereafter, developed a National Pharmacovigilance Policy and instituted an administrative structure, consisting of the National Pharmacovigilance Center (NPC) in Abuja and Zonal Pharmacovigilance Centers (ZPC) in each of the six geopolitical regions of the country.

NAFDAC also instituted the National Pharmacovigilance System which involves signal detection, collection, collation and analysis of ADRs [41]. Organizations or individuals holding a marketing

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authorization for marketing medicinal products are mandated to report any suspected ADR associated with the product they are authorized to market [41]. Healthcare providers (pharmacists, doctors and nurses) are also required by the government to report suspected ADRs, although this is not mandatory [41] as is the case in Sweden, France and Italy [42].

The primary tool for reporting ADRs in Nigeria is a structured in-take form known as the “NAFDAC Yellow Form” or “ADR Form” (https://www.nafdac.gov.ng) [Additional File 1; Figure 2]. This form is similar to the United Kingdom’s Yellow Card and has five major sections, which must all be accurately completed. A fully completed ADR form is known as the “Individual Case Safety Report” (ICSR).

The quality of an ICSR is directly proportional to the amount of clinically relevant information that is included [43-46]. On this basis, an ICSR with 100% completeness is expected to have the highest quality provided that the information included in all the sections is accurate. Poor quality ICSRs are usually quarantined by the NPC as they cannot be sent to the International Drug Monitoring Center in Uppsala, Sweden.

A typical ICSR provides the following information:

a. Patient details (name, age, sex and weight)

b. Adverse drug reaction (description, date reaction started and stopped and outcome – recovered fully, congenital abnormality, recovered with abnormality, life threatening and death)

c. Suspected drug (brand and generic names, batch number, NAFDAC number, expiry date)

d. Concomitant medicines (all medicines taken in the last three months)

e. Source of report
The reporting of ADRs in Nigeria follows two major steps:

a. Accurate completion of the ADR forms when a suspected ADR is observed by healthcare providers or reported by a patient during routine treatment of health conditions. Marketing Authorization Holders (MAH) are also expected to complete the ADR forms when suspected ADR are reported to them by patients, health institutions or the healthcare workers within and outside the country.

b. Dispatch the ICSRs to the NPC in Abuja.

The ICSRs are dispatched to the NPC in Abuja through different means. The responsibility of the NPC is to validate and analyze the submitted ICSRs and extract the relevant information into VigiBase – a proprietary web database (https://www.who-umc.org/vigibase/vigibase/) hosted at the World Health Organization (WHO) collaborating center for international drug monitoring in Uppsala, Sweden.

1.3. The pervasive problem of under-reporting of adverse drug reactions in Nigeria

The under-reporting of ADRs in Nigeria has been documented in several studies [47-50]. According to NAFDAC, only 16,500 ICSRs out of 80,000 uncompleted ADR forms distributed nation-wide for 12 years (2004 to 2016), equivalent to 1,375 ICSRs per year were submitted back to NAFDAC [51]. The WHO criteria for adequate reporting of ADRs are 200 reports per million inhabitants per year [52]. With a population of 170 million inhabitants in 2016, at least 34,000 ICSRs should have been submitted to NAFDAC instead of the 1,375 ICSRs. Furthermore, Nigeria had 323,941 healthcare workers [53-54] (consisting of Physicians, Nurses, Midwives, Pharmacists, Pharmacy-technicians, Radiographers, Medical Laboratory Scientists and Community Health Officers), [55-56] according to the 2005-2007 report of the National Professional Medical/Health Regulatory bodies. In 2015, NAFDAC reported that only 1,385 ICSRs [Additional File 2: figure
were submitted by over 323,941 workers. Given the large population of healthcare workers
and the overwhelming increase in drug consumption due to the high burden of HIV/AIDS,
Tuberculosis and Malaria, submitting only 1,385 ICSRs clearly indicates that Nigeria is facing a
major crisis of under-reporting of ADRs. Ironically, the factors that are undermining the reporting
of ADRs in other countries are rife in Nigeria and these include lack of knowledge, inaccurate
description of ADRs, poor quality reports and poor compliance to the pharmacovigilance processes
(data collection, storage, management, risk assessment and communication) [14,41,44].

The SPHAR-TI model was designed to address the challenge of under-reporting of ADR through
capacity building. Until the SPHAR-TI course, majority (71.0%) of the participants in the study
have never received training in pharmacovigilance but were working in public health institutions
or hospitals directly treating HIV/AIDS, Tuberculosis and Malaria through the respective public
health disease control programs. Some studies have reported high prevalence of ADRs emanating
from these public health programs [13, 35, 37, 38, 39, 40], thus, justifying the SPHARTI model.

1.4. The SPHAR-TI model

The SPHAR-TI model – described under “Additional File 2”, was a 12 month modular course,
modelled after the WHO accredited Structured Operational and Training Initiative (SOR-TI)
[57,58] The model incorporated six distinct but inter-related activities, referred to as the SPHAR-
TI’s principles. These are: a training workshop; participants’ mobilization; monitoring and
evaluating and providing feedback; setting up a reporting system; providing leadership and
collaborating with the government. This paper evaluated the model with the main objective of
describing its outcomes.

2. Methods
This manuscript complies with the STROBE reporting standard for observational studies.

2.1. Ethics approval

Ethics approval was given by the National Health Research Ethics Committee of Nigeria under the title: “Engaging indigenous organization to sustain and enhance clinical services for the prevention, care and treatment of HIV/AIDS in the Federal Republic of Nigeria under the President’s Emergency Plan for AIDS Relief (PEPFAR)”; Number: NHREC/01/01/2007; dated August 12, 2016. The Institute of Human Virology Nigeria, headed by Dr. Patrick Dakum, obtained this ethics clearance for all the studies conducted under its mentor-ship.

2.2. Setting

Selected health facilities and institutions in the six geopolitical regions of Nigeria constituted the setting. Nigeria has six geopolitical regions with a population of 170 million inhabitants. These regions include North-east, North-west, North-central, South-west, South-east and South-south.

2.3. Study population

The study population consisted of health care workers (Nurses, Physicians and Pharmacists) who were selected for the SPHAR-TI course based on rigorous selection criteria itemized in Table 1.

| Table 1: Participants’ selection criteria for the SPHAR-TI model |

2.4. Study design

A prospective cohort design was deployed for the evaluation of the SPHAR-TI model. Participants that attended the SPHAR-TI’s workshop (see Additional File 2) were followed up for 12 months through internet and telephone communication. Performance was evaluated based on the meetings
of milestones. Bio-demographic characteristics were recorded, and participants’ knowledge assessed at baseline. Five days after the workshop, participants’ knowledge was re-assessed without giving them a prior warning they would be re-assessed. ICSRs were submitted online every three months (31st May, 29th July, 30th September and 30th November 2016). The number of healthcare workers trained by the participants and the Pharmacovigilance Committees activated were also submitted online not later than 10th December 2016.

2.5. Outcomes of measure

The aim of the model was to improve the reporting of ADRs from both hospitals based and more importantly, community based public health programs controlling the AIDS epidemic, Tuberculosis and Malaria. The primary outcomes were knowledge gained and the number of ICSRs submitted to NAFDAC. We expected to see a significant gain in knowledge and a remarkable increase in the reporting of ADRs if the model is effective. The secondary outcomes were the health facility staff trained by the participants through the step-down training and the Pharmacovigilance Committees activated.

The secondary outcomes were evaluated because NAFDAC encourages the setting up of Pharmacovigilance Committees in health facilities as a pragmatic strategy for promoting the reporting of ADRs. During the workshop, participants were taught and encouraged to step-down the workshop and activate the committees. We expected the participants to be able to train others and set up new Pharmacovigilance Committees if the model is effective.

2.6. Evaluation of the outcomes of the model
The overall outcome of the model was assessed by comparing the number of ICSRs submitted by
the national health workforce in seven months with the number submitted by the participants in
seven months. The primary and secondary outcomes were evaluated as described below:

2.6.1. Gain in knowledge

Gain in knowledge was assessed using a structured questionnaire, consisting of 24 questions
developed by expert physicians and pharmacists in the three diseases (HIV, TB and Malaria). The
questions covered the clinical management of HIV/AIDS, Tuberculosis and Malaria and the ADRs
associated with the use of antiretroviral, anti-tuberculosis and anti-malaria drugs. The
questionnaire also assessed the knowledge of Nigeria’s ADR reporting and pharmacovigilance
system.

Prior to the commencement of the workshop, the questionnaire was administered for an hour (pre-
test). At the end of the workshop, which was five days after the pre-test, the same questionnaire
was re-administered (post-test). To minimize measurement biases, the questionnaire was
withdrawn immediately after the pre-test and participants were not warned the questionnaire would
be re-administered after the workshop. Participants did not also know the result of the pre-test
until after the post-test. The pass mark for the pre and post-tests was 45%.

2.6.2. Individual case safety reports submission

The correctness and completeness of the ICSR and the quantities submitted online were assessed.
All submitted ICSRs were manually checked for correctness and completeness and the total
number of correctly completed forms were counted and recorded in each cycle. We summed up
the number of ICSRs submitted within seven months and compared it with the amount that would have been submitted by the national health workforce in seven months in 2015.

2.6.3. Pharmacovigilance committees activated and training of health facility staff by participants

To assess the two variables, participants were given a spreadsheet for recording their activities after the workshop. The spreadsheet included the following variables:

(a). Status of the health facility

(b). Date of training

(c). Description of training

(d). Objectives of the training

(e). Mode of delivery of training content

(f). Number of doctors, nurses and pharmacists in attendance

(g). Number of Pharmacovigilance Committees activated

(h). Involvement of hospital management

(i). Collaboration with a pharmaceutical company in the training

(j). Collaboration with NAFDAC.

The completed spreadsheets were submitted to NAFDAC online at different times but not later than 10th December 2016. We extracted the number of health facility staff trained and the number of Pharmacovigilance Committees' activated into a template for analysis.
2.5.4. Statistical analysis

We applied descriptive statistics (mean, percentage and summation) in the analysis of the bio-demographic data and primary and secondary outcomes. The overall outcome of the model was analyzed by calculating the percentage increase in ADR submission using the arithmetic formula:

\[ T-M/M\times100 \]

[Where \( T = \) total number of ICSRs submitted by the participants in seven months; \( M = \) total number of ICSR submitted by the national health workforce in seven months]. According to NAFDAC, in 2015, the over 323,941 national health workforces submitted 1,385 ICSRs [Additional File 1], equivalents to 805 ICSRs in seven months. The 3000 ICSRs (\( T \)) and 805 ICSRs (\( M \)) were plucked into the arithmetic formula to determine the percentage increase in ICSRs submission.

Participants gain in knowledge was analyzed by calculating the difference between the mean pre-test and post-test scores. Summation was applied in analyzing the number of ICSR submitted by the participants, health staff trained by the participants and Pharmacovigilance Committees activated.

3. Results

Participants’ characteristics are presented in Table 2. Fifty-five out of 56 participants attended the workshop and were trained, equivalent to 98.2% attendance rate. Participants without a previous training in pharmacovigilance were more than participants that have attended pharmacovigilance training (s) in the past [39(71%) vs 16 (29.1%)].

Table 2: Participants’ characteristics, \( N = 55 \)

Table 3 compares the difference in the mean scores (gain in knowledge) among the participants. It appears participants >40 years [9.4 (SD=7.0], Pharmacists [8.5 (SD= 7.4)], and Nurses [7.6]
(SD=6.4], participants treating malaria [9.3 (SD=8.8] and those without previous training [9.5 (SD=7.8)], had remarkable gain in knowledge after the workshop.

**Table 3: Association between post test scores and participants’ characteristics**

The outcomes of the model are presented in Table 4. Participants demonstrated a significant gain in knowledge (20.4 vs 27.8 (P value < 0.001) and submitted 3000 ICSRs with 100% correctness and completeness. Compared with the 805 ICSRs submitted by more than 323,941 healthcare workers in the general population who were not SPHAR-TI trained, the percentage increase in ICSRs submission was 273%. Participants were also able to independently train 2,937 healthcare workers and activated 46 Pharmacovigilance Committees.

**Table 4: The outcome of the SPHAR-TI model**

4. **Discussion**

The major finding of this evaluation is the significant gain in knowledge observed among the participants generally. NAFDAC’s concordance on the effectiveness of the model to significantly improve the reporting of ADRs in Nigeria [Additional file 1: Figure S1] buttresses this observation and underscores the potential viability of the model to improve the reporting of ADRs in public
health programs. Furthermore, the positive outcome achieved when NAFDAC tested the model in
the training of 600 healthcare workers from ten states in Nigeria [Additional file 1: Figure S1],
suggests that the model can be replicated in countries facing similar challenge of under-reporting
of ADRs with Nigeria.

We also observed four additional outcomes. Firstly, participants developed the capacity to detect
and accurately report ADRs including the serious ADRs such as Stevens Johnson Syndrome (SJS).
Secondly, the rate of ADR reporting increased by 273%, when compared with the average
reporting rate in the general population over the past 12 years. This finding is consistent with the
findings from previous studies that examined the impact of training aimed at improving the
reporting of ADRs [31, 59]. Thirdly, participants were able to train their peers, thus, they increased
the number of healthcare workers for pharmacovigilance service delivery particularly in the
communities. In addition, participants developed the capacity to activate Pharmacovigilance
Committees in their various health facilities. This is a feat NAFDAC has persistently encouraged
in an effort to boost the reporting of ADRs in Nigeria.

We also observed two unintended outcomes of the application of the SPHAR-TI’s model. The first
is the detection and reporting of SJS by many participants. SJS is a fatal ADR associated with the
use of Nevirapine, a popular antiretroviral drug that constitutes the backbone of first line
antiretroviral regimen. This finding assures us that Nigerians are also susceptible to the ADR of
Nevirapine as reported in other climes. Further analysis of the submitted ICSRs might reveal other
life threatening ADRs in the Nigerian population, which the National Agency for the Control of
AIDS (NACA) need to pay close attention to. The second outcome is the interplay of several
factors resulting in an increase in the reporting of ADRs. The model combined at least six factors;
there is no gainsaying in concluding that training alone without the other factors could not have
yielded the results we have reported. Perhaps, the reason Nigeria and other countries are not able
to significantly address the challenge of under-reporting of ADRs despite the abundance of training
may be the over-reliance on training without combining the other factors.

We observed a surprised finding in the evaluation (table 3). Participants without prior training
tended to gain knowledge more than those who have attended pharmacovigilance trainings. The
same tendency was observed among the health care workers, with pharmacists and nurses gaining
knowledge more than the medical doctors. We do not have a viable reason for this but we suspect
that personal commitment and seriousness may have led to the difference. Participants without
prior training and the other healthcare workers were more committed to learning than the medical
doctors who presumed they already knew the content of the course.

The model holds an important lesson for sub-Saharan Africa (SSA), which has the largest public
health programs treating millions of people with HIV, Tuberculosis and Malaria. Currently, over
20 million people must be placed on antiretroviral drugs according to the new WHO treatment
guidelines for HIV [60]. The risk of “antiretroviral therapy associated ADRs” is expected to be
higher in this region than any other region in the world. Evidence from studies conducted in
developed countries where antiretroviral therapy has been offered for many years have reported a
rise of cardiometabolic disorders like type 2 diabetes mellitus and cardiovascular disease [61-65],
which have long been associated with the antiretroviral medications. In the Drug Resistant
Tuberculosis public health program, hearing loss associated with the use of the injectable
aminoglycosides (Amikacin and Kanamycin) is a major clinical challenge [66-67] and yet,
thousands of patients are using these drugs in the communities. As sub-Saharan African countries
continue to scale-up public health treatment programs in a wider global effort to end HIV and
Tuberculosis, the prevalence of ADRs will continue to increase, justifying the need for the training of healthcare providers for ADRs reporting.

Another factor that favors the training of healthcare providers for ADR reporting, which justifies the use of the SPHAR-TI model, is the acute shortage of healthcare workers in Africa. The “Brain Drain” report by Rebecca Coombes showed that the number of healthcare workers in many African countries is shrinking [68]. Ghana with a population of 20 million has only 1500 medical doctors and more than two-third of young Ghanaian doctors leave the country within three years of graduation. In Mozambique, a nation of similar size with Ghana, there are only 500 medical doctors [68]. Malawi has a worse situation; there are 12 million people but only 350 medical doctors are available to cater for all the health needs including the reporting of ADRs [68]. Nigeria appears to have the highest density of healthcare workers in Africa [37-54] but the large population size and the lack of capacity for reporting ADRs are major constrains. However, the training of healthcare workers as has been shown in several studies can improve the reporting of ADRs. The WHO in its 2013 report on “research for universal health coverage”, highlighted the need for training of healthcare workers in public health programs close to the supply and demand side of health services [69]. The structured pharmacovigilance capacity building model that we have evaluated addresses this gap in response to the WHO recommendation.

An important piece of information the SPHAR-TI model has demonstrated is that short training alone is not sufficient to stem the tide of under-reporting of ADRs. In fact, most developing countries, including Nigeria, provide trainings to healthcare workers to boost the reporting of ADRs but the crisis of under-reporting is not going away. What may be lacking are some of the factors the SPHAR-TI model has identified, which include: poor mobilization of healthcare providers, a weak monitoring and evaluation with complete absence of feedback mechanisms.
when ICSRs are submitted to central regulatory authorities, lack of a clear and practical means of
submitting ICSRs, lack of private-public collaboration, weak leadership and low motivation of the
workforce. If all these factors are combined appropriately, the reporting of ADRs could
significantly increase.

The model has some limitations that need to be considered alongside the positive outcomes. Our
participants were practicing doctors, nurses and pharmacists with some experience in the
pharmacotherapy of AIDS, tuberculosis and malaria. This knowledge may have contributed to the
knowledge gained through the SPHAR-TI training. This argument may however not hold true
because the medical doctors who are expected to have come to the training with the highest level
of knowledge and should have demonstrated higher scores compared to the pharmacists and nurses
actually scored less. The age of the participants is another factor; majority of the participants were
mid-career professionals occupying lower positions of responsibilities and were likely to be less
busy and quick learners. Elderly people with many social and professional responsibilities and
perhaps with a “slow to learn” disposition would probably have performed poorly. But again, the
results in table 3 demonstrate that participant over 40 years scored higher marks than the younger
people within the age bracket of 30-39 years. Overall, the long term impact of the model need to
be assessed; our findings in this study are only limited to the period of evaluation, which is between
10 to 12 months. However, despite these limitations, the model has provided an option for
improving the reporting of ADRs in resource limited settings.

We are recommending the use of the SPHAR-TI’s model to minimize the worrisome under-
reporting of ADRs in the developing world. As stated earlier, under-reporting of ADRs prevents
drug safety monitoring and regulation, which adds to the disease burden and mortality. Nigeria
and other developing countries may not be able to absorb additional health challenges caused by
ADRs as these countries are already overstretched by communicable and non-communicable
diseases. The SPHAR-TI model may be an effective approach that would complement existing
models of ADRs reporting in Africa and elsewhere.

**Conclusion**

The systematic and output driven training and follow-up of healthcare providers had a positive
impact on the reporting of ADRs. The SPHAR-TI principles effectively contributed to the success
of the model and are recommended to institutions or organizations providing pharmacovigilance
services in Africa and other regions with similar settings.

**Acknowledgement**

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analysis, decision to publish, or preparation of the manuscript. The views expressed in this
publication are entirely those of the authors and do not in any way represent those of their affiliated
institutions.
References


51. Speech of the Acting Director of the National Agency for Food and Drug Administration and Control, delivered on the 3rd March, 2016 in Abuja during the occasion of declaring the SPHAR-TI Workshop opened.


FIGURE LEGENDS AND TABLES

FIGURE LEGENDS

Additional file 1:

**Figure S1:** A letter from the National Agency for Food and Drug Administration and Control appreciating the Institute of Human Virology Nigeria for increasing the reporting of adverse drug reactions through the Structured Pharmacovigilance and Training Initiative.

**Figure S2:** Adverse drug reactions monitoring form (NAFDAC Yellow Form or ADR Form)
**Additional file 2:** Protocol of the Structured Pharmacovigilance and Training Initiative

### TABLES

**Table 1:** Participants’ selection criteria for the SPHAR-TI model

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<tr>
<td>1</td>
<td>Full time employee of a public health facility (non-profit health facilities that are opened to the public such as government or faith-based health institutions) providing Anti-retroviral Therapy (ART), Directly Observed Therapy (DOTS) and Roll Back Malaria (RBM) services</td>
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<tr>
<td>2</td>
<td>Directly involved in the treatment of HIV/AIDS, TB or Malaria under the ART, DOTS and RBM programs</td>
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Early or mid-career men and women with limited administrative responsibilities in the facility.

Pharmacovigilance naïve (i.e. have never been trained on Pharmacovigilance) or only received partial training in pharmacovigilance

A written Letter of Commitment to attend the workshop and also complete the monitoring and evaluation.

One reference letter attesting to the candidate’s suitability and potential to complete the course

Graduate or professional qualification or, strong recommendation by the public health program or work-place institution

Computer literacy and proven competence in the language of instruction (English)

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<td>&lt;30 years</td>
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<td>29 (52.7%)</td>
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<td>40+ years</td>
<td>21 (38.2%)</td>
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Table 2: Participants’ characteristics, N = 55
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<td><strong>Age</strong></td>
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<tr>
<td>&lt;30 years</td>
<td>5 (9.1%)</td>
<td>7.0 (2.7)</td>
<td>0.16</td>
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<td>30-39 years</td>
<td>29 (52.7%)</td>
<td>6.0 (7.3)</td>
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<tr>
<td>40+ years</td>
<td>21 (38.2%)</td>
<td>9.4 (7.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>24 (43.6%)</td>
<td>7.5 (7.7)</td>
<td>0.96</td>
</tr>
<tr>
<td>Male</td>
<td>31 (56.4%)</td>
<td>7.3 (6.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Profession</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doctors</td>
<td>11 (20.0%)</td>
<td>7.1 (6.4)</td>
<td></td>
</tr>
<tr>
<td>Pharmacists</td>
<td>34 (61.8%)</td>
<td>7.1 (7.3)</td>
<td></td>
</tr>
<tr>
<td>Nurses</td>
<td>10 (18.2%)</td>
<td>6.8 (4.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Disease area</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>39 (70.9%)</td>
<td>6.0 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>10 (18.2%)</td>
<td>6.0 (6.7)</td>
<td></td>
</tr>
<tr>
<td>Malaria</td>
<td>6 (10.9%)</td>
<td>7.9 (6.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Previous training</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>39 (70.9%)</td>
<td>7.0 (7.7)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>16 (29.1%)</td>
<td>7.5 (7.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Geopolitical Region</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North-Central</td>
<td>16 (29.1%)</td>
<td>7.1 (6.6)</td>
<td></td>
</tr>
<tr>
<td>North-West</td>
<td>3 (5.6%)</td>
<td>6.8 (6.7)</td>
<td></td>
</tr>
<tr>
<td>North-East</td>
<td>7 (12.7%)</td>
<td>9.4 (7.3)</td>
<td></td>
</tr>
<tr>
<td>South-West</td>
<td>25 (45.6%)</td>
<td>6.4 (7.1)</td>
<td></td>
</tr>
<tr>
<td>South-East</td>
<td>2 (3.6%)</td>
<td>7.5 (7.7)</td>
<td></td>
</tr>
<tr>
<td>South-South</td>
<td>2 (3.6%)</td>
<td>7.5 (7.7)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Association between post test scores and participants’ characteristics
<table>
<thead>
<tr>
<th>DESCRIPTION</th>
<th>Number (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PARTICIPANTS TRAINED</strong>¹: Participants trained at workshop vs Healthcare workers trained by participants after the workshop</td>
<td>55 vs 2937</td>
</tr>
<tr>
<td><strong>KNOWLEDGE GAIN</strong>²: Mean pre vs post test scores</td>
<td>20.4 vs 27.8 (P value&lt; 0.001)</td>
</tr>
</tbody>
</table>

Table 4: The outcomes of the SPHAR-TI model
| ADRs REPORTED<sup>3</sup>: ADR reported by SPHAR-TI trained participants vs ADR reported by Healthcare providers in the general population | 3000 ICSRs vs 805 ICSRs (percentage increase in ADR reporting = 273%) |
| PHARMACOVIGILANCE COMMITTEES<sup>4</sup>: Pharmacovigilance Committees activated by SPHAR-TI participants before the workshop vs Pharmacovigilance committees activated by participants after the workshop | 0 vs 46 |

**NOTES:**

1 = The number of participants trained at the workshop are compared with the number of healthcare workers trained by the participants after the workshop (55 vs 2937).

2 = The mean pre and post test scores (20.4 vs 27.8) are compared; the difference between the two scores is statistically significant suggesting knowledge gained.

3 = The number of ICSRs submitted to the National Agency for Food and Drug Administration (NAFDAC) by the SPHAR-TI trained participants in seven months are compared with the proportion of ICSRs submitted to NAFDAC by all the healthcare providers in Nigeria in seven months (3000 vs 805).

4 = The number of Pharmacovigilance Committees activated by the participants before they were trained is compared with the number they activated after they were trained (0 vs 46).