



Enhancing Pharmacovigilance in Sub-Saharan Africa Through Training and Mentoring: A GSK Pilot Initiative in Malawi

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Abstract

Introduction Pharmacovigilance (PV) systems to monitor drug and vaccine safety are often inadequate in sub-Saharan Africa. In Malawi, a PV enhancement initiative was introduced to address major barriers to PV.

Objective The objective of this initiative was to improve reporting of adverse events (AEs) by strengthening passive safety surveillance via PV training and mentoring of local PV stakeholders and healthcare providers (HCPs) at their own healthcare facilities (HCFs).

Methods An 18-month PV training and mentoring programme was implemented in collaboration with national stakeholders, and in partnership with the Ministry of Health, GSK and PATH. Two-day training was provided to Expanded Programme on Immunisation coordinators, identified as responsible for AE reporting, and four National Regulatory Authority representatives. Abridged PV training and mentoring were provided regularly to HCPs. Support was given in upgrading the national PV system. Key performance indicators included the number of AEs reported, transmission of AE forms, completeness of reports, serious AEs reported and timeliness of recording into VigiFlow.

Results In 18 months, 443 HCPs at 61 HCFs were trained. The number of reported AEs increased from 22 (January 2000 to October 2016) to 228 (November 2016 to May 2018), enabling Malawi to become a member of the World Health Organization Programme for International Drug Monitoring. Most (98%) AE report forms contained mandatory information on reporter, event, patient and product, but under 1% were transmitted to the national PV office within 48 h.

Conclusion Regular PV training and mentoring of HCPs were effective in enhancing passive safety surveillance in Malawi, but the transmission of reports to the national PV centre requires further improvement.

Plain Language Summary When a medicine or vaccine is made available for use, healthcare organisations maintain regular surveillance to confirm that the medicinal product is safe and effective. The efficiency of this surveillance depends mainly on the healthcare system and medical practices in place in each country. An important element is an effective procedure for identifying and reporting any unwanted medical occurrences (adverse events) after taking a medicinal product. In countries where regular safety surveillance has not been maintained, it is important to train and mentor healthcare providers on the need to be aware of adverse events and the importance of adhering to safety reporting procedures. GSK and partners conducted a pilot project in Malawi with the aim of improving adverse event reporting by training and mentoring healthcare providers. Training sessions and continuous mentoring were conducted over 18 months, involving 443 healthcare providers at 61 healthcare facilities. There was a large increase in the number of adverse events reported: from 22 in the 16-year period before the project started to 228 during the 18-month project period. This project showed that the training and mentoring programme for healthcare providers was effective in increasing the number of adverse events reported. This enabled Malawi to join the World Health Organization's international safety reporting scheme. Other countries facing similar challenges in safety surveillance systems could benefit from a similar approach.

Key Points

Many countries in sub-Saharan Africa lack the infrastructure to monitor the safety of drugs and vaccines, and healthcare providers in these regions are often not aware of safety reporting requirements.

The pilot pharmacovigilance enhancement project aimed to improve, in collaboration with national stakeholders, safety awareness and reporting among healthcare providers in Malawi.

A collaborative training and mentoring programme improved safety surveillance of drugs and vaccines and may be a suitable model for other countries facing similar challenges in pharmacovigilance.

1 Introduction

In the last decades, efforts to increase access to medicines (drugs and vaccines) in low- and middle-income countries (LMICs) have been facilitated by the World Health Organization (WHO), with support from international organisations such as the Global Fund, Gavi, the Vaccine Alliance and the United Nations Children's Fund [1, 2]. Additionally, new medicines are being developed for use primarily in sub-Saharan Africa (SSA). These include, among others, vaccines against Ebola virus disease and malaria [3, 4], and a chlorhexidine product for the prevention of omphalitis [5]. However, the introduction of new medicines is not systematically accompanied by pharmacovigilance (PV) processes to monitor medicine safety in these regions, with information on the safety profile in the post-marketing setting relying on existing suboptimal systems in many of the target countries [6]. For established products, data are primarily derived from high-income countries with well-established PV systems [7–9]. This is also problematic because the safety profile of certain products may differ between settings due to a variety of factors, including environmental and genetic influences [10–12]. It is therefore important that appropriate safety monitoring practices are in place in SSA for both established and newly launched products.

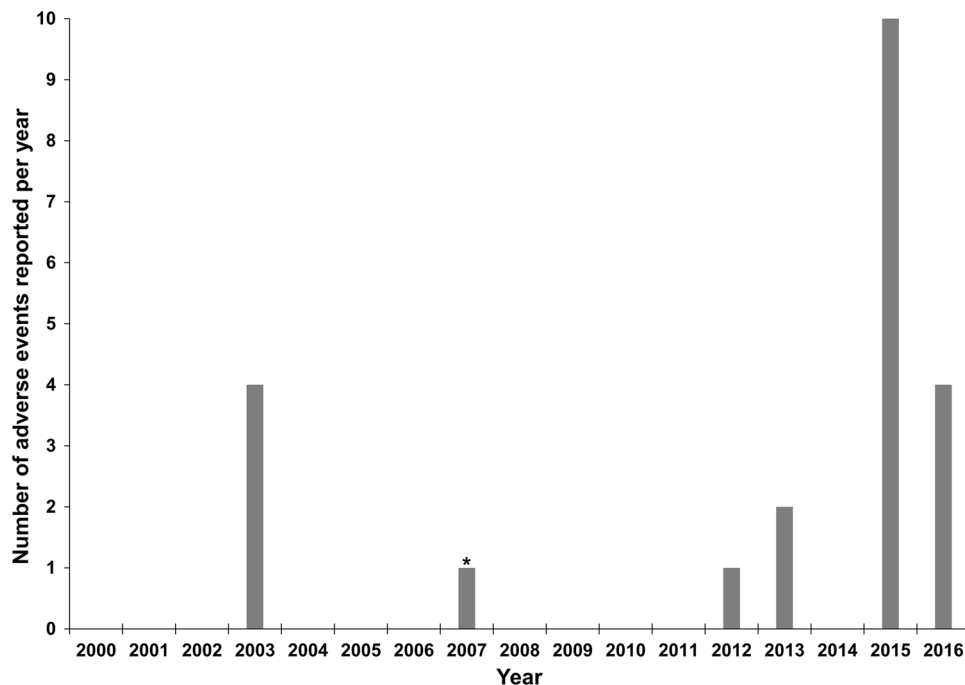
A majority of countries in SSA are classified as having minimal or basic PV systems, without the systematic framework to ensure adverse event (AE) reporting by healthcare providers (HCPs) and a lack of expertise in assessing the benefit–risk profile of products [13, 14]. Most are full or associate members of the WHO Programme for International Drug Monitoring (PIDM) [15]. However, an analysis

of global safety reporting data up to September 2015 indicated suboptimal reporting in Africa: less than 1% of the cumulative number of individual case safety reports (ICSRs) in VigiBase came from Africa, with almost half of those originating from South Africa and Morocco [10]. Many SSA countries are faced with the challenges of limited financial resources for medicine safety surveillance, inadequate technology, insufficient infrastructure and a lack of HCPs trained in PV. Challenges associated with traditional healing practices [16], the relatively low literacy level among adults, widespread self-medication and counterfeit drugs could also have an impact on AE reporting [17].

In 2016, a collaborative partnership led by GSK was initiated in three SSA countries with basic PV systems (Malawi, Côte d'Ivoire and the Democratic Republic of Congo). The initiative aimed to enhance passive safety surveillance and improve reporting of AEs by introducing spontaneous AE reporting systems and PV training and mentoring programmes for HCPs. Malawi is a low-income land-locked country in SSA, with a population of approximately 17 million, a total expenditure on health of 11.4% of the gross domestic product and physician density of 0.018 per 1000 population in 2009 [18]. Healthcare services in Malawi in 2007 were provided mainly by government facilities (54.3%), 18.9% by private for-profit owners and 13.9% by non-governmental district facilities administered by the Christian Health Association of Malawi [18]. Governmental facilities are organised in a three-tier system, consisting of primary, secondary and tertiary care, interconnected by patient referral [18]. Primary care consists of a rural network of healthcare centres run by nurses and assistants, with no doctors. For cases that cannot be handled in these healthcare centres, secondary-level care is provided by district hospitals, located in each of Malawi's 29 districts, which provide some surgical services. The tertiary tier consists of central hospitals, such as the Queen Elizabeth Central Hospital (QECH) in Blantyre, which have more advanced equipment and specialised medical personnel, and are located in the four main urban areas of Malawi [19].

The current system for monitoring drug safety in Malawi is coordinated by the Pharmacy, Medicines and Poisons Board, which is the country's National Regulatory Authority (NRA) [20]. Before project implementation, Malawi did not have a functional national PV centre and district Expanded Programme on Immunisation (EPI) coordinators were responsible for reporting the occurrence of AEs following immunisation (AEFIs) after the initiation of mass vaccination programmes. Between 2000 and 2016, the number of AEs notified per year ranged from 0 to 10 (all AEFIs) in Malawi (Fig. 1). Major barriers to safety surveillance of medicines in Malawi, as highlighted during the planning process for the initiative, included lack of knowledge of PV, fear of litigation, unavailability of AE reporting forms and

Fig. 1 Total number of adverse events reported in Malawi each year between 2000 and 2016, before project implementation in November 2016. All adverse events reported were adverse events following immunisation (AEFIs). *Serious AEFI



inadequate or unclear mechanisms for reporting. In addition, there was no national PV database and no national PV guidelines.

In this paper, we describe results following 18 months of implementation of the PV enhancement pilot project in Malawi. This was conducted through a collaboration of GSK, Malawi's Ministry of Health (MOH) via the NRA, the College of Medicine (University of Malawi, Blantyre) and PATH, a non-governmental global health organisation. The aim of the initiative was to improve reporting of AEs by strengthening passive safety surveillance via PV training and mentoring of local PV stakeholders and HCPs at their own healthcare facilities (HCFs).

2 Methods

2.1 Country Selection

Situational and gap analyses of the PV systems in SSA countries, including Malawi, were conducted by GSK to determine the capabilities of the existing systems, the level of safety surveillance and areas for improvement. Information on the gap analysis was obtained from the literature and published official documents [11, 21–23].

Malawi was selected because its PV system was classified as basic, i.e. it had a legal framework for PV and a structure was in place for AE reporting, but there was no means for signal generation and data management or risk assessment, evaluation, management and communication [14]. There was

no functioning national PV centre and Malawi was not a member of the WHO PIDM.

2.2 Project Planning and Preparation

A roadmap of the main stages of the PV enhancement pilot project in Malawi is shown in Fig. 2.

The PV enhancement project was presented and endorsed during an initiation meeting held in May 2016, with representatives from GSK, the MOH, EPI, NRA and WHO. The major challenges for the conduct of PV in Malawi were discussed and areas requiring further development and support were defined. The role of district EPI coordinators as the main PV focal points was also endorsed at this meeting, as their experience in AEFI reporting was relevant to the reporting of both AEFIs and adverse drug reactions (ADRs). Pharmacists, especially those established in tertiary and district hospitals, were also integrated as PV focal points after this meeting.

In June 2016, the project implementation plan was validated in a meeting that brought together national PV stakeholders from the MOH, the NRA, EPI, disease control programmes (HIV, tuberculosis), the Pharmacy Department of the College of Medicine, WHO, GSK and PATH.

HCFs for the pilot project (Area 25 Healthcare Centre in Lilongwe, Salima District Hospital and the QECH in Blantyre), representing a primary-, secondary- and tertiary-level facility, were initially selected, with the plan to cascade PV sensitisation to other districts in Malawi.

Key performance indicators (KPIs) for the project and target results were defined, based on the status of the existing

Fig. 2 Roadmap of the key stages of the Malawi pharmacovigilance enhancement pilot project. *ERC* expert review committee, *HCP* healthcare provider, *KPIs* key performance indicators, *MOH* Ministry of Health, *PV* pharmacovigilance

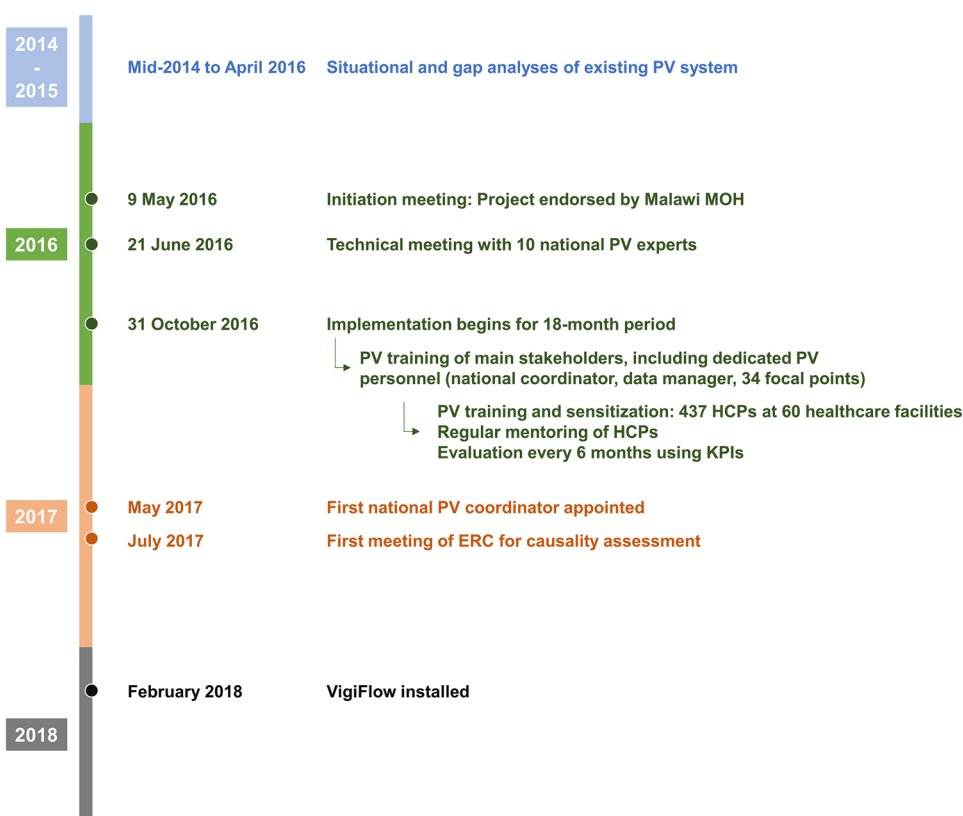


Table 1 Key performance indicators, agreed targets and actual achievements in the Malawi pharmacovigilance enhancement pilot project

Key performance indicator	Analysis period ^a (months)	Target	Achieved
Number of AEs reported	18	10	86
Proportion of AE forms transmitted from the HCF to PV office within 48 h	18	50%	< 1%
Proportion of complete AE reports	18	80%	98.2%
Proportion of serious AE reports investigated	18	100%	8.3%
Proportion of received AE forms entered into the PV database (VigiFlow) within 2 working days	18	100%	0%

AE adverse event, *HCF* healthcare facility, *PV* pharmacovigilance

^aKey performance indicators were monitored during the first 12 months of project implementation or the entire implementation period (18 months)

PV system, as presented in Table 1. The KPIs were evaluated jointly by GSK and the national stakeholders every 6 months and at the end of the project.

The roles and responsibilities of major PV stakeholders were assigned, the implementation plan was approved and related budget allocated, and communication mechanisms were established. The stakeholders approved the position of a national PV coordinator, responsible for leading and coordinating national PV activities in Malawi, effective at project start.

2.3 Project Implementation: National Pharmacovigilance (PV) System Strengthening and Capacity Building

2.3.1 National PV Centre

The national PV centre, located at the College of Medicine in Blantyre, was equipped with telephones, computers, printers and other office material. Malawi opted for VigiFlow as the national safety database for managing individual case reports and exchanging information with WHO's global database, VigiBase [24–26]. VigiFlow was installed in

February 2018 and, following training of the national PV coordinator and data manager on its use in September 2018, became functional in November 2018.

2.3.2 PV Training

PV training began in October 2016. Two types of training were delivered: basic PV training and abridged training. Training modules were assembled from material supplied by the WHO, GSK and PATH and were not product or manufacturer specific. Basic PV training was given by the College of Medicine, GSK and PATH to national PV stakeholders, the PV coordinator and PV focal points (NRA personnel, senior pharmacists and environmental health officers, including EPI coordinators) who had no prior PV training or good knowledge of PV. The training empowered the participants to deliver PV training to HCPs and consisted of a 2-day workshop on basic concepts of PV, AEFIs and ADRs, with case studies for group exercises. Refresher PV training was given to PV focal points after a year, with additional sessions on investigation of AEFIs and safety in pregnant women. The refresher also provided the opportunity for focal points to share experiences and address any challenges in the AE reporting process.

The abridged PV training targeted HCPs, primarily physicians, clinicians, nurses, pharmacists and health surveillance agents (HSAs). HCPs were trained directly at their HCFs for 1–2 h every 6 weeks by the national PV coordinator and the district PV focal point. Training aimed to create awareness of PV amongst HCPs and highlight the importance of safety surveillance and reporting of AEs. HCPs also received practical information on how to access AE report forms, complete them correctly and submit them promptly to the PV focal point.

2.3.3 PV Mentoring

Trained HCPs were mentored by GSK, the national PV coordinator and PV focal points through site visits every 6–8 weeks and/or regular phone calls with the national PV coordinator. Mentoring of HCPs was essential to sustain and expand awareness of AE surveillance and to establish and integrate PV in routine healthcare practice. It offered the opportunity to identify and address challenges in collecting and reporting AEs at the HCF and district level. Mentoring also aimed to sustain motivation of HCPs and facilitate locally adapted AE collection and reporting at each facility. For example, during sensitisations in HCFs, HCPs proposed that weekly staff meetings integrate PV sensitisation more broadly and that ward champions were used in each ward to improve AE reporting within HCFs. A ‘Meet the Focal Point’ tour was organised in April 2017 (6 months into implementation) to reach out to all PV focal points in their

respective districts, discuss the efforts made to implement PV since they received basic PV training and empower them to mentor and motivate HCPs within their districts.

Mentoring was also provided to the national PV coordinator and the data manager by GSK and PATH, supporting them in their roles and helping to address any challenges via regular phone discussions and team meetings. Assistance was also provided with sensitisation events, communication with PV experts and budget evaluation.

2.3.4 Strengthening Mechanisms for Reporting of Adverse Events (AEs)

Before project implementation, national guidelines on safety surveillance of ADRs and AEFIs were not finalised. There were no clear mechanisms for reporting and transmission of AE forms and no awareness of the availability and use of reporting tools. The AEFI form included sections on all essential information (reporter, event, patient and product) but excluded questions relevant to investigation and causality assessment. The forms were incorporated in a booklet not readily available to HCPs and only accessible to EPI coordinators and HSAs. A three-page ADR form was available but was barely used.

In absence of more detailed guidelines and adequate reporting tools, it was agreed with the PV stakeholders to report AEFIs using the WHO AEFI reporting form [27] and ADRs using the existing Malawi-specific ADR form. No specific timelines were defined for reporting AEs. However, it was agreed that AEs would be promptly reported to the national PV office. Completed AEFI forms were collected from the HCFs by the district PV focal point for transmission to the national PV office via the EPI office, while completed ADR forms were transmitted by the district PV focal point directly to the national PV office. Different means of transmitting the forms to the national PV centre were explored, including pre-paid envelopes distributed to all district HCFs nationwide, telephone calls, transmission of a snapshot of the AE form via WhatsApp¹ or by short message service (SMS), and transmission via email.

Due to delayed access to VigiFlow in Malawi, AE data received during the first 15 months of project implementation were entered into a Microsoft Excel[®] (Microsoft Corp., Redmond, WA, USA) spreadsheet at the PV centre. To foster motivation, recognition certificates were issued to PV focal points in districts with more than five reported AEs after 12 months.

¹ WhatsApp is a registered trademark of WhatsApp Inc.

Table 2 Healthcare facilities in which healthcare providers were trained and mentored in pharmacovigilance practices during the 18-month implementation period

District (total number of HCPs trained)	Number of HCFs	HCF	Department/unit	Number of HCPs trained	Mentoring done
Salima (135)	1	Salima District Hospital	Not specified	30	Y
	17	Satellite healthcare centres	Not specified	85	Y
Blantyre (60)	1	Queen Elizabeth Central Hospital	Paediatrics	20	Y
			Representation from each unit	18	Y
Mchinji (40)	1	Blantyre Adventist Hospital	Not specified	42	N
	1	Mchinji District Hospital	Not specified	20	Y
Chiradzulu (14)	1	Our Lady of Mt. Carmel Community Hospital	Not specified	20	Y
	1	Chiradzulu District Hospital	Not specified	2	Y
Lilongwe (85)	10	Healthcare centres affiliated to district	Not specified	12	Y (9)
	1	Area 25 Healthcare Centre	Not specified	30	N (several visits made; absent focal point)
Balaka (20)	1	Kamuzu Central Hospital	Pharmacists	55	Y
	1	Balaka District Hospital	Not specified	20	Y
Zomba (17)	1	Zomba Central Hospital	Not specified	17	Y
Kasungu (72)	1	Kasungu District Hospital	Not specified	21	Y
	23	14 public, 9 private HCFs	Not specified	51	Y
Total	61			443	

HCF healthcare facility, HCP healthcare provider, N no, Y yes

2.4 Project Communication

Three joint steering committee meetings, with the participation of at least two representatives from the MOH/NRA, two from GSK and one from PATH, were held during the 18-month period to review progress and challenges, as well as to endorse ways to further improve and sustain the PV system in Malawi. A meeting to that effect was also organised with national stakeholders every 6 months and two newsletters were distributed by the PV coordinator to keep PV partners informed on the progress of the project.

3 Results

3.1 PV Training

Thirty-four EPI coordinators from all nationwide districts and four NRA personnel received basic PV training and 443 HCPs had been trained at 61 HCFs (Table 2) by the end of the initial 18-month period, undergoing abridged PV training.

3.2 Evaluation of Key Performance Indicators

3.2.1 Number of AEs Reported

From 6 months into project, the number of AEs reported increased progressively (Fig. 3). Between November 2016 and November 2017, 86 AEs were reported (61 AEFIs and 25 ADRs), exceeding the KPI target of ten AEs set by the national PV stakeholders. By May 2018, 228 AEs (78 AEFIs and 150 suspected ADRs) were reported (Table 3; Fig. 3). The number of ADRs reported was higher than the number of AEFIs, probably due to ADR reports originating from Anti-Retroviral Therapy clinics close to the national PV office, where PV training and regular mentoring had been provided. Many of the other ADR reports followed mentoring and training by the PV team of the Pharmacy Department of the College of Medicine, Blantyre. Overall, 193 of 228 (84.6%) AEs were reported from PV-trained districts. AEFIs were reported from 19 districts; 57.7% (45) of all AEFIs were reported from the eight districts in which HCPs had undergone PV training (Table 3). ADRs were reported from four districts, in all of which some HCPs had received PV training (Table 3).

In the three HCFs selected initially as representative of the three-tier healthcare system, 40 AEs were reported from the QECH (tertiary care), six (all AEFIs) from the Salima

Fig. 3 Cumulative number of adverse event (AE) reports received in Malawi from November 2016 to May 2018. Total 228 AE reports: 150 adverse drug reaction reports and 78 reports of AEs following immunisation. Data for November 2016 to February 2017 are combined because no personnel were in place during this period to register adverse event reports. *Unknown* month unknown when AE report was received

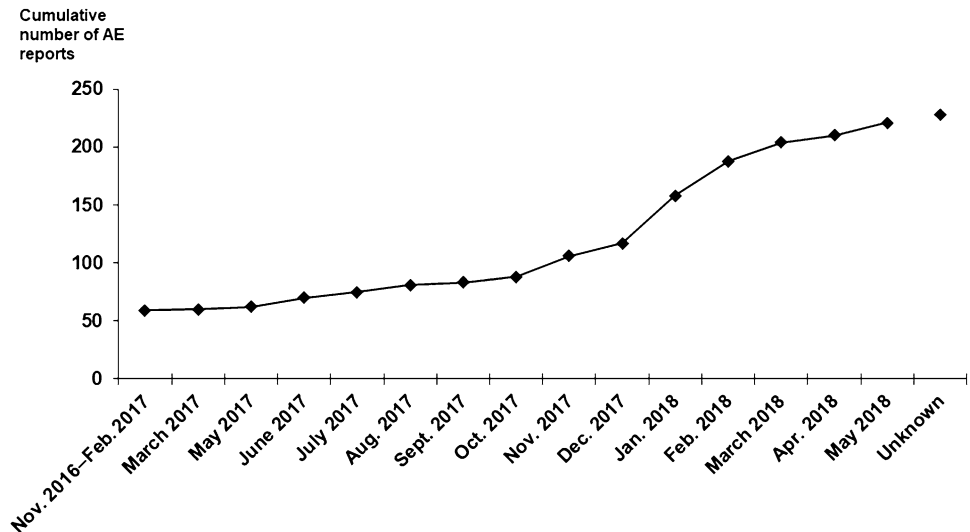


Table 3 Number of adverse events reported in each district (November 2016–May 2018)

District	Number of adverse events reported		
	ADR	AEFI	Total
Blantyre ^a	131	11	142
Kasungu ^a	6	7	13
Lilongwe ^a	10	2	12
Mchinji ^a	1	9	10
Salima ^a	0	6	6
Nsanje	0	5	5
Phalombe	0	5	5
Mulanje	0	5	5
Balaka ^a	0	5	5
Zomba ^a	0	4	4
Chitipa	0	3	3
Rumphi	0	3	3
Nkhotakota	0	3	3
Mangochi	0	3	3
Nkhatabay	0	2	2
Thyolo	0	1	1
Chiradzulu ^a	0	1	1
Ntcheu	0	1	1
Mwanza	0	1	1
Not recorded	2	1	3
Total	150	78	228

ADR adverse drug reaction, AEFI adverse event following immunisation

^aDistricts in which healthcare providers underwent pharmacovigilance training and mentoring

District Hospital (secondary care) and none from the Area 25 Healthcare Centre (primary care).

3.2.2 Transmission of AE Forms

Only two (<1%) AE reports were transmitted from the HCFs to the national PV office within 48 h (Fig. 4), well below the KPI target of 50%.

The primary route of transmission of AE reports to the national PV office was by WhatsApp mobile messages, with the remainder by telephone calls, SMS and a few by email. None of the AE reports were received via the pre-paid postal service.

3.2.3 Completeness of AE Reports

A total of 224 (98.2%) AE report forms contained mandatory information on the reporter, event, patient and product, exceeding the KPI target of 80%.

At the start of the project, although the four minimum elements of a valid report were provided in most forms, information was missing on medical history, concomitant medication/vaccination, chronological evolution of the event, laboratory test results and outcome. As training and mentoring progressed, AE reports became more complete.

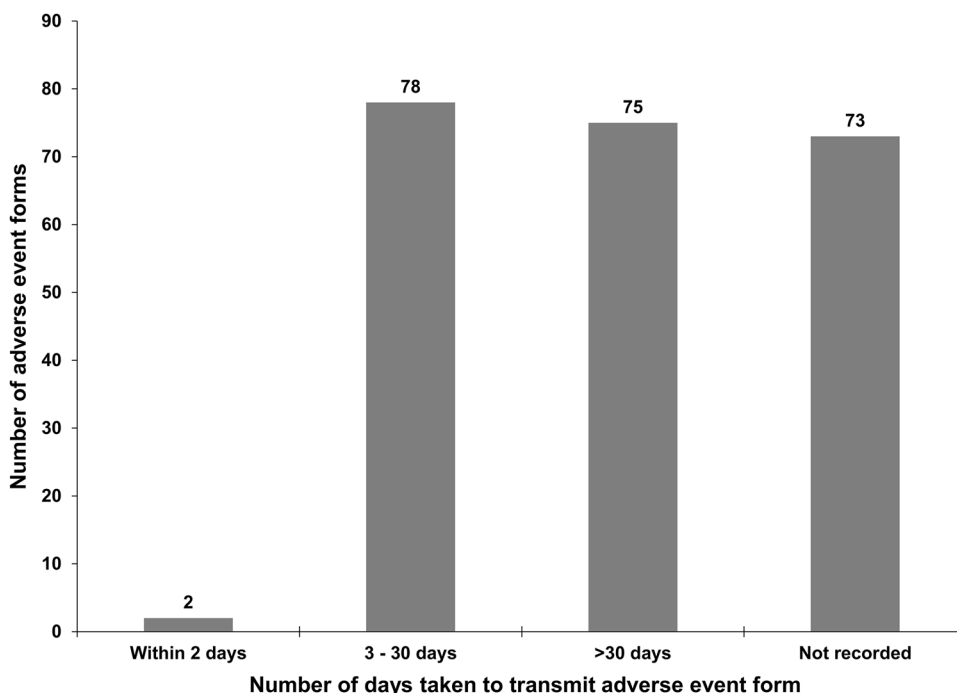
3.2.4 Serious AE Reports Investigated

Only one (8.3%) of the 12 serious AEs notified to the national PV office was investigated by the district focal point. This was far below the KPI target of 100%.

3.2.5 Timeliness of Recording AE Reports in the Individual Case Safety Report Database (VigiFlow)

On average, it took 2 months for the AE reports to be transmitted to the national PV centre. By May 2018, 40 AE

Fig. 4 Number of days taken to transmit adverse event forms from the healthcare facility to the national pharmacovigilance office



reports had been entered into VigiFlow. However, none of the AEs were entered into VigiFlow within 2 working days.

4 Discussion

This pilot initiative aimed to improve reporting of AEs for medicines in Malawi through enhancement of the passive reporting system. At the start of the project, Malawi did not have a functional national PV centre, there were no training programmes for HCPs in PV and the rate of AE reporting was very low, with a maximum of ten AEs notified per year between 2000 and 2016, all of which were AEFIs (Fig. 1). Results from the project over an implementation period of 18 months show that regular PV training and mentoring of HCPs was effective in improving passive safety surveillance and increasing AE reporting rates in all districts apart from one (Chiradzulu). The number of AE reports was highest in districts where training was provided, underscoring the benefits of regular training and mentoring. Raising PV awareness among HCPs was considered to be an essential first phase in a stepwise approach to capacity building and improved AE reporting in the context of immature PV systems.

Between 2017 and 2018, a notable increase in the number of AE reports (228 in total) was observed compared with the 2000–2016 period, during which only 22 AEFIs were reported in Malawi, despite the introduction of new medicines by public health programmes. The number of reports exceeded the agreed KPI target of ten AEs. The WHO

defined a reporting rate of at least ten AEFI reports per 100,000 surviving infants per year as indicating countries with a sustainable passive vaccine safety surveillance system [28]. With approximately 670,000 surviving infants annually [29], the expected number of reported AEFIs per year in Malawi is therefore 67. Seventy AEFIs were reported in the 12-month period November 2016 to December 2017 and, as of February 2019, data from more than 200 AE reports from Malawi had been entered into VigiFlow. The increased number of AE reports allowed Malawi to become the 135th full member of the WHO PIDM in 2019 [30].

The project initiation and planning meetings were important as they enabled transparency in decision-making and brought together for the first time the main PV stakeholders in Malawi to discuss PV. Regular communication and stakeholder meetings were also motivating in terms of the information provided on progress in improving the PV system and AE reporting, which helped to keep stakeholders on board for making transparent concerted decisions on PV. In this project, the number of AEs reported was also shown to depend on the motivation of the PV focal point. For example, the Nsanje, Phalombe and Mulanje districts reported five AEFIs each without prior sensitisation of HCPs in their facilities (Table 3), which is likely to be due to the personal motivation of the PV focal point involved and regular mentoring through calls and visits by the national PV coordinator. In Kasungu, the PV focal point reported five AEs (including two ADRs) before sensitizations were given formally to local HCPs. He was proactive in sensitising HCPs at healthcare centres in his district, including

private facilities. In the Chiradzulu district, only one AEFI was reported despite PV training and mentoring (Table 3). Here, the PV focal point was transferred soon after implementation began, and a replacement had to be provided to the PV team. Because of this and similar occurrences elsewhere, it was recommended to have back-up personnel in place and, in some facilities, an EPI coordinator–pharmacist pairing was used to facilitate PV enhancement.

Initially, the majority of HCPs had little or no knowledge of safety monitoring and AE reporting. Most had encountered AEs but were not aware that they had to be reported. In some situations where AEs were detected or notified to HCPs, reporting was hindered by unavailability of reporting forms and lack of awareness regarding reporting mechanisms. Fear of litigation was also identified as an important impediment to reporting of AEs. We found that continuous mentoring of the PV coordinator, PV focal points and HCPs was crucial to maintain motivation, adapt AE reporting procedures to the routine functioning of each HCF, implement timely measures to improve AE reporting and instil PV as a routine practice for HCPs. The mentoring programme also helped to identify and address other issues relevant to safety surveillance and make better use of existing support organisations. Some PV focal points took advantage of routine daily morning meetings of nurses and clinicians, monthly hospital staff meetings or other outlets, such as Continuing Professional Development training programmes, as a forum to deliver additional in-house sensitisations and reminders to HCPs. At the HCF level, motivated colleagues were identified in each ward or unit to coordinate AE reporting and sustain awareness. Involving hospital administration through communication of project updates also improved the engagement of HCPs within their facilities. From our experience in this project, the role of a dedicated national PV coordinator is very important for coordinating all PV activities nationwide and maintaining communication among the stakeholders for transparent concerted decisions and clarity on the way forward. In Malawi, EPI coordinators were identified as PV focal points, but it was also advantageous to actively involve pharmacists, especially in tertiary and district hospitals where they are responsible for dispensing medicines and can continue advocating for PV.

At the start of the project, the national ADR and AEFI guidelines were not yet finalised, which may partly explain the low numbers of prior AE reports. Delayed transmission of AE forms was a major challenge at all levels of the healthcare system, primarily because of the remoteness of HCFs and unclear transmission mechanisms. In these circumstances, the KPI to transmit AEs to the national PV office within 48 h was unrealistic. This issue was identified early in the project and focal points were advised to report AEs directly to the national PV coordinator by SMS or WhatsApp; the original form was subsequently collected

manually. A WhatsApp forum was created to share information among PV focal points and to improve the transmission of AEs to the national PV office. Other means of transmission, such as pre-paid postal envelopes or transmission by email, were challenging and did not reduce the transmission delays. For instance, AE forms posted in November 2016 never reached the national PV centre. Transmission was hampered by the poor internet connection in most districts.

The completeness of submitted forms was satisfactory, with 98% containing mandatory information on reporter, event, patient and product. The one-page WHO AEFI reporting form used was regarded as user-friendly because it requests the most relevant information in a clear and simple way and it includes explanatory notes on the back [27]. This was preferable to the initial reporting form, which required the name of the HCP who administered the medicine, further compounding the fear of litigation among HCPs. In contrast, the ADR reporting form used in Malawi was longer (three pages) and addressed both AE and drug quality issues; this form was subsequently modified to a one-page ADR form during the course of the project.

Limitations of this project included the absence of a functional Expert Review Committee for causality assessment at the start of implementation and the unavailability of a national safety database for most of the implementation period. Also, outcomes were affected by the absence of a permanent national PV coordinator and designated back-up. There was no official PV coordinator until 6 months into implementation, who in turn was replaced after 1 year. These issues have been addressed with the establishment of the Expert Review Committee, and the national PV centre personnel have been trained fully in AE data entry into VigiFlow for sharing into VigiBase. This pilot project could not assess sustainability since this cannot be determined over the relatively short period concerned (18 months).

AE reporting should be integrated as a routine practice for HCPs in clinical guidelines, to ensure health districts commit to their responsibility for AE reporting. Furthermore, key public health programmes, such as HIV, malaria and tuberculosis, should be engaged to harmonise PV activities within the remit of the national PV centre. Also, some organisations in Malawi, such as Médecins Sans Frontières and Riders for Health [31, 32], which are very active at remote healthcare centres on a weekly basis, could be solicited to assist in transmitting completed AE forms to the district level. Despite local enthusiasm for the project, there is still a need to expand PV sensitisation and mentoring to more HCPs in Malawi, and to evaluate means of overcoming the AE transmission delays. Moreover, it is important to adopt measures that will ensure sustainability of PV enhancement in SSA countries. Our experience from Malawi suggests it is important to utilise existing personnel (EPI coordinators and pharmacists) as PV focal points to avoid the need for

new employees, utilise national experts to train on PV at the facility level, and ensure national funding to address logistical issues related to training at facilities. It is also important for PV focal points to mentor at their facilities and peripheral healthcare centres, and transparently communicate all project challenges to the country PV experts. The ultimate vision of the project is to share experiences, lessons learned and challenges from the pilot phase, with the objective of engaging external partners in a concerted effort to roll out PV to other SSA countries. The next phase of the stepwise approach to capacity building and improved AE reporting would be to integrate safety signal detection and risk assessment, management and communication into the PV systems.

5 Conclusion

This project demonstrated that spontaneous AE reporting/passive surveillance can be improved by providing targeted technical support, such as regular in-house PV training and mentoring of HCPs at their own HCFs. This project also demonstrates the benefit of partnership between the NRA, national PV stakeholders from academia and the MOH, a non-governmental organisation and industry to positively impact and strengthen the PV system in Malawi. The lessons learnt from the 18-month PV enhancement pilot project in Malawi are invaluable for establishing more partnerships to expand the initiative nationwide and to other LMICs. General investment and improvements in healthcare systems will facilitate continued improvements in PV systems.

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Author Contributions All authors contributed to the technical details and planning of the PV enhancement pilot project. YGM, J-US, VJ, OM, CS, FC, MK and ND contributed to the data extraction, VJ, OM, CS, FC, MK and ND performed the study, YGM, VJ, OM, FC, ND, JC, CS, MK and GG contributed to the analyses, YGM, J-US, VJ, OM, OO-A, JC, CS, MK and GG conducted the analyses and interpreted the data. All authors reviewed and edited the manuscript. All authors have read and approved the final manuscript.

Compliance with Ethical Standards

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Conflict of interest VJ, JC, GG, OO-A, OO, J-US and YGM are employees of the GSK group of companies. OO-A, YGM and J-US hold shares in the GSK group of companies. YGM reports personal fees from GSK, outside the submitted work. CS reports a grant from the GSK group of companies to conduct this study. FC, ND, OM and MK report no conflict of interest.

Ethical approval Ethical approval was not required for this work.

Data sharing Data sharing not applicable to this article as no datasets were generated or analysed during the current study.







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