An investigation into the prospects of existing technologies to address the challenges faced in pharmacovigilance systems

by

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Declaration

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December 2018

Research outputs

The research outputs produced from this research includes two international conference articles, one national conference article, and a journal article.

Journal article:

- Journal article – An article titled "*Prioritising the challenges found in pharmacovigilance*" has been produced from a large portion of the content in Chapter 3 (refer to Section B.1 in Appendix B). Authors: Izak van Biljon Lamprecht; Louzanne Bam; and Imke de Kock. Status: To be submitted to an appropriate journal (national or international) for publication.

Conference articles:

- National conference article – An article titled "*An investigation into the prospects of existing technologies to address the challenges faced by pharmacovigilance systems*" has been produced from a large portion of the content in Chapter 2 (refer to Section A.1 in Appendix A). Authors: Izak van Biljon Lamprecht; Louzanne Bam; and Imke de Kock. Status: Published in the SAIIE28 conference proceedings.
- International conference article – An article titled "*Translating the pharmacovigilance challenge landscape to a lower level of abstraction: The implementation of a value chain analysis, the 5Why method, and fishbone diagrams*" has been produced based on the content in Chapter 5 (refer to Section C.1 in Appendix C). Authors: Izak van Biljon Lamprecht; Louzanne Bam; and Imke de Kock. Status: Published in the IAMOT2018 conference proceedings.
- International conference article – An article titled "*Investigating the prospects of the technology landscape to address the challenges faced in pharmacovigilance systems*" has been produced from a large portion of the content of Chapter 6 (refer to Section E.1 in Appendix E). Authors: Izak van Biljon Lamprecht; Louzanne Bam; and Imke de Kock. Status: To be submitted to the IAMOT2019 conference.

Abstract

Healthcare systems, especially those within resource-limited countries, are facing increasing pressures, which can, in part, be attributed to the struggles of balancing resource inventories, while still providing clinical care of high quality. Pharmacovigilance (PV), a system developed to ensure universal drug safety, constitutes one component of healthcare systems globally. PV systems in resource-limited countries are struggling to operate both efficiently and effectively, while continuously maintaining and ensuring universal drug safety. These PV systems are burdened by the lack of expertise and knowledge to (i) prioritise the challenges faced daily; (ii) identify the root causes of these challenges; and (iii) determine how these root causes of the challenges can be addressed by technology.

In this research, these three requirements are addressed. First, a systematic review is conducted to identify 15 challenges that are experienced in PV systems, especially those in resource-limited countries. These 15 challenges (referred to as the PV challenge landscape in this research) are prioritised with the use of: a PV system and PV challenge landscape matrix developed in this research and input from several subject matter experts. Seven challenges are regarded as priority, namely: culture, partnerships, transparency, insufficient resources, country-specific factors, technical capacity, and adverse drug-reaction under-reporting.

Second, an investigation into several translation techniques is conducted in order to determine which technique(s) is appropriate to be used to translate these challenges from a strategic to an operational level, and to identify the root causes of the challenges. The value chain analysis and the 5Why method, in combination with fishbone diagrams, are considered to be appropriate techniques. Following the implementation of these techniques, the identified root causes are once again prioritised based on inputs from SMEs in order to maintain focus on the root causes that have the most significant impact on PV systems whilst ensuring that the scope of the research remains feasible. It is concluded that 14 of the identified root causes should be prioritised for further investigation in this research.

Third, literature is reviewed to identify an appropriate technology selection framework that can be used to assess the technology landscape with regards to it being implemented in PV to address the root causes identified in this research. The technology selection framework developed by Chan & Kaufman (2010) is considered an appropriate framework, since it incorporates many elements one can associate with PV. 15 technologies that could potentially be used to address the most prominent root causes of the PV challenge landscape are identified with the use of grey literature and a focus group. With the use of Chan & Kaufman's (2010) technology selection framework, these technologies are assessed in order to determine which technologies are feasible to be implemented in PV. It is concluded that 13 of the originally identified technologies are feasible for addressing the prioritised root causes of the PV challenge landscape. Subsequently, a link between the 14 prioritised root causes of the prioritised PV challenge landscape and the 13 technologies is established, where it is described how each root cause can potentially be addressed by one or more of the 13 technologies.

This research significantly contributes to the PV system by identifying opportunities to utilise technology to address the root causes of some of the most prominent challenges in PV. Additionally, this research makes a methodological contribution by proposing a combination of techniques that can be used to: scan and prioritise the challenge landscape in PV, prioritise and identify the root causes of the challenges experienced in PV, and identify and assess potential solutions that can be used to address these root causes.

Opsomming

Gesondheidsorgstelsels, veral dié in hulpbronbeprekte lande, ondervind toenemende druk wat gedeeltelik toegeskryf kan word aan die stryd om hulpbronvoorrade te balanseer, en terselfdertyd hoë kwaliteit kliniese sorg te verskaf. *Pharmacovigilance* (*PV*), ‘n sisteem wat ontwikkel is om universele dwelmsveiligheid te verseker, vorm een komponent van gesondheidsorgstelsels wêreldwyd. *PV* stelsels in hulpbronbeperkte lande sukkel om doeltreffend en effektief te funksioneer, en terselfdertyd universele dwelmsveiligheid te handhaaf. Hierdie *PV* stelsels word belas deur die gebrek aan kundigheid en kennis om (i) die uitdagings wat daagliks aan die dag lê, te prioritiseer; (ii) die kernoorsake van hierdie uitdagings te identifiseer; en (iii) te bepaal hoe hierdie kernoorsake van die uitdagings deur tegnologie aangespreek kan word.

In hierdie navorsing word hierdie drie vereistes aangespreek. Eerstens word 'n sistematiese oorsig gedoen om 15 uitdagings wat in *PV* stelsels ervaar word, veral in die hulpbron-beperkte lande, te identifiseer. Hierdie 15 uitdagings (verwys na as die *PV*-uitdagingslandskap in hierdie navorsing) word geprioritiseer deur gebruik te maak van 'n *PV* stelsel en PV-uitdagingslandskapmatriks wat ontwikkel is in hierdie navorsing en insette van verskeie vakkundiges. Sewe uitdagings word as prioriteit beskou, naamlik: kultuur, vennootskappe, deursigtigheid, onvoldoende hulpbronne, landspesifieke faktore, tegniese kapasiteit en nadelige dwelmreaksie onderverslagdoening.

Tweedens word 'n ondersoek na verskeie translasie tegnieke gedoen om te bepaal watter tegniek(e) gepas is om hierdie uitdagings van strategiese tot operasionele vlak te transleer, en om die kernoorsake van die uitdagings te identifiseer. Die waardekettinganalise en die 5Hoekom-metode, in kombinasie met visgraatdiagramme, word as toepaslike tegnieke beskou. Na aanleiding van die implementering van hierdie tegnieke word die geïdentifiseerde kernoorsake weer geprioritiseer op grond van insette van vakkundiges om fokus te handhaaf op die kernoorsake wat die grootste impak op *PV* stelsels het, terwyl dit verseker word dat die omvang van die navorsing uitvoerbaar is. Daar word tot die gevolgtrekking gekom dat 14 van die geïdentifiseerde kernoorsake prioriteit vir verdere ondersoek in hierdie navorsing moet word.

Derdens word literatuur hersien om 'n gepaste tegnologie seleksie raamwerk te identifiseer wat gebruik kan word om die tegnologie landskap te assesseer met betrekking tot die implementering daarvan in *PV* om die kernoorsake wat in hierdie navorsing geïdentifiseer is,

aan te spreek. Die tegnologie seleksie raamwerk wat deur Chan & Kaufman (2010) ontwikkel is word beskou as 'n toepaslike raamwerk, aangesien dit baie elemente bevat wat mens met *PV* kan assosieer. 15 tegnologieë wat potensieel gebruik kan word om die belangrikste kernoorsake van die *PV*-uitdagingslandskap aan te spreek, word geïdentifiseer met die gebruik van grys literatuur en 'n fokusgroep. Met die gebruik van Chan & Kaufman (2010) se tegnologie seleksie raamwerk, word hierdie tegnologieë geassesseer om te bepaal watter tegnologie moontlik is om in *PV* geïmplementeer te word. Daar word tot die gevolgtrekking gekom dat 13 van die oorspronklik geïdentifiseerde tegnologieë haalbaar is om die geprioritiseerde kernoorsake van die *PV*-uitdagingslandskap aan te spreek. Vervolgens word 'n skakel tussen die 14 geprioritiseerde hoofoorsake van die geprioritiseerde *PV*-uitdagingslandskap en die 13 tegnologieë gevestig. Daar word beskryf hoe elke oorsaak moontlik deur een of meer van die 13 tegnologieë aangespreek kan word.

Hierdie navorsing dra aansienlik by tot die *PV*-stelsel deur geleenthede te identifiseer om tegnologie te gebruik om die kernoorsake van sommige van die prominentste uitdagings in *PV* aan te spreek. Daarbenewens maak hierdie navorsing 'n metodologiese bydrae deur 'n kombinasie van tegnieke voor te stel wat gebruik kan word om: die uitdagings landskap in *PV* te ondersoek en te prioritiseer, die kernoorsake van die uitdagings in *PV* te prioritiseer en te identifiseer, en moontlike oplossings te identifiseer en te assesseer wat gebruik kan word om hierdie oorsake aan te spreek.

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Nomenclature

Acronyms

ADE	Adverse drug event
ADR	Adverse drug reaction
AEFI	Adverse events following immunisation
AHP	Analytical hierarchy process
BPM	Business process management
CEM	Cohort event monitoring
DHP	Delphi hierarchy process
EHR	Electronic health record
EPV	Eco-pharmacovigilance
GDP	Gross domestic product
GSK	Glaxo Smith Kline
HCW	Healthcare worker
HIV	Human Immunodeficiency Virus
IAMOT	International Association for Management of Technology
IoT	Internet of Things
KAP	Knowledge, attitude, and practice
KPI	Key performance indicator
NGO	Non-governmental organisation
NPO	Non-profit organisation
PTA	Problem tree analysis
PV	Pharmacovigilance
RCA	Root-cause analysis

RMS	Resource management system
SAIIE	South African Institute for Industrial Engineering
SCM	Supply chain management
SME	Subject matter expert
TB	Tuberculosis
UK	United Kingdom
UMC	Uppsala Monitoring Centre
WAP	Wireless Application Protocol
WHO	World Health Organisation

Chapter 1: Research background

This introductory chapter provides the background for the thesis. It also provides the research rationale, problem statement, research aim and objectives, limitations and assumptions, validation strategy, key terminologies, and the research methodology.

1.1. Background

The Thalidomide disaster of the 1960s (Toklu & Uysal, 2008; Isah *et al.*, 2012) has been described as the largest man-made medical disaster in history (Vargesson, 2015). The disaster led to nearly 10 000 babies worldwide being born with extremity defects (Wang *et al.* 2009). Speculation followed on the true nature of these defects and who was to be held responsible (De Abajo, 2005). To this day, survivors of the tragedy are compensated by both government and the original manufacturers of the drug. However, the survivors still live with the consequences (Vargesson, 2015). Various researchers, including Wang *et al.* (2009); Stolk (2012); Klausen & Parle (2015) concur that this disaster made the need for drug safety monitoring and surveillance to prevent a tragedy of similar stature occurring in the future, apparent.

Subsequently, pharmacovigilance (PV) was introduced to the healthcare environment in the late 1960's (De Abajo, 2005). During this time, the World Health Organisation (WHO) unveiled the WHO Programme for International Drug Monitoring, an organisation consisting of multiple international partners aimed at international monitoring and surveillance of new and existing drugs (World Health Organization, 2002). PV enjoys much attention in this programme, now co-ordinated by the Uppsala Monitoring Centre (UMC) (World Health Organization, 2002).

1.2. Contextualisation

The WHO defines PV as the "*science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems*" (World Health Organization, 2002). Adverse drug reactions (ADRs) or adverse drug events (ADEs), which describe the unintentional and unpredicted reactions to, or side-effects of new or existing drugs, are regularly associated with PV (World Health Organization, 2014). When such unpredicted reactions or side effects occur, the ideal is that it is reported to the appropriate authorities. Depending on the degree of severity of the reaction, the report is either terminated at the national level, or sent on to the UMC (Strengthening Pharmaceutical Systems, 2009). This reporting process is illustrated in Figure 1.

In Figure 1, PV systems are described from a systems perspective. It is an illustration relating to people, functions, structures, and expected outcome and impact. People are categorised as being either reporters or evaluators. Reporters are those who report ADRs (or suspected ADRs) to the relevant authorities, known as the evaluators. Evaluators largely consist of various healthcare professionals who could do the necessary analysis to identify and categorise ADRs from the data that is reported (Strengthening Pharmaceutical Systems (SPS) 2009).

Forming part of the processes are the functions associated with PV, from ADR reporting to

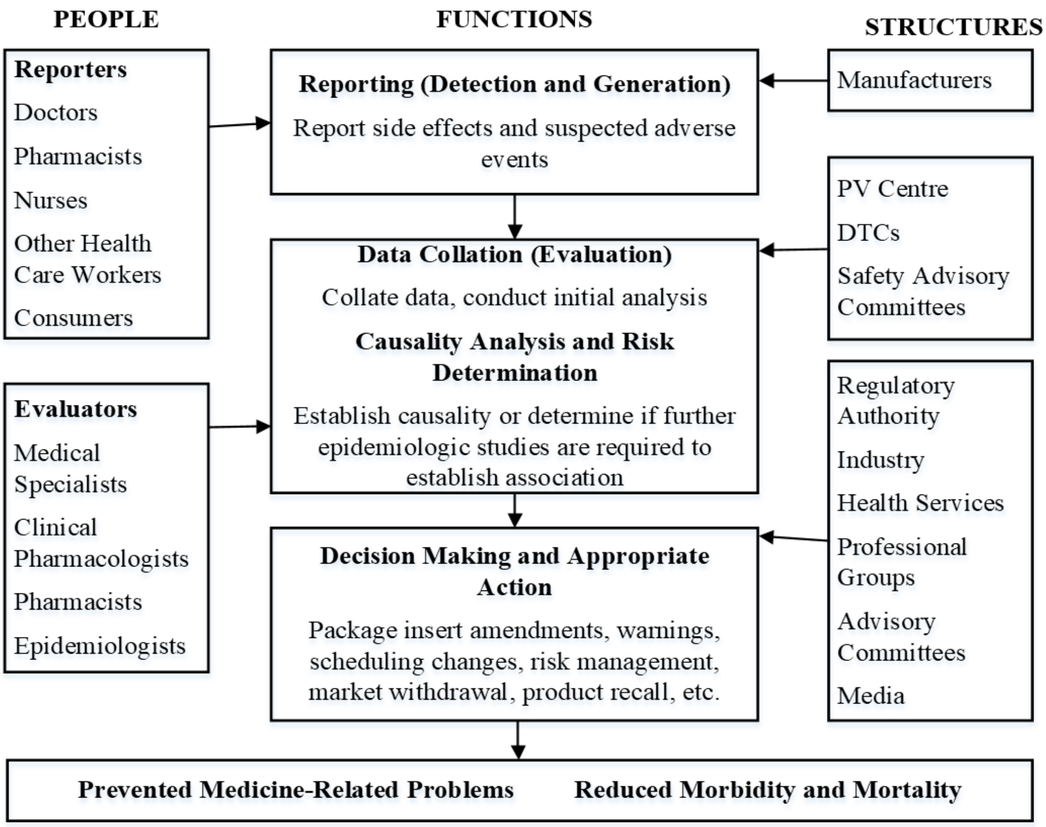


Figure 1: Illustration of PV system. (Reproduced from Strengthening Pharmaceutical Systems (SPS) (2009)).

analysis and implementation of solutions. Critical to the effective and efficient operation of these processes are the structures and bodies involved including PV organisations, medical infrastructures and networks, regulatory bodies, product manufacturers and the media. These structures, as well as the people involved, are essential in providing the necessary resources and managing the overall PV system.

The people, functions and structure's elements are said to be the building blocks of a PV system, each dependent on the other. To be both efficient and effective, the elements of the system must interact and share resources to contribute to the ultimate goal of PV: preventing medicine-related problems and associated reduced morbidity and mortality (Strengthening Pharmaceutical Systems, 2009).

Other perspectives of PV also exist. Holm, Snape, Murray-Smith, Talbot, Taylor, and Sorme (2013) refer to eco-pharmacovigilance (EPV), a developing science aimed at addressing the environmental impact of pharmaceutical products within a PV context. Environmental pharmacology is a popular alternative to the term EPV (Rahman & Khan 2015), other alternative terms include: eco-pharmacology; environmental pharmacology; pharmaco-environmentology; and eco-pharmacostewardship (Isah *et al.*, 2012).

PV is also regularly viewed from both a supply– and value chain perspective. According to Beninger (2017), effective and efficient PV requires close collaboration across its supply chain. Beninger (2017) makes specific reference to the manufacturing industry relating to PV and categorises the pharmaceutical supply chain into upstream sourcing of materials, manufacturing of products and the downstream distribution process. The importance of supply chain management (SCM) is also emphasised by Cohn *et al.* (2017) who provide a case study where poor SCM led to falsified medicines entering the Kenyan pharmaceutical supply chain.

On the other hand, operating within the stages of a supply chain, Heinrich (2015) describes the importance of pharmaceutical value chains. Heinrich (2015) specifically refers to the importance of resource management and the essential role it plays within the constrained resource environment in which PV operates. Cognizant (2012) also highlights the importance of business process management (BPM) in PV. Due to the large scope of PV, many processes are required for a PV system to function properly i.e. here BPM is essential in ensuring that these processes are managed properly.

There is agreement in literature that the contemporary scope of PV is considerably larger than that of the 1960s system (Olsson *et al.* 2010; Isah *et al.* 2012; Aljadhey *et al.* 2015). Generally, the scope of PV includes monitoring efforts related to product quality, medication errors and previously known or unknown ADRs (Strengthening Pharmaceutical Systems (SPS) 2009). Additionally, the WHO also includes the interaction of medicines, counterfeit medicines, lack of efficacy, and the abuse and misuse of medicines in the scope of their PV definition (World Health Organization, 2014).

The increasing scope of PV systems has increased the complexity and number of challenges faced within the PV landscape (Edwards, 2017; Pan, 2014). Consequently, there has been an increase in challenges such as the under-reporting of ADRs, ineffective culture, lack of transparency, and the lack of sufficient resources. Pan (2014) also states that increased pressure is put on new technological developments that are intended to counter the challenges in the PV landscape. The WHO describes how the inter-relatedness of the various stages in a PV system cause challenges that exist within the PV landscape to have a system-wide impact (World Health Organization, 2002).

The under-reporting of ADRs is an example of a prominent PV challenge that has a system-wide impact. PV systems are initiated by ADR reports, serving as the line of communication between PV authorities and the people experiencing certain ADRs (Varallo *et al.* 2014). Due to the integrated global nature of PV monitoring (as managed by the UMC), the impact of a challenge, such as under-reporting of ADRs, can also stretch beyond a specific PV system to the global PV monitoring level.

1.3. Rationale of the research

The lack of sufficient post-market drug surveillance prior to the Thalidomide incident, discussed in Section 1.2, led to the severity of this tragedy. Since then, PV has grown and contributed to much safer drug usage. The PV industry has developed relatively rapidly, pursuing improved post-market drug surveillance. This development has led to great success as the positive impact of PV on human society is evident. However, this significant growth in PV has also given rise to new challenges burdening modern PV systems, leading to increasing pressure experienced in PV systems, especially those within resource-limited settings. Moreover, many of these challenges are discussed on a high level of abstraction in literature where it is not entirely evident what the effect on these challenges are. Especially for PV systems that operate in resource-limited settings where a consortium of challenges are experienced on a daily basis, it is of utmost importance that the core effect of these challenges be known, which will make is much easier to address these challenges.

Additionally, there is also a limited number of studies that investigate the possible impact of the existing technology landscape on PV systems. Access to technology is becoming less of an obstacle, meaning more PV systems in resource-limited countries have the opportunity to investigate and implement technologies in order to address the challenges it faces.

1.4. Problem statement

Though PV is an essential aspect of ensuring drug safety, the PV system is a component of the healthcare system that is frequently poorly understood by healthcare workers and patients alike and is therefore not prioritised. PV activities are co-ordinated by the WHO to enable global monitoring to identify potential drug safety related challenges. The PV system therefore forms a complex network that is dependent on information supplied by individual healthcare workers and patients to enable monitoring at a global scale. The PV system faces a significant number of challenges, some of which could, potentially, be addressed through the application of technology. Moreover, there is a lack of appropriate strategies in PV to address the challenges faced daily. This research is concerned with: (i) which strategies can be used in PV to understand the challenges faced daily, and (ii) the question of which technologies could be leveraged to address some of the most significant root causes of challenges in the global PV system.

1.5. Research aim and objectives

The aim of this research project is to contribute towards improved PV systems, through the identification of technologies that hold the potential to address some of the challenges faced by PV systems. This will be achieved by first identifying, prioritising, and translating the existing PV challenge landscape which will provide clarity on the true effect of the PV challenge landscape on the PV system. Once the true effects, or problems, of the prioritised PV challenge landscape are identified, the possible impact of the technology landscape on the PV challenge landscape can be assessed. The research objectives that will support the achievement of the research aim include:

i. Conduct a comprehensive literature review to:
    a. Comprehensively understand the various sub-systems of which PV systems are comprised of,
    b. Identify and understand the challenges faced in the PV industry;

ii. Prioritise the PV challenge landscape to allow for more in-depth research:
    a. Clearly define and understand the prioritised PV challenge landscape;

iii. Develop a translation strategy that can be used to translate the prioritised PV challenge landscape, by doing the following:
    a. Investigate the methodologies that can be used to translate challenges from a high level of abstraction to a lower level,
    b. Select appropriate methodologies that can be used for this translation process and describe how each will be used,
    c. Implement the translation strategy to identify root causes to the prioritised PV challenges landscape,
    d. Validate and prioritise the root causes with SMEs to determine which root causes should be the focus point of this research;

iv. Investigate the technology landscape to:
   a. Identify a technology selection framework that is applicable for implementation within the PV context,
   b. Identify several technologies that can possibly be implemented within PV;

v. Implement the selected technology selection framework to assess the prioritised root causes and the technology landscape:
   a. Establish the link between the technology landscape and the prioritised root causes by describing how the technologies can be used to address these issues.

1.6. Limitations and assumptions of the research

This research project is limited due to the vast challenge landscape of PV. Many challenges exist that are both related to one another and unique to the context of the PV system. In addition to identifying the overarching challenges, focus is shifted towards challenges that have the most significant impact on PV. This allows for more in-depth research to be completed in finding solutions to the challenges. It is possible that other researchers may deem some of the other challenges that does not form part of the prioritised challenges as priority. However, the prioritised challenges are validated by SMEs, and therefore form the core of the research that follows thereafter.

Additionally, the research is also done in a general context regarding PV systems i.e. no specific PV system within a specific country is considered in isolation. The assumption made is that a general approach to identify and prioritise the PV challenge landscape will include a significant portion of the challenges faced by PV systems in specific countries.

1.7. Key terminologies

There are several key terminologies that should be explained in order to provide clarity on the meaning of these terminologies in this research. These terminologies are: PV system; partners; and technology.

1.7.1. Pharmacovigilance system

With specific reference to the entire thesis document, the phrase "PV system" is used interchangeably. In some instances, it is used to represent PV in general, or all PV systems across the globe. It is also sometimes used to represent a specific country's PV system. The intended meaning of the PV system, in this research, depends on the context in which it is used. Additionally, the phrase is used to refer to PV as a system that is constructed from of various processes or sub-systems. In all cases where it is used, it is clear which of the two intended meanings of a PV system is used.

1.7.2. Partners

With specific reference to Sections 2.8.3 and 3.5, partners represent both those who operate within PV (those directly associated and affected by PV operations), as well as those who operate outside the scope of PV i.e. those who are not directly influenced by the operations of PV, but hold the potential to affect PV. For example, partners who operate within PV include healthcare workers, the UMC, and the WHO. Partners who operate outside the scope of PV include non-profit organisations and national governments. Both these partners have the potential to influence the operation of PV in a country.

1.7.3. Technology

With specific reference to the identification of candidate technologies in Section 5.5.1, it is important to clarify how technology is defined in this research, since some might not regard some of the technologies identified as actual technologies.

There are several definitions of technology, making it difficult to determine what can be defined as technology and what not. Some may define technology as either tangible (mobile phones, computers, etc.) or intangible (software) items, whereas other may have a broader definition. Dusek (2008) argues that technology can be defined amongst four categories, namely: hardware, rules, applied science, and systems, each defining technology differently. From these categories, both Tiles & Oberdiek (1999) and Dusek (2008) concludes that anything we use in our daily lives to make our lives easier and to improve the effectiveness and efficiency of our daily activities, can be regarded as technology. For example, in a healthcare *system* (public– or private healthcare system), we use *hardware* (asthma inhaler) that have been developed by *applied sciences* (research in laboratories and clinical trials) according to certain *rules* (prescriptions) to improve our lives (treat asthma).

Using this definition of technology enables a much wider spectrum of technologies to be identified and considered in this research.

1.8. Validation strategy

Validation plays a significant role in this research. The research is firmly grounded in literature with supplementary, practical knowledge gained from consulting SMEs. These experts provide an additional perspective, filling the gaps found between literature and the real world.

Consequently, two types of validation strategies, namely informal– and formal, structured validation, are used at strategic points in this research.

The process for informal, structured validation is as follows: SMEs are contacted via email, requesting their assistance with the research. Upon indication of their willingness, they are provided with an informal, summarised version of whichever part of the research is under investigation. They are requested to read through the document, and provide feedback in the form of notes, email, or telecommunication sessions, whichever method they prefer.

The formal, structured validation process is similar to the informal, structured validation process, except for the nature and format of the information that is made available to the SMEs. SMEs are provided with a formal document that contains considerably more information than that used during the informal, structured validation process. As a result, this validation process takes longer to complete. However, this allows the SMEs to spend more time and thought on the provided information, allowing them to provide more in-depth feedback.

1.9. Research methodology

This research consists of three sections (refer to Figure 2), namely: PV, the technology landscape, and the combination of PV and the technology landscape. Each of these sections consist of different subsections. In PV, two subsections exist: the PV challenge landscape, and the PV system. In the technology landscape, the two subsections are the technology landscape, and the technology selection framework landscape. Lastly, the combination of PV and the technology landscape consists of a combination between all the subsections that have been identified here. In Figure 2, these sections and subsections are graphically depicted. Each of the subsections are investigated separately, where-after they are combined to marry PV and the technology landscape. The tools and validation strategies used during each subsection are also shown in Figure 2.

1.9.1. The pharmacovigilance system

Indicated in green in Figure 2, the PV system section consists of two stages. Firstly, PV is investigated to clearly define and understand what PV is, by making use of a literature review. Included in this stage is the definition of PV as a system, consisting of several parts. The second stage is also completed with the use of a literature review. The previously defined PV system is dissected to clearly distinguish between the different parts of a PV system, and define the activities associated with each of these parts.

1.9.2. The pharmacovigilance challenge landscape

Indicated in blue in Figure 2, the PV challenge landscape section consists of three stages. Firstly, a systematic review is conducted to identify the challenges that exist in PV, by making use of literature, grey literature, and SMEs. An informal, structured validation is then used to validate the overview of the PV challenge landscape. This is a reiterative process, meaning changes are made throughout the process based on the feedback from the validation process. This stage is followed by the prioritisation of the PV challenge landscape which relies on inputs from SMEs and a matrix that is developed in this research. Similarly, an informal, structured validation strategy is used to validate the prioritisation of the PV challenge landscape. This is also a reiterative process, similar to the previous stage. The last stage in this section is the definition and understanding of the prioritised PV challenge landscape, which is achieved with the use of a literature review.

1.9.3. The technology selection framework landscape

Indicated in purple in Figure 2, the technology selection framework landscape section that consists of three stages, each completed with the use of a literature review. Firstly, the technology selection framework landscape is investigated to identify candidate frameworks that are applicable to this research. With the use of predefined criteria, all of which are identified and described in the research, the most appropriate framework is chosen, after which it is clearly defined to understand how the framework should be implemented.

1.9.4. The technology landscape

The technology landscape section consists of two stages, the first of which is the identification of candidate technologies that can be used to address the PV challenge landscape. Given that this landscape is so large, two sources are used, namely: grey literature and a focus group. This stage is proceeded by defining the technologies, describing the exact meaning and scope of each. This process is completed with the use of a literature review. The technology landscape is shown in orange in Figure 2.

1.9.5. Combining pharmacovigilance and the technology landscape

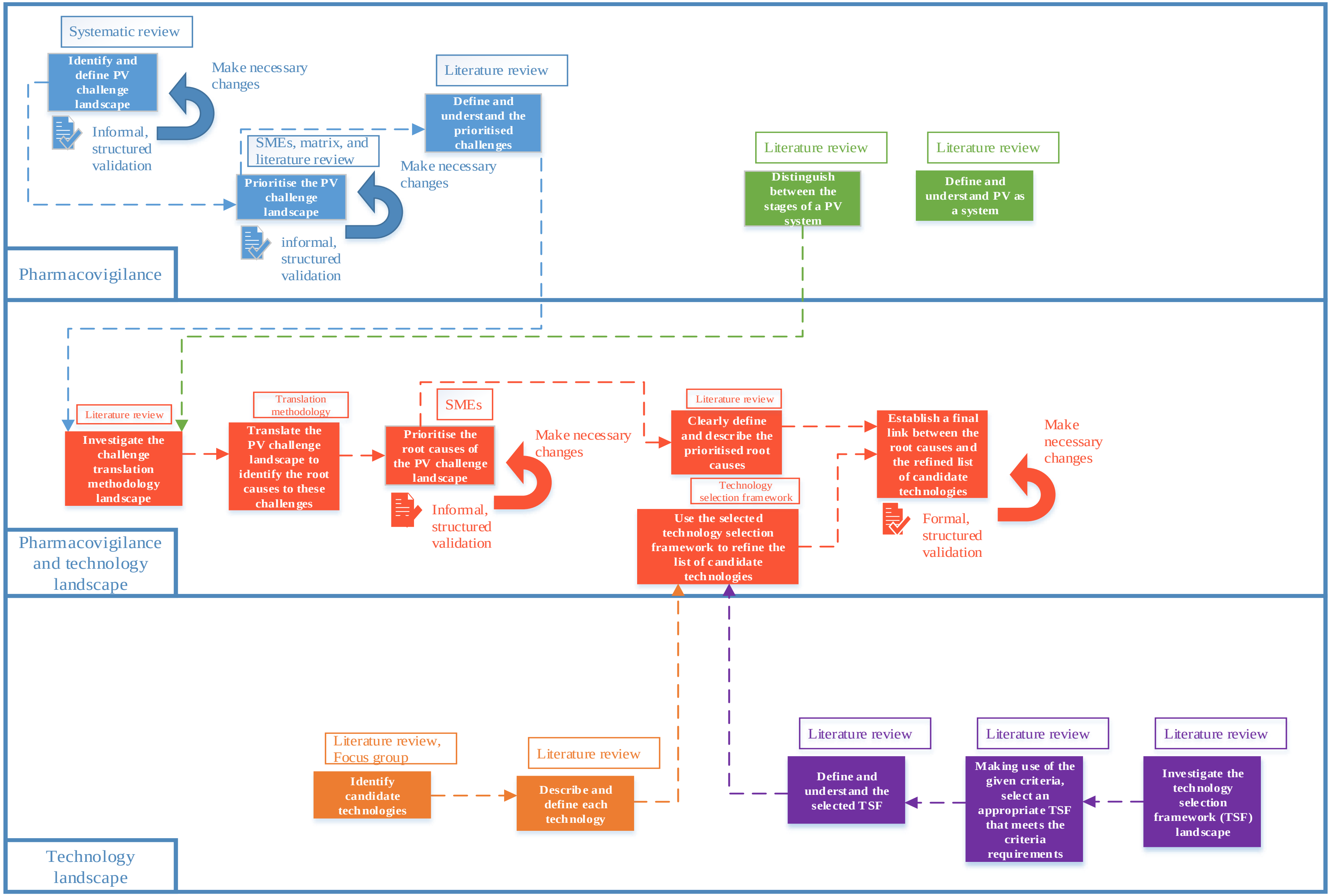
The marriage of the stages in the PV and technology landscape section is indicated in red in Figure 2. Initiated with the combination of the stages in the PV section, an investigation is launched into the translation methodology landscape to identify which methodology can be used to translate the PV challenge landscape. This process is achieved with the use of a literature review. Implementing the selected translation methodology, the PV challenge landscape is translated to identify root causes to the overarching challenges. Proceeding the translation process, the root causes are prioritised with the assistance of SMEs. This stage also incorporates an informal, structured validation, which is used to make necessary changes to the prioritised root causes. Once the root causes are prioritised, each are defined and described to create a better understanding of the exact meaning of each. This is achieved with the use of a literature review.

The stages in the technology landscape section are merged into the stage where the selected technology selection framework is used to assess the technology landscape and determine which technologies are feasible for implementation in PV. This stage, in combination with the description of the prioritised root causes, is proceeded with the process where the selected technologies are linked to the prioritised root causes. During this process, a formal, structured validation process is used to determine whether the final linkages are feasible according to various experts in PV. This validation process also allows for any necessary changes to be made to the linkages between the technologies and the root causes.

1.10. Chapter 1 conclusion

Chapter 1 provides an overview of the thesis, discussing the research background and rationale, problem statement, research aim and objectives, limitations of the research, validation strategy, key terminologies, and the research methodology. Succeeding this chapter is a study of the PV challenge landscape.

Figure 2: Research methodology roadmap.



Chapter 2: The pharmacovigilance landscape

This chapter[1] is primarily concerned with the PV landscape. The chapter is divided into two sections - the PV system and the PV challenge landscape. To gain a comprehensive understanding of the challenges faced by PV, it is valuable to first understand the composition of a PV system. This will better enable the relationships between the PV system and its challenge landscape to be discerned. Subsequently, the PV system is described, based on the system perspective presented by Strengthening Pharmaceutical Systems (2009) in Figure 3.

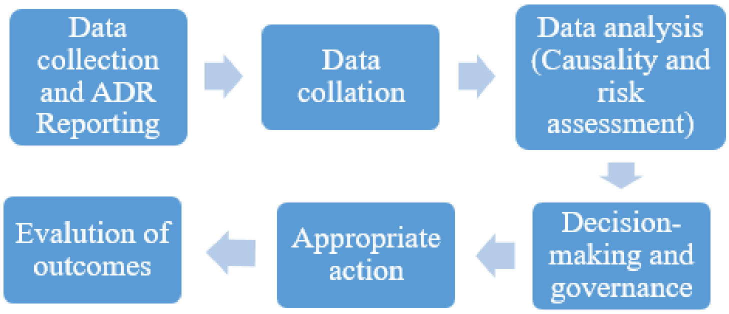


Figure 3: Stages of a PV system (Reproduced from Strengthening Pharmaceutical Systems (2009)).

2.1. Data collection and ADR reporting and data collation

ADR reporting is the cornerstone of PV (Irujo *et al.*, 2007). Serving as the starting point to a PV system, ADR reports are essential to its functionality. ADR reporting has been the subject of a number of research studies, including Hill (2014), De Abajo (2005), Irujo *et al.* (2007), and Rodrigues & Khan (2011). Hill (2014) describes five types of ADR reporting methods that are used in modern PV systems, namely: targeted reporting; cohort event monitoring; spontaneous reporting; electronic health record mining; and intensified ADR reporting. Detail on each of these reporting methods is provided in Table 1.

Hill (2014) states that the choice of most appropriate reporting method is based on three aspects: the medicine under investigation, the population of participants, and the type of reports required by the represented authorities. In support of Hill (2014), De Abajo (2005) and Irujo *et al.* (2007) dub spontaneous reporting as the first generation reporting method of PV. Spontaneous reporting is still used today, especially in developing countries, because of its relative simplicity and inexpensive nature (De Abajo, 2005).

[1] A large portion of the contents of this chapter has been published in an article that was included in the proceedings of the Southern African Institute for Industrial Engineering's 28th annual conference (SAIIE28 2018). A copy of this article is included in Section A.1 in Appendix A.

Table 1: Types of PV reporting systems. (Data source: Hill, 2014.)

PV method	Objective
Targeted reporting	To learn more about the ADR profile of a specific medicine(s) in your population or to estimate the incidence of a known ADR to a specific medicine.
Cohort event monitoring (CEM)	To gather more information on the safety profile of a new chemical entity in early post-marketing phase.
Spontaneous reporting	A functional ADR reporting system to monitor the safety of all medicines.
Electronic health record (EHR) mining	Utilise electronic health records to identify emerging drug safety issues.
Intensified ADR reporting	To enhance ADR reporting of specific medicines in early post-marketing phase.

Proceeding ADR reporting is data collation, where most ADR reports are gathered by municipal–, provincial– or national PV centres. Depending on the severity and repetition of an ADR, countries often resolve the issue internally, without consulting the UMC (Stahl *et al.* 2003). The UMC is, however, still made aware of the reported ADRs.

2.2. Causality analysis and risk assessment

Causality analysis is the process where the source of an ADR is determined with the aid of the appropriate participants and resources (Edwards, 2017). This stage is critical to the PV process, as it determines whether further investigations will be conducted. Edwards (2017) describes this stage as being dependent on detailed data, openness and the involvement of all stakeholders.

Although causality analysis methods differ in many respects, Agbabiaka *et al.* (2008) are of the opinion that they share a common goal: to arrive at a conclusion on the source of the suspect drug. Causality analysis is routine not only at the UMC, but also at PV centres around the world, allowing a wider range of stakeholders to be involved during such a process (Agbabiaka *et al.*, 2008).

Risk assessments, aimed at identifying and attending to the risk factors associated with ADRs, are used to complement causality analyses (Edwards, 2017). Risk assessments must identify the risk factors to the use of a certain drug, as well as the risks of further complications to patients after an ADR has been reported. Holden *et al.* (2003) also describe risk assessments as a collaborative effort, requiring the input of various stakeholders such as pharmaceutical companies, healthcare workers, patients, consumers and PV organisations.

2.3. Decision making and governance, appropriate action, and evaluation of outcomes

Following ADR reporting, data collation, causality analysis, and risk assessment, a decision is made on the appropriate action to be taken. Waller & Evans (2003) describe a decision-making method regularly used, known as the robust decision-making approach. The robust decision-making approach includes the following steps: analysis of evidence, which is similar to that of a causality analysis and a risk assessment described by Edwards (2017), identification of options, and final decision-making. Waller & Evans (2003) state that there is greatest scope for innovation in respect to the latter. Modern regulatory models used for decision-making consider many factors prior to taking appropriate action including the strength of the evidence, balance of risks and benefits, public health consequences, and likely effectiveness of potential preventative strategies (Waller & Evans, 2003).

Finally, Agbabiaka *et al.* (2008) emphasise the need for post-action evaluation. Following the implementation of any system, evaluation of outcomes are important to determine whether the intended results are accomplished (Strengthening Pharmaceutical Systems, 2009). Waller & Evans (2003) refer to two measures often used for measuring outcomes: the extent to which a process of PV is effective in the protection of public health; and possibilities of further improvements to be made. Waller & Evans (2003) are also of the opinion, however, that true measures of outcomes would also provide estimates of the impact of interventions on morbidity and mortality.

2.4. Introducing the pharmacovigilance challenge landscape

Each stage of a PV system is associated with a specific set of challenges and Pan (2014) states that the challenge landscape as well as the PV landscape is vast. It is therefore advantageous to this research that these challenges be identified, thereby enabling associations to be made between the challenges and the various stages of a PV system.

2.5. Research approach to the pharmacovigilance challenge landscape

Due to the large landscape of PV challenges, a systematic review was conducted to ensure that a significant portion of the existing research conducted in the challenge landscape, is considered in this research. Three academic databases were used, namely: *Scopus, Google Scholar*, and *PubMed*. The *Scopus* database was used for the primary systematic search protocol, while the *PubMed* and *Google Scholar* databases were used for snowballing and other informal search methods.

In total, 2 301 relevant documents are available based on specific search terms (these search terms are detailed in Section A.2 in Appendix A). These search terms were based on a cursory review of an initial batch of articles, uncovered on the databases via serendipitous discovery. In addition, opinions found in grey literature were used to determine the search terms used in the databases.

To reduce the number of articles to a more manageable quantity and to only look at the challenges that are identified as most relevant according to several sources, only the articles published during the year 2000 and onwards were included in the search. The abstracts were then consulted to determine the applicability of the article to the research. An important inclusion criterion was that the abstract had to contain words associated with PV, such as "*pharmacovigilance*", "*drug safety monitoring*" or "*drug safety surveillance*". The documents were filtered to 64 documents of which the majority are referenced in the proceeding section.

2.6. Succinct overview of the pharmacovigilance challenge landscape

The most prevalent PV challenges were organised into a network (Figure 4), illustrating the inter-related nature of the challenges found in the PV landscape. This was done by interpreting the suggestions made in literature, and by considering both the severity and prevalence of the challenge in literature. The dark grey blocks indicate the classification of the challenges, whereas the blue blocks indicate the specific challenges in PV. As seen in Figure 4, the overarching challenge is culture. All other challenges identified in the PV landscape fall into one of two sub-categories of culture, namely PV infrastructure and data management.

The proceeding section is limited to a succinct overview of the PV challenge landscape. This is done to demarcate the scope of the research in an effort to focus on specific challenges that are most prevalent in modern PV. Subsequently, the network of challenges is briefly discussed, providing an overview of the challenges found in PV.

2.7. Culture

PV is based on the culture of safety, where PV professionals provide the foundation upon which the principles of this culture are built (Olsen & Whalen, 2009). Literature argues that there is a need to improve the culture in modern PV systems (Edwards *et al.*, 2015). It is believed that the improvement of PV culture will lead to the improvement of the other challenges in PV, such as ADR under-reporting discussed in Section 2.9.2. It is often discussed that the improvement of PV culture requires participation across all disciplines to become a reality.

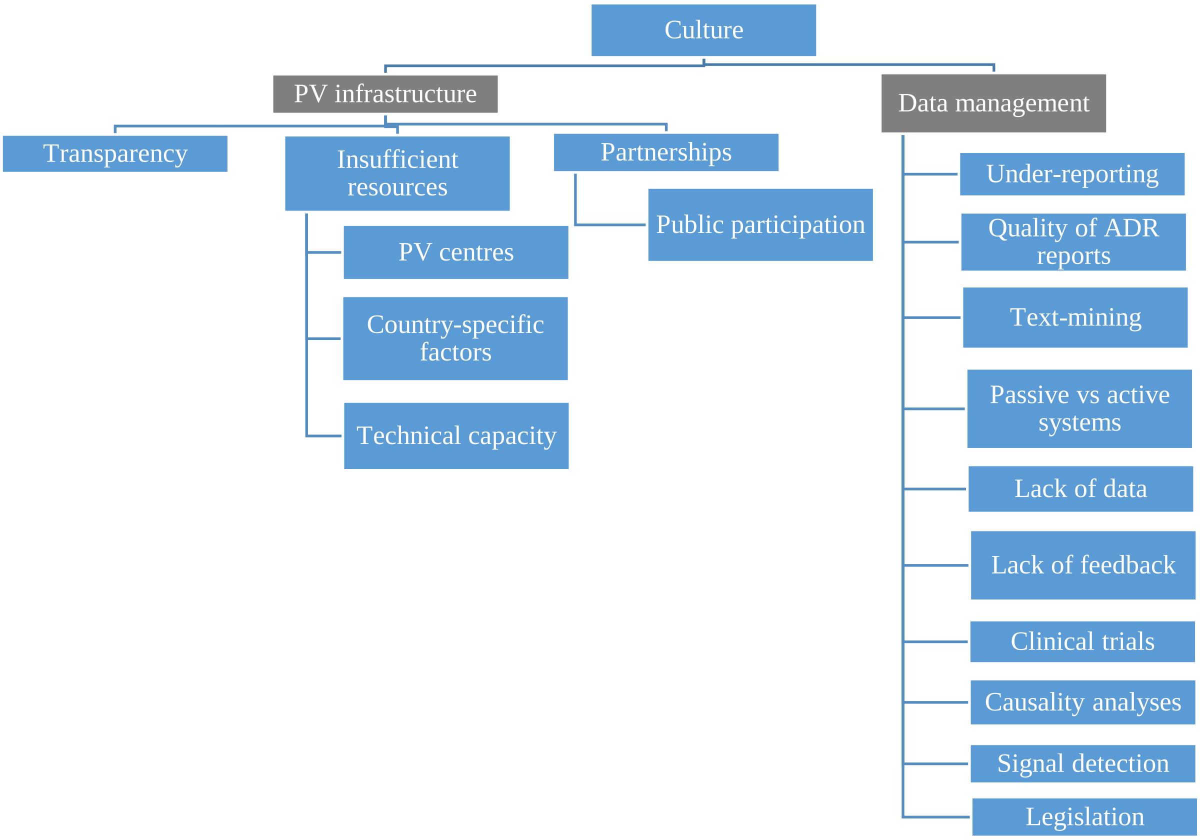


Figure 4: PV challenge landscape network.

2.8. Pharmacovigilance infrastructure

The challenges that are grouped under PV infrastructure in this research are: transparency; insufficient resources; PV centres; country-specific factors; technical capacity; partnerships; and public participation. These challenges are subsequently discussed.

2.8.1. Transparency

In close association with the culture found in PV (discussed in Section 2.7), the lack of transparency amongst the stakeholders in PV may lead to failed PV initiatives (Rubel *et al.*, 2017). It is essential that key stakeholders, especially those with the relevant experience in PV, share relevant information with their peers. This will enable participants in PV to learn of new ways in solving the problems they might be experiencing. Increasing the visibility of information in PV is critical (Rubel *et al.*, 2017), as it will support an improved drug safety culture.

It is also essential that the existence of PV systems in countries be publicly unveiled. It is described in literature that HCWs in many countries do not contribute to PV, simply because they are not aware of the existing PV infrastructure in their location.

2.8.2. Insufficient resources

It is well-known that PV operates within a resource-constrained environment (Isah *et al.*, 2012). Moreover, in developing countries where other challenges such as drought and war are of high priority, PV organisations struggle to implement new PV systems (Isah *et al.*, 2012). In these developing countries, the available resources are rather invested elsewhere, leaving little for the requirements of PV.

The resources required by PV systems are unique in specific countries e.g. a country might have the necessary expertise and manpower to assist a PV system, but lack the governmental funding. In contrast, another country might have the necessary budget but lack the required manpower (Pan, 2014). Countries experiencing this phenomena include sub-Saharan African countries (Isah *et al.*, 2012), India (Rama *et al.*, 2011), and certain South-East Asian countries (Suwankesawong *et al.*, 2016).

Common resources required by PV systems include monetary assistance, hardware and software infrastructure, expertise and training curricula amongst healthcare professionals, and common PV knowledge amongst both healthcare professionals and consumers (Isah *et al.*, 2012; Pan, 2014). PV systems are dependent on the combination of these resources and are not able to function properly without them (Isah *et al.*, 2012). Heinrich (2015) refers to effective resource management, a crucial element to the successful operation of a PV system.

2.8.2.1. Lack of pharmacovigilance centres

Serving as the base of operation for PV monitoring efforts, PV centres are important elements of the PV industry. According to Zhang *et al.* (2014), there is a certain structure or hierarchy associated with PV in general. The UMC is the international database, taking ownership of millions of ADR reports received from numerous countries each year (Rama *et al.*, 2011). Serving as a filter to these ADR reports are national PV centres, supported by provincial centres, usually located in provincial hospitals and other medical institutions. Municipal centres serve as the first line of defence, i.e. initially receiving and processing ADR reports, before sending these to PV centres further up the PV centre network hierarchy. Zhang *et al.* (2014) provide a description of the Chinese PV centre network, consisting of one national PV centre, 34 provincial centres and 400 municipal centres, all ultimately reporting to the UMC.

The challenge faced, especially in developing countries, is the gaps found within this PV centre network. The case of sub-Saharan Africa, where there are many countries with no or few municipal– and provincial centres is discussed by Isah *et al.* (2012). Olsson *et al.* (2010) and Isah *et al.* (2012) are of the opinion that this deficit is due to the lack of resources such as tangible infrastructure, human resources, training and capacity building, governance, sustainable methodologies, and innovations within a number of areas in the sub-Saharan African context. With no intermediate body to receive and filter initial ADR reports, it is difficult for healthcare professionals and consumers, in countries with no municipal– or provincial PV centre, to report ADRs to the appropriate authorities (Zhang *et al.*, 2014).

2.8.2.2. Country-specific factors

Country-specific factors refer to challenges faced by PV organisations outside the traditional resource architecture, these are described by Edwards (2017) and Härmark & Van Grootheest (2008). Closely related to the effect of the public on PV, the social factors of an area must be considered—which includes the culture, religion, age groups, and sex groups of a specific region. It is often a burden to clearly identify these factors since it requires manpower and funding that are not always readily available.

Situational factors including border regulations, policies for implementation, governmental budget constraints, conflict in countries, and environmental issues such as severe drought, must also be considered. Often governments refuse to authorise and support the implementation of new PV systems as its priorities are elsewhere (World Health Organization, 2002), thus delaying the implementation of PV systems. Similar to the case for social factors, the required resources needed to identify these situational factors are not always available, contributing to the failed deployment of PV initiatives.

2.8.2.3. Technical capacity

Technical capacity refers to the ability of individuals and teams working in PV to conduct their work efficiently and effectively. Very closely associated with the country-specific factors discussed under Section 2.8.2, Mehta (2017) is of the opinion that it deserves to be independently categorised. The challenge faced here, especially in developing countries where there are limited resource-capacities, is that the individuals or teams working within the PV systems often lack the necessary skills and experience to conduct their work effectively and efficiently.

Over the years, PV has grown to be a large and complex system. The nature of PV has changed from a single oriented discipline, to a cross-functional discipline. Individuals and teams from different a background than that of healthcare (e.g. statisticians, programmers, and engineers) are more often being consulted and involved in PV, since they offer additional perspectives that may be of benefit to PV (Mehta, 2017).

2.8.3. Partnerships

PV is a collaborative endeavour (Pan, 2014). Sustained collaboration and commitment are vital to attend to future challenges of PV (World Health Organization, 2002); World Health Organization, 2004), and ineffective partnerships pose a threat to PV (World Health Organization, 2004). Operating in a resource-constrained environment, partners in PV must sometimes provide expertise, training, political support, scientific infrastructure, and a capacity to accomplish comprehensive monitoring and investigations of the safety of medicines (Pan, 2014). Failure in providing such resources, could amount to ineffective partnerships that can lead to failed PV initiatives. In order to maintain a certain inventory of these resources, it is vital that PV organisations form lasting relationships with their partners. Management for Science (2012) emphasises the importance of relationships between partners and how failed relationships often lead to PV failures.

2.8.3.1. Public participation

The scope of PV is large (Rodrigues & Khan, 2011), as it is concerned with monitoring a wide range of new and existing drugs in several countries, therefore requiring the participation of numerous stakeholders. Consumers and patients are described as key stakeholders (BEUC, 2008), having the ability to contribute through an integrated and efficient reporting system. These direct reporting systems enable PV professionals to detect ADRs much earlier, as well as to remove the healthcare professional as filter to reporting ADRs.

However, patients and consumers have been losing faith in the pharmaceutical industry. A survey of the US public, conducted in 2006, illustrated this loss in trust with approximately 42% of public participants indicating that they are sceptical of the pharmaceutical industry (Olsen & Whalen, 2009). Similarly, a study conducted in 2007 indicated that there was a decline in public trust towards the healthcare system in some resource-constrained countries (Gilson 2006). The findings of surveys such as these serve as proof that the PV industry must shift its focus in maintaining collaboration with the consumer and patient.

2.9. Data management

In this research, there are several challenges that are grouped under data management. These challenges are: quality of ADR reports; under-reporting of ADRs; text-mining; passive versus active systems; lack of data; lack of feedback; clinical trials; causality analyses; signal detection; and legislation. These challenges are subsequently discussed.

2.9.1. Quality of ADR reports

The quality of medical data, in a PV context, is of utmost importance (François *et al.*, 2013). Without ADR reports, PV systems cannot function and literature regularly emphasises the need for advancements to be made regarding the quality of such reports (Sarker *et al.* 2015).

Spontaneous reporting is a widely used method in PV (Hill, 2014), dependent on both healthcare professionals and the consumer. However, Bandekar *et al.* (2009) describe a looming threat to spontaneous reporting: the poor quality of the reports. These quality issues, regularly found in reports by non-healthcare professionals, include issues with credibility, uniqueness, frequency, and salience of the data contained in the report (Sarker *et al.*, 2015). Such issues can be attributed to the lack of necessary PV knowledge amongst consumers.

Poor quality reports are, however, not restricted to those generated by consumers—quality issues also exist in reports generated by healthcare professionals. Such poor quality is evident in a study by Bandekar *et al.* (2009), where ADR reports from ten different countries were collected, with the objective of determining the quality of the reports. It was found that several reports lacked critical information (e.g. pregnancy status, age, sex, and allergic status), even though many of these reports were generated by healthcare professionals. Sub-Saharan African countries were rated particularly poorly, achieving below 50% with regards to the quality standard baseline.

The poor quality of ADR reports can be traced back to the culture of PV (Bandekar *et al.*, 2009). The establishment of a culture where more emphasis is put on the quality of ADR reports, as described by Edwards *et al.* (2015), may therefore contribute to the improvement of ADR reports.

2.9.2. Under-reporting of ADRs

Under-reporting of ADRs occur when healthcare workers (HCWs) (i.e. general practitioners, nurses, surgeons, pharmacists, etc.) fail to efficiently report new and existing ADRs (Herdeiro *et al.*, 2006). In the interest of consumers and patients who experience ADRs, it is crucial that all ADRs be reported to the relevant authorities to enable signal detection, leading to investigations into the specific ADR. Without ADR reports that generate signals of a problematic ADR, investigations that aim to address these problems cannot take place.

2.9.3. Text-mining

Text mining is defined as the computational process of extracting meaningful information from large amounts of unstructured text (Harpaz *et al.* 2014). In a PV context, meaningful information is regarded as information that can support ADR detection and assessment (Yang *et al.*, 2015). Contrary to popular belief, a major challenge faced in text mining, as described by. Harpaz *et al.* (2014), is not necessarily the extraction of useful information from severely unstructured text, but rather realising the value text mining holds for the PV industry. Extraction is a challenge (Yang *et al.* 2015), but advancements in software have simplified information extraction efforts (Harpaz *et al.* 2014).

The use of text-mining on social media is regularly discussed in literature (Harpaz *et al.*, 2014; Yang *et al.*, 2015; Nikfarjam *et al.*, 2015). The challenge of some PV organisations not realising the value of text mining , is evident in the late adoption rate of social media (Harpaz *et al.*, 2014). Nikfarjam *et al.* (2015) are of the opinion that this unwillingness to use social media for ADR reporting is due to the informal nature of social media. For example, consumers make use of informal words and phrases to report a suspected ADR, therefore PV organisations are sceptical of the quality of information that can be gathered from social media. Harpaz *et al.* (2014) and Yang *et al.* (2015) argue that technological developments are only contributing to an increased adoption rate of text-mining to a limited extent.

2.9.4. Passive vs active systems

Regulatory enforcement and increased accountability drive demand for the protection and welfare of patients, and forces the PV industry to be more active (also referred to as proactive) in its efforts (Lu, 2009). These regulations govern active PV systems that must include comprehensive risk management plans and signal detection and analysis throughout a clinical product's lifecycle (Lu, 2009). Active PV is not only able to respond to ADRs prior to the marketing stage of drugs, but also decreases the probability of a known ADR being experienced during such a large scale deployment (Rodrigues & Khan, 2011).

Certain modern PV systems are outdated (Giezen *et al.*, 2009). Spontaneous reporting, as described by Hill (2014), is the first ADR reporting system implemented in PV. Such reports are of a passive (also referred to as reactive) nature, depending on healthcare professionals and consumers to report ADRs after a drug has been marketed and the ADR experienced. Spontaneous reports are still widely used, increasing the pressure on PV systems in which these are prevalent to make a transition towards active operation (Rodrigues & Khan, 2011).

2.9.5. Lack of data

PV relies on good information, meaning information of sufficient quality (Pan, 2014). It is argued that a lack of data, as well as the insufficient quality of such data, burdens PV systems (Rachlis *et al.*, 2016), thereby limiting the possibility of investigations. This argument is supported by case studies conducted by Rachlis *et al.* (2016) and Weber-Schoendorfer & Schaefer (2016) that made the phenomenon of insufficient data apparent. This phenomenon is closely related to under-reporting of ADRs and the quality of ADR reports.

2.9.6. Lack of reporter feedback

A challenge faced by the PV industry, regularly overlooked by researchers, is the lack of feedback given to ADR reporters (Aljadhey *et al.*, 2015; Al Dweik *et al.*, 2016; Ríos *et al.*, 2016; de Vries *et al.*, 2016; Kabore *et al.*, 2013)). For example, a study of Saudi Arabia's PV system indicated that participants of the existing ADR reporting network see no point in reporting ADRs if they cannot get feedback and support from the country's PV authorities (Aljadhey *et al.*, 2015). As another example, a similar study completed in the UK, Netherlands, and Australia found that ADR reporters, especially patients, want personal feedback to put them at ease that their voices and opinions are heard by the relevant PV authorities (Al Dweik *et al.*, 2016).

This need for personal feedback as a sociological component of PV, is described by Ríos *et al.* (2016) as a routinely overlooked component of the PV system. The lack of adequate feedback is also evident further up the PV authority hierarchy, where gaps in the PV centre network (as described under Section 2.8.2) are regularly found.

2.9.7. Clinical trials

Clinical trials are conducted premarket and are used to determine the effect that a drug will have on consumers, as well as to identify certain ADRs that cannot be predicted in laboratory conditions (Cheaib, 2016). Similarly, Dubey & Handu (2013) state that clinical trials are important to determine the drug's effect on humans, as it cannot be directly extrapolated from preclinical animal studies.

Although the results obtained from clinical trials are beneficial to the PV industry, clinical trials are burdened by some limitations (Cheaib, 2016; Raschi *et al.*, 2016; Dubey & Handu, 2013; Härmark & Van Grootheest, 2008). Though clinical trials undoubtedly play a vital role in drug safety, they can sometimes deliver limited results (Härmark & Van Grootheest, 2008). For example, due to the limited number of patients participating, it is generally not possible to identify ADRs that occur only rarely (Cheaib, 2016). Consequently, ADRs will only be identified and investigated after a drug has been marketed to the public. Another example of the limitations of clinical trials, is a possible lack of correspondence in characteristics (e.g. age and sex), between the populations in which a drug is tested and those where it will be deployed (Dubey & Handu, 2013). This limits the potential to extrapolate results obtained from clinical trials to the population at large (Härmark & Van Grootheest 2008).

Another challenge posed by clinical trials is what is known as special control programmes developed with a specific purpose, e.g. treating malaria or HIV. In many sub-Saharan countries, the challenge is that these programmes are coordinated separately from the national PV system, and do not report ADRs to the national system. There is a need to bring together such programmes under one umbrella so that relevant experiences can be shared (Jusot, 2017).

2.9.8. Causality analyses

Establishing causality in PV is a difficult and time consuming process, requiring resources such as manpower, expertise, and funding that is often scarce and hard to come by (Edwards, 2017). Avorn & Schneeweiss (2009) refer to this issue, stating that it is a common challenge experienced in various locations. Even though a large body of ADR data exists (Avorn & Schneeweiss, 2009), the volume is often too much for causality initiatives. Like the case described earlier, undertaking the analysis of such a volume of data requires resources that are not always available. This lack of resources and the difficulty in identifying linkages between ADRs and their root cause, are hindering causality analyses from being conducted in a timely fashion.

2.9.9. Signal detection

Signal detection and its assessment is one of the most important aspects of PV (Kumar & Khan 2015). A signal is regarded as "*reported information on a possible causal relationship between an adverse event and a particular drug, of which the relationship is unknown or incompletely documented previously*" (World Health Organization, 2002). A limited number of reports, such as spontaneous ADR reports, can serve as a signal. Signal detection is thus the early detection of such signals. The early detection of signals is increasingly important to contribute to improved health amongst patients and consumers. However, modern PV signal detection systems are burdened by some challenges, including (Pontes *et al.*, 2014):

- The variance in ADR reports, especially spontaneous reports, such as quality, accuracy, and completeness;

- An ADR report is only an indication of the suspicion, opinion, or observation of an individual reporter, and does therefore not necessarily constitute an actual association to a specific drug;
- Under-reporting of ADRs;
- The unavailability of population exposure data;
- Patients are frequently not identifiable, or the case history is not clearly reported for each patient; and
- Non-compliance, medication errors, or other factors may often be related to ADRs.

The challenges described by Pontes *et al.* (2014), are closely related to the other challenges discussed in the PV challenge landscape, including ADR under-reporting, poor quality of ADR reports, lack of data, and insufficient resources. It is therefore believed that addressing those challenges might contribute to the improvement of signal detection in PV.

2.9.10. Legislation

Literature suggests that legislation in PV is multi-faceted as it is either enforced too strictly or not strictly enough. The latter is particularly the case in developing countries, also referred to as low– and middle income countries by Olsson *et al.* (2010). A questionnaire-based analysis performed by Olsson *et al.* (2010) showed that many of the participating countries indicated that there is a need for better legislation regarding PV. Although PV is covered in many developing countries' national legislation, which is proven by the fact that the countries reported that a budget exists for PV, the poor condition of PV systems in these countries suggest that these lack strength and focus (Olsson *et al.*, 2010).

On the other hand, PV legislation is sometimes too strictly enforced. This phenomenon is especially experienced in developed countries where PV systems have already exited the infant stage of development. According to Callréus (2011), legislation in such countries burden drug development, especially during the post-approval stage. This delay in the life cycle of drug development means that drugs, with the potential of helping a wide range of individuals, often enter the market later than could feasibly be achieved.

2.10. Pharmacovigilance challenge landscape and the pharmacovigilance system

As discussed in Section 2.4 on p.14, it is useful to establish in which stages of the PV system the various challenges play a role. The associations between the various stages of the PV system and the challenges that have been identified in this chapter are indicated in Table 2, which has been validated by a SME who is a PV consultant at an university. Establishing how widely a specific challenge affects the PV system is a step towards prioritising the PV challenge landscape, a necessary step in the completion of this research, as described in Chapter 1. The rationale behind the construction of Table 2 is provided in Table 3. When read in combination with the PV system illustration in Figure 1 on p.2, Table 2 enables the identification of appropriate stakeholders to be consulted in attending to the challenges and contributing to the overall improvement of PV.

2.11. Chapter 2 conclusion

In this chapter, an overview of the PV system is provided. The PV system is described from a systems perspective, clearly illustrating the stages of a PV system. Furthermore, an overview of the PV challenge landscape is provided. Finally, an association is made between the PV system and the challenge landscape.

The PV industry is riddled with challenges and it is therefore challenging to address all these challenges. To focus the scope of this research, the next chapter prioritises the PV challenge landscape based on the suggestions made from different sources.

Table 2: The PV system and the PV challenge landscape matrix.

		Challenges																	
		Culture	**Transparency**	**Insufficient resources**	**PV centres**	**Country-specific factors**	**Technical capacity**	**Partnerships**	**Public participation**	**Under-reporting**	**Quality of ADR reports**	**Text-mining**	**Passive vs. Active systems**	**Lack of data**	**Lack of feedback**	**Clinical trials**	**Causality analysis**	**Signal detection**	**Legislation**
Stages of a PV system	**ADR reporting**	X	X	X	-	X	X	X	X	X	-		X	-	-	-	-	-	X
	Data collation	X	X	X	X	X	X	X	-	-	X	X	-	X	-	X	-	X	-
	Causality analysis	X	X	X	-	X	X	X	-	-	X	X	-	X	-	X	X	-	-
	Risk assessment	X	X	X	-	X	X	X	-	-	X	X	-	X	-	X	X	-	-
	Decision-making	X	X	X	X	X	X	X	-	-	-	-	-	-	X	-	-	-	-
	Appropriate action	X	X	X	X	X	X	X	X	-	-	-	X	-	-	-	-	-	X
	Evaluation of outcomes	X	X	X	X	X	X	X	X	-	-	-	-	-	-	-	-	-	-

Table 3: Rationale behind Table 3.

Challenges associated with PV	Description
ADR reporting	
Culture and transparency	The overall culture of ADR reporting is a challenge faced in modern PV systems. ADR reporters must conform to an efficient culture and be willing to share information with their peers in order to contribute to the success of PV.
Insufficient resources	ADR reporting require certain resources to be operational. Such resources are sometimes not readily available, resulting in inefficient reporting systems.
Country-specific factors	These factors are unique to the country of implementation e.g. in many African countries, remote villages are far from hospitals and clinics. It is therefore difficult to report ADRs that might surface in these villages since the inhabitants rarely come to the hospital or clinic.
Technical capacity	Often, HCWs lack the technical skills to complete an ADR form. This might be because they were not aware of ADR reporting or were not adequately trained to do so.
Partnerships	Ineffective partnerships between ADR reporters (consumers, patients, and healthcare professionals) and the PV industry results in struggling PV systems.
Public participation	Public participation is critical as it not only increase the reach of ADR reporting, but also ensures that the rarest of ADRs are reported.
Under-reporting	Under-reporting is a major challenge of ADR reporting since not all ADRs are reported to the appropriate authorities.
Passive vs active	ADR reporting should be of active nature i.e. prior to life threatening illnesses, side-effects of a certain drug must be reported to attend to the patients or consumer in an early stage.
Legislation	In many countries, few ADRs are reported, because legislation allows only healthcare workers, not patients or consumers, to report ADRs.
Data collation	
Culture and transparency	It is of great importance that each ADR report be collated, especially the outliers that might contain the details of rare ADRs. A culture amongst healthcare workers to contribute to improve PV by doing non-mandatory work is crucial.
Insufficient resources	A collective combination of manpower, expertise and experience is required to collate all ADR reports and conduct screening and filtering of these reports.
Lack of PV centres	PV centres are needed to serve as collection points for ADR reports, also accommodating screening efforts of ADR reports.
Country-specific factors	Countries where war or drought are of more importance than PV, it is difficult for collection efforts of all ADR reports. Also, since the governments in these countries focus its efforts elsewhere, screening efforts of ADR reports are limited since the needed infrastructure and manpower are not of abundance.
Technical capacity	Persons who have the necessary experience regarding data collation are not always in abundance.
Partnerships	PV organisations need to form alliances with existing medical infrastructures to serve as consolidation centres for ADR reports.
Quality of ADR reports	During the collation and initial screening process of ADR reports, it is essential that the physical ADR reporting forms be of such quality that it can be easily categorised and triaged, especially those containing the details of rare ADRs.
Text-mining	Since ADR reports contain great detail, text-mining makes the extraction process of this data much simpler and quicker.
Lack of data	Lack of essential data such as the name of the drug believed to have caused the ADR is a challenge since more investigations are necessary to identify the drug.

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Challenges associated with PV	Description
Clinical trials	The data collected during clinical trials is often limited in its validity because of the controlled environments in which these clinical trials are carried out.
Signal detection	Prior to the investigation of certain ADRs carried out during causality analyses, a signal of an ADR must be detected through data collation.
Causality analysis and risk assessment	
Culture and transparency	The danger posed by certain rare ADRs serve as proof that thorough analyses be completed in finding solutions. It is essential that participants in these analyses share information and experience with their peers to aid one another in attending to the ADR on hand.
Insufficient resources	Similar to the above case, the lack of resources such as manpower, infrastructure, funding, and experience burdens both causality analyses and risk assessments.
Country-specific factors	Countries vary in respect to the characteristics of its inhabitants e.g. race, age and sex ratios etc. These characteristics are limiting factors to clinical trials since the effect on other participants, with different characteristics than that of the country where the trial was done, are unknown.
Technical capacity	Special skills and experience is needed to conduct causality and risk assessments. Often, there are few individuals, with these characteristics, who are available to PV.
Partnerships	It is essential that partners with the necessary expertise provide aid and take lead during these stages of the PV system.
Quality of ADR reports	The lack of proper quality in ADR reports is a limiting factor to causality analyses and risks assessments since the information on the ADR report is either missing or vague
Text-mining	Text-mining is an effective tool to use during causality analyses, as it reduces the time spent on data collection from ADR reports.
Lack of data	The lack of data is a burden to causality and risk assessments, as it limits the extent to which investigations can be done.
Clinical trials	The causality analyses and risk assessments conducted during clinical trials are limited by the fact that the trials were carried out in controlled environments.
Causality analysis	Causality analyses are regularly burdened by the lack of manpower and expertise that are not always available.
Decision making	
Culture and transparency	Transparency is needed during decision making. Peers need to share their experiences of similar ADRs in order to aid others in determining the best course of action.
Insufficient resources	The determination process during which the best course of action is decided upon, require various resources such as manpower and funding that are not always in abundance.
Lack of PV centres	The opinions of local representatives working in local PV centres, who have knowledge of the region where implementation is to be done, are needed.
Country-specific factors	Social factors, such as cultural – and religious beliefs, of the specific region must be considered during the decision making process to ensure that the community will accept and support the improvement initiative.
Technical capacity	During the decision making stage, it is beneficial that persons who have the necessary experience and skills be consulted and involved in the process. Such persons are not always in abundance.
Partnerships	Partnerships are essential to provide the necessary expertise and experience during decision making, to determine the appropriate action to be taken.

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Challenges associated with PV	Description
Lack of reporter feedback	It is essential that ADR reporters be notified that their reports have been received. Also, they need to be made aware of the decision that is taken following their report.
Appropriate action	
Culture and transparency	Similar to the previous stage of the PV system, transparency amongst peers who have experienced similar conditions of implementation are essential to increase the chances of successful implementation.
Insufficient resources	Depending on the scale of the action, resources are required to make the implementation process a reality.
Lack of PV centres	Serving as the base of operations, local PV centres are essential during the implementation process.
Country-specific	Similar to the decision making stage, it is critical that social factors such as cultural – and religious beliefs be considered during the implementation process.
Technical capacity	Implementation of new initiatives are not simple, therefore PV rely on individuals and teams who have experience in this regard to aid during this stage. However, these individuals or teams are not always available to PV.
Partnerships	During the implementation – or deployment process of the improvement initiative, partners are essential to provide aid in certain areas of these processes.
Public participation	Public members such as local leaders must be consulted during the implementation of the appropriate action to increase the chances of successful implementation.
Passive vs active systems	Due to the dangers posed by several ADRs, it is critical that active actions be taken to attend to possible ADRs before it surfaces.
Legislation	The multi-faceted nature of legislation (either too strict or too lenient) limits the range of actions that can be taken to improve PV systems.
Evaluation of outcomes	
Culture and transparency	The right mind-set towards PV evaluation is important and participants must be motivated to do the necessary evaluation. Similarly, transparency is also important to enable peers to share information on the experiences they had with similar evaluation processes.
Insufficient resources	Evaluation of outcomes cannot be done without the necessary resources such as funding and manpower. It is therefore of great importance that these resources be made available.
Lack of PV centres	Local PV centres are essential to accommodate the infrastructure required during evaluation efforts.
Country-specific factors	The hierarchy of leadership and networks within certain communities must be consulted, as well as involved in the evaluation process. This enables for ownership of evaluation efforts, increasing the reliability of the feedback provided by the relevant stakeholders.
Technical capacity	In many countries, there is a lack of people working in PV who have experience and skills regarding evaluation and continuous monitoring of PV systems.
Partnerships	Collaboration with partners with the ability to monitor and evaluate PV systems are essential.
Public participation	The public is an effective evaluator of PV initiatives since they experience the effects of these initiatives first hand.

Chapter 3: Prioritisation of the pharmacovigilance challenge landscape

In this chapter[2] the challenges that make up the PV challenge landscape are prioritised, based on suggestions gleaned from various sources. At the onset of this chapter, the importance of prioritisation, specifically within the context of PV, is highlighted. Subsequently, the method employed to prioritise the challenges identified as part of the PV challenge landscape developed in Chapter 2 is discussed. The sources that are used to prioritise the challenges in the PV challenge landscape are identified and described thereafter, and succeeded by the prioritisation of the PV challenge landscape exercise. This is then followed by a detailed description of the prioritised challenges, to provide a holistic overview of such challenges.

3.1. The importance of prioritisation

The demand for healthcare has increased substantially over the last decade, and this has increased the pressure on the healthcare industry to manage its already constrained resources to meet its clinical responsibilities (Barnieh *et al.*, 2014). This has given rise to the realisation of the importance of prioritisation, a process which governs the allocation of resources to demarcate the scope of clinical activities (Barnieh *et al.*, 2014). Prioritisation of clinical activities is not a new concept, and in fact has been a popular topic of debate since the late 1990s (Barnieh *et al.*, 2014).

Healthcare systems across the globe regard prioritisation as inescapable (Newton, 2010). This includes countries such as Norway, Sweden, the United States of America, and the United Kingdom (Sabik & Lie, 2008). Several events such as the denial of life-saving treatments, ever-expanding waiting lists, and inefficient allocation of health insurance packages were catalysts to these countries to invest more time and resources towards prioritisation (Sabik & Lie, 2008). All these healthcare systems rely heavily on different sources of funding, which are classified as either public or private. The contributions of these groups fluctuates significantly due to factors such as exchange rates, healthcare needs, and resource availability (Sabik & Lie, 2008). As a result, the resources these funding bodies and investment groups provide are often unpredictable, which further emphasises the importance of prioritisation.

[2] A significant portion of the contents of this chapter has been included in an article (shown in Section B.1 in Appendix B) that is in the process of being submitted to an appropriate journal.

However, prioritisation is challenging, and is often described as an inevitably disorganised process (Klein, 1998). Klein (1993) states that given that prioritisation is inherently the rationing of resources, healthcare systems struggle to find a balance between managing their already constrained resources and continuing to meet the demand for healthcare services. Moreover, the absence of a universally accepted framework that can be used to simplify the process of prioritisation makes this even more of a challenging process (Sabik & Lie, 2008). Therefore, organisations rely on different approaches for prioritisation, such as ad-hoc committees and advisory boards, which make use of different techniques to prioritise challenges and activities (Sabik & Lie, 2008).

When considering PV specifically, as evidenced by the systematic review conducted in Chapter 2, the PV systems, in both developed and developing countries, are experiencing an assortment of challenges. It is becoming increasingly difficult to address each of the challenges identified in this study because of the increasing requirement for resources to address these challenges effectively and efficiently. Therefore, it is essential that the challenges that are deemed most prevalent, or have the most significant impact on the PV system, be addressed as a matter of priority. By adopting this systematic approach to addressing the most prominent and impactful challenges first, it enables a process by which to systematically progress through the challenges in the PV challenge landscape.

3.2. Prioritisation process

To identify which of the challenges in the PV challenge landscape are of priority, different sources are used. The sources that are used, include: the PV system and PV challenge landscape matrix (Table 2); and SMEs. At the onset, the PV system and the PV challenge landscape matrix (Table 2) illustrate which challenges appear across the entire PV system spectrum, thus also facilitating the process of prioritising the challenges in this research. Second, suggestions by SMEs are used since they are front line participants in PV who have the necessary knowledge of the prevalent and severe challenges in PV. The SMEs consulted in this regard are shown in Table 4. Two of the SMEs are affiliated with a multi-national pharmaceutical company, whereas the other is an experienced PV researcher affiliated with a university.

Table 4: SMEs consulted to prioritise the PV challenge landscape.

	Occupation	Affiliation
1	Medical Lead Access, Regional Medical Director. Leading the preparation for the launch of a new product within severely resource constrained environments.	Multi-national pharmaceutical company
2	This SME has practical experience and knowledge in a PV enhancement project linked to Malaria vaccines.	Multi-national pharmaceutical company
3	This SME is an independent PV consultant with more than 20 years of experience within PV, including policy development and implementation.	Locally renowned university (Public Health department)

3.3. Prioritised pharmacovigilance challenge landscape

An important parameter in a prioritisation exercise such as this is the degree of impact (Ebrahim, 2013), i.e. what is the expected impact of the challenge? Defining impact, it is an iterative process, and is described as an evidence-based process of assessing the implementation and effectiveness of several actions in a specific context (Ebrahim, 2013). As seen in the definition, impact evaluation is an "*evidence-based*" process, requiring real-world data (Ebrahim, 2013). Acquiring such data is a tedious process, and due to time constraints is not included in the scope of this research. Instead, impact evaluation is incorporated during the consultations with the SMEs. I.e. if an SME indicates a specific PV challenge has a significant impact on the PV system, it is regarded as priority. Furthermore, and in support of the opinions of the SMEs, the PV systems and PV challenge landscape matrix in Table 2 is used to indicate the PV challenges that should be prioritised. When a challenge is experienced during each of the stages of a PV system, the specific challenge is regarded as a priority. This matrix in Table 2 was also validated by the previously mentioned SMEs. The results from these two sources (the SME feedback and the PV systems and PV challenge landscape matrix in Table 2) are combined in order to develop a list of challenges in PV that should be prioritised.

Consequently, the challenges that are regarded as priority (indicated as an "X" symbol), according to the PV system and PV challenge landscape matrix and the SMEs, are shown in Table 5. The challenges deemed challenges that should be prioritised are culture, transparency, insufficient resources, country-specific factors, technical capacity, partnerships, and under-reporting of ADRs Subsequently, these challenges are discussed in more detail than presented in Chapter 2, allowing for a comprehensive understanding of such challenges.

Table 5: The prioritised challenges of the PV challenge landscape.

PV challenge landscape	PV system and PV challenge landscape matrix	Opinions of SMEs
Culture	X	X
Transparency	X	X
Insufficient resources	X	X
Lack of PV centres	-	-
Country-specific factors	X	X
Technical capacity	-	X
Partnerships	X	X
Public participation	-	-
Under-reporting of ADRs	-	X
Quality of ADR reports	-	-
Text-mining	-	-
Passive vs. active systems	-	-
Lack of data	-	-
Lack of reporter feedback	-	-
Clinical trials	-	-
Causality analysis	-	-
Signal detection	-	-
Legislation	-	-

3.4. Culture in pharmacovigilance

Culture (also referred to as organisational culture) has been defined differently in many disciplines, remaining a controversial concept. Conflicting definitions of organisational culture exist, and there is constant debate over the most appropriate methods for defining and assessing culture (Bellot, 2011).

3.4.1. Defining organisational culture in pharmacovigilance

Following the introduction of culture in in Section 2.7, defining organisational culture is challenging, because of the different conceptions of culture (Bellot, 2011). In an attempt to define organisational culture from a general perspective, Naidoo & Martins (2014) define it as "*an integrated pattern of human behaviour which is unique to a particular organisation and which originated as a result of the organisation's survival process and interaction with its environment*". Culture is said to direct an organisation to goal attainment, and newly appointed employees must be taught what is regarded as the correct way of behaving (Naidoo & Martins, 2014). Another perspective of organisational culture is that it is a social construct, the product of groups and not individuals. It is based on the experiences of groups and it is unique to each organisation. It is also said to be malleable, adapting to the continual changes found in organisations, and it develops over time (Fortado & Fadil, 2012).

The definition of organisational culture given by Naidoo & Martins (2014) clearly places the focus on the behaviour of the human participants of an organisation as the manifestation of an organisation's culture. The PV system can be viewed as an organisation, consisting of different processes managed by people. Like any other organisation, groups with different multi-disciplinary backgrounds and experiences take part in PV. Considering Naidoo & Martins' (2014) definition of organisational culture, the behaviour of the individuals in these groups creates the culture in the PV system.

3.4.2. Factors that influence organisational culture

Returning to the definition of organisational culture provided in the preceding section, Naidoo & Martins (2014) emphasise that the human behaviour that manifests an organisation's culture is a response to an "*organisation's survival process and interaction with its environment*". There is agreement in literature that many factors influence organisational culture. Though these factors are sometimes unique to a specific industry or organisation, a succinct overview of some of the most salient factors are presented here to provide a general perspective on factors that may influence the organisational culture in a PV context.

First, the business environment in which an organisation operates determines its culture. Within the market, the speed of change; the level of competitiveness; the value placed on technology; and the demands of the customer; influences the values; and norms and behaviours associated with the organisational culture (Alan, 2001). Second, leadership influences organisational culture (Al-Alawi *et al.*, 2007), especially in newly created organisations (Alan 2001). Leaders help establish organisational culture through their own ambitions and actions e.g. setting standards for behaviour by being an example to the people in the organisation. Third, management practices influence organisational culture. Alan (2001) believes the way an organisation is managed[3] is likely to influence the beliefs, attitudes, and behaviours of the employees.

Last, formal and informal socialisation processes play an important role in propagating the organisational culture (Alan, 2001; Al-Alawi *et al.*, 2007). Formal socialisation activities include induction training, hosted by the managers and leaders of an organisation. On the other

[3] For the purpose of this discussion, leadership is distinguished from management based on its providing vision and long-term direction to an organisation (Alan, 2001).

hand, informal socialisation refers to individual activities within a group context. Al-Alawi *et al.* (2007) discern a distinctive relationship between these socialisation processes and the people in an organisation, stating that it is essential to focus on people and their behaviours when attempting to assess or change organisational culture. Moreover, Al-Alawi *et al.* (2007) include organisational structure, trust, information systems, and reward systems as critical success factors to organisational culture, with specific reference to the relationship between organisational culture and knowledge management.

All of these factors influence PV in some way, making it increasingly challenging to maintain a culture of universal drug safety. Furthermore, and in addition to the known factors that influence organisational culture (discussed in Section 3.4.2), additional factors are expected to affect a safety culture in PV, due to the large scope of the PV system. Examples of such factors include hierarchical networks, location specific factors such as religion and culture and resource management practices.

3.4.3. Singular versus plural organisational culture in pharmacovigilance

Since the PV system has such a large scope, the question: *"Is the culture found in PV of singular or plural origin?"* should be asked. Sprouting from the discussion of Bellot (2011) who makes reference to singular– and plural organisational culture, it should be considered whether PV has a unique yet homogenous culture, or whether there is a presence of subcultures, also referred to as nested cultures or cultural pluralism.

Cultural pluralism exists in many organisations, and it relates to different jobs, different levels of organisational status, and class (Alan, 2001). A PV system consists of several stages and different groups of role players are regarded as stakeholders within the various stages. The stakeholders that participate in PV, range from healthcare specialists to consumers and patients to administrative workers and these stakeholders display both individual and group behavioural phenomena. These behavioural aspects, reflecting the identity and purpose of the group, results in the formation of a variety of subcultures within the PV system. Subcultures also exist in PV systems that operate in different countries, where the country specific conditions influence the behaviours of the PV system's participants in a particular geographic location.

Considering that subcultures exist in PV, the question posed at the beginning of this sub-section is answered: PV culture is of plural origin since many subcultures exist in different stages of PV systems and in different locations where the PV system operates. Comprehensively understanding these subcultures is difficult due to the large scope of PV. However, since PV is based on a safety culture, these subcultures do incorporate certain shared behavioural phenomena related to a safety culture.

3.5. Partners in pharmacovigilance

Many partners exist in PV, operating from both within and outside the PV system. For instance, partners that operate within PV include the UMC, national PV centres, and healthcare workers. Partners that operate outside PV include local governments or regulators and private investors. Both these partners provide different forms of expertise, training, political support, scientific infrastructure, and a capacity to accomplish comprehensive monitoring and investigations of the safety of medicines (Pan, 2014). It is essential that sustained collaboration exists between partners, because they supply resources to a resource-constrained system. As stated in Section 2.8.3, this type of collaboration is not always achieved. Moreover, providing services and resources to the PV system may not necessarily result in a high-profit margin, hindering the establishment and maintenance of partnerships even further.

3.5.1. Different partners in pharmacovigilance

Partners in PV form an entire network of collaboration, with each partner (both operating internally and externally to PV) retaining unique expertise, resource capacities, responsibilities, and power to influence PV systems. In Table 6 the partners in PV are identified and briefly described.

As described in literature, effective and efficient PV systems that are able to operate without disruptions can only exist with assistance and support from partners. An extensive network of partners exists, making it increasingly difficult to establish and manage partnerships with all the required role players to effectively deliver PV on a global scale. Moreover, the different interests and expectations of partners further burden PV systems. In a society with increasing demand for healthcare provision, it is becoming increasingly challenging for PV systems (as well as for many other healthcare systems) to meet the demands of its partners, and for the partners to meet the needs of the PV system.

3.5.2. Comparing partners to stakeholders in pharmacovigilance

Considering the term "*stakeholders*", Mathur *et al.* (2007) describe them as "*influencers*" to certain situations. Alluding to partners in PV while still considering this description of stakeholders, one could say that "*partners*" and "*stakeholders*" are interchangeable terms, since partners also influence PV. The perspective of Mathur *et al.* (2007) on stakeholders is therefore applied to the partners in PV.

Partners have different levels of power and interest (Brugha & Varvasovszky, 2000). It is critical to the success of PV that these are defined. The levels of power and influence of various partners will differ from one country to another, however, a general estimation of both the level of power and the level of interest in PV can be determined, representing a so-called industry average. To portray the different levels of power and interest of partners in PV, a stakeholder analysis technique explained by Mathur *et al.* (2007) is used. Considering that partners and stakeholders share similar characteristics, the analysis is used to investigate partners in PV. The diagram in Figure 5 illustrates the different levels of power and interest of partners in PV. The numbers in the diagram represent the partners in PV, according to the numbering system used in Table 6

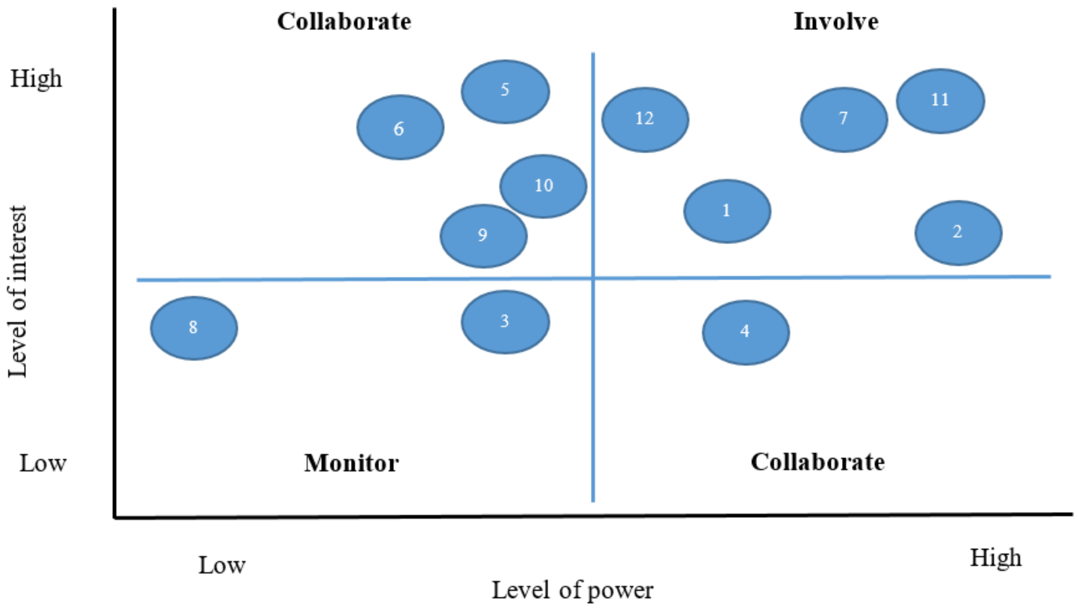

Figure 5: Level of power versus level of interest of partners in PV (based on the previously mentioned technique described by Mathur et al. *(2007)).*

Table 6: The partners that operate in PV.

Number	Partners	Brief description
1	Healthcare workers	Healthcare workers (general practitioners, nurses, pharmacists) are responsible for reporting ADRs and promoting PV.
2	Governments	Collaboration with governmental bodies are essential since they hold the power to authorise a PV system.
3	Manufacturers of hardware and software	Modern PV systems rely on software (e.g. used for text-mining and administrative purposes) and hardware (e.g. mobile phones used for patient engagement) to operate to its fullest potential.
4	Non-governmental organisations (NGOs)	NGOs in the private sector often provide essential support to PV systems, especially in the form of funding. Other NGOs also include the WHO and the UMC who provide frameworks and policies for use in PV systems.
5	Non-profit organisations (NPOs)	NPOs who already operate in a specific country can provide essential knowledge and expertise on a country that might help the planning process of a PV system.
6	Community leaders	Leaders in communities can be used to motivate the public to promote PV systems.
7	Pharmaceutical companies	Pharmaceutical companies play a major role in PV because it is their product being monitored. They also play a major role during drug risk assessments.
8	Media	The media can be utilised to promote PV in a community.
9	Public health systems (South Africa Infection Prevention and Control, Poison Control Centres, etc.)	Public health systems that already operate in a certain area can provide important information to PV organisations on different considerations that are unique to a country e.g. people's knowledge of healthcare systems. A collaboration with these health systems can be beneficial to PV, possibly offering some form of expertise and knowledge.
10	Drug administration programmes (e.g. drug administration programmes during an epidemic)	Like public health systems, drug administration programmes (e.g. malaria or HIV/AIDS vaccination programmes) can offer expertise and knowledge that might be beneficial to PV systems.

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11	PV centres (e.g. WHO Programme for International Drug Monitoring, UMC)	PV centres, especially those who form part of the high-level network described in Section 2.8.2, provide much needed frameworks, policies, models, assessment tools, and expertise used in PV systems.
12	Academic institutions	Academic institutions aid PV by conducting much needed research, aiming to improve the impact of PV.

As mentioned, the diagram in Figure 5 represents a generalised depiction of the levels of power and interest of partners in PV. A brief discussion of Figure 5, with the help of the key in Table 7, follows.

Table 7: Key used to explain the analysis of the partners in PV (Reproduced from Mathur et al. *(2007)).*

	Involve	Collaborate	Monitor
High support	Optimal	Missed opportunity	Missed opportunity
Could support (oppose)	Risk	Optimal	Missed opportunity
High threat (resistance)	Risk	Risk	Risk
Low support	Resource waste	Resource waste	Optimal

In Table 7 three actions are displayed: *involve*, *collaborate*, and *monitor*, representing the suggested actions for collaboration between partners, as described by Mathur *et al.* (2007). Depending on the level of interest, different scenarios (*optimal*, *risk*, *missed opportunity*, and *resource waste*) are possible. In an ideal world, the *optimal* state would give rise to effective and efficient collaborations between PV and its partners. In reality, however, the best PV organisations can do is to strive towards the *optimal* state.

3.5.3. Synthesising partnerships in pharmacovigilance

Focussing on the outliers shown in Figure 5, the authority of governmental bodies poses a risk to PV systems. Governments have control over all public-based systems and may therefore have the power to inhibit PV systems from being implemented in a country. Very closely related to the country-specific factors challenging PV systems (discussed in Section 2.8.2), governmental focus may be invested elsewhere. This risk of non-support must be considered by PV organisations, who must put effort into building a close collaboration with governmental bodies.

Pharmaceutical companies and PV centres are also important partners in PV. First, pharmaceutical companies are close collaborators in PV, since it is mostly their product monitored by PV systems. Active engagement is needed to ensure that these companies are consulted during causality– and risk assessments, because they can provide the necessary scientific infrastructure and resources. Second, PV centres such as the WHO Programme for International Drug Monitoring and the UMC are obvious partners and have major influence in PV, providing essential support in the form of policies, frameworks and models used by PV systems.

In the *Monitor* quadrant of the diagram shown in Figure 5, an outlier to consider is the media. Pivoting between a *risk* or a *missed opportunity*, the media is an effective tool to use during public participation (discussed in Section 2.8.3.1). Having the ability to convey important information, such as news on ADR reporting (discussed in Section 2.9.2) or providing feedback to ADR reporters (discussed in Section 2.9.6), the media can deliver messages to a wide range of consumers and patients. On the other side of the spectrum, the media also poses a risk to PV, for example, the PV system could suffer reputational damage if the media were to only report its failures. It is essential that PV systems collaborate with the media to enable balanced reporting, thereby increasing the public's awareness of PV and their willingness to participate in the system as active partners.

3.6. Transparency in pharmacovigilance

As mentioned previously, efficient and effective operation of the PV system relies on the collaboration of several partners. Collaboration on this scale is challenging to achieve and is often hindered by poor communication (Jusot 2017). Communication is one of the most important aspects of collaboration in any industry, and serves as the foundation to basic business. Transparency is a key element of communication (Jusot 2017).

Transparency is defined as "*the level of availability and accessibility of market information to its participants*" (Granados *et al.*, 2010). Transparency means that all relevant information is made available to the relevant stakeholders. In PV, and in healthcare in general, transparency is crucial because the information being shared either directly or indirectly relates to patient– and public health. There are many forms of failed transparency between stakeholders in PV, some of which are discussed in Table 8. The different forms of failed transparency in PV shown in Table 8 does not constitute an exhaustive list, but the examples provided do emphasise the need for transparency amongst the stakeholders in PV.

Table 8: Different forms of transparency between stakeholders in PV.

Transparency between stakeholders	Description
HCWs and HCWs	HCWs may fail to effectively communicate about PV-related tasks, such as capturing ADR reports on a computer, which might lead to lost ADR reports.
PV centres and HCWs	In some cases, HCWs fail to provide the right information regarding PV-related tasks (e.g. ADR reports) to PV centres who are requesting specific information, leading to wasted time for both entities since the entire process must be revisited.
PV centres and governments	As mentioned in Section 3.5.3, governments are major role-players in PV. The lack of transparency between PV centres and governments may lead to the ineffective and inefficient operation of a country's PV system.
PV centres and pharmaceutical companies	The lack of transparency between PV centres who are public entities and pharmaceutical companies who are private entities may lead to failed follow-ups of ADR reports. For example, if the former does not make ADR information available to the latter, the latter may not be able to conduct proper assessments in order to address possible ADRs associated with its product.

3.7. Insufficient resources in pharmacovigilance

In order to understand the challenge posed by insufficient resources in PV, one should first consider the differentiation between the types of resources referred to when making reference to insufficient resources in PV.

Different resources exist, ranging from tangible– to intangible resources. Tangible resources comprise of physical assets such as machinery, buildings, and equipment; whereas intangible resources comprise everything else that has no physical presence, including trademarks, software programs, and business processes (Jurevicius, 2013a). Resource management systems (RMSs) are widely used to help organisations manage these two types of resources more effectively and efficiently. Furthermore, Li *et al.* (2017) describe that the modern era of business operates under high resource-consumption rates, as well as high market-uncertainty.

According to Li *et al.* (2017), RMSs perform two core functions namely resource acquisition and resource accumulation. The latter refers to the development of resources from internal sources (e.g. expertise and experience), allowing for the expansion of an organisation's internal resources. Resource accumulation is necessary since the external market cannot provide all the required resources to an organisation (Li *et al.* 2017). Resource acquisition is concerned with procuring resources from the external market.

Imperative for active management of resource portfolios and the adoption of strategic flexibility (Li *et al.*, 2017), an effective and efficient RMS, that identifies resource acquisition and accumulation is essential (Li *et al.*, 2017).

3.7.1. Resource accumulation and resource acquisition in pharmacovigilance

Taking into consideration the market conditions described by Li *et al.* (2017), PV operates in an environment of high resource-consumption and high market-uncertainty due to an increasing demand for healthcare. To meet the increasing demand for healthcare and be strategically flexible, the PV system requires active management of its resource portfolios, including both resource accumulation and resource acquisition activities.

Resource acquisition plays a vital role in PV. PV systems rely on external partners to provide resources such as computer hardware and software, and funding. To ensure a timely supply of such resources, PV organisations and their partners must collaborate and communicate (also associated with the need for improved transparency as indicated in Section 3.6) and ensure that both parties' needs are met.

The PV system is also dependent on effectively harnessing internal resources, such as the expertise that specialists from different backgrounds can offer in formulating business models, policies, frameworks, and internal processes, through the process of resource accumulation. Resource accumulation is especially valuable as it allows for differentiated resources that have been developed specifically to accommodate the unique features of the PV system.

3.8. Country-specific factors in pharmacovigilance

In 2013, a study was conducted by numerous healthcare researchers (Tomoaia-Cotisel *et al.*, 2013) aimed at advancing both internal– and external validity of healthcare research by delivering their opinions on the importance of reporting contextual factors in healthcare research. It was stated that contextual factors are rarely reported in healthcare research, leading to failed attempts in replicating such research. The study also indicated that efforts to translate research into practice fail because contextual factors that are important for understanding and knowledgably synthesising findings across studies are not known.

Several factors, defined differently in various disciplines, affect PV. Experts from disciplines such as sociology and social anthropology are increasingly being included in the development and planning of not only PV systems, but many other healthcare initiatives such as vaccination administration programmes.

3.8.1. Distinguishing between factors that might affect pharmacovigilance

Sociocultural factors and contextual or systemic factors are closely linked to the geographical location and are considered in this section. Covering a wide range of factors that might impact PV systems, sociocultural factors distinguish between social factors such as attitudes, ethnic identities, linguistic differentiations, and power structures, as well as cultural factors such as cross-cultural differences, cultural identity, and religious beliefs (Buse et al. 2005).

Contextual factors, also referred to as systemic factors refer to political, economic and social factors, both national and international levels. Contextual factors are categorised, according to Buse *et al.* (2005), as follows:

- Situational factors: Transient or impermanent conditions such as drought and war.
- Structural factors: The relatively unchanging elements of society such as the political system, health expenditure, gross domestic product (GDP) per capita, and the degree to which the public can participate in decision-making etc.
- Cultural factors: Like sociocultural factors, cultural factors refer to aspects such as power hierarchies, linguistic differences, and religious beliefs.
- International or exogenous factors: Closely related to partnerships, collaborations are often needed to aid in the implementation and operation of systems.

There is an overlap between sociocultural factors and some of the categories of contextual factors i.e. contextual and sociocultural studies identify and assess similar influential factors. Identifying and assessing sociocultural and contextual, or systemic factors, is a complex process, requiring multi-disciplinary groups including sociologists, anthropologists, and governmental agencies (Buse et al. 2005).

3.8.2. Example of the effect of country-specific factors on pharmacovigilance

As stated earlier, country-specific factors significantly affect the operation of PV systems. A significant effect one of the country-specific factors identified in the previous section, cultural factors, is reported in PV (Varallo et al. 2014). Varallo et al. (2014) reports that there are many causes of ADR under-reporting, including causes linked to cultural factors. It is often reported that people who experience ADRs do not report it to the necessary authorities since they believe it can either be addressed by a doctor, or they feel that they do not have the authority to reach out to local healthcare facilities. It is clear that this country specific factor is a stumbling block in PV, since it reduces the number of ADR reports that are of utmost importance to PV.

Although this is only one example of the potential effects country-specific factors could have on PV systems, it is regarded as one of the most significant challenges in PV (Varallo et al. 2014). This highlights the need to address the effect country-specific factors have on PV systems.

3.9. Technical capacity

Technical capacity refers to the ability of an organisation or person conducting a specific action that is meant to achieve some outcome. This is closely related to the KAP model which is described in further detail in Section 3.10.2. Often categorised as an insufficient resource, Mehta (2017) is of the opinion that it deserves to be independently categorised, because it is such an influential aspect that is lacking in many countries, especially developing countries. Many factors contribute to the ability of an organisation or individual to exercise a specific action, which includes past experience, personal and personnel skills, ability to utilise resources, and education or training.

The only way in which experience, personal skills, and the ability to utilise resources can be achieved is by both theoretical– and practical training. Theoretical training closely relates to academic education and plays an essential role in developing foundations and thinking patterns in individuals who enter practice (Mehta 2017). Practical training is often significantly more difficult to obtain since training often conflicts with working schedules. However, Mehta (2017) is of the opinion that it is of importance that practical training is provided to those who fail to achieve the desired objectives. Practical training is in many cases considered more critical than theoretical training (Mehta 2017). Reasons for this may include that a portion of the workforce may not attended an academic institution.

The lack of technical training negatively affect PV in several ways, which include (Mehta 2017):

- PV personnel who lack the necessary technical capacity may take longer to complete PV-related tasks (e.g. capturing ADR reports on a computer).
- There is also poor human resource-efficiency because the responsibility of PV-related tasks is given to many employees who might not have the necessary skills and knowledge.

Improving technical capacity is not as simple as one might think (Mehta 2017). Not even considering the cost implications of theoretical training provided by academic education, practical training is often also very difficult to provide. Training sessions in the form of workshops and brainstorming sessions require resources that are often not available. One of these scarce resources are access to individuals who have the desired technical capacities and are able to convey their skills and experiences.

Regardless of the challenges facing technical capacity, there are several studies that conclude that the lack of technical capacity is a major obstacle in PV, and must be addressed on a large scale (Schramm *et al.*, 2017; Abubakar, Chedi, *et al.*, 2015; Abubakar & Haque 2016; Abubakar, Ismail, *et al.*, 2015; Abubakar, Simbak, *et al.*, 2015; Mehta 2017).

3.10. ADR under-reporting in pharmacovigilance

Two prominent models that explain the causes of under-reporting of ADRs are widely cited in literature, namely Inman's model of the seven deadly sins of under-reporting (Varallo *et al.*, 2014) and the KAP (knowledge, attitude and practice) model of under-reporting (Herdeiro *et al.*, 2006). Taken together, these two models provide a comprehensive overview of the lead causes of under-reporting of ADRs (Herdeiro *et al.*, 2006).

3.10.1. Inman's seven deadly sins of under-reporting

In the 1990s, Dr William Inman conducted research on PV with specific reference to the causes of under-reporting of ADRs (Varallo *et al.*, 2014). The findings of this study, known as Inman's seven deadly sins of under-reporting, are widely cited in literature (Varallo *et al.*, 2014; Hazell & Shakir, 2006; Irujo *et al.*, 2007; Rodrigues & Khan, 2011). More recent studies have confirmed the findings, specifically highlighting the ignorance, insecurity and indifference aspects of the model. (Varallo *et al.*, 2014; Rodrigues & Khan, 2011)

The so-called sins of Inman's model are (Varallo *et al.*, 2014):

- Fear: Of litigation;
- Indifference: About contributing to the general advancement of knowledge;
- Ambition: To collect and publish a personal case series;
- Guilt: At having caused an adverse effect;
- Complacency: The mistaken belief that only safe drugs are licensed;
- Ignorance: Of the need for reporting; and
- Diffidence: About reporting a mere suspicion.

A number of subsequent studies have validated Inman's model. In 2014, a study was conducted amongst hospitals and physicians in Spain (Varallo *et al.*, 2014). The objective of the study was to identify the main causes of under-reporting ADRs by health professionals in Spain. It was found that the main causes of under-reporting was ignorance, insecurity, and indifference, all associated with Inman's model (Varallo *et al.*, 2014). Also, Rodrigues & Khan (2011) conducted research with the intention of identifying the cause of under-reporting amongst surgeons and surgical wards in an unknown context. The findings of the research also correlated with Inman's model. Rodrigues & Khan (2011), Varallo *et al.* (2014) and Hazell & Shakir (2006) are all of opinion that Inman's model is and will be applicable to future PV initiatives.

Many of these so-called sins such as indifference, ambition, complacency, and diffidence strongly relate to the culture in PV (discussed in Section 3.4) and research in eliminating these sins is believed to improve the overall culture within PV.

3.10.2. KAP model

The first aspect of the KAP model is knowledge, closely related to education (Herdeiro *et al.*, 2006). The shortcomings of PV in the undergraduate and postgraduate syllabus of medical students is regularly referred to in literature (Schramm *et al.*, 2017; Abubakar, Chedi, *et al.*, 2015; Abubakar & Haque 2016; Abubakar, Ismail, *et al.*, 2015; Abubakar, Simbak, *et al.*, 2015). These shortcomings are also not unique to specific countries. Studies in Nigeria (Abubakar, Chedi, *et al.*, 2015), Malaysia (Abubakar, Ismail, *et al.*, 2015), Portugal (Herdeiro *et al.*, 2006), Turkey (Toklu & Uysal, 2008), India (KC *et al.*, 2013), and China (Su *et al.*, 2010) all discuss the need for medical students' curriculum to either include or improve PV education.

The aforementioned countries' specific studies also highlight the lack of sufficient knowledge on the correct PV practices in practicing healthcare professionals. Toklu & Uysal (2008) discuss the need for improved PV knowledge amongst community pharmacists in Turkey, Passier *et al.* (2009) the need for improved PV knowledge amongst general practitioners in the Netherlands, and Herdeiro *et al.* (2006) the need for improved PV knowledge amongst pharmacists in Portugal. Thorough knowledge of PV is a challenge, hurdling several PV initiatives to be completely successful in many countries.

Secondly, the KAP model refers to the general attitude of healthcare professionals towards PV. This element of the KAP model is closely related to the indifference and ignorance aspects of Inman's model and relates strongly to the culture aspects of the PV challenge landscape. Some examples of the role of attitude in under-reporting are given in a recent study by Shamim *et al.* (2016) who seek to build an understanding of the general attitude of physicians, pharmacists, and nurses towards PV in Pakistan. It was found that a large portion of these healthcare professionals are indifferent towards PV, with only 14.3% being aware that there was an ADR reporting organisation in Pakistan. Similarly, a study within a Spanish context also discusses the poor attitude of healthcare professionals towards PV (Varallo *et al.*, 2014). The indifference found in the Spanish context is associated with the lack of interest of healthcare professionals to register for ADR reporting and a lack of time for the many activities in the clinical routine.

Lastly, the lack of sufficient practice (relating to first-hand experience within PV, as well as skills and knowledge needed within PV) in PV is also a challenge faced in the PV industry. Closely associated with training, Varallo *et al.* (2014) is of the opinion that the lack of sufficient practice has recently surfaced and is nowadays referred to as the eighth sin of Inman's model. The lack of practice in PV is regularly referred to in literature, including Aronson (2012) discussing the need for increased, real-world PV practice amongst British healthcare professionals and Beckmann *et al.* (2014) who similarly emphasises this need in a general context.

3.10.3. Synthesising Inman's model and the KAP model in pharmacovigilance

Under-reporting of ADRs is a burden to PV systems in many countries, limiting the extent to which action can be taken to improve medicines' safety. There is a need for the culture surrounding ADR reporting (relating back to the lack of safety culture in PV as discussed in Sections 2.7 and 3.4) to improve to a state where healthcare professionals, patients, and the public feel unthreatened and assured to report ADRs (Jusot, 2017). It is important to consider that PV systems in different countries are unique, and might therefore require a comprehensive investigation to understand the attributes that affect ADR reporting (e.g. understanding how country-specific factors, described in Section 3.8, might affect ADR reporting).

3.11. Chapter 3 conclusion

The challenges described in this section are culture, transparency, insufficient resources, country-specific factors, partnerships, technical capacity and under-reporting of ADRs. These are the challenges that are identified as challenges that should be prioritised. Such challenges differ in nature and bring forth numerous additional challenges to PV. Yet, some of these challenges are inter-related (e.g. under-reporting of ADRs are in certain aspects related to the culture of PV), meaning that addressing one may also affect another. Subsequently, the challenges are further contextualised to facilitate the process of understanding and evaluating how these challenges could potentially be addressed through the use of technology.

Chapter 4: Translating the pharmacovigilance challenge landscape

This chapter[4] discusses the translation process of the prioritised PV challenge landscape from a strategic level to an operational level, i.e. identifying the root causes. An investigation into different translation methodologies is done to identify methods which would be appropriate to use in this research. One of these methods is then implemented in the PV challenge landscape, translating the prioritised PV challenge landscape.

4.1. Business levels in an organisation

In an organisation, different levels exist within the structures of the organisation, referred to as strategic–, tactical–, and operational levels (Boundless Management 2016). These levels are the foundation on which most organisations are developed, conduct planning, communicate and make decisions.

4.1.1. Strategic level

The strategic level is where an organisation develops and plans its strategy for the long-term i.e. examining where the organisation is now, deciding where it should go and planning how it will get there. The strategic level considers both the tactical– and operational level, taking into consideration the requirements of these levels to support the organisation-wide strategy. Strategic decisions are usually made by upper-management and directors, but managers on the tactical– and operational levels are consulted to give meaningful input on how they believe the organisation can achieve its strategy.

4.1.2. Tactical level

Oscillating between the strategic– and operational levels, the tactical level focusses on the actual steps that are needed to achieve the strategy of the organisation. Tending to be more short-term focussed (usually one year or less), planning on a tactical level considers the current business activities across the entire organisation, and determines the requirements that are needed to achieve the organisations' strategy.

[4] A significant portion of the contents of this chapter has been published in an article that was included in the proceedings of the International Association for the Management of Technology's 2018 annual conference (IAMOT2018). A copy of this article is included in Section C.1 in Appendix C.

4.1.3. Operational level

At the operational level, day-to-day activities are the focal point. These refer to the actual output of the organisation such as number of products manufactured daily, quality standards of these products, and worker schedule adherence. Planning on an operational level links strategic goals and objectives to that of the tactical level. The idea behind operational control is to streamline a process to minimise costs and increase efficiency.

4.2. Translating strategy into operations

Executives and managers who have not moved through the ranks of operational management and as a consequence are not familiar with operations, frequently fail to consider the influence of operations on an organisation's overall strategy (Hammer, 2004). According to both Hammer (2004) and Croxton *et al.* (2001), being aware of both the opportunities posed and the limitations associated with various operational strategies will allow these previously mentioned executives and managers to add to their strategic arsenal to become influential market players. Companies such as *Dell* and *Toyota* have shown that operational innovation offers many benefits, and Hammer (2004) is of the opinion that many other companies can learn a great deal from these companies who have been investing more towards operational management.

Provided that more effort needs to be shifted towards processes and activities related to operational management (Croxton *et al.,* 2001), there is a need to define and investigate strategic level processes and activities at an operational level. Thus, strategies need to be translated to an operational level to understand how these influence the different functions within an organisation (Naghibi & Baban, 2011). Considering this within the PV context, to propose actionable solutions to the strategic level challenges that have been identified in the PV landscape, these must be translated to an operational level. Formalising the operational level challenges in this manner will enable knowledge sharing and debate about these in literature and will enable researchers and practitioners to differentiate between the effects that these challenges have on the various functions in PV.

Hewitt-Taylor (2012) argue that, for challenges to be described on an operational level, the root causes must be identified. It is argued that it is often more feasible to address these root causes, rather than to address the challenges on a strategic level, because the root causes will represent tangible problems that can be more easily addressed.

Therefore, the rationale behind the proposition that the PV challenge landscape must be translated to a lower level of abstraction is: (i) such a translation will make it clear how strategic challenges influence the different functions in an organisation, or in the case of PV, the stages of which PV systems are composed; and (ii) identifying the root causes of strategic challenges will make it increasingly easier to address such challenges at an operational level.

Such a translation, however, is not always simple, and according to Chmutova (2015), businesses often struggle with this process, given that they fail to leverage existing methodologies in guiding the entire translation process. Some of the methodologies that have been developed for this translation process are considered in the subsequent section.

4.3. Translation methodology assessment

To identify the different methodologies that can be used to translate the PV challenge landscape, a literature review was conducted in two databases, namely *Google Scholar* and *Scopus*, as well as grey literature. Using the search terms "*root cause analysis", "translation methodologies and approaches",* and *"problem solving"*, the literature review uncovered some of the more widely used methodologies, namely root-cause analyses (RCAs), the 5Why method and fishbone diagrams, and problem tree analyses. Additionally, the 5W2H method, key performance indicators (KPIs), and value chain analyses, methods that are commonly used for analysing and defining systems in the Industrial Engineering discipline, are added to the list of methodologies that are considered for application.

4.3.1. Root cause analysis

According to Jones & Despotou (2016), RCA is by far the most widely used analysis tool for investigating problems, especially in the healthcare environment. RCAs focus on the root cause of problems, while avoiding emphasis on any mistakes made by specific individuals. Ideally, a team-based approach, where teams are composed of individuals from different backgrounds and contexts, is the best approach to conducting a RCA, as this will ensure that a range of root causes to the same problem are identified.

There are different techniques that can be used to conduct a RCA, the most popular being the 5Why method and fishbone diagrams.

4.3.1.1. 5Why method and fishbone diagrams

The 5Why method was developed by *Sakichi Toyoda*, one of the fathers of the establishment of the car company *Toyota* in the late 1940s (Warner, 2015). Adopted by the global market in the 1970s, the 5Why method became one of the most renowned methodologies able to identify the root causes of specific problems.

In essence, this form of RCA is completed by asking the *why* question, on average, five times (Warner, 2015), which will lead to the identification of the root cause of a given problem. Additionally, in order to capture the thinking processes during this exercise, a fishbone diagram can be developed, which will provide a visual representation of the possible root causes to a given problem (Pojasek, 2000; Jones & Despotou, 2016).

The 5Why method, in combination with fishbone diagrams, offers several benefits to its users, including (Pojasek, 2000):

- It is a very quick and simple method to use, provided that the user has some background and understanding of the appropriate strategy to implement the method.
- The nature of the *why* question is highly relatable, since *why* is so often asked in real-life.
- Fishbone diagrams serve as visual representations to the 5Why method, providing a holistic view of the effects that stem from a certain root cause.
- The process initiates a thinking process in the individuals that make up the team, allowing them to come up with an answer more quickly.
- The *one right answer* syndrome is eliminated since the method is a team-based approach i.e. a broad range of answers from different perspectives or departments within the organisation are given.

Regardless of the benefits offered by the 5Why method and fishbone diagrams, there are also some challenges associated with it, namely (Pojasek, 2000):

- Facilitation is needed to guide the process followed during the execution of this method in order to ensure that the participants understand how the method works.
- It is not always straightforward to answer the simple question of *why*, since many internal and external factors may affect the answer.
- When used incorrectly, these methods can lead to finger pointing i.e. one individual or group can be blamed for a mistake.

A number of studies have endorsed the efficacy of the 5Why method in combination with fishbone diagrams as a mechanism for translating problems that have been defined on a strategic level to a more tactical or operational level where some of the root causes may exist (Pojasek, 2000; Bulsuk, 2009; Sonkiya, 2014; Brundage *et al.*, 2017; Mpanza, 2016).

4.3.2. Problem tree analysis

Problem tree analyses (PTAs) visually represent problems, their causes and the effects in the form of a tree, where the problem is shown as the tree trunk, the causes as the roots, and the effect as the branches (Hewitt-Taylor, 2012). These types of analyses are comprehensive and make clear differentiation between the causes and the effects of a problem.

PTAs offer several benefits, which include (Hewitt-Taylor, 2012):

- Clearly distinguishing between the causes and the effects of problems.
- Providing a holistic overview of the different effects of a specific problem.

There are also some limitations to using PTAs, which include (Hewitt-Taylor, 2012):

- PTAs can become difficult to manage if there are too many links between causes and effects.
- The PTA development process can become tedious, given that both causes and effects must be identified.

Regardless of these limitations, PTAs offer businesses the opportunity to distinguish between the causes and the effects of a problem, leading to the identification of different links between effects and likely root causes.

4.3.3. 5W2H method

The 5W2H method is a highly efficient and simple management tool (Veyrat, 2016). It is constructed of well-defined stages, serving as structures to action planning. The name of this method originates from the questions that are asked. These questions are: "*What will be done?*", "*Why will this be done?*", "*Where will it be done?*", "*When will it be done?*", "*Who will do it?*", "*How will this be done?*" and "*How much will it cost?*" Given that strategies constantly change within the competitive market, strategies must continuously be adjusted. As a result new strategic challenges come to light. According to Veyrat (2016), going through the process of the 5W2H method will allow organisations to define their strategies, and determine how these strategic challenges can be addressed.

The 5W2H method has a variety of applications, including quality planning, purchases planning, human resource planning, and risk planning (Bau *et al.*, 2012). The simplicity of this method allows it to be used in many industries and applications such as those mentioned earlier. The 5W2H method offers many benefits, including (Bau *et al.*, 2012; Veyrat, 2016):

- It is a simple method to implement since straightforward questions are asked.

- It enables businesses to comprehensively define the problem at hand, which in turn make it simpler to identify areas where improvements are necessary.
- The simple questions enable individuals from different backgrounds and experiences to provide their input.
- The simplicity of the method allows it to be used in many different industries.

As with any methodology, there are also some limitations that might prevent businesses from fully utilising the 5W2H method, which includes:

- The method is most effective with the help of experienced facilitation.
- It is not always easy to answer the questions asked by the method, and there may be conflicting views on the correct answer.

There are arguments for and against this method, which must be weighed against one another. Veyrat (2016) is of the opinion that, when used correctly, the 5W2H method can effectively help businesses translate their strategic goals.

4.3.4. Key performance indicators (KPIs)

Most businesses make use of KPIs to translate their strategy into quantifiable and measurable objectives (Baroudi, 2014). For example, a manufacturing business' strategy may be to increase overall productivity. Measuring a business' overall productivity is most likely difficult or infeasible, therefore, operational level KPIs such as the total hours of machine downtime per day, or the total number of defective raw materials per month are used instead. These operational KPIs can be measured in a direct and standardised manner and enable businesses to determine whether productivity has increased or decreased.

Different types of KPIs exist such as absolute numbers, indexes, percentages, rankings, ratings, and ratios (Baroudi, 2014), these are regularly classified as either output KPIs or driver KPIs. Output KPIs measure the output of past activity e.g. the total sales in the last three months. In contrast, driver KPIs measure the activities that are influential to the outcome e.g. customer and employee satisfaction. Driver KPIs are often said to be more powerful than output KPIs, because these allow managers and individuals to adjust their behaviours to achieve the desired outcome (Eckerson, 2009).

Different levels of authority in a business use KPIs for different purposes, for example: executives use KPIs to define and communicate strategic goals to their managers and other employees; managers use KPIs to measure both individual and team performance, as well as guide these individuals and teams to success; and employees use KPIs to focus on what is required from them to achieve a specific outcome (Eckerson, 2009). In all applications, however, KPIs serve to guide businesses to achieve their overall strategic goals.

Using KPIs offer certain benefits, including (Baroudi, 2014):

- Increasing individual and team focus.
- Encouraging departments to meet their goals.
- Serving as a link between individual and departmental goals.
- Allowing executives, managers, and employees to identify possible areas for improvement.
- Defining and communicating both the expected and achieved performance levels.

Some potential drawbacks associated with the use of KPIs include (Baroudi, 2014):

- Unclear definitions of KPIs can negatively affect other KPIs that are crucial to the measurement of the success of a business.
- Employees will sometimes focus more on what is expected of them, rather than focus on how these expectations will be met, leading to possible health and safety risks.

Developing KPIs is often a tedious and difficult process. To minimise the risk, it is essential that businesses consult the relevant stakeholders as they may have valuable inputs that have not been considered before (Baroudi, 2014).

4.3.5. Value chain analysis

A value chain analysis is defined as "*a process where a firm identifies its primary and support activities that add value to its final product [or service] and then analyse these activities to reduce costs or increase differentiation*" (Jurevicius, 2013b). It enables businesses to identify underperforming business processes and activities, allowing them to make necessary adjustments. It also highlights influential factors (environmental factors, participating actors etc.) that affect a value chain, delivering a comprehensive image of how a value chain and its components interact. In Figure 6, an example of a value chain analysis framework is shown.

Value chain analyses offer several benefits, which include (Simister, 2011):

- It is a flexible strategic tool and can be adapted towards many different industries.
- It focusses on the activities needed to deliver the value proposition, highlighting the processes and activities that contribute to satisfying customer demand.
- It is a well-known strategic tool and has delivered insight into many industries as to how and where they need to improve.

It is also important to be aware of the limitations to using value chain analyses, which include (Simister, 2011):

- Although the value chain analysis is flexible, it is not a *plug and play* instrument, therefore necessary changes must be made to adapt the analysis to a specific industry.
- The fact that the method was originally designed for use in the manufacturing industry may deter other industries from using it.
- The scale and scope of a value chain analysis can be intimidating since it considers a value chain in its entirety.
- Though many people are familiar with the concept of a value chain analysis, few are experts, and facilitation is therefore often needed to guide the development of such an analysis.

A value chain analysis is a comprehensive strategic tool that offers many benefits, and when

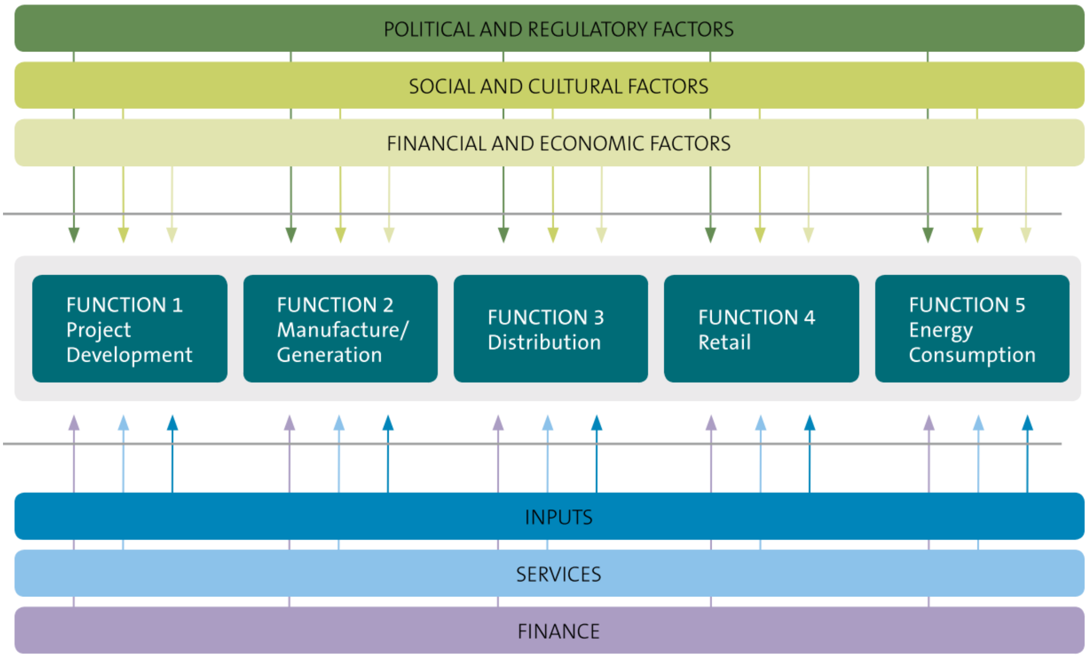

Figure 6: Example of a value chain analysis (Source: Franz et al., (2015)).

implemented with consideration and management of the limitations of the approach, it can assist businesses in making necessary improvements across their value chains to deliver a better value proposition.

4.4. Translation methodology selection

To select the most appropriate translation methodology for application to the PV system, the methodologies are compared to one another by evaluating their capability of meeting certain qualification criteria. A set of indicators that was developed by the World Health Organisation, and used to evaluate the inputs, outputs, processes, and impacts of PV systems (World Health Organization, 2014) was used as starting point when defining these qualifying criteria:

- Stakeholder identification: Does the methodology allow the user to identify the stakeholders that participate in the PV system?
- Distinguishing: Does the methodology distinguish between the different stages in the PV system?
- Flexibility: Does the methodology adapt well to different input data and structures?
- Relationship identification: Does the methodology indicate the effect that different elements may have on another?
- Reproducible: Can the methodology be reproduced by anyone, regardless of their background?
- Measurable outcome: Does the methodology deliver measurable outcomes?

The sought-after translation process consists of two stages, which, when used in combination, will contribute to the translation of the PV challenge landscape to a lower level of abstraction, where tangible problems can be defined and addressed. These stages are:

1) Defining the influence of the PV challenge landscape between the different functions, or stages, of a PV system; and
2) Identifying the root causes of the disseminated PV challenges within a PV system.

The comparison of the methodologies according to the set of qualifying criteria is shown in Table 9. Based on this analysis, the following two methodologies are selected to address the two stages of the desired translation process: 1) value chain analysis, and 2) the 5Why method and fishbone diagrams. A defining feature of both methodologies is the fact that they are flexible, making them suitable candidate methodologies for this application. The value chain analysis offers a distinct advantage in the fact that it can distinguish between the functions of a value stream, making it a suitable methodology for the first stage of the translation process. A specific benefit of the 5Why method, in combination with fishbone diagrams, is that it can assist in identifying possible relationships between different problems, and can also be relatively easily reproduced by anyone. Moreover, it was originally designed for the specific purpose of identifying root causes of problems. To provide even further justification, some examples of the success achieved via the implementation of these methodologies are provided in the following two subsections.

Table 9: Comparing the different translation methodologies.

Translation methodology	Stakeholder identification	Distinguishing	Flexibility	Relationship identification	Reproducible	Measurable outcomes
5Why and Fishbone diagrams	X	-	X	X	X	-
Problem Tree Analysis	X	-	X	X	-	-
5W2H	X	-	X	-	X	-
KPI	-	-	-	-	-	X
Value chain analysis	X	X	X	X	-	-

4.4.1. The value chain analysis

A recent report by Franz *et al.* (2015) discusses a value chain analysis conducted in the energy market system in sub-Saharan African countries. The framework (like that of Figure 6) that was used consisted of a value chain analysis, of which the energy market chain served as the foundation. The influence of additional inputs, services, finances and enabling environmental factors such as socio-cultural and political factors, were differentiated for the various functions of the energy market system. This allowed the developers to comprehensively understand the operation of the current energy market system in sub-Saharan African countries, which in turn allowed them to identify improvement initiatives (Franz *et al.*, 2015). Similarly, the United Nations also implemented a value chain analysis, which focussed on the living conditions of disabled persons. Several influential factors such as disabled rights, policies, and financial structures were identified, indicating problem areas where improvements or changes were necessary (United Nations, 2012).

The prospects of leveraging the value chain analysis for translating challenges in the PV system that have been defined at a strategic level to an operational level in a specific context is evident in these two cases. Moreover, with reference to the qualifying criteria in Table 9, value chain analyses enables the following: the user to differentiate between the stakeholders in PV ("*stakeholder identification*"); allows the user to distinguish between the different functions of a value chain or in this case a PV system ("*distinguishing*"); can be adapted towards the PV context ("*flexibility*"); and enables the user to identify any possible relationships that might be shared between the different influences in a value chain ("*relationship identification*"). The methodology therefore satisfies four of the six qualifying criteria defined in Section 4.4. This justifies the use of a value chain analysis for the first stage of the translation process i.e. defining the influence of the PV challenge landscape on the functions in a PV system.

4.4.2. The 5Why method and fishbone diagrams

There are many reported cases where the 5Why method and fishbone diagrams have enabled businesses to follow a systematic approach in identifying the root causes of challenges they are experiencing. Myszewski (2013) describes a case where an unknown company regularly produced a certain electric cable that did not conform to certain quality standards. To identify the root cause of this phenomenon, the 5Why method was used, which helped the company identify four possible root causes. Additionally, a fishbone diagram was also used to graphically present the thinking process of the 5Why method, which enabled the company to revisit previously discussed possible root causes. Another case of the successful application of the 5Why method and fishbone diagrams is described by Jones & Despotou (2016). Several hospitals based in the United Kingdom reported numerous unintended consequences from the use of electronic health records. Although these consequences are not named in the article, Jones & Despotou (2016) described that through a combination of the 5Why method and fishbone diagrams, investigators were able to identify the root causes of these consequences and were subsequently able to address the problems.

These two cases represent only a small portion of the many reported cases of the success achieved by the 5Why method and fishbone diagrams, yet they substantiate the rationale that these methodologies are suitable to support the translation of the PV challenge landscape to an operational level. Providing even further justification, and with reference to the qualifying criteria depicted in Table 9, the 5Why method, in combination with fishbone diagrams: allow the user to differentiate between the key role players in a PV system ("*stakeholder identification*"); can be adapted towards a PV context ("*flexibility*"); and can be easily reproduced by someone who might be lacking a certain degree of technical capacity ("*reproducible*"). The methodology therefore satisfies three of the six qualifying criteria defined in Section 4.4 and this justifies the use of the 5Why method and fishbone diagrams for the second stage of the translation process i.e. identifying the root causes of the PV challenge landscape.

Subsequently, an instance of the application of the two stages of the translation of the PV challenge landscape is provided through a worked example.

4.5. Stage 1: Implementation of a value chain analysis

Given that a value chain analysis cannot be reproduced by someone who does not have some form of past experience in this regard (Simister, 2011) and to map out the systematic thinking process needed to produce such an analysis, a roadmap to mediating a PV value chain analysis is proposed, clearly illustrating the steps that should be taken to complete such an exercise.

4.5.1. Roadmap to developing a pharmacovigilance value chain analysis

The roadmap, which was used to develop the PV value chain analysis in Section 4.5.2, is shown in Figure 7 and discussed in more detail in Table 10. Each stage in the roadmap is executed differently, processing different inputs to deliver specific outputs, and can be completed with the help of specific methods. The end product delivered by the roadmap is a PV value chain analysis, which is based on the framework design used by Franz *et al.* (2015), coupled with some amendments that are subsequently discussed.

Firstly, serving as the foundation of the analysis and replacing the energy market value chain, are the stages found in the generic PV system, namely data collection and ADR reporting, data collation, data analysis (causality and risk assessments), decision-making and governance, appropriate action and evaluation of outcomes, all of which are discussed in detail by Strengthening Pharmaceutical Systems (Strengthening Pharmaceutical Systems, 2009). Secondly, replacing the inputs, finances, and services level of Franz *et al.*'s (2015) framework is the PV challenge landscape. All these challenges are investigated separately, given that they are defined differently within each stage of the PV system. Lastly, substituting the environmental, political, regulatory, social and cultural factors level, are the stakeholders that participate during each stage, all of which are discussed in more detail in Table 6.

Each of the influences identified in the analysis relates to different stakeholders e.g. the lack of awareness of the importance of reporting ADRs relates specifically to healthcare workers, the public, and patients. Thus, these stakeholders embody the target population of investigations on how these challenges can be addressed. Thus, identifying the stakeholders will assist researchers to be clear on who to consult and engage with when developing a new initiative and when attempting to roll-out a new project.

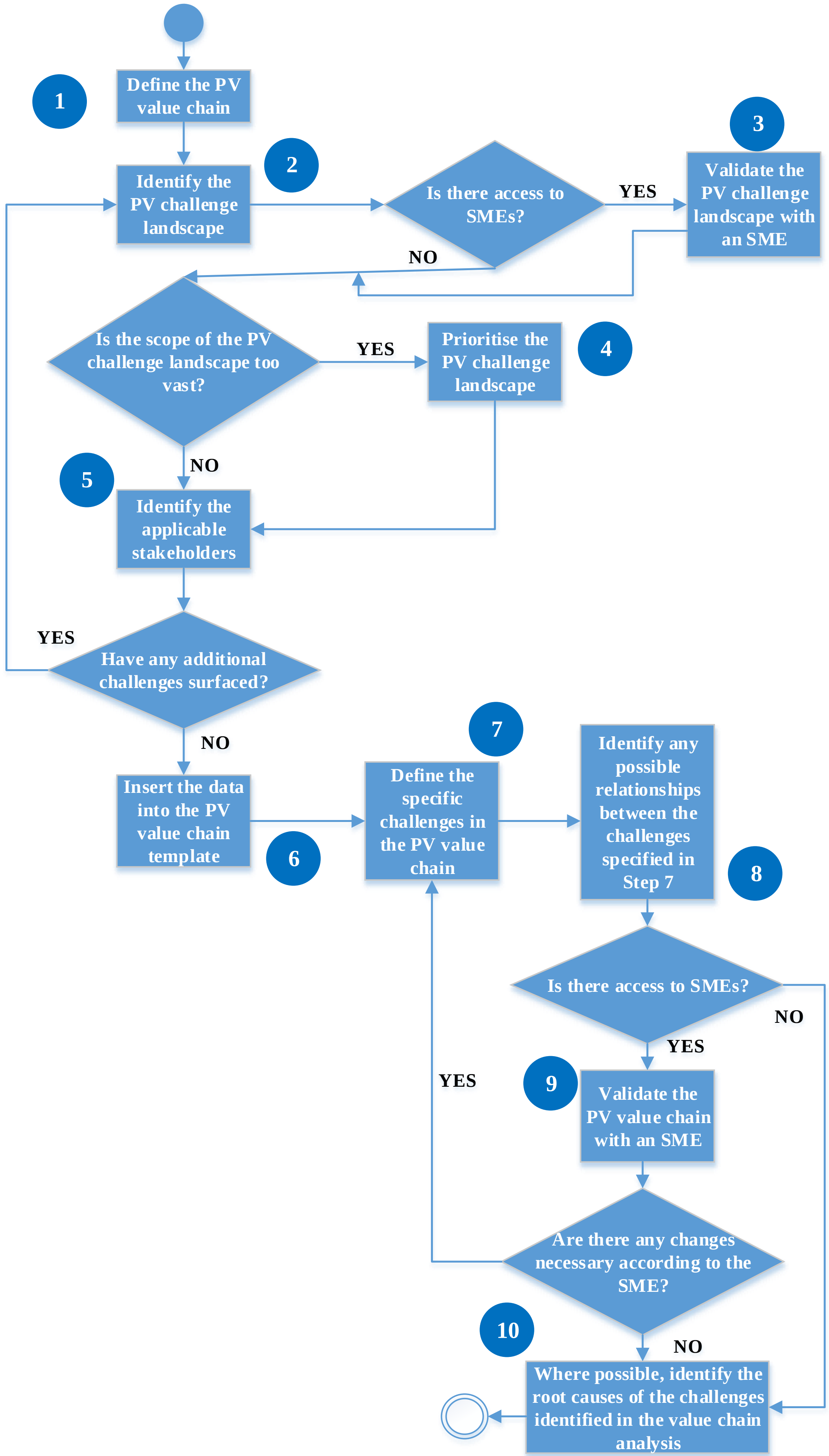

Figure 7: Roadmap to developing a PV value chain analysis.

Table 10: Description of the PV value chain analysis roadmap.

Stage	Description	Inputs	Outputs	Possible methods
1	Identify the stages that constitutes the PV system.	Literature	PV value chain	Literature review
2	On a high level of abstraction, identify the challenges that are experienced throughout the PV system.	Literature and SMEs	PV challenge landscape	Systematic review.
3	If possible, validate the PV challenge landscape with an SME.	SME	Validated PV challenge landscape	Personal or virtual interview, email correspondence, workshops.
4	In order to reduce the scope of the PV challenge landscape, prioritise the challenges that are deemed of priority.	Literature and SMEs	Prioritised PV challenge landscape	Degree of prevalence (similar to the matrix developed by Lamprecht, Bam, and de Kock (Lamprecht *et al.* 2017), Impact analysis.
5	Identify the stakeholders that participate across the PV system.	Literature and SMEs	Relevant stakeholders	-
6	Make use of the PV value chain analysis outline in Figure 8 and insert the applicable data from the previous stages.	PV value chain analysis template	Preliminary PV value chain analysis	-
7	With specific reference to each block in the analysis, identify the specific challenges that are experienced in that specific stage of the PV system, within the confines of the specific challenge.	Literature and SMEs	Preliminary PV value chain analysis	-
8	Identify which of these challenges share relationships with one another i.e. addressing the one might affect another.	Literature and SMEs	Preliminary PV value chain analysis	-
9	If possible, validate the PV value chain analysis with an SME.	SMEs	Validated PV value chain analysis	Personal or virtual interview, email correspondence, workshops.
10	In order to further translate the challenges in the PV value chain analysis, identify the root causes of these challenges.	Literature, SMEs	Root causes of the challenges	Root cause analysis or 5Why analysis.

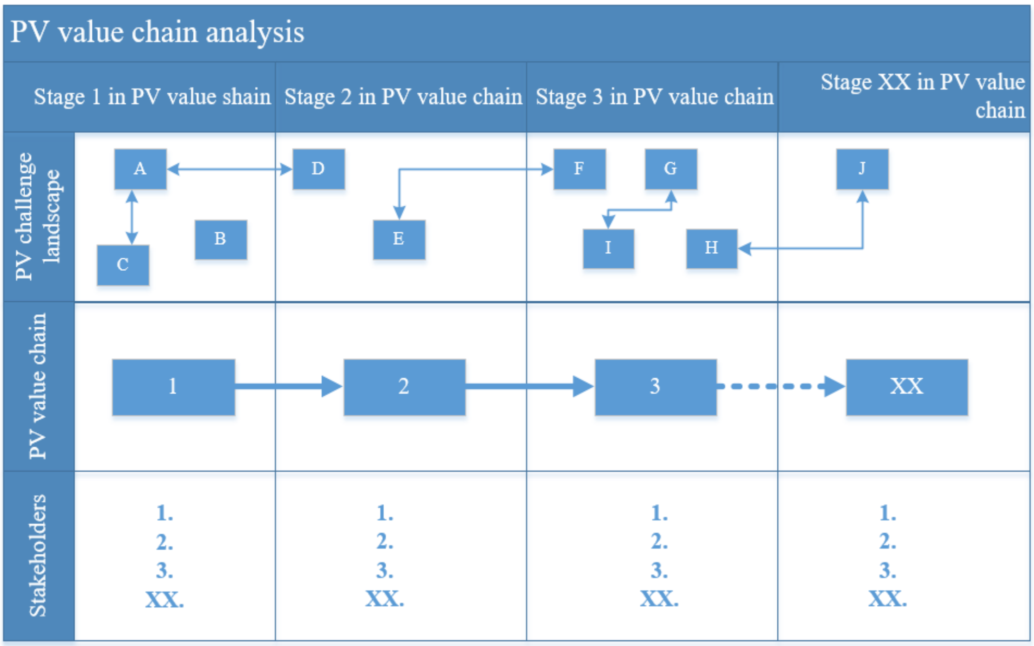

Figure 8: PV value chain analysis template.

4.5.2. The pharmacovigilance value chain analysis

Using the roadmap described in Section 4.5.1, each stage was completed to develop a PV value chain analysis (shown in Figure 9). The sections of this thesis document in which these stages have been completed are shown in Table 11. Many of the challenges identified in the analysis share relationships with others. Illustrated by double-headed arrows as in Figure 9, these relationships indicate that when the one challenge is addressed, there will either be a direct or indirect effect on the other(s).

Table 11: Sections in which the stages of the roadmap have been completed.

Stage	1	2	3	4	5	6	7	8	9	10
Section	2.1-2.3	2.6-2.10	3.1	3.3-3.10	3.5	Figure 8	4.5	4.5	4.5.2	4.6
Page number	12-14	15-24	30	32-46	36	63	60	60	63	67

4.5.3. Key points highlighted by the pharmacovigilance value chain analysis

By integrating the PV challenge landscape in the PV value chain, several key points that would have been difficult to identify by simply considering the PV challenge landscape in isolation were highlighted. The analysis also sheds some light on the relationships within the

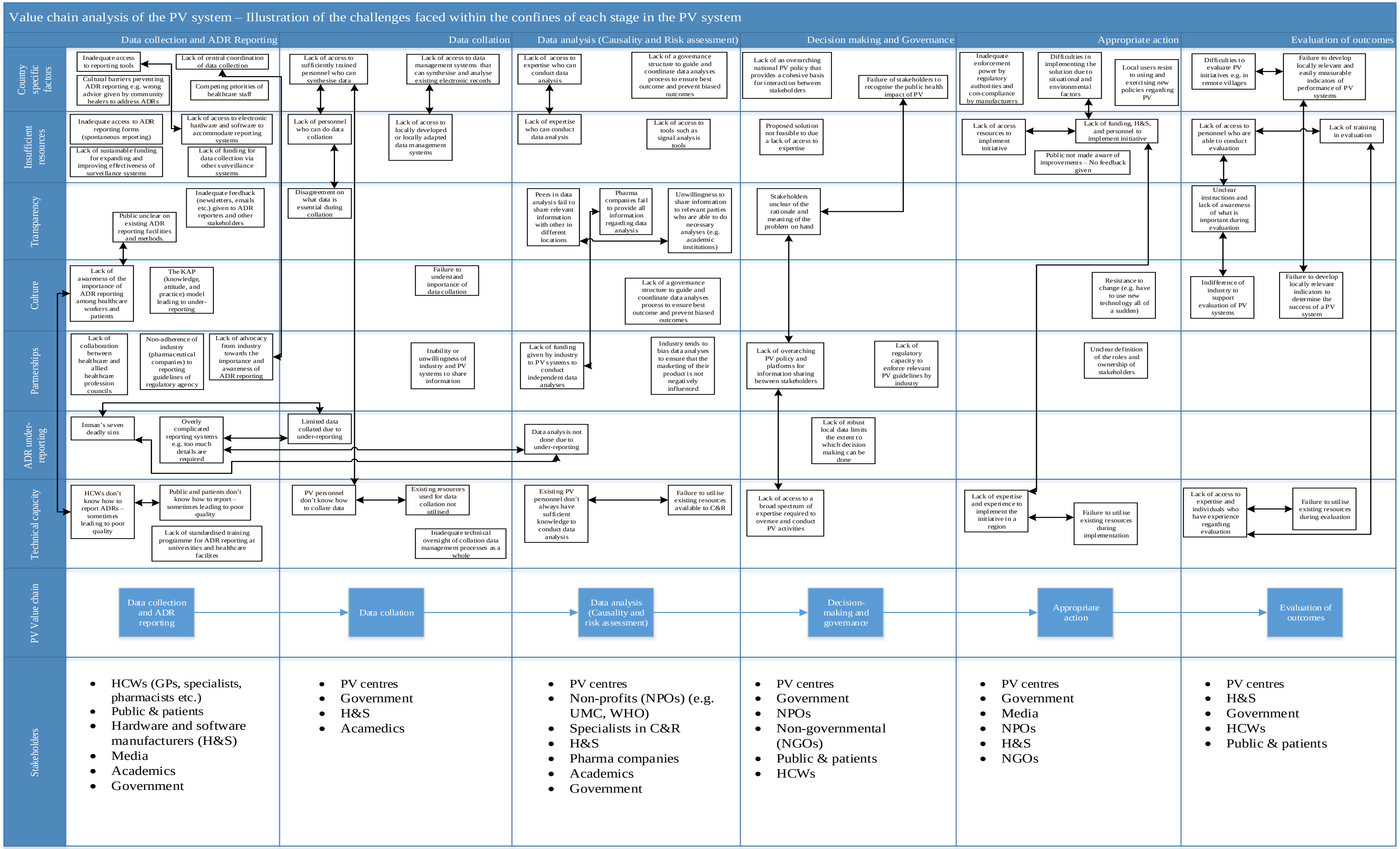

Figure 9: The PV value chain analysis.

PV challenge landscape, as well as the actual meaning of the influence of challenges in PV. These key points are briefly described in the subsequent subsections.

4.5.3.1. Prominent role players

Governmental bodies, also referred to as regulatory authorities, are key role players in PV. This is because, in most countries, regulatory authorities govern PV systems, developing the necessary policies and investing the required resources for PV systems to operate. Although some countries (e.g. South Africa) are trying to privatise a portion of the power held by regulatory authorities, these authorities will remain key role players in PV.

4.5.3.2. Snowballing effect caused by adverse drug reaction under-reporting

Within the ADR under-reporting lane, it is shown that many of the challenges in the downstream PV value chain share relationships with this phenomenon. This emphasises the limitations caused by the phenomenon of ADR under-reporting that is so often cited in literature.

4.5.3.3. Many challenges faced at the start of the pharmacovigilance value stream

Many challenges are found at the start of the PV value chain i.e. within the data collection and ADR under-reporting, and data collation stages, which highlights the limitations posed by a lack of robust qualitative and quantitative data. Data plays a major part in PV and it is therefore important that the efforts towards acquiring such data are as efficient and effective as possible.

4.5.3.4. Exchanges between country-specific factors and insufficient resources

There are frequent exchanges between the challenges associated with country-specific factors and insufficient resources Therefore, it is worthwhile exploring whether there is a causal relationship between these two strategically defined challenges. In other words, when it is found that there are insufficient resources within a certain country, it is possible that it is a unique case to that specific country, i.e. another country may not experience the same problem.

4.5.3.5. Role played by country-specific factors

Many challenges have been identified within the country-specific factors lane. This supports the rationale that an exercise such as globalisation and standardisation of PV systems on an international scale may be significantly challenging, given that PV systems in different countries are unique and are influenced by different factors.

4.5.3.6. Failure to understand the effects of pharmacovigilance

It is often the case that those within the PV system, as well as those outside–such as the partners who operate within and outside the scope of PV (described in Section 3.5)–fail to realise the importance of PV and the influence that PV has, not only on an individual patient level, but on the entire healthcare system.

4.5.3.7. Lack of access

The lack of access to resources is regularly reported in the analysis. It is not necessarily the case that the expertise, experience, funding, training, technology and other resources do not exist, but rather that PV systems are not given access to such resources. One of the main reasons for this can be attributed to the fact that PV may not be regarded as priority within a certain country. Therefore, it does not receive the necessary funding to access the required resources.

4.5.3.8. Adoption by the widespread healthcare industry

Dissecting the PV challenge landscape, shows that PV is a large and complex system with many opportunities for problems to arise. Consequently, PV needs to be adopted by the wider healthcare industry, and must be regarded as a priority, not only to those actively involved in PV, but also to those outside the boundaries of the PV system.

4.5.3.9. Lack of technical capacity

The lack of training, knowledge or practice, all of which contribute to technical capacity (as identified and described in Section 3.9), are often limiting factors in PV systems. This can be traced back to the phase before healthcare workers enter into the working environment i.e. university, college or any other form of tertiary education or training. It is essential that training starts on a tertiary level, where the basics of PV are taught.

4.5.4. Concluding stage one of the translation process

These key points all contribute to the initial translation process i.e. understanding that the PV challenge landscape affects the different stages in the PV value chain in different ways. It is critical to a system such as PV, where drug and patient safety are of primary concern, that researchers understand how the challenges affect a PV system, which will allow them to make the necessary improvements to the system.

To validate the PV value chain analysis, an SME has been consulted. The SME is an independent PV consultant at a local university. The feedback of the SME is already incorporated into the value chain analysis provided in this chapter.

To identify the root causes of challenges in the PV landscape, the second stage of the translation process proposed in Section 4.5.1 is essential. An example of this second translation step is given in the following section.

4.6. Stage 2: The 5Why method and fishbone diagrams

Up to this point, the translation of the strategically defined PV challenge landscape has reached an intermediate stage. To complete the translation, the root causes of these challenges must be identified, which will translate these challenges into tangible problems that can be addressed at an operational level. To do this, the 5Why method, in combination with fishbone diagrams, can be used. In illustration of the implementation of these methodologies, Figure 10 shows one of the fishbone diagrams used to identify root causes. As seen in Figure 10, the "*lack of robust local data limits the extent to which decision-making can be done"* is used as the base challenge. From there, the 5Why method is implemented (as discussed in Section 4.3.1.1). This allows for several possible root causes to be identified for the initial challenge.

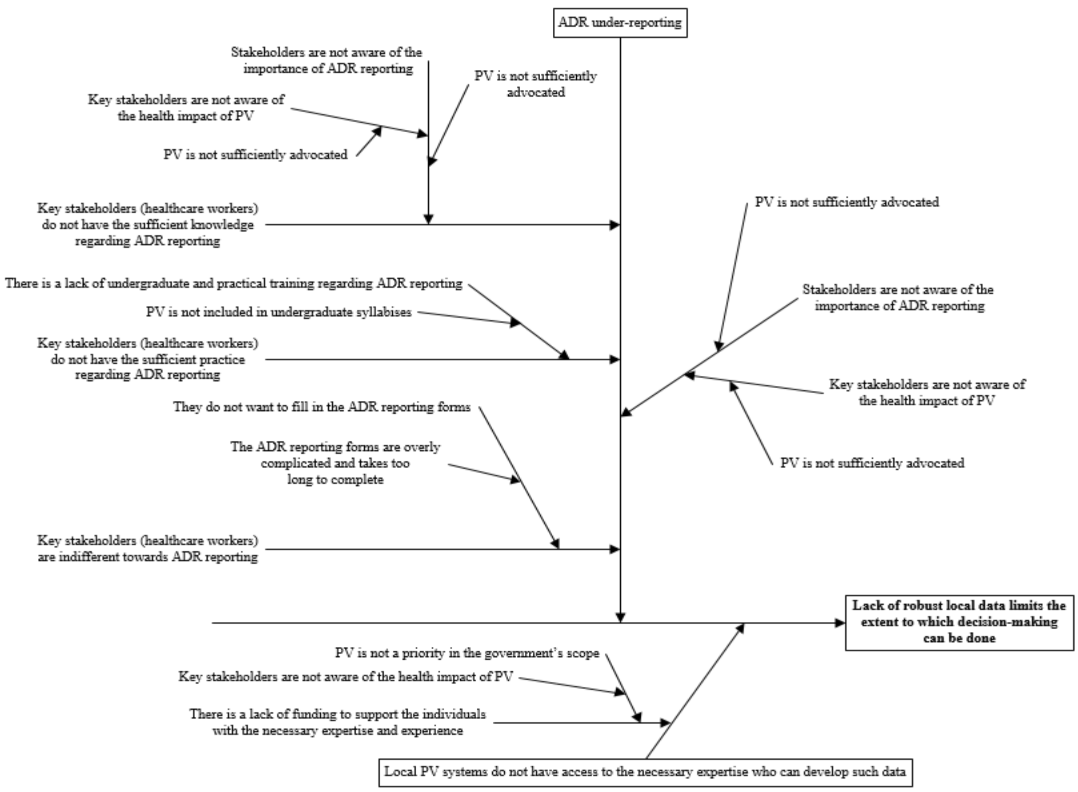

Figure 10: Example of a fishbone diagram used to identify root causes.

The 5Why method, in combination with fishbone diagrams, are implemented on the following challenges: (1) the inadequate access to ADR reporting forms (spontaneous); (2) the failure to develop locally relevant and easily measurable indicators of performance of PV systems; (3) the lack of robust local data that limits the extent to which decision-making can be done; (4) the inadequate feedback given to ADR reporters and other stakeholders; (5) the inadequate access to data management systems that can synthesise and analyse existing electronic health records; (6) failure to utilise existing resources to conduct data collection, collation, and analysis; (7) lack of overarching platforms for information sharing between stakeholders; and

(8) the lack of sufficient knowledge of existing PV personnel to conduct the necessary data analysis. Section C.2 in Appendix C contains the fishbone diagrams that have been developed to identify the root causes of these challenges.

The eight challenges listed in the previous paragraph were chosen because of their potential to highlight areas in PV where technology can be implemented to address the many challenges it faces, thereby linking to the primary topic of this research. The root causes that have been identified are shown in Table 12. These root causes highlight several key findings that are subsequently discussed.

4.6.1. Key points highlighted by the implementation of the 5Why method, in combination with fishbone diagrams

Certain key points can be concluded from the identification of the root causes, highlighting distinct features of the PV system that may not have been known before.

4.6.1.1. Wide spectrum of possible root causes

When conducting these types of analyses, it is possible to either identify numerous possible root causes of a specific problem, or only a few. This is evident from the wide spectrum of root causes identified in the examples provided. This phenomenon is a result of the nature of answering a simple "*Why?*" question, which may have more than one possible answer.

4.6.1.2. Unclear association between the possible root causes and the overall problem

Some of the root causes identified may be deemed as implausible i.e. it may seem that the root cause and the overall problem may not have anything in common, and this may make stakeholders resistant to using the 5Why methodology. For example, a root cause for the inadequate access to ADR reporting forms is the lack of funding to access software technologies. As Warner (2015) described, however, analyses such as the 5Why methodology have delivered many positive results, and therefore one should at the very least devote some effort towards investigating the possible interactions these seemingly non-associated root causes and challenges may share.

4.6.1.3. Shared root causes

As indicated by the analysis of the failure to develop locally relevant and easily measurable performance indicators of PV systems, and the lack of robust local data that limits the extent of decision-making which is supported, certain possible root causes may affect different problems. This is proof that the challenges in the PV challenge landscape share relationships, as illustrated in the PV value chain analysis in Figure 9.

4.6.1.4. Inconsistent levels of complexity

Referring to the diagrams in Section C.2 in Appendix C, the number of successive layers of root causes are inconsistent, with some challenges being traced back to several successive layers of root causes, whereas others are linked to only one or two layers of root causes. It is important to remember that the set of root causes identified in the analyses are not necessarily exhaustive, meaning that there may also be other root causes to the challenges that are not considered in this study. The process of the second translation stage merely proves that such an analysis can contribute to the identification of several root causes that can be addressed on the operational level, but, especially when one considers the vast scope of the PV system and the role of country-specific factors, it is clear that it is not feasible to generate an exhaustive set of root causes.

4.6.1.5. Root causes

The challenges identified in the PV value chain analysis can sometimes already represent the root cause of a challenge. Such a phenomenon can be seen in the last diagram in Section C.2 in Appendix C, where it is shown that there are no further root causes related to the lack of sufficient knowledge of existing PV personnel to conduct the necessary data analysis. It is already made apparent that the only possible solution to this is to provide sufficient training to these groups to equip them with the required skills and knowledge to conduct crucial data analyses.

4.6.2. Concluding stage two of the translation process

In combination with the first stage of the translation process where the influence of the PV challenge landscape on the PV value chain is investigated, the root cause analysis identifies tangible problems that may have been unknown. To organise the identified root causes, the following categories are used: funding, management, training, advocacy and technology. Organising the root causes into these categories, allows for the identification of the types of root causes that are most regularly experienced. This categorisation is shown in Table 13.

Table 12: Root causes of the challenges identified in the PV value chain analysis.

Challenge identified in the PV value chain analysis	Root causes
Inadequate access to ADR reporting forms (spontaneous)	There is a lack of funding to access software technologies that can assist the coordination of the deliveries of spontaneous ADR reporting forms. There is no existing software technology that can assist the coordination of the deliveries of spontaneous ADR reporting forms. The individuals responsible for coordinating the deliveries of spontaneous ADR reporting forms are not sufficiently trained to execute the necessary tasks. There is no designated transportation service to distribute the ADR reporting forms. The person in charge of re-ordering the ADR reporting forms is not sufficiently trained in stock control. The person in charge of re-ordering the ADR reporting forms is situated in a remote location, and as a consequence, users of the forms struggle to make contact with this person. The users of the forms have competing priorities, and simply do not have time to notify the person in charge of re-ordering the ADR reporting forms.
Failure to develop locally relevant and easily measurable indicators of performance of PV systems	Key stakeholders are not aware of the health impact of PV. There are only globally defined performance indicators that may not include features of a unique, local PV system.
The lack of robust local data that limits the extent to which decision-making can be done	PV is not sufficiently advocated to the necessary stakeholders. PV is not included in the undergraduate syllabus of healthcare tertiary education. The ADR reporting forms are overly complicated and are time-consuming. Key stakeholders are not aware of the health impact of PV.
Inadequate feedback (newsletters, emails etc.) given to ADR reporters and other stakeholders	There is no translation services that can prepare these reports for the specific context. Feedback is not deemed as a priority. The importance of feedback is not advocated sufficiently.

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Challenge identified in the PV value chain analysis	**Root causes**
Inadequate access to data management systems that can synthesise and analyse existing electronic health records	There is a lack of ownership of managing this process. Lack of access to technology to simplify this process. Lack of training provided those who report ADRs. Difficulties in providing such training to all individuals in remote locations in a timely fashion.
Failure to utilise existing resources to conduct data collection, collation, and analysis	There is no resource management system in place to manage the resource inventories. There is a lack of ownership taken to manage these resources. No training is provided to educate PV personnel on how to use these resources.
Lack of overarching platforms for information sharing between stakeholders	Lack of funding to access modern information sharing platforms. PV personnel are insufficiently trained in using existing platforms. There are no set regulations that governs the standardisation of data. It is unclear what data should be shared with which stakeholder. ADR reporters are not sufficiently trained in providing the sought after data.
Lack of sufficient knowledge of existing PV personnel to conduct necessary data analysis	Lack of sufficient knowledge of existing PV personnel to conduct necessary data analysis.

Table 13: Categorisation of the root causes.

Category	Root cause
Funding	There is a lack of funding to access software technologies that can assist the coordination of the deliveries of spontaneous ADR reporting forms. Lack of funding to access modern information sharing platforms.
Management	There is no designated transportation service to distribute the ADR reporting forms. The person in charge of re-ordering the ADR reporting forms is situated in a remote location, and as a consequence, users of the forms struggle to make contact with this person. The users of the forms have competing priorities, and simply do not have time to notify the person in charge of re-ordering the ADR reporting forms. There are only globally defined performance indicators that may not include features of a unique, local PV system. PV is not included in the undergraduate syllabus of healthcare tertiary education. There is a lack of ownership of managing this process. There is a lack of ownership taken to manage these resources. There are no set regulations that governs the standardisation of data. It is unclear what data should be shared with which stakeholder.
Training	The individuals responsible for coordinating the deliveries of spontaneous ADR reporting forms are not sufficiently trained to execute the necessary tasks. The person in charge of re-ordering the ADR reporting forms is not sufficiently trained in stock control. The ADR reporting forms are overly complicated and are time-consuming. Lack of training provided those who report ADRs. Difficulties in providing such training to all individuals in remote locations in a timely fashion. No training is provided to educate PV personnel on how to use these resources. PV personnel are insufficiently trained in using existing platforms. ADR reporters are not sufficiently trained in providing the sought after data. Lack of sufficient knowledge of existing PV personnel to conduct necessary data analysis.

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Category	Root cause
Advocacy	Key stakeholders are not aware of the health impact of PV. PV is not sufficiently advocated to the necessary stakeholders. Key stakeholders are not aware of the health impact of PV. Feedback is not deemed as a priority. The importance of feedback is not advocated sufficiently.
Technology	There is no existing software technology that can assist the coordination of the deliveries of spontaneous ADR reporting forms There is no translation services that can prepare these reports for the specific context. Lack of access to technology to simplify this process. There is no resource management system in place to manage the resource inventories.

4.6.3. Validating the root causes

Two SMEs that are employed in the pharmaceutical sector were consulted to validate the root causes identified in this section. The inputs of each of the SMEs are summarised in Table 14. In summary, the SMEs agreed that the root causes identified in this research represent some of the real-world root causes. Additionally, they added some root causes, which have already been incorporated into this research. Most importantly, they highlighted the root causes that should be regarded as priority to this research. Thus, these selected sets of root causes are investigated in the subsequent part of this research (specifically, Chapter 6).

4.7. Chapter 4 conclusion

The focus of this chapter is the translation of the PV challenge landscape from a strategic– to an operational level thus lowering the level of abstraction of the PV challenge landscape. Firstly, the concept of strategic–, tactic–, and operational levels in businesses was discussed, followed by the argument that the PV challenge landscape has thus far been described at a strategic level. This was followed by a discussion that provided the rationale for the importance of translating the strategically defined PV challenges landscape to an operational level and where it was concluded that such a process should be done in two stages. Several methodologies that could be employed during this translation process were investigated, concluding that the PV value chain analysis and the 5Why analysis, in combination with fishbone diagrams, are the most appropriate methodologies to use during the proposed two-stage translation process. Following the implementation of these methodologies executing two stages of the translation process, it became clear that the methodologies that have been implemented highlighted several key points that may have been difficult, or even impossible, to conclude if the PV challenge landscape was only defined at a strategic level. As a result, several tangible problems were identified.

The set of root causes identified during the analysis is not necessarily exhaustive, therefore it is possible that other root causes exist that are not considered in this study. It is particularly difficult to consider each possible root cause to a challenge, given that the scope of root causes differs severely based on the context in which the PV system operates. However, the analyses conducted in the two-stage translation process have identified root causes that can be assumed to lead to challenges in the PV system in a general sense. The worked example also serves as proof that these analyses can be used to identify tangible problems in PV systems that may not have been known before.

Table 14: Input from SMEs regarding root causes.

Occupation		Affiliation	Input
1	Medical Lead Access, Regional Medical Director. Leading the preparation for the launch of a new product within severely resource constrained environments.	Multi-national pharmaceutical company	The focus of this research should be towards the first two challenges taken from the PV value chain analysis i.e. inadequate access to ADR reporting forms (spontaneous); and failure to develop locally relevant and easily measurable indicators of performance of PV systems.
2	Medical Affairs Executive and Named Safety Contact for an African country.	Multi-national pharmaceutical company	The root causes identified in the study represent most of the possible root causes that exist in practice. One key issue, regarding ADR reporting, is the lack of ownership taken by healthcare workers and PV experts to report ADRs via the applicable channels. Furthermore, the root causes that were identified represent another key issue within PV; key stakeholders not understanding the importance of PV within the context of healthcare.

Chapter 5: The technology landscape

Following the translation of the PV challenge landscape to a lower level of abstraction (i.e. from a strategic to an operational level) in the previous chapter, several root causes have been identified. As stated in Chapter 1, the aim of this research is to investigate the potential of technology to address these root causes. Technology selection frameworks can be a useful tool towards achieving this aim. These frameworks facilitate the technology selection process, guiding the user by referring to key characteristics that should be considered during the selection process.

In the first section of this chapter, the technology selection framework landscape is investigated, and the selection of an appropriate framework for this research is motivated. In the second section of this chapter, the technology landscape is investigated to identify candidate technologies that can be implemented to address the root causes identified in the previous chapter.

5.1. Technology selection

In an ever-changing business environment, new technologies are frequently developed to perform specific functions. This increase in new technologies entering the market is making it increasingly difficult for businesses to determine which technologies are best suited for their needs (Shen *et al.*, 2010). It is important that the right technologies are selected because technology plays an instrumental part in any business and has the potential to either contribute to the success and growth of a business or contribute to severe monetary losses.

Consequently, businesses should follow a comprehensive process, known as the technology selection process, during which they investigate the technology landscape in an effort to find the most appropriate technologies to meet their requirements (Ruder, Pretorius & B. T. Maharaj, 2008). Considering many factors such as business processes, environmental conditions, social and cultural factors and political influences, the technology selection process compares alternative technologies in order to refine the list of technologies to those best suited for the business (Shehabuddeen *et al.*, 2006).

To provide guidance to the technology selection process, technology frameworks are used. These frameworks, developed from both a theoretical– and empirical background (Shehabuddeen *et al.*, 2006), provide essential insight into the stages that should be followed during the technology selection process and serve to highlight the influential factors that should be considered during the process (Shen *et al.*, 2010).

5.2. Technology selection frameworks

A large number of technology selection frameworks exist in literature. Although many of these technology selection frameworks incorporate generic elements, they tend to be developed with specific contexts or application areas in mind, and therefore generally also contain elements that are specifically tailored to the intended context or application area. Consequently, the literature review described in Section 5.3 did not uncover a universally acceptable technology selection framework that can be implemented within any setting.

Due to the lack of a universally accepted framework, it is recommended that the best course of action to find an appropriate technology selection framework for application in this research would be to investigate several of the frameworks that are published in literature. The choice of a technology selection framework for use in this research will be based on the following factors (the terms given in brackets are those used in Table 15): (1) Does the framework incorporate some elements of healthcare (focus)? (2) Does the framework consider resource constraints (resource constraints)? (3) Is there a focus on the patient or end-user (patient orientation)? (4) Can the framework be used within more than one context (flexibility)? (5) Can the framework be used more than once (re-evaluation)? Subsequently, the technology frameworks are assessed.

5.3. Technology selection framework assessment

A search in the *Google Scholar*, *Scopus*, and *PubMed* research databases using the search terms *"technology selection frameworks", "technology selection",* and *"technology evaluation"* revealed 15 technology selection frameworks. These frameworks are identified and briefly described in Table 16. The authors of these frameworks are also provided, as well as the context in which the frameworks were initially developed. With reference to the context in which these frameworks were developed (indicated in Table 16), many have been developed within a general context, using either quantitative– or qualitative data to make the necessary decisions. The other contexts in which the frameworks were developed include telecommunications, information technologies, aerospace and training technologies. Given that many of the frameworks were developed within a general context, the process of selecting an appropriate framework is simpler, since these frameworks do not incorporate elements that are unique to a specific industry.

After careful consideration of these frameworks, it is concluded that the framework by Chan & Kaufman (2010), titled: "*A technology selection framework for supporting delivery of patient-oriented health interventions in developing countries"* is appropriate for the purpose of this research effort.

5.4. Technology selection framework selection

As shown in Table 15, the framework by Chan & Kaufman (2010) was chosen because it embodies several of the characteristics that were deemed desirable in a framework for application to this research, as defined in Section 5.2. The framework was originally developed to support the delivery of patient-oriented health interventions in developing countries, with a specific focus on healthcare information technologies. The framework is structured around three levels (with Level 2 being sub-divided into two components), serving as filters and constraints, narrowing the decision space for selecting technologies. These levels are described in Table 17.

Table 15: Characteristics of Chan & Kaufman (2010)'s technology selection framework.

Characteristic	Explanation
Focus	The framework was initially developed to be used within developing countries, which aligns with the focus of this research.
Resource constraints	The framework has been developed for resource constrained environments, making it especially applicable to PV, since resource deficiencies are regarded as a priority challenge in PV.
Patient orientation	The framework is focussed around patient orientation, which is a major element of PV.
Flexibility	The authors propose that the conditions and settings in which the framework can be applied are dynamic i.e. in addition to the delivery of patient-oriented health interventions, the framework can be applied to other health interventions as well. The framework is designed to explore how and whether technologies can support the delivery of health interventions towards different target populations, meaning it can be used within PV where multiple stakeholders need to be considered.
Re-evaluation	The framework is not a "*once-off*" instrument that can only be used upon initial technology acquisition. It is clearly stated that the framework can be used for re-evaluation of technologies, enabling it to adapt to the rapidly changing technology environment.

Table 16: Technology selection frameworks.

Framework	Source	Description	Context in which framework is developed
Delphi technique	Shen *et al.* (2010)	A systematic collection of opinions and judgments from SMEs through a specially designed set of questionnaires.	General
Fuzzy Delphi technique	Shen *et al.* (2010)	The fuzzy Delphi technique is similar to the Delphi technique, however, uses fewer rounds of questionnaires to speed-up the process of collecting opinions.	General
Analytical hierarchy process (AHP)	Shen *et al.* (2010)	The AHP is a multi-criteria approach, making use of weights, defined at the start of the process, to determine the best alternative.	General
Delphi hierarchy process (DHP)	Khorramshahgol & Moustakis (1988)	A combination of the AHP and the Delphi method, the DHP consists of a six stage process in which both questionnaires and the mathematical approach to comparing the opinions and judgements of SMEs are used.	General
A Quantitative Model for the Evaluation of Technological Alternatives	Sharif & Sundararajan (1983)	A model that combines both quantitative and qualitative factors and then uses a mathematical model to unify the results from these factors.	General
A filter system for technology evaluation and selection	Yap & Souder (1993)	This model makes use of two filters stages, the first of which eliminates technologies based on predefined capabilities and environments of a business. This is followed by a second filter stage where in depth evaluations are done.	General
From theory to practice: challenges in operationalising a technology selection framework	Shehabuddeen *et al.* (2006)	The framework relies heavily on filters in order to reduce the number of candidate technologies under evaluation. These filters are based on certain characteristics that are used to make the decision as to which technologies will be eliminated from the process.	General

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Framework	Source	Description	Context in which framework is developed
A Technology Selection Framework for the Telecommunications Industry in Developing Countries	Ruder, Pretorius & B.T. Maharaj (2008)	This framework is based on systematic, seven phase process, relying on certain inputs in order to deliver certain outputs, ultimately unveiling a refined list of candidate technologies.	Telecommunications
A technology selection framework for supporting delivery of patient-oriented health interventions in developing countries	Chan & Kaufman (2010)	Originally developed with regards to patient-oriented technologies, this framework consists of three levels of factors (situational factors, the relationship of the technology with regards to health interventions, and empirical evidence) that serve as filters, refining the candidate technologies.	Patient-oriented health interventions
A framework for evaluating and selecting learning technologies	Zaied (2007)	This framework is based on learning technologies, and contains several criteria that have been developed based on the opinions of certain groups in universities. These criteria can ultimately be used to compare different candidate technologies that can be used as learning technologies.	Education and training
A hybrid selection model for emerging technology	Shen *et al.* (2010)	This model uses the fuzzy Delphi, AHP and patent co-citation approaches and integrates certain aspects of each to compare technologies.	General

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Framework	Source	Description	Context in which framework is developed
A decision model for information technology selection using AHP integrated TOPSIS-Grey: The case of content management systems	Oztaysi (2014)	This model makes use of a combination of the AHP method (described earlier), and the Grey-TOPSIS method (Technique for Order Preference by Similarity to Ideal Solution). The AHP method is used to determine the weight of the criteria used in the framework, which is then followed by the evaluation of the alternatives by the Grey-TOPSIS method.	Information technology
A systems approach for technology assessment and selection	Demirkıran & Altunok (2012)	This is a systematic model that uses quantitative data to determine which technologies are candidate technologies. The model also defines critical technology elements of a system that should be considered.	General
Framework for selecting the technology in public sector	Hong (2013)	This framework's focus is on technology selection in the public sector, where social and economic impact of technology plays a key role. IT uses a technique called the fuzzy analytical network process, which is a technique that can deal with ambiguity involved during the evaluation of candidate technologies.	General (with focus on the public sector)
A method for technology selection based on benefit, available schedule and budget resources (TIES method)	Kirby & Mavris (2000)	The framework is based on an eight stage process, ranging from technology identification to selection. Using customer acceptance and satisfaction as starting criteria, as well as budgetary constraints, the framework is able to identify candidate technologies.	Aerospace systems

Table 17: Description of the three levels and the associated focus areas in the technology selection framework developed by Chan & Kaufman (2010).

Level	Category in framework		Description
Level 1	Situational factors	Clinical domain	It must be clear in what clinical domain (e.g. HIV, malaria, vaccines, educational programmes etc.) the framework is to be implemented.
		Setting	This stage focusses on the influence of factors such as environmental conditions, security infrastructures for technology, and infrastructure such as internet connectivity and electricity access that will support the technology.
Level 2	Technology and health intervention	Workforce	It must be determined whether the workforce that will be using the technology is adequately skilled. There should also be supporting staff (e.g. staff support, IT staff, and technology experts etc.) who are able to ensure the effective and efficient use of technologies.
		Delivery mechanisms	The delivery of the technologies must not burden existing health intervention deliveries, and must rather meet the needs and communications of the health interventions.
	Technology and target population	Meaningful access	The target population should have meaningful access to the technology. This relates to aspects such as affordability, connectivity, and ongoing technology support.
		Use patterns	If, for instance the health intervention entails handling of sensitive information of patients, more secure and personal technology is needed. Other use habits such as the frequency in which a user checks their emails should be considered.
		Interface	The interface of the technology should be simple and appropriate for interaction. Different languages must also be available.
Level 3	Empirical evidence	Potential for application	The implementers of the framework should not only focus on the framework. They should be willing to learn from real-world implementations of similar frameworks in similar target populations.
		Research needs	Any missing links that have been found during the real-world implementation should be re-assessed to determine ways in which to improve it. For example, research into the evaluation metrics can highlight specific requirements for different technologies.

In Chapter 6, the framework developed by Chan & Kaufman (2010) will be used to link the root causes identified in Chapter 4 to the technologies that are subsequently identified in the remainder of this chapter. The framework will facilitate the selection process and ensure that essential factors (embodied within the framework) are considered.

5.5. Investigating the technology landscape

As discussed in Section 1.7, technology has a broad definition in this research. This broad view of technology is leveraged towards the benefit of this research i.e. the technologies investigated are not limited to only hardware and software. The technologies that are identified and assessed can each be used to improve the daily activities in a PV system, making it more effective and efficient.

5.5.1. Technology landscape assessment

To identify technologies that can be used to address the root causes of the prioritised PV challenge landscape, two sources were used, namely: grey literature, and a focus group. The search terms used to identify technologies in grey literature were: "*Technologies used to address* …" and "*Emerging technologies used to address* …" The prioritised challenges in PV, namely: culture, transparency, partnerships, insufficient resources, country-specific factors, ADR-under reporting and technical capacity were used in the place of the ellipses in each search term.

To ensure additional credibility, a focus group was held to populate the technology landscape investigated in this research. The participants of the focus group (one professional Industrial Engineer and researcher; and eight postgraduate students in Industrial Engineering) originate from an Industrial Engineering background, and therefore have a fairly good understanding of the role that technologies play in the modern world. Prior to the start of the focus group, each participant was sent a summarised version of this section of the research, providing some background and stating the purpose of the focus group. All the relevant information regarding the focus group is shown in Section D.1 in Appendix D, which includes the identification of the participants, the document containing the summarised version of the research discussed, and the agenda for the focus group.

Subsequently, the technologies identified with the use of the previously mentioned sources (grey literature and the focus group) are described, along with some benefits and drawbacks. It should be made clear that the technologies are all described at a high-level i.e. specific instances of these technologies are not identified. The goal of this discussion is merely to identify the technology landscape, after which the technology selection framework will be used to determine which of these technologies have the potential to be used in addressing some of the root causes identified in the previous chapter.

5.5.1.1. Resource management systems

Resource management systems are used for the planning and control of resources (Spacey, 2015). These systems manage several different types of resources, including human resources, natural resources, financial resources, tangible and intangible infrastructures and information technologies. According to Smith (2014) it is vital to have a balance between these different resources, because any system relies on a combination of many interacting resources. Resource management systems are able to provide a global view on the available resources (Smith, 2014), and facilitate the management of these resources to ensure both efficiency and effectiveness. An example of a widely used resource management system, is the SAP (Systems Applications and Products) models, developed by the SAP Company. These management systems provide organisations with the ability to improve their resource management efforts and allow them to predict their resource requirements in future business.

Regardless of the many benefits mentioned earlier, there are some drawbacks to resource management systems as well. These include high initial acquisition and installation costs of the system (software) itself, resistance of employees to integrate such a system into their everyday routine, and the need to train employees to use these systems.

5.5.1.2. Big data analytics

Big data analytics is defined as "*a data analysis methodology enabled by recent advances in technologies that support high-velocity data capture, storage and analysis*" (Zakir *et al.*, 2015).

Essentially, big data analytics allow organisations to expand their scope of data analysis to include data from unstructured databases, such as emails, mobile device outputs and sensor-generated data. Big data analytics have grown to assist organisations in analysing exceedingly large amounts of data and are able to provide large samples of statistical data that can be used to enhance analytical tool results (Russom, 2011).

There are numerous technologies that are based on big data analytics, ranging from tools such as structured query language (SQL) servers, Hadoop and SAP, to simple tools such as Microsoft Excel (Zakir *et al.*, 2015). Many of these are open source software (i.e. are freely available to the public). These tools do, however, require users to possess specific skills to effectively utilise the tools (Zakir *et al.*, 2015).

5.5.1.3. Cloud technology

Cloud technology refers to the online space that can be used to store and share data (Harris, 2017). Examples of cloud technologies include *Dropbox*, *Google Drive*, *Amazon Drive* and *Apple iCloud*. These platforms can be used for two purposes; data storage, and data sharing (Harris, 2017). This eliminates the need to store and share data on external data storage devices such as external hard-drives or flash drives that can easily be corrupted, stolen, damaged or lost.

Many cloud technology platforms are open source software (i.e. are freely available to the public). These platforms are simple to use, and can be accessed by anyone from any location, provided that they have access to the internet, both simplifying and speeding up the sharing of information with relevant parties (Baiju, 2017). There are shortcomings to cloud technology. The first is that one can only access a limited storage capacity. When this predefined capacity is exceeded, a fee must be paid to access further storage capacity. Another shortcoming is that cloud technology can only be accessed with an internet connection (Baiju, 2017).

5.5.1.4. Online teaching services

Online teaching services are popular platforms used to replace the need to physically attend a lecture (Palloff & Pratt, 2001). These platforms are delivered through the internet i.e. lectures can be accessed online. There are many forms of online teaching services, such as online classes (courses that are delivered on the Internet), or hybrid courses (a combination of traditional, face-to-face classes and online courses) (Tallent-Runnels *et al.*, 2006). In some cases, online teaching services are regarded as a form of cloud technology, however, in this research, these services are classified outside the jurisdiction of cloud technology.

Online teaching services offer several benefits. The first is the fact that individuals in remote locations can access the necessary materials at their own discretion. The cost associated with online teaching is also less than that of traditional, face-to-face lectures. There is no need for a classroom, lecturer, or transportation to and from a venue (Armstrong, 2013). Online teaching also enables users to learn at their own pace, without a constant pressure to learn a large portion of work in a short time period (Norman, 2016).

There are disadvantages to online teaching services. These platforms cannot accommodate human interaction, which is often a critical element of teaching. Also, these platforms can only be accessed with internet connectivity (Armstrong, 2013).

5.5.1.5. Remote internet accessibility

Remote internet accessibility is defined as *"the ability to access a network from a remote distance"* (Rouse, 2005). The context of this definition only refers to one part of the intended meaning of remote internet accessibility. The intended meaning refers mostly to accessing the internet in remote locations where there is often insufficient electricity and network infrastructures. Since many PV systems' scope include activities in these locations, it is necessary for the inhabitants of these locations to have access to some sort of network to share and access relevant information.

There are numerous remote internet accessibility technologies on the market. One that has recently been receiving much attention is a robust, self-powered router that provides internet service to its users, developed by a company in Kenya. This device, one of many designed by the company, has proven to work in remote locations in Kenya, and is already used by the education departments of several sub-Saharan countries (Lamprecht, 2017).

Remote internet accessibility technologies offer several benefits, which include providing access to important information, increasing economic growth of local businesses and entrepreneurs, and reducing the incidence of diseases through improved information sharing between patients and healthcare practitioners (Booth, 2003; Deloitte, 2014). There are shortcomings in these technologies, which include high initial acquisition costs, maintenance costs and skill required to operate certain devices.

5.5.1.6. Internet of Things

The internet of things (IoT) has been a popular topic of debate in many circles and is a growing technology that is receiving increasing attention and investment. It is often regarded as a subset of big data analytics. For this research, however, IoT is investigated as a separate entity. The premise of IoT is that many objects used on a daily basis are connected on a network, allowing for numerous forms of communication (Gubbi *et al.*, 2013). For example, in an ideal world, a fridge will be able to communicate with a mobile phone to notify that some products are almost empty or expired, and that these products must be replaced. Other examples of potential areas include traffic control, transportation, electricity usage (Gubbi *et al.*, 2013), and healthcare (Islam *et al.*, 2015).

IoT offers a variety of benefits. With the implementation of IoT, access to information will be improved. A broader range of information that has not been captured before will be available. Cost saving is another benefit since devices are used more efficiently and effectively, reducing costs such as water and electricity usage. Transparency is also improved with IoT, because information is shared across several platforms that can be accessed by numerous parties (Gaille, 2016; Varun, 2016).

There are shortcomings to IoT that should be considered. Firstly, there is a cost component related to the physical infrastructure that must be installed. Secondly, IoT could reduce employment since daily activities are automated. Lastly, because IoT is still in its infancy and because it is a complex network, the chances of failure are still high (Gaille, 2016; Varun, 2016).

5.5.1.7. Mobile technology

Mobile technology refers to technologies that are used for cellular communication and other related aspects (Macwan, 2017). Gaining increasing popularity and injection into new markets (Kendrick, 2013), mobile technologies have been one of the most successful technological developments (Macwan, 2017). There are many different technologies that are categorised under mobile technology, such as cellular phones, smartphones, portable computers, tablets, PDAs (personal digital assistant) and GPS devices. Many of these technologies are used in combination and interact to connect people in different locations and allow them to share many different types of information.

There are several benefits offered by mobile technologies. These technologies are mobile and can be used in nearly any location. In the healthcare industry, sharing of information enabled by mobile technology has allowed for distant healthcare monitoring. These technologies are able to transmit information much quicker, and enable individuals in remote locations to stay in contact with other communities (Kendrick, 2013).

One should consider the shortcoming of mobile technologies. There are both acquisition and maintenance costs that should be considered. Integration of mobile technologies into an existing infrastructure might also pose a problem since compatibility of devices may be a challenge. Another shortcoming is that the tangible devices might get stolen, damaged or lost and must therefore be closely monitored (Kendrick, 2013).

5.5.1.8. User videos

User videos are predominantly used for training and education. Videos are created by individuals or teams who are knowledgeable about a certain topic and shared with others to train or educate them in a specific field or guide them through a certain process. These videos are often used in education departments to train and educate both teachers and students in remote locations where it is difficult to gain physical access (Lamprecht, 2017).

There are limitations to these types of videos. The videos cannot be accessed without the necessary hardware, such as computers or tablet devices. The planning and creation of these videos must also be done meticulously, because missing or wrong information may cause complications (Lamprecht, 2017).

5.5.1.9. Block chain

Block chain is defined as "*a decentralised ledger of all transactions across a peer-to-peer network…participants can confirm transactions without the need for a central certifying authority*" (Morrison & Sinha, 2016). In simple terms, block chain allows for transactions such as payments and record sharing to occur between peers, without the need for an intermediary who manages the exchange. This technology has been receiving increased attention over the last decade, and is already used by some of the world's top professional services organisations (Hackett, 2016). The potential application areas of block chains are many, including financial services, political voting, transportation and healthcare. To provide an example of the latter, block chains can be used to share private patient related data with several parties without the risk of privacy breaches (Morrison & Sinha, 2016).

Block chain offers several benefits, such as reduced transaction costs, improved protection of private data, permanent record keeping of transactions, and increased transparency between peers (Morrison & Sinha, 2016). However, there are shortcomings to consider. The technology is still in its infancy stage, meaning that the technology and systems used are complex. There may also be a clash in priorities between regulatory agencies and organisations seeking to rely increasingly on block chain technologies since the need for external, regulatory involvement is reduced. Lastly, the implementation of block chain technologies in the contemporary setting may also create challenges with regard to integration and compatibility with existing systems (Morrison & Sinha, 2016).

5.5.1.10. Non-traditional transportation

Non-traditional transportation refers, in this case, to those modes of transportation that are not commonly used. In other words, it does not refer to transportation modes such as trucks, trains, or aeroplanes, but rather modes on a smaller scale, such as bicycles and pushcarts. Over the last decade, the *Coca Cola Company* has led the way in the exploitation of non-traditional transportation in several African countries (Berry, 2010). The areas in which the company's product is consumed are often inaccessible, because of the poor conditions of the roads leading to these areas. To address this obstacle, the *Coca Cola Company* employed local entrepreneurs to distribute their product to these areas, with the use of bicycles or pushcarts. As a consequence, the inhabitants of vastly remote locations have increased access to the products of the *Coca Cola Company* (Berry, 2010).

Non-traditional transportation services offer several benefits, which include increased local entrepreneurship and the simplification of delivery modes since no trucks are needed. There are limitations to consider, such as an increased probability of damage to the product (bicycles are unsteady and might lead to product damage) and the limitation with regards to how much product can be shifted on one delivery (there is limited space on a bicycle or pushcart).

5.5.1.11. Mobile applications

Mobile applications, better known as mobile apps, are software programmes designed for mobile devices to enable a wide array of functionalities. Mobile apps are used for a number of purposes, which include navigation, entertainment, sport, fitness, and productivity (Viswanathan, 2017). These apps can be accessed on many different platforms, such as *Google Play* or *Apple App Store*. The use of mobile apps have grown exponentially over the last decade, with an estimated 197 billion apps forecasted to be downloaded in 2017 (Viswanathan, 2017).

Mobile apps are relatively easily maintained (depending on the degree of complexity of the functionalities enabled by the app), easily modifiable for different requirements and platforms and relatively simple to develop for nearly any function. There are limitations to consider. These include a limited scope of functions that can be executed, and the need for a smartphone or tablet device to access these apps (Singh, 2017).

5.5.1.12. Educational television and radio programmes

Educational television programmes refer to programmes that incorporate different elements of education. These programmes are aired across a television network, with a wide target market. Many shows are aimed at children within a low age range (1-5 years), whereas other programmes are aimed at adults (Western Governers University, 2017). The latter may incorporate different social elements and provide essential educational aspects, such as safe sex practices and anti-drug initiatives.

There are several benefits associated with these educational television programmes. These programmes allow for a large audience to be reached, even in remote locations. It also eliminates the need for the physical presence of educators or trainers. One potential disadvantage is that the intended message of these types of programmes can be misinterpreted, which might lead to unintended behaviours. According to Ostrov *et al.* (2013), another potential disadvantage is that some of these programmes can lead to aggravated behaviours and attitudes, especially amongst the younger population.

Radio programmes, like educational television programmes, are educational programmes intended to convey a certain message of a subject to a certain target audience. However, instead of using the television, educational radio programmes are delivered across radio broadcasts. The benefits and limitations of these types of educational programmes are like educational television programmes. However, there is one additional limitation to consider, namely that radio programmes allow only for audible communication, which limits the amount of information that can be shared.

5.5.1.13. Wireless Application Protocol based messaging

Wireless Application Protocol (WAP) is a *"specification for a set of communication protocols to standardise the way that wireless devices, such as cellular telephones…can be used for Internet access, including e-mail, the World Wide Web, newsgroups, and instant messaging"* (Rouse 2010). WAP based messaging refers to messaging platforms that are based on WAP technology, such as Mxit, and *Blackberry messenger*. For this research, the well-known application, WhatsApp, is not included in these messenger platforms, since it can only be accessed with more advanced smartphones, compared to the other platforms.

WAP based messaging does not require advanced smartphones, but rather less expensive mobile technologies. It also allows for information to be shared in real-time. On the other hand, WAP based messaging can only be used within an area where there is access to a mobile network, which may be an obstacle to use in some areas.

5.5.1.14. Routine assessments

Routine assessments can be done in many ways, such as examinations, interviews, projects, or surveys. These assessments are used to assess the knowledge and experience of employees, and determines whether a specified threshold is met (Lamprecht, 2017). These assessments are used in many disciplines, such as healthcare and education. Often, it is seen as a type of incentive scheme, since some form of incentive (e.g. funding or promotions) is given to those who excel in these assessments.

Routine assessments allow for a routine check-up on the level of expertise, which enables those in management positions to intervene where necessary. These types of assessments also eliminate the need for the physical presence of an SME since the assessments are mostly done on computers. There are shortcomings to these assessments. It is possible for those being assessed to cheat i.e. get information from colleagues. Also, in some areas where there are no access to computers and internet networks, these assessments cannot be used (Lamprecht, 2017).

5.5.1.15. Game-based learning

Game-based learning is a method of incorporating educational content or learning principles into video games (Coffey, 2007). Game-based learning is the use of educational games to teach the user certain aspects of the real world. Many of these games are developed as mobile apps (described in an earlier section) and are widely available.

Game-based learning engages and motivates students with a custom learning experience and promotes long-term memory. It also contributes to the development of certain computer skills, which is a necessity in modern society. An important criticism is that this type of learning may be more distracting than more traditional teaching methods. Additionally, game-based learning can be resource intensive, since it requires a computer, tablet, or smartphone to be accessed.

5.5.2. Concluding the technology landscape assessment

There are numerous technologies that can possibly be implemented in PV to address some of the root causes identified in Chapter 4. Each of these technologies offer several benefits that could potentially be leveraged towards the improvement of PV. However, there are also some shortcomings or limitations to each of these technologies that must be considered. The potential of each technology to address some of the root causes of prominent challenges in the PV landscape will be explored in the next chapter.

5.6. Chapter 5 conclusion

This chapter is made up of two sections, namely a brief overview of technology selection frameworks, and an overview of the technology landscape that is applicable to PV. In the first section, it is argued that, for this research, it would be beneficial to select an appropriate technology selection framework for application. Several technology selection frameworks are investigated, followed by a concluding argument that justifies the selection of a specific framework that will be used in the subsequent chapter. The focus of the second part of this chapter is the technology landscape. The purpose is to identify several technologies that can possibly be leveraged towards the benefit of PV.

In the next chapter, the two sections of this chapter will be merged i.e. the technology selection framework will be used as linkage between the technologies and the root causes identified in the previous chapter. In other words, the technology selection framework will be used to create a context that provides further explanation of the root causes, which will be used to refine the list of technologies to several candidate technologies for application to each root cause.

Chapter 6: Investigating technology and root causes

In this chapter[5] the root causes identified in Chapter 4 are linked to the technologies identified in Chapter 5, using the technology selection framework developed by Chan & Kaufman (2010) as guidance. The landscape of potential technologies is condensed to a list of candidate technologies that could feasibly be used to address the challenges in PV. This is followed by establishing a link between the selected technologies and the prioritised root causes, where it is discussed which technologies can be used to address which root cause.

In the previous chapter, the primary focus was on the implementation of certain tools and techniques in order to achieve a specific outcome. In large part, this is an essential component of Industrial Engineering i.e. finding the appropriate methodologies that can be used to address a specific problem. However, this chapter moves away from this, and in fact, is a guiding discussion of qualitative data.

It should be made clear that the discussions that follow are non-exhaustive, and that the researcher is aware of this. In order to provide a maximum amount of suggestions and to provide a comprehensive overview, validation is used. This ensures that the discussions and overviews not only contain the opinion of the researcher, but also those of SMEs who have more experience in the field of PV. The validation process is described and shown in Section 6.9.

6.1. Technology selection framework implementation outline

It is important to define how each of the categories in the technology selection framework, developed by Chan & Kaufman (2010), are used to assess the technology landscape in order to make it clear exactly how the framework categories are defined for the purpose of this research. Table 18 indicates which categories of the framework are used to describe the root causes, and which to describe the technologies. The root causes are described within the clinical domain (first category in Level 1), to formulate a problem statement, where the particulars of the problem are described. The remaining category in Level 1 (setting), as well as the categories in Level 2, are used to filter the landscape of potential technologies to a set of candidate technologies that could feasibly be implemented within PV. The factors that are considered during this filtering process are: (i) the characteristics of the setting within which the technology would need to operate; (ii) the skills development required for the workforce to effectively

[5] A large portion of the contents of this chapter has been published in an article that has been submitted to the IAMOT2019 conference. A copy of this article is included in Section E.1 in Appendix E.

implement, utilise, and manage the technology; (iii) the feasibility of integrating the technology into the existing communication modalities; (iv) the degree of affordability and connectivity to determine the potential for meaningful access; and (v) the interaction with the technologies regarding interface. Once the candidate technologies have been identified, Level 3 of the framework is utilised to describe how each of the candidate technologies can be implemented within PV, by describing real-world examples of possible applications.

Table 18: Outline of how each category in the technology selection framework is used.

Level	Category in framework		Description of the assessment of each technology during each category
Level 1	**Situational factors**	**Clinical domain**	Define and describe each root cause within the context of the clinical domain, providing an explanation in the form of a problem statement.
		Setting	Define how each technology will be influenced by the environmental settings (e.g. weather conditions) and by infrastructure support (e.g. access to electricity and security measures).
Level 2	**Technology and health intervention**	**Workforce**	Describe the requirements regarding existing and additional training of users, leadership commitment, and technical expertise for each technology.
		Delivery mechanism	Describe the integration of each technology into the existing infrastructure about communication modalities, and highlight any obstacles that might surface during this stage.
	Technology and target population	**Meaningful access**	Describe the feasibility of each technology in terms of affordability and connectivity.
		Interface	Where applicable, identify essential requirements about the interface of the technology, and highlight possible obstacles that should be overcome concerning the physical interaction with the information display (e.g. screen) or input of the technology.
Level 3	**Empirical evidence**	**Potential application and research needs**	After the technology landscape has been refined to a set of candidate technologies, possible, real-world implementations of the technologies are provided, giving a tangible indication of how these technologies can be leveraged towards addressing some of the challenges in PV. Additionally, existing research and future research of technology in healthcare and pharmacovigilance is discussed.

6.2. Clinical domain-based root cause description

In order to determine which root causes should be addressed in this analysis, the suggestions made by SMEs, as described in Section 4.6.3, are used. As part of the exercise during which the root causes were validated, distinctions were made between the root causes that deserved greater attention compared to others. In essence, similar to the approach taken with the prioritisation of the PV challenge landscape in Chapter 3, the SMEs indicated which root causes should be prioritised in this research, based on their experience within the PV context. Therefore, these root causes were deemed to be of priority and form the focus of subsequent discussions. The intention is, however, not to suggest that the other root causes should be ignored, merely that it does not form part of the set of root causes prioritised for investigation in this research project. Other than the opinions of the SMEs consulted during the validation of all the identified root causes, there are two additional reasons why the selected set of root causes are singled out for further investigation:

- Some of the root causes cannot necessarily be addressed with technology alone. Instead, other interventions such as additional funding or adjusted management practices are more plausible for addressing these root causes; and
- Focussing on only a selected set of root causes reduces the scope of this research effort, allowing for a more in-depth analysis on the most important root causes, rather than a more superficial focus on a larger set of root causes.

In line with the implementation plan for the technology selection framework described in Section 6.1, the root causes summarised in Table 19[6] are described in term of the *clinical domain* category in Level 1 of the technology selection framework. This is shown in Table 20.

[6] The process of identifying root causes was described in Chapter 4. The set of root causes summarised in Table 21 were identified using fishbone diagrams documented in Section C.2 in Appendix C, with the set of root causes summarised in Table 12.

Table 19: Prioritised root causes according to the SMEs (as discussed in Section 4.6.3).

Originally identified challenge (strategic level)	**Challenge identified during Stage 1 of the translation process**	**Root causes identified during Stage 2 of the translation process**
Insufficient resources	Inadequate access to ADR reporting forms (spontaneous).	1. There is no designated transportation service to distribute the ADR reporting forms to the different facilities.
		2. The users of the forms have competing priorities, and do not have time to notify the person in charge of re-ordering the ADR reporting forms when stock is depleted.
		3. The individuals responsible for coordinating the deliveries of spontaneous ADR reporting forms are not sufficiently trained to execute these tasks.
Country-specific factors	Failure to develop locally relevant and easily measurable indicators of performance of PV systems.	1. Key stakeholders are not aware of the health impact of PV on the healthcare system.
ADR under-reporting	The lack of robust local data limits the extent to which decision-making can be done.	1. Key stakeholders are not aware of the health impact of PV on the healthcare system.
		2. PV is not included in the undergraduate syllabus of tertiary healthcare education.
		3. The ADR reporting forms are overly complicated and take too long to complete.
Transparency	Inadequate feedback (newsletters, emails etc.) given to ADR reporters and other stakeholders.	1. The importance of feedback is not sufficiently advocated.

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Originally identified challenge (strategic level)	Challenge identified during Stage 1 of the translation process	Root causes identified during Stage 2 of the translation process
Insufficient resources	Inadequate access to data management systems that can synthesise and analyse existing electronic health records.	1. There is a lack of ownership of managing the process of data management.
		2. There is a lack of training provided to those who report ADRs.
		3. There are difficulties in providing the necessary training to individuals in remote locations in a timely manner.
Insufficient resources	Failure to utilise existing resources to conduct data collection, collation, and analysis.	1. There is a lack of ownership to manage existing PV-related resources.
		2. There is a lack of training to educate PV personnel on how the available resources should be used.
		3. There is no resource management system in place to manage existing resource inventories.
Transparency	Lack of overarching platforms for information sharing between stakeholders.	1. PV personnel are not sufficiently trained in using existing platforms.
		2. It is unclear what data should be shared with which stakeholders.

Table 20: Root causes described in terms of the clinical domain.

Root cause		Clinical domain
1	There is no designated transportation service to distribute the ADR reporting forms to the different facilities.	In some settings, the transportation of the physical ADR reporting forms is challenging. There is not a designated transportation service in place that is able to collect ADR reporting forms from the location where these are created, and to transport the forms to different locations for use. Since many ADRs are still reported on a spontaneous reporting form, it is critical that these forms be readily available on demand.
2	The users of the forms have competing priorities, and do not have time to notify the person in charge of re-ordering the ADR reporting forms when stock is depleted.	Due to severe workloads, especially in sub-Saharan African countries where the healthcare system is under-resourced, healthcare practitioners forget or for other reasons fail to request that the stock of ADR reporting forms be replenished. As a result, stock-outs of ADR reporting forms within healthcare facilities are frequently experienced. This leads to frustration on the part of the healthcare workers that are responsible for reporting ADRs and ultimately results in ADRs not being reported. It is possible that, in some cases, the person in charge of managing the ADR reporting form stock is not situated in the same healthcare facility in which healthcare practitioners reside, meaning calls must be placed to request that depleted form stocks be replenished.
3	The individuals responsible for coordinating the deliveries of spontaneous ADR reporting forms are not sufficiently trained to execute these tasks.	It has been validated that in some cases, the lack of technical expertise with regards to ADR reporting form delivery management is an issue. As a result, healthcare facilities that need the reporting forms are not receiving sufficient stock. Consequently, a snowballing effect takes place where ADR reporting form stock is not replenished in time, which leads to ADR under-reporting, putting further pressure on the overall healthcare system since patients experiencing ADRs re-enter the healthcare system. Therefore, there is a need to address the lack of technical expertise with regards to the management of the delivery of ADR reporting forms.
4	Key stakeholders are not aware of the health impact of PV on the healthcare system.	Key stakeholders might not be aware of the impact of PV not only on PV itself, but also the impact it has on the entire healthcare system. When a PV system is not functioning properly, the healthcare system will experience increasing pressure. The key stakeholders among which PV awareness should be increased are patients, healthcare practitioners, nurses, and pharmacists. These stakeholders represent a group that are most exposed to ADR reporting. The obstacle that surfaces during the creation of awareness amongst these stakeholders is that existing awareness programmes struggle to reach a wide audience, especially audiences in remote locations.

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Root cause		Clinical domain
5	PV is not included in the undergraduate syllabus of tertiary healthcare education.	In some undergraduate healthcare syllabuses, PV is not deemed a priority, and therefore does not receive the necessary attention. According to Mehta (2017), it is not a simple process to change existing syllabuses to focus more attention towards PV. As a result of the lack of PV education, increasing pressure is faced in the PV system where PV-related activities, especially ADR reporting, are not executed properly. Healthcare practitioners frequently do not know how or where to report ADRs. When they do, the quality of the data they provide is poor. As many of the graduates of these programmes are currently employed in the healthcare system, the definition of this root cause within the clinical domain should be expanded to also include a lack of PV education amongst current healthcare system workers. A lack of training on ADR reporting is defined as a separate root cause in this table, the scope of training referred to here, however, extends beyond the scope of ADR reporting only to encompass an understanding of the PV system as a whole and ties in with the previous root cause to also include an understanding of the role of PV within the broader healthcare system. Like the previous root cause, the obstacle that one would expect to surface when attempting to provide PV education to the current healthcare workforce include reaching a wide audience, including audiences in strategic locations throughout a country.
6	The ADR reporting forms are overly complicated and are time-consuming.	As reported in a study by Khan (2013), in many countries patients and healthcare workers are deterred from reporting ADRs due to overly complicated ADR reporting forms, as well as the great effort required to complete each of the fields in these forms. This is a phenomenon that is especially experienced in areas where spontaneous ADR reporting forms are used. Healthcare workers do not want to fill in these long documents, and would rather divert their attention and time to attending to patients, especially when they are remunerated on a patient-basis[7]. This issue is closely related to the lack of technical capacity discussed in the third and fifth root cause discussed in this table. Each of these three root causes ties back to the lack of technical capacity.

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[7] This phenomenon is usually experienced in healthcare facilities where the healthcare worker to patient ratio is low i.e. there are only a small number of healthcare workers compared to the large number of patients. In these facilities, remuneration for healthcare workers is usually based on a patient-basis, meaning the healthcare workers (mostly doctors and specialists) are payed according to the number of patients they attend to. This is very closely related to the second root cause discussed in this table, which also relates to the competing priorities of healthcare workers.

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Root cause		Clinical domain
7	The importance of feedback is not sufficiently advocated.	The feedback referred to here is the feedback given to ADR reporters. These reporters include both patients and healthcare workers. In some countries, feedback is not regarded as a priority, which is a mind-set that should be changed. Some of the PV systems have some form of feedback system in place, however, these systems are severely limited in capabilities. The only form of feedback is in the form of a once-off, automated response once an ADR report is submitted. Thereafter, no form of feedback is provided. It is argued in this research that feedback should be regarded as a priority. As shown in a study by Al Dweik *et al*. (2016), the lack of feedback is a barrier to ADR reporting in several countries.
8	There is a lack of ownership of managing the process of data management.	The data management systems referred to here are the systems within local healthcare facilities. Since many of the staff in these facilities already have an overloaded schedule (similar to the second and sixth root causes discussed in this table), there may be a lack of ownership of managing the PV system, or in this case, the PV data management system (e.g. ensuring ADRs are reported, all the reports are collected, and the forms are captured on a computer). As a result, the PV systems in these facilities are of poor quality. It is therefore necessary to improve these PV systems, or rather PV data management systems.
9	There is a lack of training provided to those who report ADRs.	ADR under-reporting, as described numerous times in this research, is one of the major challenges in PV. Since ADR reporting is the front-end of PV, it is critical that all possible ADRs are reported. It is often reported in there is a lack of training provided to the public, patients, and healthcare workers on ADR reporting.
10	There are difficulties in providing the necessary training to individuals in remote locations in a timely manner.	This issue is closely related to the previously discussed root cause. Existing training initiatives struggle to provide the necessary ADR reporting (and broader PV-related activities) training to the public, patients, and healthcare workers in remote locations. It is severely important that individuals in these remote locations be aware of ADR reporting, since they might be the ones who, unknowingly, are experiencing ADRs.

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Root cause		Clinical domain
11	There is a lack of ownership to manage existing PV-related resources.	The resources referred to here are those intended for PV activities in local healthcare facilities, such as ADR reporting forms, computers, smartphones, tablets, and human resources. Resources form the cornerstone of any system, and should be efficiently managed. Since in many cases existing healthcare staff already have an overloaded schedule, there may be no one who is willing to take ownership of managing PV resources, and in turn, manage the PV system. It is therefore essential to intervene in these cases, by ensuring PV does not interfere with the schedules of the staff, but that PV is regarded as a priority and receives the necessary attention. This issue is closely related to the second and sixth root cause discussed in this table, which also relates to the overloaded schedules of healthcare workers.
12	Lack of training to educate PV personnel on how the available resources should be used.	Closely associated with the lack of ADR reporting training previously discussed, the lack of training provided to healthcare staff in local facilities on how PV resources should be used is proving to burden the PV system in those facilities. It is essential that staff are trained on how to manage PV resources, such as ensuring the availability of ADR reporting forms, filling in ADR reporting forms, and capturing the data on a computer. This training should not only be provided to healthcare facilities in major cities or towns, but also to facilities in remote locations.
13	There is no resource management system in place to manage existing resource inventories.	This is closely related to the two previously discussed issues that refer to the management of PV resources. It is incredibly challenging to manage these resources without some sort of system that is able to track and monitor inventories. It is not surprising that, in healthcare facilities where PV is not regarded as a priority, there are no initiatives taken to implement such a resource management system.
14	PV personnel are not sufficiently trained in using existing platforms.	The platforms referred to here are those used between healthcare workers to share information with their peers, which can be in the form of emails, online chatrooms, blogs, or cloud technologies (e.g. *Google Drive*). These technologies are available, however, are still unfamiliar to some of the staff. There is a need for some sort of training to be provided to these individuals in order to ensure that each member of a healthcare facility know how information can be shared with the relevant parties.

Following the discussions in Table 19 and Table 20, it is now clear which root causes are regarded as priority in this research. The primary focus of the subsequent research is on these prioritised root causes. Shifting focus away from the root causes and towards the technology landscape, the subsequent section investigates the feasibility of implementing the technologies identified in Section 5.5 in PV in order to address the prioritised root causes.

6.3. Determining the feasibility of the technologies

The next step, according to the implementation plan for the technology selection framework described in Section 6.1., is to analyse each of the technologies identified in Section 5.5 according to the *setting*, *workforce*, *delivery mechanism*, *meaningful access*, and *interface* categories (described in Table 18) of the technology selection framework. These categories define several key considerations that are used to determine the feasibility of implementing each technology in the PV challenge landscape.

For the sake of clarity, the 15 potential technologies that were identified for application to the PV landscape in Section 5.5 are summarised in Table 21. In the remainder of this section, each of these technologies will be analysed according to the aforementioned five categories, defined in the technology selection framework.

Prior to the investigation of the analysis of the technology landscape, some terminologies that are used by the researcher throughout the analysis are clarified. These terminologies are explained in Table 22.

Table 21: The 15 potential technologies identified for application in the PV landscape.

<table>
<tr><th colspan="4">Technology landscape</th></tr>
<tr><td colspan="2">Resource Management Systems (RMSs)</td><td>Remote internet accessibility</td><td>Educational television and radio programmes</td></tr>
<tr><td>Big data analytics</td><td>Internet of Things (IoT)</td><td>Block chain</td><td>WAP based messaging</td></tr>
<tr><td>Cloud technology</td><td>Mobile technology</td><td>Non-traditional transportation</td><td>Routine assessments</td></tr>
<tr><td>Online teaching services</td><td>User videos</td><td>Mobile applications</td><td>Game-based learning</td></tr>
</table>

Table 22: Terminologies used throughout the analysis of the technology landscape.

Terminology	Description
Feasibility	The term feasibility is used to describe whether or not it will be possible to implement a technology within a specific setting or context.
Potential	The term potential is used to describe, in this case, whether or not there is an acceptable likelihood that a technology can implemented within a specific setting or context.
Tangible	The term tangible is used to describe something that is perceptible to touch.
Intangible	The term intangible is used to describe something that cannot be touched or does not have a physical presence.
Setting	Not referring to the "setting" category used to assess the technologies, the term setting is used to describe resource limited setting, primarily in sub-Saharan Africa.
Internet connection	When referring to internet connections, intranet connections are included in the discussion.
Technical support	Technical support is used to make reference to the general need for assistance with procuring, installing, and operating hardware (computers, smartphones, tablets, etc.) and software.

6.3.1. Resource management systems (RMSs)

Each of the five categories from the technology selection framework are used to assess the feasibility of resource management systems.

6.3.1.1. Setting

Resource management systems are not tangible, but rather intangible systems that are operated with the use of tangible technologies such as computers, tablets, and smartphones. Therefore, environmental factors are not applicable for assessing the feasibility of these systems. Infrastructure support, however, is an important element. Resource management systems rely heavily on electricity supplies to be operated. In many areas in several developing countries, electricity infrastructures are not dependable, and in some cases, non-existent. As a result these systems cannot be used in such countries where there is not a dependable electricity infrastructure. Another element of infrastructure support on which resource management systems rely is internet connectivity. Many of these systems rely on information being shared across several platforms in different locations. In countries where internet connectivity is not reliable, these systems may struggle to operate effectively. This is an area where remote internet accessibility, another technology assessed in this research, can be used to provide internet connectivity to areas where it is needed.

Lastly, since resource management systems are accessed via hardware such as computers or tablets, security measures must be implemented to secure these devices from theft or vandalism.

6.3.1.2. Workforce

Resource management systems are complex, because they incorporate several elements of an already complex system i.e. PV. Due to this complexity, resource management systems tend to become increasingly complex, and challenging to effectively implement and manage. Therefore, a large portion of the strategy to implement a resource management system would entail the training of the existing workforce to operate such a system. These training sessions must encompass a substantial portion of understanding of these systems, and as a result often become time-consuming and expensive. Another consideration is the influence of leadership or individuals in influential regulatory positions. Adopting a resource management system is a significant undertaking, and will therefore require a champion in an influential position to advocate the entire process.

6.3.1.3. Delivery mechanism

Resource management systems make use of communication modalities through an internet connection. In other words, the information generated by these systems can be accessed where there is access to an internet connection. This can be an obstacle, since internet networks in several settings are not reliable (as mentioned in Section 6.3.1.1). Therefore, it may be challenging to utilise resource management systems properly.

6.3.1.4. Meaningful access

Comprehensive and complex resource management systems are expensive, regarding both acquisition and integration into an existing system. This is a major shortcoming since many countries do not have sufficient monetary resources to access these systems. There are, however, less expensive resource management systems on the market that are likely more feasible for implementation in several resource-limited settings. Additionally, resource management can be adapted, where the principles of resource management systems are implemented in more generic application software. For example, existing software such as Microsoft Excel can be used to develop a simple resource management system which measure several characteristics such as resource utilisation and availability. To further exploit resource management systems, internet connectivity should be addressed, as already pointed out in the earlier sections. In other words, these systems should be universally accessible. This can be done by supplying internet connectivity to areas where the existing infrastructures are not sustainable. A technology such as remote internet accessibility can be used to provide such an internet connectivity infrastructure.

6.3.1.5. Interface

Since resource management systems are accessed via a computer, tablet, or smartphone, interface plays a prominent role. Arguing that many employees in a workforce have limited knowledge about resource management and technology interaction, simplicity should be designed into these systems, making it easy for employees to both navigate through the system and access the necessary information.

6.3.2. Big data analytics

Only four of the five categories from the technology selection framework are used to assess the feasibility of big data analytics. *Interface* is not a relevant subject, since big data analytics mostly refers to *behind-the-scenes* software that are not visible to a user.

6.3.2.1. Setting

Similar to resource management systems, big data analytics are intangible, but rely on tangible products such as computers. Therefore, environmental factors are not applicable for assessing the feasibility of these systems. Focus should shift towards infrastructure support. Big data analytics are best utilised where there is a reliable internet connectivity. These systems gather data from several sources in different locations, making internet connectivity a requirement. However, in several developing countries, internet connectivity is not reliable and sometimes not available, therefore, implementing big data analytics will not be feasible.

6.3.2.2. Workforce

Big data analytics, similar to resource management systems, entail complex systems, algorithms, skills, and processes that are challenging for individuals, who are not familiar with the realm of big data, to understand. Therefore, a significant part of the implementation of big data analytics would be to train the existing workforce in PV to make use of the available systems and processes to capture and analyse large amounts of data. Such training will require several monetary resources to provide the necessary expertise, hardware, software, and materials. A network of technical support will also be needed, at least during the initial stages of system implementation, to provide constant assistance regarding system use and maintenance. Lastly, leadership is a critical element for the adoption of big data analytics, especially on a large scale. Leadership should provide both advocacy and guidance to the implementation of big data analytics in PV.

6.3.2.3. Delivery mechanism

The communication modalities used by big data analytics software depend on internet connections (and by implication any and all infrastructure related to internet connections) or intranet connections. It is essential that these networks are maintained (as mentioned in Section 6.3.2.1), since big data analytics collect and synthesise information from several sources in different locations. This can only be achieved when all these sources are connected to an online network, where it is possible for a single big data analytics system to gather the necessary data. The benefit of how assessed data is communicated on big data analytics software is that it offers visual representations that can be analysed by anyone with the necessary knowledge and skills.

6.3.2.4. Meaningful access

Since the operation of big data analytics software require a certain degree of knowledge and skills that may be lacking in developing countries and within the context of PV, adopting and integrating these systems into the existing infrastructure can prove to be too costly, especially within the short to medium term. However, a gradual approach may be more feasible, where smaller parts of a big data analytics system are implemented over a period of time, ultimately building the overall system. Big data analytics also significantly rely on internet or intranet connectivity (as mentioned before), meaning the existing internet network must be assessed to determine whether or not it can accommodate big data analytics systems. This can be an obstacle in several countries where the internet network is not reliable and sustainable.

6.3.3. Cloud technology

Each of the five categories from the technology selection framework are used to assess the feasibility of cloud technology.

6.3.3.1. Setting

Cloud technology, similar to the previous technologies, is intangible, and relies on tangible items such as computers to be accessed. Therefore, environmental factors are not applicable for assessing the feasibility of these technologies. Cloud technology relies on internet connectivity, and in fact, cannot be used without it. Therefore, in locations where internet connectivity is not reliable, cloud technologies cannot be used for information sharing. Technologies such as remote internet connectivity is a candidate that can be used to supply such internet connectivity networks.

6.3.3.2. Workforce

Since cloud technology is a relatively simple platform to use, the burden of training of a workforce is not as large as that of resource management systems and big data analytics. These platforms are user-friendly, allowing for easily understandable processes by which one can store and share information. However, a critical element of cloud technology, technical support, must be considered. Since cloud technology rely on internet (and intranet) networks, a well-established technical support system should be in place to provide the necessary assistance where it might be needed.

6.3.3.3. Delivery mechanism

Regardless of the fact that cloud technology relies heavily on internet networks (as mentioned before), the communication modalities are vast. In fact, it depends entirely on the data types loaded onto these platforms. These platforms allow for several types of data to be shared, such as visual displays and audio files. This is especially beneficial towards PV, where data of different types are generated in many locations.

6.3.3.4. Meaningful access

The cost component of cloud technology is negligible, since most of the platforms are freely accessible. The only noticeable cost component comes with the purchase of additional storage space, since many of these platforms offer a limited capacity of storage at no charge. Any additional storage space must be bought. However, this cost is not significant (when compared with the cost of running PV systems), since it is structured around a small, monthly fee. Similar to big data analytics, cloud technology can also only be accessed with an internet (or intranet) connection. If the internet connection is insufficient, the cost component of cloud technology will become significant, since the internet connectivity network must be installed or improved.

6.3.3.5. Interface

Since the interfaces of cloud technology platforms such as *Google Drive*[8] and *Dropbox*[9] cannot be altered, interface interaction is not a major cause for concern. A noteworthy consideration is the training that should be made available to teach a workforce on how to interact with these platforms.

6.3.4. Online teaching services

Each of the five categories from the technology selection framework are used to assess the feasibility of online teaching services.

6.3.4.1. Setting

Online teaching services, similar to the previous technologies, are intangible, and relies on tangible items, such as computers, to be accessed. Therefore, environmental factors are not applicable for assessing the feasibility of these technologies. Online teaching platforms are

[8] URL: https://www.google.com/drive
[9] URL: https://www.dropbox.com

accessed via an internet connection and require reliable internet connectivity. It cannot be used in areas where internet connectivity is not sufficient. Another form of these teaching services, user videos, can be accessed without the use of the internet.

6.3.4.2. Workforce

Training of workforce with regards to online teaching services is a negligible factor, since the workforce is not responsible for the creation of these services. The materials that are used in online teaching services are developed by experts in the particular field, and will most likely have sufficient knowledge of the creation of these materials. The two forms of training one can associate with online teaching services are teaching PV workforce on accessing these services and improving computer literacy where it may be lacking. Technical support is, to a certain degree, negligible, since the developers of the online teaching services will most probably have access to technical support. Therefore, the end-users of the materials will not require technical support. Lastly, leadership support is another factor that does not have a large footprint in the adoption of online teaching services. The only form of leadership support is in the form managers motivating their workforce to spend the time in gaining the necessary knowledge from online teaching services.

6.3.4.3. Delivery mechanism

As per definition, online teaching services can only be accessed via an internet connection (as mentioned in Section 6.3.4.1), which will be a limitation in areas where internet networks are sub-optimal for such online services. However, online teaching services offer several communication modalities i.e. data of different types can be accessed. Both visual and audio data are offered by these services. Real-time interaction, where one can interact with some expert via a chatroom or video call, is also made possible with these services.

6.3.4.4. Meaningful access

The only significant cost components of online teaching services is access to an internet connection and the subscription to the online teaching services providers. It is possible that the latter be negligible, since several online teaching services are freely available to the public. As per definition of online teaching services, a reliable internet connection is necessary to access these services (as mentioned before). Therefore, in settings with poor or non-existing internet networks, online teaching services is not a feasible option. However, user videos that do not require internet connections, can be used as an alternative. The cost associated with technical support is not as significant as the previously mentioned cost components. It should be considered as some form of technical support should be available to the users of online teaching services.

6.3.4.5. Interface

It is important to consider the level of knowledge of the audience for which online teaching services are created. This is applicable to both the workforce on a lower level of authority and responsibility and workforce on a higher level of authority, such as managers and supervisors. Learning new materials will most probably be challenging to anyone who are not familiar with the subject, and should therefore be designed to accommodate the level of knowledge of the target audience, as well as materials that challenge them to learn new skills and obtain knowledge.

6.3.5. Remote internet accessibility

Only four of the five categories from the technology selection framework are used to assess the feasibility of remote internet accessibility. *Delivery mechanism* is not a relevant subject, since the purpose of these technologies are to create and provide access to communication modalities such as emails.

6.3.5.1. Setting

Remote internet accessibility refers specifically to tangible items, such as router devices used for Wi-Fi connectivity. Therefore, environmental factors should be considered. For example, in areas with high humidity and heat or with a high frequency rainfall, devices should have a robust design to withstand such weather conditions. Another consideration is the location in which the devices will be installed, as well as usage patterns. In areas where infrastructure support is not adequate, such as poor security, provision should be made to implement certain security measures to ensure that the devices are not stolen or damaged. The aspect of power should be considered. Since some devices rely on batteries to draw power, the rate at which these batteries need replacement should be considered. Since several locations' electricity supply is unreliable, batteries should be designed to be minimally reliant on electricity supplies, but rather to rely on renewable sources, such as solar energy.

6.3.5.2. Workforce

Given that remote internet accessibility, within this context, refers to tangible products such as router devices, workforce training is a requirement. Although companies developing these devices put a great deal of effort into simplicity, there will always be a certain degree of training needed. Personnel will have to be taught how these devices should be operated to supply an internet connection, including recharging of these devices. Another aspect that should be considered is technical support. As with any form of internet connectivity network, technical support for remote internet accessibility technologies is essential. Some companies provide some form of technical assistance, via email correspondence or phone calls. However, maintaining these technical support systems in many different settings may be an obstacle.

6.3.5.3. Meaningful access

According to the researcher of this thesis, there are three significant cost components associated with remote internet accessibility, namely: acquisition, training, and maintenance. The first component is non-negotiable, since several tangible products such as router devices must be purchased in order to create a network of connectivity. Secondly, the cost associated with training a workforce on how to use the remote internet accessibility technologies should be considered. Lastly, the cost of maintaining both the hardware and software associated with remote internet accessibility technologies such as upgrades and updates respectively, should be considered. However, these maintenance costs are negligible in the short to medium term, since these technologies are designed to require few updates and upgrades. If these cost components become too significant, remote internet accessibility technologies may not be a feasible option.

6.3.5.4. Interface

The interface component of remote internet accessibility refers to the integration of the hardware (e.g. router device) into the existing infrastructure. In other words, the workforce must be trained on how hardware devices such as smartphones or computers can be connected to the network provided by the remote internet accessibility technologies. The interface pathway should be designed as simple as possible, to reduce the demand for technical support.

6.3.6. Internet of Things

Each of the five categories from the technology selection framework are used to assess the feasibility of IoT.

6.3.6.1. Setting

IoT refers to intangible software, and relies on tangible items such as computers, smartphones, or tablets to function. Therefore, environmental factors are not applicable for assessing the feasibility of these technologies. Probably the most important factor associated with IoT is internet connectivity. Since IoT functions as a network where information is shared across several platforms, internet connectivity is a requirement. It is the only way through which these networks can function. Therefore, in areas where there is a lack of internet connectivity, IoT is not feasible. Remote internet accessibility can possibly be used in support of IoT to provide the necessary internet connections.

6.3.6.2. Workforce

IoT adoption brings with it a requirement for a substantial amount of training, since the entire technology is based around both hardware and software interaction. Training to operate certain hardware devices such as computers and software platforms will be essential. The adoption of IoT on a large scale depends on significant monetary investments, and constant technical support systems. The lack of available funds to invest in such operations can hinder a large scale implementation. Therefore, small scale implementation of IoT technologies, followed by a gradual adoption of the broader system may be a more feasible course of action since it requires smaller monetary investments over a longer period of time. Another key requirement for the adoption of IoT is constant support from leadership, especially those holding influential positions, in order to encourage the workforce to utilise such systems.

6.3.6.3. Delivery mechanism

One of the several benefits offered by IoT is that it allows for different kinds of communication modalities. Once an IoT system is online, large amounts of information can be shared across several platforms, in both visual and audio configurations. Even though IoT is largely dependent on an internet network, which can be a major obstacle, the benefit of information of several types being shared across many platforms, accessible to nearly anyone, serve as a motivating factor for investments to be made towards the leveraging of IoT.

6.3.6.4. Meaningful access

If there is a lack of the necessary hardware and software, the cost component of IoT may be significant since it relies largely on hardware and software. IoT relies on the integration of several hardware and software products, by making use of complex algorithms that may be difficult to understand by those who are not familiar with IoT technology. Embedded in its name, IoT is also extremely reliant on internet connections. Therefore, in settings where internet networks are poor or non-existing, IoT may not be a feasible option (as mentioned in Section 6.3.6.1).

6.3.6.5. Interface

The interface component of IoT is similar to that of remote internet accessibility technologies i.e. the integration of IoT into the existing infrastructure. Personnel should be trained in navigating the software interfaces of IoT. These interfaces must also incorporate simplistic designs to reduce the demand for technical support.

6.3.7. Mobile technology

Each of the five categories from the technology selection framework are used to assess the feasibility of mobile technology.

6.3.7.1. Setting

Mobile technology refers to tangible technologies that can be used by almost any individual for the main purpose of communication and information sharing. Environmental factors play a significant role in the realm of mobile technologies. Regions where severe weather conditions such as constant rain, or severe heat are often recorded, require robust mobile technologies able to withstand these conditions. Also, the manner in which these technologies will be used should be considered. Robust mobile technologies is once again a suggested requirement since many of these technologies will sustain wear and tear in some way. Another consideration is the existing mobile phone network. Mobile technologies rely on these networks to function. Therefore, in areas where mobile phone networks are not sufficient, mobile technologies are not feasible. Lastly, security measures are needed to protect mobile devices from theft or vandalism.

6.3.7.2. Workforce

Given that mobile technology has reached a rather mature state in several countries and its increased penetration in developing countries' markets, the implementation of mobile technologies does not carry a large burden concerning training. In particular, mobile phones, smartphones, PDA devices, and tablets are user-friendly, reducing the need for constant training in operating these devices. However, in settings where mobile technology is not yet a mainstream technology, training is a requirement. As with many other training requirements, this training will demand monetary resources, since experts in these technologies must be consulted to assist those providing the necessary training. Technical support is another aspect to consider. Regardless of the many benefits offered by mobile technology, it is limited regarding technical issues. Reliable technical support networks will be a requirement to provide technical assistance where needed.

6.3.7.3. Delivery mechanism

Mobile technology offers two distinct communication modalities, namely: audible (phone calls) and textual communication (text messaging) (Chan & Kaufman, 2010). These modalities are already used in several contexts within PV, such as education, reminders and alerts as well as monitoring. Moreover, new generation mobile technologies add more to the existing modalities, such as Bluetooth, cameras and applications. However, these types of technologies that own all these modalities tend to be more expensive than other technologies that without these modalities, which is a cost consideration.

6.3.7.4. Meaningful access

Mobile technology is an extremely popular technology used throughout the world, and is experiencing an increasing penetration in many developing markets (Chan & Kaufman, 2010). Therefore, the cost component of mobile technologies is becoming less of an obstacle towards adopting these technologies. However, some mobile technologies, such as smartphones, are still challenging to obtain due to significant costs to supply on a large scale. Other mobile technologies such as PDA devices that have been used more often in developing countries are more feasible options (at least in the short-term) than the more advanced mobile technologies. In the long-term, efforts should be diverted towards the large-scale adoption of advanced mobile technologies, such as smartphones.

6.3.7.5. Interface

Interface interaction is an important element of mobile technologies. There are several components of interface that should be considered. Arguing that there are individuals working in PV who have limited mobile technology literacy, especially smartphone technology, overly-complicated icons, navigation pathways and menu structures may not be the sought after solution. Instead, these should be designed to be simple enough for any individual, with a certain level of training, to use on a daily basis with ease, without requiring constant support.

6.3.8. User videos

Each of the five categories from the technology selection framework are used to assess the feasibility of user videos.

6.3.8.1. Setting

User videos refer to intangible products that rely on tangible products such as computers or tablets to function. Therefore, environmental conditions are not applicable. However, certain situational factors must be considered. Since one route of accessing user videos is often via the internet, connectivity infrastructures should be sufficient and able to accommodate access to such videos. The other route to access user videos is off-line, and does not rely on internet connectivity. The hardware used to access these videos should be considered. In areas where there is no existing infrastructure to support computers, additional hardware such as tablets or smartphones should be made available. However, these devices cause additional challenges. Security measures should be implemented to protect these devices from theft or damage. Additional security measures for software should also be implemented to ensure data privacy is not breached. Tablets and smartphones are limited due to the requirement of batteries to be charges frequently.

6.3.8.2. Workforce

User videos are developed by experts in a particular field and accessed by others. There is no a significant burden associated with workforce training. A notable requirement is training the workforce in accessing these videos, and ensuring that they have the skills necessary to execute the work taught in the videos. As previously mentioned, these types of training carry a certain financial burden that should be considered. Depending on the level of knowledge of the target audience, technical support may not be a significant factor associated with user videos, since these materials are more than likely maintained by role players with access to the necessary resources. An important factor that may contribute to the successful adoption of user videos is leadership advocacy. Since user videos require the workforce to sacrifice their time, encouragement from management may be needed to motivate the workforce to put in the hours to access and learn from user videos.

6.3.8.3. Delivery mechanism

User videos offer the same communication modalities as online teaching services, except that interactive, real-time interaction is not possible. User videos only offer communication in the form of audio and visual material i.e. videos, that offer users the opportunity to access interactive materials (e.g. the process of navigating a particular software) that will equip them with the necessary skills and knowledge. Even though user videos might be offering less when compared to online teaching services, it can be argued that it is a more feasible option since it does not rely on an internet connection.

6.3.8.4. Meaningful access

A significant cost component associated with user videos is an indirect component, and is not directly related to the videos. In order to access and view these videos, one must have access to some type of hardware (e.g. smartphone, computer, tablet, or laptop). In several settings, these hardware products are not always available. Therefore, when determining the possible impact of user videos in PV, one should consider whether there is access to the necessary hardware to access these videos. Another cost component that should be considered is the cost of purchasing these videos, or purchasing access to these videos, which might be substantial.

6.3.8.5. Interface

The interface component of user videos is identical to that of online teaching services. The materials used in these videos should consider the audience. It should accommodate the level of knowledge and skills of the target audience and challenge their intellect which is needed to provide them with new skills and knowledge about a specific subject such as ADR reporting via a mobile application.

6.3.9. Block chain

Only four of the five categories from the technology selection framework are used to assess the feasibility of block chain. *Interface* is not a relevant subject, since block chain technology, like big data analytics, refers to *behind-the-scenes* software that are not visible to the user.

6.3.9.1. Setting

Block chain is an intangible product functioning beyond the immediate view of the user. Environmental factors are therefore not applicable. The impact of certain situational factors should, however, be considered. Block chain relies on internet connectivity, which suggests that the lack of infrastructure implies that block chain may not feasible. Remote internet accessibility technologies can possibly be implemented to provide internet connections which will allow for the adoption of block chain. Since block chain is still in its infancy (Iansiti & Lakhani, 2017), information technology maintenance may be needed on a frequent basis. Therefore, maintenance support systems should be put in place to ensure that the installed block chain technologies operate efficiently and effectively.

6.3.9.2. Workforce

The adoption of a large scale block chain infrastructure may require a substantial amount of training if the users of the software do not have the required knowledge and skills. Since block chain technology is largely software based, the workforce should be provided with the necessary knowledge to operate these programmes. It should be considered that such training will be largely resource dependent, especially monetary resources. Ongoing technical support should also be provided. In settings where there is no technical support infrastructure, it may be challenging to implement and integrate block chain technologies into the existing system. Lastly, leadership support should be advocated. The adoption of complex systems such as block chain technologies, and in fact any new technology, may experience a certain degree of resistance from the workforce. Therefore, advocacy from those in leadership positions will be required to champion the entire process.

6.3.9.3. Delivery mechanism

Block chain technologies, being a revolutionary innovation, offer many communication modalities, which include textual and audible communication, Bluetooth, camera, applications and internet capabilities. In combination, these modalities can possibly be leveraged to the advantage of nearly any system. These modalities are already enabling an array of functionalities in the healthcare industry, such as low bandwidth data exchange, tracking and monitoring and device synchronisation (Chan & Kaufman, 2010).

6.3.9.4. Meaningful access

Block chain technology is still in its infancy stage, even in developed countries (Iansiti & Lakhani, 2017). Multinational companies such as *PwC* and *Deloitte* have only recently started pilot projects to test the feasibility of block chain technologies (Iansiti & Lakhani, 2017). This results in a substantial monetary investment, especially in developing countries. Therefore, the integration of block chain technologies in a PV system may not receive much attention in the short to medium-term due to the monetary constraints. However, in the long term, when block chain technologies have matured, it may be a feasible option in a PV system.

6.3.10. Non-traditional transportation

Only three of the five categories from the technology selection framework are used to assess the feasibility of non-traditional transportation. *Delivery mechanism* is not relevant, since this transportation is not a new addition, but rather the exploitation of an existing transportation network. I*nterface* is not relevant, since there is no visual interaction with an electronic screen.

6.3.10.1. Setting

Environmental factors should be considered when assessing the feasibility of non-traditional transportation. Is areas where the raining seasons are long, provision should be made for the protection of the contents being transported via bicycles or pushcarts. Due to the frequent rain and possible storms, there may be delays in the delivery of the contents being transported, as well as possible damage to the contents being transported.

6.3.10.2. Workforce

Non-traditional transportation is not severely labour intensive, since existing transportation networks are exploited, ultimately creating job opportunities. A noteworthy training requirement that should be provided is to educate these transporters regarding administration behind the transportation of specific goods, such as preferred routes, locations of facilities, and the paperwork needed for confirmation of delivery. Another consideration is in the form of ownership, where an individual or team should take responsibility of the entire network of non-traditional transportation services.

6.3.10.3. Meaningful access

The need for financial support with regards to non-traditional transportation services depends largely on the existing state of an area. In other words, in areas where locals already have access to bicycles and pushcarts, the noteworthy cost component is associated with the employment of these individuals. On the other hand, if there is a lack of access to bicycles or pushcarts, the cost component becomes significant since there is a lack of access to the required transportation hardware. In such a situation, provision should be made for acquiring these modes of transportation, as well as the employment of individuals.

6.3.11. Mobile applications

Each of the five categories from the technology selection framework are used to assess the feasibility of mobile applications.

6.3.11.1. Setting

There are certain situational factors that should be considered when assessing the feasibility of mobile applications. First, access to the mobile technology (smartphones or tablets) needed to access mobile applications should be assessed. It may not feasible to develop a state of the art application if there is no access to the hardware needed to use that application. Secondly, access to an electricity infrastructure should be assessed, since the devices needed to run mobile applications must be charged on a frequent basis, which can only be done when there is reliable electricity or some form of charging station. The lack of electricity affects the feasibility of mobile applications.

6.3.11.2. Workforce

In many cases, intensive training for the use of mobile applications may not be necessary, since they are designed to be simple and easy to use. The one form of training that should receive attention is at the start of the roll-out of a new mobile application, where users are shown how to use the application. Another form of training would be to educate certain individuals who can act as technical experts to serve as technical support and provide technical assistance to those who might be struggling to use or understand a particular function within the application.

6.3.11.3. Delivery mechanism

The communication modalities offered by mobile applications depend on the development of the application. Some applications offer both audible and visual communication, whereas some offer only one of the two. It can be argued that an application offering both modalities can be more beneficial. However, it depends entirely on the context in which the application is developed, because in some cases it may not be necessary for both modalities.

6.3.11.4. Meaningful access

Since many mobile applications are freely accessible, the cost component to acquire these applications is negligible. However, there is an indirect cost to consider. Since these applications can only be accessed with hardware such as smartphones or tablets, the cost of acquiring these hardware components should be considered. In other words, in areas where there is no access to these types of technologies, the cost component of mobile applications becomes considerably more compared to areas where there is access to the necessary hardware (e.g. smartphones or tablets).

6.3.11.5. Interface

The interface component of mobile applications should receive considerable attention. Since applications are relatively easy to develop and maintain, adjustments can be made to its interface. Many applications make use of a hierarchical menu design, which is simple and easy to understand. The graphics of these application allow for easy navigation and understanding the instructions that should be followed.

6.3.12. Educational television and radio programmes

Only four of the five categories from the technology selection framework are used to assess the feasibility of educational television and radio programmes. *Workforce* is a negligible category since educational television and radio programmes do not require any form of training. These programmes are simply sent to local television and radio stations to be aired to local communities.

6.3.12.1. Setting

One critical situational factor should be considered when determining the feasibility of educational television and radio programmes, which is the local access to televisions and radios. In other words, in areas where access is limited, it may not be feasible to implement education television and radio programmes, since it will not reach a large audience.

6.3.12.2. Delivery mechanism

When referring to the communication modalities offered by educational programmes, a distinction must be made between television and radio. Educational television programmes offer two communication modalities in the form of audio and visual material. Having access to both modalities is advantageous since different kinds of information can be transferred. With reference to educational radio programmes, only audible communication is possible, since there is no visual representation of the information being discussed.

6.3.12.3. Meaningful access

Since the television and radio industry has grown considerably in the last decade, especially in sub-Saharan African countries, the cost component of the education programmes delivered across these platforms is not significant, since there is no need for the provision of televisions and radios on a large scale. However, cost component to be considered is the development of these educational programmes. There may be costs involved with purchasing these programmes for use in a specific area, or purchasing access to these programmes.

6.3.12.4. Interface

The interface component of educational programmes relates largely to those programmes aired across a television network. Many of these types of programmes are designed to be as simple as possible, easily understandable, yet manages to convey an important message. Depending on the message delivered and the mode used (television or radio), the materials on these programmes should be clear and understandable to anyone outside the realm of the context in which the programme was developed.

6.3.13. Wireless application protocol based messaging

Each of the five categories from the technology selection framework are used to assess the feasibility of wireless application protocol based messaging.

6.3.13.1. Setting

The influence of both environmental and situational factors should be considered with regards to WAP based messaging. Firstly, WAP based messaging is done via hardware, such as mobile phones or computers. In areas with high humidity and extended raining seasons, provision should be made for robust hardware, able to withstand these extreme weather conditions. Security measures are also needed to secure the hardware from theft or vandalism. Secondly, with reference to situational factors, access to electricity and mobile networks should be determined, since WAP based messaging hardware is ultimately dependent on these networks. The lack of networks indicates that WAP based messaging may not be feasible.

6.3.13.2. Workforce

WAP based messaging, similar to mobile applications, need some form of training. When such a messaging system is made available, there should be an initial training session provided to educate users on how these systems work, and how it should be used. Provisions should also be made for technical support, which will provide technical assistance on a regular basis.

6.3.13.3. Delivery mechanism

WAP based messaging, depending on the platform used, offer either audible or visual communication, or both. These communication modalities allow users to talk to one another in real-time, and also enable them to share relevant pictures and documents. For example, *MxIt* can be used to easily share pictures and communication between individuals who might not be in the same location in real time.

6.3.13.4. Meaningful access

Access to WAP based messaging may not be a significant cost component, since many of these messaging platforms are freely available. There is, however, an indirect cost consideration. The use of these messaging platforms depends largely on access to hardware such as smartphones or computers. Thus, if there is poor access to these types of hardware, the cost component becomes considerably larger, since provision must be made for these hardware devices.

6.3.13.5. Interface

The interface of WAP based messaging platforms is fairly easy to understand, since it makes use of simple menu structures and navigation pathways. There may be some degree of training required for users to understand these interfaces. This training is mostly a once-off training session, and not regularly required.

6.3.14. Routine assessments

Each of the five categories from the technology selection framework are used to assess the feasibility of routine assessments.

6.3.14.1. Setting

A key consideration with regards to routine assessments is the degree of access to the mode through which these assessments are carried out. In other words, when these assessments are done via computers, the access to computers should be assessed. In areas where there is no widespread access to computers, it may challenging to fully utilise these types of assessments. Additionally, a paper-based system can be used if there is a lack of access to computers.

6.3.14.2. Workforce

A noteworthy training component of routine assessments depends on the mode used to deliver these assessments. For example, if these assessments are done on a computer, users should be provided with training to educate them on navigation (i.e. computer literacy) and completion of the assessments. On the other hand, if a paper-based system is used, the training component is not as significant as that of a computer-based system, since there is minimal interaction with technologies such as computers.

6.3.14.3. Delivery mechanism

Depending on the type of routine assessment, the communication modalities differ. In some cases, for example assessments done on a computer, both audible and visual communication is enabled which, in some cases, allow for a wider range of information to be shared. When considering a paper-based routine assessment system, only visual communication is possible, since there is no provision for audible communication such as videos, which can be an obstacle.

6.3.14.4. Meaningful access

The cost component of routine assessments depends largely on the mode through which these assessments are delivered. For example, if the system is a computer-based assessment, there may be a cost component related to the creation of an online and computer-based platform to be used to conduct these assessments. On the other hand, if it is a paper-based system, the cost component will be structured differently. The need for several provisions such as the printing of hardcopy assessments, as well as the distribution, collection and analysis of these assessments should be considered.

6.3.14.5. Interface

Regardless of the type of routine assessment (computer– or paper-based), the interface component should be assessed carefully. Computer based assessments should have easy-to-understand menu structures and navigation pathways. The icons and graphics used to represent certain types of information (e.g. an envelope icon representing a messaging forum) should also be relevant to ensure that no-one is unclear on how to navigate these assessments. On the other hand, paper-based assessments should also be thoroughly investigated to ensure that there is no ambiguity and uncertainty, which may lead to wrong interpretations of the questions.

6.3.15. Game-based learning

Each of the five categories from the technology selection framework are used to assess the feasibility of game-based learning.

6.3.15.1. Setting

There are both environmental and situational factors to consider when assessing the setting aspect with regards to game-based learning. Firstly, the environmental impact on the hardware used to access these game-based learning platforms should be considered. Provisions should be made to supply robust hardware to areas with severe weather conditions such as high humidity and heavy rainfall. Security measures is also needed to secure these devices from theft and vandalism. A situational factor to consider is the access to electricity infrastructures needed to maintain the hardware. Therefore, in areas with a lack of access to a reliable electricity network, game-based learning may not be feasible.

6.3.15.2. Workforce

In many instances, game-based learning may need routine training sessions to educate users on the use these platforms. Since many of these game-based learning platforms regularly update or change, some form of training should be provided to educate users of the purpose of these games, and show them how the principles taught in these games reflect in real-world applications. A certain degree of technical support may also be needed, since access to games-based learning platforms requires a certain level of computer literacy, which may be a challenge in settings where some individuals may not be computer literate.

6.3.15.3. Delivery mechanism

The communication modalities offered by game-based learning depends on the type of game. In some cases, the game can be designed to contain both visual and audible information, which is in its own way advantageous, since some individuals may learn much quicker with audible and visual communication. Other game-based learning platforms may only offer visual or audible communication, which can be a limiting factor regarding the amount and quality of information shared.

6.3.15.4. Meaningful access

There are two noteworthy cost components associated with game-based learning, namely: the development of the game itself and access to these games. These costs largely depend on the context in which the game-based learning platforms are implemented.

For example, in areas where access to the hardware needed for the learning platforms is not sufficient, provision must be made to supply the hardware, implying that the cost component may become considerably larger.

It is therefore important to consider the context in which these game-based learning platforms are developed, since these context-specific factors govern the cost associated with these platforms.

6.3.15.5. Interface

Game-based learning platforms, which is essentially games on computers or smartphones, should not be too complex. The navigation pathways should be clear and simple to navigate to ensure that the principles contained in these games are correctly interpreted. Another consideration is that the visual contents in the game should be relevant to the subject at hand.

In summary, 15 technologies have been assessed according to *setting, workforce, delivery mechanism, meaningful access*, and *interface*, the categories found in Level 1 and Level 2 of the technology selection framework developed by Chan & Kaufman (2010) (the technology selection framework deemed most applicable for the purpose of this research).

6.4. Refining the technology landscape

Making use of the discussions in the previous section, the 15 technologies identified in Section 5.5.1 and assessed in Section 6.3, are refined to a selected set of technologies that are feasible for implementation in PV. Three distinct exclusion criteria are used to determine which of the technologies are to be excluded from this research, namely: (i) cost; (ii) development-time; and (iii) workforce. These three criteria are based on the opinions of the SMEs consulted during the validation process discussed in Section 6.9. These criteria are discussed in Table 23.

The technologies that are excluded (big data analytics, IoT and block chain) from the selected set of technologies are summarised in Table 24 where their exclusion is briefly motivated. These technologies are primarily excluded due to the need for a significant resources (regarding cost, development-time and workforce-intensity) in the short to medium-term.

Table 23: Exclusion criteria for technology landscape.

Criteria	Description
Cost	If a technology is deemed too resource-intensive to implement on a large scale due to the required monetary investments within the short to medium-term, it is excluded from further research.
Development-time	If it may not be possible for a technology to be developed and adapted towards a specific PV system in a specific setting within the short to medium-term, it is excluded from further research.
Workforce-intensity	If the implementation and operation of a technology would be exceptionally workforce-intensive (requiring a considerable investment towards large scale workforce training, or requiring specific individuals with specific skills) it is excluded from further research.

The selected technologies are RMS, cloud technologies, online teaching services, remote internet accessibility, mobile technologies, user videos, non-traditional transportation, mobile applications, educational television and radio programmes, WAP-based messaging, routine assessments, and game-based learning. Regarding the three exclusion criteria (cost, development-time and workforce-intensity), no significant limitations in the short to medium-term, as well as in the long-term, were identified for any of these technologies in the discussion in Section 6.3. Though some of these technologies, such as RMSs, mobile technologies, and online teaching services do require significant resources, it is argued that the implementation and adoption of these technologies are nonetheless more feasible than is the case for the excluded technologies (big data analytics, IoT, and block chain).

In the subsequent section, the link between the selected technologies and the prioritised root causes (as identified in Section 6.2) is created by describing how the technologies can be used to address the root causes.

Table 24: The technologies excluded from the selected set of technologies.

Technology	Reason for exclusion
Big data analytics	The fact that big data analytics are still only a relatively recent addition in healthcare (Raghupathi & Raghupathi, 2014), raises some cost concerns for implementation in PV, especially in resource-limited settings. Firstly, as stated under the *setting* category, big data analytics is largely dependent on reliable internet networks. In several settings, these types of internet networks may not be available, resulting in a requirement for an increased monetary investment to improve these networks. Secondly, as stated under the *workforce* category, big data analytics are labour intensive, requiring a workforce with advanced skills and knowledge to fully utilise these systems. In several settings, such a workforce is not available, and may require a substantial amount of training which may be a limiting factor due to substantial costs. Given that cost (one of the exclusion criteria) is a major limiting factor, big data analytics are excluded from subsequent research.
Internet of things (IoT)	Similar to big data analytics, and as per definition, IoT relies largely on reliable internet networks (argued under the *setting* category), which in several settings, are not available. Adopting IoT brings with it a significant amount of training requirements (as argued under the *workforce* category). A workforce that may have limited knowledge of the subject are supposed to learn complex interactions between hardware and software. Providing this type of training can be extremely resource intensive, which might deter local governments and investors from supporting such an initiative. Given that cost and workforce-intensity (two of the exclusion criteria) appear to be considerable limitations, IoT is excluded from subsequent research.
Block chain	The main reason why block chain technology is excluded is because it is still in its early stages of adoption in developed countries (as stated under the *meaningful access* category). As reported by Iansiti & Lakhani (2017), companies such as *PWC* and *Deloitte* have only recently started to pilot block chain projects. It is reasonable to expect that it will take a considerable amount of time for block chain technology to be adopted by developing countries. Given that the development time (one of the exclusion criteria) of block chain technologies may be too long, block chain technology is excluded from subsequent research.

6.5. Linking the technologies to the root causes

In order to complete the implementation of Chan & Kaufman (2010)'s technology selection framework, the *potential for application* category in Level 3 is used to describe real-world examples of how the selected technologies can be used to address the root causes in Table 20.

In Table 25, it is indicated which technologies can be used to address which root causes. This analysis is derived from the perception of the researcher, which is based on the rationale drawn from the discussions of the prioritised root causes in Table 20, and the assessment of the selected technologies in Section 6.3. The root causes are shown by numbers, following the same sequential order as in Table 20. There are two key findings that can be concluded from Table 25, these are subsequently identified and discussed.

6.5.1. Shared technologies

As seen in Table 25, the root causes can be addressed with more than one type of technology. Some of these technologies can address the root causes on their own, but most rely on other technologies to support them. For example, mobile applications can be used to address several root causes, however, these cannot function without mobile technology such as smartphones.

6.5.2. Technologies that can address several root causes

Another conclusion that can be drawn from Table 25 is that some technologies can be used to address several root causes. For example, online teaching services, user videos, mobile technology, and mobile applications are all technologies that can address several root causes. Consequently, it can be concluded that it would be beneficial to invest more in these technologies, since doing so is likely to be a cost-effective way to address several root causes.

Table 25: Illustration of which technologies can be used to address which root causes.

		Technologies											
		Resource Management Systems	**Cloud technology**	**Online teaching services**	**Remote internet accessibility**	**Mobile technology**	**User videos**	**Non-traditional transportation**	**Mobile applications**	**Educational television and radio programmes**	**WAP based messaging**	**Routine assessments**	**Game-based learning**
Root causes	**1**	-	-	-	-	X	-	X	X	-	-	-	-
	2	X	-	-	X	X	-	-	X	-	X	-	-
	3	-	-	X	X	-	X	-	-	-	-	X	X
	4	-	-	X	X	-	X	-	-	X	-	X	-
	5	-	-	X	X	-	X	-	-	-	-	X	X
	6	-	-	-	-	X	-	-	X	-	-	-	-
	7	-	-	-	-	X	-	-	X	X	X	-	-
	8	X	-	X	X	X	X	-	X	-	-	-	-
	9	-	-	X	X	-	X	-	-	X	-	-	X
	10	-	-	X	X	X	X	-	X	-	-	-	X
	11	X	-	X	X	X	X	-	X	-	-	-	X
	12	-	-	X	X	X	X	-	X	-	-	X	X
	13	X	-	-	X	-	-	-	-	-	-	-	-
	14	-	X	X	X	X	X	-	X	-	-	-	X

6.6. Possible implementations of technologies

As stated in Section 6.1, the implementation of Chan & Kaufman's (2010) technology selection framework is concluded with the implementation of Level 3, where real world examples of how the selected technologies can be used to address the root causes are described. Subsequently, each root cause is investigated separately to describe how the technologies can be used to address the specific root cause, as described in Table 20.

It should be made clear, as in previous sections, that the discussions that follow are illustrative, and do not represent an exhaustive list of possible solutions to root causes provided.

Root cause #1: There is no designated transportation service to distribute the ADR reporting forms to different facilities

Envisaged technologies: Non-traditional transportation, mobile technologies and mobile applications.

Firstly, in areas where there is a lack of designated transportation services such as delivery trucks or fleet vehicles, ADR reporting forms (those supplied by regulatory authorities) can be distributed with the use of bicycles or pushcarts. The system will work as follows: The ADR reporting forms will be collected from a central point by the individuals on bicycles or pushcarts. Each collection will be signed off to ensure that there is a paper trail to monitor the distribution of the forms. Then, the ADR reporting forms will be transported to the necessary healthcare facilities, where delivery will be confirmed by the recipient. This type of transportation network is already used by one of the world's largest beverage companies, *Coca Cola* (Berry, 2010), whom have proven its success.

The second solution is the adoption of an electronic ADR reporting form. This can be done with the use of mobile applications, in combination with mobile technologies. Electronic ADR reporting removes the need for a distribution network such as the one described earlier, since there are no tangible reporting forms in circulation. A simple solution would be to provide one or two smartphones to healthcare facilities, since it is not necessary to supply smartphones to each healthcare worker.

By making use of a mobile application, if designed correctly, the process of filling in the ADR reporting form will be simplified and much quicker, causing minimal disruption of the overloaded schedules of healthcare workers.

The mobile application also removes the need for data capturing, since the data is already electronically submitted. This will reduce the time spent on the process of converting a paper-based ADR reporting form to an electronic version, which will allow for signal detection to occur much more quickly.

Root cause #2: The users of the form have competing priorities, and simply do not have time to notify the person in charge of re-ordering the ADR reporting forms when stock is depleted

Envisaged technologies: RMS, remote internet accessibility, mobile technologies, mobile applications and WAP-based messaging.

Firstly, RMSs can be implemented to maintain a record of the movement of ADR reporting forms. If maintained, these systems can keep track of the number of ADR reporting forms used, as well as the left-over stock. Such a system will allow anyone to be aware of the ADR reporting form stock levels, enabling them to reorder new forms in time. In areas where there is not a reliable internet network, remote internet accessibility technologies can be used to provide access to internet, which will allow individuals in different locations to access the same RMS.

The second option is using mobile applications, in combination with mobile technologies. Mobile applications can be used in the same way as RMS, except for the use of mobile technologies. RMSs, as described in the earlier section, are accessed via a computer or tablet, whereas mobile applications can be accessed via smartphones. This allows the user to have constant and immediate access to the ADR reporting form stock levels. Mobile applications can also be accessed by anyone, which is beneficial in the case where the individual in charge of managing the ADR reporting form stock may be situated in a remote location where healthcare facilities may have difficulties to communicate.

Lastly, WAP-based messaging can be used to partially address this issue. Notwithstanding that WAP-based messaging cannot be used as a RMS, it can be used to address the issue of communication. By making use of these communication platforms, healthcare facilities can constantly communicate with their ADR reporting form supplier.

Root cause #3: The individuals responsible for coordinating the deliveries of spontaneous ADR reporting forms are not sufficiently trained to execute these tasks

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, game-based learning and routine assessments.

Firstly, online teaching services can be used to provide essential training to these individuals. These teaching services replace the need for a physical presence of an expert in a remote location who provides face-to-face training. Rather, training videos can be accessed via the internet, at any time and in any location. This is beneficial since the individuals who need the training can access these videos in their own time, and complete any necessary assessments in the comfort of their own workplace. Remote internet accessibility technologies can be used in support of online teaching services to provide access to internet in areas where it might be lacking.

The second option is similar to online teaching services, except that it does not require access to an internet connection. Physical copies of user videos can be distributed to different locations and accessed by those who might need the training.

The final option is with the use of game-based learning, where individuals are provided with the training in a gaming format. These types of learning platforms allow the user to learn several real-world processes in a virtual world, and allow them to understand the implications their actions might have on an overall system. In the end, individuals will be equipped with key skills that they can leverage in their daily tasks of ADR reporting form management.

In support of all three of these possibilities are routine assessments, which allow for periodic evaluation to be done in order to determine whether the individuals who are coordinating the delivery of spontaneous reporting forms have gained the necessary experience in managing ADR reporting forms. These assessments can be done in several ways, such as paper-based or using a computer, and can therefore accommodate the specific resource availabilities.

Root cause #4: Key stakeholders are not aware of the health impact of PV on the healthcare system

Envisaged technologies: Online teaching services, remote internet accessibility, routine assessments, user videos and educational television and radio programmes.

Firstly, online teaching services can be used to provide healthcare workers with the necessary knowledge and awareness of the health impact of PV. If this method is used, it should be made mandatory for healthcare workers to access and review these online learning materials, in order to ensure that they actually read through the necessary materials. Additionally, in areas where there is a lack of access to internet networks, remote internet accessibility technologies can be used to provide access to such networks. Routine assessments or assignments can be used to ensure that all healthcare workers allocate the time and effort to access online teaching services. In order to further motivate these workers, an incentive programme can be implemented whereby healthcare workers receive a certain number of points which will contribute to the yearly mandatory points they must gather in order to remain registered as professional healthcare workers. The continual professional development (CPD) programme, used by professional councils in sectors such as medicine, engineering, and accounting, is an example of such an incentive scheme.

The second option is similar to online teaching services, however, it does not require access to an internet network. Physical copies of user videos could be distributed to different locations, and viewed by relevant parties. Similar to online teaching services, these training videos do not only remove the need for the physical presence of a person knowledgeable within a specific field, but create awareness amongst healthcare workers of the impact of ADRs, which motivate them to support PV.

The third option is largely aimed at public awareness. Since many people in several locations have access to either televisions or radios, educational television and radio programmes can be used to promote PV and create awareness amongst the public. This will not only motivate the public to support and contribute to PV, but will provide them with the necessary knowledge on key aspects such as the source of ADRs, where ADRs should be reported and when to know that an ADR is experienced. An example of an educational television programme that has been broadcasted for a number of years is *Takalani Sesame*, a children's television programme aimed to improve general early childhood education, with a view to school readiness.

Root cause #5: PV is not included in the undergraduate syllabus of tertiary healthcare education

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, routine assessments and game-based learning.

As indicated by Mehta (2017), it is a difficult to change a healthcare syllabus, because there are numerous important aspects of healthcare that deserve attention. Ideally, the solution would be to include PV training in the syllabus of healthcare professionals' training. However, this can be a difficult and time-consuming project. In order to provide the necessary PV education to healthcare workers who have been minimally exposed to PV in their undergraduate training, this training can be provided in their workplace. In this instance, online teaching services can be used. These services, as described in earlier sections, remove the need for healthcare workers to take time away from their full work schedules to physically attend training sessions. Online teaching services allow them access to the necessary materials at any time they prefer while providing them with the necessary PV knowledge. In areas with poor internet networks, remote internet accessibility technologies can be implemented to create access to such networks.

Similar to online teaching services, the second option provide healthcare workers with the necessary PV knowledge in their workplace without requiring access to internet. User videos can be accessed on a computer or smartphone at any time and in any location. This reduces the pressure on healthcare workers, since they can consult these materials at their own discretion. In order to ensure that healthcare workers put in the time and effort to access either online teaching services or user videos, routine assessments can be used to assess whether the workers have gained the necessary PV knowledge such as ADR reporting. A similar point system as discussed under the previous root cause, where healthcare workers are obligated to obtain a certain number of points to maintain registration as professional healthcare workers, can be implemented.

Lastly, PV knowledge can be conveyed via game-based learning platforms. These platforms will provide its users with the necessary knowledge, such as ADR reporting, in a virtual world, which can then be implemented within the real world.

Root cause #6: The ADR reporting forms are overly complicated and are time-consuming

Envisaged technologies: Mobile applications and mobile technologies.

Two possible solutions to this issue are envisaged. As indicated in the study by Khan (2013), the time required of healthcare workers to complete overly complicated ADR reporting forms is a major barrier to ADR reporting. It is therefore important that, in order to motivate healthcare workers to continuously support PV and contribute towards the improvement of ADR reporting, any initiatives should ideally be minimally invasive and non-disruptive concerning their daily routines. In this instance, mobile applications, in combination with mobile technology, can be used. ADR reporting forms can be changed into electronic reporting forms, which can be accessed via mobile applications. Such mobile application based ADR reporting forms are already used. For example a recent development named *WEB-RADR* has been released in Burkina Faso in 2017 (Uppsala Monitoring Centre, 2017).

These forms should also be made up of as few as possible data entries, and should only serve as an initial ADR report. In order to reduce complexity during ADR analyses that takes place during a later stage in the PV system, these initial ADR reports should be somewhat standardised in order to ensure that the same information is being shared from reports originating from different countries. Once a signal has been detected (a number of ADRs have been reported in the same location), a second stage of ADR reporting can commence, where supporting information, related to the already supplied information, is submitted, resulting in a growing ADR report which contains only the relevant information.

Root cause #7: The importance of feedback is not sufficiently advocated

Envisaged technologies: Educational television and radio programmes, mobile applications, mobile technologies and WAP-based messaging.

Three possible solutions to this issue are envisaged. In order to provide feedback to the public regarding ADR reporting, educational television and radio programmes can be used. Instead of printing and distributing tangible reports, these programmes are able to reach a large audience in many different locations. This types of feedback can be done on a monthly or quarterly basis. It is important that periodic feedback is provided in order to reassure the public that any ADRs they might have reported are investigated.

An electronic ADR reporting system can be explored, with the use of a mobile application, in combination with mobile technologies. Not only may such a system reduce the time and effort required for ADR reporting, but it will also enable feedback to be provided through the application, which can be viewed by the reporter at any time.

Another form of feedback, aimed at both the public and healthcare workers, is in the form of WAP based messaging. These messaging platforms can be used to provide feedback to ADR reporters during strategic stages in the PV system, such as a notification when the ADR report is received, and when it is being investigated, and finally when certain steps are being taken to address the particular ADR. WAP based messaging is specifically aimed at resource-limited healthcare facilities who might not have access to online reports. A simple SMS might reassure healthcare workers that their voices are heard (their ADR reports are investigated), which may motivate them to regularly report ADRs.

Root cause #8: There is a lack of ownership of managing the process of data management

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, RMS, mobile applications and mobile technologies.

Firstly, two major causes of concern can be concluded from the seeming lack of ownership. It can either be the case that there is a lack of personnel with the necessary skills and appropriate training to maintain the data management system, or it can be that there are significant time constraints, thus individuals with the necessary and appropriate skills are not able to add PV data management to their schedule. Either way, both of these possible causes must be accounted for. Considering the first case, two possible technologies are envisaged (as illustrated in Table 25) to be implemented to address the issue of a lack of training. Firstly, online teaching services can be used to provide an individual or team with the necessary knowledge and skills to maintain PV data management, which in turn will motivate them to take complete ownership of that system. In areas where there is no access to internet (in order to access online teaching services), remote internet accessibility technologies can be used to provide such networks.

Secondly, similar to online teaching services, user videos can be used to provide training with regards to data management. User videos may be more practical than online teaching services in certain settings, since they do not require access to internet. However, they a drawback associated with using videos is the inability for the viewer to interact with the host in real-time.

In order to address the second cause of the lack of ownership, the issue of limited capacity for clinical activities and responsibilities, two technologies (as illustrated in Table 25) are envisaged to be implemented. Firstly, RMSs can be implemented. These systems maintain not only records of resources, but also allow for data management to be done. With a system that automatically does data management, requiring minimal interaction, individuals are expected to be less deterred from PV data management, and may feel more obliged and comfortable to take ownership of data management.

Another candidate technology is mobile applications, in combination with mobile technologies. Providing stakeholders with access to PV data management systems anywhere and at any time will facilitate the execution of their PV responsibilities and activities since they are not limited concerning the location from where they are able to perform this work. They will also most likely be able to notice any possible warnings or mistakes more rapidly.

Root cause #9: There is a lack of training provided to those who report ADRs

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, and game-based learning, and educational television and radio programmes.

Three possible solutions to this issue are envisaged. With specific aim at healthcare workers, online teaching services can be used to provide them with the necessary knowledge and skills of ADR reporting, such as how to know when a patient is experiencing an ADR, which essential data to submit on ADR reports and where to report ADRs. These services are more user-friendly when it comes to interference with the schedules of healthcare workers since they can view these materials at their own discretion and according to their own schedule. In areas where there is no access to internet networks, remote internet accessibility technologies can be used to provide access to such networks.

The second option, similar to online teaching services, is the use of user videos. These videos are minimally invasive on the schedules of healthcare workers, since it can be viewed at any time. User videos do not require access to internet networks, which in some settings is advantageous.

Lastly, game-based learning initiatives can be used to provide healthcare workers with the necessary skills to report ADRs. These virtual platforms can teach them key aspects of ADR reporting which they can implement in the real world.

Focussing on the public and the patients who can also report ADRs, educational television and radio programmes can be used to educate the public on PV-related activities, such as when to know an ADR is experienced and where ADRs can be reported. Since many people have access to either a television or radio, these educational programmes will be able to reach a large audience in remote locations.

Root cause #10: There are difficulties in providing the necessary training to individuals in remote locations in a timely manner

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, mobile applications, and mobile technologies.

Four possible solutions to this issue are envisaged. This root cause is similar to the one described in the previous section. However, it focusses on the barrier of providing training to the public and healthcare workers in remote locations. In this case, online teaching services, in combination with remote internet accessibility technologies, user videos, and game-based learning can be applied in the same manner as the case previously discussed. The fourth technology added to this list is mobile applications, in combination with mobile technologies. Given the widespread adoption of mobile technologies (not smartphone technology) in sub-Saharan African countries (Data Team, 2017), mobile applications can be used to provide training to those residing in remote locations. By making use of a technology they are familiar and comfortable with, mobile application based training can be used to supply both the public and healthcare workers with the necessary knowledge regarding ADR reporting.

Root cause #11: There is a lack of ownership to manage existing PV-related resources

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, mobile applications, mobile technologies, game-based learning and RMS.

Similar to the eighth root cause, the lack of ownership can be contributed to two possible causes. It can either be that there is a lack of personnel who have the necessary knowledge and skills to manage PV resources, or it is possible that there is simply no one who can add PV resource management to their existing portfolios. As described under the discussion of the eighth root cause in this section, the first cause can be addressed with the implementation of either online teaching services (in combination with remote internet accessibility technologies), user videos, mobile applications (in combination with mobile technologies) or game-based learning. Each of these technologies offer different ways of teaching which can be used to provide essential resource management training.

Another technology that has great potential regarding adding PV resource management to the schedule of an individual or team, is a RMS. These systems maintain electronic records of all the resources available to PV activities, and also track their movements, and therefore require a minimal degree of intervention. Therefore, if RMSs are well maintained and updated, resource management would be much simpler and less invasive to the overloaded schedules of healthcare workers.

Root cause #12: Lack of training to educate PV personnel on how available resources should be used

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, mobile applications, mobile technologies, game-based learning and routine assessments.

There are several different forms of training that can be provided to individuals in order to provide them with the necessary knowledge on how to fully utilise PV resources such as ADR reporting forms, computers and smartphones. Online teaching services (in combination with remote internet accessibility technologies), user videos, mobile applications (in combination with mobile technologies) or game-based learning are all technologies that remove the need for face-to-face interaction by providing training which can be accessed through computers, smartphones, or tablets. All these technologies are marginally invasive i.e. slightly interferes with the daily routine of healthcare workers. Additionally, and in support of these training platforms, routine assessments, which can either be paper– or computer based, can be used to assess whether or not healthcare workers have dedicated the time and effort to learn using the aforementioned learning technologies.

Root cause #13: There is no resource management system in place to manage existing resource inventories

Envisaged technologies: RMS and remote internet accessibility.

One possible solution to this issue is envisaged, namely RMSs. These systems, if well maintained, simplify the process of PV resource management by monitoring the available resources and keeping track of the movement of resources. These types of systems can also be accessed by anyone in any location, provided that there is access to an internet network, which can be provided by remote internet accessibility technologies. This can be beneficial in several ways. For example, the distribution centre for ADR reporting forms can simply log on to the RMS of a healthcare facility, check their available ADR reporting form stock, and start distributing more forms to the facility if necessary. Another instance is where the system keeps track of the available PV resources. For example, the system keeps record of who might be using a smartphone intended for ADR reporting. If something were to happen, such as vandalism or the item is lost, the individual who last used the smartphone can be tracked down.

Root cause #14: PV personnel are not sufficiently trained in using existing platforms

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, mobile applications, mobile technologies, game-based learning and cloud technologies.

The platforms referred to in this case are information sharing platforms such as emails, chatrooms, or blogs. Each of these platforms allow for different parties to communicate with one another and share relevant information. In order to provide training to healthcare workers, especially in areas where they are not familiar with these platforms, three different technologies can be used, namely: online teaching services (in combination with remote internet accessibility technologies), user videos or game-based learning. Each of these technologies, as mentioned in earlier sections, removes the need for face-to-face interaction. It also reduces the degree of interference in the daily routine of healthcare workers, since they can access these training materials at their own discretion. The one technology that can also, to a certain extent, be used to simplify the process of information sharing is cloud technology. These technologies are freely available to the public and can be used to share large amounts of data, such as ADR reports.

6.7. Concluding remarks of the link between the root causes and the technologies

In conclusion, a link between the prioritised root causes (shown in Table 20) and the selected technologies (identified in Section 6.4) have been created. It is clearly stated which of the selected technologies can possibly be used to address the prioritised root causes in this research. In most cases, there are several technologies (and combinations of technologies) that can be used to address the root causes, showing the potential of a wide range of technologies that can be investigated for implementation.

Subsequently, and in conclusion of the implementation of Chan & Kaufman's (2010) technology selection framework, the second category in Level 3, *research needs*, is addressed by providing some examples of existing studies conducted in the use of technology in PV.

6.8. Existing research in the technology landscape and pharmacovigilance

In order to provide further empirical evidence of the implementation of technology in PV, the *research needs* category in Level 3 of Chan & Kaufman's (2010) technology selection framework is used. Level 3 of Chan & Kaufman's (2010) technology selection framework entails an investigation into both existing research and implementations (case studies) of the technologies in the healthcare and PV industry, as well as an investigation into specific research needs that should be pursued to further support the existing research according to the user of the framework.

6.8.1. Research needs

There are several research needs (opportunities) that will contribute to the successful adoption of technology in PV. These research opportunities are subsequently discussed.

6.8.1.1. Further research to assess the existing conditions

There is a need for further research regarding the assessment of the current landscape of PV systems. These research initiatives should be done within the context of the categories found in Chan & Kaufman's (2010) technology selection framework, namely: setting, workforce, delivery mechanisms, meaningful access and interface. These categories, all used to assess the feasibility of the technologies identified in this research, should be used to determine the condition of the existing infrastructure within countries. In other words, research should be conducted to, considering for example the setting, determine the existing state of electricity and internet infrastructures. If it is found that these infrastructures are reliable, then it can be concluded that the technologies can possibly be implemented within these settings.

6.8.1.2. Study of existing technologies in pharmacovigilance

There are several existing studies investigating the role of technology in PV, some of which are investigating the effects of some of the technologies identified in this research. Some studies are exploring the use patterns of several technologies in developing countries, focussing on the effect it might have on the overall population health (Donner, 2008; Mishra & Singh, 2008). There is emerging research on the effect of mobile technology in PV, with a recent report by the UMC indicating the effect of mobile application-based ADR reporting (Uppsala Monitoring Centre, 2017). Closely related to this report is a study that investigated the level of understanding of simple hierarchy structures found on mobile applications amongst a specific group of South Africans (Chan & Kaufman, 2010).

Other well-known technologies that are currently used in PV are *VigiBase* (a drug safety data repository owned by the WHO), *VigiRank* (a "*data-driven predictive model for emerging safety signals*"), and V*igiGrade* ("*a tool to identify well-documented individual case reports*") (Caster *et al*., 2017; Bergvall *et al*., 2014).

6.8.1.3. Research needs relating to the excluded technologies in this research

Additionally, there is a research need, or rather opportunity, for the development and preparation of the three technologies excluded in this research, namely: big data analytics, IoT, and block chain technologies. These represent a generation of technologies that are changing the way technologies can be leveraged in the modern world. As mentioned in earlier sections, these technologies are used by several industries and businesses, and have already delivered several benefits, such as increased data privacy (block chain), technology synchronisation (IoT), and data mining (big data analytics). As a result, there is a need for further research that investigates how these technologies can be leveraged towards PV systems. The functionalities offered by these technologies hold great promise for PV, and can be leveraged towards PV, including areas such as ADR reporting (IoT), signal detection (big data analytics) and patient information protection (block chain).

6.8.1.4. Research needs related to socio-technical aspects

A key aspect of all the technologies discussed in this research that should be prioritised in future research relates to the socio-technical side of the implementation of these technologies in PV. The socio-technical aspect marries the social and technical sides of technologies. In other words, socio-technical studies determine how technologies should be designed in order for it to be accepted by a certain group of stakeholders. For example: if a technology is extremely complex to operate, a community in a remote area might not use this technology, since they are not familiar with it, and lack the technical capacity to do so. It is critical that the work building on this research incorporates the socio-technical aspect of the implementation of the suggested technologies in PV.

6.8.2. Conclusion: Research needs

In conclusion, it is clear that there are several opportunities for investigating the effect technology can have on PV. It is believed that research into the opportunity areas identified will contribute towards the improvement of PV systems, especially in resource-limited countries.

Subsequently, in order to validate the link drawn between the prioritised root causes and the selected technologies, formal, structured validation strategy is implemented.

6.9. Validating the link between the technologies and root causes

As stated in Section 1.9.5, a formal, structured validation strategy is used to validate the link drawn between the technology landscape and the prioritised root causes. Nine SMEs were contacted for the purpose of validation, However, only five (details of the SMEs are provided in Table 26) managed to respond and provide feedback. The document that was sent to each SME containing the request for validation as well as the required information is shown in Section E.2 in Appendix E. Subsequently, their feedback is summarised, showing the concerns that were raised by the SMEs, and how these concerns were addressed in the research.

6.9.1. Replacing paper-based systems with electronic ADR reporting

A concern was raised that applies to the suggestion made in the first root cause, where it is suggested that a ADR reporting form delivery system, similar to that used by *Coca-Cola*, is used to provide ADR reporting forms to healthcare facilities. The concern is two-fold. Firstly, it is said that this suggestion is not feasible, since PV systems do not have the access to resources that are comparable to that of a company such as *Coca-Cola*. However, the suggestion made in this research is aimed at resource-limited settings. Contracting local inhabitants with bicycles or push-carts is not resource-intensive and will only require minimal resources in the form of training and payment due to the delivery persons.

Table 26: Occupation and affiliation of SMEs consulted during the validation process.

	Occupation	Affiliation
1	Regional Medical Director (Kenya)	Multi-national pharmaceutical company
2	Member of PV enhancement project for Malaria (Democratic Republic of Congo)	Multi-national pharmaceutical company
3	Medical Affairs Executive and Named Safety Contact (Kenya)	Multi-national pharmaceutical company
4	PV Pharmacist, Deputy National Safety Officer (South Africa and export countries)	Multi-national pharmaceutical company
5	PV Manager (South and Southern Africa)	Multi-national pharmaceutical company

The second part of the concern relates to the nature of the proposed delivery system just mentioned, which is aimed at providing paper-based ADR reporting forms to healthcare facilities. The SMEs argued that it is not feasible to suggest that more paper-based ADR reporting forms be pushed into PV. This is understandable, given that they are resource-intensive. The suggestion made in this research is a short to medium-term solution, and is meant to be adopted by PV systems operating in severely resource-constrained settings. Electronic ADR reporting is the sought after method for reporting in PV and is suggested in this research in the form of mobile applications. However, it is not feasible at this stage to suggest that electronic ADR reporting be adopted in resource-limited settings, given that this will require a considerable amount of resources, many of them related to infrastructure, that are not necessarily currently available. In the long-term, when more resources are provided to these settings, electronic ADR reporting can be pursued.

6.9.2. Security concerns regarding mobile phones

One SME pointed out that vandalism and theft is a problem that has been reported in several healthcare systems where mobile phones were introduced, and it can possibly curb the adoption of mobile phones in PV. This issue has been pointed out in this research (Section 6.3.7), where it is mentioned that the introduction of mobile technologies in resource-limited settings do carry the risk of theft and vandalism. This is an inevitable risk which can only be managed. The introduction of mobile technologies in healthcare systems has proven to be a success. With this introduction, however, it is necessary to consider the risk of theft and vandalism, by introducing security measures to protect the hardware.

6.9.3. Failing to sensitise healthcare workers to advocate and support pharmacovigilance

Another concern that was raised is the fact that HCWs who are at the front line of reporting ADRs are not sensitised to pursue and advocate PV. Consequently, the introduction of electronic ADR reporting may not always be a feasible solution, given that these reporting systems will not be properly used, resulting in under-utilisation and resource-wastage.

This concern is raised in this research. Specifically, in order to sensitise HCWs through PV training and awareness campaigns, the technologies assessed in Sections 6.3.4, 6.3.8, 6.3.12, 6.3.14, and 6.3.15 (online teaching services, user videos, educational television and radio programmes, routine assessments and game-based learning) are all technologies specifically aimed at achieving this particular outcome. Not only are these technologies aimed at HCWs, but they are also aimed at raising PV awareness amongst the public.

6.9.4. Healthcare professionals are desensitised with regards to pharmacovigilance

One SME pointed out that in many sub-Saharan African countries, healthcare professionals are not sensitised with regards to PV. This is not necessarily due to overloaded work schedules, which is a phenomenon that is routinely used as excuse. In fact, healthcare professionals simply fail to support PV. This phenomenon is closely related to Inman's model of ADR under-reporting (discussed in Section 3.10.1), which identifies factors such as complacency, guilt and ignorance as causes for desensitised healthcare professionals.

This particular concern is addressed by one technology that is assessed in Section 6.3.14, namely routine assessments. These assessments can be used as a mechanism to sensitise healthcare professionals who fail to support PV due to reasons previously mentioned.

6.9.5. Dedicated pharmacovigilance personnel

Another concern raised by an SME is that the introduction of some technologies in PV will require dedicated PV personnel that take responsibility for PV-related activities in a healthcare facility. This concern is addressed in this research, specifically in Section 4.6.2. It is mentioned that not all of the challenges in PV can be addressed with technology, but rather finances, business process improvement, managerial changes, or a change in national PV guidelines and policies. Although this research focusses on technology, this concern has been pointed out. Additionally, this is discussed in the opportunities for future research section (Section 7.5), mentioning that a similar research approach (to that used in this research) can be used to investigate how the other challenges in PV can be addressed with management (which includes the appointment of dedicated PV personnel), financial investment and business process improvement.

6.9.6. Target audience for routine assessments

One SME raised a question, rather than a concern, regarding the target audience of the proposed use of routine assessments. It is worthwhile to briefly explain the use of routine assessments. Routine assessments are proposed in this research for the specific goal of sensitising HCWs and professionals to support and advocate PV. Specifically, routine assessments can be used to evaluate whether or not these individuals are actively supporting and pursuing PV activities such as ADR reporting.

6.9.7. Harmonisation of ADR reporting

A recommendation was made by an SME that harmonisation and standardisation of PV reporting is essential. This can definitely be achieved with the adoption of certain technologies in PV. Firstly, mobile technologies and applications can be used to standardise ADR reporting and ensure harmonisation between ADR reports from different settings and contexts. Additionally, the introduction of IoT and big data analytics will contribute to the harmonisation and standardisation of reporting in PV. Although it will still take some time for these two technologies to be adopted by PV, the capabilities they hold can be leveraged to the benefit of PV.

6.9.8. Training requirements of resource management systems

A concern regarding the training requirements for using RMSs has been raised by an SME. The training requirements associated with RMSs have been raised as a factor to consider when implementing these types of systems (specifically in the discussion of the first root cause). Initially, there is no need for complex RMSs and these will consequently not require many resources pertaining to training, making it feasible solutions in resource-limited settings. Once more resources have been devoted towards PV systems that currently operate within resource-constrained settings, more complex RMSs that have additional capabilities can be adopted. Only then will the training requirements become significant. However, as proven by the adoption of RMSs in many other industries, RMSs can be of significant benefit towards PV.

6.9.9. Providing feedback to ADR reporters

The lack of feedback given to ADR reporters is one of the prioritised challenges discussed in this research. There are several technologies that can be used to improve these feedback processes, all of which are identified and discussed in the seventh root cause. Included in the feedback from the SMEs was the statement that emails can also be used to provide feedback to ADR reporters. Although not specifically mentioned in this research, feedback in the form of emails inherently forms part of the recommendation made that electronic ADR reporting (via mobile applications or social media platforms) is needed. When comparing paper-based ADR reporting, feedback in the form of emails is possible, however, this will be time-intensive. Once an electronic ADR reporting system is implemented, automatic email replies and personal communication with ADR reporters will be possible. This will enable timely personal feedback to be provided to ADR reporters, providing them with a sense of contribution which is likely to encourage them to continue reporting and advocating ADR reporting.

6.9.10. Capacity support for pharmacovigilance data management

A suggestions was made that National Regulatory Authorities should be encouraged to invest in Integrated Information Management Systems that link to both paper-based and electronic ADR reporting to enable real-time data analysis and simplify ADR reporter feedback. Recollecting the contents of Section 6.4, three technologies (big data analytics, IoT, and block chain) were excluded from this research, primarily because these technologies are deemed too complex and expensive to feasibly be implemented in PV at present. However, in the future, once more research, investment and has been made in the development of these technologies, it can be adopted by PV. In combination, these technologies (especially IoT and big data analytics) can be used to create the sought after "*Integrated Information Management Systems that link to both paper-based and electronic ADR reporting to enable real-time data analysis and simplify ADR reporter feedback*".

6.9.11. Conclusion: SME validation

Regardless of the fact that only some of the SMEs managed to provide feedback, each of these SMEs operate in PV on a daily basis, and have relevant experience when it comes to the improvement of PV. Consequently, their feedback serves as validation of the final recommendations of this research.

6.10. Chapter 6 conclusion

The foundation of this chapter is the implementation of Chan & Kaufman's (2010) technology selection framework. Firstly, 14 prioritised root causes are used to describe the clinical domain within the PV landscape. This provides some clarity on what exactly is implied by each root cause, and also highlights some key issues that should be addressed. This is followed by an investigation into the technology landscape, where five of the categories found in Level 1 and Level 2 of Chan & Kaufman's (2010) technology selection framework (*setting, workforce, meaningful access*, *delivery mechanisms* and *interface*) are used to assess these technologies. This allows for several benefits and shortcomings to be highlighted, which are used to determine which technologies are feasible for implementation in PV. Following the implementation of this stage, the technology landscape is refined to a list of candidate technologies that can be implemented in PV. In order to complete the implementation of Chan & Kaufman's (2010) technology selection framework, Level 3 is implemented. In particular, the *potential for application* category is used to describe real-world implementations of how the technologies can be leveraged towards the addressment of these root causes. Additionally, the *research needs* category, found in Level 3, is used to briefly provide some examples of existing studies conducted in the implementation of technology in PV and to highlight some areas where further research would be beneficial.

The chapter is concluded with a validation process, where SMEs provided input and feedback on the technologies that are suggested as offering potential solutions to the prioritised root causes identified in this research. The SME feedback is summarised, to provide an overview of the most salient concerns and suggestions. Included in these summaries are discussions of how each of these concerns and suggestions are addresses in this research.

Chapter 7: Recommendations and future research

In Chapter 6, the link between the PV challenge landscape and the technology landscape is made, as discussed in Chapter 1. In particular, real-world implementations are provided to indicate how a combination of certain technologies can be leveraged towards the root causes of several of the challenges found in the PV challenge landscape. This shows that there are areas for opportunity in the PV challenge landscape for the intervention of technology to address the challenges faced on a daily basis. Subsequently, this chapter serves as the conclusion to this research. A project summary, contributions to the PV industry, key contributions offered to academic literature, achievement of the research objectives, and opportunities for future research are provided and discussed.

7.1. Project summary

In Chapter 1, a background and introduction to PV, the research rationale, problem statement, research aim and objectives, limitations and assumptions, validation strategy, and research methodology are provided and discussed. Chapter 2 deals with the initial key literature investigation into PV. Contextual information regarding PV and PV as a system is provided. Additionally, the PV challenge landscape is identified, conceptualised and elaborated on. In Chapter 3, the challenges that constitutes the PV challenge landscape is prioritised, refining the PV challenge landscape to a selected set of prioritised challenges that form the focus of the subsequent research. Each of the prioritised challenges are investigated in sufficient detail to provide a clear understanding of each challenge. The investigation of translation strategies that can be used to translate the prioritised PV challenge landscape to root causes comprises the first part of Chapter 4. This is followed by the implementation of a two stage translation process, where a PV value chain analysis, and the 5Why method, in combination with fishbone diagrams, are used to identify several root causes to which the prioritised PV challenges can be attributed to. In order to further focus the scope, the root causes that are deemed ones that could be addressed by technology were identified. After which, this set of root causes was subjected to a second prioritisation exercise during which a number of specific root causes were prioritised by SMEs. Chapter 5 consists of two parts, the first of which is an investigation into the technology selection framework landscape, where a specific framework is selected as an appropriate framework to be used in this research. The second part of Chapter 5 is geared towards an investigation of the technological landscape, where numerous technologies are identified and defined. Combining the results from Chapter 4 and Chapter 5, resulting in the foundation of Chapter 6, i.e. the implementation of the selected technology selection framework. Several categories are used to assess the prioritised root causes and the technological landscape. Consequently, specific technologies, that are deemed feasible for implementation in PV, are selected. In conclusion, the technological landscape and the prioritised root causes are linked in Chapter 6. Furthermore, each of the root causes are investigated separately, and real-world implementations of the selected technologies are provided to indicate how such technologies can be used to address the PV challenge landscape.

7.2. Research contributions to the pharmacovigilance industry

In this research it was found that a challenge faced within PV is the ability to fully comprehend the challenges PV systems face on a daily basis, and to determine how these challenges can be addressed with technology. The PV challenge landscape is ever-expanding, and the effects of the challenges are intensifying, burdening PV systems from achieving universal drug safety. As a possible solution, the feasibility of the intervention of technology to address the PV challenge landscape is investigated in this research. The solution developed in this research, is comprised of several stages, all of which contribute to addressing the barrier of understanding the true effects of the PV challenge landscape and determining how these effects can be alleviated by means of employing technology.

In this research, seven challenges (culture, transparency, partnerships, insufficient resources, technical capacity, country-specific factors and ADR under-reporting) were highlighted as priority in PV. It can be argued that these challenges are a true representation of the PV challenges that should be of priority in the real world, since these challenges were validated by SMEs.

Translating PV challenges to a lower level of abstraction is a useful step in uncovering the operational-level root causes that can potentially be addressed by technological solutions. A translation strategy, consisting of two stages, that allows one to achieve this is recommended in this research. In the first stage, the prioritised PV challenge landscape is evaluated according the stages of the PV system with the use of a PV value chain analysis, in order to understand the meaning and effect of the challenges in each stage of the PV system. During the execution of this stage, it was found that the challenges have different meanings and impacts in the different stages of the PV system, and are either based on managerial practices, business process restructuring, financial investment or technological intervention. With specific focus on the challenges that are based on technological intervention, the second stage of the translation strategy was implemented in order to identify the root causes of these challenges. It was found that there are several root causes to many of these challenges, all of which will affect the PV challenge landscape differently. Additionally, it can be concluded that the root causes identified in this research represent the root causes found in the real world, since it was validated by several SMEs. The SMEs also indicated that 14 of these root causes should be of priority in this research.

Provided with the prioritised root causes of the prioritised PV challenge landscape, PV systems can continue by determining how technologies can be leveraged towards addressing these root causes, which can be achieved with the implementation of Chan & Kaufman's (2010) technology selection framework. Several frameworks were investigated in this research, however, it was found that this specific framework is appropriate for implementation within a PV context. Prior to the implementation of this framework, candidate technologies should be identified. Fifteen technologies were identified in this research with the use of literature and a focus group. Each of these technologies can somehow be leveraged towards PV. In order to determine which of the technologies are feasible for implementation in PV, Chan & Kaufman's (2010) technology selection framework is used. Making use of the categories found in the framework (*setting*, *workforce*, *meaningful access*, *delivery mechanism* and *interface*), each of these 15 technologies were assessed, highlighting several elements that should be considered. These assessments were then used to refine these technologies to a list of 13, all of which are deemed feasible for implementation in PV. Additionally, the clinical domain category, also found in Chan & Kaufman's (2010) technology selection framework, was used to assess the prioritised root causes, clearly defining the meaning of each. Ultimately, this allowed for the link to be established between the root causes and the technologies, where it was shown which technologies can be used to address the respective root causes.

In conclusion, this research contributes to the PV industry in several ways. Not only can the final results of the research i.e. the link between the technology landscape and the PV challenge landscape root causes, be extrapolated into the existing PV system, many of the tools and techniques used in the research can be adopted by the industry. The prioritisation exercise, translation strategy, technology selection framework, and proposed technologies holds value for PV systems, and can facilitate a comprehensive understanding of the meaning and effect of the challenges faced in PV. In addition, the outlined approach can be implemented to determine which technologies can be leveraged towards the addressing the challenged faced by PV systems.

7.3. Key contributions offered to academic literature

There are several key contributions of this research that contribute to the existing academic literature, which include:

- The results of the systematic literature review constitutes a holistic overview of the challenges found in the PV challenge landscape.
- The prioritisation of the PV challenge landscape provides guidance on challenges towards which research efforts should be addressed. Since two sources are used to prioritise the PV challenge landscape (SMEs and the PV system and PV challenge landscape matrix), it can be concluded with fair certainty that these selected challenges should be of priority in PV.
- Proceeding the prioritisation of the PV challenge landscape, this research also proposes a translation strategy that can be used to translate the PV challenge landscape to a lower level of abstraction in order to identify root causes to these challenges. This translation strategy is also implemented in this research, with the likely root causes of a number of the prominent challenges in the PV landscape being identified.
- Lastly, potential technological solutions to some of the prominent root causes of challenges in the PV challenge landscape is investigated using a technology selection framework. It is believed that this is a novel contribution to PV literature, offering a new perspective on addressing the PV challenge landscape.

7.4. Achieving research objectives

The research aim and objectives, as set out in Chapter 1, have successfully been achieved in this research. In Table 27, the chapters, sections and page numbers where each of the objectives have been achieved are shown.

Table 27: Research aim and objectives achieved.

	Research aim and objectives	Chapter and Section	Page number
i.	Conduct a comprehensive literature review to:	Chapter 2	12-25
a.	Comprehensively understand the various sub-systems of which PV systems are comprised of.	2.1-2.3	12-14
b.	Identify and understand the challenges faced in the PV industry.	2.4-2.10	14-24
ii.	Prioritise the PV challenge landscape to allow for more in-depth research:	Chapter 3	27-48
a.	Clearly define and understand the prioritised PV challenge landscape.	3.3-3.10.3	32-48
iii.	Develop a translation strategy that can be used to translate the prioritised PV challenge landscape, by doing the following:	Chapter 4	49-74
a.	Investigate the methodologies that can be used to translate challenges from a high level of abstraction to a lower level.	4.3-4.3.5	51-55
b.	Select appropriate methodologies that can be used for this translation process and describe how each will be used.	4.4-4.4.2	56-59
c.	Implement the translation strategy in order to identify root causes to the prioritised PV challenges landscape.	4.5-4.6.2	60-69
d.	Validate and prioritise the root causes with SMEs in order to determine which root causes should be the main focus point of this research.	4.6.3	74
iv.	Investigate the technology landscape in order to:	Chapter 5	76-91
a.	Identify a technology selection framework that is applicable for implementation within the PV context.	5.2-5.4	77-78
b.	Identify a number of technologies that can possibly be implemented within PV.	5.5-5.5.2	83-91
v.	Implement the selected technology selection framework in order to assess the prioritised root causes and the technology landscape;	Chapter 6	92-143
a.	Establish the link between the technology landscape and the prioritised root causes by describing how the technologies can be used to address these issues.	6.6	127-137

7.5. Opportunities for future research

It is recommended that the following opportunities for future research can be explored, since each will build on this research:

i. Taking a context-specific perspective, use the technology selection framework to determine which technologies can be leveraged in addressing context-specific PV challenges. This will include an investigation into the existing technology infrastructure to determine the scale of technological implementation, i.e. to determine which technological infrastructures should be implemented in addition to the adoption of the technologies identified in this research.
ii. Determine how the technologies identified in this research can be leveraged with regards to large scale adoption and financial investment by, amongst others, developing a cost model to determine the cost implications of these technologies.
iii. Investigate the technological landscape in greater detail to determine more specifically the model types of the identified technologies that could be implemented to address the challenges in the PV challenge landscape. Given the above recommendation regarding including a context-specific perspective, this can be also be investigated within a specific context.
iv. Establish how the impact of the technologies can be monitored and evaluated to determine whether the sought after results are obtained.
v. Expand the research focus from ADRs to adverse events following immunisation (AEFIs), especially within a sub-Saharan African context. AEFIs and ADRs differ in many ways, and as a result will entail different root causes, requiring that different groups of technologies are needed to address the challenges associated with AEFIs.
vi. It has been highlighted in this research that not all challenges can be addressed with technology. Using a similar research approach, address the PV challenge landscape by redirecting focus away from technology, focusing instead on aspects such as finance, business processes, and management.

7.6. Research conclusion

Technology has developed considerably over the last couple of decades, and has become an integral part society and of many organisations. Given that technology plays such a significant role in the modern society, it is of utmost importance for the value of technology in PV to be realised, especially in resource-limited countries. To address the challenges burdening PV systems, it is evident from the recommendations made in this research that existing technologies can be used. Not only are the majority of the technologies identified in this literature already in existence, they are also already well developed, with a higher degree of access compared to a decade ago. Moreover, the three technologies (big data analytics, IoT, and block chain) excluded from this research hold substantial potential for PV, and can most definitely benefit PV systems once further developed.

When healthcare systems, especially those within resource-limited countries, adopt technology on a large scale, PV systems might benefit significantly. Since PV is a component of the healthcare system that few patients or members of the general public are likely to have interacted with, it can easily be overlooked when investment in the healthcare sector is made. By leveraging technology in healthcare, and proving its benefit and value, investors may be more likely to invest in the adoption of technology in PV.

The value of technology in PV is already starting to gain publicity in several countries; however, many of these countries operate within resource-rich environments. Although this is a positive outcome, one can argue the case that PV systems in resource-limited countries are significantly more important, because of large scale disease burdens such as HIV, tuberculosis and malaria. It is important for the gap between PV systems in developing– and developed countries to be narrowed. This will allow for more research to be conducted in the adoption of technology in PV systems in these countries, which will ultimately contribute to the realisation of universal drug safety.

7.7. Chapter 7 conclusion

This chapter serves as conclusion to this research. It provides the project summary, research contributions to the PV industry, key attributes offered to academic literature, sections and page numbers where the research objectives were achieved, opportunities for future research, and the research conclusion.

References

Abubakar, A.R., Ismail, S., et al., 2015. Comparative study on drug safety surveillance between medical students of Malaysia and Nigeria. *Therapeutics and Clinical Risk Management*, pp.1015–1025.

Abubakar, A.R., Chedi, B.A., et al., 2015. Perception of Nigerian medical students on adverse drug reaction reporting. *Journal of Advanced Pharmaceutical Technology and Research*, 6(4), pp.154–158.

Abubakar, A.R. & Haque, M., 2016. Pharmacovigilance Practice : The Current Challenges and the Gaps in the Medical Students ' Curriculum. *Journal of Applied Pharmaceutical Science*, 6(05), pp.210–215.

Abubakar, A.R., Simbak, N. Bin & Haque, M., 2015. Pharmacovigilance Study : Awareness among Medical Students of a New Medical School of Malaysia. *International Journal of Pharmaceutical Research*, 7(1), pp.83–88.

Agbabiaka, T.B., Savović, J. & Ernst, E., 2008. Methods for causality assessment of adverse drug reactions: a systematic review. *Drug Safety*, 31(1), pp.21–37. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18095744.

Al-Alawi, A.I., Al-Marzooqi, N.Y. & Mohammed, Y.F., 2007. Organizational culture and knowledge sharing: critical success factors. *Journal of Knowledge Management*, 11(2), pp.22–42. Available at: http://www.emeraldinsight.com/doi/10.1108/13673270710738898.

Alan, W., 2001. Understanding organisational culture and the implications for corporate marketing. *European Journal of Marketing*, 35(3/4), pp.353–367.

Al Dweik, R. et al., 2016. Factors affecting patient reporting of adverse drug reactions: a systematic review. *British Journal of Clinical Pharmacology*, (November).

Aljadhey, H. et al., 2015. A qualitative exploration of the major challenges facing pharmacovigilance in Saudi Arabia. *Saudi Medical Journal*, 36(9), pp.1097–1102.

Armstrong, S., 2013. What Are The Advantages And Disadvantages Of Online Learning? *eLearning Industry*. Available at: https://elearningindustry.com/advantages-and-disadvantages-of-online-learning [Accessed January 30, 2018].

Aronson, J.K., 2012. Balanced prescribing – principles and challenges. *British Journal of Clinical Pharmacology*, 74(4), pp.566–572.

Avorn, J. & Schneeweiss, S., 2009. Managing Drug-Risk Information — What to Do with All Those New Numbers. *The New England Journal of Medicine*, 361(7), pp.647–649.

Baiju, N.T., 2017. 5 advantages and disadvantages of Cloud Storage. *Big Data Made sSmple*, pp.4–6. Available at: http://bigdata-madesimple.com/5-advantages-and-disadvantages-of-cloud-storage/ [Accessed January 30, 2018].

Bandekar, M.S., Anwikar, S.R. & Kshirsagar, N.A., 2009. Theories of attempted suicide: Should they differ from theories of completed suicide? *Pharmacoepidemiology and Drug Safety*, 6(5), pp.188–191.

Barnieh, L., Donaldson, C. & Manns, B., 2014. Health care prioritization : a clinician's duty. *Canadian Journal of Kidney Health and Disease*, 1(27), pp.1–5.

Baroudi, R., 2014. Key performance indicators: Winning tips and common challenges. *EY Performance Journal*, 6(2), pp.36–43.

Bau, L.M.S. et al., 2012. Organizational ergonomics of occupational health methods and processes in a Brazilian oil refinery. In *Work 41*. pp. 2817–2821.

Beckmann, J. et al., 2014. Teaching Pharmacovigilance: the WHO-ISoP Core Elements of a Comprehensive Modular Curriculum. *Drug Safety*, 37(10), pp.743–759.

Bellot, J., 2011. Defining and assessing organizational culture. *Nursing forum*, 46(1), pp.29–37.

Beninger, P., 2017. Opportunities for Collaboration at the Interface of Pharmacovigilance and Manufacturing. *Clinical Therapeutics*, 39(4), pp.702–712. Available at: http://dx.doi.org/10.1016/j.clinthera.2017.03.010.

Bergvall, T., Niklas Norén, G. & Lindquist, M., 2014. VigiGrade: A tool to identify well-documented individual case reports and highlight systematic data quality issues. *Drug Safety*, 37(1), pp.65–77.

Berry, S., 2010. How Coca-Cola's distribution system works. *ColaLife*. Available at: http://www.colalife.org/2010/12/19/how-coca-colas-distribution-system-works/ [Accessed February 26, 2018].

BEUC, 2008. A STRONG , TRANSPARENT AND PROACTIVE PHARMACOVIGILANCE SYSTEM. , pp.1–8. Available at: www.beuc.eu.

Booth, N., 2003. Can business benefit from remote access? *ComputerWeekly.com*. Available at: http://www.computerweekly.com/feature/Can-business-benefit-from-remote-access [Accessed January 31, 2018].

Boundless Management, 2016. Strategic, Tactical, and Operational Control. *Boundless Management*. Available at: https://www.boundless.com/management/textbooks/boundless-management-textbook/control-8/types-of-control-62/strategic-tactical-and-operational-control-313-3960/ [Accessed August 4, 2017].

Brugha, R. & Varvasovszky, Z., 2000. Stakeholder analysis: a review. *Health Policy and Planning*, 15(3), pp.239–246. Available at: https://academic.oup.com/heapol/article-lookup/doi/10.1093/heapol/15.3.239.

Brundage, M.P. et al., 2017. Smart Manufacturing Through a Framework for a Knowledge-Based Diagnosis System. In M. P. Brundage, ed. *ASME 2017 International Manufacturing Science and Engineering Conference*. Los Angeles: Research Gate, pp. 1–9. Available at: http://proceedings.asmedigitalcollection.asme.org/proceeding.aspx?doi=10.1115/MSEC2017-2937.

Bulsuk, K., 2009. Using a Fishbone (or Ishikawa) Diagram to Perform 5-why Analysis. *Toyota Production System*. Available at: http://www.bulsuk.com/2009/08/using-fishbone-diagram-to-perform-5-why.html [Accessed October 4, 2017].

Buse, K., Mays, N. & Walt, G., 2005. *Making Health Policy* N. Black & R. Raine, eds., Berkshire, England: McGraw-Hill Education.

Callréus, T., 2011. The New EU Legislation on Pharmacovigilance and Changing Models for Drug Development. *Drug Safety*, 34(6), pp.529–531.

Caster, O. et al., 2017. vigiRank for statistical signal detection in pharmacovigilance: First results from prospective real-world use. *Pharmacoepidemiology and Drug Safety*, 26(8), pp.1006–1010.

Chan, C. V. & Kaufman, D.R., 2010. A technology selection framework for supporting delivery of patient-oriented health interventions in developing countries. *Journal of Biomedical Informatics*, 43(2), pp.300–306. Available at: http://dx.doi.org/10.1016/j.jbi.2009.09.006.

Cheaib, N., 2016. Pharmacovigilance in Clinical Trials: Current Practice and Challenges. *Accountability in Research*, 23(1), pp.23–30. Available at: http://www.tandfonline.com/doi/full/10.1080/08989621.2014.956868%0Ahttp://www.ncbi.nlm.nih.gov/pubmed/26528639.

Chmutova, I., 2015. Bank’s financial management technologies forming at strategic and operational levels. *Economic Annals-XXI*, 9, pp.73–77.

Coffey, H., 2007. Digital game-based learning. *Learn NC*. Available at: http://www.dfpp.univr.it/documenti/Avviso/all/all036209.pdf [Accessed February 26, 2018].

Cognizant, 2012. *The Future of Pharmacovigilance : Five Imperatives that Will Drive Improved Business Outcomes*, Available at: https://www.cognizant.com/industries-resources/life_sciences/The-Future-of-Pharmacovigilance-Five-Imperatives-that-Will-Drive-Improved-Business-Outcomes.pdf.

Cohn, J. et al., 2017. When falsified medicines enter the supply chain : Description of an incident in Kenya and lessons learned for rapid response Published by : Palgrave Macmillan Journals Stable URL : http://www.jstor.org/stable/43287941 When falsified medicines enter the su. *Journal of Public Health Policy*, 34(1), pp.22–30.

Croxton, K.L. et al., 2001. The Supply Chain Management Processes. *The International Journal of Logistics Management*, 12(2), pp.13–36.

Data Team, 2017. In much of sub-Saharan Africa, mobile phones are more common than access to electricity. *The Economist*. Available at: https://www.economist.com/graphic-detail/2017/11/08/in-much-of-sub-saharan-africa-mobile-phones-are-more-common-than-access-to-electricity [Accessed July 16, 2018].

De Abajo, F.J., 2005. Improving pharmacovigilance beyond spontaneous reporting. *International Journal of Pharmaceutical Medicine*, 19(4), pp.209–218.

Deloitte, 2014. *Value of connectivity: Economic and social benefits of expanding internet access*, Available at: https://www2.deloitte.com/content/dam/Deloitte/ie/Documents/TechnologyMediaCommunications/2014_uk_tmt_value_of_connectivity_deloitte_ireland.pdf.

Demirkıran, Z.K. & Altunok, T., 2012. A Systems Approach for Technology Assessment and Selection. In *Digital Avionics Systems Conference (DASC)*. Williamsberg, VA, USA: IEEE, pp. 1–11.

Deshpande, S., Basil, M.D. & Basil, D.Z., 2009. Factors Influencing Healthy Eating Habits Among College Students: An Application of the Health Belief Model. *Health Marketing Quarterly*, 26(2), pp.145–164. Available at: http://www.tandfonline.com/doi/abs/10.1080/07359680802619834.

De Vries, S.T. et al., 2016. Factors Influencing the Use of a Mobile App for Reporting Adverse Drug Reactions and Receiving Safety Information: A Qualitative Study. *Drug Safety*, 40, pp.443–455. Available at: http://link.springer.com/10.1007/s40264-016-0494-x.

Donner, J., 2008. Research approaches to mobile use in the developing world: A review of the literature. *Information Society*, 24(3), pp.140–159.

Dubey, A. & Handu, S.S., 2013. Are we pharmacovigilant enough in ophthalmic practice? *Indian Journal of Ophthalmology*, 61(5), pp.226–229.

Dusek, V., 2008. *Philosophy of Technology: An Introduction*, United Kingdom: Blackwell Publishing. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18427953%5Cnfile:///C:/Users/morganya/Documents/My eBooks/academic/Dusek, Val. Philosophy of Technology An Introduction.pdf.

Ebrahim, A., 2013. Let’s Be Realistic About Measuring Impact. *Harvard Business Review*, pp.1–2. Available at: https://hbr.org/2013/03/lets-be-realistic-about-measur.html

[Accessed July 21, 2017].

Eckerson, W.W., 2009. *Performance management strategies: How to Create and Deploy Effective Metrics*, Available at: https://www.microstrategy.com/strategy/media/downloads/white-papers/tdwi_performance-management-strategies.pdf.

Edwards, B. et al., 2015. Guiding Principles of Safety as a Basis for Developing a Pharmaceutical Safety Culture. *Current Drug Safety*, 2, pp.135–139.

Edwards, I.R., 2017. Causality Assessment in Pharmacovigilance: Still a Challenge. *Drug Safety*, 40(5), pp.365–372.

Fortado, B. & Fadil, P., 2012. The four faces of organizational culture. *Competitiveness Review: An International Business Journal*, 22(4), pp.283–298. Available at: http://www.emeraldinsight.com/doi/10.1108/10595421211247132.

François, A. et al., 2013. How can the Quality of Medical Data in Pharmacovigilance , Pharmacoepidemiology and Clinical Studies be Guaranteed ? *Société Française de Pharmacologie et de Thérapeutique*, 68(4), pp.217–223.

Franz, M. et al., 2015. *Building Energy Access Markets: A Value Chain Analysis of Key Energy Market Systems*, Eschborn. Available at: http://www.euei-pdf.org/sites/default/files/files/field_pblctn_file/150907_euei_value-chain_en_rz_03_web_0.pdf.

Gaille, B., 2016. 16 Pros and Cons of the Internet of Things. *BrandonGaille.com*. Available at: https://brandongaille.com/16-pros-and-cons-of-the-internet-of-things/ [Accessed January 31, 2018].

Giezen, T.J., Mantel-Teeuwisse, A.K. & Leufkens, H.G., 2009. Pharmacovigilance of Biopharmaceuticals - Challenges Remain. *Drug Safety*, 32(10), pp.811–817.

Gilson, L., 2006. Trust in health care : Theoretical perspectives and research needs. *Journal of Health Organization and Management*, 20(5), pp.359–375.

Granados, N., Gupta, A. & Kauffman, R.J., 2010. Information Transparency in Tusiness-to-Consumer Markets: Concepts, Framework, and Research Agenda. *Information Systems Research*, 21(2), pp.207–226.

Gubbi, J. et al., 2013. Internet of Things (IoT): A Vision, Architectural Elements, and Future Directions. *Future Generation Computer Systems*, 29(7), pp.1645–1660. Available at: https://arxiv.org/pdf/1207.0203.pdf?ref=theiotlist.

Hackett, R., 2016. Wait, What is Blockchain? *Fortune*. Available at: http://fortune.com/2016/05/23/blockchain-definition/ [Accessed February 8, 2018].

Hammer, M., 2004. Deep Change : How Operational Innovation Can Transform Your

Company. *Harvard Business Review*, (April), pp.1–20.

Härmark, L. & Van Grootheest, A.C., 2008. Pharmacovigilance: Methods, recent developments and future perspectives. *European Journal of Clinical Pharmacology*, 64(8), pp.743–752.

Harpaz, R. et al., 2014. Text Mining for Adverse Drug Events : the Promise , Challenges , and State of the Art. *Drug Safety*, 37, pp.777–790.

Harris, M., 2017. What is Cloud Storage? *LifeWire*. Available at: https://www.lifewire.com/what-is-cloud-storage-2438541 [Accessed January 30, 2018].

Hazell, L. & Shakir, S.A.W., 2006. Under-Reporting of Adverse A Systematic Review. *Drug Safety*, 29(5), pp.385–396.

Heinrich, M., 2015. Quality and safety of herbal medical products : regulation and the need for quality assurance along the value chains. *British Journal of Clinical Pharmacology*, 80(1), pp.62–66.

Herdeiro, M.T. et al., 2006. Influence of Pharmacists ' Attitudes on Adverse Drug Reaction Reporting A Case-Control Study in Portugal. *Drug Safety*, 29(4), pp.331–340.

Hewitt-Taylor, J., 2012. Identifying, analysing and solving problems in practice. *Nursing Standard*, 26(40), pp.35–41. Available at: https://www.researchgate.net/profile/Eduardo_Cittadini/publication/262911808_Participatory_Analysis_of_the_Sweet_Cherry_Sector_in_Argentinian_South_Patagonia/links/5656edfb08ae4988a7b51232.pdf.

Hill, G., 2014. Pharmacovigilance methods: the spectrum of PV. [Online video]. Available at: https://www.youtube.com/watch?v=lAhzeDxMp1s [Accessed April 15, 2017].

Holden, W.L., Juhaeri, J. & Dai, W., 2003. Benefit-risk analysis: A proposal using quantitative methods. *Pharmacoepidemiology and Drug Safety*, 12(7), pp.611–616.

Holm, G. et al., 2013. Implementing Ecopharmacovigilance in Practice : Challenges and Potential Opportunities. *Drug Safety*, 36, pp.533–546.

Hong, J., 2013. Framework for selecting the technology in public sector. *Information*, 16(11), pp.7895–7904.

HRCloud, 2017. HR Software & HRMS Solutions for Business. Available at: https://www.hrcloud.com/.

Iansiti, M. & Lakhani, K.R., 2017. The Truth About Blockchain. *Harvard Business Review*, 3(January-February), pp.3–11.

Irujo, M. et al., 2007. Factors that Influence Under-Reporting of Suspected Adverse Drug Reactions among Community Pharmacists in a Spanish Region. *Drug Safety*, 30(11), pp.1073–1082.

Isah, A.O. et al., 2012. Specific features of medicines safety and pharmacovigilance in Africa.

Therapeutic advances in drug safety, 3(1), pp.25–34. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4110828&tool=pmcentrez&rendertype=abstract.

Islam, S.M.R. et al., 2015. The Internet of Things for Health Care : A Comprehensive Survey. *IEEE Access*, 3, pp.678–708. Available at: http://ieeexplore.ieee.org/xpl/articleDetails.jsp?arnumber=7113786.

Jones, R.W. & Despotou, G., 2016. Root cause analysis and health informatics. In *14th International Conference on Informatics, Management and Technology in Healthcare*. Athens: Studies in health technology and informatics, pp. 131–134. Available at: http://dx.doi.org/10.3233/978-1- 61499-664-4-131.

Jurevicius, O., 2013a. Resource based view. *Strategic Management Insight*, p.1. Available at: https://www.strategicmanagementinsight.com/topics/resource-based-view.html [Accessed June 28, 2017].

Jurevicius, O., 2013b. Value Chain Analysis. *Strategic Management Insight*. Available at: https://www.strategicmanagementinsight.com/tools/value-chain-analysis.html [Accessed August 18, 2017].

Jusot, V., 2017. Correspondence. 20 July, Stellenbosch.

Kabore, L. et al., 2013. Pharmacovigilance systems in developing countries: An evaluative case study in Burkina Faso. *Drug Safety*, 36(5), pp.349–358.

KC, S. et al., 2013. Knowledge about adverse drug reactions reporting among healthcare professionals in Nepal. *International Journal of Risk and Safety in Medicine*, 25, pp.1–16.

Kendrick, J., 2013. Mobile technology: The amazing impact on our lives. *Mobile News*. Available at: http://www.zdnet.com/article/mobile-technology-the-amazing-impact-on-our-lives/ [Accessed February 2, 2018].

Khan, T.M., 2013. Community pharmacists' knowledge and perceptions about adverse drug reactions and barriers towards their reporting in Eastern region, Alahsa, Saudi Arabia. *Therapeutic Advances in Drug Safety*, 4(2), pp.45–51.

Khorramshahgol, R. & Moustakis, V.S., 1988. Delphic hierarchy process (DHP): a methodology for priority setting derived from the Delphi method and analytical hierarchy process. *European Journal of Operational Research*, 37(3), pp.347–354.

Kirby, M.R. & Mavris, D.N., 2000. A method for technology selection based on benefit, available schedule and budget resources. In *2000 World Aviation Conference*. San Diego, CA: American Institute of Aeronautics and Astronautics (AIAA), pp. 1–15. Available at: http://arc.aiaa.org/doi/pdf/10.2514/6.2000-5563.

Klausen, S.M. & Parle, J., 2015. 'Are we going to stand by and let these children come into the world?': the impact of the 'Thalidomide Disaster' in South Africa, 1960–1977. *Journal of Southern African Studies*, 41(4), pp.735–752. Available at: http://www.tandfonline.com/doi/full/10.1080/03057070.2015.1047181.

Klein, R., 1993. Dimensions of rationing: who should do what? *British Medical Journal*, 307, pp.309–131.

Klein, R., 1998. Puzzling out Priorities: Why We Must Acknowledge That Rationing Is a Political Process. *British Medical Journal*, 317(7164), pp.959–960.

Kumar, A. & Khan, H., 2015. Signal detection and their assessment in pharmacovigilance. *Open Pharmaceutical Sciences Journal*, 2, pp.66–73.

Lamprecht, A.J., 2017. Personal interview. 10 October, Western Cape Department of Education Headquarters.

Lamprecht, I.V.B., Bam, L. & de Kock, I.H., 2017. An investigation into the prospects of existing technologies to address the challenges faced by pharmacovigilance systems. In *SAIIE28: Taking up Stewardship*. Vanderbijlpark: SAIIE, pp. 1–17. Available at: https://www.saiie.co.za/saiie28.

Li, Y. et al., 2017. How Do Resource Structuring and Strategic Flexibility Interact to Shape Radical Innovation? *Journal of Product Innovation Management*, 34(4), pp.471–491. Available at: http://doi.wiley.com/10.1111/jpim.12389.

Lu, Z., 2009. Information technology in pharmacovigilance : Benefits , challenges , and future directions from industry perspectives. *Drug, Healthcare and Patient Safety*, 1, pp.35–45.

Macwan, U., 2017. Mobile Technology , Its Importance , Present And Future Trends. *Finextra*. Available at: https://www.finextra.com/blogposting/14000/mobile-technology-its-importance-present-and-future-trends [Accessed February 2, 2018].

Management for Science, 2012. Pharmacovigilance. , p.35.1-35.19.

Mathur, V.N. et al., 2007. Defining, identifying and mapping stakeholders in the assessment of urban sustainability. In M. Horner et al., eds. *International Conference on Whole Life Urban sustainability and its Assessment*. Glasgow, p. 18. Available at: https://dspace.lboro.ac.uk/xmlui/handle/2134/5202.

Mehta, U., 2017. Personal interview. 21 August, School of Public Health (UCT).

Mishra, S. & Singh, I.P., 2008. mHealth: a developing country perspective. In *Making the eHealth connection*. Bellagio, Italy, pp. 1–9. Available at: http://ehealth-connection.org/files/conf-materials/mHealth_ A Developing Country Perspective_0.pdf.

Morrison, A. & Sinha, S., 2016. A primer on blockchain (infograohic). *PWC Emerging Technology*. Available at: http://usblogs.pwc.com/emerging-technology/a-primer-on-blockchain-infographic/ [Accessed February 8, 2018].

Mpanza, Z., 2016. Identifying the root causes contributing to defects in order to minimize scrap. In *2016 International Conference on Industrial Engineering and Operations Management*. Kuala Lumpur: IEOM Society International, pp. 1139–1146. Available at: http://ieomsociety.org/ieom_2016/pdfs/318.pdf.

Myszewski, J.M., 2013. On improvement story by 5 whys. *The TQM Journal*, 25(4), pp.371–383. Available at: http://www.emeraldinsight.com/doi/10.1108/17542731311314863.

Naghibi, M.A. & Baban, H., 2011. Strategic Change Management: The Challenges Faced by Organizations. *International Proceedings of Economics Development and Research*, 4, pp.542–544.

Naidoo, P. & Martins, N., 2014. The relationship between organizational culture and work engagement: A multilevel investigation. *Problems and Perspectives in Management*, 12(4), pp.433–441.

Newton, R., 2010. Six Symptoms of Poor Prioritisation. *Corporate Geek*, pp.407–407. Available at: http://www.corporategeek.info/six-symptoms-poor-prioritisation [Accessed November 9, 2017].

Nikfarjam, A. et al., 2015. Pharmacovigilance from social media: Mining adverse drug reaction mentions using sequence labeling with word embedding cluster features. *Journal of the American Medical Informatics Association*, 22(3), pp.671–681.

Norman, S., 2016. Advantages Of Online Learning: Education Without Leaving Home. *eLearning Industry*. Available at: https://elearningindustry.com/5-advantages-of-online-learning-education-without-leaving-home [Accessed January 30, 2018].

Olsen, A.K. & Whalen, M.D., 2009. Public Perceptions of the Pharmaceutical Industry and Drug Safety and the Culture of Safety. *Drug Safety*, 32(10), pp.805–810.

Olsson, S. et al., 2010. Pharmacovigilance activities in 55 low-and middle-income countries: A questionnaire-based analysis. *Drug Safety*, 33(8), pp.689–703.

Ostrov, J.M., Gentile, D.A. & Mullins, A.D., 2013. Evaluating the effect of educational media exposure on aggression in early childhood. *Journal of Applied Developmental Psychology*, 34(1), pp.38–44. Available at: http://dx.doi.org/10.1016/j.appdev.2012.09.005.

Oztaysi, B., 2014. A decision model for information technology selection using AHP integrated TOPSIS-Grey: The case of content management systems. *Knowledge-Based Systems*, 70, pp.44–54.

Palloff, R.M. & Pratt, K., 2001. *Lessons from the Cyberspace Classroom: The Realities of Online Teaching*, San Francisco: Jossey-Bass. Available at: https://books.google.co.za/books?hl=en&lr=&id=36GLHRvTELMC&oi=fnd&pg=PR9&dq=online+teaching&ots=8n_1hUxCUP&sig=6Ku1I_cFJfZyhzD-

nHlsJnuFf_4#v=onepage&q=online teaching&f=false.

Pan, G.J.D., 2014. Ongoing Challenges in Pharmacovigilance. *Drug Safety*, 37, pp.1–8.

Passier, A. et al., 2009. Reporting of Adverse Drug Reactions by General Practitioners. *Drug Safety*, 32(10), pp.851–858.

Pojasek, R.B., 2000. Asking "Why?" five times. *Environmental Quality Management*, 10(1), pp.79–84.

Pontes, H., Clément, M. & Rollason, V., 2014. Safety signal detection: The relevance of literature review. *Drug Safety*, 37(7), pp.471–479.

Rachlis, B. et al., 2016. Targeted Spontaneous Reporting: Assessing Opportunities to Conduct Routine Pharmacovigilance for Antiretroviral Treatment on an International Scale. *Drug Safety*, 39(10), pp.959–976.

Raghupathi, W. & Raghupathi, V., 2014. Big data analytics in healthcare: promise and potential. *Health Information Science and Systems*, 2(1), p.3. Available at: http://link.springer.com/10.1186/2047-2501-2-3.

Rahman, S.Z. & Khan, R.A., 2015. Pharmaco Environmentology – Aligning Pharmacovigilance with Environment. *Pharma Times*, 47(8).

Rama, P., Rodrigues, P.A. & Georgy, A., 2011. Asian Journal of Pharmaceutical and Clinical Research PHARMAOVIGILANCE : PERSPECTIVES AND FUTURE CHALLENGES IN INDIAN SCENARIO. *Asain Journal of Pharmaceutical and Clinical Research*, 4(4), pp.1–4.

Raschi, E. et al., 2016. Adverse events associated with the use of direct-acting oral anticoagulants in clinical practice: Beyond bleeding complications. *Polish Archives of Internal Medicine*, 126(7–8), pp.552–561.

Ríos, O.M. et al., 2016. A comprehensive intervention for adverse drug reactions identification and reporting in a Pediatric Emergency Department. *International Journal of Clinical Pharmacy*, 38(1), pp.80–87.

Rodrigues, G.S. & Khan, S.A., 2011. Pharmacovigilance Among Surgeons and in Surgical Wards : Overlooked or Axiomatic ? *Indian Journal of Surgery*, 73(1), pp.4–8.

Rouse, M., 2005. Remote Access. *TechTarget*. Available at: http://searchmidmarketsecurity.techtarget.com/definition/remote-access [Accessed January 30, 2018].

Rouse, M., 2010. WAP (Wireless Application Protocol). *TechTarget*. Available at: http://searchmobilecomputing.techtarget.com/definition/WAP [Accessed February 26, 2018].

Rubel, M.R.B. et al., 2017. Adapting technology : effect of high-involvement HRM and organisational trust. *Behaviour and Information Technology*, 36(1), pp.281–293.

Ruder, K.A., Pretorius, M.W. & Maharaj, B.T., 2008. A technology selection framework for the telecommunications industry in developing countries. In *IEEE International Conference on Communications*. Beijing, pp. 5490–5493.

Ruder, K.A., Pretorius, M.W. & Maharaj, B.T., 2008. A technology selection framework for the telecommunications industry in developing countries. In *IEEE International Conference on Communications*. IEEE, pp. 5490–5493.

Russom, P., 2011. *Big data analytics*, Available at: https://vivomente.com/wp-content/uploads/2016/04/big-data-analytics-white-paper.pdf.

Sabik, L.M. & Lie, R.K., 2008. Priority setting in health care: Lessons from the experiences of eight countries. *International Journal for Equity in Health*, 7(1), p.4. Available at: http://equityhealthj.biomedcentral.com/articles/10.1186/1475-9276-7-4.

Sarker, A. et al., 2015. Utilizing social media data for pharmacovigilance: A review. *Journal of Biomedical Informatics*, 54, pp.202–212. Available at: http://dx.doi.org/10.1016/j.jbi.2015.02.004.

Schramm, G.E. et al., 2017. Implementation of an interprofessional clinical pharmacology selective learning experience for pharmacy residents and medical students. *American Journal of Health-System Pharmacy*, 74(6), p.397.

Shamim, S. et al., 2016. Adverse drug reactions (ADRS) reporting : awareness and reasons of under-reporting among health care professionals , a challenge for pharmacists. *SpringerPlus (2016)*, 5, pp.1–8.

Sharif, M.N. & Sundararajan, V., 1983. A quantitative model for the evaluation of technological alternatives. *Technological Forecasting and Social Change*, 24(1), pp.15–29.

Shehabuddeen, N., Probert, D. & Phaal, R., 2006. From theory to practice: Challenges in operationalising a technology selection framework. *Technovation*, 26(3), pp.324–335.

Shen, Y.C. et al., 2010. A hybrid selection model for emerging technology. *Technological Forecasting and Social Change*, 77(1), pp.151–166. Available at: http://dx.doi.org/10.1016/j.techfore.2009.05.001.

Simister, P., 2011. Advantages & Disadvantages Of Value Chain Analysis. *Differentiate Your Business*. Available at: http://www.differentiateyourbusiness.co.uk/the-advantages-disadvantages-of-value-chain-analysis [Accessed August 18, 2017].

Singh, V., 2017. Pros & Cons of Apps and Website: Which is Better Option? *YourStory*. Available at: https://yourstory.com/mystory/5d1d4981fe-pros-cons-of-apps-and-website-which-is-better-option- [Accessed February 26, 2018].

Smith, N., 2014. 5 Key Principles to Resource Management. *LiquidPlanner*. Available at:

https://www.liquidplanner.com/blog/5-key-principles-resource-management/ [Accessed February 1, 2018].

Sonkiya, S., 2014. Cause And Effect Diagram- Fishbone Diagram Analysis. *Project Quality Management*. Available at: https://www.izenbridge.com/blog/cause-and-effect-diagram-fishbone-diagram-analysis/ [Accessed October 4, 2017].

Spacey, J., 2015. 11 Types of Resource Management. *Simplicable*. Available at: https://simplicable.com/new/resource-management [Accessed February 1, 2018].

Stahl, M. et al., 2003. Assessing the Impact of Drug Safety Signals from the WHO Database Presented in SIGNAL. *Drug Safety*, 26(10), pp.721–727. Available at: http://www.scopus.com/inward/record.url?eid=2-s2.0-19244382600&partnerID=tZOtx3y1.

Stolk, R.P., 2012. Screening for diabetes. *British Medical Journal*, 335(September), p.462.

Strengthening Pharmaceutical Systems (SPS). *Supporting Pharmacovigilance in Developing Countries: The Systems Perspective*. Submitted to the U.S. Agency for International Development by the SPS Program. Arlington, VA: Management Sciences for Health.

Stretcher, V. & Rosenstock, I.M., 1997. The Health Belief Model. In *Health Behavior and Health Education: Theory, Research and Practice*. Jones and Bartlett Publishers, pp. 31–36.

Su, C., Ji, H. & Su, Y., 2010. Hospital pharmacists ' knowledge and opinions regarding adverse drug reaction reporting in Northern China y. *Pharmacoepidemiology and Drug Safety*, 19, pp.217–222.

Suwankesawong, W. et al., 2016. Pharmacovigilance activities in ASEAN countries. *Pharmacoepidemiology and Drug Safety*, 25, pp.1061–1069.

Tallent-Runnels, M.K. et al., 2006. Teaching Courses Online: A Review of the Research. *Review of Educational Research*, 76(1), pp.93–135. Available at: http://rer.sagepub.com/cgi/doi/10.3102/00346543076001093.

Tiles, M. & Oberdiek, H., 1999. *Living in a Technological World 27*, United Kingdom: Routledge.

Toklu, H.Z. & Uysal, M.K., 2008. The knowledge and attitude of the Turkish community pharmacists toward pharmacovigilance in the Kadikoy district of Istanbul. *Pharmacy World & Science*, 30, pp.556–562.

Tomoaia-Cotisel, A. et al., 2013. Context Matters : The Experience. *Annals of Family Medicine*, 11(Supp 1), pp.115–123.

United Nations, 2012. *UNPRPD Strategic and Operational Framework*, New York. Available at: http://www.undp.org/content/dam/undp/library/Poverty Reduction/Inclusive development/UNPRPD_SOF_web_April2012.pdf.

Uppsala Monitoring Centre, 2017. *The quest for evidence*, Uppsala. Available at: https://view.publitas.com/uppsala-monitoring-centre/uppsala-reports-77_web/page/1.

Varallo, F.R. et al., 2014. Causes for the underreporting of adverse drug events by health professionals : a systematic review. *Rev Esc Enferm USP*, 48(4), pp.739–747.

Vargesson, N., 2015. Thalidomide-induced teratogenesis: History and mechanisms. *Birth Defects Research*, 105(2), pp.140–156. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26043938%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4737249%5Cnhttp://doi.wiley.com/10.1002/bdrc.21096.

Varun, B., 2016. What are pros and cons of Internet of Things? *PixelCrayons*. Available at: https://www.pixelcrayons.com/blog/industry-news/what-are-pros-and-cons-of-internet-of-things/ [Accessed January 31, 2018].

Veyrat, P., 2016. How did the 5W2H method earn its name? *Heflo*. Available at: https://www.heflo.com/blog/action-plan/5w2h-method/ [Accessed August 16, 2017].

Viswanathan, P., 2017. What is a Mobile Application? *LifeWire*. Available at: https://www.lifewire.com/what-is-a-mobile-application-2373354 [Accessed February 26, 2018].

Waller, P.C. & Evans, S.J.W., 2003. A model for the future conduct of pharmacovigilance. *Pharmacoepidemiology and Drug Safety*, 12(1), pp.17–29.

Wang, X. et al., 2009. Active Computerized Pharmacovigilance Using Natural Language Processing, Statistics, and Electronic Health Records: A Feasibility Study. *Journal of the American Medical Informatics Association*, 16(3), pp.328–337. Available at: http://dx.doi.org/10.1197/jamia.M3028.

Warner, J., 2015. Is the "5 Why" Method Still a Useful Tool? *Ready To Manage*. Available at: http://blog.readytomanage.com/is-the-5-why-method-still-a-useful-tool/ [Accessed August 16, 2017].

Weber-Schoendorfer, C. & Schaefer, C., 2016. Pregnancy outcome after tocilizumab therapy in early pregnancy-case series from the German Embryotox Pharmacovigilance Center. *Reproductive Toxicology*, 60, pp.29–32. Available at: http://dx.doi.org/10.1016/j.reprotox.2016.01.002.

Western Governers University, 2017. Teaching Strategies for Using Educational Movies in the Classroom. *Western Governors University*. Available at: https://www.wgu.edu/blogpost/teaching-strategies-using-educational-television-classroom# [Accessed February 26, 2018].

World Health Organization, 2004. *Pharmacovigilance : ensuring the safe use of medicines*, Available at: www.who.org.

World Health Organization, 2002. *The Importance of Pharmacovigilance - Safety Monitoring of medicinal products*, Available at: http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf.

World Health Organization, 2014. WHO pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. , (1), pp.4–6. Available at: http://apps.who.int/iris/bitstream/10665/186642/1/9789241508254_eng.pdf.

Yang, M., Kiang, M. & Shang, W., 2015. Filtering big data from social media - Building an early warning system for adverse drug reactions. *Journal of Biomedical Informatics*, 54, pp.230–240. Available at: http://dx.doi.org/10.1016/j.jbi.2015.01.011.

Yap, C.M. & Souder, W.E., 1993. A filter system for technology evaluation and selection. *Technovation*, 13(7), pp.449–469.

Zaied, A.N., 2007. A Framework for Evaluating and Selecting Learning Technologies. *The International Arab Journal of Information Technology*, 4(2), pp.141–147.

Zakir, J., Seymour, T. & Berg, K., 2015. Big Data Analytics. *Issues in Information Systems*, 16(2), pp.81–90.

Zhang, L. et al., 2014. Pharmacovigilance in China: Current Situation, Successes and Challenges. *Drug Safety*, 37(10), pp.765–770.

Appendix A: Chapter 2 supporting content

This appendix provides the supporting content of Chapter 2. In this appendix, two sections are provided, namely:

- Section A.1: SAIIE28 annual conference article – This section contains the article that was published in the SAIIE28 annual conference proceedings, produced from a large portion of the content in Chapter 2 of this thesis.
- Section A.2: Structured literature search protocol – This section contains the structured literature search protocol, referenced in Section 2.5, used during the literature search in order to identify the PV challenge landscape.

Section A.1: SAIIE28 annual conference article

An investigation into the prospects of existing technologies to address the challenges faced by pharmacovigilance systems

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ABSTRACT

Pharmacovigilance (PV) is defined as the science and activities relating to drug safety surveillance, i.e. the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. Even though substantial progress has been made over the past several decades to improve the effectiveness and efficiency of PV systems, literature suggests that the vast majority of PV systems are still burdened by similar challenges. Typical challenges often relate to aspects considered to have the ability to facilitate improved PV, i.e. engaging the public, building collaborations and partnerships, incorporating informatics into PV systems, adopting a global (standardised) approach, and assessing the impact of efforts. Furthermore, researchers argue that these challenges are not new and have been, and still is, pivotal research objectives within PV studies.

Advances in science and technology over the past couple of decades have seen technologies being developed, and subsequently successfully employed, to address similar challenges in other industries. The impact of these technologies are described in literature, proving their success. This paper argues the case for such technologies within PV systems, proposing a research agenda for identifying technologies that hold the potential to address the challenges faced by PV systems.

OPSOMMING

Pharmacovigilance (*PV*) word gedefinieer as die wetenskap en aktiwiteite wat verband hou met farmaseutiese dwelm veiligheid toesig, dit wil sê, die opsporing, assessering, verstaan en voorkoming van ongunstige gevolge of enige ander dwelm-verwante probleem. Ten spyte van die aansienlike vordering oor die afgelope paar jaar om die effektiwiteit en doeltreffendheid van *PV* sisteme te verbeter, stel literatuur steeds voor dat 'n groot deel van *PV* sisteme steeds belas word met soortgelyke uitdagings. Tipiese uitdagings hou dikwels verband met aspekte met die vermoë om verbeterde *PV* te fasiliteer, dit wil sê, die innemendheid van die publiek, die verbetering van samewerking en vennootskappe, die inkorporëring van informatika in *PV* sisteme, die aanneming van 'n globale (gestandaardiseerde) benadering, en die assessering van die impak van pogings. Verder argumenteer navorsers dat hierdie uitdagings nie nuut is nie en was, en is steeds, deurslaggewende navorsingsdoelwitte in *PV* studies.

Vorderings in wetenskap en tegnologie oor die afgelope paar jaar het leiding gegee tot ontwikkelings in tegnologie wat gevolglik suksesvol onderneem is, wat soortgelyke uitdagings in ander nywerhede aanspreek. Die impak van hierdie tegnologieë word beskryf in literatuur en dien as bewys van die sukses behaal deur hierdie tegnologieë. Hierdie navorsingsverslag beweer die toepassing van hierdie tegnologieë en stel 'n navorsingsagenda voor vir die identifikasie van sulke tegnologie wat die potensiaal het om die uitdagings in *PV* aan te spreek.

1. INTRODUCTION: Background

The Thalidomide disaster of the 1960s ((Toklu & Uysal 2008); (Isah et al. 2012)) has been described as the largest man-made medical disaster in history (Vargesson 2015), that led to nearly 10 000 babies worldwide being born with extremity defects (Wang et al. 2009). Speculation followed on the true nature of these defects and whom is to be held responsible (De Abajo 2005). To this day survivors of the tragedy are compensated by both government and the original manufacturers of the drug, however, they still live with the consequences (Vargesson 2015). Various researchers (including Wang *et al.* (Wang et al. 2009); De Abajo (Stolk 2012); and Klausen & Parle (Klausen & Parle 2015)) concur that this disaster made the need for drug safety monitoring and surveillance to prevent a tragedy of similar stature occurring in the future apparent.

Subsequently, pharmacovigilance (PV) was introduced to the healthcare environment in the late 1960's (De Abajo 2005). At this time, the World Health Organisation (WHO) unveiled the WHO Programme for International Drug Monitoring, an organisation consisting of multiple international partners aimed at international monitoring and surveillance of new and existing drugs (World Health Organization 2002). PV enjoys much attention in this programme, now co-ordinated by the Uppsala Monitoring Centre (UMC) (World Health Organization 2002).

THE PHARMACOVIGILANCE SYSTEM

The WHO defines PV as the "*science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems*" (World Health Organization 2002). Regularly associated with PV are adverse drug reactions (ADRs) or adverse drug events (ADEs) which describe the unintentional and unpredicted reactions to, or side-effects of new or existing drugs (World Health Organization 2014). When such unpredicted reactions or side effects occur, the ideal is that it is reported to the appropriate authorities. Depending on the degree of severity of the reaction, the report is either terminated at the national level or sent on to the UMC (Strengthening Pharmaceutical Systems (SPS) 2009).

Referring to the nature of PV, the WHO describe it as being based on surveillance (World Health Organization 2004). It is therefore reasonable to expect that, at least at an abstract systems level, the PV challenge landscape will share some characteristics with other surveillance based industries. More specifically, it is reasonable to expect that at least some of the challenges faced in the PV landscape will be similar to those faced in other surveillance based industries.

The common ground that exists between the PV challenge landscape and other industries is clear in the resource management (in particular human resource management) use case described by Rabiul *et al.* (Rubel et al. 2017). A study is conducted in a software based model known as high-involvement human resource management (Rubel et al. 2017), which is implemented in a variety of organisations, delivering good results in terms of increased organisational process efficiency and reduced human resource expenses.

The use case illustrates the relationship that exists between PV and other industries, both requiring resource management in general and human resource management in particular. It is clear that there are existing technological developments that can have a beneficial impact on PV. Prior to the investigation of such developments, the PV system and the PV challenge landscape are described, providing an understanding of the current condition of PV. This allows for the research to pinpoint exactly where in the PV landscape improvements are necessary.

2. The PV system

PV is described from a systems perspective by the organisation Strengthening Pharmaceutical Systems (Strengthening Pharmaceutical Systems (SPS) 2009), who categorise the PV system into people, functions, structures, and expected outcome and impact. This systems view of PV is briefly described in this section.

Within the PV system, people are categorised as either reporters or evaluators (Strengthening Pharmaceutical Systems (SPS) 2009). Reporters are those who report ADRs (or suspected ADRs) to the relevant authorities, known as the evaluators. Evaluators largely consist of various healthcare professionals whom have the ability to do the necessary analysis to identify and categorise ADRs from the data that is reported. Forming part of the processes are the functions associated with PV, from ADR reporting to analysis and implementation of solutions. Critical to the effective and efficient operation of these processes are the structures and bodies involved including PV organisations, medical infrastructures and networks, regulatory bodies, product manufacturers, and the media (Strengthening Pharmaceutical Systems (SPS) 2009). These structures, as well as the people involved, are essential in providing the necessary resources and managing the overall PV system.

A PV system consists of several sequential stages. Figure 1 provides an overview of the six stages (Strengthening Pharmaceutical Systems (SPS) 2009).

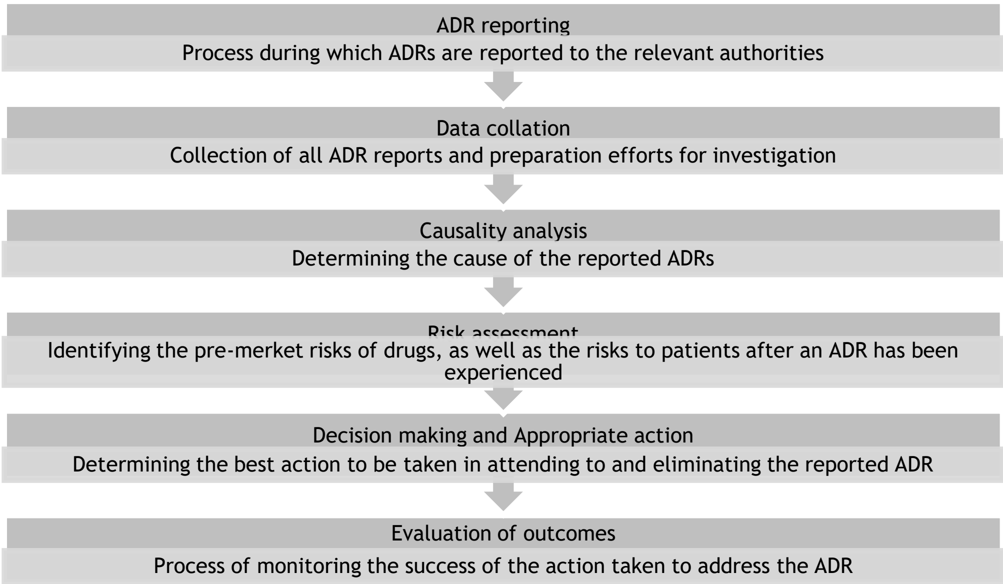

Figure 1: Stages of a PV system

As one would expect, the increasing scope of PV systems has increased the complexity and number of challenges faced within the PV landscape ((Edwards 2017) and (Pan 2014)), giving rise to challenges such as the under-reporting of ADRs, ineffective culture, lack of transparency, and the lack of sufficient resources. Pan (Pan 2014) also states that increased pressure is put on new technological developments that are intended to counter the challenges in the PV landscape. The WHO describes how the inter-relatedness of the various stages in a PV system cause challenges that exist within the PV landscape to have a system-wide impact (World Health Organization 2002). The under-reporting of ADRs is an example of a prominent PV challenge that has a system-wide impact. PV systems are initiated by ADR reports, serving as the line of communication between PV authorities and the people experiencing certain ADRs (Varallo et al. 2014). Due to the integrated global nature of PV monitoring (as managed by the UMC), the impact of a challenge such as under-reporting of ADRs can also stretch beyond a specific PV system to the global PV monitoring level.

3. Overview of the PV challenge landscape

Each stage of a PV system is associated with a specific set of challenges and Pan (Pan 2014) states that the PV challenge landscape is vast. It is therefore advantageous to this research that these challenges be identified, enabling associations to be made between the challenges and the various stages of a PV system where they are likely to have an impact.

Due to the large landscape of PV challenges, a systematic review was conducted in order to ensure that a significant portion of existing research conducted in the challenge landscape is considered in this research. Three academic databases were used, namely: Scopus, Google Scholar and PubMed. The Scopus database was used for the primary systematic search protocol while the PubMed and Google Scholar databases were used for snowballing and other informal search methods. In total, 2301 relevant documents are available based on specific search terms (these search terms are detailed in Appendix 1). These search terms were based on the suggestions made by the articles found on the databases. Also, suggestions made by grey literature were used as search terms. To reduce the number of articles to a more manageable quantity, only the articles published during the year 2000 and onwards were included in the search. Then, the abstracts were consulted to determine the applicability of the article to the research. An important inclusion criteria was that the abstract had to contain words associated with PV, such as “pharmacovigilance”, “drug safety monitoring”, or “drug safety surveillance”. The documents were filtered to 64 documents of which the majority are referenced in the proceeding section.

Shown in Figure 2, the most prevalent PV challenges were organised into a network, illustrating the inter-related nature of the PV challenge landscape. This was done by interpreting the suggestions made by literature, taking into account both the severity and prevalence of the challenge. The PV challenge landscape has been organised into two categories, namely partnerships and ADR reporting, both overarched by culture:

- Culture can be regarded as an overarching element of the PV challenge landscape, underpinning the other challenges in PV. The suggestion that the improvement of PV culture will contribute to the improvement of the entire PV system is regularly made by literature ((Olsen & Whalen 2009); and (Rodrigues & Khan 2011)).
- Partners are regarded as essential to a system such as PV, responsible for providing essential resources. The public is a key partner in PV, as they can be utilised across the PV spectrum, especially during ADR reporting ((World Health Organization 2002); and (World Health Organization 2004)).

- ADR reporting is widely regarded as one of the most important stages of a PV system (Hill 2014), as it serves as the starting point for the PV system providing the data on which the system relies to identify ADRs.

Each of the challenges presented in Figure 2 are briefly described in the following section, providing a succinct overview of the PV challenge landscape.

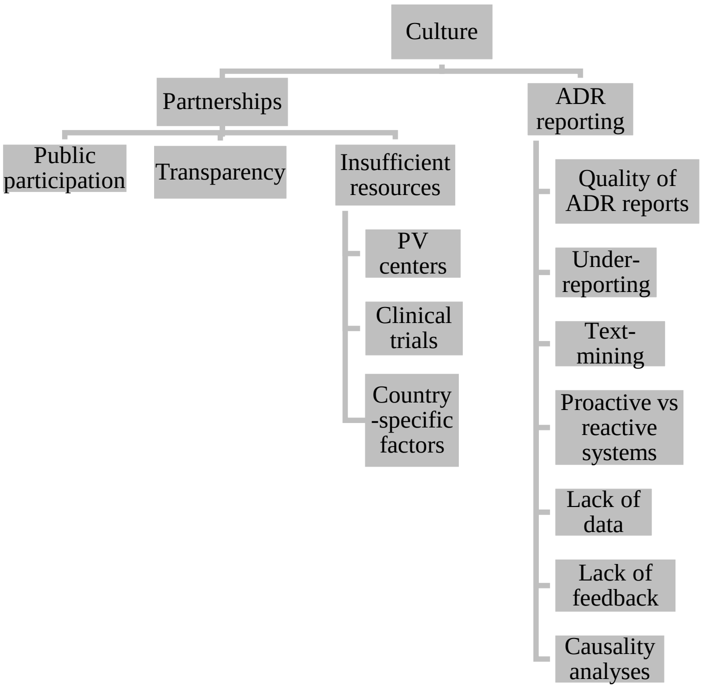

Figure 2: The PV challenge landscape network

3.1. Culture

PV is based on the culture of safety, where PV professionals provide the foundation upon which the principles of this culture is built (Olsen & Whalen 2009). Literature, however, argues that there is a need to improve the culture in modern PV systems (Rodrigues & Khan 2011). It is believed that the improvement of PV culture will give lead to the improvement of the other challenges in PV, as illustrated in Figure 2. It is often discussed that the improvement of PV culture requires participation across all disciplines in order to become a reality.

The culture of PV is closely related to both Inman's – and the KAP models of under-reporting (Rodrigues & Khan 2011), discussed in Section 3.3.2. To achieve this culture, the challenges presented by these models should be investigated. This is also the opinion of Rodrigues & Khan (Rodrigues & Khan 2011), who refer to the need to develop a safety culture, associated with the reporting of ADRs, amongst surgeons and surgical wards. The establishment of a culture of safety amongst healthcare professionals across the globe is time-sensitive (Edwards et al. 2015), emphasising the need for the timely establishment of such a culture.

3.2. Partnerships

PV is a collaborative endeavour (Pan 2014). Sustained collaboration and commitment are vital to attend to future challenges of PV ((World Health Organization 2002); and (World Health Organization 2004)). However, ineffective partnership is a threat to PV (World Health Organization 2004). Operating in a resource constrained environment, partners in PV must sometimes provide expertise, training, political support, scientific infrastructure, and a capacity to accomplish comprehensive monitoring and investigations of the safety of medicines (Pan 2014). Failure in providing such resources, ineffective partnerships can lead to failed PV initiatives. In order to maintain a certain inventory of these resources, it is vital that PV organisations form lasting relationships with its partners. Management for Science (Management for Science 2012) emphasises the importance of relationships between partners and how failed relationships often lead to failures.

3.2.1. Public participation

The scope of PV is large (Rodrigues & Khan 2011), as it monitors a wide range of new and existing drugs in several countries, therefore requiring the participation of numerous stakeholders. Consumers and patients are described as key stakeholders (BEUC 2008), having the ability to contribute through an integrated and efficient reporting system. These direct reporting systems enables PV professionals to detect ADRs much earlier, as well as remove the healthcare professional as filter to reporting ADRs.

However, patients and consumers have been losing faith in the pharmaceutical industry. A survey of the US public, conducted in 2006, illustrated this loss in trust with approximately 42% of public participants indicating that they are sceptical of the pharmaceutical industry (Olsen & Whalen 2009). Similarly, a study conducted in 2007 on similar participants also indicated that the public had indeed lost confidence in the pharmaceutical industry (Olsen & Whalen 2009). Surveys such as these serve as proof that the PV industry must shift its focus in maintaining collaboration with the consumer and patient.

3.2.2. Transparency

In close association with the culture found in PV, the lack of transparency amongst the stakeholders in PV may lead to failed PV initiatives (Edwards et al. 2015). It is essential that key stakeholders, especially those with the relevant experience in PV, share information with their peers. This will enable participants in PV to learn of new ways in solving the problems they might be experiencing. Increasing the visibility of information in PV is critical (Edwards et al. 2015), as it will support an improved drug safety culture.

3.2.3. Insufficient resources

It is well-known that PV operate within a resource constrained environment (Isah et al. 2012). Especially in developing countries where other challenges such as drought and war are of high priority, PV organisations struggle to implement new PV systems (Isah et al. 2012). In these countries the available resources are rather invested elsewhere, leaving little for the requirements of PV.

The resources required by PV systems are unique in specific countries e.g. a country might have the necessary expertise and manpower to assist a PV system but lack the governmental funding, whereas another country might have the necessary budget but lack the required manpower (Pan 2014). Countries experiencing this phenomena include Sub-Saharan African countries (Isah et al. 2012), India (Rama et al. 2011), and certain South-East Asian countries (Suwankesawong et al. 2016). Common resources required by PV systems include monetary assistance, hardware and software infrastructure, expertise and training curricula amongst healthcare professionals, and common PV knowledge amongst both healthcare professionals and consumers ((Isah et al. 2012); and (Pan 2014)). PV systems are dependent on the combination of these resources and are not able to function properly without it (Isah et al. 2012). Heinrich (Heinrich 2015) make reference to effective resource management, a crucial element to the successful operation of a PV system.

Lack of PV centres

Serving as the base of operation for PV monitoring efforts, PV centres are important elements of the PV industry. Zhang *et al.* (Zhang et al. 2014) describes the PV centre network: the UMC is the international database, taking ownership of millions of ADR reports received from numerous countries each year (Rama et al. 2011). Serving as filter to such ADR reports are national PV centres, supported by provincial centres, usually located in provincial hospitals and other medical institutions. Lastly, municipal centres serve as the first line of defence i.e. initially receiving and processing ADR reports before sending it to PV centres further up the PV centre network hierarchy. Zhang *et al.* (Zhang et al. 2014) provides a description of the Chinese PV centre network, consisting of one national PV centre, 34 provincial centres and 400 municipal centres, all reporting to the UMC.

The challenge faced, especially in developing countries, are the gaps found within this PV centre network. The Sub-Saharan Africa case where there are many countries with no or few municipal – and provincial centres is discussed by Isah *et al.* (Isah et al. 2012). Olsson *et al.* (Olsson et al. 2010) and Isah *et al.* (Isah et al. 2012) are of the opinion that this deficit is due to the lack of resources such as tangible infrastructure, human resources, training and capacity building, governance, sustainable methodologies, and innovations within a number of areas in the Sub-Saharan Africa context. With no intermediate body to receive and filter initial ADR reports, it is difficult for healthcare professionals and consumers, in countries with no municipal – or provincial PV centre, to report ADRs to the appropriate authorities (Zhang et al. 2014).

Clinical trials

Clinical trials are conducted premarket and are used to determine the effect that a drug will have on consumers, as well as to identify certain ADRs that cannot be predicted in laboratory conditions (Cheaib 2016). Similarly, Dubey & Handu (Dubey & Handu 2013) state that clinical trials are important to know the drug's effect on humans as it cannot be directly extrapolated from preclinical animal studies. Although the results detained from clinical trials are beneficial to the PV industry, clinical trials are burdened by some limitations ((Cheaib 2016); (Raschi et al. 2016); (Dubey & Handu 2013); and (Härmark & Van Grootheest 2008)).

Though clinical trials undoubtedly play a vital role in drug safety, they can sometimes deliver limited results (Härmark & Van Grootheest 2008). For example, due to the limited number of patients participating, it is generally not possible to identify ADRs that occur rarely (Cheaib 2016) and such ADRs will therefore only be identified and investigated after a drug has been marketed to the public. Another example of the limitation to clinical trials, is a possible lack of correspondence in characteristics (e.g. age and sex) between the populations in which a drug is tested and those where it will be developed post-market (Dubey & Handu 2013). This limits the extrapolation of results obtained from clinical trials to the population at large (Härmark & Van Grootheest 2008).

Country-specific factors

Country-specific factors refer to challenges faced by PV organisations outside the traditional resource architecture and are described by Edwards (Edwards 2017) and Härmark & Van Grootheest (Härmark & Van Grootheest 2008). Closely related to the effect of the public on PV, the social factors of an area must be considered which includes the culture, religion, age groups, and sex groups of a specific region. It is often a burden to clearly identify these factors, since it requires manpower and funding that are not always available.

Situational factors which refer to border regulations, policies for implementation, governmental budget constraints, conflict in countries, and environmental issues such as severe drought must also be considered. Often governments refuse to authorise and support the implementation of new PV systems since its priorities are elsewhere (World Health Organization 2002), delaying the implementation of PV systems. Similar to the social factors, the required resources needed to identify these factors are not always available, proving to contribute to the failed deployment of PV initiatives.

3.3. ADR reporting

ADR reporting is widely regarded as the starting point of a PV system. An ADR report is present across the entire PV system, serving as source of information to the relevant authorities conducting the investigations into the ADR query. Furthermore, many ADR reporting techniques exist in practice including spontaneous reporting, targeted reporting, cohort event monitoring, and electronic health record mining (Hill 2014).

3.3.1. Quality of ADR reports

The quality of medical data, in a PV context, is of utmost importance (François et al. 2013). Without ADR reports, PV systems cannot function and literature regularly emphasises the need for advancements to be made with regards to the quality of such reports (Sarker et al. 2015).

Spontaneous reporting is a widely used method in PV (Hill 2014), dependent on both healthcare professionals and the consumer. However, Bandekar *et al.* (Bandekar et al. 2009) describes a looming threat to spontaneous reporting: the poor quality of the reports. These quality issues, regularly found in reports by non-healthcare professionals, include issues with credibility, uniqueness, frequency, and salience of the data contained in the report (Sarker et al. 2015). Such issues can be motivated by the lack of necessary PV knowledge amongst consumers.

However, poor quality reports are not restricted to those generated by consumers, but is also generated by healthcare professionals. Such poor quality is evident in a study by Bandekar *et al.* (Bandekar et al. 2009), where ADR reports from ten different countries were collected, with the objective of determining the quality of the reports. It was found that several reports lacked critical information (e.g. pregnancy status, age, sex, and allergic status), regardless of the fact that many of these reports were generated by healthcare professionals. Sub-Saharan African countries were rated particularly poorly, achieving below 50% with regards to the quality standard baseline.

The poor quality of ADR reports can be traced back to the culture of PV (Bandekar et al. 2009). The establishment of a culture where more emphasis is put on the quality of ADR reports, as described by Edwards *et al.* (Edwards et al. 2015), may therefore contribute to the improvement of ADR reports.

3.3.2. ADR under-reporting

Under-reporting of ADRs occur when healthcare workers (HCWs) (general practitioners, nurses, surgeons, pharmacists etc.) fail to efficiently report new and existing ADRs. Two prominent models that explain the causes of under-reporting are widely cited in literature namely Inman's model of the seven deadly sins of under-reporting and the KAP (knowledge, attitude, and practice) model of under-reporting. Taken together, these two models provide a comprehensive overview of the causes of under-reporting of ADRs. The KAP model is said to be the leading cause, in association with Inman's model, of under-reporting of ADRs (Herdeiro et al. 2006).

Inman's seven deadly sins of under-reporting

In the 1990s Dr William Inman conducted research on PV with specific reference to the causes of under-reporting (Varallo et al. 2014). This study, known as Inman's seven deadly sins of under-reporting, is widely cited in literature ((Varallo et al. 2014); (Hazell & Shakir 2006); (Irujo et al. 2007); and (Rodrigues & Khan 2011)). More recent studies ((Varallo et al. 2014); and (Rodrigues & Khan 2011)) have confirmed the findings, specifically highlighting the ignorance, insecurity and indifference aspects of the model.

The so-called sins of Inman's model are:

- Fear: Of litigation,
- Indifference: About contributing to the general advancement of knowledge,
- Ambition: To collect and publish a personal case series,
- Guilt: At having caused and adverse effect,
- Complacency: The mistaken belief that only safe drugs are licensed,
- Ignorance: Of the need for reporting, and
- Diffidence: About reporting a mere suspicion.

Many of these so-called sins such as indifference, ambition, complacency, and diffidence strongly relate to the culture in PV and research in eliminating these sins is believed to improve the overall culture within PV.

KAP model

The first aspect of the KAP model is knowledge, closely related to education according to Herdeiro *et al.* (Herdeiro et al. 2006). The shortcomings of PV in the undergraduate and postgraduate syllabus of medical students is regularly referred to in literature ((Schramm et al. 2017); (Abubakar, Chedi, et al. 2015); (Abubakar & Haque 2016); (Abubakar, Ismail, et al. 2015); and (Abubakar, Simbak, et al. 2015)). These shortcomings are also not unique to specific countries. Studies in Nigeria (Abubakar, Chedi, et al. 2015), Malaysia (Abubakar, Ismail, et al. 2015), Portugal (Herdeiro et al. 2006), Turkey (Toklu & Uysal 2008), India (KC et al. 2013), and China (Su et al. 2010) all discuss the need for medical students' curriculum to either include or improve PV education.

The aforementioned country specific studies also highlight the lack of sufficient knowledge on the correct PV practices in practicing healthcare professionals. Toklu & Uysal (Toklu & Uysal 2008) discuss the need for improved PV knowledge amongst community pharmacists in Turkey, Passier *et al.* (Passier et al. 2009) the need for improved PV knowledge amongst general practitioners in Netherlands, and Herdeiro *et al.* (Herdeiro et al. 2006) the need for improved PV knowledge amongst pharmacists in Portugal. It is clear that thorough knowledge of PV is a challenge, hurdling several PV initiatives to be completely successful in many countries.

Secondly, the KAP model refers to the general attitude of healthcare professionals towards PV. This element of the KAP model is closely related to the indifference and ignorance aspects of Inman's model and also strongly relates to the culture aspects of the PV challenge landscape. Some examples of the role of attitude in under-reporting are given in a recent study by Shamim *et al.* (Shamim et al. 2016) who seek to build an understanding of the general attitude of physicians, pharmacists, and nurses towards PV in Pakistan. It was found that a large portion of these healthcare professionals are indifferent towards PV, with only 14.3% being aware that there was an ADR reporting organisation in Pakistan. Similarly, a study within a Spanish context also discuss the poor attitude of healthcare professionals towards PV (Varallo et al. 2014). The indifference found in the Spanish context is associated with the lack of interest of healthcare professionals to register for ADR reporting and a lack of time for the many activities in the clinical routine.

Lastly, the lack of sufficient practice in PV is also a challenge faced in the PV industry. Closely associated with training, Varallo *et al.* (Varallo et al. 2014) is of the opinion that the lack of sufficient practice has recently surfaced and is nowadays referred to as the eight sin of Inman's model. The lack of practice in PV is regularly referred to in literature, including Aronson (Aronson 2012) discussing the need for increased, real-world PV practice amongst British healthcare professionals, and Beckmann *et al.* (Beckmann et al. 2014) who similarly emphasises this need in a general context.

3.3.3. Text-mining

Text mining is defined as the computational process of extracting meaningful information from large amounts of unstructured text (Harpaz et al. 2014). In a PV context, meaningful information is regarded as information that can support ADR detection and assessment (Yang et al. 2015). Contrary to popular belief, a major challenge faced in text mining, as described by Harpaz *et al.* (Harpaz et al. 2014), is not necessarily the extraction of useful information from severely unstructured text, but rather realising the value text mining holds for the PV industry (Harpaz et al. 2014). Extraction is a challenge (Yang et al. 2015), but advancements in software have simplified information extraction efforts (Harpaz et al. 2014).

The use of text-mining on social media is regularly discussed in literature ((Harpaz et al. 2014); (Yang et al. 2015); and (Nikfarjam et al. 2015)). The challenge of some PV organisations not realising the value of text mining, as described by Harpaz *et al.* (Harpaz et al. 2014), is evident in the late adoption rate of social media. Nikfarjam *et al.* (Nikfarjam et al. 2015) is of opinion that this unwillingness to use social media for ADR reporting is due to the informal nature of social media i.e. consumers make use of informal words and phrases to report a suspected ADR, therefore PV organisations are sceptical of the quality of information that can be gathered from social media. Harpaz *et al.* (Harpaz et al. 2014) and Yang *et al.* (Yang et al. 2015) argue that technological developments are only contributing to an increased adoption rate of text-mining to a limited extent.

3.3.4. Proactive versus reactive systems

Regulatory enforcement and increased accountability demands for the protection and welfare of patients, forces the PV industry to be more proactive in its efforts (Lu 2009). These regulations govern proactive PV systems that must include comprehensive risk management plans and signal detection and analysis throughout a clinical product's lifecycle (Lu 2009). Proactive PV is not only able to respond to ADRs prior to the marketing stage of drugs, but also decreases the probability of a known ADR to be experienced during such a large scale deployment (Rodrigues & Khan 2011).

Certain modern PV systems are outdated (Giezen et al. 2009). Spontaneous reporting, as described by Hill (Hill 2014), is the first ADR reporting system implemented in PV. Such reports are of reactive nature, depending on healthcare professionals and consumers to report ADRs after a drug has been marketed and the ADR experienced. Spontaneous reports are still widely used, increasing the pressure on PV systems in which these operate to make a transition towards proactive operation (Rodrigues & Khan 2011).

Existing PV systems struggle with the reactive to proactive conversion process ((Lu 2009); and (Giezen et al. 2009)). It is simpler to design a proactive PV system from scratch than to convert an existing PV system to a proactive mode of operation. Resistance to change is a major cause of this struggling transformation since it is well known that people often prefer an existing system rather than having to learn the functions of a new system (Hill 2014).

3.3.5. Lack of data

PV relies on good information i.e. information of proper quality (Pan 2014). It is argued that the lack of the physical data as well as the quality of such data burdens PV systems (Rachlis et al. 2016), limiting the possibility of investigations. Pan (Pan 2014) also discusses the limitation to current PV data. This argument is supported by case studies conducted by Rachlis *et al.* (Rachlis et al. 2016) and Weber-Schoendorfer & Schaefer (Weber-Schoendorfer & Schaefer 2016) that made the phenomenon of insufficient data apparent. This phenomenon is closely related to under-reporting and the quality of ADR reports.

3.3.6. Lack of reporter feedback

A challenge faced by the PV industry, regularly overlooked by researches, is the lack of feedback given to ADR reporters ((Aljadhey et al. 2015); (Al Dweik et al. 2016); (Ríos et al. 2016); (De Vries et al. 2016); and (Kabore et al. 2013)). A study of Saudi Arabia's PV system indicated that participants of the existing ADR reporting network see no point in reporting ADRs if they cannot get feedback and support from the country's PV authorities (Aljadhey et al. 2015).

A similar study completed in the UK, Netherlands, and Australia found that ADR reporters, especially patients, want personal feedback to put them to ease that their voices and opinions are heard by the relevant PV authorities (Al Dweik et al. 2016).

This need for personal feedback as a sociological component of PV is described by Rios *et al.* (Ríos et al. 2016) as a routinely overlooked component of the PV system. The lack of adequate feedback is also evident further up the PV authority hierarchy, where gaps in the PV centre network are regularly found.

3.3.7. Causality analysis

Establishing causality in PV is a difficult and time consuming process, requiring resources such as manpower, expertise, and funding that is often scarce and hard to come by (Edwards 2017). Avorn & Schneeweiss (Avorn & Schneeweiss 2009) make reference to this issue, stating that it is a common challenge experienced in various locations. Even though a large body of ADR data exists (Avorn & Schneeweiss 2009), the volume is often too much for causality initiatives. Similar to the case described earlier, undertaking such a volume of data require resources that are not always available. This lack of resources and the difficulty in identifying linkages between ADRs and its source are hindering causality analyses from being conducted in a timely fashion.

4. Relationship between the PV system and the challenge landscape

As discussed in Section 2, literature suggests that relationships exist between the stages of a PV system and the challenge landscape. Table 1 depicts the proposed relationships between the challenges (as organised in Figure 2) and the stages of a PV system (as shown in Figure 1).

Table 1illustrates where exactly in the PV system the challenge landscape has an impact. From the table it is evident that challenges such as partnerships, culture, and transparency are prominent and the dominant positioning of these three challenges in the typology of the challenge landscape presented in Figure 2 is thus supported. Cognisant of the vast number of challenges that exist in the PV landscape, Table 1 can be useful in assisting to direct future research efforts by enabling researchers to prioritise those challenges that have the most far-reaching impact on the PV system. Thus encouraging more in-depth research in specific challenges that are likely to have a system-wide positive impact.

Table 1: Relationship between a PV system and the challenge landscape.

Stages of a PV system / Challenge landscape	ADR reporting	Data collation	Causality analysis	Risk assessment	Decision-making	Appropriate action	Evaluation of outcomes
Culture	X	X	X	X	X	X	X
Partnerships	X	X	X	X	X	X	X
Public participation	X					X	X
Transparency	X	X	X	X	X	X	X
Insufficient resources	X	X	X	X	X	X	X
Lack of PV centres		X			X	X	X
Clinical trials		X	X	X			
Country-specific factors	X	X	X	X	X	X	X
Quality of ADR reports		X	X	X			
ADR under-reporting	X						
Text-mining		X	X	X			
Proactive vs reactive systems	X					X	
Lack of data		X	X	X			
Lack of reporter feedback					X		
Causality analysis			X	X			

5. Prospects of technological developments from other industries

As discussed in the introductory chapter, it is believed that PV shares common characteristics with other surveillance based industries. The ever increasing environment of technological developments (such as tangible hardware, software, business processes, frameworks, and models) in various industries that have a similarity to PV, is believed to hold the potential to address aspects of the PV challenge landscape.

Limited research has been conducted with regards to the prospects of existing technological developments to address the challenges faced by PV systems, therefore, this section is limited to a brief overview of the existing technological developments. Subsequently, a succinct overview of three technological developments, believed to have a possible impact on the PV challenge landscape, is provided.

5.1. Improving PV transparency with *Workmate*

As discussed in Section 3.2.2., transparency, especially between key stakeholders, is a challenge faced in PV. Literature often claims that transparency in PV is essential as it allows for healthcare workers to share experiences with certain ADRs and support one another in attending to such ADRs.

A software program, *Workmate,* a human resource management system developed by *HRCloud,* an organisation developing software models for human resource management purposes (HRCloud 2017), can be used for the general improvement of transparency in PV. It enables users, in this case PV stakeholders, to share experiences and recognise peers' work and achievements. This software has the capacity to improve transparency in PV, as well as contribute to the improvement of PV culture.

5.2. Understanding the attitudes, perceptions and behaviours of stakeholders in PV with the Health Belief Model

The health belief model is a popular theory used in health education and health promotion, first developed in the 1950s as a way to explain why medical screening programs offered by the US Public Health Service were not successful (Stretcher & Rosenstock 1997). The model consists of various elements, with the ultimate goal of identifying the attitudes, perceptions and behaviours of participants towards certain health services. It has been applied in various contexts, especially in nutritional studies (Deshpande et al. 2009).

This model can also be applied in the PV industry, enabling researchers to understand the phenomenon of the ADR under-reporting. Directly associated with Inman's model and the KAP model discussed in Section 3.3.2., the attitudes of both healthcare workers and the public can be determined. This allows for research to determine the appropriate actions to be taken to address the findings of the health belief model.

5.4. Partnership Success Model

Literature makes reference to various business partnership models that have the capacity to aid the establishment of partner relationships. One of these models, the partnership success model, can be used to contribute to improved partnership management in PV. This model states that in order to achieve success in partnerships, certain attributes must be established. These attributes are the key characteristics of partnerships such as commitment and trust, communication behaviours such as information sharing and participation from all parties, and finally effective conflict resolution techniques (Hill 2014).

5.5. Conclusion: Potential of technology to contribute to PV

It is evident that there are existing technological developments that can be used to address the PV challenge landscape. Further investigation of other technological developments such as algorithms developed for big data analysis, existing resource management systems, sociological studies to understand the country-specific factors, and transition models for changing reactive reporting systems into proactive systems, is therefore motivated as there is reason to believe that these may have the capacity to address aspects of the PV challenge landscape.

6. Conclusion and further research

The association made between a PV system and the PV challenge landscape is discussed in this paper. A succinct overview of the PV challenge landscape is provided, where it is made clear that PV culture is in need of improvement. This can be done by addressing the challenges arising from PV culture. The associations made between the PV system and the PV challenge landscape illustrates the challenges that are most prevalent, making it clear that research in these challenges is necessary.

A succinct overview of the prospects of existing technological developments in addressing the PV challenge landscape is provided. This shows that there are technological developments, used outside the PV context, which can be applied to the PV challenge landscape.

For further research, subject matter experts and literature will be essential in prioritising the PV challenge landscape, allowing for more in-depth research to be conducted in the most prevalent challenges in PV, which will allow for a comprehensive understanding of these challenges. Subsequently, research into the prospects of technological developments in industries that experience similar challenges than that of PV can continue.

7. References

De Abajo, F.J., 2005. Improving pharmacovigilance beyond spontaneous reporting. *International Journal of Pharmaceutical Medicine*, 19(4), pp.209–218.

Abubakar, A.R., Ismail, S., et al., 2015. Comparative study on drug safety surveillance between medical students of Malaysia and Nigeria. *Therapeutics and Clinical Risk Management*, pp.1015–1025.

Abubakar, A.R., Chedi, B.A., et al., 2015. Perception of Nigerian medical students on adverse drug reaction reporting. *Journal of Advanced Pharmaceutical Technology and Research*, 6(4), pp.154–158.

Abubakar, A.R. & Haque, M., 2016. Pharmacovigilance Practice : The Current Challenges and the Gaps in the Medical Students ' Curriculum. *Journal of Applied Pharmaceutical Science*, 6(05), pp.210–215.

Abubakar, A.R., Simbak, N. Bin & Haque, M., 2015. Pharmacovigilance Study : Awareness among Medical Students of a New Medical School of Malaysia. *International Journal of Pharmaceutical Research*, 7(1), pp.83–88.

Agbabiaka, T.B., Savović, J. & Ernst, E., 2008. Methods for causality assessment of adverse drug reactions: a systematic review. *Drug Safety*, 31(1), pp.21–37. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18095744.

Al-Alawi, A.I., Al-Marzooqi, N.Y. & Mohammed, Y.F., 2007. Organizational culture and knowledge sharing: critical success factors. *Journal of Knowledge Management*, 11(2), pp.22–42. Available at: http://www.emeraldinsight.com/doi/10.1108/13673270710738898.

Alan, W., 2001. Understanding organisational culture and the implications for corporate marketing. *European Journal of Marketing*, 35(3/4), pp.353–367.

Aljadhey, H. et al., 2015. A qualitative exploration of the major challenges facing pharmacovigilance in Saudi Arabia. *Saudi Medical Journal*, 36(9), pp.1097–1102.

Armstrong, S., 2013. What Are The Advantages And Disadvantages Of Online Learning? *eLearning Industry*. Available at: https://elearningindustry.com/advantages-and-disadvantages-of-online-learning [Accessed January 30, 2018].

Aronson, J.K., 2012. Balanced prescribing – principles and challenges. *British Journal of Clinical Pharmacology*, 74(4), pp.566–572.

Avorn, J. & Schneeweiss, S., 2009. Managing Drug-Risk Information — What to Do with All Those New Numbers. *The New England Journal of Medicine*, 361(7), pp.647–649.

Baiju, N.T., 2017. 5 advantages and disadvantages of Cloud Storage. *Big Data Made sSmple*, pp.4-6. Available at: http://bigdata-madesimple.com/5-advantages-and-disadvantages-of-cloud-storage/ [Accessed January 30, 2018].

Bandekar, M.S., Anwikar, S.R. & Kshirsagar, N.A., 2009. Theories of attempted suicide: Should they differ from theories of completed suicide? *Pharmacoepidemiology and Drug Safety*, 6(5), pp.188-191.

Barnieh, L., Donaldson, C. & Manns, B., 2014. Health care prioritization : a clinician's duty. *Canadian Journal of Kidney Health and Disease*, 1(27), pp.1–5.

Baroudi, R., 2014. Key performance indicators: Winning tips and common challenges. *EY Performance Journal*, 6(2), pp.36–43.
Bau, L.M.S. et al., 2012. Organizational ergonomics of occupational health methods and processes in a Brazilian oil refinery. In *Work 41*. pp. 2817–2821.
Beckmann, J. et al., 2014. Teaching Pharmacovigilance: the WHO-ISoP Core Elements of a Comprehensive Modular Curriculum. *Drug Safety*, 37(10), pp.743–759.
Bellot, J., 2011. Defining and assessing organizational culture. *Nursing forum*, 46(1), pp.29–37.
Beninger, P., 2017. Opportunities for Collaboration at the Interface of Pharmacovigilance and Manufacturing. *Clinical Therapeutics*, 39(4), pp.702–712. Available at: http://dx.doi.org/10.1016/j.clinthera.2017.03.010.
Bergvall, T., Niklas Norén, G. & Lindquist, M., 2014. VigiGrade: A tool to identify well-documented individual case reports and highlight systematic data quality issues. *Drug Safety*, 37(1), pp.65–77.
Berry, S., 2010. How Coca-Cola's distribution system works. *ColaLife*. Available at: http://www.colalife.org/2010/12/19/how-coca-colas-distribution-system-works/ [Accessed February 26, 2018].
BEUC, 2008. A STRONG , TRANSPARENT AND PROACTIVE PHARMACOVIGILANCE SYSTEM. , pp.1–8. Available at: www.beuc.eu.
Booth, N., 2003. Can business benefit from remote access? *ComputerWeekly.com*. Available at: http://www.computerweekly.com/feature/Can-business-benefit-from-remote-access [Accessed January 31, 2018].
Boundless Management, 2016. Strategic, Tactical, and Operational Control. *Boundless Management*. Available at: https://www.boundless.com/management/textbooks/boundless-management-textbook/control-8/types-of-control-62/strategic-tactical-and-operational-control-313-3960/ [Accessed August 4, 2017].
Brugha, R. & Varvasovszky, Z., 2000. Stakeholder analysis: a review. *Health Policy and Planning*, 15(3), pp.239–246. Available at: https://academic.oup.com/heapol/article-lookup/doi/10.1093/heapol/15.3.239.
Brundage, M.P. et al., 2017. Smart Manufacturing Through a Framework for a Knowledge-Based Diagnosis System. In M. P. Brundage, ed. *ASME 2017 International Manufacturing Science and Engineering Conference*. Los Angeles: Research Gate, pp. 1-9. Available at: http://proceedings.asmedigitalcollection.asme.org/proceeding.aspx?doi=10.1115/MSEC2017-2937.
Bulsuk, K., 2009. Using a Fishbone (or Ishikawa) Diagram to Perform 5-why Analysis. *Toyota Production System*. Available at: http://www.bulsuk.com/2009/08/using-fishbone-diagram-to-perform-5-why.html [Accessed October 4, 2017].
Buse, K., Mays, N. & Walt, G., 2005. *Making Health Policy* N. Black & R. Raine, eds., Berkshire, England: McGraw-Hill Education.
Callréus, T., 2011. The New EU Legislation on Pharmacovigilance and Changing Models for Drug Development. *Drug Safety*, 34(6), pp.529–531.
Caster, O. et al., 2017. vigiRank for statistical signal detection in pharmacovigilance: First results from prospective real-world use. *Pharmacoepidemiology and Drug Safety*, 26(8), pp.1006–1010.
Chan, C. V. & Kaufman, D.R., 2010. A technology selection framework for supporting delivery of patient-oriented health interventions in developing countries. *Journal of Biomedical Informatics*, 43(2), pp.300–306. Available at: http://dx.doi.org/10.1016/j.jbi.2009.09.006.
Cheaib, N., 2016. Pharmacovigilance in Clinical Trials: Current Practice and Challenges. *Accountability in Research*, 23(1), pp.23–30. Available at: http://www.tandfonline.com/doi/full/10.1080/08989621.2014.956868%0Ahttp://www.ncbi.nlm.nih.gov/pubmed/26528639.
Chmutova, I., 2015. Bank's financial management technologies forming at strategic and operational levels. *Economic Annals-XXI*, 9, pp.73–77.
Coffey, H., 2007. Digital game-based learning. *Learn NC*. Available at: http://www.dfpp.univr.it/documenti/Avviso/all/all036209.pdf [Accessed February 26, 2018].
Cognizant, 2012. *The Future of Pharmacovigilance : Five Imperatives that Will Drive Improved Business Outcomes*, Available at: https://www.cognizant.com/industries-resources/life_sciences/The-Future-of-Pharmacovigilance-Five-Imperatives-that-Will-Drive-Improved-Business-Outcomes.pdf.
Cohn, J. et al., 2017. When falsified medicines enter the supply chain : Description of an incident in Kenya and lessons learned for rapid response Published by : Palgrave Macmillan Journals Stable URL : http://www.jstor.org/stable/43287941 When falsified medicines enter the su. *Journal of Public Health Policy*, 34(1), pp.22–30.
Croxton, K.L. et al., 2001. The Supply Chain Management Processes. *The International Journal of Logistics Management*, 12(2), pp.13-36.
Data Team, 2017. In much of sub-Saharan Africa, mobile phones are more common than access to electricity. *The Economist*. Available at: https://www.economist.com/graphic-detail/2017/11/08/in-much-of-sub-saharan-africa-mobile-phones-are-more-common-than-access-to-electricity [Accessed July 16, 2018].
Deloitte, 2014. *Value of connectivity: Economic and social benefits of expanding internet access*, Available at: https://www2.deloitte.com/content/dam/Deloitte/ie/Documents/TechnologyMediaCommunications/2014_uk_tmt_value_of_connectivity_deloitte_ireland.pdf.
Demirkıran, Z.K. & Altunok, T., 2012. A Systems Approach for Technology Assessment and Selection. In *Digital Avionics Systems Conference (DASC)*. Williamsberg, VA, USA: IEEE, pp. 1–11.
Deshpande, S., Basil, M.D. & Basil, D.Z., 2009. Factors Influencing Healthy Eating Habits Among College Students: An Application of the Health Belief Model. *Health Marketing Quarterly*, 26(2), pp.145–164. Available at:

http://www.tandfonline.com/doi/abs/10.1080/07359680802619834.
Donner, J., 2008. Research approaches to mobile use in the developing world: A review of the literature. *Information Society*, 24(3), pp.140–159.
Dubey, A. & Handu, S.S., 2013. Are we pharmacovigilant enough in ophthalmic practice? *Indian Journal of Ophthalmology*, 61(5), pp.226–229.
Dusek, V., 2008. *Philosophy of Technology: An Introduction*, United Kingdom: Blackwell Publishing. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18427953%5Cnfile:///C:/Users/morganya/Documents/My eBooks/academic/Dusek, Val. Philosophy of Technology An Introduction.pdf.
Al Dweik, R. et al., 2016. Factors affecting patient reporting of adverse drug reactions: a systematic review. *British Journal of Clinical Pharmacology*, (November).
Ebrahim, A., 2013. Let's Be Realistic About Measuring Impact. *Harvard Business Review*, pp.1–2. Available at: https://hbr.org/2013/03/lets-be-realistic-about-measur.html [Accessed July 21, 2017].
Eckerson, W.W., 2009. *Performance management strategies: How to Create and Deploy Effective Metrics*, Available at: https://www.microstrategy.com/strategy/media/downloads/white-papers/tdwi_performance-management-strategies.pdf.
Edwards, B. et al., 2015. Guiding Principles of Safety as a Basis for Developing a Pharmaceutical Safety Culture. *Current Drug Safety*, 2, pp.135–139.
Edwards, I.R., 2017. Causality Assessment in Pharmacovigilance: Still a Challenge. *Drug Safety*, 40(5), pp.365–372.
Fortado, B. & Fadil, P., 2012. The four faces of organizational culture. *Competitiveness Review: An International Business Journal*, 22(4), pp.283–298. Available at: http://www.emeraldinsight.com/doi/10.1108/10595421211247132.
François, A. et al., 2013. How can the Quality of Medical Data in Pharmacovigilance , Pharmacoepidemiology and Clinical Studies be Guaranteed ? *Société Française de Pharmacologie et de Thérapeutique*, 68(4), pp.217–223.
Franz, M. et al., 2015. *Building Energy Access Markets: A Value Chain Analysis of Key Energy Market Systems*, Eschborn. Available at: http://www.euei-pdf.org/sites/default/files/files/field_pblctn_file/150907_euei_value-chain_en_rz_03_web_0.pdf.
Gaille, B., 2016. 16 Pros and Cons of the Internet of Things. *BrandonGaille.com*. Available at: https://brandongaille.com/16-pros-and-cons-of-the-internet-of-things/ [Accessed January 31, 2018].
Giezen, T.J., Mantel-Teeuwisse, A.K. & Leufkens, H.G., 2009. Pharmacovigilance of Biopharmaceuticals - Challenges Remain. *Drug Safety*, 32(10), pp.811–817.
Gilson, L., 2006. Trust in health care : Theoretical perspectives and research needs. *Journal of Health Organization and Management*, 20(5), pp.359–375.
Granados, N., Gupta, A. & Kauffman, R.J., 2010. Information Transparency in Tusiness-to-Consumer Markets: Concepts, Framework, and Research Agenda. *Information Systems Research*, 21(2), pp.207–226.
Gubbi, J. et al., 2013. Internet of Things (IoT): A Vision, Architectural Elements, and Future Directions. *Future Generation Computer Systems*, 29(7), pp.1645–1660. Available at: https://arxiv.org/pdf/1207.0203.pdf?ref=theiotlist.
Hackett, R., 2016. Wait, What is Blockchain? *Fortune*. Available at: http://fortune.com/2016/05/23/blockchain-definition/ [Accessed February 8, 2018].
Hammer, M., 2004. Deep Change : How Operational Innovation Can Transform Your Company. *Harvard Business Review*, (April), pp.1–20.
Härmark, L. & Van Grootheest, A.C., 2008. Pharmacovigilance: Methods, recent developments and future perspectives. *European Journal of Clinical Pharmacology*, 64(8), pp.743–752.
Harpaz, R. et al., 2014. Text Mining for Adverse Drug Events : the Promise , Challenges , and State of the Art. *Drug Safety*, 37, pp.777–790.
Harris, M., 2017. What is Cloud Storage? *LifeWire*. Available at: https://www.lifewire.com/what-is-cloud-storage-2438541 [Accessed January 30, 2018].
Hazell, L. & Shakir, S.A.W., 2006. Under-Reporting of Adverse A Systematic Review. *Drug Safety*, 29(5), pp.385–396.
Heinrich, M., 2015. Quality and safety of herbal medical products : regulation and the need for quality assurance along the value chains. *British Journal of Clinical Pharmacology*, 80(1), pp.62–66.
Herdeiro, M.T. et al., 2006. Influence of Pharmacists ' Attitudes on Adverse Drug Reaction Reporting A Case-Control Study in Portugal. *Drug Safety*, 29(4), pp.331–340.
Hewitt-Taylor, J., 2012. Identifying, analysing and solving problems in practice. *Nursing Standard*, 26(40), pp.35–41. Available at: https://www.researchgate.net/profile/Eduardo_Cittadini/publication/262911808_Participatory_Analysis_of_the_Sweet_Cherry_Sector_in_Argentinian_South_Patagonia/links/5656edfb08ae4988a7b51232.pdf.
Hill, G., 2014. Pharmacovigilance methods: the spectrum of PV. [Online video]. Available at: https://www.youtube.com/watch?v=lAhzeDxMp1s [Accessed April 15, 2017].
Holden, W.L., Juhaeri, J. & Dai, W., 2003. Benefit-risk analysis: A proposal using quantitative methods. *Pharmacoepidemiology and Drug Safety*, 12(7), pp.611–616.
Holm, G. et al., 2013. Implementing Ecopharmacovigilance in Practice : Challenges and Potential Opportunities. *Drug Safety*, 36, pp.533–546.
Hong, J., 2013. Framework for selecting the technology in public sector. *Information*, 16(11), pp.7895–7904.
HRCloud, 2017. HR Software & HRMS Solutions for Business. Available at: https://www.hrcloud.com/.
Iansiti, M. & Lakhani, K.R., 2017. The Truth About Blockchain. *Harvard Business Review*, 3(January-February),

pp.3–11.
Irujo, M. et al., 2007. Factors that Influence Under-Reporting of Suspected Adverse Drug Reactions among Community Pharmacists in a Spanish Region. *Drug Safety*, 30(11), pp.1073–1082.
Isah, A.O. et al., 2012. Specific features of medicines safety and pharmacovigilance in Africa. *Therapeutic advances in drug safety*, 3(1), pp.25–34. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4110828&tool=pmcentrez&rendertype=abstract.
Islam, S.M.R. et al., 2015. The Internet of Things for Health Care : A Comprehensive Survey. *IEEE Access*, 3, pp.678–708. Available at: http://ieeexplore.ieee.org/xpl/articleDetails.jsp?arnumber=7113786.
Jones, R.W. & Despotou, G., 2016. Root cause analysis and health informatics. In *14th International Conference on Informatics, Management and Technology in Healthcare*. Athens: Studies in health technology and informatics, pp. 131–134. Available at: http://dx.doi.org/10.3233/978-1- 61499-664-4-131.
Jurevicius, O., 2013a. Resource based view. *Strategic Management Insight*, p.1. Available at: https://www.strategicmanagementinsight.com/topics/resource-based-view.html [Accessed June 28, 2017].
Jurevicius, O., 2013b. Value Chain Analysis. *Strategic Management Insight*. Available at: https://www.strategicmanagementinsight.com/tools/value-chain-analysis.html [Accessed August 18, 2017].
Jusot, V., 2017. Correspondence. 20 July, Stellenbosch.
Kabore, L. et al., 2013. Pharmacovigilance systems in developing countries: An evaluative case study in Burkina Faso. *Drug Safety*, 36(5), pp.349–358.
KC, S. et al., 2013. Knowledge about adverse drug reactions reporting among healthcare professionals in Nepal. *International Journal of Risk and Safety in Medicine*, 25, pp.1–16.
Kendrick, J., 2013. Mobile technology: The amazing impact on our lives. *Mobile News*. Available at: http://www.zdnet.com/article/mobile-technology-the-amazing-impact-on-our-lives/ [Accessed February 2, 2018].
Khan, T.M., 2013. Community pharmacists' knowledge and perceptions about adverse drug reactions and barriers towards their reporting in Eastern region, Alahsa, Saudi Arabia. *Therapeutic Advances in Drug Safety*, 4(2), pp.45–51.
Khorramshahgol, R. & Moustakis, V.S., 1988. Delphic hierarchy process (DHP): a methodology for priority setting derived from the Delphi method and analytical hierarchy process. *European Journal of Operational Research*, 37(3), pp.347–354.
Kirby, M.R. & Mavris, D.N., 2000. A method for technology selection based on benefit, available schedule and budget resources. In *2000 World Aviation Conference*. San Diego, CA: American Institute of Aeronautics and Astronautics (AIAA), pp. 1–15. Available at: http://arc.aiaa.org/doi/pdf/10.2514/6.2000-5563.
Klausen, S.M. & Parle, J., 2015. 'Are we going to stand by and let these children come into the world?': the impact of the 'Thalidomide Disaster' in South Africa, 1960–1977. *Journal of Southern African Studies*, 41(4), pp.735–752. Available at: http://www.tandfonline.com/doi/full/10.1080/03057070.2015.1047181.
Klein, R., 1993. Dimensions of rationing: who should do what? *British Medical Journal*, 307, pp.309–131.
Klein, R., 1998. Puzzling out Priorities: Why We Must Acknowledge That Rationing Is a Political Process. *British Medical Journal*, 317(7164), pp.959–960.
Kumar, A. & Khan, H., 2015. Signal detection and their assessment in pharmacovigilance. *Open Pharmaceutical Sciences Journal*, 2, pp.66–73.
Lamprecht, A.J., 2017. Personal interview. 10 October, Western Cape Department of Education Headquarters.
Lamprecht, I.V.B., Bam, L. & de Kock, I.H., 2017. An investigation into the prospects of existing technologies to address the challenges faced by pharmacovigilance systems. In *SAIIE28: Taking up Stewardship*. Vanderbijlpark: SAIIE, pp. 1–17. Available at: https://www.saiie.co.za/saiie28.
Li, Y. et al., 2017. How Do Resource Structuring and Strategic Flexibility Interact to Shape Radical Innovation? *Journal of Product Innovation Management*, 34(4), pp.471–491. Available at: http://doi.wiley.com/10.1111/jpim.12389.
Lu, Z., 2009. Information technology in pharmacovigilance : Benefits , challenges , and future directions from industry perspectives. *Drug, Healthcare and Patient Safety*, 1, pp.35–45.
Macwan, U., 2017. Mobile Technology , Its Importance , Present And Future Trends. *Finextra*. Available at: https://www.finextra.com/blogposting/14000/mobile-technology-its-importance-present-and-future-trends [Accessed February 2, 2018].
Management for Science, 2012. Pharmacovigilance. , p.35.1-35.19.
Mathur, V.N. et al., 2007. Defining, identifying and mapping stakeholders in the assessment of urban sustainability. In M. Horner et al., eds. *International Conference on Whole Life Urban sustainability and its Assessment*. Glasgow, p. 18. Available at: https://dspace.lboro.ac.uk/xmlui/handle/2134/5202.
Mehta, U., 2017. Personal interview. 21 August, School of Public Health (UCT).
Mishra, S. & Singh, I.P., 2008. mHealth: a developing country perspective. In *Making the eHealth connection*. Bellagio, Italy, pp. 1-9. Available at: http://ehealth-connection.org/files/conf-materials/mHealth_ A Developing Country Perspective_0.pdf.
Morrison, A. & Sinha, S., 2016. A primer on blockchain (infograohic). *PWC Emerging Technology*. Available at: http://usblogs.pwc.com/emerging-technology/a-primer-on-blockchain-infographic/ [Accessed February 8, 2018].
Mpanza, Z., 2016. Identifying the root causes contributing to defects in order to minimize scrap. In *2016 International Conference on Industrial Engineering and Operations Management*. Kuala Lumpur: IEOM

Society International, pp. 1139–1146. Available at: http://ieomsociety.org/ieom_2016/pdfs/318.pdf.

Myszewski, J.M., 2013. On improvement story by 5 whys. *The TQM Journal*, 25(4), pp.371–383. Available at: http://www.emeraldinsight.com/doi/10.1108/17542731311314863.

Naghibi, M.A. & Baban, H., 2011. Strategic Change Management: The Challenges Faced by Organizations. *International Proceedings of Economics Development and Research*, 4, pp.542–544.

Naidoo, P. & Martins, N., 2014. The relationship between organizational culture and work engagement: A multilevel investigation. *Problems and Perspectives in Management*, 12(4), pp.433–441.

Newton, R., 2010. Six Symptoms of Poor Prioritisation. *Corporate Geek*, pp.407–407. Available at: http://www.corporategeek.info/six-symptoms-poor-prioritisation [Accessed November 9, 2017].

Nikfarjam, A. et al., 2015. Pharmacovigilance from social media: Mining adverse drug reaction mentions using sequence labeling with word embedding cluster features. *Journal of the American Medical Informatics Association*, 22(3), pp.671–681.

Norman, S., 2016. Advantages Of Online Learning: Education Without Leaving Home. *eLearning Industry*. Available at: https://elearningindustry.com/5-advantages-of-online-learning-education-without-leaving-home [Accessed January 30, 2018].

Olsen, A.K. & Whalen, M.D., 2009. Public Perceptions of the Pharmaceutical Industry and Drug Safety and the Culture of Safety. *Drug Safety*, 32(10), pp.805–810.

Olsson, S. et al., 2010. Pharmacovigilance activities in 55 low-and middle-income countries: A questionnaire-based analysis. *Drug Safety*, 33(8), pp.689–703.

Ostrov, J.M., Gentile, D.A. & Mullins, A.D., 2013. Evaluating the effect of educational media exposure on aggression in early childhood. *Journal of Applied Developmental Psychology*, 34(1), pp.38–44. Available at: http://dx.doi.org/10.1016/j.appdev.2012.09.005.

Oztaysi, B., 2014. A decision model for information technology selection using AHP integrated TOPSIS-Grey: The case of content management systems. *Knowledge-Based Systems*, 70, pp.44–54.

Palloff, R.M. & Pratt, K., 2001. *Lessons from the Cyberspace Classroom: The Realities of Online Teaching*, San Francisco: Jossey-Bass. Available at: https://books.google.co.za/books?hl=en&lr=&id=36GLHRvTELMC&oi=fnd&pg=PR9&dq=online+teaching&ots=8n_1hUxCUP&sig=6Ku1I_cFJfZyhzD-nHlsJnuFf_4#v=onepage&q=online teaching&f=false.

Pan, G.J.D., 2014. Ongoing Challenges in Pharmacovigilance. *Drug Safety*, 37, pp.1–8.

Passier, A. et al., 2009. Reporting of Adverse Drug Reactions by General Practitioners. *Drug Safety*, 32(10), pp.851–858.

Pojasek, R.B., 2000. Asking "Why?" five times. *Environmental Quality Management*, 10(1), pp.79–84.

Pontes, H., Clément, M. & Rollason, V., 2014. Safety signal detection: The relevance of literature review. *Drug Safety*, 37(7), pp.471–479.

Rachlis, B. et al., 2016. Targeted Spontaneous Reporting: Assessing Opportunities to Conduct Routine Pharmacovigilance for Antiretroviral Treatment on an International Scale. *Drug Safety*, 39(10), pp.959–976.

Raghupathi, W. & Raghupathi, V., 2014. Big data analytics in healthcare: promise and potential. *Health Information Science and Systems*, 2(1), p.3. Available at: http://link.springer.com/10.1186/2047-2501-2-3.

Rahman, S.Z. & Khan, R.A., 2015. Pharmaco Environmentology – Aligning Pharmacovigilance with Environment. *Pharma Times*, 47(8).

Rama, P., Rodrigues, P.A. & Georgy, A., 2011. Asian Journal of Pharmaceutical and Clinical Research PHARMAOVIGILANCE : PERSPECTIVES AND FUTURE CHALLENGES IN INDIAN SCENARIO. *Asain Journal of Pharmaceutical and Clinical Research*, 4(4), pp.1–4.

Raschi, E. et al., 2016. Adverse events associated with the use of direct-acting oral anticoagulants in clinical practice: Beyond bleeding complications. *Polish Archives of Internal Medicine*, 126(7–8), pp.552–561.

Ríos, O.M. et al., 2016. A comprehensive intervention for adverse drug reactions identification and reporting in a Pediatric Emergency Department. *International Journal of Clinical Pharmacy*, 38(1), pp.80–87.

Rodrigues, G.S. & Khan, S.A., 2011. Pharmacovigilance Among Surgeons and in Surgical Wards : Overlooked or Axiomatic ? *Indian Journal of Surgery*, 73(1), pp.4–8.

Rouse, M., 2005. Remote Access. *TechTarget*. Available at: http://searchmidmarketsecurity.techtarget.com/definition/remote-access [Accessed January 30, 2018].

Rouse, M., 2010. WAP (Wireless Application Protocol). *TechTarget*. Available at: http://searchmobilecomputing.techtarget.com/definition/WAP [Accessed February 26, 2018].

Rubel, M.R.B. et al., 2017. Adapting technology : effect of high-involvement HRM and organisational trust. *Behaviour and Information Technology*, 36(1), pp.281–293.

Ruder, K.A., Pretorius, M.W. & Maharaj, B.T., 2008. A technology selection framework for the telecommunications industry in developing countries. In *IEEE International Conference on Communications*. Beijing, pp. 5490–5493.

Ruder, K.A., Pretorius, M.W. & Maharaj, B.T., 2008. A technology selection framework for the telecommunications industry in developing countries. In *IEEE International Conference on Communications*. IEEE, pp. 5490–5493.

Russom, P., 2011. *Big data analytics*, Available at: https://vivomente.com/wp-content/uploads/2016/04/big-data-analytics-white-paper.pdf.

Sabik, L.M. & Lie, R.K., 2008. Priority setting in health care: Lessons from the experiences of eight countries. *International Journal for Equity in Health*, 7(1), p.4. Available at: http://equityhealthj.biomedcentral.com/articles/10.1186/1475-9276-7-4.

Sarker, A. et al., 2015. Utilizing social media data for pharmacovigilance: A review. *Journal of Biomedical*

Informatics, 54, pp.202–212. Available at: http://dx.doi.org/10.1016/j.jbi.2015.02.004.

Schramm, G.E. et al., 2017. Implementation of an interprofessional clinical pharmacology selective learning experience for pharmacy residents and medical students. *American Journal of Health-System Pharmacy*, 74(6), p.397.

Shamim, S. et al., 2016. Adverse drug reactions (ADRS) reporting : awareness and reasons of under-reporting among health care professionals , a challenge for pharmacists. *SpringerPlus (2016)*, 5, pp.1–8.

Sharif, M.N. & Sundararajan, V., 1983. A quantitative model for the evaluation of technological alternatives. *Technological Forecasting and Social Change*, 24(1), pp.15–29.

Shehabuddeen, N., Probert, D. & Phaal, R., 2006. From theory to practice: Challenges in operationalising a technology selection framework. *Technovation*, 26(3), pp.324–335.

Shen, Y.C. et al., 2010. A hybrid selection model for emerging technology. *Technological Forecasting and Social Change*, 77(1), pp.151–166. Available at: http://dx.doi.org/10.1016/j.techfore.2009.05.001.

Simister, P., 2011. Advantages & Disadvantages Of Value Chain Analysis. *Differentiate Your Business*. Available at: http://www.differentiateyourbusiness.co.uk/the-advantages-disadvantages-of-value-chain-analysis [Accessed August 18, 2017].

Singh, V., 2017. Pros & Cons of Apps and Website: Which is Better Option? *YourStory*. Available at: https://yourstory.com/mystory/5d1d4981fe-pros-cons-of-apps-and-website-which-is-better-option- [Accessed February 26, 2018].

Smith, N., 2014. 5 Key Principles to Resource Management. *LiquidPlanner*. Available at: https://www.liquidplanner.com/blog/5-key-principles-resource-management/ [Accessed February 1, 2018].

Sonkiya, S., 2014. Cause And Effect Diagram- Fishbone Diagram Analysis. *Project Quality Management*. Available at: https://www.izenbridge.com/blog/cause-and-effect-diagram-fishbone-diagram-analysis/ [Accessed October 4, 2017].

Spacey, J., 2015. 11 Types of Resource Management. *Simplicable*. Available at: https://simplicable.com/new/resource-management [Accessed February 1, 2018].

Stahl, M. et al., 2003. Assessing the Impact of Drug Safety Signals from the WHO Database Presented in SIGNAL. *Drug Safety*, 26(10), pp.721–727. Available at: http://www.scopus.com/inward/record.url?eid=2-s2.0-19244382600&partnerID=tZOtx3y1.

Stolk, R.P., 2012. Screening for diabetes. *British Medical Journal*, 335(September), p.462.

Strengthening Pharmaceutical Systems (SPS), 2009. *Supporting Pharmacovigilance in Developing Countries The Systems Perspective*,

Stretcher, V. & Rosenstock, I.M., 1997. The Health Belief Model. In *Health Behavior and Health Education: Theory, Research and Practice*. Jones and Bartlett Publishers, pp. 31–36.

Su, C., Ji, H. & Su, Y., 2010. Hospital pharmacists ' knowledge and opinions regarding adverse drug reaction reporting in Northern China y. *Pharmacoepidemiology and Drug Safety*, 19, pp.217–222.

Suwankesawong, W. et al., 2016. Pharmacovigilance activities in ASEAN countries. *Pharmacoepidemiology and Drug Safety*, 25, pp.1061–1069.

Tallent-Runnels, M.K. et al., 2006. Teaching Courses Online: A Review of the Research. *Review of Educational Research*, 76(1), pp.93–135. Available at: http://rer.sagepub.com/cgi/doi/10.3102/00346543076001093.

Tiles, M. & Oberdiek, H., 1999. *Living in a Technological World 27*, United Kingdom: Routledge.

Toklu, H.Z. & Uysal, M.K., 2008. The knowledge and attitude of the Turkish community pharmacists toward pharmacovigilance in the Kadikoy district of Istanbul. *Pharmacy World & Science*, 30, pp.556–562.

Tomoaia-Cotisel, A. et al., 2013. Context Matters : The Experience. *Annals of Family Medicine*, 11(Supp 1), pp.115–123.

United Nations, 2012. *UNPRPD Strategic and Operational Framework*, New York. Available at: http://www.undp.org/content/dam/undp/library/Poverty Reduction/Inclusive development/UNPRPD_SOF_web_April2012.pdf.

Uppsala Monitoring Centre, 2017. *The quest for evidence*, Uppsala. Available at: https://view.publitas.com/uppsala-monitoring-centre/uppsala-reports-77_web/page/1.

Varallo, F.R. et al., 2014. Causes for the underreporting of adverse drug events by health professionals : a systematic review. *Rev Esc Enferm USP*, 48(4), pp.739–747.

Vargesson, N., 2015. Thalidomide-induced teratogenesis: History and mechanisms. *Birth Defects Research*, 105(2), pp.140–156. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26043938%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4737249%5Cnhttp://doi.wiley.com/10.1002/bdrc.21096.

Varun, B., 2016. What are pros and cons of Internet of Things? *PixelCrayons*. Available at: https://www.pixelcrayons.com/blog/industry-news/what-are-pros-and-cons-of-internet-of-things/ [Accessed January 31, 2018].

Veyrat, P., 2016. How did the 5W2H method earn its name? *Heflo*. Available at: https://www.heflo.com/blog/action-plan/5w2h-method/ [Accessed August 16, 2017].

Viswanathan, P., 2017. What is a Mobile Application? *LifeWire*. Available at: https://www.lifewire.com/what-is-a-mobile-application-2373354 [Accessed February 26, 2018].

De Vries, S.T. et al., 2016. Factors Influencing the Use of a Mobile App for Reporting Adverse Drug Reactions and Receiving Safety Information: A Qualitative Study. *Drug Safety*, 40, pp.443–455. Available at: http://link.springer.com/10.1007/s40264-016-0494-x.

Waller, P.C. & Evans, S.J.W., 2003. A model for the future conduct of pharmacovigilance. *Pharmacoepidemiology and Drug Safety*, 12(1), pp.17–29.

Wang, X. et al., 2009. Active Computerized Pharmacovigilance Using Natural Language Processing, Statistics, and Electronic Health Records: A Feasibility Study. *Journal of the American Medical Informatics Association*, 16(3), pp.328–337. Available at: http://dx.doi.org/10.1197/jamia.M3028.

Warner, J., 2015. Is the “5 Why” Method Still a Useful Tool? *Ready To Manage*. Available at: http://blog.readytomanage.com/is-the-5-why-method-still-a-useful-tool/ [Accessed August 16, 2017].

Weber-Schoendorfer, C. & Schaefer, C., 2016. Pregnancy outcome after tocilizumab therapy in early pregnancy-case series from the German Embryotox Pharmacovigilance Center. *Reproductive Toxicology*, 60, pp.29–32. Available at: http://dx.doi.org/10.1016/j.reprotox.2016.01.002.

Western Governers University, 2017. Teaching Strategies for Using Educational Movies in the Classroom. *Western Governors University*. Available at: https://www.wgu.edu/blogpost/teaching-strategies-using-educational-television-classroom# [Accessed February 26, 2018].

World Health Organization, 2004. *Pharmacovigilance : ensuring the safe use of medicines*, Available at: www.who.org.

World Health Organization, 2002. *The Importance of Pharmacovigilance - Safety Monitoring of medicinal products*, Available at: http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf.

World Health Organization, 2014. WHO pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. , (1), pp.4-6. Available at: http://apps.who.int/iris/bitstream/10665/186642/1/9789241508254_eng.pdf.

Yang, M., Kiang, M. & Shang, W., 2015. Filtering big data from social media - Building an early warning system for adverse drug reactions. *Journal of Biomedical Informatics*, 54, pp.230–240. Available at: http://dx.doi.org/10.1016/j.jbi.2015.01.011.

Yap, C.M. & Souder, W.E., 1993. A filter system for technology evaluation and selection. *Technovation*, 13(7), pp.449–469.

Zaied, A.N., 2007. A Framework for Evaluating and Selecting Learning Technologies. *The International Arab Journal of Information Technology*, 4(2), pp.141–147.

Zakir, J., Seymour, T. & Berg, K., 2015. Big Data Analytics. *Issues in Information Systems*, 16(2), pp.81–90.

Zhang, L. et al., 2014. Pharmacovigilance in China: Current Situation, Successes and Challenges. *Drug Safety*, 37(10), pp.765–770.

Appendix 1: structured literature search protocol

As described in Section 3, a structure search protocol was followed to identify literature for inclusion in the review of the PV challenge landscape. In total, 33 searches were conducted, the protocol used for each search is detailed in Table 2. The “W/” operator indicated in the table is used in Scopus to denote that terms must appear within the specified number of words from one another.

Table 2: Structured literature review search protocol.

Search ID	Search terms
1	pharmacovigilance AND challenge*

2	adverse AND drug AND reaction AND area* W/3 improvement*
3	adverse AND drug AND reaction AND area* W/1 improvement*
4	adverse W/0 drug W/0 event OR reaction* AND area* W/1 improvement*
5	limitation* AND clinical AND trials AND pharmacovigilance
6	limitation* W/1 clinical AND trials AND pharmacovigilance
7	pharmacovigilance AND culture
8	pharmacovigilance AND culture AND challenge
9	pharmacovigilance AND feedback
10	pharmacovigilance AND feedback AND challenge*
11	pharmacovigilance AND feedback AND limitation*
12	adverse AND drug AND reaction AND report* AND feedback
13	pharmacovigilance AND minimal W/0 data
14	adverse AND drug AND reaction AND report* AND minimal W/0 data
15	adverse AND drug AND reaction AND report* AND lack W/0 of W/0 data
16	pharmacovigilance AND education
17	pharmacovigilance AND education AND limitation
18	pharmacovigilance AND expertise
19	adverse AND drug AND reaction AND expertise
20	adverse AND drug AND reaction AND expertise AND challenge
21	adverse AND drug AND reaction AND training AND challenge
22	adverse AND drug AND reaction AND training AND limit*
23	adverse AND drug AND reaction AND partner*
24	adverse AND drug AND reaction AND partner* AND challenge
25	pharmacovigilance AND proactive
26	pharmacovigilance AND proactive W/0 system
27	pharmacovigilance AND public AND participation*
28	adverse AND drug AND reaction AND public AND participation*
29	adverse AND drug AND reaction AND consumer* AND challenge
30	adverse AND drug AND reaction AND report* AND poor W/0 quality
31	adverse AND drug AND reaction AND report* AND text-mining
32	adverse AND drug AND reaction AND report* AND under-reporting
33	pharmacovigilance AND under-reporting AND challenge

Section A.2: Structured literature search protocol

Search	Search terms
1	pharmacovigilance AND challenge*
2	adverse AND drug AND reaction AND area* W/3 improvement*
3	adverse AND drug AND reaction AND area* W/1 improvement*
4	adverse W/0 drug W/0 event OR reaction* AND area* W/1 improvement*
5	limitation* AND clinical AND trials AND pharmacovigilance
6	limitation* W/1 clinical AND trials AND pharmacovigilance
7	pharmacovigilance AND culture
8	pharmacovigilance AND culture AND challenge
9	pharmacovigilance AND feedback
10	pharmacovigilance AND feedback AND challenge*
11	pharmacovigilance AND feedback AND limitation*
12	adverse AND drug AND reaction AND report* AND feedback
13	pharmacovigilance AND minimal W/0 data
14	adverse AND drug AND reaction AND report* AND minimal W/0 data
15	adverse AND drug AND reaction AND report* AND lack W/0 of W/0 data
16	pharmacovigilance AND education
17	pharmacovigilance AND education AND limitation
18	pharmacovigilance AND expertise
19	adverse AND drug AND reaction AND expertise
20	adverse AND drug AND reaction AND expertise AND challenge
21	adverse AND drug AND reaction AND training AND challenge
22	adverse AND drug AND reaction AND training AND limit*
23	adverse AND drug AND reaction AND partner*
24	adverse AND drug AND reaction AND partner* AND challenge
25	pharmacovigilance AND proactive
26	pharmacovigilance AND proactive W/0 system
27	pharmacovigilance AND public AND participation*
28	adverse AND drug AND reaction AND public AND participation*
29	adverse AND drug AND reaction AND consumer* AND challenge
30	adverse AND drug AND reaction AND report* AND poor W/0 quality
31	adverse AND drug AND reaction AND report* AND text-mining
32	adverse AND drug AND reaction AND report* AND under-reporting
33	pharmacovigilance AND under-reporting AND challenge

Appendix B: Chapter 3 supporting content

This appendix provides the supporting content of Chapter 3. In this appendix, one section is provided, namely:

- Section B.1: Journal article – This section provides the article that has been produced from a large portion of the content on Chapter 3. During the time of this thesis hand-in, an applicable journal is still being decided upon.

Section B.1: Journal article

Prioritising the challenges found in pharmacovigilance

Izak van Biljon Lamprecht; Louzanne Bam; Imke de Kock

Abstract

Background: The scope of pharmacovigilance is constantly expanding. As a consequence, an increasing number of challenges burden pharmacovigilance systems. From literature it is clear that there are numerous challenges of varying severity and impact that influence the many functions in pharmacovigilance. In order to address these challenges, researchers and practitioners are investigating, developing and implementing an array of solutions, but are however, struggling to address the challenges in the pharmacovigilance challenge landscape. As a result, some of the challenges that have a severe impact on pharmacovigilance systems are not addressed. In order to counteract the exclusion of challenges with the most significant impact on pharmacovigilance systems, prioritisation of the pharmacovigilance challenge landscape is essential, as this will enable researchers and practitioners to shift their focus to the challenges that warrant the greatest attention.

Methods: Several techniques that can be used to guide the research process were investigated. A set of techniques were subsequently selected and used to prioritise the pharmacovigilance challenge landscape. With the use of literature, the prioritised challenges are discussed in detail in order to provide a clearer understanding of each.

Results: Due to the lack of a universally accepted technique, a technique or combination of techniques, deemed suitable and applicable for the specific context, can be implemented. Following the implementation of two prioritisation techniques, it was found that there are seven challenges within the pharmacovigilance challenge landscape that should be prioritised, namely: (i) culture; (ii) transparency; (iii) partnerships; (iv) insufficient resources; (v) country-specific factors; (vi) adverse drug reaction under-reporting; and (vii) technical capacity.

Conclusions: As the pharmacovigilance challenge landscape is becoming an increasing burden for pharmacovigilance systems in numerous countries, it is becoming progressively difficult to address each of these challenges. Consequently, prioritisation has become essential, especially in countries where the available resources to pharmacovigilance are severely constrained. This paper thus proposes that emphasis be placed on the seven challenges that are identified to be of priority, as it is argued that the identified challenges to be prioritised represent a set of challenges that have the most significant impact on pharmacovigilance.

Keywords: pharmacovigilance; challenge landscape; prioritisation.

Background

Following the Thalidomide tragedy in the 1960s, pharmacovigilance (PV) was introduced to healthcare [1]. Defined as the "science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems" by the World Health Organisation (WHO) [2], the functions, resources, and stakeholders in PV collaborate to optimise drug benefits and minimise the risks of existing and newly marketed drugs. In the last decade, PV has been the recipient of much research and investments, which has led to an expansion of activities, ranging from drug efficacy, drug misuse, and drug interactions [2].

As a consequence of this increasing scope of PV the capacity for challenges has also grown, and has led to numerous PV systems in many countries being burdened with an array of problems. Especially in developing countries where resources are scarce, these challenges are limiting the extent to which PV systems can execute the necessary activities both effectively and efficiently [3]. Much research and investments, from both private – and regulatory bodies, have been devoted to these struggling PV systems in an effort to address some of the challenges experienced. However, when consulting literature, it is clear that many PV systems still experience problems, many of which are unique to a specific context.

Following a literature review, Lamprecht *et al.* [4] identified a large portion of the challenges faced by modern PV systems, including challenges related to culture, transparency, resources, PV centres, country-specific factors, technical capacity, partnerships, public participation, adverse drug reaction (ADR) under-reporting, quality of ADR reports, text-mining, lack of data, clinical trials, causality assessments, signal detection, and legislation. It is evident that the PV challenge landscape is vast, containing many different challenges of dissimilar impact and severity. Addressing each of these challenges simultaneously is difficult, therefore, prioritisation is needed.

Arguing the importance of prioritisation

The demand for healthcare has increased substantially over the last decade, and as a result has increased the pressures on the healthcare industry to manage its already constrained resources to meet its clinical responsibilities [5]. This has given rise to the realisation of the importance of prioritisation, a process which governs the allocation of resources in an effort to demarcate the scope of clinical activities. Prioritisation of clinical activities is not a new concept, and in fact has been a popular topic of debate in the late 1990s.

Healthcare systems across the globe regard prioritisation as inescapable [6], including countries such as Norway, Sweden, United States of America, and the United Kingdom [7]. Several events such as the denial of life-saving treatments, ever-expanding waiting lists, and inefficient allocation of health insurance packages were catalysts to these countries to invest more time and resources towards prioritisation [7]. All of these healthcare systems rely heavily on different sources of funding, which are classified as either public or private. The provisions these groups offer fluctuates severely, be it because of factors such as exchange rates, healthcare needs, or resource availabilities [7]. As a result, the invaluable resources these groups provide are often unreliable, which only further emphasises the importance of prioritisation.

However, prioritisation is extremely difficult, and is often described as an inevitably messy process [8]. Provided with the argument of Klein [9] who states that prioritisation is inherently the rationing of resources, healthcare systems struggle to find a balance between managing its already constrained resources and continuously meeting the demand for healthcare services. Moreover, the absence of a universally accepted framework that can be used to simplify the process of prioritisation makes this even more of a difficult process [7]. Therefore, countries rely on different approaches to prioritisation, such as ad hoc committees and advisory boards, all of which make use of different techniques to prioritise challenges and activities.

Redirecting attention towards PV, as evidenced by the literature review completed by Lamprecht *et al.* [4], the PV systems in both developed and developing countries are experiencing an assortment of challenges. It is becoming increasingly difficult to address each of the challenges because of an unbalanced resource supply and demand system [4], therefore, it is essential that the challenges that are most prevalent, or have the largest impact on the PV system, be addressed first. By addressing these challenges first, will one be able to systematically progress through the PV challenge landscape and address the challenges along the way.

Methods

As discussed, prioritisation has become a major topic of debate in healthcare, which has led to the development of numerous techniques that can guide such a process. Given that there is no universally accepted prioritisation technique [7], the context in which these techniques can be used differs severely. Regardless, these techniques can be leveraged to simplify and guide the process of prioritisation, or in this case, the prioritisation of the PV challenge landscape.

A literature review was conducted in order to identify prioritisation techniques that are still being used today. Both literature and grey literature were consulted, using the following search protocols: "prioritisation methods", "prioritisation techniques", and "how to prioritise challenges".

Following an investigation into the various prioritisation techniques that were identified in the literature review, it was decided that two of the techniques will be used to prioritise the PV challenge landscape, namely the Action Priority matrix and the system and challenge landscape matrix. A brief description of each technique is subsequently provided.

The Action Priority matrix

The Action Priority matrix measures issues on a two axis graph in terms of two parameters, namely: impact and effort [11], or importance and satisfaction [12]. Also relying on a group of theoretically and practically knowledgeable individuals to rate the issues, the Action Priority matrix is divided into four quadrants, named: low effort and high impact, high effort and high impact, low effort and low impact, and high effort and low impact issues [11]. Researchers can then decide which quadrant's issues they want to focus on. Usually, the two quadrants that receive the most attention are low effort and high impact, and high effort and high impact [12]. Both these quadrants embody certain benefits and risks which researchers must consider when deciding which issues will be addressed first.

The system and challenge landscape matrix

The system and challenge landscape matrix is a prioritisation technique that has been developed by Lamprecht at al. [4]. This matrix to compare the PV system to the PV challenge landscape. The matrix serves as a visual representation, indicating which challenges are experienced during which stages of the PV system. Challenges that were experienced during each stage of the PV system were deemed as priority. Such a matrix is highly flexible, and can be adapted towards nearly any industry [4].

The development process of both prioritisation techniques

The PV challenge landscape identified by Lamprecht *et al.* [4] was used as foundation to the prioritisation exercise. As previously mentioned, two prioritisation techniques (the Action Priority matrix and the system and challenge landscape matrix) were used to prioritise the PV challenge landscape. Following the implementation of the techniques, the obtained results were combined in order to establish which PV challenges should be prioritised.

In order to complete the Action priority matrix, three subject matter experts from different backgrounds were consulted. The role of each subject matter expert is subsequently described:

i. The first subject matter experts in the Regional Medical Director in Kenya, who is leading the preparation for the launch of a new product within severely resource-constrained environments.

ii. The second subject matter expert is an expert in the field of PV with several years of practical experience, and is actively involved in PV enhancement projects linked to Malaria vaccines in the Democratic Republic of Congo.

iii. The third subject matter expert is a Medical Affairs Executive and named safety contact for Kenya.

In order to develop a system and challenge landscape matrix, the same subject matter experts as those consulted during the development of the Action Priority matrix were consulted, as well as an additional subject matter expert, whose role is subsequently described.

i. The fourth subject matter expert, a PhD recipient, is a PV consultant for the South African National Department of Health with more than 20 years of experience in PV, and has been actively involved in many PV-related projects in several countries.

Following the prioritisation of the PV challenge landscape, literature was consulted in order to investigate each of the prioritised challenges. This was done to develop a better understanding of the impact of each challenge on PV.

Results

Combining the results from both prioritisation techniques, it was found that there are seven challenges within the PV challenge landscape that should be prioritised, namely: culture, transparency, partnerships, insufficient resources, country-specific factors, ADR under-reporting, and technical capacity. These challenges relate in large part to a sub-Saharan African context since each of the subject matter experts work within these settings. Subsequently, these challenges are described in more detail.

Culture

PV is based on the culture of safety, where PV professionals provide the foundation upon which the principles of this culture is built [13]. Literature, however, argues that there is a need to improve the culture in modern PV systems [14]. The culture of drug safety is not always sufficiently advocated, leading to several additional challenges within PV, such as ADR under-reporting. Consequently, it is argued that the improvement of PV culture will give lead to the improvement of some of the other challenges in PV.

There are three aspect of culture that is critical to consider, namely: definition, influential factors, and assessment. By taking these aspects into consideration, it would be much easier to identify opportunities for improving the culture of PV.

Defining culture

Diverting focus from PV, and focussing on culture is an abundance of literature that one can draw from. As an initial step towards improving culture, it is essential to understand how culture is defined. Naidoo & Martins [16] defines culture as “an integrated pattern of human behaviour which is unique to a particular organisation and which originated as a result of the organisation’s survival process and interaction with its environment”. Another perspective of culture is that it is a social construct, the product of groups and not individuals. It is based on the experiences of groups and it is unique to each organisation. It is also said to be malleable, adapting to the continual changes found in organisations, and develops over time [17].

The definition of culture, as described by Naidoo & Martins [16], clearly situates the limelight on the human participants of culture. In particular, groups operating across the spectrum of processes in an organisation are pinnacle to establish an effective and efficient culture in an organisation [17]

PV is an organisation, consisting of different processes managed by people. Similar to any other organisation, groups with different multi-disciplinary backgrounds and experiences take part in PV. Considering Naidoo & Martins' [16] definition of culture, these groups are responsible for the establishment of a culture in PV which is focussed on patient and consumer safety. In an effort to improve this safety culture, research should focus more on the individual behaviour phenomena of the groups working in PV. For instance, under-reporting of ADRs is routinely found in PV, proving to burden the PV system. Since people (e.g. healthcare workers, consumers, and patients) are responsible for reporting ADRs, focus should be more towards understanding the behaviours of these groups regarding ADR reporting.

Factors that influence culture

There is agreement in literature that many factors influence culture. Many researchers identify specific factors affecting culture, however, these factors are sometimes unique to a specific industry or organisation. Preferably, the underlying factors that influence culture gives a general perspective on culture since these factors are not necessarily unique to a specific industry, simplifying its application in a PV context.

Firstly, the business environment in which an organisation operates determines its culture. Within the market, the speed of change, the level of competitiveness, the value placed on people with regards to technology, and the demands of the customer influence the values, norms and behaviours one would associate with culture [18]. Secondly, leadership is regarded as an influence to culture [19], especially newly created organisations [18]. Leaders help establish culture through their own ambitions and actions i.e. setting the standards by being an example to the people in the organisation.

Thirdly there are management practices. Alan [18] is of the opinion that the manner in which an organisation is managed is likely to influence the beliefs, attitudes, and behaviours of the employees. There should be a fine balance between management and leadership, where the latter is regarded as the vision and long-term direction of an organisation through visions and strategy [18].

Lastly there is the formal and informal socialisation processes ([18]; and [19]). Formal socialisation activities include training and induction training, hosted by the managers and leaders of an organisation. On the other hand, informal socialisation refers to individual behaviours within a group context. Al-Alawi *et al.* [19] draws a distinctive relationship between these socialisation processes and the people in an organisation, stating that it is essential to focus on people and their behaviours when attempting to assess or change culture. Moreover, Al Alawi *et al.* [19] include organisational structure, trust, information systems, and reward systems as critical success factors to culture, with specific reference to the relationship between culture and knowledge management.

Each of the above mentioned factors have an impact on the way culture is established and maintained, as it helps to develop a basis on which an effective and efficient culture is built.

Assessing culture

It can be concluded from literature that many conceptualisations of culture are of deep, intangible phenomena not easily objectified [15]. Organisations often struggle to determine objectives that can be used to assess its culture [20]. There is much debate over the most effective culture assessment techniques, and if it should be of qualitative and quantitative nature. Supporters of a qualitative approach blame quantitative approaches to be unable to capture the subjective and unique aspects of culture, whereas opponents of qualitative approaches asserted that a comparison between cultures is not possible using this approach [15]. There is, however, the possibility of combining qualitative and quantitative approaches, able to help develop a more detailed understanding of all the layers of culture within an organisation [21].

A range of assessment tools with differing characteristics exist, all of which have limitations in terms of their scope, ease of use, and measurement capabilities. Examples of such tools include the Competing Values Framework, the Quality Improvement Implementation Survey, the Culture Inventory, and Harrison's Organisational Ideology Questionnaire [21]. The choice of assessment tool depends on how an organisation conceptualise culture, the purpose of the assessment, intended use of the results, and the availability of resources. Scott el al. [21] identifies several culture assessment tools that can be used within the healthcare setting (e.g. the Corporate Culture Questionnaire, Hofstede's Culture Questionnaire, and the Core Employee Opinion Questionnaire), but states that researchers searching for the ideal assessment tool will be frustrated, since no such tool exist. Bellot [15] is also of the opinion that no ideal culture assessment tool exist, since no organisation share identical cultures.

In order to address the shortcomings of culture in PV, the three aspects (definition, influential factors, and assessment) of culture should be combined in order to firstly understand the current culture in PV, and secondly to determine where areas for improvement exist.

Transparency

In close association with the culture found in PV, the lack of transparency amongst the stakeholders in PV may lead to failed PV initiatives [22]. It is essential that key stakeholders, especially those with the relevant experience in PV, share relevant information with their peers. This will enable participants in PV to learn of new ways in solving the problems they might be experiencing. Increasing the visibility of information in PV is critical [22], as it will support an improved drug safety culture.

It is also essential that the existence of PV systems in countries be publically unveiled. It is described in literature that healthcare workers in many countries do not contribute to PV, simply because they are not aware of the existing PV infrastructure in their location.

Understanding transparency within pharmacovigilance

There are many stakeholders that participate in PV environment. To allow PV systems to operate efficiently and effectively, these stakeholders (also referred to as partners in later discussions) must collaborate and ensure the success of PV systems. A collaboration of this scale is difficult, and is often burdened by the lack of communication. Communication is one of the most important aspects of collaboration in any industry, and serves as the foundation to basic business [23]. With communication comes transparency, which is also a crucial element of any collaboration.

Transparency is defined as “the level of availability and accessibility of market information to its participants” [24]. In essence, transparency means that all relevant information is made public, and shared between the relevant stakeholders. In PV, and also in healthcare in general, transparency is crucial because the information being shared either directly or indirectly relates to patient and public health.

One of the major challenges faced in PV is to ensure transparency between all stakeholders. There are many stakeholders that participate in PV (healthcare workers, non-governmental organisations, PV centres, governments, pharmaceutical manufacturers, academic institutions etc.). It is extremely difficult to ensure transparency between each of these stakeholders, since each has different priorities and expectations from a PV system. It is essential that transparency between these stakeholders be improved in order to aggregate a disseminated PV system, which can ultimately be leveraged towards the benefit of PV. This can be achieved by improving communication, and developing policies that govern the way in which information is shared in PV.

Partnerships

PV is a collaborative endeavour [25]. Sustained collaboration and commitment are vital to attend to future challenges of PV ([2]; and [26]). However, ineffective partnership is a threat to PV [26]. Operating in a resource-constrained environment, partners (also referred to as stakeholders in earlier discussions) in PV must sometimes provide expertise, training, political support, scientific infrastructure, and a capacity to accomplish comprehensive monitoring and investigations of the safety of medicines [25]. Failure in providing such resources, ineffective partnerships can lead to failed PV initiatives. In order to maintain a certain inventory of these resources, it is vital that PV organisations form lasting relationships with its partners. A publication by Management for Science [27] emphasises the importance of relationships between partners, and further states that failed relationships often lead to failures in business.

Partnership success factors

Characteristics of successful partnerships include common purpose and goals, high motivation, having the right people and the right leadership, maintaining balanced relationships, trust and respect, and good communication [28]. Moreover, literature often makes reference to success factors, and how these are essential to ensure effective and efficient partnerships. Casey [28] provides the following foundational success factors, stating that they are a requirement in any partnership: trust and value between partners, leadership and change management, a partnership framework, communication, equity and involvement in decision-making, and power distribution.

These success factors constitute examples of best practice for partnership formation and, without effective management, these partnerships are likely to fail [28]

In conclusion, it is critical to those within PV systems to understand that the partners with whom they collaborate have different levels of power and interest. Naturally, it would be of value to PV systems to maintain sustainable collaborations with partners who show deep interest in PV, and who also have high levels of power that can have a beneficial influence on PV systems.

Insufficient resources

It is well-known that PV operate within a resource-constrained environment in several countries [29]. Especially in developing countries where other challenges such as drought and war are of high priority, PV organisations struggle to implement new PV systems [29]. In these countries the available resources are rather invested elsewhere, leaving little for the requirements of PV.

Another challenge associated with insufficient resources is that the resources requirements of PV systems are unique in specific countries e.g. a country might have the necessary expertise and manpower to assist a PV system, but lack the governmental funding, whereas another country might have the necessary budget but lack the required manpower [25]. Countries experiencing this phenomena include Sub-Saharan African countries [29], India [30], and certain South-East Asian countries [31]. Common resources required by PV systems include monetary assistance, hardware and software infrastructure, expertise and training curricula amongst healthcare professionals, and common PV knowledge amongst both healthcare professionals and consumers ([29]; and [25]). PV systems are dependent on the combination of these resources and are not able to function properly without it [29].

Forasmuch as it is not feasible to conclude that the resource deficiencies burdening PV systems can be addressed by simply providing more resources to such systems, the focus should be towards the improved management of the existing resource portfolios. This type of resource management is made possible by assessing the value offered by the already used resources in PV. A model that embodies some aspects of resource management is the resource based view (RBV), able to assess organisation's resource portfolios based on certain characteristics and attributes. Models such as this assess the value of resources, allowing PV organisations to better manage their resources.

A resource-based view of pharmacovigilance

PV is not necessarily a profit-gaining industry, therefore there is some limitation to the implementation of the RBV in PV. However, many of the characteristics and attributes on which RBV is based can be used to assess the value offered by resources in PV.

First-off, reference can be made to the similarities of sustained competitive advantage between profit-gaining organisations and PV. In a business where much focus is on profit margins, sustained competitive advantage is a critical element as it allows for increased profits. Considering PV, a great deal of emphasis should be placed on the sustainability aspect sustained competitive advantage. With an increasing demand for healthcare, PV is more and more under severe pressure to monitor a wide range of medicines, while still giving attention to other activities such as causality and risk assessments. Since PV is so important in ensuring drug safety, it is even clearer that it should be able to do so, both now and in the future, under the difficult conditions just described.

Secondly, the RBV states that resources should be heterogeneous. In the context of PV, large inventories of resources with disparate roles and capacities to address diverse activities in PV exist. These resource portfolios must be managed and maintained to ensure that PV goals are constantly achieved.

Two resource attributes, value and organisation, on which the RBV is based, can be applied to the assessment of resources in PV. Firstly, the value posed by the resources in PV must be determined. Operating in a resource-constrained environment, non-value adding resources must be identified, allowing for resource requirements to be identified. Once the exact resource requirements are identified, steps can be taken to either develop or acquire the required resources. The second resource attribute, the question of organisation, determines whether PV systems are organised and able to effectively and efficiently utilise the existing resources for exploitation and to capture value. Failure in being organised and utilising all available resources, PV systems will struggle to meet healthcare demands.

Country-specific factors

Country-specific factors refer to challenges faced by PV organisations outside the traditional resource architecture and are described by Edwards [35] and Härmark & Van Grootheest [36]. A number of factors, defined differently in various disciplines, affect PV. Disciplines such as sociology and social anthropology are receiving more attention and are included in the development and planning of not only PV systems, but also many other healthcare initiatives such as vaccination administration programmes. These disciplines, as well as a range of other disciplines, are capable of identifying different factors such as human behavioural traits that might affect the implementation, operation, or maintenance of PV systems.

Influential factors that might affect pharmacovigilance

Often, the factors that are relevant to this section are defined differently in literature. Two categorisations of such factors exist, namely sociocultural factors and contextual – or systemic factors. Distinguishing between consortiums of factors, these categorisations make reference to a range of different factors that PV organisations should consider.

Covering a wide range of things that might impact PV systems, sociocultural factors distinguish between social factors such as attitudes, ethical identities, linguistic differentiations, and power structures, as well as cultural factors such as cross-cultural differences, cultural identity, and religious beliefs.

Other types of factors that might influence the operation of PV systems are contextual factors, also referred to as systemic factors. These refer to political, economic and social factors, both national and international. Contextual factors are categorised, according to Buse *et al.* [37], as follows:

i. Situational factors: Transient or impermanent conditions such as drought and war.

ii. Structural factors: The relatively unchanging elements of society such as the political system, health expenditure, gross domestic product (GDP) per capita, and the degree to which the public is allowed to participate in decision-making etc.

iii. Cultural factors: Similar to sociocultural factors, cultural factors refer to aspects such as power hierarchies, linguistic differences, and religious beliefs.

iv. International or exogenous factors: Closely related to partnerships, collaborations are often needed to aid in the implementation and operation of systems.

Some of the categories of contextual factors are similar to that of sociocultural factors. Often used interchangeably, contextual – and sociocultural studies identify and assess similar influential factors. Identifying and assessing sociocultural and contextual – or systemic factors are not simple, requiring multiple, multi-disciplinary individuals or groups such as sociologists, anthropologists, and governmental agencies. Proving to challenge PV systems, these individuals and groups must be employed, saturating the already constrained resource portfolios of PV. Regardless, it is essential that these factors be identified and assessed to determine its possible effect on PV systems.

Impact of sociocultural – and contextual factor: Case studies

Many case studies that describe the impact of sociocultural – and contextual factors, particularly in healthcare, exist in literature. Subsequently, some case studies are provided to indicate the beneficial results delivered by the identification and assessment of sociocultural – and contextual factors, emphasising its importance in PV.

In 2007, a study was conducted to determine the association between contextual factors and breast cancer screening amongst women in the United States. The study found that two factors led to the limited breast cancer screening. First, high unemployment rates gave way to poverty i.e. women could not afford regular breast cancer screenings. The second factor was the increased aged population. Elderly women tend to reject the need for breast cancer screening, feeling it is not of importance to them. The research allowed for American health authorities to develop new policies to improve access towards breast cancer screening to the women most affected by these two contextual factors [38].

Assessing the contextual factors influencing resource utilisation in nursing, a study conducted in 2006 found that resource utilisation amongst nurses was influenced by several contextual factors. These factors are the role of nurses, multi-faceted access to resources, organisational culture, multi-faceted support systems, time for research activities, and provision of education. Though limited research exist in this regards, the authors suggested that the identification of these contextual factors would allow healthcare institutions to better manage its resources made available to nurses [40].

In 2013, a study was conducted by numerous healthcare researchers who aimed at advancing both internal – and external validity of healthcare research by delivering their opinions of the importance of reporting contextual factors. It was stated that contextual factors are rarely reported in healthcare research, leading to failed attempts in replicating such research. The efforts to translate research into practice fail because contextual factors which are important for understanding and knowledgably synthesising findings across studies are not known. The opinions from all researchers were synthesised, where it was found that everyone suggested that the identification of contextual factors during healthcare research is an important stage that must be incorporated in future research [41].

Lastly, a study conducted in 2007 aimed at identifying the cultural factors that affected children's oral healthcare amongst different ethnic groups (African-American, Chinese, Latino, and Filipino) in San Francisco, California. Lack of knowledge about primary teeth were barriers to early preventative care in all ethnic groups. In all groups, family carers, especially elders, influenced access to preventative care. Also, dental fear, whether derived from community beliefs or personal negative dental experiences, greatly influenced attitudes towards preventative dental care. The study concluded that many similarities and differences exist amongst the ethnic groups in how cultural beliefs and experiences influence children's access to oral healthcare [42].

These case studies show the importance of identifying and assessing contextual – and sociocultural factors, particularly in healthcare. Literature suggests that these factors are routinely left out of healthcare research [41], burdening the healthcare systems in many countries. It can be concluded that healthcare initiatives, such as PV, can be improved by focussing more on the identification and assessment of these factors.

Adverse drug reaction under-reporting

Under-reporting of ADRs occur when healthcare workers (general practitioners, nurses, surgeons, pharmacists etc.) fail to efficiently report new and existing ADRs [43]. In the interest of consumers and patients who experience ADRs, it is crucial that all ADRs be reported to the relevant authorities. This will give way to signal detection, leading to investigations into the specific ADR. Without ADR reports that generate signals of a problematic ADR, investigations that aim to address these problems cannot take place.

Two prominent models that explain the causes of under-reporting are widely cited in literature namely Inman's model of the seven deadly sins of under-reporting and the KAP (knowledge, attitude, and practice) model of under-reporting. Taken together, these two models provide a comprehensive overview of the causes of under-reporting of ADRs. The KAP model is said to be the leading cause, in association with Inman's model, of under-reporting of ADRs [43].

Inman's seven deadly sins of under-reporting

In the 1990s Dr William Inman conducted research on PV with specific reference to the causes of under-reporting [44]. This study, known as Inman's seven deadly sins of under-reporting, is widely cited in literature ([44]; [45]; [46]; and [47]). More recent studies ([44]; and [47]) have confirmed the findings, specifically highlighting the ignorance, insecurity and indifference aspects of the model.

The so-called sins of Inman's model are:

i. Fear: Of litigation,

ii. Indifference: About contributing to the general advancement of knowledge,

iii. Ambition: To collect and publish a personal case series,

iv. Guilt: At having caused an adverse effect,

v. Complacency: The mistaken belief that only safe drugs are licensed,

vi. Ignorance: Of the need for reporting, and

vii. Diffidence: About reporting a mere suspicion.

In 2014, a study was conducted amongst hospitals and physicians in Spain. The objective of the study was to identify the main causes for under-reporting of ADRs by health professionals in Spain. It was found that the main causes of under-reporting were ignorance, insecurity, and indifference, all associated with Inman's model [44].

Also, Rodrigues & Khan [47] conducted research with the intention of identifying the cause of under-reporting amongst surgeons and surgical wards in an unknown context. The findings of the research correlated with Inman's model. Rodrigues & Khan [47], Varallo *et al.* [44], and Hazell & Shakir [45] are all of opinion that Inman's model is and will be applicable to future PV initiatives.

Many of these so-called sins such as indifference, ambition, complacency, and diffidence strongly relate to the culture in PV and research in eliminating these sins is believed to improve the overall culture within PV.

KAP model

The first aspect of the KAP model is knowledge, closely related to education [43]. The shortcomings of PV in the undergraduate and postgraduate syllabus of medical students is regularly referred to in literature ([48]; [49]; [50]; [51]; and [52]). These shortcomings are also not unique to specific countries. Studies in Nigeria [49], Malaysia [51], Portugal [43], Turkey [1], India [53], and China [54] all discuss the need for medical students' curriculum to either include or improve PV education.

The aforementioned country specific studies also highlight the lack of sufficient knowledge on the correct PV practices in practicing healthcare professionals. Toklu & Uysal [1] discuss the need for improved PV knowledge amongst community pharmacists in Turkey, Passier *et al.* [55] the need for improved PV knowledge amongst general practitioners in Netherlands, and Herdeiro *et al.* [43] the need for improved PV knowledge amongst pharmacists in Portugal. It is clear that thorough knowledge of PV is a challenge, hurdling several PV initiatives to be completely successful in many countries.

Secondly, the KAP model refers to the general attitude of healthcare professionals towards PV. This element of the KAP model is closely related to the indifference and ignorance aspects of Inman's model and also relates strongly to the culture aspects of the PV challenge landscape. Some examples of the role of attitude in under-reporting are given in a recent study by Shamim *et al.* [56] who seek to build an understanding of the general attitude of physicians, pharmacists, and nurses towards PV in Pakistan. It was found that a large portion of these healthcare professionals are indifferent towards PV, with only 14.3% being aware that there was an ADR reporting organisation in Pakistan. Similarly, a study within a Spanish context also discuss the poor attitude of healthcare professionals towards PV [44]. The indifference found in the Spanish context is associated with the lack of interest of healthcare professionals to register for ADR reporting and a lack of time for the many activities in the clinical routine.

Lastly, the lack of sufficient practice in PV is also a challenge faced in the PV industry. Closely associated with training, Varallo *et al.* [44] is of the opinion that the lack of sufficient practice has recently surfaced and is nowadays referred to as the eight sin of Inman's model. The lack of practice in PV is regularly referred to in literature, including Aronson [57] discussing the need for increased, real-world PV practice amongst British healthcare professionals, and Beckmann *et al.* [58] who similarly emphasises this need in a general context.

Synthesising Inman's model and the KAP model in PV

Under-reporting of ADRs is a burden to PV systems in many countries, limiting the extent to which action can be taken to improve medicine safety. There is a need for the culture surrounding ADR reporting to improve to a state where healthcare professionals, patients, and the public feel unthreatened and assured to report ADRs. Achieving such a culture is possible when especially healthcare professionals are sensitised and aware of the benefits posed by PV towards patient safety [23].

There is argument that ADR under-reporting can be improved by a range of solutions including standardised and universal reporting systems, simplified ADR reporting forms, decentralised PV systems, and electronic reporting forms. Regardless of the many possible solutions like those just mentioned, one must still consider that PV systems in different countries are unique, therefore requiring a comprehensive investigation to understand the attributes that affect ADR reporting (e.g. understanding how country-specific factors might affect ADR reporting).

Technical capacity

Technical capacity refers to the ability of a person conducting a specific action that is meant to achieve a specific outcome. Often categorised as an insufficient resource, Mehta [59] is of the opinion that it deserves to be independently categorised, because it is such an influential aspect that is lacking in many countries, especially developing countries Many factors contribute to the ability of an individual to exercise a specific action, which includes past experience, personal skills, ability to utilise resources, and academic education.

The only way in which experience, personal skills, and the ability to utilise resources can be achieved is by both theoretical – and practical training. Theoretical training closely relates to academic education, and plays an essential role in developing foundations and thinking patterns in individuals who enter practice. Practical training is often much more difficult to obtain, since training often clashes with the working schedules. However, Mehta [59] is of the opinion that it is of great importance that practical training is provided to those who fail to achieve the desired objectives.

An improvement in technical capacity offer many benefits to PV, which includes:

i. PV personnel will be able to complete their work even quicker.

ii. They will also be able to deliver work of much better quality standards.

iii. Since many PV systems operate in resource saturated environments, improving the technical capacity of existing personnel eliminates the need to appoint more employees i.e. one individual will be able to do the work of two or more.

iv. Improving technical capacity will also increase resource utilisation, which may convince investors to supply wider consortiums of resources.

However, improving technical capacity is not as simple as one might think. Not even considering the cost implications of theoretical training in the form of academic education, practical training is often very difficult to provide as well. Training sessions in the form of workshops and brainstorming sessions require resources that are often not available. Also, individuals who have the desired technical capacities are needed to convey their skills and experiences onto those who are in need of it. Similar to the issues of gathering all the necessary resources, these individuals are not in abundance.

Regardless of the challenges facing technical capacity, Mehta [59] is of the opinion that it is crucial that these challenges be overcome, because technical capacity is a challenge in many PV systems.

Conclusion

Increasing pressure can be attributed to an increasing demand for healthcare services, as well as an unsteady and unpredictable supply of resources, is burdening many healthcare systems in several countries. Included in these healthcare systems is PV, a system that is clearly still experiencing several challenges when consulting literature. In order to alleviate some of the pressures by starting to address some of these challenges, prioritisation has become a critical stage that is impossible to overlook. Consequently, this forms the core argument of this paper. The importance of prioritising PV challenge landscape is advocated in this paper, and some evidence as to why it is necessary is provided, which includes resource deficiencies and improper resource rationing. In order to prioritise the PV challenge landscape, the results from two prioritisation techniques that have been developed are combined.

Consequently, it can be concluded that there are seven challenges in PV that should be of priority, namely: culture, transparency, partnerships, insufficient resources, and country-specific factors, ADR under-reporting, and technical capacity.

Many of these challenges are interrelated i.e. addressing one may affect another. For example, when ADR under-reporting is advocated properly, it would contribute to the improvement of the culture of PV. Many of these challenges are, as per definition, severely challenging to address, especially in developing countries where resources are constrained. Regardless, it is an absolute necessity that more focus, especially from a research point of view, be diverted towards addressing these seven challenges in PV. These challenges represent a set of challenges that, when properly addressed, will have a large beneficial impact of PV systems, which will ultimately contribute to overall drug safety, which is the foundation of PV.

Declaration

Abbreviations

PV: Pharmacovigilance

WHO: World Health Organisation

ADR: Adverse drug reaction

RBV: Resource based view

KAP: Knowledge, Attitude, and Practice

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and material

The data that support the findings of this study are available from the authors of this paper.

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Authors' contributions

IL made substantial contributions to the conception and design of the information in this paper. Both LB and IDK reviewed this paper in an attempt to make suggestions where changes to the content provided should be made, and gave final approval for this version to be published. All three authors are accountable for all of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References

[1] H. Z. Toklu and M. K. Uysal, The knowledge and attitude of the Turkish community pharmacists toward pharmacovigilance in the Kadikoy district of Istanbul, Pharm. World Sci., vol. 30, pp. 556–562, 2008.
[2] World Health Organization, The Importance of Pharmacovigilance - Safety Monitoring of medicinal products, 2002.
[3] Strengthening Pharmaceutical Systems, Supporting Pharmacovigilance in Developing Countries The Systems Perspective, 2009.
[4] I. V. B. Lamprecht, L. Bam, and I. H. de Kock, An investigation into the prospects of existing technologies to address the challenges faced by pharmacovigilance systems, in SAIIE28: Taking up Stewardship, 2017, pp. 1–17.
[5] L. Barnieh, C. Donaldson, and B. Manns, Health care prioritization : a clinician's duty, Can. J. Kidney Heal. Dis., vol. 1, no. 27, pp. 1–5, 2014.
[6] R. Newton, Six Symptoms of Poor Prioritisation, Corporate Geek, 2010. [Online]. Available: http://www.corporategeek.info/six-symptoms-poor-prioritisation. [Accessed: 09-Nov-2017].
[7] L. M. Sabik and R. K. Lie, Priority setting in health care: Lessons from the experiences of eight countries, Int. J. Equity Health, vol. 7, no. 1, p. 4, 2008.
[8] R. Klein, Puzzling out Priorities: Why We Must Acknowledge That Rationing Is a Political Process, Br. Med. J., vol. 317, no. 7164, pp. 959–960, 1998.
[9] R. Klein, Dimensions of rationing: who should do what?, Br. Med. J., vol. 307, pp. 309–131, 1993.
[10] J. Calltorp, Priority setting in health policy in Sweden and a comparison with Norway, Heal. Policy 50, vol. 50, no. 1–2, pp. 1–22, 1999.
[11] Coach Federation, The Action Priority Matrix, International Coach Federation, 2014. [Online]. Available: https://coachfederation.org/blog/index.php/3694/. [Accessed: 22-Nov-2017].
[12] Z. Song, Analysis on Satisfaction Degree of School-Enterprise Cooperation in Application-oriented Undergraduate Base on Two-dimensional Scale, Boletín Técnico, vol. 55, no. 7, pp. 92–97, 2017.
[13] A. K. Olsen and M. D. Whalen, Public Perceptions of the Pharmaceutical Industry and Drug Safety and the Culture of Safety, Drug Saf., vol. 32, no. 10, pp. 805–810, 2009.
[14] B. Edwards, M. Gold, A. K. Olsen, and M. D. Whalen, Guiding Principles of Safety as a Basis for Developing a Pharmaceutical Safety Culture, Curr. Drug Saf., vol. 2, pp. 135–139, 2015.
[15] J. Bellot, Defining and assessing organizational culture., Nurs. Forum, vol. 46, no. 1, pp. 29–37, 2011.
[16] P. Naidoo and N. Martins, The relationship between organizational culture and work engagement: A multilevel investigation, Probl. Perspect. Manag., vol. 12, no. 4, pp. 433–441, 2014.
[17] B. Fortado and P. Fadil, The four faces of organizational culture, Compet. Rev. An Int. Bus. J., vol. 22, no. 4, pp. 283–298, 2012.
[18] W. Alan, Understanding organisational culture and the implications for corporate marketing, Eur. J. Mark., vol. 35, no. 3/4, pp. 353–367, 2001.
[19] A. I. Al-Alawi, N. Y. Al-Marzooqi, and Y. F. Mohammed, Organizational culture and knowledge sharing: critical success factors, J. Knowl. Manag., vol. 11, no. 2, pp. 22–42, 2007.

[20] P. Pronovost and B. Sexton, Assessing safety culture: guidelines and recommendations, Br. Med. J., vol. 14, pp. 231–233, 2005.
[21] T. Scott, R. Mannion, H. Davies, and M. Marshall, The Quantitative Measurement of Organizational Culture in Health Care : A Review of the Available Instruments, HSR Heal. Serv. Res., vol. 38, no. 3, pp. 923–945, 2003.
[22] M. R. B. Rubel, D. M. H. Kee, N. N. Rimi, and Y. M. Yusoff, Adapting technology : effect of high-involvement HRM and organisational trust, Behav. Inf. Technol., vol. 36, no. 1, pp. 281–293, 2017.
[23] V. Jusot, Correspondence. 20 July, Stellenbosch. 2017.
[24] N. Granados, A. Gupta, and R. J. Kauffman, Information Transparency in Tusiness-to-Consumer Markets: Concepts, Framework, and Research Agenda, Inf. Syst. Res., vol. 21, no. 2, pp. 207–226, 2010.
[25] G. J. D. Pan, Ongoing Challenges in Pharmacovigilance, Drug Saf., vol. 37, pp. 1–8, 2014.
[26] World Health Organization, Pharmacovigilance : ensuring the safe use of medicines, 2004.
[27] Management for Science, Pharmacovigilance. p. 35.1-35.19, 2012.
[28] M. Casey, Partnership - Success factors of interorganizational relationships, J. Nurs. Manag., vol. 16, no. 1, pp. 72–83, 2008.
[29] A. O. Isah, S. N. Pal, S. Olsson, A. Dodoo, and R. S. Bencheikh, Specific features of medicines safety and pharmacovigilance in Africa., Ther. Adv. drug Saf., vol. 3, no. 1, pp. 25–34, 2012.
[30] P. Rama, P. A. Rodrigues, and A. Georgy, Asian Journal of Pharmaceutical and Clinical Research PHARMAOVIGILANCE : PERSPECTIVES AND FUTURE CHALLENGES IN INDIAN SCENARIO, Asain J. Pharm. Clin. Res., vol. 4, no. 4, pp. 1–4, 2011.
[31] W. Suwankesawong, T. Dhippayom, C. Kongkaew, and W.-C. Tan-Koi, Pharmacovigilance activities in ASEAN countries. Pharmacoepidemiol. Drug Saf., vol. 25, pp. 1061–1069, 2016.
[32] M. Heinrich, Quality and safety of herbal medical products : regulation and the need for quality assurance along the value chains, Br. J. Clin. Pharmacol., vol. 80, no. 1, pp. 62–66, 2015.
[33] O. Jurevicius, Resource based view, Strategic Management Insight, 2013. [Online]. Available: https://www.strategicmanagementinsight.com/topics/resource-based-view.html. [Accessed: 28-Jun-2017].
[34] J. Kraaijenbrink, J. C. Spender, and A. J. Groen, The Resource-Based View : A Review and Assessment of Its Critiques, J. Manage., vol. 36, no. 1, pp. 349–372, 2010.
[35] I. R. Edwards, Causality Assessment in Pharmacovigilance: Still a Challenge, Drug Saf., vol. 40, no. 5, pp. 365–372, 2017.
[36] L. Härmark and A. C. Van Grootheest, Pharmacovigilance: Methods, recent developments and future perspectives, Eur. J. Clin. Pharmacol., vol. 64, no. 8, pp. 743–752, 2008.
[37] K. Buse, N. Mays, and G. Walt, Making Health Policy. Berkshire, England: McGraw-Hill Education, 2005.
[38] D. Litaker and A. Tomolo, Association of Contextual Factors And Breast Cancer Screening: Finding New Targets to Promote Early Detection, J. Women's Heal., vol. 16, no. 1, pp. 36–45, 2007.
[39] D. K. Brazier, Influence of contextual factors on health-care leadership, Leadersh. Organ. Dev. J., vol. 26, no. 2, pp. 128–140, 2005.
[40] J. M. M. Meijers, M. A. P. Janssen, G. G. Cummings, L. Wallin, C. A. Estabrooks, and R. Y.G. Halfens, Assessing the relationships between contextual factors and research utilization in nursing: Systematic literature review, J. Adv. Nurs., vol. 55, no. 5, pp. 622–635, 2006.
[41] A. Tomoaia-Cotisel *et al.*, Context Matters : The Experience, Ann. Fam. Med., vol. 11, no. Supp 1, pp. 115–123, 2013.
[42] I. V. Hilton, S. Stephen, J. C. Barker, and J. A. Weintraub, Cultural factors and children's oral health care: A qualitative study of carers of young children, Community Dent. Oral Epidemiol., vol. 35, no. 6, pp. 429–438, 2007.
[43] M. T. Herdeiro, A. Figueiras, J. Polonia, and J. Gestal-Otero, Influence of Pharmacists ' Attitudes on Adverse Drug Reaction Reporting A Case-Control Study in Portugal, Drug Saf., vol. 29, no. 4, pp. 331–340, 2006.
[44] F. R. Varallo, S. de O. P. Guimaraes, S. A. R. Abjaude, and P. de C. Mastroianni, Causes for the underreporting of adverse drug events by health professionals : a systematic review, Rev Esc Enferm USP, vol. 48, no. 4, pp. 739–747, 2014.
[45] L. Hazell and S. A. W. Shakir, Under-Reporting of Adverse A Systematic Review, Drug Saf., vol. 29, no. 5, pp. 385–396, 2006.
[46] M. Irujo, G. Beitia, M. Bes-Rastrollo, A. Figueiras, S. Hernandez-Diaz, and B. Lasheras, Factors that Influence Under-Reporting of Suspected Adverse Drug Reactions among Community Pharmacists in a Spanish Region, Drug Saf., vol. 30, no. 11, pp. 1073–1082, 2007.
[47] G. S. Rodrigues and S. A. Khan, Pharmacovigilance Among Surgeons and in Surgical Wards : Overlooked or Axiomatic ?, Indian J. Surg., vol. 73, no. 1, pp. 4–8, 2011.

[48] G. E. Schramm, P. P. Narayanan, D. S. Chutka, and W. T. Nicholson, Implementation of an interprofessional clinical pharmacology selective learning experience for pharmacy residents and medical students, Am. J. Heal. Pharm., vol. 74, no. 6, p. 397, 2017.
[49] A. R. Abubakar, B. A. Chedi, K. G. Mohammed, and M. Haque, Perception of Nigerian medical students on adverse drug reaction reporting, J. Adv. Pharm. Technol. Res., vol. 6, no. 4, pp. 154–158, 2015.
[50] A. R. Abubakar and M. Haque, Pharmacovigilance Practice : The Current Challenges and the Gaps in the Medical Students ' Curriculum, J. Appl. Pharm. Sci., vol. 6, no. 5, pp. 210–215, 2016.
[51] A. R. Abubakar, S. Ismail, N. I. A. Rahman, and M. Haque, Comparative study on drug safety surveillance between medical students of Malaysia and Nigeria, Ther. Clin. Risk Manag., pp. 1015–1025, 2015.
[52] A. R. Abubakar, N. Bin Simbak, and M. Haque, Pharmacovigilance Study : Awareness among Medical Students of a New Medical School of Malaysia, Int. J. Pharm. Res., vol. 7, no. 1, pp. 83–88, 2015.
[53] S. KC, P. Tragulpiankit, I. R. Edwards, and S. Gorsanan, Knowledge about adverse drug reactions reporting among healthcare professionals in Nepal, Int. J. Risk Saf. Med., vol. 25, pp. 1–16, 2013.
[54] C. Su, H. Ji, and Y. Su, Hospital pharmacists ' knowledge and opinions regarding adverse drug reaction reporting in Northern China, Pharmacoepidemiol. Drug Saf., vol. 19, pp. 217–222, 2010.
[55] A. Passier, K. van Grootheest, M. ten Napel, and E. van Puijenbroek, Reporting of Adverse Drug Reactions by General Practitioners, Drug Saf., vol. 32, no. 10, pp. 851–858, 2009.
[56] S. Shamim *et al.*, Adverse drug reactions (ADRS) reporting : awareness and reasons of under-reporting among health care professionals , a challenge for pharmacists, SpringerPlus (2016), vol. 5, pp. 1–8, 2016.
[57] J. K. Aronson, Balanced prescribing – principles and challenges, Br. J. Clin. Pharmacol., vol. 74, no. 4, pp. 566–572, 2012.
[58] J. Beckmann *et al.*, Teaching Pharmacovigilance: the WHO-ISoP Core Elements of a Comprehensive Modular Curriculum, Drug Saf., vol. 37, no. 10, pp. 743–759, 2014.
[59] U. Mehta, Personal interview. 21 August, School of Public Health (UCT). 2017.

Appendix C: Chapter 4 supporting content

This appendix provides the supporting content of Chapter 4. In this appendix, two sections are provided, namely:

- Section C.1: IAMOT2018 annual conference article – This section contains article that was produced from a large portion of the content in Chapter 4, and published in the IAMOT2018 annual conference proceedings.
- Section C.2: Implementation of the 5Why method, illustrated by fishbone diagrams – This section contains the fishbone diagrams, referenced in Section 4.6, that illustrate the implementation of the 5Why method. These diagrams identify several possible root causes to specific PV challenges.

Section C.1: IAMOT2018 annual conference article

Translating the pharmacovigilance challenge landscape to a lower level of abstraction: The implementation of a value chain analysis, the 5Why method, and fishbone diagrams

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ABSTRACT

While substantial progress has been made over the last decade to address the prevalent challenges faced by pharmacovigilance (PV) systems, many such systems are still experiencing various challenges. Considering that PV challenges identified in literature are often described on a strategic level and that no PV system is the same, there is a failure to understand the influence of these challenges within their specific contexts. Moreover, there is a shortage of research that proposes appropriate methodologies to translate these strategically defined challenges to an operational level, where it would be much simpler to: (i) understand the effects these might have on a PV system, and (ii) realise the potential of leveraging existing technologies to address these challenges.

Thus, the rationale as to why it is important to translate strategic level challenges to an operational level is discussed in this paper. The potential of existing methodologies that can assist and guide this translation process is also investigated. A selected set of methodologies are implemented as an example, describing the influence of strategically defined challenges on the functions in PV and identifying the root causes of these challenges. Lastly, the prospects of existing technologies that can address these challenges are discussed.

Key words: *Pharmacovigilance; challenge landscape; translation; value chain analysis; 5Why method; fishbone diagrams; technology landscape.*

INTRODUCTION: BACKGROUND

In the 1960s, an international health disaster was experienced. A pharmaceutical company introduced Thalidomide, a drug which was marketed as a sedative and anti-emetic in pregnancy. Following the release of Thalidomide, reports of infants being born with severe birth defects flooded the healthcare system. Worldwide, it was reported that nearly 10 000 infants were born with such defects, which affected the development of extremities (Toklu & Uysal (2008) and Isah *et al.* (2012)). Following these events, it was clear that there was a dire need to develop a system where the effects of newly marketed and existing drugs were constantly monitored to prevent a similar tragedy such as that of the Thalidomide case (Wang *et al.* (2009); Stolk (2012); and Klausen & Parle (2015)). Subsequently, such a system was developed, and came to be known as pharmacovigilance (PV) (De Abajo 2005).

PV is defined as the “science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems” (World Health Organization 2002). Ultimately, the goal of PV is to optimise benefits and minimise the risks, of newly marketed and existing drugs, at both the individual and population level. In the last decade, PV has been the recipient of a great deal of research and investment, and has grown to become an important facet of healthcare (World Health Organization 2002). This considerable growth, however, has led to PV becoming a ubiquitous system with an increasing scope.

The expansion of activities have led to numerous challenges that burden modern PV systems (Pan 2014). Challenges from both a systems – and clinical perspective prevent optimal service delivery and resource utilisation within PV systems, and limits the extent to which PV can operate both effectively and efficiently

(Strengthening Pharmaceutical Systems (SPS) 2009). In an effort to identify these challenges, Lamprecht *et al.* (2017) conducted a systematic review, and prioritised the following challenges: unsupported culture of drug safety, lack of partnerships, lack of transparency, insufficient resources, country-specific factors serving as barriers, adverse drug reaction (ADR) under-reporting, and lack of technical capacity.

An investigation of these challenges established that most are described on a high level of abstraction i.e. at a strategic level. In other words, literature tends to argue that these challenges burden PV systems in many countries, but fails to provide additional information as to the specific influences these challenges have on the different functions within PV. The root causes of these challenges in different contexts are also not identified in literature. The subsequent section argues the importance of translating the strategically defined challenges in PV to an operational level in order to realise the influence and root causes of these challenges.

RATIONALE BEHIND THE IMPORTANCE OF TRANSLATING STRATEGICALLY DEFINED CHALLENGES

Strategic management is often the so-called golden child of an organisation, receiving far greater attention than operational management. Executives and managers who have not moved through the ranks of operational management and as a consequence are not familiar with operations, frequently fail to consider the influence of operations on an organisation's overall strategy (Hammer 2004). According to both Croxton *et al.* (2001) and Hammer (2004), being aware of both the opportunities posed and the limitations associated with various operational strategies will allow these previously mentioned executives and managers to add to their strategic arsenal to become influential market players.

Provided that more effort needs to be shifted towards processes and activities related to operational management (Croxton *et al.* 2001), there is a need to define and investigate strategic level processes and activities at an operational level. Thus, strategies need to be translated to an operational level to understand how these influence the different functions within an organisation (Naghibi & Baban 2011). Considering this within the PV context, in order to propose actionable solutions to the strategic level challenges that have been identified in the PV landscape, these must be translated to an operational level. Formalising the operational level challenges in this manner will enable knowledge sharing and debate about these in literature, and will enable researchers and practitioners to differentiate between the effects these challenges have on the various functions in PV.

Hewitt-Taylor (2012) argue that, in order for challenges to be described at an operational level, the root causes must be identified. It is argued that it is often more feasible to investigate these root causes, rather than addressing the challenges on an strategic level, because the root causes will deliver tangible problems that can be more easily addressed.

Therefore, the rationale behind the proposition that the PV challenge landscape must be translated to a lower level of abstraction is (i) such a translation will make it clear how strategic challenges influence the different functions in an organisation, or in the case of PV, the stages of which PV systems are composed, and (ii) identifying the root causes of strategic challenges will make it increasingly easier to address such challenges at an operational level.

Such a translation, however, is not always simple, and according to Chmutova (2015), business often struggle severely with this process, given that they fail to leverage existing methodologies in guiding the entire process. Some of the methodologies that have been developed for this translation process are considered in the subsequent section.

TRANSLATION METHODOLOGY ASSESSMENT

In order to identify the different methodologies that can be used to translate the PV challenge landscape, a literature review was conducted in two databases, namely Google Scholar and Scopus, as well as grey literature. Using the search terms "root cause analysis", "translation methodologies and approaches", and "problem solving", the literature review uncovered some of the more widely used methodologies, namely root-cause analyses (RCAs), the 5Why method and fishbone diagrams. Additionally, the 5W2H method, key performance indicators (KPIs), and value chain analyses, methods that are commonly used for analysing and defining systems in the Industrial Engineering profession, are added to the list of methodologies that are considered for application.

Root cause analysis

According to Jones & Despotou (2016), the RCA is by far the most widely used analysis tool for investigating problems, especially in the healthcare environment. RCAs focus on the root cause of problems, while avoiding emphasis on any mistakes made by specific individuals. Ideally, a team-based approach, where teams are composed of individuals from different backgrounds and contexts, is the best approach to conducting a RCA, as this will ensure that a range of root causes to the same problem be identified.

There are different techniques that can be used to conduct a RCA, the most popular being the 5Why method and Fishbone diagrams.

The 5Why method and fishbone diagrams

The 5Why method was developed by Sakichi Toyoda, one of the fathers of the establishment of the car company Toyota in the late 1940s (Warner 2015). Adopted by the global market in the 1970s, the 5Why method became one of the most renowned methodologies, able to identify the root causes of specific problems.

In essence, this form of RCA is completed by asking the Why question, on average, five times (Warner 2015), which will lead to the root cause of a given problem. Additionally, in order to capture the thinking processes during this exercise, a fishbone diagram can be developed, which will provide a visual representation of the possible root causes to a given problem (Pojasek (2000) and Jones & Despotou (2016)).

The 5Why method, in combination with fishbone diagrams, offer several benefits to its users, including (Pojasek 2000): (i) it is a very quick and simple tool to use; (ii) the nature of the Why question is highly relatable, since Why is so often asked in real-life; (iii) fishbone diagrams serve as visual representations to the 5Why method, providing a holistic view of the effects that stem from a certain root cause; (iv) the process initiates a thinking process in the individuals of the team, allowing them to come up with an answer more quickly; and (v) the one right answer syndrome is eliminated since the method is a team-based approach i.e. a broad range of answers from different departments are given.

Regardless of the benefits offered by the 5Why method and fishbone diagrams, there are also some challenges associated with it, namely (Pojasek 2000): (i) facilitation is needed to optimise the results of the method, and the facilitator(s) should have some experience in the method; (ii) it is not always simple to answer the simple question of Why, since many environmental factors may affect the answer; and (iii) when used incorrectly, these methods can lead to finger pointing i.e. one individual or group can be blamed for a mistake.

A number of studies (Pojasek (2000); Bulsuk (2009); Sonkiya (2014); Mpanza (2016); and Brundage *et al.* (2017)) have endorsed the efficacy of the 5Why method in combination with fishbone diagrams as a mechanism for translating problems that have been defined on a strategic level to a more tactical – or operational level where some of the root causes may exist.

5W2H

The 5W2H method is a highly efficient and simple management tool, constructed of well-defined stages which serve as structures to action planning (Veyrat 2016). The name of this method originates from the questions that are asked. These questions are: "*What will be done?*", "*Why will this be done?*", "*Where will it be done?*", "*When will it be done?*", "*Who will do it?*", "*How will this be done?*", and "*How much will it cost?*" Given that strategies constantly change within the competitive market, strategies must be continuously adjusted, and as a result new strategic challenges come to light. According to Veyrat (2016), going through the process of the 5W2H method will allow organisations to define their strategies, and determine how these goals will be achieved.

The 5W2H method offer many benefits, including (Bau *et al.* (2012) and Veyrat (2016)): (i) it is a simple method to implement since straightforward questions are asked; (ii) it enables businesses to comprehensively define the problem at hand, which in turn make it simpler to identify areas where improvements are necessary; (iii) the simple questions enables individuals from different backgrounds and experiences to provide their input; and (iv) the simplicity of the method allows it to be used in many different industries.

As with any methodology, there are also some challenges that might burden businesses to effectively use the 5W2H method, which includes: (i) the method is most beneficial when there is a facilitating individual or team who has experience with the method; and (ii) it is not always simple to answer the questions asked by the method, and there may be conflicting views on the correct answer.

It is clear that there are pros and cons to this method, which must be weighed against one another. On balance, however, Veyrat (2016) is of the opinion that when used correctly, the 5W2H method can effectively help businesses translate their strategic goals.

Key performance indicators

Most businesses make use of KPIs to translate their strategy into some quantifiable and measurable objective (Baroudi 2014). For example, a manufacturing business's strategy may be to increase overall productivity. Measuring a business's overall productivity is most likely difficult or infeasible, therefore, operational level KPIs such as the total hours of machine downtime per day, or the total number of defective raw materials per month are used instead. These operational level KPIs can be measured in a direct and standardised manner and enable businesses to determine whether productivity has increased or decreased.

The specific benefits that KPIs offer includes (Baroudi 2014): (i) increasing individual and team focus; (ii) encouraging departments to meet their goals; (iii) serving as a link between individual and departmental goals; (iv) allowing executives, managers, and employees to identify possible areas for improvement; and (v) defining and communicating both the expected and achieved performance levels.

Some potential drawbacks associated with the use of KPIs include (Baroudi 2014): (i) unclear definitions of KPIs can negatively affect other KPIs that are crucial to the measurement of the success of a business; and (ii) employees may sometimes focus more on what is expected of them, rather than focus on how these expectations will be met, leading to possible health and safety risks.

Developing KPIs is often a tedious and difficult process. To avoid this, it is essential that businesses consult the relevant stakeholders as they may have valuable inputs that have not been considered before (Baroudi 2014).

Value chain analysis

A value chain analysis is defined as "a process where a firm identifies its primary and support activities that add value to its final product [or service] and then analyse these activities to reduce costs or increase differentiation" (Jurevicius 2013b). It enables businesses to identify underperforming business processes and activities, allowing them to make necessary adjustments. It also highlights influential factors (environmental factors, participating actors etc.) that affect a value chain, delivering a comprehensive image of how a value chain and its components interact.

Value chain analyses offer several benefits, which include (Simister 2011): (i) it is a flexible strategy tool, and can be adapted towards many different industries; (ii) it focusses on the activities needed to deliver value proposition, highlighting the processes and activities that contribute to delivering the customer demand; and (iii) it is a well-known strategic tool, and has delivered insight to many industries as to how and where they need to improve.

It is also important to be aware of the limitations to using value chain analyses, which include (Simister 2011): (i) although the value chain analysis is flexible, it is not a plug and play instrument, therefore necessary changes must be made to adapt the analysis to a specific industry; (ii) knowing that value chain analysis was originally designed for use in the manufacturing industry may deter other industries from using it; (iii) the scale and scope of a value chain analysis can be intimidating, since it considers a value chain in its entirety; and (iv) though many people are familiar with the concept of a value chain analysis, few are experts, and facilitation is therefore often needed to guide the development of such an analysis.

A value chain analysis is a comprehensive strategic tool that offers many benefits, and when implemented properly and the limitations are considered and managed, it can assist businesses in making necessary improvements across its value chain in order to deliver a better value proposition.

TRANSLATION METHODOLOGY SELECTION

In order to select the most appropriate translation methodology for application to the PV system, the methodologies are compared to one another by evaluating their capability of meeting certain qualification criteria. These criteria were developed based on a set of indicators, developed by the World Health Organisation, used to evaluate the inputs, outputs, processes, and impacts of PV systems (World Health Organization 2014), and incorporates some conditions set by the authors of this paper. These qualifying criteria are:

- Stakeholder identification: Does the methodology allow the user to identify the stakeholders that participate in the PV system?
- Distinguishing: Does the methodology distinguish between the different stages in the PV system?
- Flexibility: Does the methodology adapt well to different input data and structures?
- Relationship identification: Does the methodology indicate the effect that different elements may have on the other?
- Reproducible: Can the methodology be reproduced by anyone, regardless of their background?
- Measurable outcome: Does the methodology deliver measurable outcomes?

The sought after translation process consists of two stages, which, in unison, will contribute to the translation of the PV challenge landscape to a lower level of abstraction, where tangible problems can be defined and addressed. These stages are: (1) defining the influence of the PV challenge landscape by differentiating between the different functions, or stages, of a PV system; and (2) identifying the root causes of the differentiated PV challenges within a PV system.

The comparison of the methodologies according to the set of qualifying criteria is shown in Table 1. Based on this analysis, the following two methodologies are selected to address the two stages of the desired translation process: 1) value chain analysis, and 2) the 5Why method and fishbone diagrams. The use of these methodologies are further advocated in the subsequent sections.

Table 1: Comparing the different translation methodologies.

Translation methodology	Stakeholder identification	Distinguishing	Flexibility	Relationship identification	Reproducible	Measurable outcomes
5Why and Fishbone diagrams	X		X		X	
Problem tree analysis			X	X		
5W2H	X		X		X	
KPIs						X

Value chain analysis	**X**	**X**		**X**		

The value chain analysis

A recent report by Franz *et al.* (2015) discusses a value chain analysis conducted in the energy market system in sub-Saharan African countries. This analysis allowed the developers to comprehensively understand the operation of the current energy market system in sub-Saharan African countries, which in turn allowed them to identify improvement initiatives with regards to specified inputs, services, finances, and enabling factors (Franz *et al.* 2015). Similarly, the United Nations also implemented a value chain analysis, which focussed on the living conditions of disabled persons. Several influential factors such as disabled rights, policies, and financial structures were identified, indicating problem areas where improvements or adjustments were necessary (United Nations 2012).

The prospects of leveraging the value chain analysis for translating challenges in the PV system that have been defined at a strategic level to an operational level in a specific context is evidenced by these two cases. Moreover, with reference to the qualifying criteria in Table 1, value chain analyses enables the user to differentiate between the stakeholders in PV ("Stakeholder identification"), distinguishes between the different functions of a value chain or in this case a PV system ("Distinguishing), can be adapted towards the PV context ("Flexibility"), and enables the user to identify any possible relationships that might be shared between the different influences in a value chain ("Relationship identification"). The methodology therefore satisfies four of the six qualifying criteria defined in the previous section and this justifies the use of a value chain analysis for the first stage of the translation process i.e. defining the influence of the PV challenge landscape on the functions in a PV system.

The 5Why method and fishbone diagrams

There are many reported cases where the 5Why method and fishbone diagrams have enabled businesses to follow a systematic approach in identifying the root causes of challenges they are experiencing. Myszewski (2013) describes a case where an unknown company used these analyses to identify certain root causes with regards to quality deficiencies found in a product manufactured by this company.

Another reported case of the successful application of the 5Why method and fishbone diagrams is described by Jones & Despotou (2016). A number of hospitals based in the United Kingdom reported numerous unintended consequences from the use of electronic health records. Though these consequences are not named in the article, Jones & Despotou (2016) described that through a combination of the 5Why method and fishbone diagrams, investigators were able to identify the root causes of these consequences, and were subsequently able to address the problems.

These two cases support the rationale that these methodologies are suitable to support the translation of the PV challenge landscape to an operational level. Providing even further justification, the 5Why method, in combination with fishbone diagrams, allows the user to differentiate between the key role players in a PV system ("Stakeholder identification"), can be adapted towards a PV context ("Flexibility"), and can be easily reproduced by someone who might be lacking a certain degree of technical capacity ("Reproducible"). The methodology therefore satisfies three of the six qualifying criteria defined in the previous section and this justifies the use of the 5Why method in combination with fishbone diagrams for the second stage of the translation process i.e. identifying the root causes of the PV challenge landscape.

Subsequently, an example of the application of the two stages of the translation of the PV challenge landscape is provided through a worked example.

STAGE 1: IMPLEMENTATION OF THE VALUE CHAIN ANALYSIS

Following the argument that the value chain analysis can be used for the purpose of the first stage of the proposed translation process, a PV value chain analysis is developed in the subsequent section.

The pharmacovigilance value chain analysis

The PV value chain analysis is shown in Appendix 1. Many of the challenges identified in the analysis share relationships with others. Illustrated by double-headed arrows, these relationships indicate that when the one challenge is addressed, there will either be a direct or indirect effect on the other(s).

The PV value chain analysis has been developed in a general context, taking no specific location into consideration. In order to further ensure that the analysis is even more accurate, it can be developed within a specific context where specific challenges to a specific context are investigated.

Regardless, the PV value chain analysis has been validated by a subject matter expert who have sufficient experience in the PV industry, and endorsed the use of such an analysis.

Key points highlighted by the pharmacovigilance value chain analysis

By disseminating the PV challenge landscape in the PV value chain, the PV value chain analysis has highlighted several key points that would have been difficult to identify by simply considering the PV challenge landscape in isolation. The analysis also *sheds some light* on the relationships within the PV challenge landscape, as well as the actual meaning of the influence of challenges in PV. These key points are briefly described in subsequent subsections.

Prominent role players

Governmental bodies, also referred to as regulatory authorities, are key role players in PV. This is because, in most countries, regulatory authorities govern PV systems, developing the necessary policies and investing the required resources for PV systems to operate. Though some countries (e.g. South Africa) are trying to shift a portion of the power held by regulatory authorities outside their jurisdiction, these authorities will still play a major part in PV systems.

Snowballing effect caused by adverse drug reaction under-reporting

Within the ADR under-reporting lane, it is shown that many of the challenges in the downstream PV value chain share relationships with this phenomenon, emphasising the limitations caused by ADR under-reporting that are so often described in literature.

Many challenges faced at the start of the pharmacovigilance value stream

Many challenges are found at the start of the PV value chain i.e. within the data collection and ADR under-reporting, and data collation stages, which highlights the limitations posed by a lack of robust qualitative and quantitative data. Data plays a major part in PV, and it is therefore of great importance that the efforts towards acquiring such data be made as efficient and effective as possible.

Exchanges between country-specific factors and insufficient resources

There are frequent exchanges between the challenges associated with country-specific factors and insufficient resources, therefore it is worthwhile exploring whether there is a causal relationship between these two strategically defined challenges. In other words, when it is found that there are insufficient resources within a certain country, it is possible that it is a unique case to that specific country i.e. another country may not experience the same problem.

Role played by country-specific factors

Many challenges have been identified within the country-specific factors lane. This only highlights the rationale that globalisation and standardisation of PV systems on an international scale is not feasible, given that PV systems in different countries are unique, and are influenced by different factors.

Failure to understand the effects of pharmacovigilance

It is often the case that there is a failure amongst those within the PV spectrum, as well as those outside, to fathom the importance of PV, and the major influence it not only has on an individual level, but also the effect it has on the entire healthcare industry.

Lack of access

The lack of access to resources is regularly reported in the analysis. It is not necessarily the case that the expertise, experience, funding, training, technology, and other resources do not exist, but rather that PV systems are not given access to such resources. One of the main reasons for this can be attributed to the fact that PV is not classified as priority within a certain country.

Adoption by the widespread healthcare industry

Disseminating the PV challenge landscape, shows that PV is a large and complex system with much room for problems, and therefore needs to be adopted by the widespread healthcare industry i.e. it must be a priority not only to those actively involved in PV, but also to those outside the spectrum of PV, to aid PV in its activities.

Lack of technical capacity

The lack of training, knowledge, or practice, all of which are attributed to technical capacity, are often limiting factors in PV systems. This can be directly traced back to the pre-entering phase into the healthcare environment i.e. university, college, or any other form of tertiary education. Training needs to start on a tertiary level, where the basics of PV are taught.

Concluding stage one of the translation process

These key point all contribute to the initial translation process i.e. understanding that the PV challenge landscape affects the different stages in the PV value chain in different ways. It is critical to a system such as PV, where drug and patient safety are of primary concern, that researchers understand how the challenges affect a PV system, which will allow them to make the necessary improvements to the system.

In order to identify the root causes of challenges in the PV landscape, the second stage of the translation process proposed in this paper is essential, an example of this second translation step is given in the following section.

STAGE 2: IMPLEMENTATION OF THE 5WHY METHOD AND FISHBONE DIAGRAMS

Up to this point, the translation of the strategically defined PV challenge landscape has reached an intermediate stage. To complete the translation, the root causes of these challenges must be identified, which will translate these challenges to tangible problems that can be addressed at an operational level. In order to do this, the 5Why method, in combination with fishbone diagrams, can be used. To illustrate the implementation of these methodologies, the root causes of three of the challenges in the PV value chain analysis are identified, namely: (i) inadequate access to ADR reporting forms (spontaneous); (ii) failure to develop locally relevant and easily measurable indicators of performance of PV systems; and (iii) the lack of robust local data that limits the extent to which decision-making can be done. Appendix 2 contains a fishbone diagram illustrating the application of the 5Why method to each of these three challenges. The key findings are briefly discussed in the remainder of this section.

In summary, the possible root causes that have been identified for the inadequate access to ADR reporting forms (spontaneous) are:

i) There is a lack of funding to access software technologies to assist the coordination of the deliveries of spontaneous ADR reporting forms.

ii) There is no existing software technology that can assist the coordination of the deliveries of spontaneous ADR reporting forms.

iii) The individuals responsible for coordinating the deliveries of spontaneous ADR reporting forms are not sufficiently trained in this regard.

iv) There is no designated transportation service to distribute the ADR reporting forms.

v) The person in charge of re-ordering the ADR reporting forms is not sufficiently trained in stock control.

vi) The person in charge of re-ordering the ADR reporting forms is situated in remote location, and as a consequence, users of the forms struggle to notify the person.

vii) The users of the forms have competing priorities, and simply do not have time to notify the person in charge of re-ordering the ADR reporting forms.

The identified potential root causes for the failure to develop locally relevant and easily measurable indicators of performance of PV systems are:

i) Key stakeholders are not aware of the health impact of PV.

ii) There are only globally defined indicators of performance that may not include features of a unique, local PV system.

The possible root causes of the lack of robust local data that limits the extent to which decision-making can be done have been identified as:

i) PV is not sufficiently advocated to the necessary stakeholders.

ii) PV is not included in the undergraduate syllabus of healthcare tertiary education.

iii) The ADR reporting forms are overly complicated and takes too long to complete.

iv) Key stakeholders are not aware of the health impact of PV.

These examples show the systematic thinking process behind the identification of the root causes by using the 5Why method in combination with fishbone diagrams. Subsequently, the key points that were highlighted during this process are discussed.

Key points highlighted by the implementation of the 5Why method, in combination with fishbone diagrams

Certain key points that can be concluded from these analyses, highlighting several distinct features that may not have been known before.

Wide spectrum of possible root causes

When conducting these types of analyses, it is possible to either identify numerous possible root causes of a specific problem, or only a few. This is evident from the wide spectrum of root causes identified in the examples provided. This phenomenon is a result of the nature of answering a simple "Why?" question, which may have more than one possible answer.

Unclear association between root causes and the overall problem

Some of the root causes identified may be deemed as *far-fetched* i.e. it may seem that the root cause and the overall problem may not have anything in common, and this may make stakeholders resistant to using the 5Why methodology. For example, a root cause for the inadequate access to ADR reporting forms is the lack of funding to access software technologies. As Warner (Warner 2015) described, however, these types of analyses have delivered many positive results, and therefore one should at the very least put some effort into investigating the possible interactions these seemingly non-associated root causes and challenges may share.

Shared root causes

As indicated by the analysis of the failure to develop locally relevant and easily measurable indicators of performance of PV systems, and the lack of robust local data that limits the extent to which decision-making can be done, certain possible root causes may affect different problems. This is proof that the challenges in the PV challenge landscape share relationships, as illustrated in the PV value chain analysis.

Concluding stage two of the translation process

In combination with the initial translation process where the influence of the PV challenge landscape on the PV value chain is investigated, the root cause analysis identifies tangible problems that have not been previously known. Further investigations into these root causes can commence, and solutions can be developed in terms of technology, funding, or general managerial strategies.

LEVERAGING THE TECHNOLOGY LANDSCAPE

The translation of the PV challenge landscape has delivered tangible problems, many of which are described on an operational level. Some of these operational challenges offer investigators the opportunity to investigate the prospects of the technology landscape and determine how these technologies can be leveraged towards addressing some of these problems. Subsequently, examples of some of these technologies are provided.

Online teaching services

Already proven to deliver desirable outcomes within the educational environment (Lamprecht 2017), online teaching services have been successfully implemented to address the issue of the lack of technical capacity. Frequently found in PV, and emphasised in this paper, the lack of technical capacity refers to the lack of essential theoretical – and practical knowledge. Online teaching services are able to provide these essential skills to individuals in different contexts.

Big data analysis

As highlighted by second stage of the translation process, the lack of existing software to manage data in PV is a challenge affecting different areas in PV. In order to accommodate for the large amount of data circulating in PV, big data analysis software can be used to collect, synthesise, and analyse data. This will enable researchers and practitioners in PV to manage large amounts of data, and identify signals of adverse events much quicker. This will also eliminate the snowballing effect caused by ADR under-reporting, because the necessary data is readily available and analysed.

Cloud technology

Cloud technology, which is essentially an information sharing platform, can be implemented to address the issue of the lack of advocacy of PV systems. One component of this lack of advocacy is the challenge of sharing information with the necessary stakeholders. Cloud technology platforms such are easy-to-use software that can be used to share large amounts of data with many stakeholders, making them aware of the effects caused by PV and the importance of maintaining and supporting these systems.

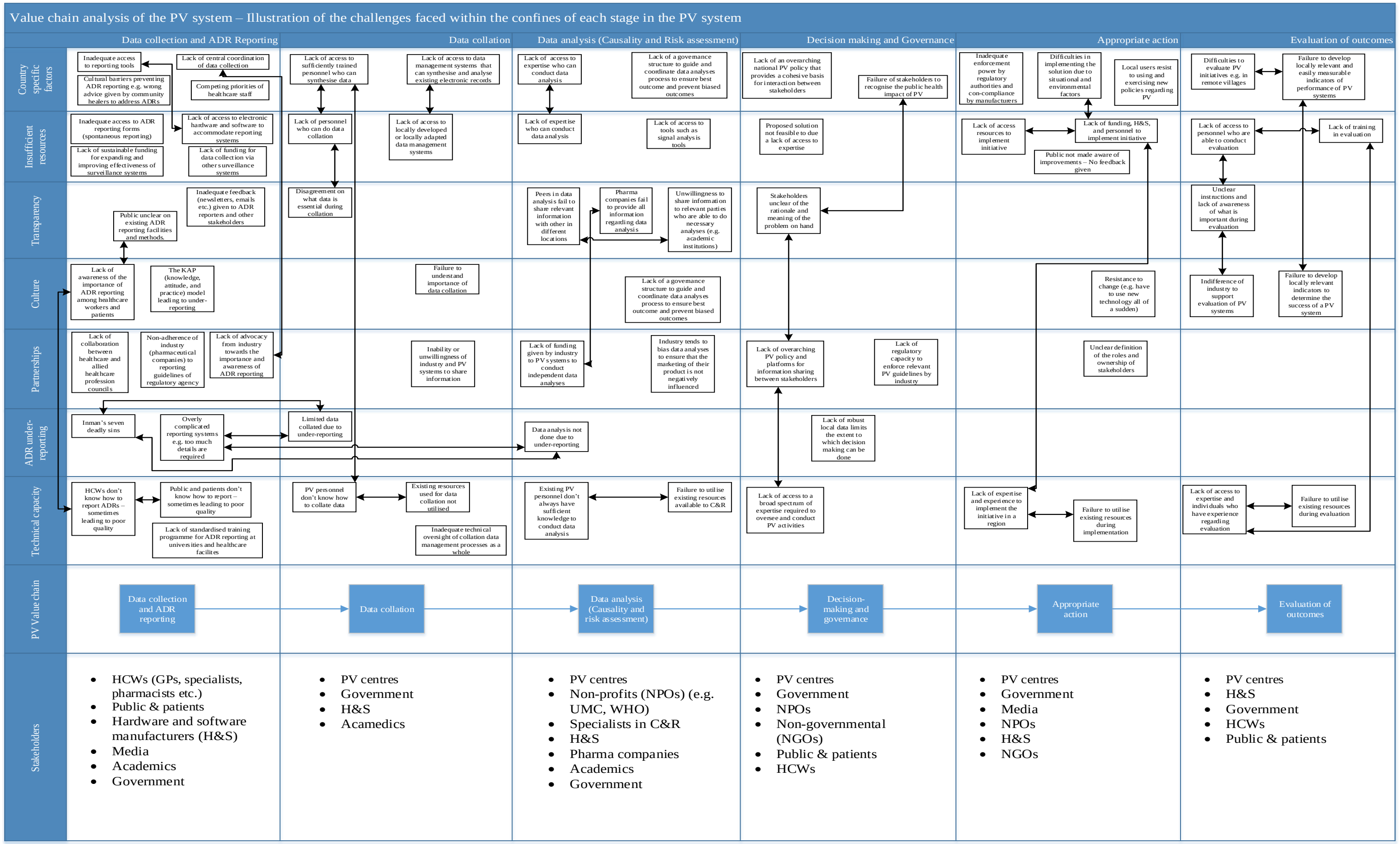
CONCLUSION AND FUTURE RESEARCH

In this paper, the translation of the PV challenge landscape to a lower level of abstraction is the main focus point. It is concluded that this translation process is best achieved via two stages, which are (i) the identification of the influence of the PV challenge landscape in the PV value chain, and, (ii) the identification of the root causes of these challenges. In order to complete these stages, the prospects of several methodologies are investigated, and by making use of a set of qualification criteria, two candidate methodologies are chosen, namely the value chain analysis (used for stage one of the translation process) and the 5Why method in combination with fishbone diagrams (used for stage two of the translation process). As an illustration of the implementation of these methodologies and the associated benefits they offer, examples are provided, followed by a summary of the key points that can be concluded from the application of each of these methodologies to the PV landscape. Finally, candidate technologies are identified that can be leveraged towards addressing the challenges in PV.

Following the two stages of the translation process, is became clear that the methodologies that have been implemented highlighted several key points that may have been difficult, or even impossible, to conclude. As a result, the proposed approach to translating the PV challenge landscape can be used in future studies in an attempt to develop solutions to the many problems that burden PV systems.

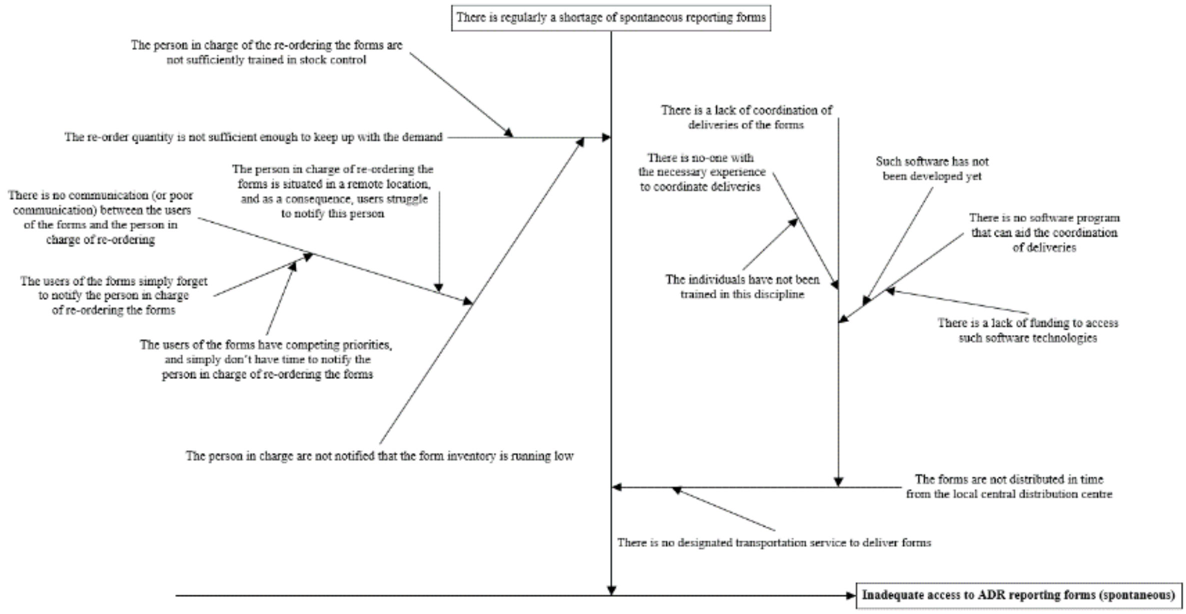
Both stages of the translation process of the PV challenge landscape identified several tangible problems and operational challenges that can be addressed with technology. The technologies identified in the paper represent only a portion of the technology landscape, and there are many other technologies that can be investigated. Regardless, the success already achieved by these technologies in other industries such as the educational industry increase the probability that these technologies can be used to address the PV challenge landscape.

APPENDIX 1: THE PHARMACOVIGILANCE VALUE CHAIN ANALYSIS

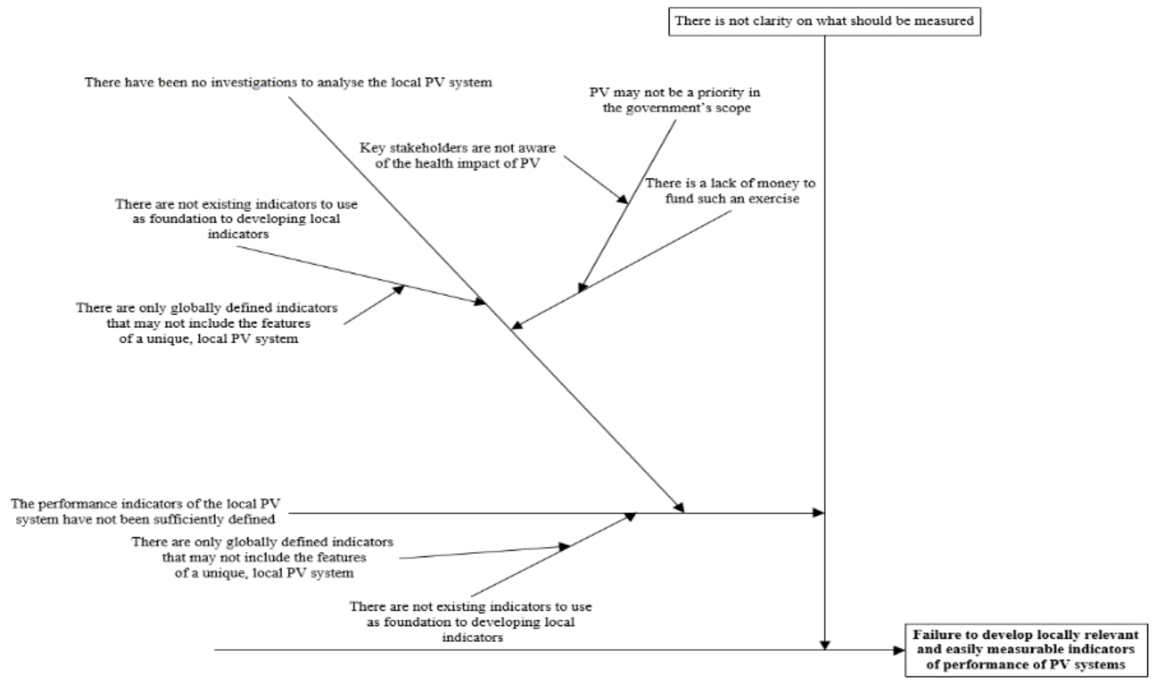


APPENDIX 2: IMPLEMENTATION OF THE 5WHY METHOD, ILLUSTRATED BY FISHBONE DIAGRAMS

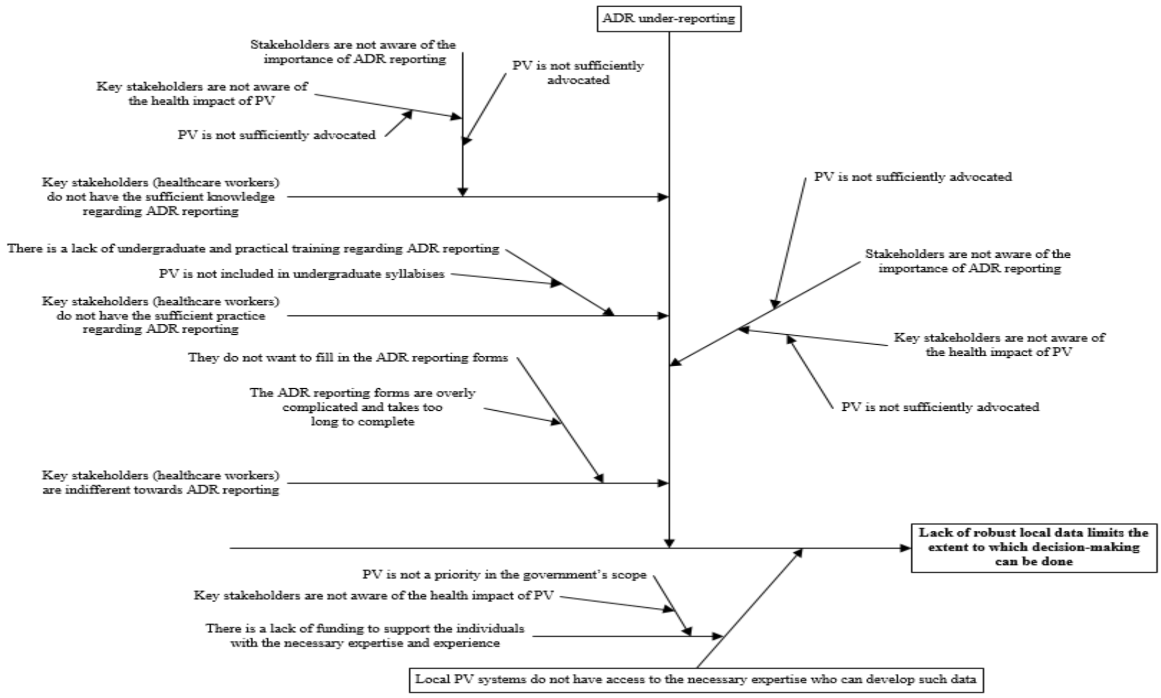
1. Inadequate access to ADR reporting forms (spontaneous).



2. Failure to develop locally relevant and easily measurable indicators of performance of PV systems.



3. Lack of robust local data limits the extent to which decision-making can be done



REFERENCES

De Abajo, F.J., 2005. Improving pharmacovigilance beyond spontaneous reporting. *International Journal of Pharmaceutical Medicine*, 19(4), pp.209–218.

Abubakar, A.R., Ismail, S., et al., 2015. Comparative study on drug safety surveillance between medical students of Malaysia and Nigeria. *Therapeutics and Clinical Risk Management*, pp.1015–1025.

Abubakar, A.R., Chedi, B.A., et al., 2015. Perception of Nigerian medical students on adverse drug reaction reporting. *Journal of Advanced Pharmaceutical Technology and Research*, 6(4), pp.154–158.

Abubakar, A.R. & Haque, M., 2016. Pharmacovigilance Practice : The Current Challenges and the Gaps in the Medical Students ' Curriculum. *Journal of Applied Pharmaceutical Science*, 6(05), pp.210–215.

Abubakar, A.R., Simbak, N. Bin & Haque, M., 2015. Pharmacovigilance Study : Awareness among Medical Students of a New Medical School of Malaysia. *International Journal of Pharmaceutical Research*, 7(1), pp.83–88.

Agbabiaka, T.B., Savović, J. & Ernst, E., 2008. Methods for causality assessment of adverse drug reactions: a systematic review. *Drug Safety*, 31(1), pp.21–37. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18095744.

Al-Alawi, A.I., Al-Marzooqi, N.Y. & Mohammed, Y.F., 2007. Organizational culture and knowledge sharing: critical success factors. *Journal of Knowledge Management*, 11(2), pp.22–42. Available at: http://www.emeraldinsight.com/doi/10.1108/13673270710738898.

Alan, W., 2001. Understanding organisational culture and the implications for corporate marketing. *European Journal of Marketing*, 35(3/4), pp.353–367.

Aljadhey, H. et al., 2015. A qualitative exploration of the major challenges facing pharmacovigilance in Saudi Arabia. *Saudi Medical Journal*, 36(9), pp.1097–1102.

Armstrong, S., 2013. What Are The Advantages And Disadvantages Of Online Learning? *eLearning Industry*. Available at: https://elearningindustry.com/advantages-and-disadvantages-of-online-learning [Accessed January 30, 2018].

Aronson, J.K., 2012. Balanced prescribing – principles and challenges. *British Journal of Clinical Pharmacology*, 74(4), pp.566–572.

Avorn, J. & Schneeweiss, S., 2009. Managing Drug-Risk Information — What to Do with All Those New Numbers. *The New England Journal of Medicine*, 361(7), pp.647–649.

Baiju, N.T., 2017. 5 advantages and disadvantages of Cloud Storage. *Big Data Made sSmple*, pp.4–6. Available at: http://bigdata-madesimple.com/5-advantages-and-disadvantages-of-cloud-storage/ [Accessed January 30, 2018].

Bandekar, M.S., Anwikar, S.R. & Kshirsagar, N.A., 2009. Theories of attempted suicide: Should they differ from theories of completed suicide? *Pharmacoepidemiology and Drug Safety*, 6(5), pp.188–191.

Barnieh, L., Donaldson, C. & Manns, B., 2014. Health care prioritization : a clinician's duty. *Canadian Journal of Kidney Health and Disease*, 1(27), pp.1–5.

Baroudi, R., 2014. Key performance indicators: Winning tips and common challenges. *EY Performance Journal*, 6(2), pp.36–43.

Bau, L.M.S. et al., 2012. Organizational ergonomics of occupational health methods and processes in a Brazilian oil refinery. In *Work 41*. pp. 2817–2821.

Beckmann, J. et al., 2014. Teaching Pharmacovigilance: the WHO-ISoP Core Elements of a Comprehensive Modular Curriculum. *Drug Safety*, 37(10), pp.743–759.

Bellot, J., 2011. Defining and assessing organizational culture. *Nursing forum*, 46(1), pp.29–37.

Beninger, P., 2017. Opportunities for Collaboration at the Interface of Pharmacovigilance and Manufacturing. *Clinical Therapeutics*, 39(4), pp.702–712. Available at: http://dx.doi.org/10.1016/j.clinthera.2017.03.010.

Bergvall, T., Niklas Norén, G. & Lindquist, M., 2014. VigiGrade: A tool to identify well-documented individual case reports and highlight systematic data quality issues. *Drug Safety*, 37(1), pp.65–77.

Berry, S., 2010. How Coca-Cola's distribution system works. *ColaLife*. Available at: http://www.colalife.org/2010/12/19/how-coca-colas-distribution-system-works/ [Accessed February 26, 2018].

BEUC, 2008. A STRONG , TRANSPARENT AND PROACTIVE PHARMACOVIGILANCE SYSTEM. , pp.1–8. Available at: www.beuc.eu.

Booth, N., 2003. Can business benefit from remote access? *ComputerWeekly.com*. Available at: http://www.computerweekly.com/feature/Can-business-benefit-from-remote-access [Accessed January 31, 2018].

Boundless Management, 2016. Strategic, Tactical, and Operational Control. *Boundless Management*. Available at: https://www.boundless.com/management/textbooks/boundless-management-textbook/control-8/types-of-control-62/strategic-tactical-and-operational-control-313-3960/ [Accessed August 4, 2017].

Brugha, R. & Varvasovszky, Z., 2000. Stakeholder analysis: a review. *Health Policy and Planning*, 15(3), pp.239–246. Available at: https://academic.oup.com/heapol/article-lookup/doi/10.1093/heapol/15.3.239.

Brundage, M.P. et al., 2017. Smart Manufacturing Through a Framework for a Knowledge-Based Diagnosis System. In M. P. Brundage, ed. *ASME 2017 International Manufacturing Science and Engineering Conference*. Los Angeles: Research Gate, pp. 1–9. Available at: http://proceedings.asmedigitalcollection.asme.org/proceeding.aspx?doi=10.1115/MSEC2017-2937.

Bulsuk, K., 2009. Using a Fishbone (or Ishikawa) Diagram to Perform 5-why Analysis. *Toyota Production System*. Available at: http://www.bulsuk.com/2009/08/using-fishbone-diagram-to-perform-5-why.html [Accessed October 4, 2017].

Buse, K., Mays, N. & Walt, G., 2005. *Making Health Policy* N. Black & R. Raine, eds., Berkshire, England: McGraw-Hill Education.

Callréus, T., 2011. The New EU Legislation on Pharmacovigilance and Changing Models for Drug Development. *Drug Safety*, 34(6), pp.529–531.

Caster, O. et al., 2017. vigiRank for statistical signal detection in pharmacovigilance: First results from prospective real-world use. *Pharmacoepidemiology and Drug Safety*, 26(8), pp.1006–1010.

Chan, C. V. & Kaufman, D.R., 2010. A technology selection framework for supporting delivery of patient-oriented health interventions in developing countries. *Journal of Biomedical Informatics*, 43(2), pp.300–306. Available at: http://dx.doi.org/10.1016/j.jbi.2009.09.006.

Cheaib, N., 2016. Pharmacovigilance in Clinical Trials: Current Practice and Challenges. *Accountability in Research*, 23(1), pp.23–30. Available at: http://www.tandfonline.com/doi/full/10.1080/08989621.2014.956868%0Ahttp://www.ncbi.nlm.nih.gov/pubmed/26528639.

Chmutova, I., 2015. Bank's financial management technologies forming at strategic and operational levels. *Economic Annals-XXI*, 9, pp.73–77.

Coffey, H., 2007. Digital game-based learning. *Learn NC*. Available at: http://www.dfpp.univr.it/documenti/Avviso/all/all036209.pdf [Accessed February 26, 2018].

Cognizant, 2012. *The Future of Pharmacovigilance : Five Imperatives that Will Drive Improved Business Outcomes*, Available at: https://www.cognizant.com/industries-resources/life_sciences/The-Future-of-Pharmacovigilance-Five-Imperatives-that-Will-Drive-Improved-Business-Outcomes.pdf.

Cohn, J. et al., 2017. When falsified medicines enter the supply chain : Description of an incident in Kenya and lessons learned for rapid response Published by : Palgrave Macmillan Journals Stable URL : http://www.jstor.org/stable/43287941 When falsified medicines enter the su. *Journal of Public Health Policy*, 34(1), pp.22–30.

Croxton, K.L. et al., 2001. The Supply Chain Management Processes. *The International Journal of Logistics*

Management, 12(2), pp.13–36.
Data Team, 2017. In much of sub-Saharan Africa, mobile phones are more common than access to electricity. *The Economist*. Available at: https://www.economist.com/graphic-detail/2017/11/08/in-much-of-sub-saharan-africa-mobile-phones-are-more-common-than-access-to-electricity [Accessed July 16, 2018].
Deloitte, 2014. *Value of connectivity: Economic and social benefits of expanding internet access*, Available at: https://www2.deloitte.com/content/dam/Deloitte/ie/Documents/TechnologyMediaCommunications/2014_uk_tmt_value_of_connectivity_deloitte_ireland.pdf.
Demirkıran, Z.K. & Altunok, T., 2012. A Systems Approach for Technology Assessment and Selection. In *Digital Avionics Systems Conference (DASC)*. Williamsberg, VA, USA: IEEE, pp. 1–11.
Deshpande, S., Basil, M.D. & Basil, D.Z., 2009. Factors Influencing Healthy Eating Habits Among College Students: An Application of the Health Belief Model. *Health Marketing Quarterly*, 26(2), pp.145–164. Available at: http://www.tandfonline.com/doi/abs/10.1080/07359680802619834.
Donner, J., 2008. Research approaches to mobile use in the developing world: A review of the literature. *Information Society*, 24(3), pp.140–159.
Dubey, A. & Handu, S.S., 2013. Are we pharmacovigilant enough in ophthalmic practice? *Indian Journal of Ophthalmology*, 61(5), pp.226–229.
Dusek, V., 2008. *Philosophy of Technology: An Introduction*, United Kingdom: Blackwell Publishing. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18427953%5Cnfile:///C:/Users/morganya/Documents/My eBooks/academic/Dusek, Val. Philosophy of Technology An Introduction.pdf.
Al Dweik, R. et al., 2016. Factors affecting patient reporting of adverse drug reactions: a systematic review. *British Journal of Clinical Pharmacology*, (November).
Ebrahim, A., 2013. Let's Be Realistic About Measuring Impact. *Harvard Business Review*, pp.1–2. Available at: https://hbr.org/2013/03/lets-be-realistic-about-measur.html [Accessed July 21, 2017].
Eckerson, W.W., 2009. *Performance management strategies: How to Create and Deploy Effective Metrics*, Available at: https://www.microstrategy.com/strategy/media/downloads/white-papers/tdwi_performance-management-strategies.pdf.
Edwards, B. et al., 2015. Guiding Principles of Safety as a Basis for Developing a Pharmaceutical Safety Culture. *Current Drug Safety*, 2, pp.135–139.
Edwards, I.R., 2017. Causality Assessment in Pharmacovigilance: Still a Challenge. *Drug Safety*, 40(5), pp.365–372.
Fortado, B. & Fadil, P., 2012. The four faces of organizational culture. *Competitiveness Review: An International Business Journal*, 22(4), pp.283–298. Available at: http://www.emeraldinsight.com/doi/10.1108/10595421211247132.
François, A. et al., 2013. How can the Quality of Medical Data in Pharmacovigilance , Pharmacoepidemiology and Clinical Studies be Guaranteed ? *Société Française de Pharmacologie et de Thérapeutique*, 68(4), pp.217–223.
Franz, M. et al., 2015. *Building Energy Access Markets: A Value Chain Analysis of Key Energy Market Systems*, Eschborn. Available at: http://www.euei-pdf.org/sites/default/files/files/field_pblctn_file/150907_euei_value-chain_en_rz_03_web_0.pdf.
Gaille, B., 2016. 16 Pros and Cons of the Internet of Things. *BrandonGaille.com*. Available at: https://brandongaille.com/16-pros-and-cons-of-the-internet-of-things/ [Accessed January 31, 2018].
Giezen, T.J., Mantel-Teeuwisse, A.K. & Leufkens, H.G., 2009. Pharmacovigilance of Biopharmaceuticals - Challenges Remain. *Drug Safety*, 32(10), pp.811–817.
Gilson, L., 2006. Trust in health care : Theoretical perspectives and research needs. *Journal of Health Organization and Management*, 20(5), pp.359–375.
Granados, N., Gupta, A. & Kauffman, R.J., 2010. Information Transparency in Tusiness-to-Consumer Markets: Concepts, Framework, and Research Agenda. *Information Systems Research*, 21(2), pp.207–226.
Gubbi, J. et al., 2013. Internet of Things (IoT): A Vision, Architectural Elements, and Future Directions. *Future Generation Computer Systems*, 29(7), pp.1645–1660. Available at: https://arxiv.org/pdf/1207.0203.pdf?ref=theiotlist.
Hackett, R., 2016. Wait, What is Blockchain? *Fortune*. Available at: http://fortune.com/2016/05/23/blockchain-definition/ [Accessed February 8, 2018].
Hammer, M., 2004. Deep Change : How Operational Innovation Can Transform Your Company. *Harvard Business Review*, (April), pp.1–20.
Härmark, L. & Van Grootheest, A.C., 2008. Pharmacovigilance: Methods, recent developments and future perspectives. *European Journal of Clinical Pharmacology*, 64(8), pp.743–752.
Harpaz, R. et al., 2014. Text Mining for Adverse Drug Events : the Promise , Challenges , and State of the Art. *Drug Safety*, 37, pp.777–790.
Harris, M., 2017. What is Cloud Storage? *LifeWire*. Available at: https://www.lifewire.com/what-is-cloud-storage-

2438541 [Accessed January 30, 2018].
Hazell, L. & Shakir, S.A.W., 2006. Under-Reporting of Adverse A Systematic Review. *Drug Safety*, 29(5), pp.385–396.
Heinrich, M., 2015. Quality and safety of herbal medical products : regulation and the need for quality assurance along the value chains. *British Journal of Clinical Pharmacology*, 80(1), pp.62–66.
Herdeiro, M.T. et al., 2006. Influence of Pharmacists ' Attitudes on Adverse Drug Reaction Reporting A Case-Control Study in Portugal. *Drug Safety*, 29(4), pp.331–340.
Hewitt-Taylor, J., 2012. Identifying, analysing and solving problems in practice. *Nursing Standard*, 26(40), pp.35–41. Available at: https://www.researchgate.net/profile/Eduardo_Cittadini/publication/262911808_Participatory_Analysis_of_the_Sweet_Cherry_Sector_in_Argentinian_South_Patagonia/links/5656edfb08ae4988a7b51232.pdf.
Hill, G., 2014. Pharmacovigilance methods: the spectrum of PV. [Online video]. Available at: https://www.youtube.com/watch?v=lAhzeDxMp1s [Accessed April 15, 2017].
Holden, W.L., Juhaeri, J. & Dai, W., 2003. Benefit-risk analysis: A proposal using quantitative methods. *Pharmacoepidemiology and Drug Safety*, 12(7), pp.611–616.
Holm, G. et al., 2013. Implementing Ecopharmacovigilance in Practice : Challenges and Potential Opportunities. *Drug Safety*, 36, pp.533–546.
Hong, J., 2013. Framework for selecting the technology in public sector. *Information*, 16(11), pp.7895–7904.
HRCloud, 2017. HR Software & HRMS Solutions for Business. Available at: https://www.hrcloud.com/.
Iansiti, M. & Lakhani, K.R., 2017. The Truth About Blockchain. *Harvard Business Review*, 3(January-February), pp.3–11.
Irujo, M. et al., 2007. Factors that Influence Under-Reporting of Suspected Adverse Drug Reactions among Community Pharmacists in a Spanish Region. *Drug Safety*, 30(11), pp.1073–1082.
Isah, A.O. et al., 2012. Specific features of medicines safety and pharmacovigilance in Africa. *Therapeutic advances in drug safety*, 3(1), pp.25–34. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4110828&tool=pmcentrez&rendertype=abstract.
Islam, S.M.R. et al., 2015. The Internet of Things for Health Care : A Comprehensive Survey. *IEEE Access*, 3, pp.678–708. Available at: http://ieeexplore.ieee.org/xpl/articleDetails.jsp?arnumber=7113786.
Jones, R.W. & Despotou, G., 2016. Root cause analysis and health informatics. In *14th International Conference on Informatics, Management and Technology in Healthcare*. Athens: Studies in health technology and informatics, pp. 131–134. Available at: http://dx.doi.org/10.3233/978-1- 61499-664-4-131.
Jurevicius, O., 2013a. Resource based view. *Strategic Management Insight*, p.1. Available at: https://www.strategicmanagementinsight.com/topics/resource-based-view.html [Accessed June 28, 2017].
Jurevicius, O., 2013b. Value Chain Analysis. *Strategic Management Insight*. Available at: https://www.strategicmanagementinsight.com/tools/value-chain-analysis.html [Accessed August 18, 2017].
Jusot, V., 2017. Correspondence. 20 July, Stellenbosch.
Kabore, L. et al., 2013. Pharmacovigilance systems in developing countries: An evaluative case study in Burkina Faso. *Drug Safety*, 36(5), pp.349–358.
KC, S. et al., 2013. Knowledge about adverse drug reactions reporting among healthcare professionals in Nepal. *International Journal of Risk and Safety in Medicine*, 25, pp.1–16.
Kendrick, J., 2013. Mobile technology: The amazing impact on our lives. *Mobile News*. Available at: http://www.zdnet.com/article/mobile-technology-the-amazing-impact-on-our-lives/ [Accessed February 2, 2018].
Khan, T.M., 2013. Community pharmacists' knowledge and perceptions about adverse drug reactions and barriers towards their reporting in Eastern region, Alahsa, Saudi Arabia. *Therapeutic Advances in Drug Safety*, 4(2), pp.45–51.
Khorramshahgol, R. & Moustakis, V.S., 1988. Delphic hierarchy process (DHP): a methodology for priority setting derived from the Delphi method and analytical hierarchy process. *European Journal of Operational Research*, 37(3), pp.347–354.
Kirby, M.R. & Mavris, D.N., 2000. A method for technology selection based on benefit, available schedule and budget resources. In *2000 World Aviation Conference*. San Diego, CA: American Institute of Aeronautics and Astronautics (AIAA), pp. 1–15. Available at: http://arc.aiaa.org/doi/pdf/10.2514/6.2000-5563.
Klausen, S.M. & Parle, J., 2015. 'Are we going to stand by and let these children come into the world?': the impact of the 'Thalidomide Disaster' in South Africa, 1960–1977. *Journal of Southern African Studies*, 41(4), pp.735–752. Available at: http://www.tandfonline.com/doi/full/10.1080/03057070.2015.1047181.
Klein, R., 1993. Dimensions of rationing: who should do what? *British Medical Journal*, 307, pp.309–131.

Klein, R., 1998. Puzzling out Priorities: Why We Must Acknowledge That Rationing Is a Political Process. *British Medical Journal*, 317(7164), pp.959–960.

Kumar, A. & Khan, H., 2015. Signal detection and their assessment in pharmacovigilance. *Open Pharmaceutical Sciences Journal*, 2, pp.66–73.

Lamprecht, A.J., 2017. Personal interview. 10 October, Western Cape Department of Education Headquarters.

Lamprecht, I.V.B., Bam, L. & de Kock, I.H., 2017. An investigation into the prospects of existing technologies to address the challenges faced by pharmacovigilance systems. In *SAIIE28: Taking up Stewardship*. Vanderbijlpark: SAIIE, pp. 1–17. Available at: https://www.saiie.co.za/saiie28.

Li, Y. et al., 2017. How Do Resource Structuring and Strategic Flexibility Interact to Shape Radical Innovation? *Journal of Product Innovation Management*, 34(4), pp.471–491. Available at: http://doi.wiley.com/10.1111/jpim.12389.

Lu, Z., 2009. Information technology in pharmacovigilance : Benefits , challenges , and future directions from industry perspectives. *Drug, Healthcare and Patient Safety*, 1, pp.35–45.

Macwan, U., 2017. Mobile Technology , Its Importance , Present And Future Trends. *Finextra*. Available at: https://www.finextra.com/blogposting/14000/mobile-technology-its-importance-present-and-future-trends [Accessed February 2, 2018].

Management for Science, 2012. Pharmacovigilance. , p.35.1-35.19.

Mathur, V.N. et al., 2007. Defining, identifying and mapping stakeholders in the assessment of urban sustainability. In M. Horner et al., eds. *International Conference on Whole Life Urban sustainability and its Assessment*. Glasgow, p. 18. Available at: https://dspace.lboro.ac.uk/xmlui/handle/2134/5202.

Mehta, U., 2017. Personal interview. 21 August, School of Public Health (UCT).

Mishra, S. & Singh, I.P., 2008. mHealth: a developing country perspective. In *Making the eHealth connection*. Bellagio, Italy, pp. 1–9. Available at: http://ehealth-connection.org/files/conf-materials/mHealth_ A Developing Country Perspective_0.pdf.

Morrison, A. & Sinha, S., 2016. A primer on blockchain (infograohic). *PWC Emerging Technology*. Available at: http://usblogs.pwc.com/emerging-technology/a-primer-on-blockchain-infographic/ [Accessed February 8, 2018].

Mpanza, Z., 2016. Identifying the root causes contributing to defects in order to minimize scrap. In *2016 International Conference on Industrial Engineering and Operations Management*. Kuala Lumpur: IEOM Society International, pp. 1139–1146. Available at: http://ieomsociety.org/ieom_2016/pdfs/318.pdf.

Myszewski, J.M., 2013. On improvement story by 5 whys. *The TQM Journal*, 25(4), pp.371–383. Available at: http://www.emeraldinsight.com/doi/10.1108/17542731311314863.

Naghibi, M.A. & Baban, H., 2011. Strategic Change Management: The Challenges Faced by Organizations. *International Proceedings of Economics Development and Research*, 4, pp.542–544.

Naidoo, P. & Martins, N., 2014. The relationship between organizational culture and work engagement: A multilevel investigation. *Problems and Perspectives in Management*, 12(4), pp.433–441.

Newton, R., 2010. Six Symptoms of Poor Prioritisation. *Corporate Geek*, pp.407–407. Available at: http://www.corporategeek.info/six-symptoms-poor-prioritisation [Accessed November 9, 2017].

Nikfarjam, A. et al., 2015. Pharmacovigilance from social media: Mining adverse drug reaction mentions using sequence labeling with word embedding cluster features. *Journal of the American Medical Informatics Association*, 22(3), pp.671–681.

Norman, S., 2016. Advantages Of Online Learning: Education Without Leaving Home. *eLearning Industry*. Available at: https://elearningindustry.com/5-advantages-of-online-learning-education-without-leaving-home [Accessed January 30, 2018].

Olsen, A.K. & Whalen, M.D., 2009. Public Perceptions of the Pharmaceutical Industry and Drug Safety and the Culture of Safety. *Drug Safety*, 32(10), pp.805–810.

Olsson, S. et al., 2010. Pharmacovigilance activities in 55 low-and middle-income countries: A questionnaire-based analysis. *Drug Safety*, 33(8), pp.689–703.

Ostrov, J.M., Gentile, D.A. & Mullins, A.D., 2013. Evaluating the effect of educational media exposure on aggression in early childhood. *Journal of Applied Developmental Psychology*, 34(1), pp.38–44. Available at: http://dx.doi.org/10.1016/j.appdev.2012.09.005.

Oztaysi, B., 2014. A decision model for information technology selection using AHP integrated TOPSIS-Grey: The case of content management systems. *Knowledge-Based Systems*, 70, pp.44–54.

Palloff, R.M. & Pratt, K., 2001. *Lessons from the Cyberspace Classroom: The Realities of Online Teaching*, San Francisco: Jossey-Bass. Available at: https://books.google.co.za/books?hl=en&lr=&id=36GLHRvTELMC&oi=fnd&pg=PR9&dq=online+teaching&ots=8n_1hUxCUP&sig=6Ku1I_cFJfZyhzD-nHlsJnuFf_4#v=onepage&q=online teaching&f=false.

Pan, G.J.D., 2014. Ongoing Challenges in Pharmacovigilance. *Drug Safety*, 37, pp.1–8.

Passier, A. et al., 2009. Reporting of Adverse Drug Reactions by General Practitioners. *Drug Safety*, 32(10),

pp.851–858.
Pojasek, R.B., 2000. Asking "Why?" five times. *Environmental Quality Management*, 10(1), pp.79–84.
Pontes, H., Clément, M. & Rollason, V., 2014. Safety signal detection: The relevance of literature review. *Drug Safety*, 37(7), pp.471–479.
Rachlis, B. et al., 2016. Targeted Spontaneous Reporting: Assessing Opportunities to Conduct Routine Pharmacovigilance for Antiretroviral Treatment on an International Scale. *Drug Safety*, 39(10), pp.959–976.
Raghupathi, W. & Raghupathi, V., 2014. Big data analytics in healthcare: promise and potential. *Health Information Science and Systems*, 2(1), p.3. Available at: http://link.springer.com/10.1186/2047-2501-2-3.
Rahman, S.Z. & Khan, R.A., 2015. Pharmaco Environmentology – Aligning Pharmacovigilance with Environment. *Pharma Times*, 47(8).
Rama, P., Rodrigues, P.A. & Georgy, A., 2011. Asian Journal of Pharmaceutical and Clinical Research PHARMAOVIGILANCE : PERSPECTIVES AND FUTURE CHALLENGES IN INDIAN SCENARIO. *Asain Journal of Pharmaceutical and Clinical Research*, 4(4), pp.1–4.
Raschi, E. et al., 2016. Adverse events associated with the use of direct-acting oral anticoagulants in clinical practice: Beyond bleeding complications. *Polish Archives of Internal Medicine*, 126(7–8), pp.552–561.
Ríos, O.M. et al., 2016. A comprehensive intervention for adverse drug reactions identification and reporting in a Pediatric Emergency Department. *International Journal of Clinical Pharmacy*, 38(1), pp.80–87.
Rodrigues, G.S. & Khan, S.A., 2011. Pharmacovigilance Among Surgeons and in Surgical Wards : Overlooked or Axiomatic ? *Indian Journal of Surgery*, 73(1), pp.4–8.
Rouse, M., 2005. Remote Access. *TechTarget*. Available at: http://searchmidmarketsecurity.techtarget.com/definition/remote-access [Accessed January 30, 2018].
Rouse, M., 2010. WAP (Wireless Application Protocol). *TechTarget*. Available at: http://searchmobilecomputing.techtarget.com/definition/WAP [Accessed February 26, 2018].
Rubel, M.R.B. et al., 2017. Adapting technology : effect of high-involvement HRM and organisational trust. *Behaviour and Information Technology*, 36(1), pp.281–293.
Ruder, K.A., Pretorius, M.W. & Maharaj, B.T., 2008. A technology selection framework for the telecommunications industry in developing countries. In *IEEE International Conference on Communications*. Beijing, pp. 5490–5493.
Ruder, K.A., Pretorius, M.W. & Maharaj, B.T., 2008. A technology selection framework for the telecommunications industry in developing countries. In *IEEE International Conference on Communications*. IEEE, pp. 5490–5493.
Russom, P., 2011. *Big data analytics*, Available at: https://vivomente.com/wp-content/uploads/2016/04/big-data-analytics-white-paper.pdf.
Sabik, L.M. & Lie, R.K., 2008. Priority setting in health care: Lessons from the experiences of eight countries. *International Journal for Equity in Health*, 7(1), p.4. Available at: http://equityhealthj.biomedcentral.com/articles/10.1186/1475-9276-7-4.
Sarker, A. et al., 2015. Utilizing social media data for pharmacovigilance: A review. *Journal of Biomedical Informatics*, 54, pp.202–212. Available at: http://dx.doi.org/10.1016/j.jbi.2015.02.004.
Schramm, G.E. et al., 2017. Implementation of an interprofessional clinical pharmacology selective learning experience for pharmacy residents and medical students. *American Journal of Health-System Pharmacy*, 74(6), p.397.
Shamim, S. et al., 2016. Adverse drug reactions (ADRS) reporting : awareness and reasons of under-reporting among health care professionals , a challenge for pharmacists. *SpringerPlus (2016)*, 5, pp.1–8.
Sharif, M.N. & Sundararajan, V., 1983. A quantitative model for the evaluation of technological alternatives. *Technological Forecasting and Social Change*, 24(1), pp.15–29.
Shehabuddeen, N., Probert, D. & Phaal, R., 2006. From theory to practice: Challenges in operationalising a technology selection framework. *Technovation*, 26(3), pp.324–335.
Shen, Y.C. et al., 2010. A hybrid selection model for emerging technology. *Technological Forecasting and Social Change*, 77(1), pp.151–166. Available at: http://dx.doi.org/10.1016/j.techfore.2009.05.001.
Simister, P., 2011. Advantages & Disadvantages Of Value Chain Analysis. *Differentiate Your Business*. Available at: http://www.differentiateyourbusiness.co.uk/the-advantages-disadvantages-of-value-chain-analysis [Accessed August 18, 2017].
Singh, V., 2017. Pros & Cons of Apps and Website: Which is Better Option? *YourStory*. Available at: https://yourstory.com/mystory/5d1d4981fe-pros-cons-of-apps-and-website-which-is-better-option- [Accessed February 26, 2018].
Smith, N., 2014. 5 Key Principles to Resource Management. *LiquidPlanner*. Available at: https://www.liquidplanner.com/blog/5-key-principles-resource-management/ [Accessed February 1, 2018].
Sonkiya, S., 2014. Cause And Effect Diagram- Fishbone Diagram Analysis. *Project Quality Management*. Available

at: https://www.izenbridge.com/blog/cause-and-effect-diagram-fishbone-diagram-analysis/ [Accessed October 4, 2017].

Spacey, J., 2015. 11 Types of Resource Management. *Simplicable*. Available at: https://simplicable.com/new/resource-management [Accessed February 1, 2018].

Stahl, M. et al., 2003. Assessing the Impact of Drug Safety Signals from the WHO Database Presented in SIGNAL. *Drug Safety*, 26(10), pp.721–727. Available at: http://www.scopus.com/inward/record.url?eid=2-s2.0-19244382600&partnerID=tZOtx3y1.

Stolk, R.P., 2012. Screening for diabetes. *British Medical Journal*, 335(September), p.462.

Strengthening Pharmaceutical Systems (SPS), 2009. *Supporting Pharmacovigilance in Developing Countries The Systems Perspective*,

Stretcher, V. & Rosenstock, I.M., 1997. The Health Belief Model. In *Health Behavior and Health Education: Theory, Research and Practice*. Jones and Bartlett Publishers, pp. 31–36.

Su, C., Ji, H. & Su, Y., 2010. Hospital pharmacists ' knowledge and opinions regarding adverse drug reaction reporting in Northern China y. *Pharmacoepidemiology and Drug Safety*, 19, pp.217–222.

Suwankesawong, W. et al., 2016. Pharmacovigilance activities in ASEAN countries. *Pharmacoepidemiology and Drug Safety*, 25, pp.1061–1069.

Tallent-Runnels, M.K. et al., 2006. Teaching Courses Online: A Review of the Research. *Review of Educational Research*, 76(1), pp.93–135. Available at: http://rer.sagepub.com/cgi/doi/10.3102/00346543076001093.

Tiles, M. & Oberdiek, H., 1999. *Living in a Technological World 27*, United Kingdom: Routledge.

Toklu, H.Z. & Uysal, M.K., 2008. The knowledge and attitude of the Turkish community pharmacists toward pharmacovigilance in the Kadikoy district of Istanbul. *Pharmacy World & Science*, 30, pp.556–562.

Tomoaia-Cotisel, A. et al., 2013. Context Matters : The Experience. *Annals of Family Medicine*, 11(Supp 1), pp.115–123.

United Nations, 2012. *UNPRPD Strategic and Operational Framework*, New York. Available at: http://www.undp.org/content/dam/undp/library/Poverty Reduction/Inclusive development/UNPRPD_SOF_web_April2012.pdf.

Uppsala Monitoring Centre, 2017. *The quest for evidence*, Uppsala. Available at: https://view.publitas.com/uppsala-monitoring-centre/uppsala-reports-77_web/page/1.

Varallo, F.R. et al., 2014. Causes for the underreporting of adverse drug events by health professionals : a systematic review. *Rev Esc Enferm USP*, 48(4), pp.739–747.

Vargesson, N., 2015. Thalidomide-induced teratogenesis: History and mechanisms. *Birth Defects Research*, 105(2), pp.140–156. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26043938%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4737249%5Cnhttp://doi.wiley.com/10.1002/bdrc.21096.

Varun, B., 2016. What are pros and cons of Internet of Things? *PixelCrayons*. Available at: https://www.pixelcrayons.com/blog/industry-news/what-are-pros-and-cons-of-internet-of-things/ [Accessed January 31, 2018].

Veyrat, P., 2016. How did the 5W2H method earn its name? *Heflo*. Available at: https://www.heflo.com/blog/action-plan/5w2h-method/ [Accessed August 16, 2017].

Viswanathan, P., 2017. What is a Mobile Application? *LifeWire*. Available at: https://www.lifewire.com/what-is-a-mobile-application-2373354 [Accessed February 26, 2018].

De Vries, S.T. et al., 2016. Factors Influencing the Use of a Mobile App for Reporting Adverse Drug Reactions and Receiving Safety Information: A Qualitative Study. *Drug Safety*, 40, pp.443–455. Available at: http://link.springer.com/10.1007/s40264-016-0494-x.

Waller, P.C. & Evans, S.J.W., 2003. A model for the future conduct of pharmacovigilance. *Pharmacoepidemiology and Drug Safety*, 12(1), pp.17–29.

Wang, X. et al., 2009. Active Computerized Pharmacovigilance Using Natural Language Processing, Statistics, and Electronic Health Records: A Feasibility Study. *Journal of the American Medical Informatics Association*, 16(3), pp.328–337. Available at: http://dx.doi.org/10.1197/jamia.M3028.

Warner, J., 2015. Is the "5 Why" Method Still a Useful Tool? *Ready To Manage*. Available at: http://blog.readytomanage.com/is-the-5-why-method-still-a-useful-tool/ [Accessed August 16, 2017].

Weber-Schoendorfer, C. & Schaefer, C., 2016. Pregnancy outcome after tocilizumab therapy in early pregnancy-case series from the German Embryotox Pharmacovigilance Center. *Reproductive Toxicology*, 60, pp.29–32. Available at: http://dx.doi.org/10.1016/j.reprotox.2016.01.002.

Western Governers University, 2017. Teaching Strategies for Using Educational Movies in the Classroom. *Western Governors University*. Available at: https://www.wgu.edu/blogpost/teaching-strategies-using-educational-television-classroom# [Accessed February 26, 2018].

World Health Organization, 2004. *Pharmacovigilance : ensuring the safe use of medicines*, Available at: www.who.org.

World Health Organization, 2002. *The Importance of Pharmacovigilance - Safety Monitoring of medicinal products*, Available at: http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf.

World Health Organization, 2014. WHO pharmacovigilance indicators: A practical manual for the assessment of pharmacovigilance systems. , (1), pp.4–6. Available at: http://apps.who.int/iris/bitstream/10665/186642/1/9789241508254_eng.pdf.

Yang, M., Kiang, M. & Shang, W., 2015. Filtering big data from social media - Building an early warning system for adverse drug reactions. *Journal of Biomedical Informatics*, 54, pp.230–240. Available at: http://dx.doi.org/10.1016/j.jbi.2015.01.011.

Yap, C.M. & Souder, W.E., 1993. A filter system for technology evaluation and selection. *Technovation*, 13(7), pp.449–469.

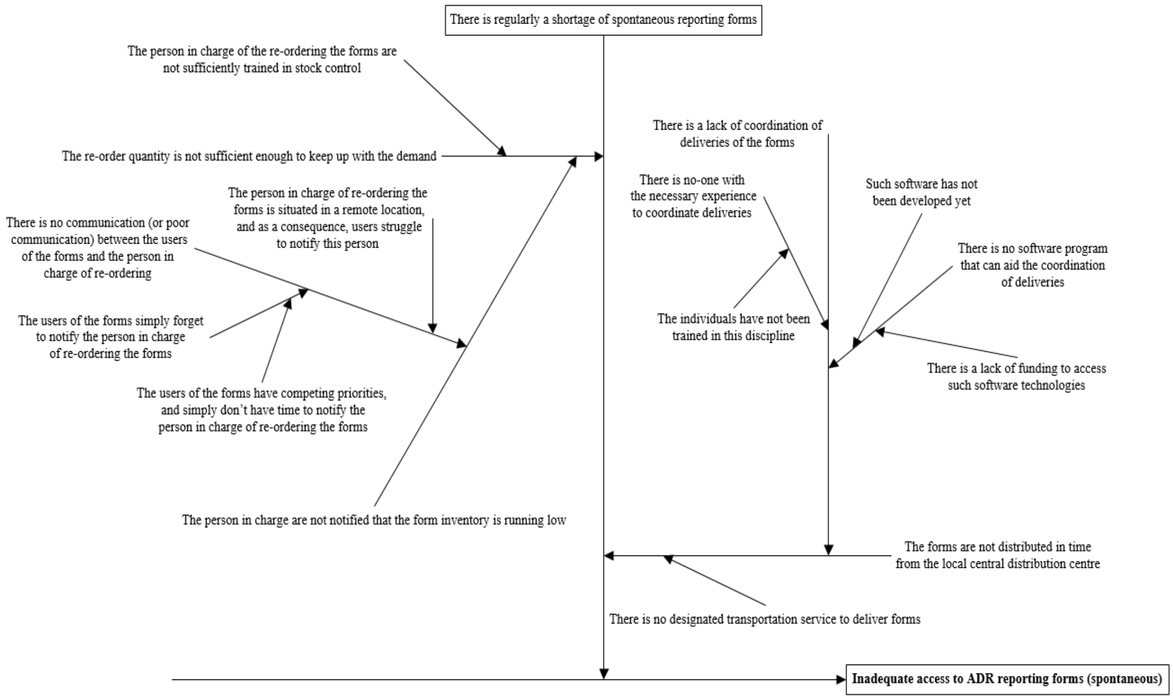
Zaied, A.N., 2007. A Framework for Evaluating and Selecting Learning Technologies. *The International Arab Journal of Information Technology*, 4(2), pp.141–147.

Zakir, J., Seymour, T. & Berg, K., 2015. Big Data Analytics. *Issues in Information Systems*, 16(2), pp.81–90.

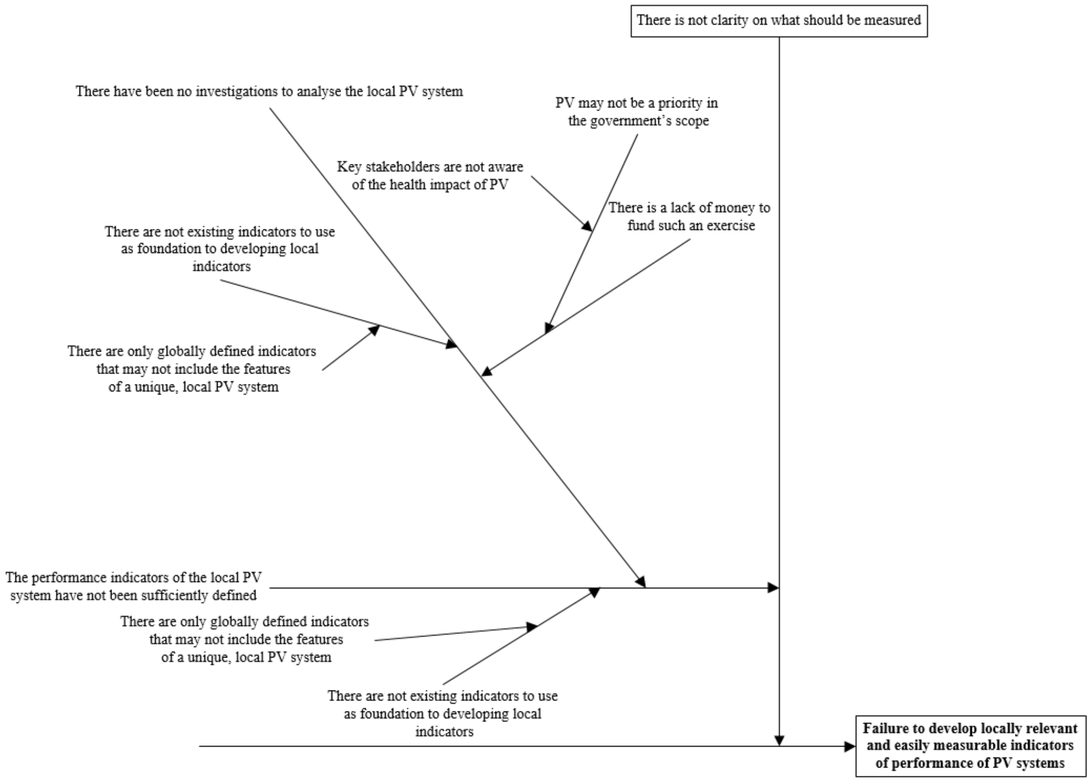
Zhang, L. et al., 2014. Pharmacovigilance in China: Current Situation, Successes and Challenges. *Drug Safety*, 37(10), pp.765–770.

Section C.2: Implementation of the 5Why method, illustrated by fishbone diagrams.

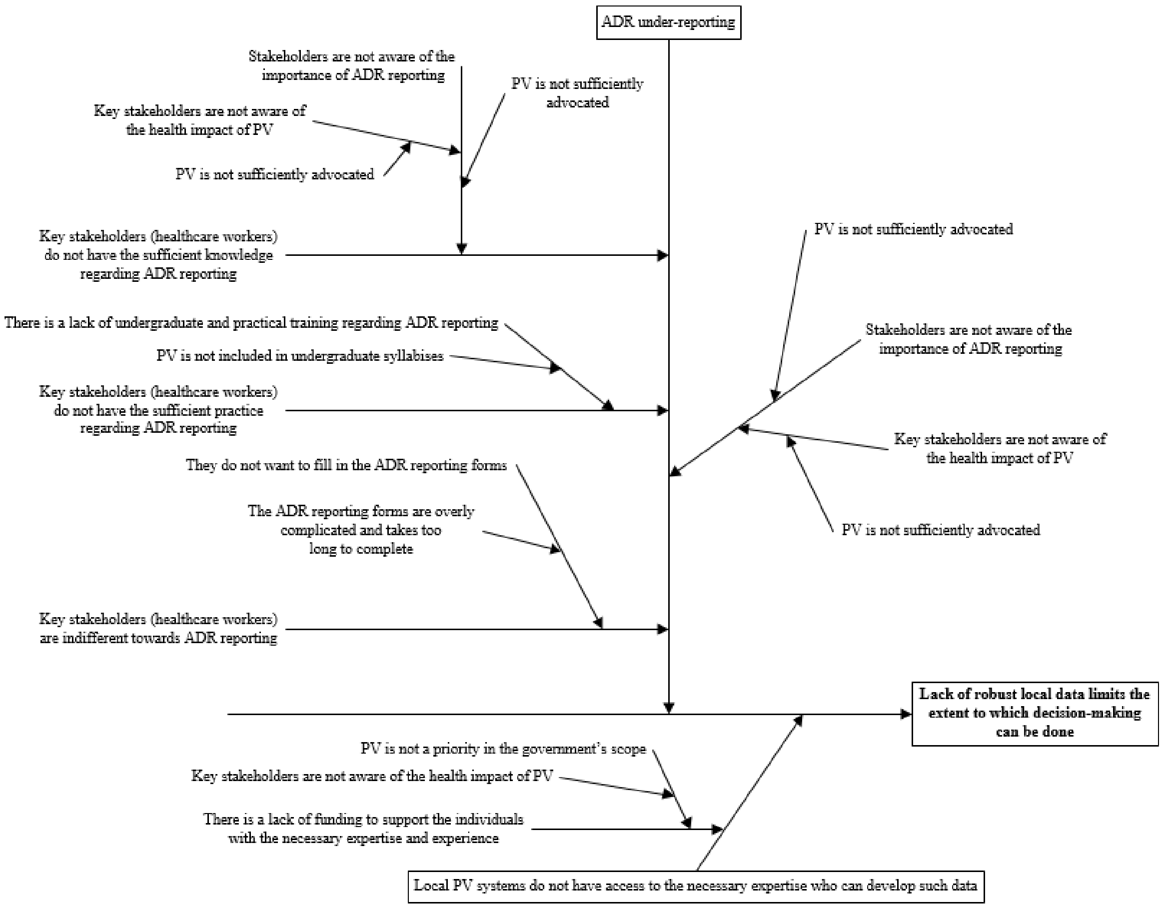
1. Inadequate access to ADR reporting forms (spontaneous)



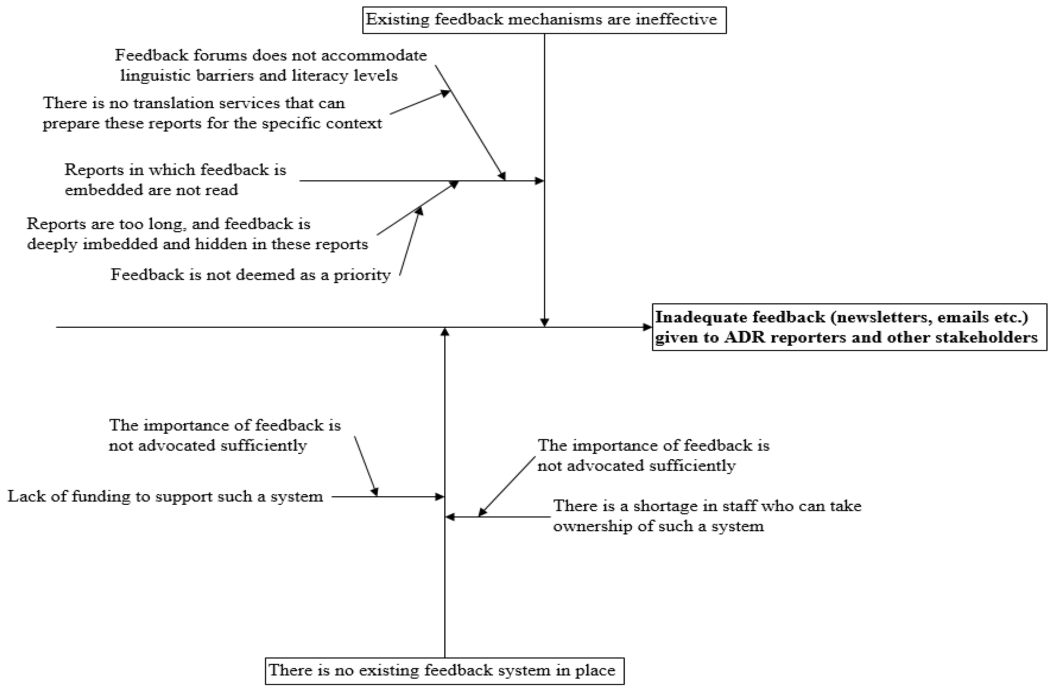
2. Failure to develop locally relevant and easily measurable indicators of performance of PV systems.



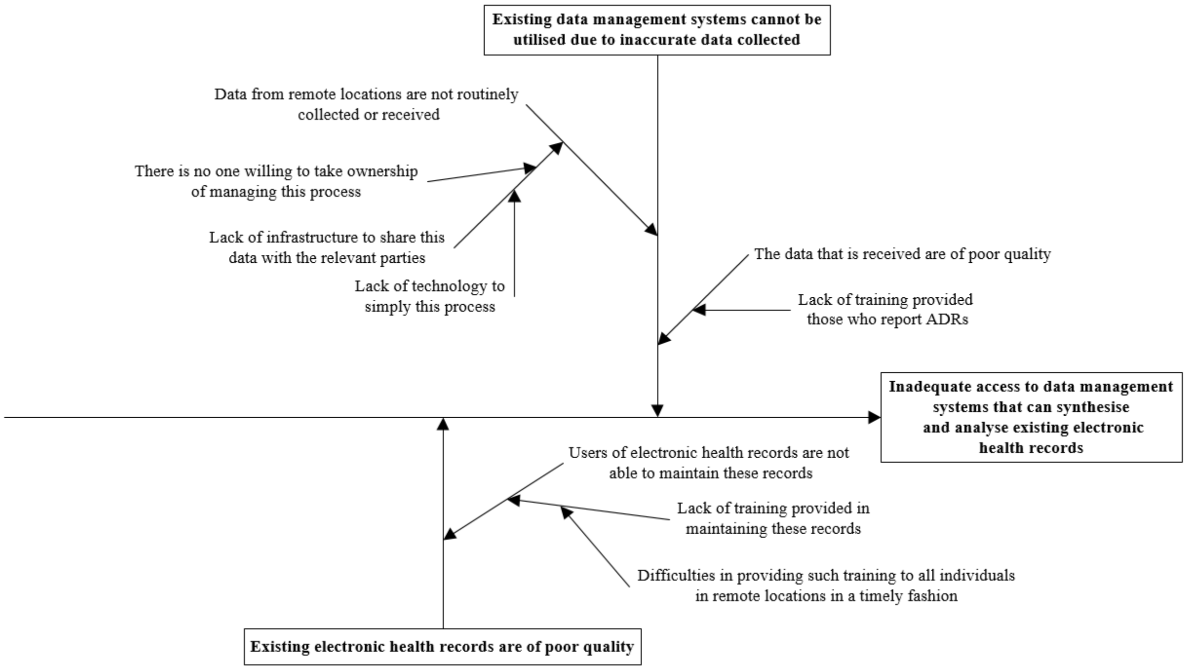
3. Lack of robust local data limits the extent to which decision-making can be done.



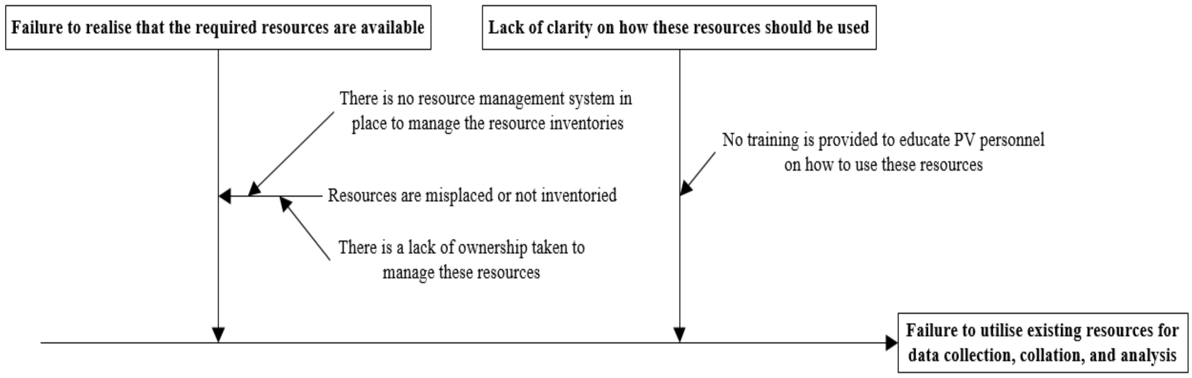
4. Inadequate feedback (newsletters, emails etc.) given to ADR reporters and other stakeholders.



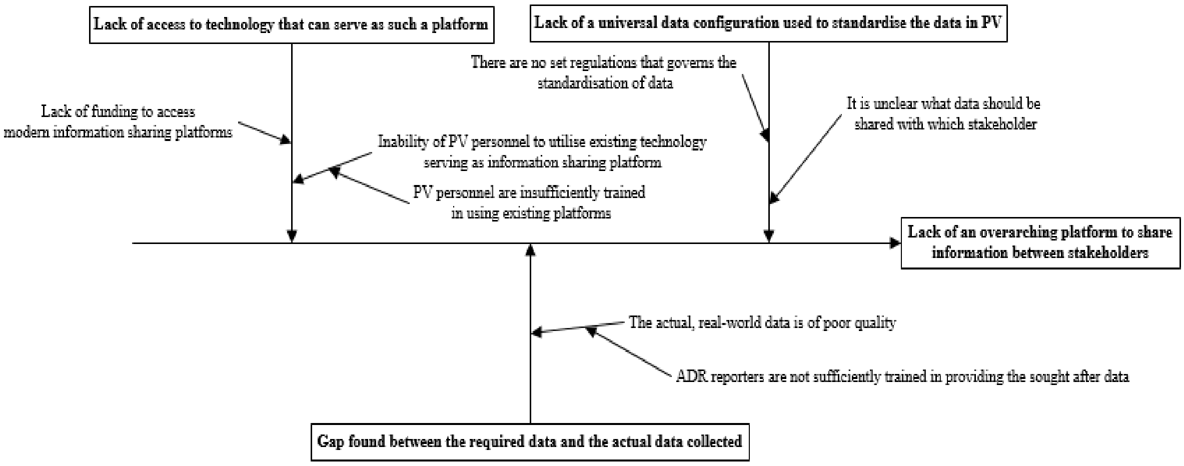
5. Inadequate access to data management systems that can synthesise and analyse existing electronic health records.



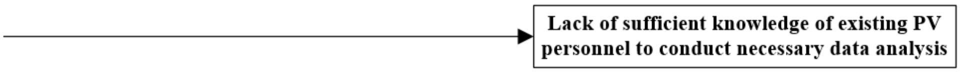
6. Failure to utilise existing resources to conduct data collection, collation, and analysis.



7. Lack of overarching platforms for information sharing between stakeholders.



8. Lack of sufficient knowledge of existing PV personnel to conduct necessary data analysis



Appendix D: Chapter 5 supporting content

This appendix provides the supporting content of Chapter 5. In this appendix, one section is provided, namely:

- Section D.1: Focus group session details – This section contains the information regarding the focus group referenced in Section 5.5.1. The document that was issued to the participants of the focus group session is shown, containing the relevant details discussed during the session.

Section D.1: Focus group session details

Connecting technology to the pharmacovigilance challenge landscape – Focus group: Discussion and feedback (23 February 2018)

Background

This document constitutes research in the field of pharmacovigilance (PV). The purpose of the research is to determine where technology can be implemented in PV to address some of the challenges faced in the system. Taking no specific context into consideration, the research is conducted from a general lens. In other words, the research does not state that the Nokia 3310 should be used to improve communication in the PV system that focusses on the malaria vaccine programme in Kenya, Nairobi. Instead, it is stated that mobile technology should be used to address the shortcomings in communication in the PV system. The more specified version where specific models of technologies are proposed will constitute an add-on project.

At this stage in time, the PV challenge landscape, with the use of a systematic review, has been identified. It was found that the challenge landscape is incredibly vast, meaning there are numerous challenges with different degrees of impact on PV. Consequently, is was decided that the PV challenge landscape should be refined with the use of prioritisation. It was argued that this will reduce the research scope, and ensure that the challenges with the largest footprint in PV be addressed.

Subsequently, the prioritised challenges are: culture, transparency, partnerships, insufficient resources, country-specific factors, technical capacity, and adverse drug reaction (ADR) under-reporting. A brief description of each is provided at the end of this document.

Looking at the description of each of these challenges, it is clear that they are described on a high, strategic level. In other words, these challenges do not make specific reference to tangible problems that provide some clarification as to the true effect these challenges have on a PV system. Therefore, in order to clarify the true meaning and effect of the prioritised PV challenge landscape, a translation process was used.

This translation process consisted of two stages. The first stage served as an interim stage, where the PV challenge landscape was disseminated into the PV system i.e. the meaning and effect of each challenge during each stage of a PV system were described. Using this stage as foundation, the second stage of the translation process made use of a 5Why analysis to identify possible root causes to these PV challenges. The results of both translation stages are shown in the end of this document.

Purpose of the focus group

As stated in the beginning of this document, this research is looking at the technology landscape, and determines which technologies can be used to address the PV challenge landscape i.e. the root causes identified by the translation process. In order to identify these technologies, two sources are used, namely: grey literature and a focus group. These two sources ensures that the process used to identify candidate technologies is credible.

Therefore, the purpose of this focus group is to identify candidate technologies that can be used to address some of the root causes of the PV challenge landscape, as well as describe possible, real-world implementations of these candidate technologies into the PV system. The suggested technologies should not make reference to specific models, but rather high-level categorisations of the technologies. For example: this research will focus on the use of smartphone technologies, rather than the IPhone X.

Agenda of focus group

The agenda of the focus group is as follows:

1. Welcoming
2. Discussion of the background of the research

3. Discussion of the translation process described in the provided document
4. Identification of candidate technologies and possible implementations

Example of focus group output

This is an example of the sought after output of this focus group. The two columns in **Bold** portray the intended output.

Technology	PV challenge	Stage 1 challenge	Root cause	Real-world implementation
Online teaching services	Insufficient resources	Inadequate access to data management systems that can synthesise and analyse existing electronic health records	Lack of training provided those who report ADRs.	**Online teaching services can be used to provide several ADR reporters (practitioners, nurses, patients etc.) with the necessary know-how of how and where an adverse drug reaction should be reported.**

Culture

PV is based on the culture of safety, where PV professionals provide the foundation upon which the principles of this culture is built (Olsen & Whalen 2009). Literature, however, argues that there is a need to improve the culture in modern PV systems (Edwards *et al.* 2015). It is believed that the improvement of PV culture will give lead to the improvement of the other challenges in PV. It is often discussed that the improvement of PV culture requires participation across all disciplines in order to become a reality.

The culture of PV is closely related to ADR under-reporting (Rodrigues & Khan 2011). To achieve this culture the challenges presented by these models should be investigated. This is also the opinion of Rodrigues & Khan (2011), who refer to the need to develop a safety culture, associated with the reporting of ADRs, amongst surgeons and surgical wards. The establishment of a culture of safety amongst healthcare professionals across the globe is time-sensitive (Edwards *et al.* 2015), emphasising the need for the timely establishment of such a culture.

Transparency

In close association with the culture found in PV, the lack of transparency amongst the stakeholders in PV may lead to failed PV initiatives (Rubel *et al.* 2017). It is essential that key stakeholders, especially those with the relevant experience in PV, share relevant information with their peers. This will enable participants in PV to learn of new ways in solving the problems they might be experiencing. Increasing the visibility of information in PV is critical (Rubel *et al.* 2017), as it will support an improved drug safety culture.

It is also essential that the existence of PV systems in countries be publically unveiled. It is described in literature that HCWs in many countries do not contribute to PV, simply because they are not aware of the existing PV infrastructure in their location.

Partnerships

PV is a collaborative endeavour (Pan 2014). Sustained collaboration and commitment are vital to attend to future challenges of PV (World Health Organization (2002); and World Health Organization (2004)). However, ineffective partnership is a threat to PV (World Health Organization 2004). Operating in a resource constrained environment, partners in PV must sometimes provide expertise, training, political support, scientific infrastructure, and a capacity to accomplish comprehensive monitoring and investigations of the safety of medicines (Pan 2014). Failure in providing such resources, ineffective partnerships can lead to failed PV initiatives. In order to maintain a certain inventory of these resources, it is vital that PV organisations form lasting relationships with its partners. Management for Science (2012) emphasises the importance of relationships between partners and how failed relationships often lead to failures.

Insufficient resources

It is well-known that PV operate within a resource constrained environment (Isah *et al.* 2012). Especially in developing countries where other challenges such as drought and war are of high priority, PV organisations struggle to implement new PV systems (Isah *et al.* 2012). In these countries the available resources are rather invested elsewhere, leaving little for the requirements of PV.

The resources required by PV systems are unique in specific countries e.g. a country might have the necessary expertise and manpower to assist a PV system but lack the governmental funding, whereas another country might have the necessary budget but lack the required manpower (Pan 2014). Countries experiencing this phenomena include Sub-Saharan African countries (Isah *et al.* 2012), India (Rama *et al.* 2011), and certain South-East Asian countries (Suwankesawong *et al.* 2016). Common resources required by PV systems include monetary assistance, hardware and software infrastructure, expertise and training curricula amongst healthcare professionals, and common PV knowledge amongst both healthcare professionals and consumers (Isah *et al.* (2012); and Pan (2014)). PV systems are dependent on the combination of these resources and are not able to function properly without it (Isah *et al.* 2012). Heinrich (2015) make reference to effective resource management, a crucial element to the successful operation of a PV system.

Country-specific factors

Country-specific factors refer to challenges faced by PV organisations outside the traditional resource architecture and are described by Edwards (2017) and Härmark & Van Grootheest (2008). Closely related to the effect of the public on PV, the social factors of an area must be considered which includes the culture, religion, age groups, and sex groups of a specific region. It is often a burden to clearly identify these factors, since it requires manpower and funding that are not always available.

Situational factors which refer to border regulations, policies for implementation, governmental budget constraints, conflict in countries, and environmental issues such as severe drought must also be considered. Often governments refuse to authorise and support the implementation of new PV systems since its priorities are elsewhere (World Health Organization 2002), delaying the implementation of PV systems. Similar to the social factors, the required resources needed to identify these factors are not always available, proving to contribute to the failed deployment of PV initiatives.

Technical capacity

Technical capacity refers to the ability of individuals and teams working in PV to conduct their work efficiently and effectively. Very closely associated with the country-specific factors, Mehta (2017) is of the opinion that it deserves to be independently categorised. The challenge faced here, especially in developing countries where there are limited resource capacities, is that the individuals or teams working within the PV systems often lack the necessary skills and experience to conduct their work effectively and efficiently.

Over the years, PV has grown to be a large and complex system. The nature of PV has changed from a single oriented discipline to a cross-functional discipline. Individuals and teams from different background than that of healthcare (e.g. statisticians, programmers, and engineers) are more often being consulted and involved in PV, since they offer additional perspectives that may be of benefit to PV (Mehta 2017).

Under-reporting of ADRs

Under-reporting of ADRs occur when healthcare workers (HCWs) (general practitioners, nurses, surgeons, pharmacists etc.) fail to efficiently report new and existing ADRs (Herdeiro *et al.* 2006). In the interest of consumers and patients who experience ADRs, it is crucial that all ADRs be reported to the relevant authorities. This will give way to signal detection, leading to investigations into the specific ADR. Without ADR reports that generate signals of a problematic ADR, investigations that aim to address these problems cannot take place.

PV challenge	Result from stage 1	Results from stage 2: Possible root causes
Insufficient resources	Inadequate access to ADR reporting forms (spontaneous)	There is a lack of funding to access software technologies that can assist the coordination of the deliveries of spontaneous ADR reporting forms. There is no existing software technology that can assist the coordination of the deliveries of spontaneous ADR reporting forms. The individuals responsible for coordinating the deliveries of spontaneous ADR reporting forms are not sufficiently trained to execute the necessary tasks. There is no designated transportation service to distribute the ADR reporting forms. The person in charge of re-ordering the ADR reporting forms is not sufficiently trained in stock control. The person in charge of re-ordering the ADR reporting forms is situated in a remote location, and as a consequence, users of the forms struggle to make contact with this person. The users of the forms have competing priorities, and simply do not have time to notify the person in charge of re-ordering the ADR reporting forms.
Country-specific factors	Failure to develop locally relevant and easily measurable indicators of performance of PV systems	Key stakeholders are not aware of the health impact of PV. There are only globally defined performance indicators that may not include features of a unique, local PV system.
ADR under-reporting	The lack of robust local data that limits the extent to which decision-making can be done	PV is not sufficiently advocated to the necessary stakeholders. PV is not included in the undergraduate syllabus of healthcare tertiary education. The ADR reporting forms are overly complicated and are time-consuming. Key stakeholders are not aware of the health impact of PV.
Transparency	Inadequate feedback (newsletters, emails etc.) given to ADR reporters and other stakeholders	There is no translation services that can prepare these reports for the specific context. Feedback is not deemed as a priority. The importance of feedback is not advocated sufficiently.
Insufficient resources	Inadequate access to data management	There is a lack of ownership of managing this process. Lack of access to technology to simplify this process. Lack of training provided those who report ADRs.

	systems that can synthesise and analyse existing electronic health records	Difficulties in providing such training to all individuals in remote locations in a timely fashion.
Insufficient resources	Failure to utilise existing resources to conduct data collection, collation, and analysis	There is no resource management system in place to manage the resource inventories. There is a lack of ownership taken to manage these resources. No training is provided to educate PV personnel on how to use these resources.
Transparency	Lack of overarching platforms for information sharing between stakeholders	Lack of funding to access modern information sharing platforms. PV personnel are insufficiently trained in using existing platforms. There are no set regulations that governs the standardisation of data. It is unclear what data should be shared with which stakeholder. ADR reporters are not sufficiently trained in providing the sought after data.
Technical capacity	Lack of sufficient knowledge of existing PV personnel to conduct necessary data analysis	Lack of sufficient knowledge of existing PV personnel to conduct necessary data analysis.

Appendix E: Chapter 6 supporting content

This appendix provides the supporting content of Chapter 6. In this appendix, two sections are provided, namely:

- Section E.1: IAMOT2019 annual conference article – This section contains the article that was produced from a large portion of the content in Chapter 6. At the time of this thesis hand-in date, this article is still in the process of being submitted to the IAMOT2019 conference.
- Section E.2: Formal, structured validation document – This section contains the document that was sent to the various SMEs during the formal, structured validation process described in Section 6.9. In this document, some background to the validation request is provided, containing relevant information that the SMEs required to be able to provide the necessary feedback. The document also contains a summarised version of the research area where validation was required.

Section E.1: IAMOT2019 annual conference article

An investigation into the prospects of the technology landscape to address challenges faced in pharmacovigilance systems

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ABSTRACT

It is regularly reported that in many healthcare related activities in resource-limited settings are experiencing several challenges. Included in this range of struggling activities is pharmacovigilance (PV). In PV systems, a consortium of challenges are experienced, especially from a systems perspective i.e. challenges faced by the daily operations of PV systems. When consulting literature, it is clear that PV systems in resource-limited settings are struggling to operate both efficiently and effectively, while maintaining high standards of drug safety associated with a wide range of activities included in its scope. There is a wide range of research that investigates several solutions that can be implemented to assist and improve PV systems in resource-limited settings. Included in this research is a growing interest in the role of technology in PV. Provided that there has been profound developments experienced in the technology landscape, many of which have been developed with resource-limited settings in mind, there is a growing degree of interest in the role these technological developments can have in PV.

Consequently, the prospects of the technology landscape are investigated in this paper, and it is argued how several of these technologies can be leveraged towards the benefit of PV systems in resource-limited settings. Firstly, several root causes associated with the challenges experienced within PV systems are identified and described. This is followed by an investigation into the technology landscape where a consortium of technologies are identified which have the potential to be implemented within PV. Lastly, and in conclusion, the previously identified root causes of the PV challenge landscape are linked to the aforementioned technology landscape, where it is discussed how these technologies can possibly be leveraged towards addressing these challenges, and contribute towards the improvement of PV systems in resource-limited settings.

Key words: pharmacovigilance; technology landscape; resource-limited settings

INTRODUCTION: BACKGROUND

Pharmacovigilance (PV) was introduced in the late 1960s, following the well-known Thalidomide tragedy which severely affected thousands of new-born infants across the world (Toklu & Uysal (2008) and Isah et al. (2012)). According to the World Health Organisation, PV can be defined as the "science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems" (World Health Organization 2002). Essentially, PV was developed with the purpose of ensuring universal drug safety, ultimately contributing to a healthier population.

In recent years, the development and increase of pharmaceutical products, as well as the several delivery mechanisms of these products, PV systems have started to experience and increasing number of challenges (Pan 2014), both from a systems – and clinical perspective (Strengthening Pharmaceutical Systems 2009). The latter has been the recipient of many investigations and research, and has experienced considerate improvements. However, when shifting focus towards the challenges faced from a systems perspective, Lamprecht et al. (2017) found that there are still many challenges burdening PV systems from operating both effectively and efficiently, which include minimal investment from PV stakeholders in supporting PV culture, the lack of transparency amongst several role players, and the lack of technical capacity. Especially in resource-limited settings, PV systems are burdened by these types of challenges (Pan 2014), and are in need of an innovative solution that can address these challenges in not only the short – to medium-term, but also sustainable solutions that will address these challenges in the long-term.

Consulting literature, Lamprecht et al. (2017) that there are and have been research that addresses some of these challenges, however, failed to find research that approaches these challenges from (i) a technology perspective and (ii) a general perspective (not developed with a specific context or setting in mind). With this in mind, this research paper addresses the challenges found in PV systems on a general scale through a technology lens.

TECHNOLOGY IN PHARMACOVIGILANCE

It is well known that the technology landscape is exceedingly broad, with a range of technologies being invented, developed, and improved for many industries. PV systems in several countries have reaped the benefits offered by these technologies, and have managed to leverage these technologies to address the challenges it faces on a daily basis. For instance, a mobile application that can be used for adverse drug reaction (ADR) reporting, which was developed by the Web-RADR consortium, have contributed significantly towards the increase and simplification of ADR reporting in several European countries (De Vries et al. 2016). However, as the researchers if this paper argue, the PV systems in countries such as the United Kingdom and the United States of America, are much better equipped for the large-scale adoption of technologies to address the challenges it faces when compared to PV systems that operate in resource-limited countries, such as many sub-Saharan African countries.

Considering the previously mentioned Web-RADR mobile application used for ADR reporting; this technology was only recently piloted in a sub-Saharan African country (Uppsala Monitoring Centre 2017). Also, as pointed out by Mehta (2017), South Africa has also only recently introduced a mobile application based ADR reporting system. It is evident that in resource-limited settings, it can be argued that it significantly more challenging to implement and adopt a technology in PV systems compared to that of more developed countries, since there is not a readily-available, broad range of resources.

Provided that there is an opportunity for research to be conducted in investigating the effect technology can have on PV systems, the primary aim of this paper is the following: Identify different technologies that can be used to address challenges faced in PV systems, especially those within resource-limited settings. Subsequently, the PV challenge landscape is identified, as well as several root causes of these challenges.

THE ROOT CAUSES OF THE PHARMACOVIGILANCE CHALLENGE LANDSCAPE

In order to identify the PV challenge landscape, the research conducted by Lamprecht et al. (2018) is used. Lamprecht et al. (2018) conducted a literature review in order to identify, in general, the PV challenge landscape. Realising that it would be more beneficial towards PV systems, Lamprecht et al. (2018) prioritised the PV challenge landscape, ending up with the following challenges which were regarded as priority in PV: culture, transparency, partnerships, insufficient resources, country-specific factors, ADR-under reporting, and technical capacity. Additionally, in order to identify the root causes of these challenges, Lamprecht et al. (2018) implemented an innovative translation strategy, and managed to identify numerous root causes.

In order to focus primarily on the root causes that would have a significant effect on PV, the root causes identified by Lamprecht et al. (2018) were prioritised. Firstly, two subject matter experts (SMEs) were consulted in order to prioritise the root causes identified by Lamprecht et al. (2018), based on their personal experience and knowledge. Secondly, an exclusion criterion was also used to further filter root causes, which is: if the root cause cannot be addressed with the implementation of a technology, but rather with other interventions such as additional funding or business process restructuring, it was excluded from the research.

Consequently, 13 root causes were identified as priority, and therefore forms the primary focus of this research paper. These 13 root causes are identified and described within the clinical domain of PV in Table 1. Subsequently, the technology landscape is investigated in order to identify several potential technologies that can be leveraged towards the benefit of PV systems by addressing the root causes in Table 1.

THE TECHNOLOGY LANDSCAPE

In order to identify technologies that can be used to address the root causes of the prioritised PV challenge landscape, two sources were used, namely: grey literature, and a focus group. The search terms used to identify technologies in grey literature were: “Technologies used to address …” and “Emerging technologies used to address …” The prioritised challenges in PV, as identified by Lamprecht et al. (2018), namely: culture, transparency, partnerships, insufficient resources, country-specific factors, ADR-under reporting, and technical capacity were used in the place of the ellipses in each search term.

To ensure additional credibility, a focus group was held to further populate the technology landscape investigated in this research. The participants of the focus group originate from an Industrial Engineering background, and therefore have an understanding of the role technologies play in the modern world. Subsequently, the technologies identified with the use of the previously mentioned sources (grey literature and the focus group) are described, along with some benefits and drawbacks.

Resource management systems

Resource management systems (RMSs) are used for the planning and control of resources (Spacey 2015). These systems manage several different types of resources, including human resources, natural resources, financial resources, tangible and intangible infrastructures, and information technologies. According to Smith (2014) it is vital to have a balance between these different resources, because any system relies on a combination of many interacting resources. RMSs are able to provide a global view on the available resources (Smith 2014), and facilitate the management of these resources to ensure both efficiency and effectiveness. Some of the more widely used RMSs are known as SAP (Systems Applications and Products) models, developed by the SAP Company. These management systems provide organisations with the ability to improve their resource management efforts, and allows them to predict their resource requirements in future business.

Regardless of the many benefits mentioned earlier, there are some drawbacks to RMSs as well. These include high initial acquisition and installation costs of the system (software) itself, resistance of employees in integrating such a system into their everyday routine, and the need for training employees in operating these systems.

Table 1: The prioritised root causes of the PV challenge landscape.

Root cause		Clinical domain
1	**The users of the forms have competing priorities, and do not have time to notify the person in charge of re-ordering the ADR reporting forms when stock is depleted.**	Due to severe workloads, especially in sub-Saharan African countries where the healthcare system is under-resourced, healthcare practitioners forget or for other reasons fail to request that the stock of ADR reporting forms be replenished. As a result, stock-outs of ADR reporting forms within healthcare facilities are frequently experienced. This leads to frustration on the part of the healthcare workers that are responsible for reporting ADRs and ultimately results in ADRs not being reported. It is possible that, in some cases, the person in charge of managing the ADR reporting form stock is not situated in the same healthcare facility in which healthcare practitioners reside, meaning calls must be placed to request that depleted form stocks be replenished.
2	**The individuals responsible for coordinating the deliveries of spontaneous ADR reporting forms are not sufficiently trained to execute these tasks.**	It has been validated that in some cases, the lack of technical expertise with regards to ADR reporting form delivery management is an issue. As a result, healthcare facilities that need the reporting forms are not receiving sufficient stock. Consequently, a snowballing effect takes place where ADR reporting form stock is not replenished in time, which leads to ADR under-reporting, putting further pressure on the overall healthcare system since patients experiencing ADRs re-enter the healthcare system. Therefore, there is a need to address the lack of technical expertise with regards to the management of the delivery of ADR reporting forms.
3	**Key stakeholders are not aware of the health impact of PV on the healthcare system.**	Key stakeholders are not aware of the impact of PV not only on PV itself, but also the impact it has on the entire healthcare system—when a PV system is not functioning properly, the healthcare system will experience increasing pressure. The key stakeholders among which PV awareness should be increased are patients, healthcare practitioners, nurses, and pharmacists. These stakeholders represent a group that are most exposed to ADR reporting. The obstacle that surfaces during the creation of awareness amongst these stakeholders is that existing awareness programmes struggle to reach a wide audience, especially audiences in remote locations.
4	**PV is not included in the undergraduate syllabus of tertiary healthcare education.**	In some undergraduate healthcare syllabuses, PV is not deemed a priority, and therefore does not receive the necessary attention. According to Mehta (2017), it is not a simple process to change existing syllabuses to focus more attention towards PV. As a result of the lack of PV education, increasing pressure is faced in the PV system where PV related activities, especially ADR reporting, are not executed properly. Healthcare practitioners frequently do not know how or where to report ADRs, and when they do, the quality of the data they provide is poor. As many of the graduates of these programmes are currently employed in the healthcare system, the definition of this root cause within the clinical domain should be expanded to also include a lack of PV education amongst current healthcare system workers. A lack of training on ADR reporting is defined as a separate root cause in this table, the scope of training referred to here, however, extends beyond the scope of ADR reporting only to encompass an understanding of the PV system as a whole and ties in with the previous root cause to also include an understanding of the role of PV within the broader healthcare system. Similarly to the previous root cause, the obstacle that

		one would expect to surface when attempting to provide PV education to the current healthcare workforce include reaching a wide audience, including audiences in strategic locations throughout a country.
5	**The ADR reporting forms are overly complicated and are time-consuming.**	As reported in a study by Khan (2013), in many countries patients and healthcare workers are deterred from reporting ADRs due to overly complicated ADR reporting forms, as well as the great effort required to complete each of the fields in these forms. This is a phenomenon that is especially experienced in areas where spontaneous ADR reporting forms are used. Healthcare workers do not want to fill in these long documents, and would rather divert their attention and time to attending to patients, especially when they are remunerated on a patient-basis[10]. This issue is closely related to the lack of technical capacity discussed in the third and fifth root cause discussed in this table. Each of these three root causes ties back to the lack of technical capacity.
6	**The importance of feedback is not sufficiently advocated.**	The feedback referred to here is the feedback given to ADR reporters. These reporters include both patients and healthcare workers. In some countries, feedback is not regarded as a priority, which is a mind-set that should be changed. Some of the PV systems have some form of feedback system in place, however, these systems are severely limited in capabilities. The only form of feedback is in the form of a once-off, automated response once an ADR report is submitted. Thereafter, no form of feedback is provided. It is argued in this research that feedback should be regarded as a priority. As shown in a study by Al Dweik et al. (2016), the lack of feedback is a barrier to ADR reporting in several countries.
7	**There is a lack of ownership of managing the process of data management.**	The data management systems referred to here are the systems within local healthcare facilities. Since many of the staff in these facilities already have an overloaded schedule (similar to the second and sixth root causes discussed in this table), there may be a lack of ownership of managing the PV system, or in this case, the PV data management system (e.g. ensuring ADRs are reported, all the reports are collected, and the forms are captured on a computer). As a result, the PV systems in these facilities are of poor quality. It is therefore necessary to improve these PV systems, or rather PV data management systems.
8	**There is a lack of training provided to those who report ADRs.**	ADR under-reporting, as described numerous times in this research, is one of the major challenges in PV. Since ADR reporting is the front-end of PV, it is critical that all possible ADRs are reported. It is often reported in there is a lack of training provided to the public, patients, and healthcare workers on ADR reporting.
9	**There are difficulties in providing the necessary training to individuals in remote locations in a timely manner.**	This issue is closely related to the previously discussed root cause. Existing training initiatives struggle to provide the necessary ADR reporting (and broader PV related activities) training to the public, patients, and healthcare workers in remote locations. It is severely important that individuals in these remote locations be aware of ADR reporting, since they might be the ones who, unknowingly, are experiencing ADRs.

[10] This phenomenon is usually experienced in healthcare facilities where the healthcare worker to patient ratio is low i.e. there are only a small number of healthcare workers compared to the large number of patients. In these facilities, remuneration for healthcare workers is usually based on a patient-basis, meaning the healthcare workers (mostly doctors and specialists) are payed according to the number of patients they attend to. This is very closely related to the second root cause discussed in this table, which also relates to the competing priorities of healthcare workers.

10	**There is a lack of ownership to manage existing PV-related resources.**	The resources referred to here are those intended for PV activities in local healthcare facilities, such as ADR reporting forms, computers, smartphones, tablets, and human resources. Resources form the cornerstone of any system, and should be efficiently managed. Since in many cases existing healthcare staff already have an overloaded schedule, there may be no one who is willing to take ownership of managing PV resources, and in turn, manage the PV system. It is therefore essential to intervene in these cases, by ensuring PV does not interfere with the schedules of the staff, but also ensuring that PV is regarded as a priority and receives the necessary attention. This issue is closely related to the second and sixth root cause discussed in this table, which also relates to the overloaded schedules of healthcare workers, especially in resource-limited settings.
11	**Lack of training to educate PV personnel on how the available resources should be used.**	Closely affiliated with the lack of ADR reporting training previously discussed, the lack of training provided to healthcare staff in local facilities on how PV resources should be used is proving to burden the PV system in those facilities. It is essential that staff be trained on how to manage PV resources, such as ensuring the availability of ADR reporting forms, filling in ADR reporting forms, and capturing the data on a computer. This training should not only be provided to healthcare facilities in major cities or towns, but also to facilities in remote locations.
12	**There is no resource management system in place to manage existing resource inventories.**	This is closely related to the two previously discussed issues that refer to the management of PV resources. It is incredibly challenging to manage these resources without some sort of system that is able to track and monitor inventories. It is not unexpected that, in healthcare facilities where PV is not regarded as a priority, there are no initiatives taken to implement such a resource management system.
13	**PV personnel are not sufficiently trained in using existing platforms.**	The platforms referred to here are those used between healthcare workers to share information with their peers, which can be in the form of emails, online chatrooms, blogs, or cloud technologies (e.g. *Google Drive*). These technologies are available, however, are still unfamiliar to some of the staff. There is a need for some sort of training to be provided to these individuals in order to ensure that each member of a healthcare facility know how information can be shared with the relevant parties.

Cloud technology

Cloud technology refers to the online space that can be used to store and share data (Harris 2017). Examples of cloud technologies include Dropbox, Google Drive, Amazon Drive, and Apple iCloud. These platforms can be used for two purposes; data storage, and data sharing (Harris 2017). This eliminates the need to store and share data on external data storage devices such as external hard-drives or flash drives that can easily be corrupted, stolen, damaged, or lost.

Many cloud technology platforms are open source software (i.e. are freely available to the public). These platforms are simple to use, and can be accessed by anyone in any location, provided that they have access to the internet, both simplifying and speeding up the sharing of information with relevant parties (Baiju 2017). There are also some drawbacks to cloud technology, the first of which is that one can only access a limited storage capacity. When this predefined capacity is exceeded, a fee must be paid to access further storage capacity. Another drawback is that cloud technology can only be accessed with an internet connection (Baiju 2017).

Online teaching services

Online teaching services are popular platforms used to replace the need to physically attend a lecture (Palloff & Pratt 2001). These platforms are delivered through the internet i.e. lectures can be accessed online. There are many forms of online teaching services, such as online classes (courses that are delivered on the Internet), or hybrid courses (a combination of traditional, face-to-face classes and online courses) (Tallent-Runnels et al. 2006). In some cases, online teaching services are regarded as a form of cloud technology, however, in this research, these services are classified outside the jurisdiction of cloud technology.

Online teaching services offer several benefits, the first of which is the fact that individuals in remote locations can access the necessary materials at their own discretion. The costs associated with online teaching is also less than that of a traditional, face-to-face lectures. There is no need for a classroom, lecturer, or transportation to and from a venue (Armstrong 2013). Online teaching also enables users to learn at their own pace, without a constant pressure to learn a large portion of work in a short time period (Norman 2016). There are also some drawbacks to online teaching services. These platforms cannot accommodate human interaction, which is in many cases a critical element of teaching. Also, these platforms can only be accessed with internet connectivity (Armstrong 2013).

Remote internet accessibility

Remote internet accessibility is defined as "the ability to access a network from a remote distance" (Rouse 2005). The context of this definition, however, only refers to one part of the intended meaning of remote internet accessibility. The intended meaning refers in large part to accessing internet in severe remote locations where there is not necessarily sufficient electricity and network infrastructures. Since many PV systems' scope include activities in these locations, it is necessary for the inhabitants of these locations to have access to some sort of network in order to share and access relevant information.

Remote internet accessibility technologies offer several benefits, which include providing access to important information, increasing economic growth of local businesses and entrepreneurs, and reducing the incidence of diseases through improved information sharing between patients and healthcare practitioners (Booth (2003) and Deloitte (2014)). There are also some drawbacks to these technologies, which include high initial acquisition costs, maintenance costs, and providing training for operating certain devices.

Mobile technology

Mobile technology refers to technologies that are used for cellular communication and other related aspects (Macwan 2017). Gaining increasing popularity and injection into new markets (Kendrick 2013), mobile technologies have been one of the most successful technological developments (Macwan

2017). There are many different technologies that are categorised under mobile technology, such as cellular phones, smartphones, portable computers, tablets, PDAs (personal digital assistant) and GPS devices. Many of these technologies are used in combination, and interact to connect people in different locations and allow them to share many different types of information.

There are several benefits offered by mobile technologies. By definition, these technologies are mobile, and can be used in nearly any location. In the healthcare industry, sharing of information enabled by mobile technology has allowed for distant healthcare monitoring. Also, these technologies are able to transmit information much quicker, and enable individuals in remote locations to stay in contact with other communities (Kendrick 2013). One should also consider the drawbacks of mobile technologies. There are both acquisition and maintenance costs that should be considered. Integration of mobile technologies into an existing infrastructure might also pose a problem, since compatibility of devices may be a challenge. Another drawback is that the tangible devices might either get stolen, damaged, or lost, and must therefore be closely monitored (Kendrick 2013).

User videos

User videos are particularly used for the purpose of training and education. Videos are created by individuals or teams who are knowledgeable about a certain topic, and shared with others to train or educate them in the specific field, or guide them through a certain process. These videos are often used in education departments to train and educate both teachers and students in remote locations where it is difficult to gain physical access (Lamprecht 2017). There are also some drawbacks to these types of videos. The videos cannot be accessed without the necessary hardware, such as computers or tablet devices. The planning and creation of these videos must also be done meticulously, because missing or wrong information may cause complications.

Mobile applications

Mobile applications, better known as mobile apps, are software programmes designed for mobile devices to enable a wide array of functionalities. Mobile apps are used for a number of purposes, which include navigation, entertainment, sport, fitness, and productivity (Viswanathan 2017). These apps can be accessed on many different platforms, such as Google Play or Apple App Store. The use of mobile apps have grown exponentially over the last decade, with an estimated 197 billion apps forecasted to be downloaded in 2017 (Viswanathan 2017).

Mobile apps are relatively easily maintained (depending on the degree of complexity of the functionalities enabled by the app), easily modifiable for different requirements and platforms, and relatively simple to develop for nearly any function. There are, however, also some drawbacks to consider. These include a limited scope of functions that can be executed, and the need for a smartphone or tablet device to access these apps (Singh 2017).

Educational television and radio programmes

Educational television programmes refer to programmes that incorporate different elements of education. These programmes are aired across a television network, with a wide target market. Many shows are aimed at children within a low age range (1-5 years), whereas other programmes are aimed at adults (Western Governers University 2017). The latter may incorporate different social elements and provide essential educational aspects, such as safe sex practices and anti-drug initiatives.

There are several benefits associated with these educational television programmes. These programmes allow for a large audience to be reached, even in remote locations. It also eliminates the need for a physical presence of educators or trainers. One potential drawback is that the intended message of these types of programmes can be misinterpreted, which might lead to unintended behaviours. According to Ostrov et al. (2013), another potential drawback is that some of these programmes can lead to aggravated behaviours and attitudes, especially amongst the younger population.

Radio programmes, similar to educational television programmes, are educational programmes intended to convey a certain message of a particular subject to a certain target audience. However, instead of using the television, educational radio programmes are delivered across radio broadcasts. The benefits and drawbacks of these types of educational programmes are similar to educational television programmes. However, there is one additional drawback to consider, namely that radio programmes allow only for audible communication, which limits the amount of information that can be shared.

Wireless Application Protocol based messaging

Wireless Application Protocol (WAP) is a "specification for a set of communication protocols to standardise the way that wireless devices, such as cellular telephones…can be used for Internet access, including e-mail, the World Wide Web, newsgroups, and instant messaging" (Rouse 2010). In particular, WAP based messaging refers to messaging platforms that are based on WAP technology, such as Mxit, and Blackberry messenger. For the purpose of this research, the well-known application, WhatsApp, is not included in these messenger platforms, since it can only be accessed with more advanced smartphones, compared to the other platforms. WAP based messaging does not require advanced smartphones, but rather less expensive mobile technologies. It also allows for information to be shared in real-time. On the other hand, WAP based messaging can only be used within an area where there is access to a mobile network, which may be an obstacle to use in some areas.

Routine assessments

Routine assessments can be done in many different ways, such as examinations, interviews, projects, or surveys. These assessments are used to assess the knowledge and experience of employees, and determines whether a specified threshold is met (Lamprecht 2017). These assessments are used in many disciplines, such as healthcare and education. Often, it is seen as a type of incentive scheme, since some form of incentive (e.g. funding or promotions) is given to those who excel in these assessments.

Routine assessments allow for a routine check-up on the level of expertise, which enables those in management positions to intervene where necessary. These types of assessments also eliminate the need for the physical presence of a SME, since the assessments are mostly done on computers. There are also some drawbacks to these assessments. It is possible for those being assessed to cheat i.e. get information from colleagues. Also, in some areas where there is not access to computers and internet networks, these assessments cannot be used (Lamprecht 2017).

Game-based learning

Game-based learning is a method of incorporating educational content or learning principles into videos games (Coffey 2007). In essence, game-based learning is the use of educational games to teach the user certain aspects of the real world. Many of these games are developed as mobile apps (described in an earlier section), and are widely available.

Game-based learning engages and motivates students with a custom learning experience, and promotes long-term memory. It also contributes to the development of certain computer skills, which is a necessity in modern society. An important criticism is that this type of learning may be more distracting than more traditional teaching methods. Additionally, game-based learning can also be resource intensive, since it requires a computer, tablet, or smartphone to be accessed.

Concluding the technology landscape

It is clear that there are several technologies that can potentially be leveraged towards addressing the prioritised root causes identified in Table 1. Many of these technologies can be used in conjunction with one another in order to maximise the benefits to PV. For example, remote internet accessibility technologies can be used to supplement online teaching services and cloud technologies by providing an internet or intranet network. Thus, there are several different possible solutions to the root causes in Table 1. Subsequently, the potential implementations of the technologies to address the root causes in Table 1 are discussed.

ADRESSING THE ROOT CAUSES OF THE PHARMACOVIGILANCE CHALLENGE LANDSCAPE

It should be made clear that the discussions that follow are non-exhaustive, and in no way is it implied that these potential implementations of the technologies are the only solutions to the root causes of the PV challenge landscape. Subsequently, a guiding overview is provided where it is explained how each of the prioritised root causes in Table 1 can potentially be addressed with the use of the technologies identified in the previous section.

Root cause #1: The users of the form have competing priorities, and simply do not have time to notify the person in charge of re-ordering the ADR reporting forms when stock is depleted

Envisaged technologies: RMS, remote internet accessibility, mobile technologies, mobile applications, and WAP-based messaging.

Firstly, RMSs can be implemented to maintain a record of the movement of ADR reporting forms. If maintained, these systems can keep track of the number of ADR reporting forms used, as well as the left-over stock. Such a system will allow anyone to be aware of the ADR reporting form stock levels, enabling them to reorder new forms in time. In areas where there is not a reliable internet network, remote internet accessibility technologies can be used to provide access to internet, which will allow individuals in different locations to access the same RMS.

The second option is using mobile applications, in combination with mobile technologies. Mobile applications can be used in the same way as RMS, except with the use of mobile technologies. RMSs, as described in the earlier section, are accessed via a computer or tablet, whereas mobile applications can be accessed via smartphones. This allows the user to have constant and immediate access to the ADR reporting form stock levels. Mobile applications can also be accessed by anyone, which is beneficial in the case where the individual in charge of managing the ADR reporting form stock may be situated in a remote location where healthcare facilities may have difficulties to communicate.

Lastly, WAP-based messaging can be used to partially address this issue. Regardless that WAP-based messaging cannot be used as a RMS, it can be used to address the issue of communication. By making use of these communication platforms, healthcare facilities can constantly communicate with their ADR reporting form supplier.

Root cause #2: The individuals responsible for coordinating the deliveries of spontaneous ADR reporting forms are not sufficiently trained to execute these tasks

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, and game-based learning, routine assessments.

Firstly, online teaching services can be used to provide essential training to these individuals. These teaching services replace the need for a physical representation of an expert in a remote location who provides face-to-face training. Rather, training videos can be accessed via the internet, at any time and in any location. This is beneficial since the individuals who need the training can access these videos in their own time, and complete any necessary assessments in the comfort of their own workplace. Remote internet accessibility technologies can be used in support of online teaching services to provide access to internet in areas where it might be lacking. The second option is similar to online teaching services, except that it does not require access to an internet connection. Physical copies of user videos can simply be distributed to different locations and accessed by those who might need the necessary training.

The final option is with the use of game-based learning, where individuals are provided with the necessary training in a gaming format. These types of learning platforms allows the user to learn several real-world processes in a virtual world, and allows them to understand the implications their actions might have on an overall system. In the end, individuals will be equipped with key skills that they can leverage in their daily tasks of ADR reporting form management.

In support of all three of these possible solutions are routine assessments, which allows for periodic evaluation to be done in order to determine whether the individuals who are coordinating the delivery of spontaneous reporting forms have gained the necessary experience in managing ADR reporting forms.

Root cause #3: Key stakeholders are not aware of the health impact of PV on the healthcare system

Envisaged technologies: Online teaching services, remote internet accessibility, routine assessments, user videos, and educational television and radio programmes.

Firstly, online teaching services can be used to provide healthcare workers with the necessary knowledge and awareness of the health impact of PV. If this method is used, it should be made mandatory for healthcare workers to access and review these online learning materials, in order to ensure that they actually do read through the necessary materials. Additionally, in areas where there is a lack of access to internet networks, remote internet accessibility technologies can be used to provide access to such networks. Routine assessments or assignments can be used to ensure that all healthcare workers put in the time and effort to access online teaching services. In order to further motivate these workers, an incentive programme can be implemented whereby healthcare workers receive a certain number of points which will contribute to the yearly, mandatory points they must gather in order to remain registered as professional healthcare workers. The continual professional development (CPD) programme, used in the engineering realm, is an example of such an incentive scheme.

The second option is similar to online teaching services, however, it does not require access to an internet network. Physical copies of user videos are simply distributed to different locations, and viewed by certain parties. Similar to online teaching services, these training videos do not only remove the need for the physical presence of a person knowledgeable within a specific field, but also creates awareness amongst healthcare workers of the impact of ADRs, which motivates them to support PV.

The third option is largely aimed at public awareness. Since many people in several locations have access to either televisions or radios, educational television and radio programmes can be used to promote PV, and create awareness amongst the public. This will not only motivate the public to support and contribute to PV, but will provide them with the necessary knowledge on key aspects such as the source of ADRs, where ADRs should be reported, as well as when to know that an ADR is experienced.

Root cause #4: PV is not included in the undergraduate syllabus of tertiary healthcare education

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, routine assessments, and game-based learning.

As indicated by Mehta (2017), it is a difficult to change a healthcare syllabus, because there are numerous important aspects of healthcare that deserve attention. Ideally, the solution would be to include PV training in the syllabus of healthcare training, however, this can be difficult and time-consuming. Therefore, in order to provide the necessary PV education to healthcare workers who have been minimally exposed to PV in their undergraduate training, some focus should be shifted towards providing this training in their workplace. In this instance, online teaching services can be used. These services, as described in earlier sections, removes the need for healthcare workers to take time away from their overloaded schedules to physically attend training sessions. In areas with poor internet networks, remote internet accessibility technologies can be implemented to create access to such networks.

Similar to online teaching services, the second option provides healthcare workers with the necessary PV knowledge in their workplace, however, does not require access to internet. User videos can be accessed on a computer or smartphone at any time and in any location. This reduces the pressure on healthcare workers, since they can consult these materials at their own discretion. In order to ensure that healthcare workers do put in the time and effort to access either online teaching services or user videos, routine assessments can be used to assess whether the workers have gained the necessary PV knowledge such as ADR reporting. A similar point system as that discussed under the previous root cause, where healthcare workers are obligated to obtain a certain number of points to maintain registered as professional healthcare workers, can also be used.

Lastly, PV knowledge can be conveyed via game-based learning platforms. These platforms will provide its users with the necessary knowledge in a virtual world, such as ADR reporting, which can then be implemented within the real world.

Root cause #5: The ADR reporting forms are overly complicated and are time-consuming

Envisaged technologies: Mobile applications and mobile technologies.

Two possible solutions to this issue are envisaged. As indicated in the study by Khan (2013), the time required of healthcare workers to complete overly complicated ADR reporting forms is a major barrier to ADR reporting. It is therefore important that, in order to motivate healthcare workers to continuously support PV and contribute towards the improvement of ADR reporting, any initiatives should ideally be minimally invasive, and disrupt daily routines of healthcare workers minimally. In this instance, mobile applications, in combination with mobile technology, can be used. ADR reporting forms can be changed into electronic reporting forms, which can be accessed via mobile applications. Such mobile application based ADR reporting forms are already being used, including a recent development, named WEB-RADR, which has been released in Burkina Faso in 2017 (Uppsala Monitoring Centre 2017).

These forms should also be made up of as little as possible data entries, and should only serve as an initial ADR report. In order to reduce complexity during ADR analyses that takes place during a later stage in the PV system, these initial ADR reports should be identical in different countries (i.e. a standardised reporting form). Once a signal has been detected (a number of ADRs have been reported in the same location), a second stage of ADR reporting can commence, where supporting information, related to the already supplied information, is submitted, resulting in a growing ADR report which contains only the relevant information.

Root cause #6: The importance of feedback is not sufficiently advocated

Envisaged technologies: Educational television and radio programmes, mobile applications, and mobile technologies, WAP-based messaging.

Three possible solutions to this issue are envisaged. In order to provide feedback to the public regarding ADR reporting, educational television and radio programmes can be used. Instead of printing and distributing tangible reports, these programmes are able to reach a large audience in many different locations. These types of feedback can be done on a monthly or quarterly basis. It is just important that periodic feedback be provided in order to reassure the public that any ADRs they might have reported are being investigated.

An electronic ADR reporting system can also be investigated, with the use of mobile application, in combination with mobile technologies. Not only may such a system reduce the time and effort required for ADR reporting, but it will also enable feedback to be provided through the application, which can be viewed by the reporter at any time.

Another form of feedback, aimed at both the public and healthcare workers, is in the form of WAP based messaging. These messaging platforms can be used to provide feedback to ADR reporters during strategic stages in the PV system, such as a notification when the ADR report is received, and when it is being investigated, and finally if certain steps are being taken to address the particular ADR. WAP based messaging is specifically aimed at resource-limited healthcare facilities who might not have access to online reports. A simple SMS might reassure healthcare workers that their voices are heard (their ADR report is being investigated), which may motivate them to regularly report ADRs.

Root cause #7: There is a lack of ownership of managing the process of data management

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, RMS, mobile applications, and mobile technologies.

Firstly, two major causes of concern can be concluded from the seeming lack of ownership. It can either be the case that there is a lack of personnel with the necessary skills and appropriate training to maintain the data management system, or it can be that there is significant time constraints, thus individuals with the necessary and appropriate skills are not able to add PV data management to their schedule. Either way, both of these possible causes must be accounted for. Considering the first case, two possible technologies are envisaged to be possibly implemented to address the issue of a lack of training. Firstly, online teaching services can be used to provide an individual or team with the necessary knowledge and skills to maintain PV data management, which in turn will motivate them to take complete ownership of that system. In areas where there is not access to internet (in order to access online teaching services), remote internet accessibility technologies can be used to provide such networks.

Secondly, similar to online teaching services, user videos can be used to provide training with regards to data management. User videos may be more practical online teaching services in certain settings, since they do not require access to internet. However, they are limited with regards to the degree of interaction there is between the host and the viewer.

In order to address the second cause of the lack of ownership, the issue of limited capacities for clinical activities and responsibilities, two technologies are envisaged to be possible implemented. Firstly, RMSs can be implemented. These systems maintains not only records of resources, but it also allows for data management to be done. With a system that automatically does data management, requiring minimal interaction, individuals will less deterred from PV data management, and will feel more obliged and comfortable to take ownership of data management.

Another candidate technology are mobile applications, in combination with mobile technologies. Providing someone with anywhere, anytime access to PV data management systems will simplify their responsibilities and activities since they are not limited with regards to their location from where they are supposed to work, and they will be able to notice any possible warnings or mistakes much quicker.

Root cause #8: There is a lack of training provided to those who report ADRs

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, and game-based learning, and educational television and radio programmes.

Three possible solutions to this issue are envisaged. With specific aim at healthcare workers, online teaching services can be used to provide them with the necessary knowledge and skills of ADR reporting, such as how to know when a patient is experiencing an ADR, which essential data to submit on ADR reports, and where to report ADRs. These services are more user-friendly when it comes to interference with the schedules of healthcare workers since they can view these materials at their own discretion and according to their own schedule. In areas where there is no access to internet networks, remote internet accessibility technologies can be used to provide access to such networks. The second option, similar to online teaching services, are user videos. These videos are minimally invasive on the schedules of healthcare workers, since it can be viewed at any time. Also, user videos does not require access to internet networks, which in some settings is advantageous. Lastly, game-based learning initiatives can be used to provide healthcare workers with the necessary skills on how to report ADRs. These virtual platforms can teach them key aspects of ADR reporting which they can implement in the real-world.

Focussing on the public and the patients who can also report ADRs, educational television and radio programmes can be used to educate the public on PV related activities, such as when to know an ADR is experienced and where ADRs can be reported. Since many people have access to either a television or radio, these educational programmes will be able to reach a large audience in remote locations.

Root cause #9: There are difficulties in providing the necessary training to individuals in remote locations in a timely manner

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, mobile applications, and mobile technologies.

Four possible solutions to this issue are envisaged. This root cause is similar to the one described in the previous section, however, focusses on the barrier of providing training to the public and healthcare workers in remote locations. In this case, online teaching services, in combination with remote internet accessibility technologies, user videos, and game-based learning can be applied in the same manner as the case previously discussed. The fourth technology that is added to this list are mobile applications, in combination with mobile technologies. Given the widespread adoption of mobile technologies (not smartphone technology) in sub-Saharan African countries (Data Team 2017), mobile applications can be used to provide training to those residing in remote locations. By making use of a technology they are already familiar and comfortable with, mobile application based training can be used to supply both the public and healthcare workers with the necessary knowledge regarding ADR reporting.

Root cause #10: There is a lack of ownership to manage existing PV-related resources

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, mobile applications, mobile technologies, game-based learning, and RMS.

Similar to the eighth root cause described, the lack of ownership can be contributed to two possible causes. It can either be that there is a lack of personnel who has the necessary knowledge and skills to manage PV resources, or it is possible that there is simply no one who can add PV resource management to their existing portfolios. As described under the discussion of the eighth root cause, the first cause can be addressed with the implementation of either online teaching services (in combination with remote internet accessibility technologies), user videos, mobile applications (in combination with mobile technologies), or game-based learning. Each of these technologies offer different ways of teaching which can be used to provide essential resource management training.

Another technology that has great potential with regards to adding PV resource management to the schedule of an individual or team, is a RMS. These systems maintains electronic records of all the resources available to PV activities, and also tracks their movements, and therefore requires a minimal degree of intervention. Therefore, if RMSs are well maintained and updated, resource management would be made much simpler, and is therefore minimally invasive to the overloaded schedules of healthcare workers.

Root cause #11: Lack of training to educate PV personnel on how available resources should be used

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, mobile applications, mobile technologies, game-based learning, and routine assessments.

There are several different forms of training that can be provided to individuals in order to provide them with the necessary knowledge on how to fully utilise PV resources such as ADR reporting forms, computers, and smartphones. Online teaching services (in combination with remote internet accessibility technologies), user videos, mobile applications (in combination with mobile technologies), or game-based learning are all technologies that remove the need for face-to-face interaction, by providing training which can be accessed through computers, smartphones, or tablets. All these technologies are minimally invasive i.e. slightly interferes with the daily routine of healthcare workers. Additionally, and in support of these training platforms, routine assessments, which can either be paper– or computer based, can be used to assess whether or not healthcare workers have put in the time and effort to learn from the aforementioned learning technologies.

Root cause #12: There is no resource management system in place to manage existing resource inventories

Envisaged technologies: RMS and remote internet accessibility.

One possible solution to this issue is envisaged, namely RMSs. These systems, if well maintained, simplify the process of PV resource management by monitoring the available resources, as well as keeping track of the movement of resources. These types of systems can also be accessed by anyone in any location, provided that there is access to an internet network, which can be provided by remote internet accessibility technologies. This can be beneficial in several ways. For example, the distribution centre for ADR reporting forms can simply log on to the RMS of a healthcare facility, check their available ADR reporting form stock, and start distributing more forms to the facility if necessary. Another example is where the system keeps track of the available PV resources. For example, the system keeps record of who might be using a smartphone intended for ADR reporting. If something where to happen, such as vandalism or the item is lost, the individual who last used the smartphone can be tracked down.

Root cause #13: PV personnel are not sufficiently trained in using existing platforms

Envisaged technologies: Online teaching services, remote internet accessibility, user videos, mobile applications, mobile technologies, game-based learning, and cloud technologies.

The platforms referred to in this case are information sharing platforms such as emails, chatrooms, or blogs. Each of these platforms allow for different parties to communicate with one another, and share relevant information. In order to provide training to healthcare workers, especially in areas where they are not familiar with these platforms, three different technologies can be used, namely: online teaching services (in combination with remote internet accessibility technologies), user videos, or game-based learning. Each of these technologies, as mentioned in earlier sections, removes the need for face-to-face interaction. It also reduces the degree of interference in the daily routine of healthcare workers, since they can access these training materials at their own discretion. The one technology that can also, to a certain extent, be used to simplify the process of information sharing is cloud technology. These technologies are freely available to the public, and can be used to share large amounts of data, such as ADR reports.

CONCLUDING REMARKS

From the discussions in the previous section, it is clear that there are indeed numerous technologies that can potentially be implemented in PV systems that operate in resource-limited settings. In many instances, there are several technologies that can be either individually, or in supplement of another, implemented to address a specific root cause. For instance, remote internet accessibility technologies can be used to provide internet or intranet networks on which other technologies rely, such as online teaching services and cloud technologies. Additionally, routine assessments can also be used to supplement user videos and online teaching services, by providing a platform where the target audiences can be assessed whether or not they are gaining the necessary skills and knowledge. Consequently, it is clear that there is value in investigating the technology landscape, and determine how it can be leveraged to address the challenges faced in PV systems.

CONCLUSION

In this paper, the potential effects that the technology landscape can have on struggling PV systems are explained. Firstly, several root causes of the PV challenge landscape is identified, representing a set of prioritised root causes that are believed to have a significant effect on the PV challenge landscape. Secondly, the technology landscape is investigated, identifying several technologies that can potentially be leveraged towards the benefit of PV. Lastly, a guiding overview is provided, where it is explained how each of the prioritised root causes can be addressed with the technologies identified in this paper.

Subsequently, it is clear from the discussions in this paper that there are several opportunity areas where the role of technology in PV can be investigated. Many of these technologies offer several benefits that can be leveraged towards the benefit of PV in the short –, medium –, and long-term. Provided with the increasing attention being diverted towards sustainability, there are also additional technologies that have not been mentioned in this paper that can be used to address the challenges in PV in the long-term. Technologies such as block chain, Internet of Things, and big data analytics are all exciting technologies that are creating waves of enthusiasm in the modern world, and have the potential to significantly benefit PV systems in resource-limited settings in the long-term.

It is not a secret that technology has completely changed the modern world, and that nearly all industries have benefitted significantly from its investments in technology. In order to ensure that PV systems, especially those in resource-limited settings, become sustainable systems that are able to maintain and ensure universal drug safety, there should be an increasing amount of investment and research devoted towards adopting new, innovative technologies in PV systems across the globe.

REFERENCES

Armstrong, S., 2013. What Are The Advantages And Disadvantages Of Online Learning? eLearning Industry. Available at: https://elearningindustry.com/advantages-and-disadvantages-of-online-learning [Accessed January 30, 2018].

Baiju, N.T., 2017. 5 advantages and disadvantages of Cloud Storage. Big Data Made sSmple, pp.4–6. Available at: http://bigdata-madesimple.com/5-advantages-and-disadvantages-of-cloud-storage/ [Accessed January 30, 2018].

Berry, S., 2010. How Coca-Cola's distribution system works. ColaLife. Available at: http://www.colalife.org/2010/12/19/how-coca-colas-distribution-system-works/ [Accessed February 26, 2018].

Booth, N., 2003. Can business benefit from remote access? ComputerWeekly.com. Available at: http://www.computerweekly.com/feature/Can-business-benefit-from-remote-access [Accessed January 31, 2018].

Coffey, H., 2007. Digital game-based learning. Learn NC. Available at: http://www.dfpp.univr.it/documenti/Avviso/all/all036209.pdf [Accessed February 26, 2018].

Data Team, 2017. In much of sub-Saharan Africa, mobile phones are more common than access to electricity. The Economist. Available at: https://www.economist.com/graphic-detail/2017/11/08/in-much-of-sub-saharan-africa-mobile-phones-are-more-common-than-access-to-electricity [Accessed July 16, 2018].

Deloitte, 2014. Value of connectivity: Economic and social benefits of expanding internet access, Available at: https://www2.deloitte.com/content/dam/Deloitte/ie/Documents/TechnologyMediaCommunications/2014_uk_tmt_value_of_connectivity_deloitte_ireland.pdf.

Al Dweik, R. et al., 2016. Factors affecting patient reporting of adverse drug reactions: a systematic review. British Journal of Clinical Pharmacology, (November).

Gaille, B., 2016. 16 Pros and Cons of the Internet of Things. BrandonGaille.com. Available at: https://brandongaille.com/16-pros-and-cons-of-the-internet-of-things/ [Accessed January 31, 2018].

Gubbi, J. et al., 2013. Internet of Things (IoT): A Vision, Architectural Elements, and Future Directions. Future Generation Computer Systems, 29(7), pp.1645–1660. Available at: https://arxiv.org/pdf/1207.0203.pdf?ref=theiotlist.

Hackett, R., 2016. Wait, What is Blockchain? Fortune. Available at: http://fortune.com/2016/05/23/blockchain-definition/ [Accessed February 8, 2018].

Harris, M., 2017. What is Cloud Storage? LifeWire. Available at: https://www.lifewire.com/what-is-cloud-storage-2438541 [Accessed January 30, 2018].

Isah, A.O. et al., 2012. Specific features of medicines safety and pharmacovigilance in Africa. Therapeutic advances in drug safety, 3(1), pp.25–34. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4110828&tool=pmcentrez&rendertype=abstract.

Islam, S.M.R. et al., 2015. The Internet of Things for Health Care : A Comprehensive Survey. IEEE Access, 3, pp.678–708. Available at: http://ieeexplore.ieee.org/xpl/articleDetails.jsp?arnumber=7113786.

Kendrick, J., 2013. Mobile technology: The amazing impact on our lives. Mobile News. Available at: http://www.zdnet.com/article/mobile-technology-the-amazing-impact-on-our-lives/ [Accessed February 2, 2018].

Khan, T.M., 2013. Community pharmacists' knowledge and perceptions about adverse drug reactions and barriers towards their reporting in Eastern region, Alahsa, Saudi Arabia. Therapeutic Advances in Drug Safety, 4(2), pp.45–51.

Lamprecht, A.J., 2017. Personal interview. 10 October, Western Cape Department of Education Headquarters.

Lamprecht, I., Bam, L. & de Kock, I.H., 2018. Translating the pharmacovigilance challenge landscape to a lower level of abstraction: The implementation of a value chain analysis, the 5Why method, and fishbone diagrams. In International Association for Management of Technology 2018. Birmingham, United Kingdom: IAMOT, pp. 1–19. Available at: www.aston.ac.uk/aston-business-school/iamot2018.

Lamprecht, I.V.B., Bam, L. & de Kock, I.H., 2017. An investigation into the prospects of existing technologies to address the challenges faced by pharmacovigilance systems. In SAIIE28: Taking up Stewardship. Vanderbijlpark: SAIIE, pp. 1–17. Available at: https://www.saiie.co.za/saiie28.

Macwan, U., 2017. Mobile Technology , Its Importance , Present And Future Trends. Finextra. Available at: https://www.finextra.com/blogposting/14000/mobile-technology-its-importance-present-and-future-trends [Accessed February 2, 2018].

Mehta, U., 2017. Personal interview. 21 August, School of Public Health (UCT).

Morrison, A. & Sinha, S., 2016. A primer on blockchain (infograohic). PWC Emerging Technology. Available at: http://usblogs.pwc.com/emerging-technology/a-primer-on-blockchain-infographic/ [Accessed February 8, 2018].

Norman, S., 2016. Advantages Of Online Learning: Education Without Leaving Home. eLearning Industry. Available at: https://elearningindustry.com/5-advantages-of-online-learning-education-without-leaving-home [Accessed January 30, 2018].

Ostrov, J.M., Gentile, D.A. & Mullins, A.D., 2013. Evaluating the effect of educational media exposure on aggression in early childhood. Journal of Applied Developmental Psychology, 34(1), pp.38–44. Available at: http://dx.doi.org/10.1016/j.appdev.2012.09.005.

Palloff, R.M. & Pratt, K., 2001. Lessons from the Cyberspace Classroom: The Realities of Online Teaching, San Francisco: Jossey-Bass. Available at: https://books.google.co.za/books?hl=en&lr=&id=36GLHRvTELMC&oi=fnd&pg=PR9&dq=online+teaching&ots=8n_1hUxCUP&sig=6Ku1I_cFJfZyhzD-nHlsJnuFf_4#v=onepage&q=online teaching&f=false.

Pan, G.J.D., 2014. Ongoing Challenges in Pharmacovigilance. Drug Safety, 37, pp.1–8.

Rouse, M., 2005. Remote Access. TechTarget. Available at: http://searchmidmarketsecurity.techtarget.com/definition/remote-access [Accessed January 30, 2018].

Rouse, M., 2010. WAP (Wireless Application Protocol). TechTarget. Available at: http://searchmobilecomputing.techtarget.com/definition/WAP [Accessed February 26, 2018].

Russom, P., 2011. Big data analytics, Available at: https://vivomente.com/wp-content/uploads/2016/04/big-data-analytics-white-paper.pdf.

Singh, V., 2017. Pros & Cons of Apps and Website: Which is Better Option? YourStory. Available at: https://yourstory.com/mystory/5d1d4981fe-pros-cons-of-apps-and-website-which-is-better-option- [Accessed February 26, 2018].

Smith, N., 2014. 5 Key Principles to Resource Management. LiquidPlanner. Available at: https://www.liquidplanner.com/blog/5-key-principles-resource-management/ [Accessed February 1, 2018].

Spacey, J., 2015. 11 Types of Resource Management. Simplicable. Available at: https://simplicable.com/new/resource-management [Accessed February 1, 2018].

Strengthening Pharmaceutical Systems, 2009. Supporting Pharmacovigilance in Developing Countries The Systems Perspective, Available at: http://apps.who.int/medicinedocs/en/d/Js18813en/.

Tallent-Runnels, M.K. et al., 2006. Teaching Courses Online: A Review of the Research. Review of Educational Research, 76(1), pp.93–135. Available at: http://rer.sagepub.com/cgi/doi/10.3102/00346543076001093.

Toklu, H.Z. & Uysal, M.K., 2008. The knowledge and attitude of the Turkish community pharmacists toward pharmacovigilance in the Kadikoy district of Istanbul. Pharmacy World & Science, 30, pp.556–562.

Uppsala Monitoring Centre, 2017. The quest for evidence, Uppsala. Available at: https://view.publitas.com/uppsala-monitoring-centre/uppsala-reports-77_web/page/1.

Varun, B., 2016. What are pros and cons of Internet of Things? PixelCrayons. Available at: https://www.pixelcrayons.com/blog/industry-news/what-are-pros-and-cons-of-internet-of-things/ [Accessed January 31, 2018].

Viswanathan, P., 2017. What is a Mobile Application? LifeWire. Available at: https://www.lifewire.com/what-is-a-mobile-application-2373354 [Accessed February 26, 2018].

De Vries, S.T. et al., 2016. Factors Influencing the Use of a Mobile App for Reporting Adverse Drug Reactions and Receiving Safety Information: A Qualitative Study. Drug Safety, 40, pp.443–455. Available at: http://link.springer.com/10.1007/s40264-016-0494-x.

Western Governers University, 2017. Teaching Strategies for Using Educational Movies in the Classroom. Western Governors University. Available at: https://www.wgu.edu/blogpost/teaching-strategies-using-educational-television-classroom# [Accessed February 26, 2018].

World Health Organization, 2002. The Importance of Pharmacovigilance - Safety Monitoring of medicinal products, Available at: http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf.

Zakir, J., Seymour, T. & Berg, K., 2015. Big Data Analytics. Issues in Information Systems, 16(2), pp.81–90.

Section E.2: Formal, structured validation document

An investigation into the prospects of technologies in order to address the challenges faced in PV

After almost 18 months of research, I have finally reached a conclusion, or rather recommendation to my research. It is absolutely critical that these recommendations be validated by subject matter experts in order to determine whether or not they are feasible and credible within PV. Therefore, I would like to ask for your assistance in this process.

Brief summary of research

Given that I have completed a very large portion of my research and have conducted a great deal of work, I would like to provide a brief summary of the work I completed in order to reach this stage. This will provide some context to the research I would like you to review.

1. Starting the research, I investigated the PV system, where I consulted literature and subject matters experts in order to understand PV and the PV system.
2. Following this, I conducted a systematic literature review to identify the PV challenge landscape, which included challenges related to PV culture, insufficient resources, and technical capacity.
3. Realising that the PV challenge landscape is too large, I decided to prioritise the landscape in an effort to divert my focus towards the challenges that have the largest impact on PV.
4. Following the prioritisation of the PV challenge landscape, I induced a translation process in order to translate the prioritised PV challenge landscape to a lower level of abstraction. This was done because the initially defined PV challenges, identified via literature, were all described on a strategic level (or high level of abstraction), which made it particularly difficult to understand the true effect these challenges have on PV.
5. Following the translation process, I found that there are several tangible problems (or root causes) that made it clear what are the effects of the initially defined PV challenge landscape on PV.
6. Similar to the first prioritisation exercise in number three, I prioritised these root causes in order to divert my research focus on the most important root causes.
7. The nature of my research is to draw a link between the technology landscape and the PV challenge landscape. Therefore, I identified several technologies that can be leveraged towards PV.

8. Using a technology selection framework, I determined that there are some technologies that are not feasible for implementation in PV, and have accordingly excluded these from my research. The remaining technologies were each assessed with regards to setting, workforce, delivery mechanisms, communication modalities, and in some cases, interface.
9. Using the root causes of the prioritised PV challenge landscape and the technologies identified, I was able to draw a link between the PV challenge landscape and the technology landscape. In other words, I identified and discussed which technologies can be used to address which root cause.

Subsequently, I require validation for the last (number 9) stage of this research.

What I need from you

I need you to read through the research that I am providing below, and give some form of feedback (notes, email correspondence, or phone call) where you mention whether or not you think the recommendations are feasible, both presently and in the future of PV (with specific focus on Section 3 of the provided research). If there are sections where you do not agree, or where you think there are additional areas for opportunities, you are welcome to make suggestions.

If you need any further clarification, please feel free to contact me via email (17574846@sun.ac.za) or by phone (+27714182564).

Research summary

In order to reduce the demand for reading through too much information, I am only providing you with a certain portion of the research, which includes:

1. The prioritised root causes described within the clinical domain, in a table format.
2. A matrix showing which technology can be used to address which root cause.
3. The discussion of each root cause where the different candidate technologies are identified – You can mainly focus on this section.

Section 1

For the purpose of reducing the number of pages of this document, Section 1 of this document contains the exact same table as Table 20 on p.98 of this research document.

<u>Section 2:</u>

For the purpose of reducing the number of pages of this document, Section 2 of this document contains the exact same table as Table 25 on p.126 of this research document.

<u>Section 3:</u>

For the purpose of reducing the number of pages of this document, Section 3 of this document contains the exact same information found in Section 6.6 on p.127 of this research document.