LEADERSHIP AND MANAGEMENT IN IMPLEMENTING HEALTH INFORMATION TECHNOLOGY IN PHARMACOVIGILANCE

KEERTHANA T

Department of Health Informatics

Rutgers, The State University of New Jersey

Abstract

The information technology (IT) has transformed the world of health care and clinical medicine with better quality, effectiveness, and lesser cost. The IT has blended and collaborated into clinical safety practice and worldwide pharmacovigilance systems for safety signal detection in the timely manner. The health IT adoption have profoundly altered the conduct of clinical research, practice of medicine, and medicinal safety supervision. While spontaneous reporting in adverse events remains a keystone of pharmacovigilance in the regulatory situations, and is indispensable for signal detection, there is necessary for additional active surveillance. Devoid of knowledge and information on application and on the extent of utilization, spontaneous reports are incapable to ascertain and establish the frequency of an adverse drug reactions (ADR) of a product, or its safety. The more systematic and robust epidemiological approaches that take into account the limits of spontaneous reporting or premarketing and post marketing research and studies are obligatory to address these key drug safety queries. There is significant need to incorporate health information systems into post marketing surveillance programs.

Keywords: pharmacovigilance, health IT adoption, adverse drug reactions, post marketing surveillance

I. Introduction

A. Definition of pharmacovigilance

According to (World Health Organization, 2002), Pharmacovigilance also recognized as drug safety, is the pharmacological science and activities in relation to the collecting, detecting, assessing, monitoring, and preventing of adverse effects with medicinal or therapeutic related products, also connected with its safety and complications. Associated with this general definition, the fundamental purpose of pharmacovigilance is to prevent harm from adverse reactions in humans that occur from the usage of medicinal or therapeutic related products, besides the reputations of marketing agreement and in relation to the complete life cycle of these medicinal or therapeutic products.

B. Defining health information technology

Health information technology defines the areas of information technology used in design, development, application and usage and maintenance of the health data information systems for the healthcare organizations. (Wallask and DelVecchio, 2018) The significance of healthcare has evolved from the combination of the technology and regulatory guidelines which enhance the quality of patient care. Electronic health record (EHR) and electronic data capture (EDC) is key component of the health IT and includes all the vital information of the patient and is shared to various healthcare professionals. This act of health data exchange between the group of healthcare organizations enters into the interoperability pact and agreements.

C. Background -Progress of interoperability in healthcare

The Unites states plays a major role in interoperability developing standards for the computer systems to communicate and standardize specific terms and their connections within the

healthcare industry. The protocols for networking data, transmitting email, and improving other security and encryption schemes has been established and designed to secure confidential and sensitive patient information by the government. In the past few years, the efficiency of the healthcare systems to work attach, share and use patient records throughout the hospital ecosystem was evidently seen. There are many success stories in Spain that demonstrated that interoperability between various healthcare systems is possible even with the complexity of interoperability. The Electronic Health Record project inaugurated in 2006, which has given controlled access to patient information from any kind of care, which was primary or specialized. The success story was throughout the Spanish territory, the project to design interoperable electronic prescriptions, which was inaugurated in 2015. In 2017, among 17 autonomous communities, 9 communities were incorporated into standardized national electronic prescription system. (EhCOS, 2016)

II. The importance of implementing a systematic pharmacovigilance.

A. Why is it important to implement Health information technology on Pharmacovigilance?

The outline of the pharmacovigilance starts with safety information and coming from various sources, including the clinical trials, drug safety protocols, spontaneous reports and review literatures and every single incoming component has a potential risk to be monitored and safeguard. The drug safety product manager is assigned with safety specific issues which include large number of SAEs, case report forms and other safety projects. It is important to implement health information technology in pharmacovigilance for the risk assessment during the clinical product development while performing in laborious manner. (Fig 1) Through (Adverse Drug

reaction (ADRs) and electronic data capture (EDC) technologies, the pharmacovigilance has fostered and encouraged the international standards and practices. The drug safety researched now identify the drugs and analyses the safety information throughout the world in the confidential manner by health information exchange (HIE) and yet work in the benefit. These is lot of advantages on EDC than maintaining the paper records, data collection and randomization, validation. The data safety can also be challenging in the paper-based systems of the pharmacovigilance departments. (Lu Z, 2009)

Patient portals are platform which access the information between the patient and the healthcare professional for better patient care and access to information. This information includes the history, visits, laboratory results, discharge summaries, allergies, and other sensitive information about the patient care as well. This information can be required for the pharmacovigilance which is made easy by the implementation of Health IT (S Geyer, 2015)

B. Uses of health information technology in today's healthcare management.

The interoperability is defined as the ability of different information systems including the devices and applications for accessing, exchanging, and integrating the data in a coordinated manner within the set boundaries to supply timely and seamless portability of knowledge and optimize the health of the individual and populations worldwide. Health care data exchange designs application interface and standards the data to be accesses and shared appropriately and securely across the healthcare ecosystem with all necessary settings from respective stake holders and individuals. (HIMSS,2020)

Within the healthcare industry, the ability of various information systems different framework application to communicate, retrieve and exchange the data for information is defined as

Interoperability. The use of standard and data exchange frameworks shares this information to various healthcare providers and professionals including pharmacies, patients, hospitals, and all the other places where the application can be used. (HIMSS,2010)

C. Benefits of the implementation to healthcare providers and towards patient safety

Quality of care is the degree to which health services for individuals and populations increase the prospect of desired health outcomes and are steady with current professional knowledge. Patient safety is one aspect of quality, where quality includes not only avoiding preventable damage, but also making appropriate care accessible—providing effective services to those who could benefit. (Donaldson, M. S., Corrigan, J. M., & Kohn, L. T., 2000)

The Healthcare organizations require to employ validated safety practices to also focus on declining the rate of errors in the recording as well as medication process as these are most vulnerable zones. The healthcare industry has responded to concerns by adopting latest available technologies implementation with an existing system to ensure minimum errors with maximum care and safety. (Sittig, D. F., & Singh, H. 2011).

Five foundational components critical to delivering quality health care services are health care workers; health care facilities; medicines, devices, and other technologies; information systems; and financing. To ensure that quality is built into the foundations systems, governments, policy makers, health system leaders, patients and clinicians should ought to work together to:

- To safeguard a high-quality health workforce and excellence across all health care facilities.
- To make sure safe and effective use of medicines, devices, and other technologies.

- To safeguard effective use of health IT and develop financing mechanisms that support continuous quality improvement.

APPROACHES TAKEN BY SECTORS OF THE HEALTHCARE INDUSTRY

Healthcare IT Professionals - The entire healthcare industry is using the technology for enormous improvement in safety, for example SNOMED CT which is wonderful tool and performs important tasks such as recording healthcare data capture and storage with widespread use for taking right decisions for doctors. This data helps several clinical platforms to adopt successful and innovative cure with better patient outcomes. It also provides ready to use case studies for serious and rare diseases thereby, avoiding errors.

Health Insurance companies - Insurance providers need to focus on quality by cutting all unnecessary cause with push up the cost of healthcare without any addition of value for the patient. Research data has indicated that if Medicare operated at a level like top 10% performers in healthcare, it could improve the quality of care provided and lower cost by 20%. The major obstacle is the measurement of value through clinical outcomes data of which is not adequate presently.

Physicians and doctors - Many doctors as well as Healthcare providers have taken the initiatives to transform the sector by implementing adequate quality safety and cost cutting measures, thereby providing efficient care while maintaining safety and optimizing clinical outcomes.

Nurses – In the healthcare industries in particular, the nursing staff has also undergone excellent change through better training as well as availability of the technology deployment of which minimizes errors. Nursing staff is more reactive, responsive, and accountable, Due to improved

work atmosphere as well as employee practices adopted by most healthcare facilities about staff. High attrition rates among staff post all healthcare professionals to focus on key issues and execute all necessary enhancements to provide the more beneficial and safe work atmosphere for staff, simultaneously, impacting the quality of output rendered by them.

As part of the evidence of implemented practices that can improve health care safety, a set of five principles that it has confidence in can be usefully applied to the design of safe healthcare ecosystems like a small group practice, a hospital, or a large health care system. These include (1) delivering leadership (2) respect for human limits in the design process (3) fostering effective team functioning (4) forecasting the unexpected and (5) creating a learning and training environment. This also helps them to define all processes within the Healthcare and underline the successful practices and implement them across the board. Most of the healthcare processes are flexible, for implementation, therefore recognizing best practices and implementing them through the deployment of standard data storage practices can prove to be immensely beneficial. (Sittig, D. F., & Singh, H. ,2011).

III. Policies and regulations in Pharmacovigilance

A. Adverse event reporting

In pharmacovigilance, adverse event reporting is the foundation, and therefore closely monitored by regulatory authorities. The health information technology can be also used to report the adverse event which involves the receipt of study information, data entry, overall trails assessment, distribution of survey forms, AE reporting, and archiving of AE data and documentation for analysis. According to (ICH E2A ,1994) the definition of adverse events,

adverse drug reactions unexpected adverse drug reactions, and serious adverse events are described below.

1. **Adverse event (or adverse experience)**

   It is defined as any untoward medical incidence in a patient or clinical investigative subject administered a pharmaceutical product and which does not certainly have to have a pivotal relationship with this treatment. An adverse event (AE) can be a harmful and accidental sign (including an unusual laboratory finding), manifestation, or infection transiently associated with the use of a therapeutic/medical product, regardless of whether considered identified with the therapeutic/Medicinal product.

2. **Adverse drug reactions (ADRs)**

   In the pre-endorsement clinical trial involvement in brand-new drug and or its new uses, especially as the medicinal doses may not be clearly stated, any accidental and unintended reactions associated with this drug can be identified as adverse drug reactions. The response to the drug or therapeutic products means that a causal relationship between a drug and an adverse event is at least a rational possibility for example the relationship can't be precluded. The foremost concern for the clinical trial participants patients, clinicians, and regulatory agencies is the ADRs which lead them to substantial morbidity and mortality about the drugs in phase IV of the clinical trials. (Lavertu et al, 2021)

3. **Unexpected adverse drug reaction**

   Any adverse reaction with more severity and is not very inconsistent with the application and recommended product information. These types of adverse events are defined as “serious” centered upon participant event effect or case standards typically correlated with incidents that create a risk to a participant's life or functioning abilities.

4. **Seriousness of the adverse event**

   It is defined as the interaction of drug with any untoward medical incidence with any dose that consequences in death, is life-threatening, necessitates inpatient hospitalization or extension of existing hospitalization, outcomes in obstinate or significant debility and incapability or results in a genetic anomaly and birth defects. Significant clinical events that may not be directly or rapidly hazardous or fatal or result in hospitalization, however, may endanger the participant or expected drugs to anticipate one of the different results documented in the sense of seriousness like demise, life-threatening, hospitalization or prolonged existing hospitalization, extreme inability or debility, genetic anomaly, or birth defects, deciding whether the adverse event of reaction is serious or not. (Borja, J., Donado, E., & Souto, M. 2004)

5. **Coding of the adverse events**

   AE reporter also called verbatim is used in coding the terminology from the medical coding dictionary and process the adverse coding event. Currently in pharmacovigilance MedDRA is the most commonly used medical coding dictionary's main goal of coding is to convert the adverse event information to already existing terminology as per the coding dictionary and thus can be used for identification and analysis.(MedDRA,2020)

6. **Clinical trial reporting**

   In pharmacovigilance, AE reporting ensues when study participants or the patients would exhibit ant experience any kind of untoward event during any time of the clinical trials. The adverse events that are non-serious are usually captured separately at a different level lower than pharmacovigilance. The system captures the data and regulates the information based on the questionnaire which must be filled by the participant or the

medical monitor in a timely pattern throughout the clinical trial. Close monitoring and reporting ensure fewer casualties and a degree of seriousness. This can be achieved by alerting systems using clinical decision supports systems and analyzing the seriousness of the adverse event. (Santoro, A.,et al.,2017)

The clinical trials SAE (Serious adverse event) management includes

- To ensure criteria to report cases for review for accuracy and completeness
- To allocate the case numbers to all new SAEs
- the medical monitor should obtain the causality assessment in 24 hours
- To obtain all supporting documentation like Discharge summaries, autopsy reports and diagnostics reports which is related to the participant or subject involved in SAE.
- Outlining according to ICH guidance and describing safety narratives including all the relevant information.

B. Standard operating procedures

A standard operating procedure is a written set of instructions on a document to follow a regular or repetitive activity by the organization. According to (ICH, 2014) SOP is also defined as detailed written set of guidelines to accomplish standardization of the performance of a certain function. The enhancement and operation of SOPs are an essential part of a effective quality system as it provides entities with the knowledge and information to perform and deliver a job accurately, and accelerates stability in the quality and reliability of a product.

IMPLEMENTING SOP

While implementing the SOP is in working area, the very important step is to train or retrain the user who performs. Every individual should pursue the exact same procedure with each and

every step-in detail to report the adverse events, or else individual may decipher significance in several other ways resulting in inconsistency. SOP implemented will assure to increase quality of therapeutic /medicinal product by providing safety and efficacy which will ultimately increase the better outcomes.

MANAGEMENT OF SOP

Clinical research organizations should have planned and designed SOP on preparation, approval, revision, and control of standard operating procedures for better administration and management of SOPs. Generally, administrative aspects of the SOP system such as distribution of the therapeutic products among the patient/ participants and filing are well managed. The pharmacovigilance director is reporting for the approval of the SOPs and should safeguard the usage and execution in the organization. (Santoro, A.,et al.,2017)

C. Clinical quality management systems

A Clinical quality management system (CQMS) is required for reporting safety processes, review data, and documentation. The objective of a CQMS is to safeguard the pharmacovigilance activities which are performed with the highest of the ethical standards and correspond to regulatory requirements and responsibilities to any contractual partners. The components of CQMS include policy with a quality, SOPs, procedures for quality control, key performance indicators (KPIs), employment descriptions, and training and education plans.
A CQMS plays a crucial role in continuous process improvement. each process is reviewed through quality control steps within the process which can be accomplished also by the health information technology. The consequence of the quality control is evaluated compared to previously defined KPIs.

To assure quality check within the pharmacovigilance department is to make sure that quality is being managed by the assigned team players and their safeguard their responsibilities and that all quality issues are being addressed. (Suzzane et al., 2013)

IV. Roles and responsibilities

A. Pharmacovigilance director

The head of pharmacovigilance performs a crucial role in the pharmacovigilance department and is ultimately responsible for overall safety and risk management activities performed within the division. Usually, the director is required to have many years of experience in pharmacovigilance and be authorized personnel on pharmacovigilance rules and regulations along with reporting requirements. In addition to providing leadership and oversight within the department, the head of pharmacovigilance acts as a senior resource throughout the company on matters such as safety strategy, regulatory and safety risk management, safety compliance, and safety quality assurance. (Suzzane et al., 2013)

B. Pharmacovigilance manager

The pharmacovigilance or drug safety product manager (DSPM) is a qualified member of the pharmacovigilance department assigned to supervise specific safety products, usually when large numbers of safety staff are required. The clinical projects requiring a DSPM include studies with large numbers of SAEs, case reports, studies with clinical endpoints that are also SAEs, projects involving a number of different safety functions for example, case reporting and regulatory submission, literature review, and aggregate reporting), and other safety projects of special interest. (Suzzane et al., 2013)

C. Medical monitor

ICH-GCP does not define or describe the responsibilities of a medical monitor. A physician or other qualified individual, separate from the principal investigator, who is responsible for medical and safety monitoring of research subjects for conditions that may arise during the conduct of a clinical trial. The role of the medical monitor is to be the clinical team's advocate for subject safety and wellbeing. This extends beyond individual patient safety monitoring and may include medical assessment of the clinical study protocol for feasibility, upfront risk analysis, input into decisions on study design, treatment regimens, comparator selection, medical interpretation of data, and input into data analysis and report generation. During the study the medical monitor is an important member of the clinical project team. Responsibilities include interaction with site investigators to provide them with known information on the product under study, ongoing assessment of the medical and safety aspects of the medicinal product, serving as the medical consultant to the project team. (Suzzane et al., 2013)

D. Drug safety Associate

The role of a DSA is to monitor and track SAEs, serious and non-serious ADRs, and other medically related product information. It is paramount to ensure the timely processing and reporting of such evidence in accordance with company and regulatory reporting timelines. The DSA usually has an educational background in one of the life sciences; it is also advantageous to have a working knowledge of medical terminology. Many DSAs are nurses, pharmacists, or other allied health professionals. The DSA works under the supervision of the DSPM, director of drug safety, QPPV, or medical monitor. Some of the other functions performed by the DSA include, but are not limited to, developing safety plans and other SSPs; providing input to and

reviewing study safety tracking reports for accuracy and quality; maintaining electronic and paper files; supplementary the medical monitor with the documentation and processing of routine exceptions and rescreen approvals; performing safety review of clinical [case report forms (CRFs)] and patient laboratory data; liaising with sponsors, investigational sites, and/or reporters regarding. (Suzzane et al., 2013)

E. Health information systems specialist

The large amounts of data involved, numerous databases and technology systems are required to manage the daily workflow associated with pharmacovigilance, including individual case management and aggregate data analysis. This requires staff who have backgrounds in information technology (IT). In some cases, these staff are further specialized in the creation, validation, and maintenance specifically of safety systems. In smaller companies, the safety systems specialist may be part of the IT department, assigned as needed to support pharmacovigilance.

F. Medical assistant

The medical assistant plays an important role in maintaining efficient and accurate organization of documents and information within the department by providing administrative support to the pharmacovigilance team. In some cases, medical assistants may be trained as data entry personnel and can assist in the data entry of safety information into appropriate safety databases. Filing; faxing; assisting with the planning and organization of meetings, teleconferences, and training sessions; maintaining meeting minutes; handling mailing activities; responding SAE hotline and other departmental telephone lines; documenting contacts and submitting to appropriate personnel; maintaining office supplies and equipment; creating, maintaining and

auditing work tracking systems; and ensuring accuracy and audit readiness of the departmental files and file room are the duties of the medical monitor.

G. Drug safety trainer

Pharmacovigilance staff should be prepared for in terms of their knowledge of the rules, regulations, SOPs, and confidentiality requirements surrounding the specific protocol or project, as well as safety reporting regarding clinical research subjects and their data. In the current dynamic environment encompassing pharmacovigilance and risk management, ongoing training for pharmacovigilance staff is important to maintain awareness of current global and local regulations, policies, and guidelines. This training includes subject matter training on the therapeutic area of the product under enhancement and specific training on the science related to the investigational product. Training related exclusively to pharmacovigilance is continuous, with more senior staff reviewing and mentoring the junior staff. However, staff specifically committed to performing pharmacovigilance training is usually essential. All training modules should be documented and filed appropriately. (Suzzane et al., 2013)

V. Strategies and challenges in execution of pharmacovigilance system

A. Leadership and health care management strategies

The pharmacovigilance department should be comprised of the drug safety physician, drug safety associate, and medical assistant to start the functional process. This team also should comprise of a few DSAs, a single physician providing medical review, and one or two medical assistants for administrative support and assistance. Pharmacovigilance teams may be formed by product or by therapeutic area or may be segregated into premarketing and post marketing groups, based on the volume of the company and the number of employees. Global pharmacovigilance capacity can

permit around-the-clock pharmacovigilance, with world-wide systems it can be successful, constant processes and workflows, satisfactory and ongoing training, and excellent verbal skills across regions.

B. Oraganizational collaboration and teamwork

Pharmacovigilance matrix structures are very common. Successful pharmacovigilance requires cross-functional, cross-regional, and cross-cultural partnership and cooperation. Within the pharmacovigilance department, safety case administering, and assessment may take place in several locations, especially if some steps in the workflow are offered in low-cost centers.

The pharmacovigilance staff, as members of the clinical development team, also communicate about the work process regularly with clinical trial site investigators, research associates, project managers, statistical analysts, and medical writers. Additionally, pharmacovigilance staff impartial of the clinical team may work with the committee members to provide or clarify the safety information needed for clinical endpoint review or for periodic DSMB meetings. (Suzzane et al., 2013)

VI. Health data information review for safety and efficacy of the drug.

According to AHIMA, the performance measurement of the collected data and reporting initiatives are through public and private partnerships. The healthcare professionals are the front ways to collect and report data for quality, public health and performance and financial measurements. The absence of data standard can concern the issues in 1. Difficulty in data acquisition from the electronic systems.2. Complicated data mining and coordination efforts.3. Intensive data mapping efforts by health care professional to link systems to performance measurement data requirements.4. Disparate information systems between the

healthcare organizations.5. Conflicts between the administrative data sets. The data standard has been changed and the current issues are related with variations that may exist at the data element and data definition level are as follows – 1. Variations in data element descriptive titles.2. Difference in data element definitions and value with performance measurement systems.3. Discrepancies in data element formats.4. Disparate sources in the medical documentation where the data is retrieved.5. Variation from the source of data where it has been referred for the health care professional.6. Discrepancies between the software products used for the data collection.7. Difference in the granularity of the patient specific or aggregated data submitted. AHIMA is closely monitoring the activities and is also involved in efforts to standardize the data used for performance measurement and supporting the key industry efforts, researching the variations among performance measurement systems, and providing content expertise. (Crystal & Susan, 2007)

VII. Risk Management

The risk management represents the activity and pyramid of the pharmacovigilance as represented in (Fig. 2), and the activities are the conclusion and assessment of all the adverse events and various drug safety data, and the review of the data collected and identification, analysis and interpretation of the safety signals. The significant safer issue may include 1) Provisional suspending of the enrollment 2) Termination of the study 3) Termination of the drug/therapeutic product 4) Executing the Risk management plan or risk evaluation and mitigation strategy 5) Revising the safety protocols.

A. Data safety mitigation

A medicinal product is only approved based on specified indication(s), at the time of authorization, the benefit of risk is only judged positive for the aimed population. Not all actual and potential risks would have been discovered when an initial approval is obtained. Additionally, there would be many different subgroups of population or patients enrolled for the clinical trial whose is at greater risk than that for the aimed population.

The single risk can be managed and considered under four steps, 1) risk detection, *2)* risk assessment, 3) risk minimization and 4) risk communication. Any single therapeutic or medicinal product will have various risks accompanying it and these risks will related to severity, and single patient and public health impact

B. Evaluation of the strategies and risks

The objective of both the Risk management Plan (RMP) and the Risk evaluation and Mitigation Strategy (REMS) is to reduce the risks related to a therapeutic/ medicinal product through the new interventions and to convey those risks to participants of the clinical trails, patients and as well as healthcare professionals. The components of the evaluation may contain therapeutic or medication guides or patient package information, a comprehensive plan regarding the safety issues, and also few essential elements to pledge the safe use of a product such as mandatory laboratory testing or prescriber training, and also an implementation plan and a assessment with timely schedules. The RMP or REMS can be created during any time of the clinical development, but very frequently they are presented as part of the marketing presentation of the drug. The RMPs are consistently obliged as part of the comprehensive report of the pharmacovigilance system. In the USA, if there is a reason to suspect that one may be necessary the regulatory authorities can request a plan, considering upon non-clinical data, early use data,

class data for the medicinal compound, or other factors as well. If brand new safety data becomes obtainable after regulatory approval, the regulatory authorities may call for a REMS or an updated RMP. Additional pharmacovigilance can also be included in the plan like active surveillance, clinical trials, epidemiological trials, dedicated training, or restricted access. These mentioned activities required to be sufficient to reduce the likelihood of detriment so that benefits of the drug or medicinal products should outweigh the risks.

C. Execution of the risk management plan

As part of the execution plan of the risk management, the model must also consider the mixture of knowledge on several risks with the aim of safeguarding that the benefits surpass the risks by the best possible margin both for the individual participant or patient and at the population level. This risk management strategy comprises two parts a) pharmacovigilance and b) risk minimization. By drug safety measure and monitoring it encompasses to reduce the risk leading to adverse events.

VIII. Conclusion

There is a need for an interoperable information technology framework across the global healthcare industry to advance the outcome of the practices by various healthcare professionals. This framework can be used and manipulated for developing new techniques and methods to provide better health, therapeutic products to optimize the pharmacovigilance to improvise the ability to integrate and access the health records across the healthcare ecosystem with drug / medicinal products over decades. To ensure the process the leadership and management strategies also should be safeguarded by the team members of the pharmacovigilance departments. Globally pharmacovigilance can be centralized in a across few regions, there would

be better communication and process flow between different regions worldwide. Few functions may be competently operated in low-cost regions because of the knowledge acquired from the global information systems on the drug safety protocols and listed to the WHO regarding the safety guidelines. To outsourcing IT, to performing pharmacovigilance and risk management have enough exposure and training to execute those services, and that they are sufficiently educated in the regulations associated with pharmacovigilance. From safety audits, SOPs, medical and safety monitoring, case management, operating pharmacovigilance databases, trend analysis, and also reporting periodic safety reports to regulatory authorities, principal investigators, and institutional review boards can be accomplished by embedding the information systems into pharmacovigilance.

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FIGURES

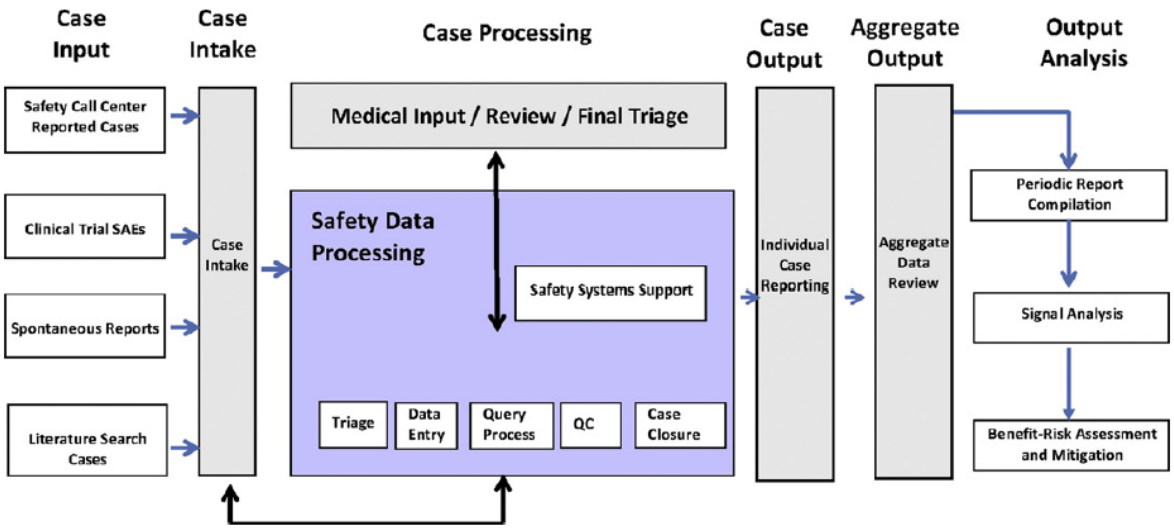

Figure 1. A flow diagram reviews the important activities associated with pharmacovigilance

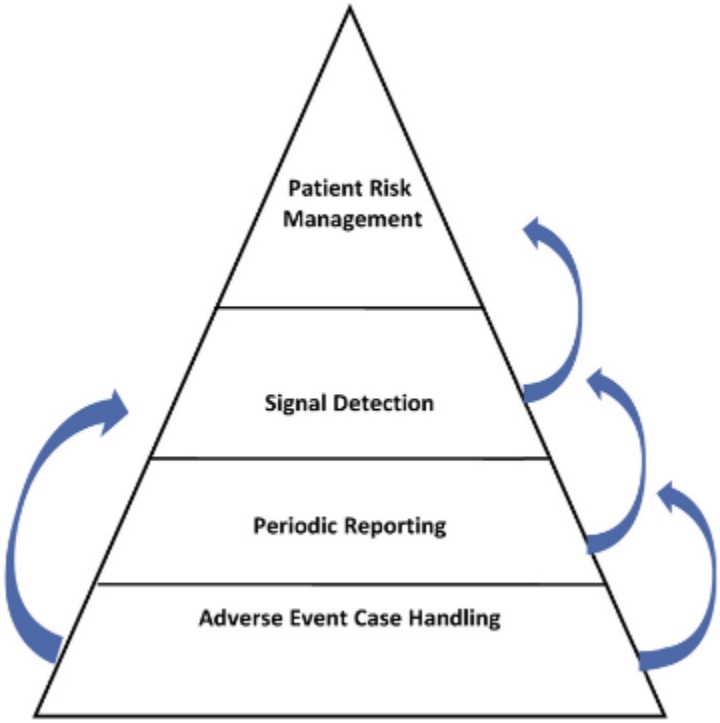

Figure 2. The risk management represents the activity and pyramid of the pharmacovigilance