1. **Introduction**

Pharmacovigilance is defined as, “the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problem, pharmacovigilance rapidly developed on a worldwide basis as a defined discipline following the thalidomide tragedy in 1961. [1] Since then, the requirements, tools and methods used in pharmacovigilance have matured into a well developed skill set. Further, there have been many useful developments with direct contributions to global public health (eg, the establishment of the World Health Organization Pharmacovigilance Programme, the development of Council for International Organizations of Medical Sciences (CIOMS) Working Group reports). But the health care environment on which the more gradual evolution of pharmacovigilance as a discipline has been predicated is itself now changing more rapidly and dramatically, in large part due to technological advances that have occurred over the past decade.[1][2]

Thus, it would be of significant value to plan for how the established infrastructure and practices of pharmacovigilance, as presently configured, will need to change in the near future in order to meet these substantial challenges. The American Medical Informatics Association defines biomedical informatics as “the interdisciplinary field that studies and pursues the effective uses of biomedical data, information, and knowledge for scientific inquiry, problem solving and decision making, motivated by efforts to improve human health.” Over the past several years, the field of biomedical informatics has been successful in establishing definitions and principles that have coalesced into a coherent approach to health care and health care data. Driven primarily by non pharmacovigilance interests in social media and the availability of large-scale datasets, the field of pharmacovigilance has begun to benefit from the application of techniques found in informatics, such as the well-developed methods of gathering useful safety data from novel sources, including electronic health records. These approaches are yielding useful insights, but to date they have been primarily isolated efforts applied only to current issues in the field. There has, in fact, been no systematic assessment of the role of informatics in enhancing the field of pharmacovigilance, an assessment that has the potential to lead to new insights, developments, and opportunities. [3][4]

Pharmacovigilance lacks a fundamental research model for the future that would provide clarity in scope and direction and could point to areas in which a greater focus of effort would produce benefits. In addition, such an approach would help to identify which basic concepts already in place in pharmacovigilance may be in need of updating in order to take full advantage of the wealth of data, technologies and methods being developed today in other, closely related areas. Thus, this article brings a novel lens to pharmacovigilance, looking at the evolution and development of the field of pharmacovigilance from the perspective of biomedical informatics with the explicit goal of providing a foundation for discussion of the future direction of pharmacovigilance as a discipline. [2][4]

The discipline of pharmacovigilance is rooted in the aftermath of the thalidomide tragedy of 1961. It has evolved as a result of collaborative efforts by many individuals and organizations, including physicians, patients health authorities, Universities, industry, the World Health Organization, the Council for International Organizations of Medical Sciences, and the International Conference on Harmonisation. Biomedical informatics is rooted in technologically based methodologies and has evolved at the speed of computer technology. The purpose of this review is to bring a novel lens to pharmacovigilance, looking at the evolution and development of the field of pharmacovigilance from the perspective of biomedical informatics, with the explicit goal of providing a foundation for discussion of the future direction of pharmacovigilance as a discipline.[5]

1. **Aim & Objective of Pharmacovigilance**

The WHO promote the safe use of medicines at country level by developing policies, norms, standards and guidelines for pharmacovigilance. They also providing a platform for Member States to meet and collaborate on pharmacovigilance issues. WHO also run public health programmes, training courses and other activities to promote pharmacovigilance.[6][7]

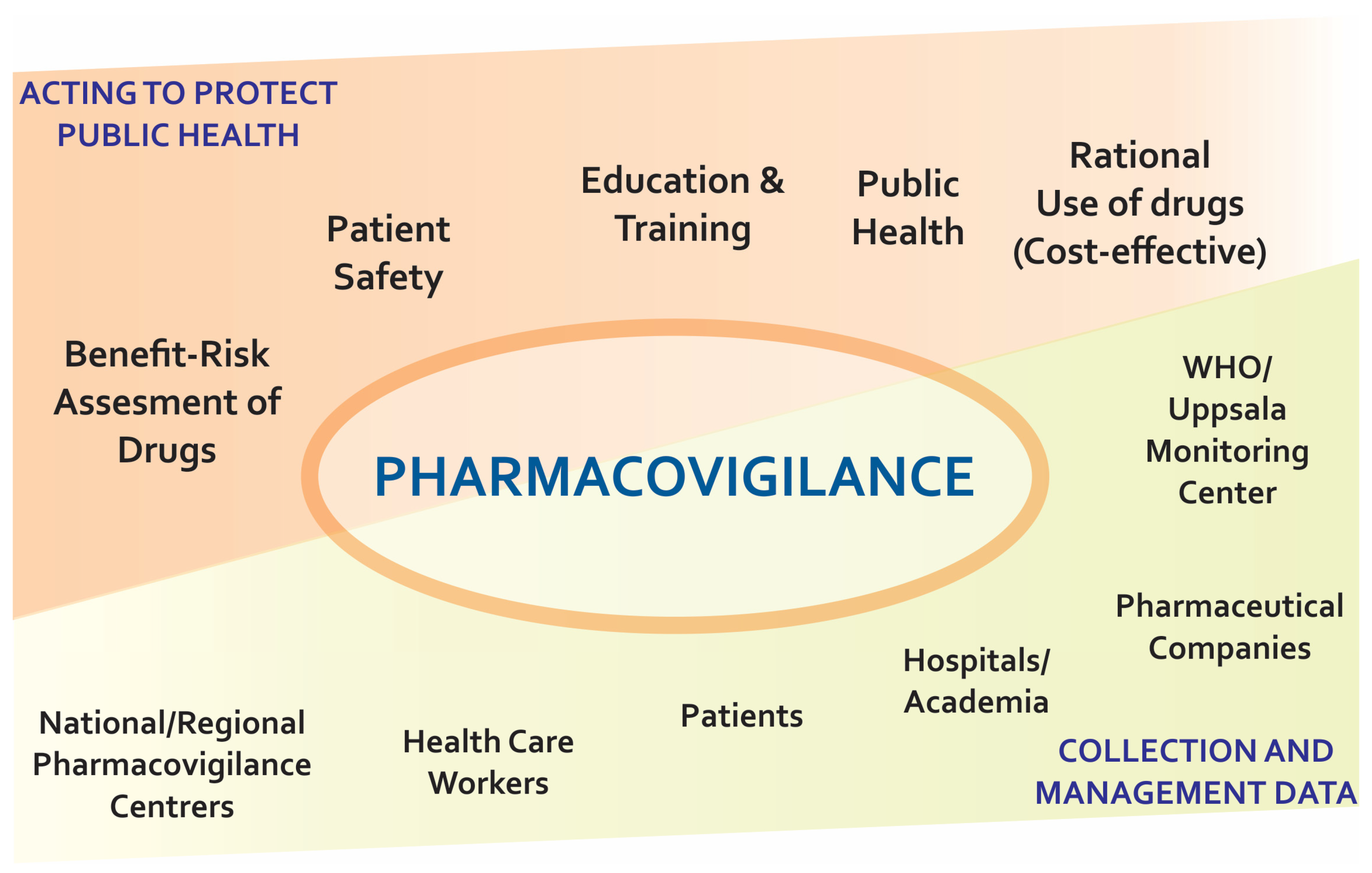
1. Preventing harm from adverse reactions in humans arising from the use of authorised medicinal products within or outside the terms of marketing authorisation or from Occupational exposure.
2. Promoting the safe and effective use of medicinal products, in particular through providing timely information about the safety of medicinal products to patients, healthcare professionals and the public.
3. The main objectives of pharmacovigilance involve exhibiting the efficacy of drugs by monitoring their adverse effect profile for many years from the lab to the pharmacy; tracking any drastic effects of drugs improving public health and safety in relation to the use of medicines.
4. In addition, encouraging the safe, rational and cost-effective use of drugs promoting understanding, education and clinical training in pharmacovigilance and effective communication to the generic public.[2][7]
5. Providing information to consumers, practitioners and regulators on the effective use of drugs along with designing programs and procedures for collecting and analyzing reports from patients and clinicians conclude to the objectives of pharmacovigilance studies.
6. Safety of patients is the most important and global responsibility. Different types of medicines are used since the ancient ages and various rules and regulations were formed in the modern era. Pharmacovigilance improves the patient safety.
7. Increase the awareness of healthcare professionals and the public on the understanding of the importance of Pharmacovigilance.
8. To develop an effective ADR reporting channel, such as the online reporting system.[1]
9. To educate all the parties to participate actively in the pharmacovigilance reporting system.
10. **Review of Literature**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Sr.No. | Title of Paper | Research Methodology | Relevance of Study | Reference |
| 01 | Pharmacovigilance and Biomedical Informatics: A Model for Future Development | Rapidly developing innovation in biomedical informatics pose a challenge to pharmacovigilance. | Pharmacovigilance and ADR reporting of healthcare. | Paul Beninger, A. Michael |
| 02 | Informatics applied to pharmacovigilance: Future perspectives | Contribution to the infrastructural development of pharmacovigilance | Activities related to detection, assesment, under standing and prevention of ADR | Michael M., Annamaria |
| 03 | Information technology in pharmacovigilance: Benefits, challenges, and future directions from industry perspectives | Risk assessment during clinical product development needs to be conducted in a thorough and rigorous manner | The development and use of standard-based pharmacovigilance system with integration connection to electronic medical records, electronic health records. | Zhengwu Lu |
| 04 | Bioinformatics Accelerates the Major Tetrad: A Real Boost for the Pharmaceutical Industry | Bioinformatics and pharmacovigilance promoted both sample analyzes and interpretation of drug side effects | The role of bioinformatics has been highlighted in DDD, proteomics, genetics, modeling, miRNA discovery and assessment | Tapan Behl |

1. **Current Scenario of Pharmacovigilance and Biomedical Informatics in India**
   1. **Pharmacovigilance Study**

Pharmacovigilance is a branch of pharmacological science encompassing all scientific and data gathering activities relating to the detection, assessment, understanding and prevention of adverse events of medicines and medical devices. The extent and pace of change promise to accelerate with the integration of biomedical informatics, analytics, artificial intelligence, and machine learning. This progress has implications for the development of the next generation of PV professionals who will need to be trained in entirely new skill sets to lead continued improvements in the safe use of pharmaceuticals.[3][8]

A century-long history of many tragic events has played a critical role in shaping the present-day drug development structures and processes, none more so than those concerned with pharmacovigilance (PV). The present review describes the core PV functions of case management, signal management, and benefit–risk management. It also covers the breadth of scope of safety-related activities that a present-day pharmaceutical company must be prepared to manage, most of which are likely to reside in a department charged with PV responsibilities. This review does not concern safety-related issues of medical devices, the intricacies of combination products, or companion diagnostics. [8]



***Fig.1*** *Scope of Pharmacovigilance*

The World Health Organization has defined PV as the “science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems.” PV is commonly considered to have begun as a separate, identifiable activity in the United States with passage of the Drug Efficacy Amendments of 1962, that were legislated in response to the thalidomide catastrophe that had occurred in Europe. However, there is an earlier history that played an important role in shaping the statute. As early as 1952, the US Food and Drug Administration (FDA) had actively sought information concerning a growing safety issue with the use of chloramphenicol. FDA conducted a survey through its 16 district offices of hospitals, clinics, and medical schools in cities with populations >100,000 to collect reports of aplastic anemia and blood dyscrasias associated with use of chloramphenicol. Thus, a pilot activity of careful, systematic review of individual case reports organized in response to a drug safety concern was codified in the KefauverHarris Amendments of 1962 as a required corporate responsibility of evaluation and timely reporting. This early response has continued to evolve into the present-day core function of Case Management.[9][10][11]

* 1. **Challenges of Pharmacovigilance**

There are well-known inherent issues in systematically analyzing and interpreting voluntarily submitted data involving multiple drugs, medical conditions, and events per report, without the benefit of a research protocol, randomization and a control group of persons taking the placebo. Other difficulties include chronic under-reporting, occasional publicity-driven and litigation-driven episodes of over-reporting and misreporting, incomplete and missing information and inconsistencies and changes over time in reporting and naming/coding practices. In addition, there is considerable uncertainty regarding the quality and completeness of the information contained in each data field, including dosage, formulation type, timing of exposure, and length of exposure and follow-up and in estimating the corresponding product exposure and background rate of adverse events. The extraction of useful information from this database presents multiple challenges, including managing, storing, querying, and analyzing such a large amount of data, and resolving event and drug dictionary problems and data miscoding. There is a need for analytical methods that are capable of systematically screening this database to identify potential serious adverse events of concern in such a noisy background that properly balance the concerns for excessive signaling and accounting for background noise. Another challenge will be determining rules to trigger an alert, when to consider a signal likely enough to be real to warrant follow-up, and when a signal needs to be elevated to represent a potential safety risk. If data mining analysis was performed on data for millions of people taking thousands of drugs, statistic significance could emerge as data on a drug–event relationship accumulate, even after adjustment for repeated testing. Such P value-driven thresholds could result from the size of the population and the strength of the supposed association.

Taking account of multiple covariates such as severity of adverse events, whether a safe alternative treatment is available, or how much benefit the drug provides will likely cut down the list to prioritize focused follow-up. Propagation Neural Network (BCPNN) methodology to calculate the Information Component (IC) value for drug-event combinations for drugs belonging to the Anatomic Therapeutic Chemical (ATC) classes of the cardiovascular system, musculoskeletal system, and nervous system (number of reports = 51,270) where only the suspected drug was considered, and also where both concomitant and suspected drugs were considered using data from the Swedish Drug Information System and reported that the proportion of “type C” reactions signaled when considering both concomitant and suspected drugs as compared with suspected drugs only.

Conversely, taking action prematurely on the basis of inadequate data could result in unnecessary confusion and harmful discontinuations of useful treatments. We cannot know now what inputs will be optimal for each decision analysis. But stating such inputs transparently up front will help to clarify the decision-making process of regulators who will have to act on these signals. It will also facilitate the communication of decisions, by enabling regulators to frame recommendations or actions in terms of prestated assumptions about acceptable risks for a given product. If such tools are applied well, the system will be able to provide early notice of adverse drug effects that have previously taken years to discover. It seems that there is a fine balance of judgment on public warnings on possible hazards. Caution needs to be exercised to issue public announcement on unreal hazards. An excessively high threshold for warnings would keep real risks hidden too long, but an excessively low threshold could undermine public trust in clinical products, the surveillance system, and the entire medical world.

Proper implementation of the pharmacovigilance technology solution will require expertise in intelligibly communicating information about risks in relation to benefits to clinicians and patients alike. Challenge area also lies in clinical process re-engineering to ensure modern pharmacovigilance technology systems are configured, tailored, and implemented in the context of addressing safety process improvements and organizational needs to support daily clinical safety operations. In the past four decades from the thalidomide tragedy to the recent drug recalls, companies have used pharmacovigilance methods to identify rare, easily identified safety problems. During the same four decades, we have seen the growth of a fragmented clinical or healthcare system that lacks a unifying infrastructure. As a result, this system operates primarily in reaction to rather than in anticipation of major pharmaceutical safety events. As drug consumption has increased and the public has grown to expect greater drug safety, the traditional reactive approach has proven largely incapable of addressing both shifts in public expectations and regulatory and media scrutiny. This reality has revealed improvement areas involved in patient safety operations: organizational alignment, operations management, data management, and risk management.[10]

* 1. **Biomedical Informatics**

Bioinformatics is a term that refers to the collection and evaluation of scientific data by employing computational techniques, integrating the biological information comprising of proteins, genes, cells, robotics, medical information, and ecosystems with technological mediums such as databases, software, tools, etc. Bioinformatics was completely established as a significant field by the 1990s, with an established role in the scientific paradigm.[12]

The pharmacological therapies are available for only 30% of the diseases identified, as per the investigations, and many biological targets for numerous diseases are yet to be identified. Bioinformatics integrates biostatistical aspects and computational techniques with biomedical sciences, like genetics, proteomics, epidemiology, and genomics. [14]

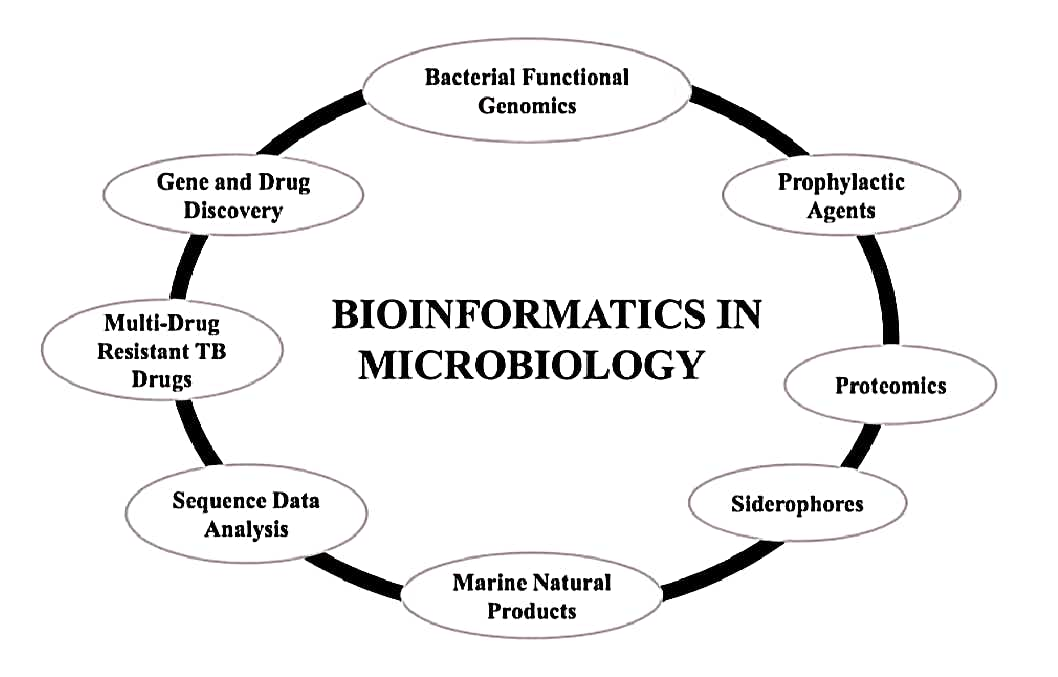
Bioinformatics aims to enable data analysis, management, and interpretation from observational investigations and biological studies, therefore targeting implementation and development of databases, biological inference and interpretation, as well as data evaluation and mining, which is very well managed by the National Center for Biotechnology Information (NBCI), European Bioinformatics Institute (EBI), Riken (Japanese National Research and Development Agencies), etc. Bioinformatics has been introduced in the pharmaceutical industry on the basis of two significant aspects, computational chemistry and molecular biology, where the latter is a specific and targeted approach, focusing on genetics and sequencing of data, which is a necessary biomedical tool, while the former emphasizes structural analysis more than biological applications, comprising crystallographic techniques, protein-structure determination, etc. Molecular biologists adopt a sequence-based approach to bioinformatics, whereas computational chemists employ bioinformatics in terms of protein structures. In the pharmaceutical industry, bioinformatics has occupied a fundamental position by facilitating the management and organization of novel developments and sectors, such as pharmacovigilance, which provides a significant basis for drug development and research, and enables the identification, evaluation, prevention, and understanding of the adverse effects or reactions as a result of drug administration. “Biomedical informatics” is defined by the American Medical Informatics as an interdisciplinary approach developed to evaluate and understand the utilization of information and data of biomedical importance, along with knowledge for scientific inquiry, decisive ability, and analytical thinking to solve problems, synergized by steps to enhance human health. [15]

The techniques associated with bioinformatics have been found to benefit the objectives of the pharmaceutical and medical sector, due to the availability of large-scale datasets, such as methodologies of collecting useful safety information from newer resources, such as electronic health records. Pharmacovigilance has been reported to be influenced by basic principles of bioinformatics, such as storage, decision making, computational skills, data generation, retrieval, use, communication, or sharing, which enable the production of a suitable framework to promote the organization of events associated with pharmacovigilance. The healthcare system has reached the so-called “third wave” of digitalization, according to McKinsey, due to the application of innovative techniques, which are patient centric, targeting the development of required services, which further propagates more intense innovations in pharmacovigilance and the healthcare sector.[13][15]

* 1. **Bioinformatics in Microbiology**

The research in the antimicrobial paradigm has resulted in the discovery of potential anti-microbial drug candidates; however, the elevating number of antimicrobial resistance bacteria has triggered the need to develop more efficient and novel antimicrobial drug candidates. The novel genetic data can cause changes in the protein structure, which impacts the ability to carry antibiotics, enzyme-mediated inactivation of drugs, and structural alterations during interactions between bacteria and drugs. Furthermore, numerous natural compounds can be used to fight against such infections, on account of their antimicrobial properties, which are referred to as antimicrobial peptides (AMPs).[16]

Bioinformatics-associated advancements in bacterial transcriptome provide a greater understanding of varying microbial adaptations in conditions of environmental stress, which will aid in the development of novel AMPs. The tools and techniques associated with bioinformatics ameliorate and short-list the total number of lead candidates to be employed as drugs and recognizes the efficient therapeutic agents. Additionally, there are numerous forms of advantages of bioinformatics in the microbiology field.



***Fig. 2*** *Bioinformatics in multiple assets of microbiology—proteomics, bacterial functional genomics, gene and drug discovery, siderophores, marine natural products, sequence data analysis, multi-drug-resistant tuberculosis (TB) drugs, and prophylactic agents.*

Novel approaches by employing rapid DNA–DNA alignment with Bowtie to the metal gear solid (MGS) database, resulting in more specific alignments. Alignment of metagenomic reads is enabled by HUMAnN2 to NCBI UniRef microbial genomes. Another metagenomic tool, MGS-Fast, aids in DNA alignment, and its gene annotation is related to KEGG and IGC. Multiple operational taxonomic units (OTU), which depict bacteria, which are uncultured, are developed by direct polymerase chain reaction (PCR) amplified 16S gene sequencing. About 1,719,541 16S rRNA sequences of bacteria are contained in rRNA database, SILVA, with 99% level of identity into 645,151 representative sequences. Antimicrobial resistance in pathogens has triggered the development of novel antimicrobial candidates. Siderophores provided newer approaches for the establishment of suitable targets for antibiotic discovery. The siderophore receptors are located on the cell membrane of the pathogen and facilitate entry of the antibiotic and produce a black.[17]

Antimicrobial resistance in pathogens has triggered the development of novel antimicrobial candidates. Siderophores provided newer approaches for the establishment of suitable targets for antibiotic discovery. The siderophore receptors are located on the cell membrane of the pathogen and facilitate entry of the antibiotic and produce a black hole due to deficiency of iron. Detailed study of biosynthetic pathways of siderophores permits the development of significant targets to facilitate hindering of these siderophores in pathogenic agents, which regulate pathogenic virulence, referred to as the Trojan Horse Strategy, which prevents the pathogen from becoming resistant to the drug candidate. Antimicrobial resistance is accelerating from proto resistance to uncurable clinical pathogens. The effective therapy of resistant infections and discovery of novel drugs is facilitated by genotype data. For instance, the estimation of resistance phenotype from genotype is enabled by the Comprehensive Antibiotic Resistance Database (CARD), which acquires curated mechanisms for resistance to data, genes as well as their targets, for resource establishment for the generation of an algorithm for the estimation of resistance to antibiotics. The Resistance Gene Identifier (RGI) in the CARD presently gives an estimation of resistant genes, evaluates genome assemblies, and gives a comprehensive account of estimated genes resistant to antibiotics as well as targeted groups of drugs.[16][17]

1. **Informatics as an Organizing Principle for Identifying Areas in Need of Development**

From a historical perspective, the intertwining technological developments in computerized data processing and storage, with the increasing awareness of drug safety issues and pharmacovigilance principles, only sparingly interacted with one another over the mid-to-late decades of the twentieth century. It was not until the latter part of the twentieth century that computer technology began to have a noticeable impact on pharmacovigilance activities, for example, in safety-database management and in algorithmic queries of the safety database, which eventually led the way to changes in virtually every other aspect of pharmacovigilance. The original technological drivers for change in pharmacovigilance were the dramatically faster processing speeds, vastly larger storage capacities, and increasing automation of repetitive tasks, all occurring while continually decreasing costs.[18][19]

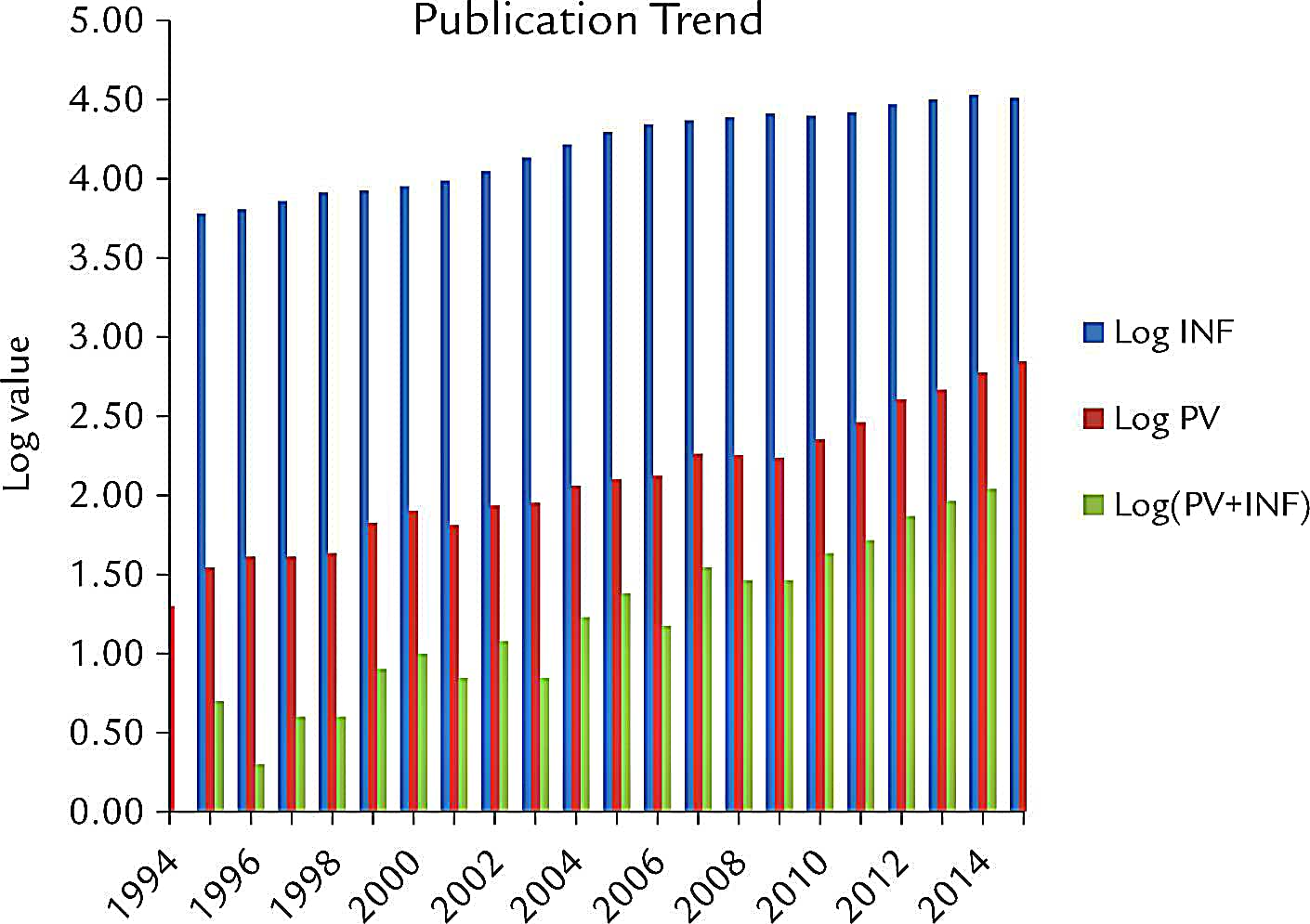
These categories provide a useful framework for organizing pharmacovigilance activities. Innovations have led health care to the cusp of what McKinsey calls the “third wave” of digitization: a patient-centric focus with the development of services to meet the anticipated needs. This focus is driving even deeper innovations in health care and, by extension, pharmacovigilance. These trends are finding expression in social media, “big data,” analytics and communication and have set the stage for entirely new operating models that have been emerging in health care but not as yet in pharmacovigilance. By surveying pharmacovigilance activities in a biomedical informatics context, we hope to provide a model structure that will allow for open discussion of the gaps that exist today, and the future work needed to encourage the pharmacovigilance community to keep up with the rapid pace of change that is affecting all of present day health care. We have also identified examples of presently available applicable technologies/methodologies in and we have attempted to assess the maturity of the applicable technologies/methodologies as well as the degree to which it has had an impact on the field of pharmacovigilance, with the intent of drawing attention to those areas that may benefit from further development.

There are also other influences on the evolving developments within the field of pharmacovigilance that help to characterize the environment in which pharmacovigilance is being practiced.[20][21]

1. **Regulatory Developments**

Through the deliberative processes of CIOMS, Health Authorities, particularly the European Medicines Agency, have made significant contributions to the development of new pharmacovigilance disciplines, specifically Benefit–Risk Management and Signal Management. Health Authorities have increasingly required the use of secured, standardized electronic formats for the submission of regulatory documents, including pharmacovigilance reporting for medical products in development and following approval for marketing.

Secured formats are also required for communications and auditing activities. However, Health Authorities have been slower to develop regulatory structures for certain other topics. For example, consumers, as early adopters of social media applications, commonly discuss adverse experiences associated with the use of prescription and non prescription medications on pharmaceutical company websites and far more commonly share such information on noncompany websites. Seeking answers to their questions, consumers have consulted websites, blogs, chat rooms, and other online forums to obtain answers that span over a range of sophistication and detail.[22][21]



***Fig. 3*** *Publication trend for the log10 value of the numbers of publications identified in PubMed by the search terms informatics (INF), pharmacovigilance (PV), and pharmacovigilance þ informatics (PV þ INF), beginning from the year of the publication of the first article to include PV þ INF (1994) through 2015.*

The slowness in Health Authorities’ response to this rapidly evolving area has contributed to the heterogeneity of approaches across jurisdictions, as suggested by recent web postings. Health Authorities have developed their own separate approaches to the growing concerns, with no apparent evidence of harmonization or even the development of collaborative standards across jurisdictions. Commercial interests have established businesses to create their own opportunities in anticipation of eventual Health Authority decisions to enter into the larger web discussions. Globalization and Opportunities Globalization has created its own pressures, beginning with economics. All of the core disciplines of pharmacovigilance (case management, signal management, benefit risk management) and accompanying documentation can be transmitted and accessed electronically anywhere, at any time. Business contracts can go to the lowest bidder who can demonstrate quality in their value contributions to work products that the company is comfortable sharing, which is consistent with the experience-supported theoretical work of Coase. The changing economic landscape has led to major offshore outsourcing of the case management discipline and the organizational movement of these activities to pharmacovigilance operations.[23][24]

These same offshore businesses are also moving into the realm of periodic report preparation, including periodic benefit risk evaluation reports, with success. These activities are likewise being managed by pharmacovigilance operations.Trained Talent The shortage of talent trained in key quantitative and technological skills is the greatest challenge that industry faces, including the pharmaceutical industry. The European Union has responded to this challenge through the creation of the Innovative Medicines Initiative, a public–private partnership that provides academic infrastructure for the education and training of highly skilled researchers for the many professions in the pharmaceutical sector. There are no comparable certifications or degrees that are generally recognized credentials for pharmacovigilance employment in the United States, although several programs have developed offerings over the past decade.[23][3]

Further, the increasing organizational pressure on these skills emphasizes the growing need for professionals who are specially trained in these cyber skill sets. The biopharmaceutical industry, which tends to have the capacity to specialize in more highly specific skill sets, may consider emphasizing these skills in recruiting for global safety officers, pharmacovigilance scientists, and pharmacovigilance operations specialists. On the Horizon The impact of the technological innovations over the past decade will be more than matched by the prospects of innovations that are rapidly developing even in the near future. Following are a few examples of work that can be expected to have a direct impact on pharmacovigilance. Massively Large Linked Data Practitioners in pharmacovigilance and epidemiology have been linking datasets for years, primarily from pharmacovigilance databases and claims datasets. More recently, datasets that focus on electronic health records and social media have been mined for adverse events. There is some evidence that linking large amounts of data together, far larger than has been done previously, can lead to better adverse-events detection. Whereas in the past only a few types of data have been combined, soon we can expect to see many more varied types of data and vastly larger amounts of data being linked together in observational research sets. Biomedical informatics methodologies, which have the potential to combine, maintain, and analyze massively large linked datasets, will be crucial for pharmacovigilance practitioners to understand. As a practical matter, however, there is no assurance that massively large linked datasets will necessarily result in better and/or sooner signal detection. More effective detection will require properly defined metrics and long- term follow-up data for assessment.[24][25][3]

1. **Globalization and Opportunities**

Globalization has created its own pressures, beginning with economics. All of the core disciplines of pharmacovigilance (case management, signal management, benefit–risk management) and accompanying documentation can be transmitted and accessed electronically anywhere, at any time. Business contracts can go to the lowest bidder who can demonstrate quality in their value contributions to work products that the company is comfortable sharing, which is consistent with the experience-supported theoretical work of Coase. The changing economic landscape has led to major offshore outsourcing of the case management discipline and the organizational movement of these activities to pharmacovigilance operations. These same offshore businesses are also moving into the realm of periodic report preparation, including periodic benefit–risk evaluation reports, with success.These activities are likewise being managed by pharmacovigilance operations. [26]

* 1. **Trained Talent**

The shortage of talent trained in key quantitative and technological skills is the greatest challenge that industry faces, including the pharmaceutical industry. The European Union has responded to this challenge through the creation of the Innovative Medicines Initiative a public–private partnership that provides academic infrastructure for the education and training of highly skilled researchers for the many professions in the pharmaceutical sector. There are no comparable certifications or degrees that are generally recognized credentials for pharmacovigilance employment in the United States, although several programs have developed offerings over the past decade.

Further, the increasing organizational pressure on these skills emphasizes the growing need for professionals who are specially trained in these cyber skill sets. The biopharmaceutical industry which tends to have the capacity to specialize in more highly specific skill sets may consider emphasizing these skills in recruiting for global safety officers pharmacovigilance scientists and pharmacovigilance operations specialists.

* 1. **On the Horizon**

The impact of the technological innovations over the past decade will be more than matched by the prospects of innovations that are rapidly developing even in the near future. Following are a few examples of work that can be expected to have a direct impact on pharmacovigilance.

* + 1. **Massively Large Linked Data**

Practitioners in pharmacovigilance and epidemiology have been linking datasets for years, primarily from pharmacovigilance databases and claims datasets. More recently, datasets that focus on electronic health records and social media have been mined for adverse events. There is some evidence that linking large amounts of data together, far larger than has been done previously, can lead to better adverse-events detection. Whereas in the past, only a few types of data have been combined, soon we can expect to see many more varied types of data and vastly larger amounts of data being linked together in observational research sets. Biomedical informatics methodologies, which have the potential to combine, maintain, and analyze massively large linked datasets, will be crucial for pharmacovigilance practitioners to understand. As a practical matter, however, there is no assurance that massively large linked datasets will necessarily result in better and/or sooner signal detection. More effective detection will require properly defined metrics and longterm follow-up data for assessment.[27]

**7.2.2.** **Mobile/Wearables**

Health care providers, payers, and biotech/pharmaceutical companies are all interested in using data generated by mobile devices and wearable sensors. The concept of a “digital biomarker,” that is, a mobile or wearable sensor that could be considered the equivalent of a biological biomarker, is rapidly evolving. There are already research projects investigating the use of “smart apps” and mobile devices in clinical trials, postmarketing studies, maintenance of health conditions, and remote emergency care. It is clear, from even a cursory survey of the activities in this area, that these devices have the potential to profoundly change the type and amount of data that are available for pharmacovigilance uses and, thus, present the same challenges to pharmacovigilance encountered in trying to understand how best to use social media data, but on an even greater scale.[27]

**7.2.3**. **Blockchain**

Blockchain technology has received the most exposure in the news through its use in Bitcoin, a digital asset and payment system invented by Satoshi Nakamoto. However, whereas Bitcoin is a financial asset, the technology behind it, the blockchain, can be used far beyond the financial technology world. Blockchain is a type of broadly (often globally) distributed database that stores a permanent and tamper-proof ledger of transaction data. There are suggestions for the use of block- chain technology to secure electronic health record, clinical trial, and personal health care data.

1. **The Future of Pharmacovigilance Technology**

The challenges to manage drug safety efficiently and to adhere to regulatory requirements create the strong impression that widespread adoption of pharmacovigilance is inevitable. As an instrument of reform, pharmacovigilance has attributes that ensure its attractiveness to many groups in a politically and economically divided health care system that is struggling with seemingly insurmountable problems of cost and quality and postmarketing clinical studies as well.

Regulatory bodies such as FDA and European Medicines Agency (EMEA) are intensifying safety regulations, therefore boosting the adoption rates of pharmacovigilance systems by biopharmaceutical firms. However, the apparent certainty of pharmacovigilance adoption needs to be constantly reexamined due to considerations of a number of challenging issues. One is whether the current standardization initiatives in reaching interoperability between differential clinical or e-health systems among several standard consortiums such as CDISC, HL7, NCI, and FDA will have any effect on pharmacovigilance. If so, to what extent such implementation level standard may bring changes and affect ongoing pharmacovigilance monitoring activities? On the technical architecture perspective, will modern pharmacovigilance technology system offer multi-tier web based application framework so that even a new clinical standard definition causes minimum modification behind the scene? This certainly presents a challenge call to pharmacovigilance technology vendors to partner with pharmaceutical firms and health care providers to offer flexible, configurable, scalable, and interoperable pharmacovigilance technology solutions to meet the future pharmacovigilance needs in:

1. increasing globalization;
2. web-based sales and information;
3. broader safety concerns linked to the patterns of drug use within society;

d) collaborative working approach among biopharmaceutical firms, health providers, regulatory agencies, insurance payers, CROs, standards consortiums, and central laboratories.[28]

A second debatable question is whether, if the apparent automation of technical edit checks of pharmacovigilance offers systematic assurance, their definition, range, threshold determination, or data-mining statistical methodology associated with alert or signal triggering requires some level of standardizations to enable consolidated efforts, comparability, and interoperability. If so, achieving this goal requires multiple stakeholders’ contribution and collaboration, among which clinical safety science and statistical modeling matter experts will play ongoing critical roles in ensuring deliverability and objectivity. The primary purpose of these technical autochecks within GPVP are to send alerts or signals, based on pre-defined and configurable thresholds or ranges, to the reviewers e-mail box for assessment as to whether it is a true signal. It is vital that the clinical safety monitors be assured that any data or sets of data that may have a causal link to one of their drugs be detected as an alert for further evaluation by the clinical risk assessor.

The modern pharmacovigilance system will have the potential to identify and quantify adverse-event signals with unprecedented power and performance. Such data-mining capability coupled with improving standards will provide great benefits to optimize medications’ safety and benefit–risk relationships. Setting up the system to function and ensuring its interoperability with multiple other systems such as clinical data management system, coding applications, clinical trial management system, or product performance system will be a daunting task yet achievable, but making sure the alerts or signals it generates are epidemiologically rigorous and clinically valuable will be of paramount criticality. Ultimately, knowing what data mining numbers mean for practice, confirming potential signal or safety risk via further case report or case-series, and communicating that meaning effectively and promptly will present the biggest challenges of all. Collectively, modern pharmacovigilance system is a tool like all other IT ventures, and one still likely to be driven by humans.[28][27][20]

1. **Activity and Application of Biomedical Informatics**

From [Genetics](https://leverageedu.com/blog/bsc-genetics/) and Toxicology to Mycology and Radiobiology, there are scores of [branches of Biology](https://leverageedu.com/blog/branches-of-biology/) to specialize in. And out of the many, Bioinformatics is one of the intriguing fields which enables you to identify, evaluate, store, and retrieve biological information. Being an interdisciplinary field of study, it incorporates various facets of [Computer Science](https://leverageedu.com/blog/category/computer-science/), [Statistics](https://leverageedu.com/blog/category/statistics/), and [Biology](https://leverageedu.com/blog/category/biology/) to develop software applications for understanding the biological data like DNA sequencing, protein analysis, evolutionary genetics, etc. Not only restricted to [Medicine](https://leverageedu.com/blog/category/medicine/), but the [scope of Bioinformatics](https://leverageedu.com/blog/scope-of-bioinformatics/) is spread across Microbial Genome as well as in the field of [Agriculture](https://leverageedu.com/blog/category/agriculture/). So, in this blog, we will explore more such exciting applications of Bioinformatics.[29][30]

Bioinformatics has various applications in medicine ranging from research in genes, drugs to prevention. Let’s take a look at the applications of bioinformatics in medicine:

* 1. **Pharmaceuticals:**

 Bioinformatics researchers have played a quintessential role in pharmaceutical research especially for infectious diseases. Moreover, bioinformatics has also innovated personalised medicine research thus bringing new discoveries in terms of drugs that can be personalized to someone’s genetic pattern.

* 1. **Prevention:**

Just like pharmaceuticals, bioinformatics can be combined with epidemiology to create preventive medicine by understanding causes of health issues, community healthcare infrastructure, disease patterns, etc.

* 1. **Therapy:**

 Bioinformatics can also be useful for gene therapy especially for individual genes that have been adversely affected. This application of bioinformatics has been researched by genetics scientists who have found that someone’s genetic profile can be better with the help of bioinformatics.

* 1. **Drug Discovery**

Drug discovery is one of the main applications of Bioinformatics. [Computational biology](https://leverageedu.com/blog/computational-biology/), an essential element of bioinformatics help scientists to analyse the disease mechanism process and validate new and cost-effective drugs. If we consider the COVID 19 outbreak, bioinformatics can be effectively used to produce an effective drug at a low cost.

* 1. **Veterinary Sciences**

The course of research in Veterinary Science has achieved an advanced level with the help of Bioinformatics. In this field, the application of Bioinformatics ranges specifically focuses on sequencing projects of animals including cows, pigs, and sheep. This has led to the development in overall production as well as the health of livestock. Moreover, Bioinformatics has helped scientists to discover new tools for the identification of vaccine targets.

* 1. **Crop Improvement**

Another important application of bioinformatics is in crop improvement. It makes effective usage of proteomic, metabolomic, genetic, and agricultural crop production to develop strong, more drought-resistant, and insect-resistant crops. Thereby enhancing the quality of livestock and making them disease resistant.

* 1. **Gene Therapy**

A popular branch of Biology, Gene Therapy is a process through which genetic materials are incorporated into unhealthy cells in order to treat, cure as well as prevent diseases. Analyzing protein targets, identifying cancer types, evaluating data, assessing MicroRNA, etc are some of the applications of Bioinformatics in Gene Therapy.

* 1. **Biotechnology**

For those who want to establish a [career in Biotechnology](https://leverageedu.com/blog/career-in-biotechnology/) must know that there are a wide range of applications of Bioinformatics in this field. Apart from understanding the genes and genomes, the bioinformatics tools and programs are used to compare the gene pair alignment in order to identify the functions of genes and genomes. Furthermore, it is also used in molecular modelling, docking, annotation and dynamic, etc.

* 1. **Waste Clean up**

Another important application of bioinformatics is in waste clean up. Here, the primary objective is to identify and assess the DNA sequencing of bacteria and microbes in order to use them for sewage cleaning, removing radioactive waste, clearing oil spills, etc. Did you know that as per the Guinness Book of world records, Bacterium Deinococcus Radiodurans is considered as the world’s toughest bacterium?

* 1. **Microbial Genome**

Microbial Genomes comprises of all the genetic material including chromosomal and extra-chromosomal components of bacteria and eukaryotes. And when it comes to the application of Bioinformatics, this is an important area. Apart from evaluating genome assembly, Bioinformatics tools also help in conducting DNA sequencing for application in areas including health and energy.

* 1. **Evolutionary Studies**

One of the great American scientists, Theodosius Dobzhansky rightly said, “Nothing in biology makes sense except in the light of evolution.” In order to understand biological problems and improve the quality of life, evolutionary studies play a decisive role. Through bioinformatics, one can compare the genomic data of different species and identify their families, functions, and characteristics.

* 1. **Bioinformatics Tools**

Bioinformatic tools have helped in drug discoveries, veterinary sciences, crop improvement, forensics are many more fields. Different bioinformatics tools have their own applications. Bioinformatics applications include sequence analysis, molecular modeling, molecular dynamics, etc.[30][31][27]

1. **Future Prospect and Conclusion**

The bioinformatics assets can be modified to further improve the diagnostic and detection criteria and procedures in the healthcare sector. The employment of bioinformatics tools in the growing fields of pharmacovigilance and genomic sequencing holds great future benefits. Future transformations in the techniques and tools of bioinformatics can aid in better understanding drug resistance and microbial virulence, which can facilitate effective management of viral infections. There are numerous health disorders for which proper and reliable treatments are not yet available, such as cancer, HIV-AIDS, neurodegenerative diseases, etc. There is an absence of a significant research model in pharmacovigilance that would aid in providing a focused direction and scope of this field in the future, resulting in potential benefits. [31]

The bioinformatics-based computational techniques can facilitate the acceleration of the drug development criteria, which can further result in the development of more active therapeutic candidates with limited toxicity profiles. Furthermore, the decision-making tools and comprehensive models can aid in transforming the conventional processes of drug delivery from single target to ‘function first’ as well as phenotypic selection methods, targeting systematic networks. Taking into account the pandemic situation, the researchers can investigate and evaluate the SNPs associated with the affected host body, and computational primer design algorithms can be used to design modified forms of newer primers of genes or nucleotides. Therefore, the bioinformatics approaches would facilitate simulation, identification, and prediction of the progression of the disease and responses of the drug candidates, for elevating the uses, safety profiles, and impact of newer and existing drugs, thereby strengthening the healthcare system. Bioinformatics has accelerated the field of biomedical sciences and has potentiated the clinical and general aspects of the healthcare system. The review focuses on giving a detailed account of the significance of bioinformatics in the pharmaceutical industry and pharmacovigilance, followed by the fundamental assets of bioinformatics-based tools and databases in drug discovery and development. The value of translational bioinformatics approaches intensifies the development and discovery of suitable drug candidates, where the manuscript enlists numerous databases in tabular forms. Moreover, bioinformatics has been reported to be employed to accelerate microRNA research and clinical genomic sequencing, where it is assessed for its potential in -omic technologies and studies. The role of bioinformatics approaches in microbiology is explained owing to its significance in gene and drug discovery, proteomics, sequence data analysis, bacterial functional genomics, and the development of multi-drug resistant TB drugs, prophylactic agents, marine natural products, siderophores, and so on. In addition, the authors reveal the positive outcomes of this tech-driven strategy in the management of the current COVID-19 pandemic, where its involvement in next-generation sequencing, genome-wide association study, and computeraided drug design tends to strengthen the fight against the pandemic. In addition, the review aims to provide a clarified image of bioinformatics and invokes the necessity of technological tools, databases, and software, thereby attracting the readers and researchers to exhibit future assessment of this field to facilitate acceleration and elevated efficiency of the healthcare system.[32]

1. **Result and Discussion**

Inter-relationship of Pharmacovigilance and Biomedical Informatics Pharmacovigilance has developed a set of practical activities based on the combination of clinical needs, regulatory obligations, and epidemiologic methods. These activities have coalesced into defined skill sets over the past 1 to 2 decades, facilitated by the unprecedented innovative developments in biomedical informatics and a globalized economic environment, and driven by significant philosophical developments in regulatory thinking. Deliberative organizations such as CIOMS have focused on creating a common vocabulary and infrastructure and have established a record of unprecedented development through its working groups. Collaborative organizations such as European Network of Centres for Pharmacoepidemiology and Pharmacovigilance have built extensive structures on this foundation. Yet the essential tools for accomplishing these goals, which largely fall within the discipline of biomedical informatics, have not received much explicit attention in pharmacovigilance circles. In the pharmacovigilance literature of the past several years, 2 papers have drawn attention to informatics. described several topical pharmacovigilance issues that concern informatics, including data mining Internet-based data, recent success with the Mini Sentinel system, and the need for standards in dealing with large, population-based data- bases. focused attention on informatics as applied to adverse drug reaction reporting systems. In the informatics literature, articles are of note.[32][33]

The first, discussed building a data set of drug drug interaction information from publicly available sources.

The second, provides an overview of infrastructural frameworks and statistical methodologies that facilitate data mining in several international jurisdictions.

The third, in the closely related area of public health, provides a survey of advances in public health and epidemiology informatics based on a public health paradigm.

The fourth, in another closely related area of data sciences, discusses the research potential of having access to the clinical experience of hundreds of millions of patients across the globe through collaboration between observational health data sciences and informatics. The literature that is reflective of the scholarship at this interface has otherwise trailed the exponential growth of the disciplines independently.

* 1. **Biomedical Informatics Lens**

Model for identifying specific areas of biomedical informatics that interface with pharmacovigilance, and for highlighting those areas in need of attention. Explicit focus on this model can help to generate and to accelerate interest in setting an agenda for future work and development of work products to meet regulatory needs and commercial interests. The typical pharmacovigilance workflow that has evolved includes the following basic components: single case collection and standardization, database storage, regulatory reporting, signal monitoring, signal generation, and signal strengthening and, finally, collection of relevant information for periodic reporting. However, there is the presumption that the data from this workflow represent the universe of available data that can contribute to an actionable determination, and for which the sponsor can be held accountable with regard to regulatory compliance. Social media and massively large linked datasets disrupt this presumption. They are newly available sources of relevant data that are not dependent on CIOMS reports completed by health care providers or consumers. These data are representative of a new phase in the digitization of health care, and they are elements of a new, deep well of near-limitless, passively generated information from highly heterogeneous sources. The data may come from patients themselves, from claims datasets, or from health surrogates such as smart phone applications and wearable, biomarker sensors. They represent challenges both in terms of the connectivity and other compatibility aspects of the technologies and the assessment of the potential information through conventional pharmacovigilance methods, and they are largely manageable, also through the use of methodologies developed in the field of informatics. However, challenges remain  
nonetheless. For example, the US Food and Drug Administration, in its White Paper on the topic, identifies continuing issues, including heterogeneity of report quality, over-reporting, and duplicate reporting, all of which contribute to the significant occurrence of false-positive signals. Also notably, rare reports may represent the most significant challenge. Thus, judgment remains a crucial human contribution to the overall signal management process that will continue to be a necessary complement to the progress in biomedical informatics innovations. It is reasonable to ask what the evidence is for the benefits of this technology. For example, data mining, utilizing either frequentist or Bayesian approaches for the detection of adverse events in Health Authority maintained databases, has been successful in properly identifying drug-event pairs.

As a result, the pharmaceutical industry has invested significant resources in commercially supported activity over the past decade. However, a recent systematic review of 49 studies of drug-event pairs showed that none of the safety signals have been detected exclusively by means of data mining methods. Further, new types of questions follow. With processed-data information that is qualitatively different from explicitly generated adverse-events reports, what responsibility does the sponsor have to mine sources that, unlike the well-structured and pharmacovigilance-oriented data models of US FDA Adverse Event Reporting System, Eudravigilance, and VigiBase, represent significant challenges to conventional pharmacovigilance approaches because they are constantly changing in nature through reconfiguration, exchange, and/or merger? When the amount of information exceeds anything that could be completely or comprehensively processed by an individual sponsor, how do the rules of sponsor accountability and compliance apply? Thus, this would be an opportune time to discuss how these sources, and other sources still on the drawing board or in the imagination, of data and information are likely to affect the core components of pharmacovigilance, as they are presently practiced.

* 1. **Generation and Capture of Data**

This category, in particular, observational patient health care data, smartphone applications, digital bio- markers, wearable and other general wellness devices, includes the areas most intensively under development in the market today. Patients with chronic diseases who are taking multiple medications on long-term bases represent a special challenge to the discernment of signals of interest and the development of actionable assessments. These circumstances also represent an opportunity to develop the types of linkages of these varied sets of source data that can allow for particular attention to the potential for obtaining longitudinal data. At least 1 biotech/pharmaceutical company has partnered with a technology company to explicitly bring increased speed, greater capacity, and new analytic capabilities to the full life cycle of pharmacovigilance activities. All of these activities have to take into account privacy, variably compatible platforms, the need for standardization, analysis for trends, and assessment for signals of interest. Interest in the practical and ethical issues concerning control and access will also continue to grow.

An example of the potential benefits is illustrative. A pharmaceutical company has designed an application to take advantage of the technological capabilities of the smartphone in making multiple determinations per day of 6 parameters for patients with Parkinson disease: voice, balance, gait, dexterity, rest tremor, and postural tremor. By streaming these daily quality-of-life metrics in real-world conditions to a central command center, a patient’s medications can be readily and confidently fine-tuned. In the near future, it is likely that an algorithm will perform this task, and do so even more efficiently. On a population level, a benefit risk assessment can take on a longitudinal dimension for these expanded daily metrics that can have implications for drug development. Transversal Activities Cross-cutting activities are not presented in because they do not readily fit into the informatics model, but they are worth mentioning because of their general, relative prominence in health care informatics and their gradual emergence in pharmacovigilance. These include the following: Metrics for standard measures of progress and controls Dashboards for management briefings and status of governance activities Tracking for daily management of workflow Security for every aspect of corporate and individual privacy with regard to data and information management and control Potential for Broader Engagement Future prospects are bright at all levels. Existing professional organizations in these disciplines can contribute to developments by sponsoring cross functional workshops, establishing working groups and special interest groups around hot topics and by creating sections of the organization dedicated to the cross-functional aspects of pharmacovigilance and biomedical informatics that are of interest to its membership. Journals may also call for special topics to spur interest.

1. **References**
2. Gilbert D., ‘Bioinformatics software resources’. Brief. Bioinform. 2004; 5, 300–304.
3. Huang D.W., Sherman B.T., Lempicki R.A., ‘Bioinformatics enrichment tools: Paths toward the comprehensive functional analysis of large gene lists’. Nucleic Acids Res. 2009; 37, 1–13.
4. Teufel A., Krupp M., Weinmann A., Galle P.R., ‘Current bioinformatics tools in genomic biomedical research’. Int. J. Mol. Med. 2006; 17, 967–973.
5. Luscombe N., Greenbaum D., Gerstein M., ‘Review: What is bioinformatics. An introduction and overview’. Yearb. Med. Inform. 2001; 1, 2.
6. Mandal S., Mandal S.K., ‘Rational drug design’. Eur. J. Pharmacol. 2009; 625, 90–100.
7. Katara P., ‘Role of bioinformatics and pharmacogenomics in drug discovery and development process’. Netw. Model. Anal. Health Inform. Bioinform. 2013; 2, 225–230.
8. Thibaut U., ‘Bioinformatics and rational drug design: Tools for discovery and better understanding of biological targets and mode of action of drugs’. Scand. J. Gastroenterol. 2002; 37, 95–99.
9. Ferrer C., Orozco M., ‘Use of Bioinformatics tools for the annotation of disease-associated mutations in animal models’. Proteins Struct. Funct. Bioinform. 2005; 61, 878–887.
10. Moore J.H., Rhodes C.H., ‘Integration of molecular and cellular pathogenesis: A bioinformatics approach’. In Molecular Pathology Amsterdam, The Netherlands, 2009; 219–224.
11. Lyall A., ‘Bioinformatics in the pharmaceutical industry’. Trends Biotechnol. 1996; 14, 308–312.
12. Dal Pan G.J., ‘Ongoing challenges in pharmacovigilance’. Drug Saf. 2014; 37, 1–8.
13. Bhangale R., Vaity S., Kulkarni N., ‘A day in the life of a pharmacovigilance case processor’. Perspect. Clin. Res. 2017; 8, 192.
14. Bungau C., Blaga F., Gherghea C., ‘Kaizen Implementation for Cost Reduction in Manufacturing Process Product’. Driver Control Board, University of Oradea, Romania, 2014; pp. 55–58.
15. Daina L.G., Sabau M., Daina C.M., Neamt u, C. Tit, D.M. Buhas, C.L. Bungau, C. Aleya, L. Bungau, S. ‘Improving performance of a pharmacy in a Romanian hospital through implementation of an internal management control system’. Sci. Total Environ. 2019; 675, 51–61.
16. Grewal, A. Kataria, H. Drawan, I. ‘Literature search for research planning and identification of research problem’. Indian J. Anaesth. 2016; 60, 635–639.
17. Murray-Rust, P. ‘Bioinformatics and drug discovery’. Curr. Opin. Biotechnol. 1994; 5, 648–653.
18. Yan Q., ‘Translational Bioinformatics and Systems Biology Methods for Personalized Medicine’ Academic Press: Cambridge, MA, USA, 2017.
19. Boland M.R., Jacunski A., Lorberbaum T., Romano J.D., Moskovitch R.,Tatonetti N.P. ‘Systems biology approaches for identifying adverse drug reactions and elucidating their underlying biological mechanisms’. Wiley Interdiscip. Rev. 2016; 8, 104–122.
20. Prathipati P., Mizuguchi K. ‘Systems biology approaches to a rational drug discovery paradigm’. Curr. Top. Med. Chem. 2016; 1009–1025.
21. Chautard E., Thierry-Mieg N., Ricard-Blum S. ‘Interaction networks: From protein functions to drug discovery. A review. Pathol’. Biol. 2009; 57, 324–333.
22. Vlasblom J., Jin K., Kassir S., Babu M. ‘Exploring mitochondrial system properties of neurodegenerative diseases through interactome mapping’. J. Proteom. 2014; 100, 8–24.
23. A Dunn D., Apanovitch D., Follettie M., He T., Ryan T. ‘Taking a systems approach to the identification of novel therapeutic targets and biomarkers’. Curr. Pharm. Biotechnol. 2010- 11; 721–734.
24. Vandamme D., Minke B.A., Fitzmaurice W., Kholodenko B.N., Kolch W. ‘Systems biology-embedded target validation: Improving efficacy in drug discovery’. Wiley Interdiscip. Rev. 2014, 6, 1–11.
25. Ryall K.A, Tan A.C. ‘Systems biology approaches for advancing the discovery of effective drug combinations’. J. ChemInform. 2015; 7.
26. Wathieu H., T Issa N., W Byers S., Dakshanamurthy S. ‘Harnessing polypharmacology with computer-aided drug design and systems biology’. Curr. Pharm. Des. 2016- 22; 3097–3108.
27. Kunz M., Liang C., Nilla S., Cecil A., Dandekar T. ‘The drug-minded protein interaction database (DrumPID) for efficient target analysis and drug development’. Database 2016.
28. Schreyer A.M., Blundell T.L. ‘CREDO: A structural interactomics database for drug discovery’. ‘Database’ 2013.
29. Wang C., Hu G., Wang K., Brylinski M., Xie L., Kurgan L. ‘PDID: Database of molecular-level putative protein–drug interactions in the structural human proteome’. ‘Bioinformatics’ 2016; 32, 579–586.
30. Beninger P., ‘Pharmacovigilance: An Overview’’ Clinical Therapeutics. 2018; 1991-2004.
31. Menniti M., Menniti A., Patanè M., Esposito S., Giofrè C., Aiello R., Russo E. ‘Informatics applied to pharmacovigilance: Future perspectives’ Journal of Pharmacology and Pharmacotherapeutics, 2013; S43-S45.
32. Beninger P., Ibara A.M. ‘Pharmacovigilance and Biomedical Informatics:A Model for Future Development’ Clin Ther. 2016; 2514–2525.
33. Lu Z. ‘Information technology in Pharmacovigilance: Benefits, challenges, and future directions from industry perspectives’ Drug Healthcare and Patient Safety 2009; 35–45.
34. Rohilla A., SinghN., KumarV., Sharma M.K., Dahiya A., Kushnoor A. ‘Pharmacovigilance: Needs and Objectives’. Journal of Advanced Pharmacy Education & Research 2012 ;2, 201-205.