Commentary

Pharmacovigilance and Biomedical Informatics: A Model for Future Development

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ABSTRACT

Purpose: 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.

Methods: For this review, we searched [publication trend for the $\log_{10}$ value of the numbers of publications identified in PubMed] using the key words [informatics (INF), pharmacovigilance (PV), pharmacovigilance þ informatics (PV þ INF)], for [study types] articles published between [1994-2015]. We manually searched the reference lists of identified articles for additional information.

Implications: Biomedical informatics has made significant contributions to the infrastructural development of pharmacovigilance. However, there has not otherwise been a systematic assessment of the role of biomedical informatics in enhancing the field of pharmacovigilance, and there has been little cross-discipline scholarship. Rapidly developing innovations in biomedical informatics pose a challenge to pharmacovigilance in finding ways to include new sources of safety information, including social media, massively linked databases, and mobile and wearable wellness applications and sensors. With biomedical informatics as a lens, it is evident that certain aspects of pharmacovigilance are evolving more slowly. However, the high levels of mutual interest in both fields and intense global and economic external pressures offer opportunities for a future of closer collaboration. (*Clin Ther*. 2016;38:2514–2525)

Key words: adverse drug reactions, biomedical informatics, Internet, pharmacoepidemiology, pharmacovigilance.

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, p. 7."[1] As described by Grootheest, pharmacovigilance rapidly developed on a worldwide basis as a defined discipline following the thalidomide tragedy in 1961.[2] Since then, the requirements, tools, and methods used in pharmacovigilance have matured into a well-developed skill set. Further, there have been many

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useful developments with direct contributions to global public health (eg, the establishment of the World Health Organization Pharmacovigilance Programme,[3] the development of Council for International Organizations of Medical Sciences (CIOMS) Working Group reports[4]). 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.[5–7] 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."[8] 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.[9]

Driven primarily by nonpharmacovigilance 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.[10] 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. 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.

MATERIALS AND METHODS

For this review, we searched [publication trend for the $\log_{10}$ value of the numbers of publications identified in PubMed] using the key words [informatics (INF), pharmacovigilance (PV), phar-macovigilance þ informatics (PV þ INF)], for [study types] articles published between [1994-2015]. We manually searched the reference lists of identified articles for additional information. Articles that were [exclusion criteria, eg duplicates] were excluded.

RESULTS

The literature search yielded [406,285] articles, of which [4733] were included in the present review. [702] articles were excluded because [all articles were included in the present review].

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. For comparison, we note that for home computer storage capacities, we have moved from gigabyte (10^9 bytes) into terabyte (10^{12} bytes) capacities. In the commercial realm, we are in the petabyte (10^{15} bytes) range with Facebook, for example, building out to exabyte (10^{18} bytes) storage capacity,[11] and in cybersecurity, government intelligence agencies are venturing into zettabyte (10^{21} bytes) storage capacity, the amount of data that can be stored on 250 billion DVDs.[12]

With ample speed and capacity have come opportunities for the explicit application of the basic concepts

Table I. Pharmacovigilance activities and the application of biomedical informatics.

Pharmacovigilance Category	Definition
Technological or methodologic maturity	
High (H)	In common practice; well-supported by research and practical use
Medium (M)	Established research with practical use in at least 1 area/industry
Low (L)	Primarily research based, with some application to industry or academic research area
Pharmacovigilance maturity	
Common	In common, global and ubiquitous use in standard pharmacovigilance use and applications; typically has been in use for more than several years
Growing	Has been used in mainstream pharmacovigilance work and applications although use may be limited; approach or technology only recently applied to pharmacovigilance use cases even though technology or methods themselves may be well established
Emerging	Limited use to date in standard pharmacovigilance practice and applications; support for use found primarily in research publications or anecdotal use; use and application may be emerging, but not yet widely adopted
Speculative	Application to pharmacovigilance theoretical only or supported by limited research; no adoption as of yet in standard pharmacovigilance practice

of informatics to pharmacovigilance: generation of information, storage, retrieval, use, decision making, computation, and sharing/communication.[8] These categories provide a useful framework for organizing pharmacovigilance activities (Tables I and II).

Innovations have led health care to the cusp of what McKinsey[33] 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 Table II 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 (Table I), with the intent of drawing attention to those areas that may benefit from further development.

Contributing Factors

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. These are worth brief mention.

Increase In Awareness, Interest, and Scholarship

Evidence of the significant potential for the application of informatics to pharmacovigilance can be seen in the increasing volume of scholarship. Here, the log-based numbers of publications in the Figure show how the literature on pharmacovigilance and in informatics separately has grown exponentially over the past several decades, but at substantially lower rates in the sparse overlap of pharmacovigilance + informatics. This sparse rate of overlap suggests that thoughtful scholarship has been emerging over the past several decades within each discipline individually but, as yet, has shown less recognition of the potential for explicit cross-fertilization.

Table II. Primary pharmacovigilance application in biomedical informatics context.

Application	Technologies/Methods	Tech Maturity	Pharmacovigilance Maturity
Representation of data/storage			
Representation of pharmacovigilance/AE data: Traditional data models common; emerging data models for "big data" still emerging for applications in pharmacovigilance	Relational database technology; industry-standard pharmacovigilance systems; E2B data model for adverse events data; common data model (Sentinel); semantic tools for data linking (eg, Hadoop,[13] Gliimpse [recently acquired by Apple][14])	H/M	Emerging/common
Generation and capture of data			
Noncomputable information; data capture; single case reporting (eg, CIOMS, MedWatch); single case reporting; translation; noncomputable pharmacovigilance information, such as pdf of AE reports in which an image is sent but the information is locked in the image vs available to be read by computers	Paper/facsimile; call center technologies; electronic submission of noncomputable information; e-mail, pdf files; human expertise relied on heavily for quality	H	Common
Computable information: E2B submissions of ICSRs (global industry use)	Computable structured information (Standard Generalized Markup Language [SGML] [ISO 8879];[15] Extensible Markup Language [XML], etc); web services; Natural Language Programming (see Decision making)	H	Common
Claims data	Relational Data Base, linking, statistical programming	H	Common
Observational health care data; clinical trial; postmarketing for single case reports and trending, hypothesis testing (eg, Sentinel); for clinical trial data transferred in digital form, still needs review for ICSRs; Sentinel uses electronic health records and common data model to test tolerability hypotheses	EHRs; registries; mobile; web services (eg, JavaScript Object Notation;[16] application program interfaces)[17]	H	Emerging
Smartphone applications: applications for reporting or for specific conditions (eg, MedWatcher[18] smart phone application)	Mobile technology; web services	M	Emerging
"Digital biomarkers": use as "digital biomarkers" in specific diseases (eg, Parkinson disease) or for specific physical analogues (eg, cardiac monitoring)	Wearable sensor technology (eg, Accelerating Medical Innovation[19] [sponsored by NASA])	L	Speculative
Social media (broad term involving data capture, storage, retrieval, decision making)	Various mobile, web applications (eg, Medwatcher,[18] Epidemico[20])	H	Emerging

(continued)

Table II. (continued).

Application	Technologies/Methods	Tech Maturity	Pharmacovigilance Maturity
Access and retrieval			
Linking various types of data to generate signals/test hypotheses; data models, coding (see Representation)	Linked data (eg, Uniform Resource Identifier,[21] Resource Description Framework,[22] Social Psychophysiological Research & Quantitative Methods Laboratory,[23] DeepMind[24])	H	Growing
Computation			
Finding associations in data, pattern matching and recognition; no use yet in pharmacovigilance	Artificial neural networks;[25] Bayesian analyses[26]	L, M	Speculative; emerging/ growing
Emerging/data provenance; no use yet in pharmacovigilance; used in banking, personal EHRs, models for use in computed tomography, other uses	Blockchain[27–30]	M	Speculative
Decision making			
Translation; detection; social media; literature surveillance; used in detection from unstructured text; used in detection and triage of AEs from social media	Natural Language Programming (eg, NLP[31])	H	Emerging/growing
AE detection; disproportionality signal detection; AE classification; triage; conventional use in epidemiology detection of signals in industry databases; and literature searching; recent use in automated detection of AEs from clinical systems; used in triage of AEs from social media	Algorithmic computing	H	Growing/common
Hypothesis generation and testing; common: Freedom of Information Act on established pharmacovigilance datasets; claims data; growing: combined use of observational datasets of all types; requires development of novel analytical techniques	Large datasets/data mining/algorithms, pattern matching; machine learning[32]	H	Growing/common
Sharing/communication			
Written	Text to stakeholders; early warning to Health Authorities	H/M	Speculative; emerging

CIOMS = Council for International Organizations of Medical Sciences; ICSRs = individual case study reports.

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 (CIOMS IV[34]) and Signal Management (CIOMS VIII[35]).

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.[36,37] 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 nonprescription 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 on-line forums to obtain answers that span over a range of sophistication and detail.[38]

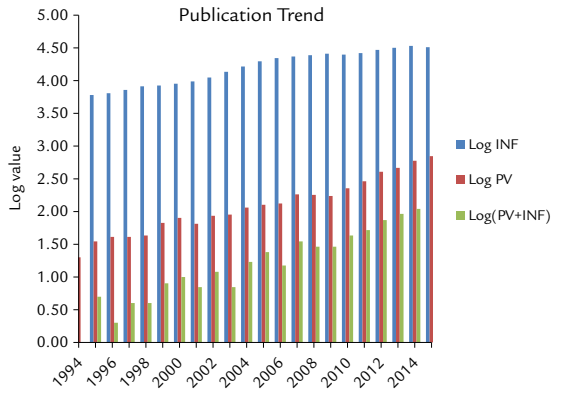

Figure. Publication trend for the $\log_{10}$ value of the numbers of publications identified in PubMed by the search terms *informatics* (INF), *pharmacovigilance* (PV), and *pharmacovigilance* + *informatics* (PV + INF), beginning from the year of the publication of the first article to include PV + 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.[39,40] 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.[20,41]

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.[42] 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.[43]

These same offshore businesses are also moving into the realm of periodic report preparation, including periodic benefit–risk evaluation reports, with success.[43] 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.[44] The European Union has responded to this challenge through the creation of the Innovative Medicines Initiative,[45] 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.[46]

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[47] and social media[48] 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.[49] 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.[50] 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.

Mobile/Wearables

Health care providers, payers, and biotech/pharmaceutical companies are all interested in using data generated by mobile devices and wearable sensors.[51] 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.[19] 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.[52] 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.

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.[27] 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.[28] There are suggestions for the use of blockchain technology to secure electronic health record, clinical trial, and personal health care data,[29] and the US government has already sponsored a challenge for the use of blockchain in health care application.[30]

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.[53] 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. Dal Pan[10] 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 databases. Menniti et al[54] focused attention on informatics as applied to adverse drug reaction reporting systems.

In the informatics literature, 4 articles are of note. The first, by Ayvaz et al,[55] discussed building a dataset of drug–drug interaction information from publicly available sources. The second, by Shibata and Hauben,[56] provides an overview of infrastructural frameworks and statistical methodologies that facilitate data mining in several international jurisdictions. The third, by Dixon et al,[57] 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, by Hripcsak et al,[58] 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 2 disciplines independently.

Biomedical Informatics Lens

Tables I and II provide a 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[59] 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.[60] 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.[61]

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.

Generation and Capture of Data

This category, in particular, observational patient health care data, smartphone applications, digital biomarkers, 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.[62] 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.[63]

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.[64] 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 Tables I and II 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[65]

Dashboards for management briefings and status of governance activities[66]

Tracking for daily management of workflow[67]

Security for every aspect of corporate and individual privacy with regard to data and information management and control[68]

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.

CONCLUSIONS

Biomedical informatics has played a key, often near-invisible, role in developing much of the technological infrastructure of pharmacovigilance. The pace of change is accelerating, with influence expected to deepen in the field of health care. One approach would be for those in the field of pharmacovigilance to recognize that we are living in a world in which possibly useful information is ubiquitous, coming from very many, highly heterogeneous sources. Thus, pharmacovigilance should consider developing structures to facilitate its evolution as a discipline from its past course of largely unstructured changes to a more deliberate, prospective approach for adapting to the changes that are underway. The use of biomedical

informatics as an organizing principle has the potential to facilitate this process.

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CONFLICTS OF INTEREST

The authors have indicated that they have no conflicts of interest with regard to the content of this article.

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