Developing a Bioinformatics and Medication Management Research Network

By Gene D. Morse, PharmD, Werner Ceusters, MD, Russell Bessette, MD, Thomas Furlani, PhD, Ranjit Singh, MD, Amy Hayward, BS, James Notaro, RPh, PhD, Linda Catanzaro, PharmD, Karl Fiebelkorn RPh, MBA, Anthony Billittier, MD, Daniel Porreca, Bruce A. Holm

Abstract

The Institute of Medicine has identified the opportunities that may enhance the quality of our health care system and enhance patient safety. In addition to emphasizing evidence-based medication use, transitioning the current medication use system to one that integrates health information technology through the use of electronic health records, ePrescribing, bar code technology and personal medication records will be a key component of future multidisciplinary models. We have established a Bioinformatics and Medication Management Research Network (BMMRN) comprised of a statewide collaborative effort with a bioinformatics infrastructure that will facilitate the design and implementation of research in this area. Our initial efforts are examining: 1) systems and data transfer methods used across health systems, 2) optimal communication approaches that are compliant with state regulations, 3) novel design criteria for an ontology that will facilitate data collection and interpretation, 4) the use of a central computing facility to facilitate communication among institutions. The BMMRN coordinating center is located in the New York State Center of Excellence in Bioinformatics and Life Sciences at the University at Buffalo.

Background

The Challenge of Providing Pharmacotherapeutic Individualization for Patients: Pharmacotherapeutic individualization is an approach to drug therapy that considers patient-specific characteristics to optimize therapeutic interventions. The initial factors involved in pharmacotherapeutic individualization include those that contribute to the ability of a patient to access, understand and participate in their disease treatment. An additional set of factors including an individual patient's pharmacokinetic characteristics, pharmacodynamic responses and pharmacogenetic variation also are considered to be important factors that contribute to the therapeutic response to a medication. Furthermore, the drug development process that leads to medication approval, usually results in the provision of fixed doses (except for certain pediatric and oncology medications), providing the same prescribed dose to all patients. Additional factors such as co-morbidities contribute to medication management. These broad areas within the field of clinical pharmacology are now recognized as integral research areas in all drug development programs that strive to identify patients that are most likely to derive therapeutic benefit with minimal toxicity. These "individualization" factors provide the rationale for the broad profiling of drug-drug interactions and form the basis for the clinical measurement of drugs in therapeutic drug monitoring (TDM) programs. *Clinical pharmacogenomics* is the application of genetic tests to identify patient characteristics that may place an individual at risk for drug-drug interactions, serious adverse drug effects or a suboptimal response to treatment. While clinical pharmacogenomics is now included in most drug development programs, the clinical application of genomic testing will require additional clinical investigation to identify the patients that will benefit most (positive or negative predictive value). In addition, education of clinicians as to optimal use genomic testing will also be a key factor in successful clinical translation of genomics.

The extensive amount of pharmacokinetic, pharmacodynamic and pharmacogenomic data that is now included in product labeling information has led to an acute need for health professionals to receive education and evidence-based guidance in order to optimize the translation of clinical pharmacology information into individualized therapeutic approaches. Furthermore, recent recommendations from the Institute of Medicine have advocated greater integration of information technology and multidisciplinary approaches to facilitate evidence-based pharmacotherapy, reduce medication errors and enhance patient safety.

Bioinformatics, Ontology and Medication Management

Diverse data sources have resulted from the expansive use of medications in society, with data residing in multiple storage sites including hospitals, medical practices, pharmacy dispensing records and health insurance claims databases. This volume of data necessitates that automatic approaches be integrated to augment the rate and accuracy of data interpretation. In this project, tasks such as information retrieval, information extraction, and data mining will be facilitated through a linked semiotics and ontology approach.[1,2]

Prescribing Errors: In order to rectify the ubiquitous problems in our system of healthcare and the well-being of our citizens, human error must be reduced by creating a robust system that is capable of learning, evolving, and recognizing errors, as well as predicting adverse drug reactions (ADRs)

and/or contraindications.[3-5] Prescribing errors by providers are considered to be the most common type of avoidable medication error.[6-11] The National Academy of Sciences estimates that at least 1.5 million Americans are sickened, injured or killed each year by errors in prescribing, dispensing and taking medications, and months after the publication of this report, the Institute of Medicine confirmed these numbers. Following up on its influential 2000 report on medical errors of all kinds, the institute, a branch of the National Academies, undertook the most extensive study ever of medication errors in response to a request made by Congress in 2003 when it passed the Medicare Modernization Act. The report found errors to be not only harmful and widespread, but very costly as well. The extra expense of treating drug-related injuries occurring in hospitals alone was estimated conservatively to be $3.5 billion a year.

Medication Dispensing Errors: In addition to prescribing errors, the second most costly (in terms of both fiscal and human loss) to the current system of operation are dispensing errors at the pharmacy level.[3] The national awakening of healthcare professionals to medication safety issues is evidenced by the reaction to the Institute of Medicine's report To Err Is Human. This report stimulated discussion of the fundamental questions "Is there a dispensing error problem?" and "If so, what is its nature and magnitude?" Answering these questions is important for identifying needed interventions (e.g., automation, training) and justifying their associated expense. Case studies using observational and auditing systems in outpatient pharmacies have detected error rates ranging from 0.2% to 10%. Using conservative estimates of a 1% dispensing error rate and an annual total of 3 billion dispensed prescriptions, a projected 30 million errors would occur each year in United States.

Pharmacovigilance: The third most costly aspect of the current system is what is loosely termed pharmacovigilance, the science of collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medications with a view to identify new information about associated hazards and to optimally prevent harm to patients. Less common side effects and Adverse Drug Reactions (ADRs) are often unknown at the time a drug enters the market. Post marketing pharmacovigilance uses tools such as data mining and investigation of case reports to identify the relationships between drugs and ADRs. Spontaneous reporting is the core data-generating system of international pharmacovigilance but the resulting reports are almost always submitted voluntarily. One major weakness is under-reporting, though the figures vary greatly between counties and in relation to minor and serious ADRs. A system that removes the human error component and automates the process of reporting may be the key to further improving the quality of life of patients receiving medications.

Bioinformatics and Medication Management Research Network (BMMRN): The BMMRN was developed by the New York State Center of Excellence in Bioinformatics and Life Sciences (CoEBLS) and the University at Buffalo (UB) School of Pharmacy and Pharmaceutical Sciences (UB-SPPS) to establish a bioinformatics infrastructure that conducts medication management research in areas that include health information and health care technology innovation. The Patient Safety Center (PSC) of the NYS Department of Health has formalized a collaboration with CoEBLS and UB-SPPS to provide a coordinating center for statewide initiatives that address patient safety and reduction in medication errors through ePrescribing. The Center for Computational Analysis in the CoEBLS provides the central repository for BMMRN database. The Center for Computational Research is a leading academic supercomputing facility that maintains a high-performance computing environment, high-end visualization laboratories, and support staff with expertise in scientific computing, software engineering, grid computing, visualization, advanced database design, and networking. Our Ontology Research Group has published extensively in areas such as Electronic Health Records, Expert Systems, Natural Language Understanding and Ontology. In 2005, the group introduced a radically new approach to data management called "Referent Tracking" (RT), which rests on the principle that globally unique and singular identifiers should be given to all entities in reality about which data are collected in a database. In contrast to other approaches, RT allows integration between data at different levels of abstraction and granularity, a key issue of the BMMRN work plans.

Clinical Medication Management Programs: UB SPPS has been developing a number of pharmacist-directed, multidisciplinary medication management programs since early 2000. The activities of these programs include individual patient visits with the pharmacist, electronic medical record reviews, prospec-

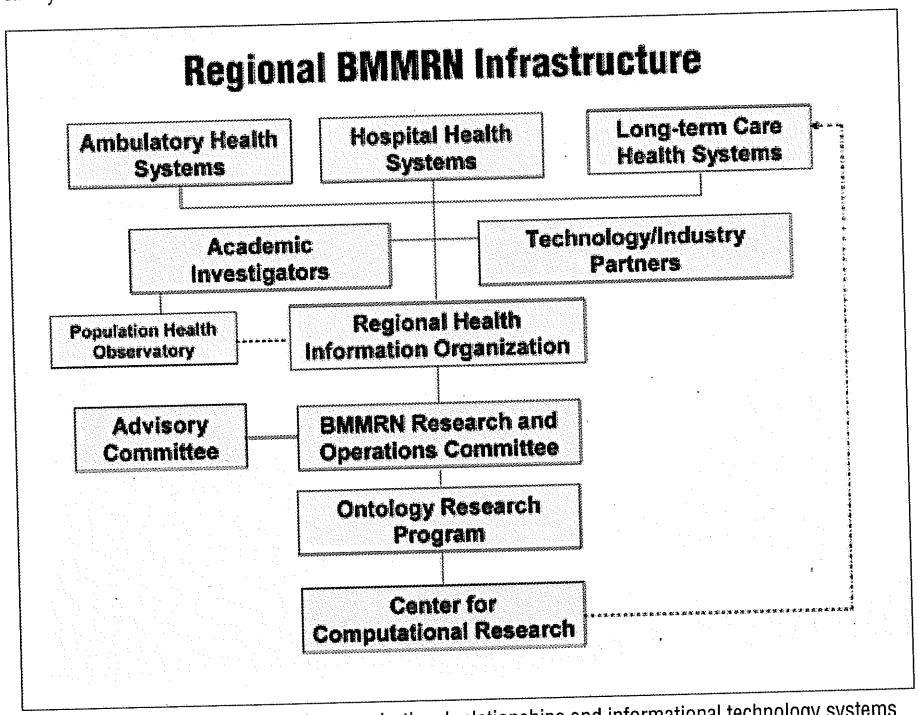

Figure 1: Schematic illustrating the organizational relationships and informational technology systems that contribute to the planned regional BMMRN "hubs".

tive medication reviews, and the provision of evidence-based pharmacotherapy recommendation communicated through individual electronic or printed responses to providers. Metrics to quantify clinical outcomes are developed within each program and input is sought from health insurance plans as to outcomes that are accepted as best practice for selected disease state management. Metrics to quantify economic aspects of the program are also adapted from published literature that utilized incremental costs associated with benefits derived from attaining unit decrements in the outcome metrics.

The UB Pharmacotherapy Information Center (PIC) provides a central resource to the BMMRN for evidence-based medication and drug class reviews. A joint effort between the UB SPPS and the Health Sciences Library, the PIC has been established as a mechanism for integrated education and research opportunities related to medication use. Training of students in the Doctor of Pharmacy program as well as post-doctoral pharmacy residents in the UB residency programs has been incorporated as they conduct supervised pharmacoinformatics activities.

We anticipate that the pilot project will lead to an efficient infrastructure that will be well-positioned to conduct collaborative clinical and translational research projects. This growth of this collaboration is well timed in that new approaches to systems-based translational research and a new collaborative emanating from HRSA are encouraging the development of programs similar to the BMMRN enhance patient safety through clinical pharmacy programs. An overall summary of our vision for regional BMMRN "hubs" is provided in Figure 1. Our current project will complete an analysis to determine the optimal approach to organizing the collaborative group of hospital practitioners, community pharmacies and health information technology applications that will lead to the multi-site infrastructure. The information to be collected for each regional unit/program will include regional hospitals and health care facilities with electronic health records that also have ePrescribing capabilities, regional investigators with an interest in participating in a collaborative research project, community practitioners with an interest and capability to provide patient outcomes, and software and hardware capabilities for contributing to research activities. Some of the potential research questions to be addressed by the BMMRN are outlined in Figure 2.

The BMMRN mission encompasses recent

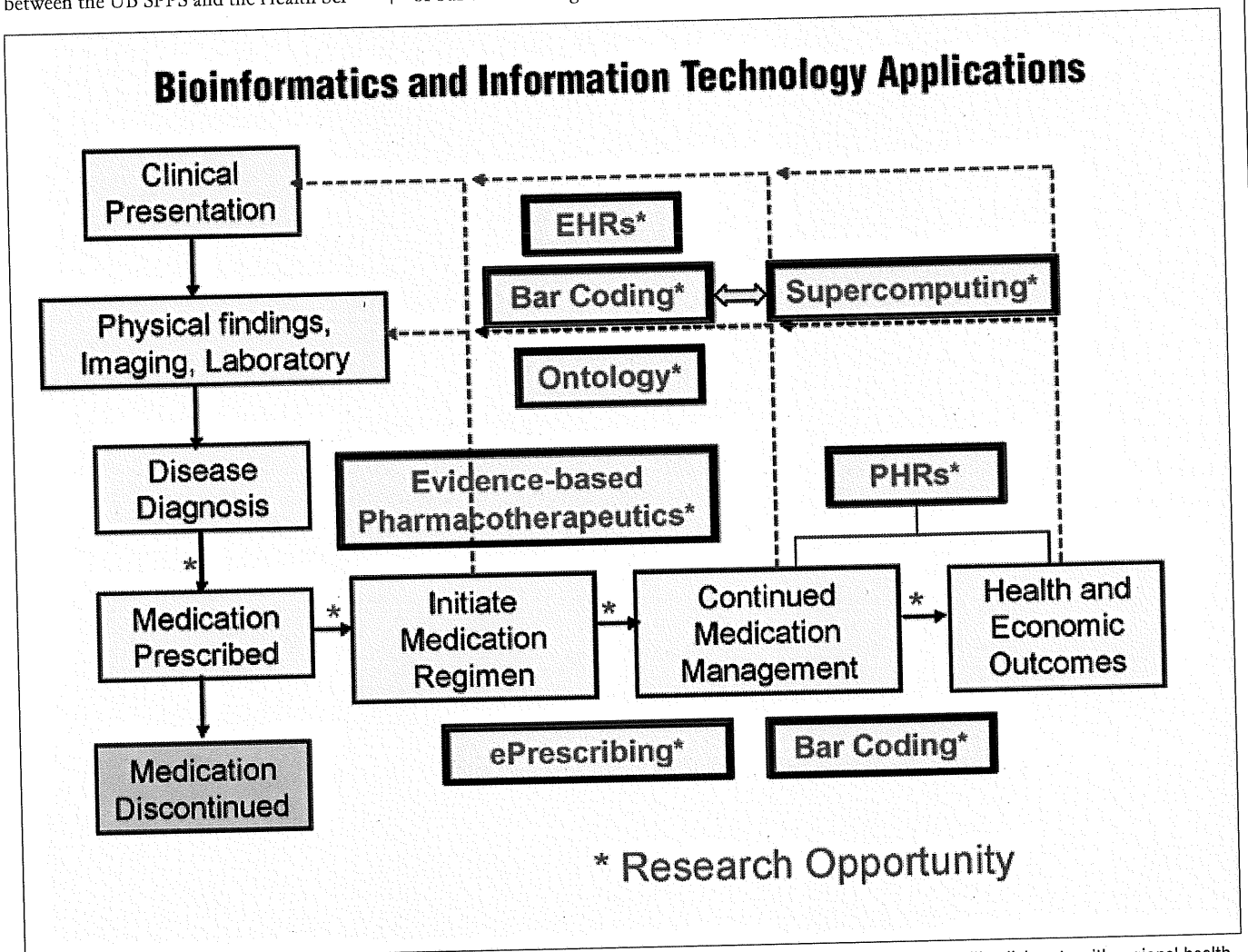

Figure 2: Diagram illustrating the development of a Bioinformatics and Medication Management Research Network that will collaborate with regional health systems and medication management programs.

statutes, regulations and policies including Medicare Part D Prescription Drug Coverage, FDA bar code regulations, JCAHO 2008 National Patient Safety Goals, IOM Preventing Medication Errors, 2007 Report Federal ONCHIT legislation, AHRQ and CMS Pharmacy Quality Alliance. In addition, CMS Pay for Performance Never Events Reimbursement Model and the Federal Patient Safety and Quality Improvement Act which established Patient Safety Organizations (PSO) are addressed by the BMMRN.

Discussion

Medication management has been recognized as an important component of the health care system that requires integration of biomedical informatics, a multidisciplinary approach and the inclusion of pharmacists as members of the healthcare team that can facilitate pharmacotherapeutic individualization. Pharmacotherapeutic individualization is an approach to drug therapy that emphasizes the characteristics of each patient when a therapeutic intervention is required and utilizes a comprehensive approach to medication prescribing and monitoring.[23-25] The initial factors involved in pharmacotherapeutic individualization include those that contribute to the ability of a patient to access, understand and participate in their disease treatment. Subsequently, an additional set of factors including an individual patient's pharmacokinetic characteristics, pharmacodynamic responses and pharmacogenetic variation contribute to the therapeutic response to a medication. The program we have developed includes each of these factors, although selected ones such as pharmacogenetics remains at the interface of practice and research. While methods to identify interindividual differences in pharmacokinetics, pharmacodynamic responses and pharmacogenetics may contribute to individualization, additional complicating factors such as co-morbidities also contribute. These broad areas within the field of clinical pharmacology are now recognized as integral aspects of medication management as the considerable amount of pharmacokinetic, pharmacodynamic and pharmacogenetic data that is now included in product labeling information has led to an acute need for health professionals to receive education and evidence-based guidance in order to optimize therapeutic strategies. Recent recommendations from the Institute of Medicine have advocated greater integration of information technology and multidisciplinary approaches to reduce medication errors and enhance patient safety. The contribution of a pharmacist to medication management has been previously described in ambulatory care, acute care and long-term care settings. However, many of these reports have not included the important aspects of medical practice integration and health insurance plan reimbursement based on a prospectively agreed set of outcome metrics.

The preceding article has been condensed to accommodate space requirements. However, a full-length version of the article can be found on the CPhA website by visiting the "Research Articles" section of the California Pharmacist page.

About the Authors

Gene D. Morse, PharmD, FCCP, BCPS is the Associate Dean of Clinical and Translational Research at the State University of New York, University at Buffalo School of Pharmacy and Pharmaceutical Sciences and Director of Translational Pharmacology Core at the NYS Center of Excellence in Bioinformatics and Life Sciences.

References

1. Ceusters W, Capolupo M, De Moor G, Devlies J. Introducing Realist Ontology for the Representation of Adverse Events. In: Eschenbach C, Gruninger M. (eds.) Formal Ontology in Information Systems, IOS Press, Amsterdam, 2008 (forthcoming).

2. Ceusters W, Jan Lorré, Annelies Harnie, Bert Van Den Bossche. Developing natural language understanding applications for healthcare: a case study on interpreting drug therapy information from discharge summaries. Proceedings of IMIA-WG6, Medical Concept and Language Representation, Phoenix, 1999;124-130.

3. Institute of Medicine. http://www.iom.edu/. 2006.

4. IOM report recommends comprehensive strategies to reduce medication errors. *Hosp Health Netw* 2006;80(8):69-70.

5. Young D. IOM panel reviews lessons for medication safety. *Am J Health Syst Pharm* 2005;62:1340-2.

6. Lubell J, DoBias M. Medication errors persist: IOM. Report highlights steps to reduce severity, frequency. *Mod Healthc* 2006;36(29):10.

7. Young D. IOM advises CPOE, other technology for preventing medication errors. *Am J Health Syst Pharm* 2006;63(17):1578, 80.

8. ASHP Calls for Personal Medication List. http://www.ashp.org/s_ashp/article_press.asp. 2008.

9. Weingart SN, Hamrick HE, Tutkus S, et al. Medication safety messages for patients via the web portal: The MedCheck intervention. *Int J Med Inform* 2008;77(3):161-8.

10. Galvin L, McBeth S, Hasdorff C, Tillson M, Thomas S. Medication bar coding: to scan or not to scan? *Comput Inform Nurs* 2007;25(2):86-92.

11. Hatton RC. Issues in medication safety. *Am J Health Syst Pharm* 2007;64(1):22; author reply.

12. Witkowski P. Case study: novel ways automation enhances medication safety. *Am J Health Syst Pharm* 2007;64(14 Suppl 9):S21-3; quiz S4-6.

13. Skibinski KA, White BA, Lin LI, Dong Y, Wu W. Effects of technological interventions on the safety of a medication-use system. *Am J Health Syst Pharm* 2007;64(1):90-6.

14. Hagland M. Right patient, right dose... Medication management is getting an IT makeover at safety - conscious healthcare organizations. *Health Inform* 2006;23(9):52, 4-7.

15. U.S. Hospitals Embrace Barcodes for Point-of-Care Safety. Release Date: 1/29/2008, Business Wire via NewsEdge Corporation. 2008.

16. Flynn EA BK, Carnahan BJ. National Observational Study of Prescription Dispensing Accuracy and Safety in 50 Pharmacies. *J Am Pharm Assoc* 2003;43(2):191-200.

17. Stoop AP, Bal R, Berg M.OZIS and the politics of safety: Using ICT to create a regionally accessible patient medication record. *Int J Med Inform* 2007;76 Supp 1:229-35.

18. Mulder D. Minimizing mistakes. Beloit Memorial Hospital is focused on bedside bar coding to help eliminate medication errors. *Health Inform* 2007;24(9):52-3.

19. Payton J, Leder W, Hord E. Bar Code Medication Administration system improves patient safety. *J Ark Med Soc* 2007;104(4):84-5.

20. Robertson WO. Issues in medication safety. *Am J Health Syst Pharm* 2007;64(1):21-2; author reply.

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