Prescriptome analytics : an opportunity for clinical pharmacy

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In a recent editorial, Barry L Carter indicated that there is a need for clinical pharmacy to implement the highest quality research that will help address the mission to « extend the frontiers of clinical pharmacy » (1). To help reaching this goal, the involvement of clinical pharmacy in the projects dealing with clinical data warehouses (CDW) may be an opportunity. Indeed, in the hospital setting, a CDW is a real time database that stores data from diverse clinical sources of hospitalized patients. Typical data types often found within CDW include: prescription data, clinical laboratory test results, patient characteristics, radiology reports and images, hospital admission summary, discharge and transfer summaries. Providing that data storage has been carried out for a long period of time, CDW can provide a wealth of knowledge about patients, their medical conditions and outcome that may be used for retrospective epidemiological studies.

More specifically, CDW allow a longitudinal retrospective survey of the drugs prescribed in patients before, during and after an hospitalization stay. The precise and comprehensive knowledge of the drugs prescribed within a time frame in a patient allows the evaluation of the exposure to prescribed drugs, i.e., to her/his prescriptome. Analysis of prescription data within CDW by data mining of clinical data may be called prescriptome analytics.

CDW are sometimes merged between hospitals, leading to huge set of clinical data accessible to analytics. Such hospital CDW can sometimes be connected with ambulatory-outpatient healthcare databases (e.g., national health insurance system database) that contain individualized demographic, anonymous, and comprehensive data on health spending reimbursements.

Initiatives are being currently organized at institutional, regional and/or at national levels to make heath data accessible to the different stakeholders among which health professionals and researchers through consortium sharing and exploiting health big data (2). A recent national initiative in France has led to the Health Data Hub (HDH) project whose mission was to identify the data sources to be integrated in the national system of health data, and to propose an organization and a regulatory environment for the HDH (3).

Prescriptome analytics

Besides individual clinical pharmacy that we practice every day to care for patients in our different institutions, we should take initiative to foster the development of clinical pharmacy at a population level. The prescriptome analytics from clinical data warehouses should be considered as an opportunity for clinical pharmacists to foster such evolution. The recent and rapid growth of the number of publications retrieved in Pubmed using “clinical pharmacy” and “big data” or “machine learning” is a significant marker of this evolution (Figure 1).

Prescriptome analytics has been shown of interest to identify at a population level risk factors associated to hospital readmission (4), drug-drug interactions (5,6) and to decipher the role of drugs and of patient characteristics in developing acute or chronic conditions (7) (Table 1).

It may also be helpful to study therapeutic discontinuations of care at transition points (at hospitalization entrance and at hospital discharge). It seems obvious that such studies will have an impact on our daily practice and should improve patient care.

Such studies (i.e., by the secondary use of data) may help to push the boundaries because there are faster and cheaper to implement since there is no need to collect data that are stored in CDW. Furthermore, in some cases it could allow access to big data (i.e., when the volume of data calculated as Log (n x P) is higher than 7, where n is the number of patients and p is the number of variables collected by patient, 8) to obtain a high statistical power and to evidence rare events.

Predictive algorithms

Leveraging retrospective analytics from CDW may help the development of predictive models to predict and potentially prevent adverse events such as hospital readmission (9), the identification or stratification of patients with a high risk of drug-related adverse events (10), and the development of personalized medication therapy by identifying medication pathways for a particular patient (11).
Hence, the development of machine learning algorithms (i.e., via the so-called « artificial intelligence ») could improve care for patients and health care outcomes in combining predictive analytics and preventive measures.
However, expectations from advanced algorithms for personalized medicine should be tempered since there are currently far from being able to recommend the right drug dosing for a specific patient, and major bottlenecks have to be overcome in a multidisciplinary effort (12, 13).
Clinical pharmacists should be watchful to this evolution, and be proactive to integrate the consortia (scientific and economic consortia from both public and private sector) being implemented so that our professional and scientific input will be accounted for.

Thinking outside the box

The traditional deductive reasoning on which is based the hypothesis-driven research is now challenged in the era of petabyte information (14). Indeed, data-driven (hypothesis-neutral) research analysis on massive volume of data with advanced algorithms may help us discover unknown or unexpected things by identifying connections or correlations between variables, and unknown features driving clinical outcomes.
As such, data-driven research – as a new way of looking at data - should be considered as a novel and additional tool of scientific research, and clinical pharmacy should benefit from this evolution. Such studies could be incentive for the development of research in clinical pharmacy, and could help address the mission to « extend the frontiers of clinical pharmacy ».
While the classical hypothesis-driven scientific method will obviously not become obsolete, such new approach may favor serendipity that often leads to major breakthroughs, and be an opportunity for clinical pharmacy.

In conclusion, times to come will offer clinical pharmacists unique opportunities to be more involved in prescriptome analytics, and to expand research horizon in clinical pharmacy as well as its visibility as an academic discipline. This will require specific curricula to provide a suitable background in pharmacoepidemiology and informatics coding to foster our integration in the large multidisciplinary consortia established for such studies on health big data. Integrating databases from different institutions may be an opportunity to promote collaborations at a national or international scale on shared research questions, and to lead to more comprehensive and relevant findings.

Beyond, the development of predictive analytics with machine learning algorithms could have the potential to redesign the way we care for patients in our institutions for a more personalized medication therapy, and we should be prepared for this evolution.

These new avenues are not only exciting by cutting-edge research they will permit but also by the benefits they will provide to the patients and to the society.

i. Compliance with Ethical Standards: yes.

ii. Funding : None.

iii. Conflicts of interest : None.

Database	Cohort of 1,275 patients with psychiatric diseases from Mount Sinai Data Warehouse	61,190 prescriptions and corresponding INR from Danish administrative healthcare registries	10,506 statins prescriptions from Rennes University Hospital warehouse (eHOP)	16,593 patients from AKI cohort, and 14,514 from the CKD cohort exposed to PPIs from HMO in western New York
Objective	To identify prescription medications, side effects, and drug-drug interaction-induced side effects associated with readmission risk	To investigate whether drug–drug interactions were discoverable without prior hypotheses using data mining (warfarin–drug interactions as the prototype)	To describe prevalence, nature, and level of severity of potential statin drug-drug interactions	To study association between PPI use and risk of AKI and of CKD
Methods	Bayesian logistic regression models to evaluate the association of prescription data with 30-day readmission risk.	Random forest method to identify important variables	Automatic DDI identification performed using a Java-algorithm from patient's drug administrations from CDW and OrientDB database containing statins DDI's datasets. Spark cluster computing framework used to perform multithreaded tasks.	Logistic regression models to estimate the odds ratios for the association between PPI exposure and risk of AKI and CKD
Result	Find factors that could help to lower readmission rates in patients with mental illness.	Data mining to discover unknown drug–drug interactions in cardiovascular medicine	The more significant DDIs (contra-indication) were reported for transporter-based DDI involving OATP1B1	PPIs are independently associated with AKI and CKD.
Reference	4	5	6	7

Table 1. Examples of studies based on prescriptome analytics.

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Figure 1 : Evolution of the number of publications using « clinical pharmacy » and « machine learning » or « big data ». Data retrieved from Pubmed using Medline trend. The number of publication at May 2019 is 35.