

The Role of Pharmacists in Data Based Medicine & RxISK.org

The Problem

Consumers of drugs are not adequately informed about drug effects or protected by the regulatory framework under which drugs are brought to the market in Canada, the U.S. or Europe, which puts them in a poor position to make informed judgments about medicines. Efficacy has been overstated in various ways, risks have been all but ignored, and real advances in drugs that provide cures for serious medical problems have taken a back seat to “lifestyle” drugs that offer little improvement on and sometimes greater hazards than previously available treatments.

Drugs get to market in 2012 by clearing short-term clinical trials. Where once such trials were a gate into the market after which close clinical observation helped map the appropriate and safe use of a treatment, now they are marketing tools for branded drugs, and they trump clinical observation. Clinical trials have become such an important marketing tool for branded drugs that companies ensure that only favorable results get on the record. They withhold results that are inconsistent with the image they want for their drug. Recent studies estimate that about 50% of trial data remains unpublished. Among trials that are published, a large proportion are “ghostwritten”; that is, the studies are done by drug companies who pay prominent academics to put their names on the research. Frequently, studies are manipulated in various ways to understate the rate of occurrence of adverse events.

The voices of patients outlining their real experiences are no longer heard, and healthcare practitioners have ever greater difficulty believing the evidence of their own eyes regarding treatment related effects that patients are experiencing. Awareness that drugs are the source of so much damage is not well understood. Doctors tend to attribute problems to conditions inherent in their patients, and the patients do not question the wisdom of their physicians. Only between 1% and 5% of serious adverse events are reported to the FDA.

This situation has made prescription drugs the fourth leading cause of death in the U.S., and in some domains of care they are likely the leading cause of death and disability with economic impacts that have never been properly addressed. The direct and indirect cost of the fallout has been estimated at \$100 billion USD. To the extent that consumers are aware, they have become disenchanted with both doctors and pharmaceutical companies.

A Role for Pharmacists

In recent years both patient and pharmacist reporting of serious adverse events has been encouraged by regulators in both North America and Europe. Studies have shown that patient reporting is often more accurate than reporting by doctors. Still, comprehensive uptake by patients has yet to take root because the prior culture of adverse event reporting militates against reporting in four respects.

First, reporting originated as a pen and paper system and has yet to fully embrace the possibilities offered by electronic and internet based reporting.

Second, with the rise of controlled trials individual reports have often been seen as anecdotal. That is, they are assumed to be either inaccurate or one-off events without implications for the patient population at large.

Third, current systems have not availed of the possibilities of teamwork between patients and pharmacists to enhance the quality of reporting.

Fourth, the possibilities of real time feedback to all parties in care have not been realized.

Fifth, there is a perception that patients do not have the necessary knowledge of the indications for treatment or the mechanisms of action of medicines to report adequately, even though studies now suggest patients reported in greater and more adequate detail than doctors.

The lack of an effective system to collect data from patients has left the field of adverse event identification to drug companies through their clinical trials, and this has resulted in a serious bias in available data

Many have commented on these deficiencies but we are actively trying to find a solution. Data Based Medicine Global Limited (DBM) has designed a system to work around this bias and facilitate healthcare teamwork between pharmacists, doctors and patients. Patients will be encouraged to visit the DBM website, RxISK.org, through various means, including the kind of short checklist so often used in pharmaceutical company ads, search engine optimization, and a social media campaign. The website will guide patients through a series of questions to assess if their medication or a medication interaction may be the source of problems. For patients, the process of systematically assessing the potential risks of their medication will serve to educate and empower them, both important factors in removing system bias.

The interaction of patients with RxISK will generate a report for them to take to their pharmacist and/or doctor as the basis for discussion. The intention is to identify more adverse drug events, earlier, and to provide a structured and factual report to aid the pharmacist or doctor. Ideally this will lead to further input to the reporting process from either pharmacist or doctor and advice re management.

The RxISK Report™ will enable the pharmacist and/or doctor reviewing the information entered by the patient to supplement it where appropriate. This may involve the addition by the pharmacist of further information to the submission in a manner that endorses the likelihood of a linkage or identification of factors that reduce that likelihood. Importantly no re entry of demographic data etc will be required of the healthcare professionals. There is also no need to submit a separate report to the regulator. RxISK will do this.

Data privacy will be protected – patients will choose who they bring their Rxisk Report to and only data they choose to share will be forwarded to the regulator in their country. All aggregate data will be anonymized.

There are a number of steps in the reporting process where a pharmacist is likely to have readier access to relevant information than either the patient or doctor, such as the availability of prior reports of comparable adverse events. In addition to supplementing the material in the report, the pharmacist will be in a position to gate-keep referrals to the doctor. Where appropriate, the doctor (or other prescriber) can then intervene to switch medication, change dose, or introduce an antidote.

Spending a few minutes checking the patient's information on the site will be more than offset by the improved quality of information and improved efficiency and satisfaction in future interactions between pharmacist and patient.

Spending a few minutes checking the patient's information on the site will lead to improved quality of information and improved efficiency and satisfaction in future interactions between pharmacist and patient.

It will also provide insights that improve processes of care in a wider context. It is easy to ignore a notification of a report of an ADR submitted to a regulator where the patient voice is erased. Providing the patient voice in narrative stories and long term consequences as part of the data promotes awareness of ADRs at a much deeper level and will encourage vigilance in managing other patients.

Increasingly this kind of clinical input by pharmacists is reimbursable and for this purpose RxISK reports will also provide a paper trail for pharmacists to demonstrate their involvement.

Public knowledge of drug side effects, following revelations about Avandia and Vioxx (for example) has introduced a new skepticism on the part of patients. In the past few years an unprecedented number of books have been published challenging the role of drugs in modern health care. Patient reporting of adverse events to the FDA has increased much faster than physician reporting, to the point that patient reporting will soon exceed reporting by health care professionals. Against this background, trust between patients and their pharmacist is likely to become an ever more crucial factor in the successful management of medicines in the future, particularly if prescribing extends beyond doctors, and with an aging population taking ever more medicines.

Digital recording of treatment related events makes it possible to enhance the quality of reports in a number of important respects.

- First, the availability space, and freedom from the confines of fixed checklists will allow patients to report on as many aspects of a problem in as much detail as they wish.
- Second, the option of saving and returning to online reports is more user-friendly. This will encourage patients to explore domains not currently tapped such as the impact of an adverse event on their circumstances which may include important economic impacts such as loss of job.
- Third, it also allows implementation of more detailed causality algorithms than found in traditional reporting systems.

- Fourth, during the reporting process a web-based system can give reporters (patients, pharmacists and doctors) detailed feedback on related reports from relevant medications in a manner that has not been possible hitherto.

RxISK.org is not just about reporting events on treatment. It promotes patient-centered therapy, an approach that has been endangered in recent years.

In many areas of therapeutics the primary determinant of a treatment's effectiveness lies in patient compliance and compliance is more influenced by patient perceptions of safety than of efficacy. Despite this we have an increasing focus in therapeutics on efficacy and comparative efficacy. RxISK's approach aims at complementing the current emphasis on comparative efficacy found in much of medicine, with a focus on comparative safety. This we believe has the potential to foster greater gains in treatment effectiveness than are likely to arise from an exclusive emphasis on comparative efficacy.

By encouraging patients to visit the site to find out if their medications are causing problems, and by providing a structured assessment tool, RxISK has the ability to identify problems years earlier than the current system, in which valuable early warning signs, if they are captured at all, are buried in individual patient records and not accessible for analysis. Even a small number of reports of the same problem on RxISK will trigger questions and provide health care professionals with valuable clues about potential drug effects. This will be especially important for new drugs.

For patients the active management of the risks of treatment has a greater potential to foster gains in treatment effectiveness than anything else.

The Practicalities of Pharmacist Involvement

In practical terms we envisage working closely with both hospital and community-based pharmacists. DBM will offer pharmacists access to data currently not available, or partially available at a hefty price from such services as FDABLE, which formats and creates reports from FDA's database of adverse events.

RxISK will make this database available for pharmacists to interrogate for prior reports of events not currently listed in the label for a medication or reported in the world literature. It will also be possible to interrogate this database by age, gender, ethnicity, country, time of the year of reporting and a range of other variables, in addition to establishing whether certain events are disproportionately reported.

As soon as reporting to RxISK.org begins, pharmacists will also have access to the data stored there. The RxISK database will be much richer than FDA's database in terms of the quality of reports, along with the availability of statistics on patient reporting, pharmacist or doctor reporting and joint reporting, as well as containing economic and quality of life data not available anywhere else.

In addition to the above benefits, RxISK will offer patient specific and problem specific information that cannot be accessed anywhere else.

The patient specific information includes:

1. A patient timeline that will facilitate investigation of problems.
2. Tag Clouds that will reveal the concerns that the typical patient has about the impact of particular treatments on their day-to-day lives. For example FDA currently classifies miscarriages under 'other' – in other words not serious. We will have patients offer their assessment of the impact of events on them like this and will make this data available. This assessment we hope will move forward discussions about medicines to a more patient centered view so that potential adverse effects that are not just common or medically important, but are of most importance **to patients** are flagged.

The problem specific information includes:

1. RxISK data will have a global reach.
2. RxISK will offer Heat-maps giving the distribution of reports that may alert and enable pharmacists to explore events that may be clustering in their local area in a manner not possible hitherto.
3. RxISK's Heat-maps will allow pharmacists to track the evolution of new therapeutic issues over time.
4. RxISK information will be real time, in contrast to information from the scientific literature which is commonly at least a year behind events and FDA data which is 6-9 months after the event. The availability of information in real time will enable pharmacists to play a greater role in shaping and interpreting data on treatment related events and their management than has been possible hitherto.
5. RxISK provides a facility that notifies pharmacists of any updates on further developments connected to the reported problem or drug – closing the feedback loop to allow the pharmacist to support patients in an ongoing and constructive way, avoiding the 'black hole' of current reporting systems.

RxISK.org will offer pharmacists information that is as useful and detailed for therapy purposes, as the kind of information that has been sold by companies like IMS health to pharmaceutical companies for business purposes has been. There will be no other source of such information and there will be no cost.

Optimizing Pharmacist Input

The optimal point to make patients aware of the existence of RxISK.org is the point at which medication is dispensed. By making patients aware of RxISK.org and how it can empower them, the pharmacist can establish a vital partnership with the patient.

Pharmacists have a critical role in the management of adverse events, and RxISK.org provides a tool that supports and strengthens this role. The RxISK Report creates a window of opportunity for connection with patients – to let them know they are being taken seriously.

An increasing number of provinces and states are recognizing the importance of input by pharmacists by adding prescription refills to their reimbursable clinical services. This strengthened role is becoming even more important, given current prescription-only arrangements for branded drugs.

Prescription-only arrangements for medicines were put in place to help manage the risk of adverse events, by reducing the likelihood of such events through an arrangement that would restrict the use of medicines to confirmed indications. But, in fact, once an adverse event happens prescription-only arrangements risk aggravating the problem. Doctors are at present the only way out of these problems for patients who may not know that their treatment is their problem.

In this hostage situation, patients all too often fail to voice their concerns and doctors are not trained to realize that patients may be having difficulties they cannot voice – these are the dynamics of Stockholm syndrome.

Aside from patient reluctance to complain about drug side effects to their doctors, doctors are further biased by virtue of the fact they have inaugurated treatment and are now being called on to recognize that their choice of treatment is causing problems. This medical bias is aggravated whenever enthusiastic marketing of a branded product over-hypes its benefits and minimizes its hazards. As a result of these dynamics, pharmacists are increasingly seen today as more likely to offer a disinterested source of information than doctors.

RxISK.org will allow pharmacists to build on this professional position and become more active members of the healthcare team.

Pharmacology Visions

RxISK.org will open up a series of new therapeutic domains. It is not possible to anticipate all of the ways the new information and new interventions will impact on clinical care but we expect that it will encourage a dynamic and iterative process and we hope to work closely with pharmacists to realize the full potential of the system.

DBM's ultimate aim is to change the culture of healthcare, and to do this through science. Our goal is to restore a proper balance among patients, doctors and others involved in healthcare – putting greater weight on the evidence of their own direct experience and less on information from marketing. This process will improve the value of feedback provided to pharmaceutical companies.

We expect that good descriptions of treatment-related events (phenotypes), allied with access to adequate numbers of similar phenotypes will help us pinpoint the biomechanisms underpinning particular effects, and in some cases to pinpoint a genetic basis for these effects.

These steps will advance pharmacological and physiological knowledge but will also provide an understanding that may yield antidotes for problems or genetic screening tests to avoid treatment related risks and equally will transform the observations of doctors, pharmacists and patients into credible sources of data.

Beyond this, the current focus on treatment efficacy for specific conditions has caused healthcare practitioners to become less observant about the full range of effects drugs may have. Data about many of these effects, if mined properly, can offer leads on understanding important aspects of both physiology and behavior.

But in addition a proper appreciation of the wider range of effects a medicine may have is still one of the most fertile and cost-effective avenues for the development of new drugs, as evidenced by Latisse, Viagra, the use of antibiotics for ulcers and other discoveries.

In every other part of the health system the discussion is around empowering patients and providing opportunities for involving them in improving the quality and safety of their care. RxISK will provide pharmacists with a real opportunity to empower patients and help them become an active rather than a passive part of making medicines safer for us all.

About Us

The founders of Data Based Medicine and its website RxISK.org, Professors David Healy, Kal Applbaum, Dee Mangin, Brenda Gallie, Nancy Olivieri and Ralph Edwards have unrivalled domain experience in medicine, medical anthropology and pharmacy when it comes to championing the need for generating and making available a full range of data on the effects of treatment and delivering medical care on a global basis.