25 YEARS OF PHARMACOEPIDEMIOLOGIC INNOVATION: THE SASKATCHEWAN HEALTH ADMINISTRATIVE DATABASES

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2010 marked the 25th anniversary of population-based pharmacoepidemiology research in Saskatchewan. In 1985, the province's administrative healthcare utilization databases, with prescription drug data as a central element, became available for studies requiring the linkage of drug exposure data with health outcomes information for the first time. The opportunity presented by the databases was recognized by having *in situ* a PhD-qualified Provincial Epidemiologist (RW), who was aware of the keen worldwide interest in linked drug exposure and health outcomes data in the early 1980s following the occurrence of several safety issues not identified by existing pharmacovigilance systems. This milestone was marked by the publication of the first population-based pharmacoepidemiology study using the Saskatchewan data.[1]

In an invited editorial accompanying the article, Hugh Tilson, at the time Head of Epidemiology, Surveillance and Policy Research at Glaxo Wellcome and a founding member of the International Society for Pharmacoepidemiology (ISPE),[2] wrote "The emergence of the Saskatchewan Health Care System databases as an epidemiologic tool reflected in the article by Dr Roy West … warrants far more than enthusiastic editorial review ... Indeed, if the public policy significance of these databases were truly understood, their emergence would be front page news in the science section of every public medium."[3] This visionary comment marked the debut of dependable and accessible record linkage of individual-level administrative data on prescription drugs dispensed in the outpatient setting with data on hospital discharges, physician service claims and vital statistics from over 90% of the one million residents of Saskatchewan for population-based evaluations of the use of drugs and their outcomes.[4,5] With close to 200 publications based on the data authored by leading Canadian and international researchers,[6] the Saskatchewan databases have proven to be an extremely important resource for population-based pharmacoepidemiologic research over the past 25 years.[7-16]

Individual databases covering cancer registrations, hospital separations, physician service claims and prescription drug dispensing were available in Saskatchewan prior to 1985, but the drug data had not been linked with the other data. The historic changes that occurred in 1985 included not only a demonstration of the value of linking the drug data with healthcare utilization outcomes, but also the establishment of an appropriate and reliable procedure for data access and the streamlining of the provincial approval process for access by the creation of a single point of contact within Saskatchewan Health (currently the Epidemiology and Research Unit) for obtaining data (additional details on the databases, the access approval process and the charging policy are available elsewhere[6]). These highly significant developments provided the impetus for a major step forward for pharmacoepidemiologic research worldwide.

The Saskatchewan record linkage scheme has several key advantages.[17] Firstly, the data cover an extensive period of time (1976 to the present).[4,5] Secondly, since 2006, data on all medications dispensed at provincial community pharmacies to all residents are now recorded regardless of who pays for the prescription (the policy framework under which data on beneficiaries of federal drug programs may be used for research is still being developed, but the ability to use them will

enhance the capabilities of the data resource). Before 2006, only data on medications in the Saskatchewan Formulary (over 3,500 products[5]) dispensed to beneficiaries of the provincial drug plan are available; those excluded are residents whose drug costs are covered by the federal government, notably Registered Indians. Many data systems in Canada and internationally only have drug data on sub-groups of the population (e.g. older adults and social assistance recipients, or employed individuals and their families), which is a major weakness since disease and drug use are rarely confined to specific population segments.

Thirdly, the existence of the central coordination office in the Saskatchewan Ministry of Health facilitates data access, which can be difficult in other Canadian provinces due to data use being restricted to a small group of academic researchers or a lack of coordination for data access, especially when databases are controlled by different organizations.[18,19] Finally, unlike several other systems, hospital records which generated the computer data are accessible (under strict protocols) so that additional crucial clinical information can be obtained.[14] Access to original records has also proved to be invaluable for validation purposes. Saskatchewan data have been subjected to numerous validation studies, including cancer, cardiovascular, respiratory and psychiatric diagnoses, and have generally been found to be accurate and reliable for most of the conditions evaluated.[20-24]

The value of the Saskatchewan data has been recognized internationally as the authors cited here[3,7,10-12,15] and elsewhere[5,6] testify. Moreover, the data were the only resource from outside the United States in the Food and Drug Administration's Cooperative Agreements with six data systems selected to provide data for FDA post-marketing studies of safety, effectiveness and other issues between 1994 and 2002.[25]

Saskatchewan data have been used to study medications that treat a wide variety of indications, e.g. respiratory, cardiovascular, musculoskeletal, psychiatric, metabolic, renal, hepatic and oncologic conditions, and a similarly broad range of treatment outcomes.[5,6] Results from these studies have especially demonstrated important findings in the treatment of asthma,[7] type 2 diabetes,[9] arthritis[10] and cardiovascular disorders.[11,13] The data have also been used to quantify the risks of pharmacotherapy in congenital malformations,[1] falls in older adults,[8] life-threatening blood disorders[14] and cancer,[12] and to provide information on the risks of gastrointestinal hemorrhage with non-steroidal anti-inflammatory drugs,[10] cardiac arrhythmias with cisapride,[15] and myocardial infarction with cyclooxygenase-2 inhibitors,[11] to name but a few topics. In addition, the data have been used for broader applications, such as adverse drug reaction monitoring and studies of disease burden and outcomes of chronic disease management,[12,13,16] providing valuable information for decision makers. Furthermore, access to data has been provided to several students from Saskatchewan and other provinces for their theses,[6] thus contributing to the training of future pharmacoepidemiology researchers.

Many of the findings of studies using Saskatchewan data have provided insights into the gastrointestinal, renal, hepatic and cardiovascular risks of using selective and non-selective cyclooxygenase-2 inhibitors,[10,11] and cardiovascular and cancer risks encountered in the use of sulfonylureas for type 2 diabetes,[9] which have contributed to changes in treatment recommendations. Studies using provincial data also provided evidence in the ongoing controversies around the use of β-agonists and inhaled corticosteroids in the treatment of asthma.[7] More broadly, the data have been used in post-marketing studies that have identified and quantified real-world benefits of drugs (effectiveness), their risks, and cost-effectiveness.

In addition to the farsighted comment about the pharmacoepidemiologic importance of the databases in his 1985 editorial, Tilson expressed the hope that "as concerned persons in health plans and health care organizations … contemplate harnessing the power of the computer for improved administration, they learn from the Saskatchewan example and design these systems to be compatible with other applications which provide the general public a greater benefit" and also that "those with existing automated systems will find a way to make these databases available for good epidemiology in protection of the public's health."[3] In many ways, his desires came true. The availability of the Saskatchewan databases for population-based pharmacoepidemiologic and

health services research and the use made of them has been a catalyst for the development or extension of similar systems in other Canadian provinces[18,19] and the United States. The number of administrative healthcare utilization databases used for pharmacoepidemiologic research has increased greatly over the last 25 years.[17] In Manitoba, for example, where the focus for many years was on health services research without pharmaceutical data, the drug data were linked into the system in the late 1990s.[26]

The opportunities presented by the Saskatchewan data for pharmacoepidemiology research have also contributed to other significant developments. The ISPE was formed following a groundbreaking symposium in Regina, Saskatchewan[27], organized by the provincial Ministry of Health and attended by founders of the Society including Tilson and its first chair. The symposium addressed the use of large-scale drug databases for improving pharmacotherapy and health outcomes. ISPE's first annual meeting took place in Minneapolis the following year. The Canadian Association for Population Therapeutics (CAPT), which developed from the Canadian Pharmacoepidemiology Forum, was established in 1996 in Saskatoon, Saskatchewan, with a mission to advance population-based research of therapeutic interventions to improve the health outcomes of Canadians.[28] CAPT can also trace its roots back to the establishment of the Saskatchewan databases as a pharmacoepidemiology resource since over 50% of its founding members either worked in Saskatchewan Health or used the data in research studies. In addition, the impetus provided by the Saskatchewan data to the development of other provincial systems has led to Canada having, on a per capita basis from ISPE membership information[29*] one of the larger pharmacoepidemiologic research communities globally. Many of its members have used Saskatchewan data in their research and are engaged in the recent formation of the Canadian Institutes for Health Research's Drug Safety and Effectiveness Network,[30] which will be heavily dependent upon provincial administrative databases for its work.

In 1985, Tilson was fully aware of the crucial need for an appropriate balance between patient confidentiality and access to anonymized data noting that "the responsible public officials of the Province of Saskatchewan have approached this one just right, with meticulous care to ensure that no one without need and right to know and without working under the oath to government office may ever have direct access to data."[3] Few Canadian systems have managed to achieve the same degree of balance between patient confidentiality and reasonable access to data as Saskatchewan.[6,31] In contrast, some Canadian provinces restrict data access to internal government analysts or specifically designated groups of local academic researchers, citing patient confidentiality as the reason.[19] This argument appears to have limited validity because Quebec, the province with the strongest privacy legislation in Canada, also allows access to its data, under appropriate contractual conditions, to all types of researchers. The more open approach of allowing access to a wide spectrum of researchers increases the value of the data because the different perspectives tend to generate more diverse research, clinical and policy applications for the data.

The emphasis for Saskatchewan's health system includes investing in information technologies to support better access to information for patient care, which may enhance the scope and quality of data available for research. One recent development is the ability to link the existing databases with the provincial immunization registry which, since several new vaccines have been introduced recently and others are on the horizon, is a valuable tool for assessing their impact. Other initiatives, such as further development of a centralized laboratory information system, would strengthen the data resources for drug effectiveness studies. As personalized medicine becomes more practicable, the data may also provide a starting point for pharmacogenetic studies.

The availability of anonymized individual-level data linking drug dispensing and health outcome information from the Saskatchewan databases to all legitimate researchers, subject to a detailed contract, was a key milestone in pharmacoepidemiology that resulted in a major new resource becoming accessible for research in

[*] Data are from 2006, but recent membership estimates from the ISPE website support Canada's significant role.

Canada and globally. Knowledge learned from their use has led to important improvements in patient health and significant methodological developments in pharmacoepidemiologic research over the last 25 years. The impact has been felt around the world.

Disclaimer

Dr. Rawson is a pharmacoepidemiologist at GlaxoSmithKline and an Adjunct Professor at the University of Waterloo, Ms. Downey is Director, Epidemiology and Research Unit, Saskatchewan Ministry of Health, Dr. Maxwell is a Professor with the University of Calgary, and Dr. West is Professor Emeritus at the Memorial University of Newfoundland. The views expressed are those of the authors and do not necessarily represent those of their employers or any other organization.

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