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Alison Kathleen Middlebro'
AUTEUR DE LA THÈSE / AUTHOR OF THESIS

M.Sc. (Epidemiology)
GRADE / DEGREE

Department of Epidemiology and Community Medicine
FACULTÉ, ÉCOLE, DÉPARTEMENT / FACULTY, SCHOOL, DEPARTMENT

A Proposal for Surveillance and Case Registry of Schizophrenia in Ontario

TITRE DE LA THÈSE / TITLE OF THESIS

Ian McDowell
DIRECTEUR (DIRECTRICE) DE LA THÈSE / THESIS SUPERVISOR

CO-DIRECTEUR (CO-DIRECTRICE) DE LA THÈSE / THESIS CO-SUPERVISOR

Doug Coyle

Brenda Wilson

Gary W. Slater
Le Doyen de la Faculté des études supérieures et postdoctorales / Dean of the Faculty of Graduate and Postdoctoral Studies

A PROPOSAL FOR SURVEILLANCE AND CASE REGISTRY OF SCHIZOPHRENIA IN ONTARIO

Alison Kathleen Middlebro'

Thesis submitted to the Faculty of Graduate and Postdoctoral Studies in partial fulfillment of the requirements for the MSc degree in Epidemiology

Epidemiology and Community Medicine
Faculty of Medicine
University of Ottawa

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Abstract

Schizophrenia is an illness causing impairment in thinking and functioning in many realms of everyday life. It is considered one of the most disabling of mental illnesses. This thesis considers the impact of schizophrenia in Ontario, including elevated mortality, degree of disability, economic impact. Some known risk factors for schizophrenia are increasingly common in Ontario, such as urban exposure, and a history of immigration. The impact of the illness in Ontario makes schizophrenia a good candidate for surveillance and case registry in this province.

This thesis reviews the required elements of a surveillance system, including case definition and potential data sources and applies them to surveillance of schizophrenia in Ontario. The thesis then proposes a surveillance system and linked case registry based on combined OHIP, discharge abstract and mental health care administrative data, and outlines the necessary steps in implementation and evaluation of the system.

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Dedicated to Brian, Colin, Malcolm and Adrian.

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Preface

Schizophrenia is an illness causing impairment in thinking and functioning in many realms of everyday life for the affected individual, and is considered to be one of the most disabling of mental illnesses. Onset of the illness is typically in adolescence or young adulthood, with the peak age for first admissions to hospital with schizophrenia between 20 and 29 years of age (1).

Our understanding of the aetiology of schizophrenia is limited. Genetic studies suggest that schizophrenia is the result of many genes of small effect interacting with environmental exposures (2). In the context of this lack of understanding, a surveillance system for schizophrenia, especially if it includes individual case level data, would provide a valuable basis from which to conduct research into the aetiology of the disease, possibly identifying new risk factors for further investigation. Surveillance of incident cases over the course of their illness would assist in evaluating current treatment and early intervention efforts, as well as any future preventative efforts. Epidemiological studies have identified some risk factors for schizophrenia, mostly occurring in the pre- and perinatal periods. With the long latency period between exposure and development of disease, and the non-specific nature of risk factors such as birth complications, preventative measures targeting these factors would be better evaluated using population level surveillance than conventional trials. Due to the high human and financial costs associated with schizophrenia, recognition of any trends in incidence and prevalence would also be relevant in health services planning, forming an additional purpose for surveillance of this illness.

This thesis discusses the value of a provincial surveillance system and linked case registry for schizophrenia in Ontario, and considers the theoretical and practical issues to be resolved in designing such a system. The thesis then proposes a design for a surveillance system and linked registry and outlines the necessary steps in implementation of the system.

The general features of surveillance are reviewed in Chapter 1. To argue the case for surveillance of schizophrenia in Ontario, Chapter 1 also outlines the scope of the problem by reviewing the human and financial costs associated with schizophrenia, as well as the known epidemiology of schizophrenia and how this could impact the occurrence of the disease in Ontario.

The required elements for a surveillance system for schizophrenia are discussed in Chapter 2, and practical considerations for implementation and evaluation of the proposed system are discussed in Chapter 3.

Chapter 1:
The purpose of, and potential uses for, a surveillance system for schizophrenia

1.1 Surveillance systems

According to Last, surveillance is 'the ongoing collection, collation, and analysis of data and the timely dissemination of information to those who need to know so that action can be taken' (3). The collection and collation of data about chronic disease, its analysis and its dissemination to those responsible for planning and delivering services are essential to rational, planned action in health care.

The purposes of surveillance for any disease include monitoring trends and changes in disease incidence (as illustrated by the National Diabetes Surveillance System or NDSS, and by surveillance for congenital anomalies) , identifying at-risk groups or risk factors for illness, planning services for current and projected future needs (cancer surveillance is used for estimating future needs for care), informing policy, evaluating disease prevention and treatment measures (for example the Canadian Joint Replacement Registry, or CJRR) and generating hypotheses for detailed etiological studies of disease. For infectious disease, the rapid identification of cases and intervention to stop the spread of disease are important reasons for surveillance. Surveillance for chronic disease is less time sensitive but can identify areas of increased incidence and contribute to the understanding of risk factors and aetiology.

Surveillance may be passive (relying on data gathered for other purposes, such as physician remuneration, for case identification) or it may be active (taking active

measures to identify cases). Active surveillance is more labour intensive, but is appropriate where timely identification of every case is important to public health, as with a virulent communicable disease. Passive surveillance leaves the counting of cases to systems that may be in place for administrative purposes or that are available to the individual clinician without direct contact by the surveillance team, and may form a more suitable and less costly method for surveillance of a chronic disease such as schizophrenia. In the case of schizophrenia, the public health consequences of missing a small number of cases would be less significant than in the case of a communicable disease. Usefulness of the surveillance data could be limited however, if large numbers of cases were missed through a bias in the data gathering system.

Surveillance of chronic or non-communicable disease has become more widely practiced when and where the leading causes of morbidity and mortality have shifted from infectious diseases to chronic conditions. In Canada the National Diabetes Surveillance System (NDSS) has proved an important tool for measuring the rising prevalence of diabetes and recognizing at-risk groups such as aboriginal people. This information is essential for local, provincial and national planning of health services and has highlighted the need for research in the area. Most provinces and territories have established surveillance systems for congenital abnormalities (4), and there are also surveillance systems in Canada for cardiovascular deaths, and for other common chronic conditions.

According to Buehler, a surveillance system must include a case definition, an understanding of the population under surveillance, the cycle of surveillance which should include not only information gathering but also plans for analysis and

dissemination of results, and plans to address confidentiality concerns, as well as an actual method of gathering data. Information gathering for surveillance can be conducted using different sources, depending on the needs dictated by the situation and availability of data sources. Sentinel reports, surveys, notifiable disease reports, health data systems and disease registries have all been used as sources of data for conducting surveillance (5). Each of the elements listed by Buehler as applied to surveillance of schizophrenia will be considered in Chapter 2.

In general terms, surveillance is widely recognized as an important approach to disease control and health care planning (5,10-12). However, a decision to assign resources to the surveillance of one health condition, intervention or risk factor over another must be based on specific criteria. Teutsch suggests criteria for justifying surveillance, based on a range of quantitative measures combined with a consensus approach of public health experts, to define conditions with significant public health impact. He also included new and emerging health issues that would not meet the purely quantitative criteria. Teutsch's proposed quantitative criteria are i) frequency (incidence, prevalence, mortality), ii) severity (case-fatality ratio, hospitalization rate, disability rate, quality-adjusted life years lost), iii) cost (direct and indirect costs), iv) preventability, v) communicability, and vi) public interest (11).

1.1.1 Case registries

Surveillance systems may use information from case registries, but a true case registry maintains records of individual cases that can be used for more than immediate

public health intervention or case counting, and so goes a step further than surveillance (3).

A disease registry is a compiled list of cases of diagnosed disease, usually followed longitudinally, and includes more than basic demographic information. Disease registries record and classify all or almost all cases of a diagnosed disease in a defined population, and can thus provide a detailed picture of incidence, course and outcomes for that disease that cannot be gained from surveillance alone. Examples such as cancer registries can also track clinical interventions and provide access for patients to research trials (5). Cancer registries are widely used and accepted around the world including Canada (6). A registry may include data on environmental or other exposures. Another type of case registry involves the compilation of cases receiving a particular intervention. An example of this in Canada is the Canadian Joint Replacement Registry (CJRR). The Canadian Institute for Health Information (CIHI) in partnership with orthopaedic surgeons and hospitals across the country maintains the CJRR. The CJRR follows cases over time in order to track revisions of the original joint replacement and other outcomes (7). Case registries do not perform the same function as surveillance, although they can complement surveillance by recording and compiling information missing from surveillance records. Case registries can track individual cases over a long period and thus offer information about the history prior to diagnosis, as well as clinical interventions and outcomes that may not be captured in population-level surveillance.

Case registry may include detailed record keeping and maintenance, based on contacts with a particular treatment centre, or may be a less detailed compilation of only basic information about cases generated from other systems such as administrative data.

1.1.2 Surveillance and case registry of mental disorders

Curiously, surveillance for mental illnesses is not common, despite the significant cost and burden of disability associated with these conditions. The specific economic, social and health services impact of schizophrenia will be reviewed below.

The complexity of case definition, the degree to which mental illness may go untreated, and the stigma associated with self identification and disclosure of a mental illness, are all factors that may have contributed to the lack of surveillance, and are issues to be considered in a surveillance system for schizophrenia. However, the human suffering and years of disability associated with schizophrenia are compelling reasons to direct more attention to this illness.

Care for people with mental illness now occurs in many different health care settings, and also in other settings such as social service agencies and correctional facilities, which makes even simple case counting more complex than it once was[1]. Because of this complexity, surveillance for schizophrenia that relies on data gathered for other purposes should include several data sources and then remove duplicate entries. This would avoid biases that might be associated with using a single data source for an illness that is encountered in medical, social, and legal settings.

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[1] In the past, when a larger proportion of people with severe mental illness resided in large psychiatric institutions (in Ontario and other provinces often referred to as 'the provincial psych hospitals' or PPHs), the basic epidemiology of mental illness was easier to describe. Records kept by these institutions provide a sad reminder of those individuals who spent time there for conditions that could now be treated in a less custodial or invasive manner, but they do provide a fascinating picture of the epidemiology of the conditions treated at those locations Thus, Gregory (1959) used records from 1954-1958 from an Ontario hospital (58)l, and Smith et al (2006) used records from the early 20th century in British Columbia(136) In Ontario the de-institutionalization of those with severe mental illness occurred through the closing or transforming of the PPHs, which continues at this time. The ongoing changes at long serving institutions such as the Queen Street facility in Toronto which is now part of the Centre for Addiction and Mental Health (CAMH), and the Brockville Psychiatric Hospital (now Mental Health Centre) in Eastern Ontario are late examples The Queen St site of CAMH is a descendant of the 'Provincial Lunatic Asylum' that opened at the same location in 1850 (137)

Case registries for mental conditions, particularly psychotic illness, are used in many European regions and a few regions outside Europe. These registries have provided information for service planning in those regions as well as providing data for epidemiological studies of mental illness (8,9). Much of the known epidemiology of schizophrenia comes from the European case registries, especially those in Scandinavia. In Canada, a small scale example of a registry for schizophrenia exists in Kingston, Ontario, where records of schizophrenia cases treated at hospital inpatient, outpatient and emergency departments at the three hospitals in Kingston were linked from 1984 to 2001 for counting purposes as well as for collection of longitudinal data on service use. Valuable information for planning and research purposes could be gained concerning service use, long term outcomes and risk factors or predictors of the clinical course of illness from a registry or record linkage approach at the provincial or even national level. A case registry approach, in addition to population level surveillance, would add considerably to what could be gained just from surveillance of schizophrenia in Ontario. The costs and burden associated with schizophrenia would seem to make this epidemiological approach well worth while.

1.2 The case for surveillance of schizophrenia

1.2.1 Criteria for justifying a surveillance system

The case for surveillance of schizophrenia can be made using Teutsch's six criteria for justifying surveillance, applied to the illness. These are i) frequency (incidence, prevalence, mortality), ii) severity (case-fatality ratio, hospitalization rate, disability rate, quality-adjusted life years lost), iii) cost (direct and indirect costs), iv) preventability, v) communicability, and vi) public interest (11). Of the six factors, Teutsch does not

further define preventability except to note that surveillance, as a public health activity, is undertaken with the expectation that some kind of control measure may be taken, or may be developed in future. As schizophrenia is not a communicable disease, communicability will not be considered as a useful factor. Public interest is also not further defined but will be considered here both as public perception and relevance to the Ontario population.

Disease frequency

Although schizophrenia is a disease with low prevalence (estimated at 0.2% to 2%) (13), the personal, social and economic costs associated with the illness are substantial. The costs of building and maintaining a surveillance system can be justified by the likely planning and research benefits for this condition. McGrath et al. quoted a wide range of incidence rates in a systematic review of 55 schizophrenia incidence studies from 25 countries. The central 80% of these rates lie in the range of 7.7 to 43 per 100 000 (14). Many studies of incidence and prevalence of schizophrenia in national populations and in specific subpopulations have been carried out in Scandinavian countries where national registry-based research makes comprehensive case identification and linkage of data more feasible and these studies have shown significantly different rates of illness in some subgroups within national populations (8,15-17).

Elevated mortality in people with schizophrenia is due to suicide risk as well as various medical causes. The lifetime suicide risk among people with schizophrenia is estimated to be 9-13% (18). Chronic diseases such as diabetes, respiratory illness and cardiovascular disease also contribute to an excess morbidity and mortality for people with schizophrenia, as the standardized mortality rate for people with schizophrenia is

about 2.5 (19). This is probably due to the social determinants of health such as poor living conditions, lower education levels, and lower rates of employment and income that disproportionately affect those with mental illness and particularly schizophrenia (20), as well as illness related conditions such as poor hygiene and side effects of antipsychotic medications. People with schizophrenia may have less access to primary care, and the care they do receive may be less effective (21). The current evidence suggests that this mortality gap is increasing (19).

Disease severity

The severity of schizophrenia is high, as indicated by all of Teutsch's suggested indicators except case-fatality rate. Deaths are not generally attributed directly to schizophrenia, but as discussed above, there is a significant mortality due to suicide, and elevated rates of accidental death and premature mortality from other chronic illnesses. The level of disability and the hospitalization rate associated with schizophrenia in Canada are high and these criteria clearly support surveillance for the illness. The Global Burden of Disease study found that 2.8% of years lived with disability (YLDs) were attributed to schizophrenia and that schizophrenia was the eighth cause of disability adjusted life years (DALYs) for people aged 15 to 44 years (22). A study of perceptions of disability in several countries showed that schizophrenia was ranked third among disabling conditions on average by all respondents, and was ranked first within the results for Canada only (23). The economic and social burden of mental illness including schizophrenia are recognized as significant (24,13), supporting the argument for a schizophrenia surveillance system.

Social and occupational impairment are often associated with schizophrenia. Severe or very severe levels of social disability can be found in more than 60% of people diagnosed with schizophrenia, compared to approximately 5% of people diagnosed with a mood disorder who experience the same level of social disability (25). Many people with schizophrenia in Canada are unable to maintain paid employment and are over-represented in the unemployed (20).

A prospective study of outcomes for patients receiving 'routine clinical care' in Canada found a two-year hospitalization rate of 36.6% before the commencement of the study, and a rate of 19.8% at two-year follow up (26). This study included only people receiving routine care and available for follow up during the study and so excluded patients unwilling to be followed. Hospitalization rate likely varies from one region to another depending on access to ambulatory, emergency and inpatient services, and local programs linking police, the court system and mental health care.

Although Teutsch proposes hospitalization rate as an indicator of severity, in the case of schizophrenia incarceration rate should be considered as well, as people with schizophrenia are over-represented in jails. Prevalence of schizophrenia in prison populations has been estimated to be at least three times the general prevalence rate, and possibly higher (27).

Schizophrenia is associated with an increased risk of violent behaviour. Most studies carried out since the 1980s show a diagnosis of schizophrenia to be associated with a two to four fold increase in the risk for violence compared with the general population. Depending on the definitions of violence used the risk may be greater, although percentage of violence in the community attributable to those with

schizophrenia is less than 10%, as the diagnosis of schizophrenia is a less important predictor of violent behaviour than more common risk factors such as gender and substance abuse. Substance abuse alone carries a higher risk than schizophrenia alone, and the effect of the two combined is additive (27).

Clinical course

The course of schizophrenia is variable and the reasons for this are unknown, so to be truly useful surveillance for schizophrenia should be able to capture this variable course. This would support research into prognostic factors and perhaps into early interventions. Long- term outcomes in schizophrenia are generally poorer than those for other psychiatric illness, although a small proportion of patients show a good degree of recovery or long periods of remission (28). Suicide is an outcome for 9% to 13% of people with schizophrenia, most often in the first ten years after diagnosis (18). Because of the variable course, each incident case identified by surveillance cannot be assumed to remain in the pool of active prevalent cases; care will be needed in defining precisely how to handle cases in apparent remission. However, the proportion of incident cases that recover and so should not be considered prevalent is both unclear and likely variable depending on the geographic or cultural location. Discovering the reasons for this forms another justification for developing a surveillance system.

A ten-year World Health Organization (WHO) study showed that over a two to five year follow-up from a diagnosis of schizophrenia, up to 60% of subjects living in the developed world had a continuous course with no complete remission, while 22% experienced complete remission for greater than 75% of their follow-up time. Of note,

the study found that the course of illness was less severe and degree of disability associated with the illness was lower in subjects in the developing world, with 36% having a continuous or episodic course without complete remission, and 38% experiencing complete remission for more than 75% of their follow up time (29).

The course of schizophrenia is often described as falling into one of three patterns: improvement and recovery; episodic course with periods of fair functional recovery between episodes; and a chronic and deteriorating course. However, Andreasen states 'this concept has been present for many years as the 'rule of thirds'... (but) the rule of thirds had no empirical basis' (30). The comment is part of an editorial on the need to establish standard remission criteria for schizophrenia that would support predictions of course of illness. Long term course of illness is also difficult to assess precisely in schizophrenia due to loss to follow-up of cases in community samples, and the bias towards a chronic course in samples drawn from institutional residents, as well as the lack of standardized criteria for remission or other outcomes. A surveillance system for schizophrenia would have to be designed to handle the complexity of cases who at one time met the diagnostic criteria but who may currently be in remission, or who may follow an episodic course, as opposed to a more straightforward chronic course.

A surveillance system that generates longitudinal data about cases could provide important evidence on long term effects of early intervention at the individual level, as well as on the effects of broad changes in social policy such as sentencing practices in the court system, or income and housing supports to low wage earners, on health

outcomes. Such a system located in Ontario would provide data that would reliably describe the course of illness in this province.

Cost

The cost associated with schizophrenia is high for a condition of low incidence because of frequent hospitalizations and the degree of disability associated with the illness (31). The cost of illness can be estimated in several ways; estimation depends upon assumptions about prevalence and on calculating the attributable costs in health care and social service sectors. Knapp et al. reviewed a number of studies, mostly from Europe and North America, on the costs of schizophrenia. Most studies included direct as well as indirect costs due to lost productivity of the individual affected by illness and of family members acting as caregivers. Although studies use different reference years and different currencies, most estimate the direct health care cost of schizophrenia to be between 1.5% and 3% of national health care expenditures (32).

In a study of the costs of schizophrenia in Canada for 1996, direct and indirect costs were estimated to be equivalent to 0.3% of the Canadian gross domestic product for that year (33). Direct and indirect costs of schizophrenia in Canada for 2004 were estimated at CAN$ 6.85 billion (34), with the largest part of that (CAN$4.83 billion) being the indirect costs of lost productivity associated with premature mortality, and morbidity. Direct costs within health care and other sectors amounted to CAN$2.02 billion. The authors included hospitalization and professional billings, residential care, costs of antipsychotic medications, administration of income assistance, and incarceration costs in the direct health care and non-healthcare costs. Costs associated with police and

judicial system contacts other than actual incarceration for people with schizophrenia were not included. Goeree cites CIHI data reporting 32 538 hospital separations for 2004, including acute and non-acute (PPH) hospital separations, and a staggering 2 366 722 hospital days from both types of hospitals combined (34). Both Canadian studies noted that many assumptions were made about prevalence, mortality, morbidity, employment levels and other cost factors. In sensitivity analysis, the most influential factor on the final cost estimate was illness prevalence, which is not known for Ontario or Canada but would be known through surveillance.

Cost of illness, as well as cost effectiveness of treatment studies, are complex issues with mental illness and a detailed review of such studies will not be included in this chapter. However, two related points relevant to schizophrenia are worth mention. First, the cost-effectiveness of schizophrenia treatment is widely acknowledged to be low compared to treatment of other higher prevalence mental illnesses such as depression (35,36). The second issue is that inclusion of values such as equity and recognition of severity of illness in an analysis of spending on schizophrenia will support continued funding of treatment and care for people with schizophrenia. Consideration that the risks of not treating are accrued beyond the individual with the illness, but fall to family members and to the general population in the case of disruptive or violent behaviour, should also be included in any analysis of treatment costs (35).

Schizophrenia is an illness whose impact and costs, whether measured by hospital days, years lived with disability, loss of productivity, morbidity and premature mortality, or individual and family burden, are significant. Surveillance of schizophrenia could play an important part in planning clinical services, research into causes and treatment for

schizophrenia, and allocating resources within the health research and clinical care envelopes. As etiological research in schizophrenia advances and leads to interventions, surveillance would also play an essential part in evaluating any large scale prevention or early intervention efforts.

Preventability

The preventability of a disease, or the possibility of understanding and mitigating its impact, is an important consideration for introducing surveillance, along with factors such as cost and severity. Preventability can include primary prevention of an illness by preventing its initial development, secondary prevention through early detection and arresting its progression, and tertiary prevention through mitigation of the impact of illness. All of these can be considered in judging the suitability of a condition for surveillance (37).

Primary prevention of schizophrenia is a topic of speculative and research interest (36,38,39) but proven primary prevention strategies do not currently exist. The evaluation of primary prevention strategies aimed at perinatal risk factors would benefit from a surveillance system as the time elapsed between such prevention measures and the time of maximum risk for incident cases would be twenty or more years.

Secondary prevention, or early detection and treatment to improve the clinical course of schizophrenia, offers a compelling reason to support surveillance of illness. Schizophrenia is a condition known to be associated with delays and barriers to receiving treatment and the mean period elapsing between the actual onset of psychosis and first contact for treatment is over a year in addition to a prodromal phase that may last more than a year (40). Although delays in seeking contact with health care providers on the

part of the patient and family will result in cases falling outside the reach of surveillance, there are also delays between the time of contact with a health care provider after the onset of psychosis and the time of initiation of adequate treatment. A fascinating Ontario study of people presenting at a clinic for first episode psychosis showed the median delay between contacting a care provider after the onset of psychosis and initiation of adequate treatment was 5.1 weeks, with a few people experiencing very long delays, causing the mean to be 44.6 weeks. The types of first contact after onset included (in descending order) emergency departments or other hospital based services, family physicians, psychiatrists, and other types of service including school counsellors, psychologists or social workers (41). Some patients may not be recognized as suffering from psychosis at contact, but some will receive diagnoses within the schizophrenia spectrum (this will be discussed under case definition in Chapter 2) at the time of first contact and would thus appear within surveillance. The gap between a diagnosis of psychotic illness and initiation of adequate treatment is important information that could be provided by surveillance and linked case registry at the provincial or at a local level. This would offer an indicator of quality of treatment for psychosis and would allow targeted services and education for care providers where most needed to decrease the delay in initiation of adequate treatment. The possibility of influencing the course of illness through early intervention early in a first psychotic episode, or even intervention at a prodromal stage is the focus of much current clinical and research activity. There is evidence that the duration of psychosis preceding initiation of treatment is associated with a poorer outcome in short and medium term follow-up (42-44). The introduction of specialized 'first episode psychosis' services in Canada and elsewhere resulted from findings

demonstrating the value of early intervention. The possibility of increasing the proportion of people with a first episode who have a milder course of illness is an exciting current in schizophrenia research, often carried out in these specialized services.

Tertiary prevention or mitigation of the health effects of people with diagnosed disease would be supported by surveillance of schizophrenia as a way of reviewing whether people once diagnosed have ongoing contact with appropriate health care. The question of how surveillance of schizophrenia can or should be used to improve care by supporting secondary or tertiary prevention efforts will be discussed in Chapter 2.

Known risk factors and public interest

Public interest is the last criterion from Teutsch's suggested list for considering a condition for surveillance. Although not defined by Teutsch, this can be considered both as the public's actual level of interest in the condition, and what is relevant to public health in that particular population. Public perception of schizophrenia in Canada is of a severely disabling illness, ranked as the most disabling possible condition by Canadian respondents in a WHO survey (23).

A number of known or suspected risk factors or correlates are linked with the incidence of schizophrenia. Some of these are more likely than others to affect the incidence and prevalence of schizophrenia in the Ontario population and thus are of greater public interest in this province. Age, sex, season of birth, perinatal influences, family history, immigration status, exposure to an urban environment, and socioeconomic status are all associated with incidence and prevalence of schizophrenia. They will be considered here in terms of their potential effect on incidence and prevalence of the illness in Ontario.

There is much still to be learned about the epidemiology of schizophrenia and much of what is known is drawn from large registries located in Europe, and American surveys. Surveillance of the illness in Ontario would help to complete the epidemiological picture in a Canadian context.

1.2.2 The Epidemiology of schizophrenia

Age

The incidence of schizophrenia peaks in the age group 20-29 years for both men and women, with a mean age of first hospitalization of 29 years for men and 35 for women, based on Canadian national data reported in 1977 (1). Due to cases in remission, and also due to the differential mortality rate for people with schizophrenia, prevalence will be lower in an older population. This is relevant to rates of illness in regions or subpopulations such as Aboriginal people where a difference in age structure from the larger population can result in higher crude prevalence of the illness. Age structure of the population is relevant in planning health services, but age standardization would have to be used if using provincial or regional level surveillance data for research purposes. Date of birth should be included in records for surveillance so that any cohort effects can be detected.

Sex

Schizophrenia is slightly more common in men than in women, with an odds ratio (OR) of 1.4 according to recent meta analyses (45), although this finding is not

universally accepted as for many years schizophrenia was believed to affect men and women in equal numbers (46). Women do have a later age at onset of illness on average, as well as a different distribution of age of onset, and on average a slightly less severe course of illness than men (1,29,47). Although these findings have led to various etiological theories they are not unique or exaggerated in the Canadian setting. Inclusion of sex in case records will allow analysis to include this as a factor in longer term outcomes and other research.

Season of birth

A small excess of winter births in people with schizophrenia has been shown in the Northern Hemisphere (48,49). This intriguing finding has not so far led to specific etiological findings, although exposure to common seasonal viruses or vitamin D levels at critical points in gestation has been postulated. This excess has been found in many settings and is not of special interest in the Canadian or Ontario setting, as the effect can be assumed to occur in Ontario based on the many replication studies in existence. Although the relative risk associated with winter birth is small, it is estimated to have a population attributable risk of over 0.1 or 10% because large numbers of people are born in winter (15). Inclusion of an accurate date of birth with each record will ensure this can be confirmed in the Ontario population.

Perinatal influences

Perinatal risk factors are not unique in the Ontario population, but these factors are of interest in this setting. With a well developed public health system, and publicly funded health care, intervention to mitigate some prenatal and perinatal risks should be

possible in Ontario as these exposures become better understood. Surveillance will be an important part of establishing a baseline against which to evaluate any public health interventions aimed at prenatal and perinatal risk factors for schizophrenia.

A number of specific prenatal and perinatal conditions have been related to an increased risk of schizophrenia. Some are clearly proxy variables for a more specific but unidentified exposure, such as winter birth described above. Obstetric complications examined as a group and individually as pre-eclampsia, Rh incompatibility and events causing hypoxia, have all been shown to elevate the risk for schizophrenia, with odds ratios of up to 2(50). Exposure to influenza or rubella *in utero* has been associated with elevated risk (51).

Increasing paternal age has also been associated with an increased risk of schizophrenia, with a relative risk increasing gradually with age and reaching 2.02 for fathers aged 45-49 and slightly higher for fathers aged over 50 compared to fathers aged less than 25 in an Israeli population (52). This is of interest in Ontario and the rest of Canada where parental age has increased in the last decades. Parental age at first birth is influenced by social and economic factors and changed considerably through the 20th century in Canada. Average age for men at marriage and maternal age at first birth are both approximations of trends in paternal age. Average age for men at marriage was in the late twenties in the period 1921 to 1941, reflecting difficult economic times. The average age at marriage dropped for the middle years of the twentieth century, affected by factors such as the Second World War and the economic boom of the years after the war. Average age at marriage then rose again at the end of the century to return to the late twenties again for men by the 1990s. In 1997, 31% of first births in Canada were to

mothers over 30 years of age. Ten years earlier these represented only 19% of births in Canada (53).

Many of these risk factors are not specific to schizophrenia (for example exposure to rubella *in utero* or events causing hypoxia have other potential negative outcomes), and because of the long time between exposure and manifestation of disease, ongoing surveillance is necessary for monitoring of the impact of demographic and social trends, as conventional trials would be unable to track the outcome of interventions in the prenatal period.

Urban birth

Urban birth has been studied in a number of settings, particularly where large case registries, or record linkage are available (49). These studies have shown a relative risk of developing schizophrenia of over 2 for those born in an urban area compared to those born in a rural area (for example 2.4 in Denmark (15)). A large Danish study showed an increasing response with increasing length of exposure to the urban environment (54). In their 2001 study Pedersen and Mortensen showed that when urban birth and length of urban residence from birth to age 15 were both included in a model therefore controlling for each variable, the independent effect of urban birth became insignificant. They suggest that the urban birth association detected in other studies may be a rough proxy for urban residence in infancy and childhood. They were able to demonstrate a dose response relationship between number of years in an urban environment, as well as degrees of urban density, and the risk for schizophrenia. The highest risk category of 15

years in the densest urban area had a relative risk of 2.75 compared to the reference category of living 15 years in the most rural area.

The risk associated with urban birth or residence is of great interest and worthy of study in Ontario. In 2006, 85% of the Ontario population lived in an urban area, compared to the national average of 80% (55), and the rate of urban residence in Ontario has increased steadily since the beginning of the 20th century. Mortensen et al. (15) estimated the population attributable risk (PAR) of urbanization in Denmark to be 34%. In other words, if the risk associated with urban birth could be reduced to that of the reference category of rural birth, 34% of cases could be avoided. Although the relative risk was found to be less than 3, the widespread exposure in the population of urban birth means the PAR is large, and this will be the case in Ontario as well.

Trends over time

The incidence rate and course of schizophrenia may change over time, with some studies showing a decline in incidence in various European populations in the 1960s to the 1980s (46,56) as a general trend or as a cohort effect in small populations. The existence of these trends is not universally accepted (57). Such trends might not be captured in the Ontario population using small samples or periodic surveys of the community, or via contacts with the health care system, but could be detected with a more comprehensive surveillance system. Any evidence demonstrating cohort or time effects could contribute to an understanding of the aetiology of the disease, and possibly its prevention. The elevated relative risk of development of schizophrenia in the offspring of older fathers is an example of a cohort effect that may be influenced by

broad historical events that alter the demographic and reproductive patterns of a population.

Migration

Immigration has been shown in many studies to be associated with an elevated risk of developing schizophrenia, and of other forms of psychotic illness. Most of these studies examine immigrant populations in northern Europe and the UK, although there are older studies from North America recognizing birth in another country as a risk factor for mental illness. A study of 1000 consecutive admissions to a provincial psychiatric hospital in south-western Ontario in the mid 1950s showed that while 18.8% of all admissions were foreign born, 23% of admissions for schizophrenia were foreign born (58). The national proportion of the foreign born population in 1951 was 15% (59). Elevated risks for developing schizophrenia have been demonstrated in immigrants in Denmark (15), and among different immigrant groups in the UK, in Sweden, and the Netherlands.

The increased risk of developing schizophrenia for migrants may be the most relevant known risk factor for the Ontario population. According to 2006 census data, the percentage of the Canadian population that was foreign born was 19.8%, the highest since 1931. The national rate was second only to the rate in Australia among western countries. In Australia, 22.2% of the population was foreign born. The proportion of foreign born residents in Ontario in 2006 was the highest in Canada, at 28.3%, and this is also the highest proportion in the history of the province (60). Because of high rates of immigration to the urban areas in Ontario, this risk factor may influence incidence rates sufficiently to alter population based estimates of incidence and prevalence of disease

based on older community studies. An editorial in the Canadian Journal of Psychiatry states 'North American psychiatry is poised to make an important contribution to the world literature simply by determining whether rates of psychosis among migrants to the United States and Canada are also elevated' (61).

The potential contribution to the literature on the association of migration with schizophrenia and psychotic illness claimed by this editorial is one of the important arguments for surveillance of schizophrenia in Ontario. An understanding of the large impact that the known risk factors including migration might have on the need for health services in Ontario is another. This can be quantified by estimating the PAR. Population attributable risk is 'the incidence of a disease in a population that is associated with (attributable to) exposure to the risk factor' (3).

The population attributable risk related to the risk factor of migration can be calculated using the relative risk from a recent review of mostly European studies of migration and schizophrenia, and the current proportion of Ontario residents who were born outside the country. A meta-analysis of studies of migration and schizophrenia from 1970 to 2003 found a relative risk of 2.7 for first generation migrants (those born in another country) (62). Using the formula shown in Figure 1.1 (63) the PAR for migration in Ontario can be estimated at 0.325. This suggests that over 30% of the illness seen in Ontario is associated with migration if the relative risk seen in European studies can be applied to Ontario. This takes into account first generation, international migrants only. There are also elevated risks of developing schizophrenia in second generation migrants (62,64), and possibly in internal migrants (people moving within Canada), as discussed below.

Population attributable risk for immigrants in Ontario (first generation only)

$$AR_p = \frac{N_1 (R_1 - R_0)}{N_1 R_1 + N_0 R_0} = \frac{p(RR-1)}{p(RR-1)+1}$$

Where $p = \frac{N_1}{N_1 + N_0}$

And N_1 = number exposed, and N_0 = number unexposed.

So p = proportion exposed to the risk factor (63).

Where RR = 2.7 (62)

And p = 0.283 (60),

Then $AR_p = \frac{.283 (2.7 - 1)}{.283 (2.7 - 1) + 1} = .325$

Figure 1.1 Population attributable risk for schizophrenia for immigrants in Ontario

Pedersen and Mortensen (54) examined the effect of migration within Denmark, considering whether the move was to an area of higher urban density, and also whether the move was within or between small municipal regions. The study showed that moves between regions up to age 15 years were associated with a small but significant increased risk for later developing schizophrenia. The relative risk for someone with three or more moves between the ages of 5 and 10 years was 1.28, and the relative risk for a single move between municipalities between the age of 13 and 15 years old was 1.45, and the relative risk of three or more such moves for the same age group was 2.49. The authors

state 'Denmark is a small homogeneous country... distances are small...' (pg 1040). This study had the power to detect and untangle several effects of fairly small size because it was based on a cohort of 1.89 million people drawn from the extensive birth and residence records and a psychiatric case registry maintained in Denmark, both national in scope. The effects described are fairly small, but if they are occurring in Ontario they could exert larger effects given the extent of migration to our largest cities, especially Toronto. Many people migrating to cities and suburban areas in this province are not considered 'immigrants' for census purposes because they come from other Canadian provinces or more remote regions of Ontario. In these situations both the physical distance and the cultural change associated with an interprovincial move could be greater than would be experienced by moving within Denmark. For example, in Ontario in 2006 there were close to 186 000 interprovincial migrants to Ontario over the five years previous to the census (60). This is a five year cumulative incidence of interprovincial migration, not a prevalence, so the prevalence of 'rest of Canada-born' Ontario residents would be higher. The large number of international migrants combined with the number of interprovincial or inter-regional migrants in this province suggests that surveillance of schizophrenia in Ontario would be of great value in health services planning and targeting of resources to areas most at risk. It also suggests that Ontario surveillance would be an excellent source of data to study the migration effect in North America, where the history and scale of immigration are different from that of Europe.

Socioeconomic status

Socioeconomic status is known to be associated with schizophrenia but the direction of causality is unclear. Due to the age of onset of illness, and the nature of the

symptoms, which often prevent or interrupt secondary or post-secondary education, people with schizophrenia disproportionately experience the 'drift effect' and become unemployed and poor. Studies attempting to distinguish social causation from social drift have looked at the occupation of the patient's father at the time of birth of the identified patient. These studies have had inconsistent findings, with some showing the distribution of occupations to be similar to the larger population. Bresnahan and Susser suggest in their review that the effect of socioeconomic status on the risk of developing schizophrenia 'the weight of evidence suggests that (it) has at most a modest effect on risk' (65). While the association between socioeconomic status and schizophrenia is not known to be exaggerated in Ontario, information from surveillance could identify regions or even neighbourhoods that should receive intervention based on a high prevalence of disease.

Family history

Family history of a first degree relative with schizophrenia carries a higher relative risk for developing the disease than any other risk factor. Most estimates place the relative risk associated with either parent or a sibling between 7 and 10, with a higher relative risk for identical twins (2,15). While family history has been the subject of much interest regarding genetic causes of schizophrenia, it appears now that genetic influences are complex, varied, may include small influences from many genes, as well as environmental influences. First degree relatives of people with schizophrenia may exhibit non-specific signs that are shared with their affected relatives, such as increased ventricular size and subtle abnormalities in eye tracking. However, family history has little value in predicting who is at risk of developing the disease due to the relatively

small numbers in a population who have this exposure, and the proportion of people who develop the illness despite not having an affected family member (15). There could be value in targeting some primary prevention measures at family members considered at risk, such as concerted education and information regarding the potential effects of marijuana on a vulnerable person, but this should be combined with more population based strategies as knowledge about risk factors increases (38). Surveillance linked to registry based data may make it easier to consider the interaction between the environment and the genetic make-up of affected and non affected individuals.

1.3 Proceeding with surveillance of schizophrenia in Ontario

I conclude that the introduction of surveillance for schizophrenia in Ontario is supported using Teutsch's criteria for introduction of surveillance (11). In addition to the contribution that accurate descriptive epidemiology might make to aetiological understanding, there is a basic need for accurate prevalence and incidence estimates at the regional and higher levels to allow for good planning of mental health services. The delivery of mental health services has undergone major changes in the last decades in many places including Ontario with the focus shifting from long term, institutional care to community based care. The publication 'Making it Happen' (66,67) describes the direction for mental health care in Ontario as planned by the Ministry of Health and Long Term Care, the major funder of mental health services in the province. This will be a continuum of care that provides different levels of intensity of service to individuals depending on the severity and course of their illness. The ability to plan for different parts of service delivery depends not only on simple incidence numbers but also a

predictive model of course of illness and outcomes for those diagnosed with schizophrenia. Surveillance could identify prevalence of illness in groups or regions that might require specialized service delivery models. It could identify schizophrenia and related illness and if it included a longitudinal case follow-up it would include data on the course of illness. Basic surveillance data supplemented with a case registry for those cases with ongoing treatment contact could support etiological and other research on causes and interventions for schizophrenia.

McGrath in his 2005 paper 'Myths and plain truths about schizophrenia epidemiology' states 'schizophrenia is a group of disorders marked by variability on many criteria... there are gradients across space and across time. The more gradients we find, the more candidate exposures we can generate. At long last we will be able to 'gain traction' on the epidemiological landscape' (45). The Canadian epidemiological landscape of schizophrenia remains to be systematically mapped, but this process could be started in Ontario by using and combining existing data sources to arrive at as complete a system as possible. Such a population level system would fulfil the need for data for service planning, and if it included longitudinal record linkage, could generate data that would serve the research, planning and clinical care agendas. Much can be learned from earlier efforts at mapping the landscape. Chapter 2 will examine some of the more important North American surveys and studies of the epidemiology of schizophrenia and other mental illness. Chapter 2 will also consider the essential elements (5) of a surveillance system for schizophrenia.

Chapter 2 Essential components of a surveillance system for schizophrenia

The required components for surveillance systems in general were listed in Chapter 1. Chapter 2 will consider each of these elements as they apply to surveillance of schizophrenia. Case definition, an understanding of the population under surveillance, the cycle of surveillance including information gathering and also plans for analysis and dissemination of results, and plans to address confidentiality concerns will be considered (5). Some of these elements, for example analysis and dissemination, will not differ greatly in the case of schizophrenia from surveillance for other chronic disease; but some of these elements are more complex for mental illness in general than for chronic physical conditions. Case definition, for example, is a complex issue in the surveillance of mental illness, and even schizophrenia, one of the more stable diagnostic categories in use in current psychiatry, presents its problems. The various sources for gathering of information for surveillance will also be considered in Chapter 2. These include surveys, administrative health data and disease registries, sentinel reports and notifiable disease reports (5).

2.1 Case Definition

Case definition is an essential part of the design of a surveillance system, but case definition in psychiatric epidemiology is a complex issue, as classification systems have changed over time, and simple diagnostic tests to support binary 'caseness' do not exist for most diagnoses. Three related questions must be resolved concerning case definition

for a surveillance system for schizophrenia. First, what classification systems for mental illness, and for schizophrenia specifically, are available and what will be the implications of using a given classification system? Second, which disorders do we want to capture and which do we want to exclude, assuming an acceptable method for case identification according to a classification system? These questions relate to the clinical and practical issues in distinguishing schizophrenia from other psychotic illness, as well as the desirability (or not) of doing so for research and health services planning purposes. Third, for the purposes of data collection for surveillance, what will be considered the acceptable equivalent of the gold standard for case identification? Given the lack of a diagnostic test, the 'gold standard' in identification of cases in psychiatry is usually considered to be the 'competent clinician' conducting an interview (68), using standard diagnostic criteria such as are defined in the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV), or the International Classification of Diseases tenth edition (ICD-10). For example, if a surveillance system is to use discharge abstracts for case identification, a physician discharge diagnosis of schizophrenia might be considered necessary and sufficient, although the sensitivity and specificity of discharge diagnoses in identifying individuals who meet DSM-IV criteria may be imperfect. (The accuracy of discharge diagnoses will be addressed later in Chapter 2). In the case of a community health survey, a structured interview based on DSM criteria and administered by a trained lay interviewer may be considered an acceptable identification method for cases of mental illness.

Narrow criteria based on rules that include or exclude individuals from a diagnostic category can give high specificity and reliable data for etiological research using comparison

studies. Such narrow criteria based on diagnostic categories may also lead to a biased epidemiological picture as case identification may be dependant on prolonged contact with a physician. Broader criteria based either on presence of symptoms or on collapsing several narrow diagnostic definitions can give better sensitivity, as well as supporting research on the broad effects of psychiatric symptoms on functioning in the community (68). A classification system based on physician evaluation of a patient's symptoms against a set of criteria is narrower and rule based, while a community survey asking about the presence of depressive or psychotic symptoms uses broader, self-assessed criteria to identify cases. These may both be acceptable for different purposes as the narrow criteria will usually have a high specificity and identify cases of illness that are fairly homogeneous, while the survey looking for the presence of certain symptoms may identify cases that are not receiving treatment, and cases will represent a broader spectrum of severity of illness.

Psychiatric illness is currently classified using either the WHO's ICD-10, or the American Psychiatric Association's DSM, fourth edition with revisions to the text. Although there is much overlap between these two systems, they do not perfectly align in their current versions (69). For a number of major mental illnesses, including schizophrenia, there are also research diagnostic criteria, which are typically narrowly defined to support high specificity.

2.1.1 The DSM and the standardization of psychiatric diagnosis in Canada

The Diagnostic and Statistical Manual of Mental Disorders (DSM) is the classification system for psychiatric disorders devised and adopted by the American Psychiatric Association. The most recent edition, DSM-IV with text revisions (DSM-IV-TR), is used in medical training and practice across the United States and Canada. It is

used in undergraduate medical education in Canada as the standard definition of the various psychiatric conditions, and little or no reference to any other classification systems is routinely made in teaching, although this has not always been the case. An understanding of how psychiatric diagnosis in Canada arrived at its present state will help clarify the potential pitfalls associated with DSM diagnoses, and allow a planned surveillance system relying on current DSM classification to 'make a virtue of necessity'.

In the immediate post-war Canada, medical school curricula reflected the various currents present in psychiatry at the time: the biological, descriptive, and the psychotherapeutic. These gradually became more integrated, starting with the more descriptive approach introduced by the first version of the DSM in 1952. Further standardization of physician education in psychiatry was supported by the inclusion of psychiatry as a subject in the Medical Council of Canada Examinations starting in 1969 (70). In the brief essay 'Psychiatry in Canada from 1951 to 2001' Greenland et al state that the DSM 'classification system... had a profound effect on the training and practice of psychiatry in Canada' (71) (pg. 9). Canadian medical schools have worked towards a shared blueprint for the organization of undergraduate psychiatric education through a national organization of directors of undergraduate psychiatric education (70). This means that the amount of exposure of each medical student to different psychiatric settings and populations could vary considerably, although the academic content regarding diagnosis would be consistently based on the DSM, and graduates of the various schools would have to write the same exam. Residency education in psychiatry does allow for the exposure of the resident to a variety of clinical settings and populations, and is also based on the DSM system for diagnosis. The system for

recruitment of residents changed in Canada in 1984. Starting in that year, residents were drawn almost exclusively from the medical student pool. Before that, psychiatry had traditionally drawn up to two thirds of its residents from foreign-trained physicians and from practicing physicians wanting to return for graduate education in psychiatry (72) meaning that residents were coming from a wider variety of undergraduate medical programs. The change meant that psychiatric residents come from a more homogeneous medical education in the pre-residency years than was previously the case, despite the remaining variation in undergraduate education across Canada. This shared training has supported the consistent national use of the DSM diagnostic tradition.

Any surveillance system for schizophrenia based on large existing databases in Ontario will necessarily be surveillance for DSM defined illness. DSM defined schizophrenia is also the most useful definition for international comparison (73), but it is not without limitations. Understanding the history and some criticism of the current DSM classification system will guide the planning of surveillance built around DSM case definitions, to make it as useful as possible to future users.

2.1.2 The classification of mental illness and the evolution of the DSMs

A brief glimpse into the history of psychiatric nosology, and some of the features and criticisms of the DSM, particularly in its classification of psychotic disorders, will help clarify the implications of DSM diagnostic categories for surveillance of schizophrenia. It will also illustrate the challenge of deriving a classification of schizophrenia from data sources such as population surveys, guiding our judgment of these as potential sources of surveillance data.

North American psychiatric hospitals in the middle to late nineteenth century housed people with a collection of conditions, many of which would now be seen as 'organic' (and acknowledging that the term 'organic' was removed from the DSM-IV). These would have included syphilis (general paresis), Huntington's Disease, nutritional deficiencies which manifest in neurological or behavioural change, and dementias as well as schizophrenia and bipolar disorders. The increase in organic conditions seen in the American hospitals by the later 19th century was mirrored by an increasingly biologically based understanding of the severely ill population and a 'therapeutically nihilistic' approach to patients (74) compared to the early 19th century. Increased understanding of the pathology behind some of these conditions has moved them at least partly out of the domain of psychiatry and into other medical specialties. However as organic conditions such as advanced syphilis began to be recognized and understood in terms of discrete aetiologies, the classification of, and therapeutic interest in, the remaining conditions increased by the early decades of the 20th century. Interest in the conditions seen in outpatients also grew at this time and the outpatient clinical setting fostered a more psychodynamic and psychosocial orientation to the understanding of psychiatric illness.

The recognition of the need for some kind of systematic classification in American psychiatry led in 1917 to the development of a list of psychiatric disorders by the precursor to the American Psychiatric Association. The list was essentially based on the classifications developed by Emil Kraepelin, who separated mood disorders including bipolar disorder from schizophrenia[2] and who assumed these conditions had

[2] The origins of the classifications systems now in use by psychiatry come from descriptions of symptoms in case histories, and nosological assignments of these symptoms by a number of clinicians working in the late nineteenth century and the first half of the twentieth century Two of the most influential of these were Emil Kraepelin and Sigmund Freud. Both drew on observations and theoretical

discrete etiologies that would soon be mapped onto discrete pathologies visible on autopsy as was the case with the recently identified 'organic' conditions (75). This list and several other classification systems developed by different bodies were in use in the US by the 1940s. In 1952 the first Diagnostic and Statistical Manual of Mental Disorders (DSM) was published, with successive editions in 1968 (II), 1980 (III), 1987 (III-Revised or III-R), 1994 (IV) and 2000 (IV-Text Revision or TR). DSM-V will probably appear in 2012 or later (69).

The recent DSMs describe and define disorders using polythetic criteria. This means that for most disorders there are no single necessary or sufficient symptoms as criteria, but rather lists of grouped symptoms or presenting features, some combination of which must be present in order for a given diagnosis to be made. Although the accompanying text may refer to typical findings seen in diagnostic tests, laboratory results are not included in the criteria.

The diagnostic criteria for schizophrenia in the current edition of the DSM (DSM-IV-TR) are the presence for at least one month of two or more symptoms from a list of five – this forms Criterion A. In addition, the individual must exhibit a social or occupational impairment compared to before onset, or compared to an expected age appropriate norm. The total duration of symptoms must be six months or more. Thus,

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works of their predecessors and many contemporaries, but space does not permit mention of others. Freud saw an outpatient population in his clinic and his nosological distinctions based on his formulations of underlying psychopathology describe this population. Freud's contributions were more explicitly theoretical than Kraepelin's, and psychodynamic theory dominated North American psychiatry by the middle of the 20th century

Kraepelin was a physician who saw a more severely impaired, institutionalized population, and his case histories reflected observations over time of a severely and often persistently mentally ill group Kraepelin's accompanying nosological distinctions apply more or less to what would now be considered the Axis I disorders of schizophrenia, bipolar disorder and unipolar depression(75) , and provided a framework for the current distinctions between those illnesses when they all present with psychotic symptoms.

the duration of symptoms is a necessary condition; the social or occupational impairment is a necessary condition (but surely not one unique to schizophrenia), but the actual presenting psychiatric symptoms are polythetic. Hallucinations and delusions, which could be considered characteristic of schizophrenia, are not necessary if the individual shows other symptoms from the list. The exception to the polythetic Criterion A list is the presence of hallucinations that take the form of auditory hallucinations of a commentary on the individual's actions or two or more voices conversing, in which case only the one symptom from the list is required. This rather complex combination of requirements (which will be more fully described below) reflects to some degree the varied historical conceptualizations of schizophrenia.

Schizophrenia has been described for many centuries, although there is uncertainty about its aetiology and about the precise borders that might separate it from other forms of mental illness. Kraepelin emphasized the chronic course and poor prognosis of the illness along with the psychotic symptoms, separating it from other conditions that may include psychotic symptoms but show a more episodic or remitting course. The DSM-IV-TR definition also attempts to separate schizophrenia from other psychotic presentations that might in cross section look like schizophrenia, but resolve fairly quickly, by including the requirement for a minimum duration of symptoms of six months. Kraepelin also distinguished schizophrenia from mood disorders that may present with psychosis (in part based on the different prognosis associated with the conditions). This distinction is reflected in the DSM and will be discussed below. Other theorists emphasized the lack of integration of will, thought, feeling and action. Eugen Bleuler used the term schizophrenia to describe the condition, in reference to this splitting

or disorganization of the mind. These symptoms are reflected in the DSM Criterion A list of symptoms, which includes symptoms of thought disorder along with affective flattening, avolition and alogia (69). Because of the polythetic Criterion A, it is possible to diagnose schizophrenia if several of these symptoms are present, in the absence of delusions or hallucinations, as long as the impairment and duration criteria are met. Another conceptualization of schizophrenia reflected in the DSM-IV-TR definition is that of Kurt Schneider. Schneider emphasized the presence of delusions regarding others being in control of one's thoughts or actions, or others being aware of one's thoughts or auditory hallucinations of voices talking to or about the individual, as diagnostic of schizophrenia. This view is reflected in the Criterion A note indicating that the presence of this type of delusion or hallucination alone is enough to satisfy Criterion A (76). The DSM-IV states that duration and impairment criteria must still be satisfied.

The definition in DSM-IV-TR attempts to capture the serious impairment and potentially chronic course of the illness, but to recognize the diversity in presentations with some patients remaining fairly organized with elaborate delusions and others presenting with very disorganized thoughts and behaviour. Other DSM psychotic conditions that may cause less functional impairment, or have a shorter duration, are described and classified under different names, and will be discussed below.

2.1.3 Criticism of the DSM and of psychiatric nosology

Psychiatry, as a discipline or medical specialty, faces many criticisms from within and from outside medicine, much of it focused on the various DSMs. Some general criticism of the DSM are described below, as well as some criticisms specific to the categorization of psychotic illnesses.

Some critics have cited the increase in the number of diagnoses contained in successive editions of the DSM. Houts compares DSM-IV's increase in diagnostic categories over previous editions with the description of advances in science through classification systems of the philosopher of science Carl Hempel (77). Houts shows that while scientific progress according to Hempel would be illustrated by a reduction in the number of categories, or at least an explanation of the categories by more and more general laws that order those categories, this cannot be claimed for the recent versions of the DSM. Houts criticizes the claim that the diagnostic proliferation in psychiatry simply parallels a similar process in physical medicine. He examines several diagnostic categories from physical medicine showing that where there have been increases each of these can be attributed to a technological diagnostic advance that supports a new diagnostic category by mapping it onto a demonstrable, previously unknown pathological change, a process without parallel in psychiatry. Houts is also highly critical of the methods through which some of the decisions regarding the content of DSM-III were made, that is, consensus of appointed committees, and mediation of disputes by a senior editor rather than unbiased literature review of the best available evidence.

While the DSM-III was recognized for its innovation in introducing the multiaxial format and regrouping of disorders into categories that were more empirically based, the American Psychiatric Association's continuing revision of the DSM at relatively short intervals has been criticized as possibly financially motivated, at least in part, and as having diminishing returns in improvements (78).

Houts, as well as Wallace (74), both point out the inevitable failure of a classification to meet the objective of being 'atheoretical' – an aspiration of the later

DSMs. Wallace emphasizes the importance of acknowledging the impossibility of a taxonomic system that does not have certain assumptions built into it, as a way of ensuring that future editions of DSM are not seen as representing a truth that is independent of values in a way that previous editions (edition II forward) have been: 'DSM-I, although chock-full of theoretical and etiological presuppositions, did not claim to have escaped them. This century's most respected philosophers of science... have held this to be logically and empirically impossible for any classificatory system in any field of the basic natural sciences, much less for the value-laden and extraordinarily multivariable-burdened psychosocial and clinical sciences' (74) (pg 81). Wallace points to the importance of clinician observed behaviour in cross-section, and the relative lack of reference to the patient's subjective history or life events in the description of the disorders as evidence of an implicit theoretical stance in the classification of medical disorders.

Canadian psychiatrists Goldbloom and Garfinkel in their essay 'The next 50 years' acknowledge the importance of the DSMs in moving psychiatry forward by making diagnostic reliability possible; yet they criticize 'the valuing of reliability over validity' and also criticize nosology that lacks reference to an explicit theoretical underpinning. They state their concern that the supremacy of the descriptive DSMs has led to the training of psychiatrists who are 'without sophisticated psychological training (in either classical psychodynamic theory or more recent and well validated psychosocial interventions) or a solid grounding in neuroscience' (79) (pg. 262).

The dichotomous nature of the various definitions of illness in the DSM is not unique to psychiatry, but does impose an artificial structure on what may be a more

continuous distribution of symptoms in the population. Rose and Barker state 'for most acquired diseases the real question in population studies is not 'has he got it?' but 'how much of it has he got?'' (80). In the case of schizophrenia this view is supported by findings that the presence of delusions or hallucinations for example, occurs in some people who do not meet the criteria for the psychotic disorders (76,81). The continuum of psychiatric symptoms could occur both as a continuity between absence and presence of illness, and between mental illnesses that are currently classified as discrete, and even mutually exclusive.

The most commonly suggested alternative to the case definition by criteria that is used by DSM as well as ICD is a dimensional model (81-83). This would separate symptoms such as delusions and hallucinations from other symptom groups such as thought disorder or negative symptoms such as avolition. This is theoretically appealing because it would allow individual patients to register different scores or degrees of impairment in each category depending on their presentation, and would allow natural patterns of symptoms to be captured rather than choosing one diagnosis over another in the hierarchical way currently set out by DSM. Whether this type of classification is supported by further research and is adopted in a future edition of the DSM remains to be seen, as dichotomous case definition has great value for the clinician who must make decisions regarding individual treatment. While there are conceptual limitations of a dichotomous classification, as Rose and Barker state 'the research worker may be content to describe his distributions, but for the man of action dichotomy is unavoidable...' (80). Surveillance based on, and serving a clinical care system, will be tied to this type of operational definition as long as they are widely in use in the clinical setting, but the

limitations may be mitigated by careful supplementary surveys and samples using other measures, and by including conditions defined by DSM to be psychotic disorders that do not meet all the criteria for schizophrenia.

2.1.4 Affective and non-affective psychosis

The distinction between psychotic disorders and affective disorders, including those accompanied by psychotic symptoms, dates back over 100 years to Emil Kraepelin's description of psychotic symptoms in what he separated as schizophrenia (Kraepelin's term was dementia praecox) and bipolar disorder (Kraepelin's manic-depressive insanity).[3] Although the DSMs have claimed to be 'atheoretical', the continuing separation of affective and non-affective psychoses under different headings in the DSMs has been the subject for some debate. Crow, for example, believed that the psychotic illnesses, including bipolar disorder, are different expressions of a single disease and will prove to have a common aetiology (84). The continuing separation of these conditions in current diagnostic classification systems may also shape the types of questions asked in the research context, for example by excluding participants from 'first episode psychosis' studies if they have a diagnosis of an affective disorder with psychosis (85). The differences in symptom combinations, prognosis and long term outcome

[3] His classification was based both on the presenting symptoms observed in his patients and the course of illness over time. Schizophrenia was seen as the more chronic, deteriorating condition, and included what we would now refer to as both positive and negative symptoms, and bipolar disorder was seen to be episodic, to present with mood-congruent psychotic symptoms and show a better long-term prognosis This distinction between the two groups of psychotic disorders was supported and expanded by other clinicians and researchers and incorporated into the DSM and ICD classification systems (86) Kraepelin, as well as other clinicians working in the late 19th and early 20th centuries, would have postulated a link between the groups of symptoms observed clinically and divided theoretically into separate diseases, and anatomical or cellular abnormalities, as well as other causal factors In the case of the two categories of psychotic illness described by Kraepelin, no such corresponding findings in neuroanatomy or aetiology materialized during that period, but the dichotomy has remained in subsequent classification systems (75)

continue to support a clustering of patients around the affective and non affective psychosis types but whether and where there is true discontinuity between these is not clear (83,85,86).

2.1.5 Schizophrenia and other psychotic disorders in the DSM

In developing a surveillance system for schizophrenia, we must decide how broadly to cast the diagnostic net. In its section 'schizophrenia and other psychotic disorders' the DSM-IV-TR includes schizophrenia (including subtypes), schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder and diagnostic categories for psychotic disorders secondary to substance use, secondary to other medical illness, and psychosis 'not otherwise specified'. Because the relationship of schizophrenia to some of the other psychotic disorders is unknown, and because of the possibility of 'diagnostic instability' of some of the DSM-IV disorders, the inclusion or exclusion of each of these disorders as cases for surveillance must be carefully considered. The diagnosis 'schizotypal personality disorder' is also included in DSM-IV, although not in the psychotic disorders section, and will also be considered. The DSM approach to defining schizophrenia was briefly described earlier; the following sections describe the definition of the other, related disorders.

2.1.6 Schizophrenia in DSM-IV

The DSM-IV uses both the criterion A list of symptoms, at least two of which must be present in order to diagnose schizophrenia, along with a six-month duration of symptoms, and a requirement that impairment in functioning must also be present. The

criterion A list includes delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behaviour, negative symptoms such as affective flattening, alogia or avolition. The diagnosis can be made if only one of these symptoms is present, 'if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behaviour or thoughts, or two or more voices conversing with each other' (as long as the duration and impairment criteria are also met) (69). There is also a criterion that distinguishes schizophrenia from a mood disorder with psychotic features, based on the timing of when mood symptoms and psychotic symptoms are present. The diagnosis should be made only if the patient's condition is not due to substance use, a medical condition, or autism or other pervasive developmental disorder. The diagnosis of schizophrenia can be further sub classified into paranoid, disorganized, catatonic, undifferentiated, and residual types. These subtypes should be captured by surveillance when they are available, for the information they may provide about prominent symptoms, although is not clear what the meaning of these subtypes is etiologically. Family studies have failed to show an increased risk for a particular subtype in family members of an affected person, although the familial risks for schizophrenia in general are well documented (87).

2.1.7 Schizophreniform Disorder

Schizophreniform disorder is described in DSM-IV as meeting the diagnostic criteria for schizophrenia except for the duration of symptoms and the requirement for functional impairment. The duration of symptoms is from one to less than six months. The diagnosis can be made provisionally if the individual continues to exhibit symptoms but the six months have not elapsed. At six months the diagnosis could be changed to

schizophrenia if symptoms continue to the criteria for schizophrenia. Of note, the ICD-10 diagnostic category for schizophrenia includes a requirement for duration of symptoms of only one month, and does not require functional impairment, and is thus essentially a single diagnostic category that encompasses the DSM-IV diagnostic categories of schizophrenia and schizophreniform disorder (69).

To exclude the DSM-IV schizophreniform disorder from surveillance would exclude valuable information about the incidence of shorter duration psychotic illness, as well as the record of first onset of psychosis in cases where the individual has a psychotic episode meeting full criteria for schizophrenia at a later date. As discussed in Chapter 1 the possibility of secondary prevention would argue for the inclusion of early cases in surveillance and a possible case registry, even when full criteria for schizophrenia are not met. Inclusion of schizophreniform disorder would also make a database from an Ontario surveillance system more compatible with ICD-10 based databases. Hence, schizophreniform disorders should thus be included in the case definition, but as a separate category from schizophrenia, allowing flexibility without losing information.

2.1.8 Schizoaffective disorder

In their *DSM-IV-TR Guidebook,* First, Frances and Pincus, themselves editors of the DSM-IV-TR, state that schizoaffective disorder 'fills a necessary and important hole in the diagnostic system, but unfortunately it does not do its job very well' (69) (pg 172). The criteria for diagnosis of this disorder include symptoms meeting the criteria for a mood disorder occurring at the same time as psychotic symptoms as described in the criteria for schizophrenia, but where the psychotic symptoms occur for at least two weeks in the absence of the mood symptoms. If the psychotic symptoms occur only in the

presence of mood symptoms, the diagnosis should be a mood disorder. The authors acknowledge the difficulties in applying the criteria and that 'this disorder is often unreliably diagnosed' (69) (pg 175). The requirement for significant presence of psychotic symptoms in the absence of mood symptoms, as well as the presence of mood symptoms that would meet the criteria for a mood disorder for a period of time during an episode of illness that includes both psychotic and mood symptoms is an attempt to provide a boundary for the clinician between what are classified in DSM-IV as schizophrenia and other psychotic disorders and what are classified as mood disorders (many of which may include psychotic symptoms). Diagnostic stability has been reported to be poor both in cross-section and over time (86) and this should be considered when using any resulting data for research purposes. However, cases diagnosed with schizoaffective disorder should clearly be captured, under separate coding from schizophrenia, as the group would include people with prominent psychotic symptoms. Retaining this group will be important for service planning and also to ensure ongoing usefulness and flexibility of surveillance data if diagnostic criteria change regarding concurrent psychosis and mood symptoms.

2.1.9 Other psychotic disorders in DSM-IV

Several other diagnoses are listed in the DSM as other psychotic disorders. These will be considered individually for inclusion in surveillance. As schizophrenia is probably part of a spectrum of psychotic disorders and of subclinical states as discussed earlier, the inclusion of related disorders under separate coding in surveillance for schizophrenia will give a clearer epidemiological picture and also support the usefulness

of surveillance data if the boundaries between some of these disorders change in future editions of the DSM.

Delusional disorder is a diagnosis made where delusions present for more than a month, in the absence of other psychotic symptoms of schizophrenia. Functional ability is generally not impaired, except where it is as a direct result of the delusional content. This diagnosis should be included in the cases collected by a surveillance system, but coded separately so the information on severity and functional impairment will not be lost for the purpose of planning of mental health services.

Brief psychotic disorder is a recommended diagnosis for cases exhibiting a checklist of symptoms for a period of one day to one month, with a return to the premorbid functional level. Unlike schizophreniform disorder described above, the diagnosis should not be made provisionally: it should not be made until it is clear that the individual has recovered the premorbid level of function and the symptoms have resolved in one month or less. It could be useful to collect cases meeting the diagnostic criteria for brief psychotic disorder for the purposes of research looking at vulnerability to psychosis, or investigating spectrum disorders, however cases should clearly be coded separately from schizophrenia, as the ongoing service needs would be different from what would be required for individuals with psychotic illness of longer duration and causing functional impairment.

'Shared psychotic disorder' is a diagnosis to be used when an individual shares a delusion with another person, but does not suffer from a primary psychotic disorder. This diagnosis was previously known as *folie à deux*. It should be included as a case under its

own coding, as it is relevant to service planning, and also may represent a group of people with vulnerability to psychosis but without the complete expression.

The diagnostic category of psychosis secondary to substance use is described in DSM-IV as being potentially related to street drug or alcohol use, or related to side effects of other prescription medications especially in older adults, or to accidental exposure to toxins (69). Although there is an etiological assumption implicit in the diagnosis, this should still be captured in a surveillance system for schizophrenia. The possible cause-and-effect relationships between primary psychotic illness and substance abuse remain unclear, but there is good evidence that substance abuse can precede and likely cause lasting psychotic illness at least for some street drugs and at least in a subset of vulnerable individuals (88). These cases should therefore be captured under their own diagnostic category. Some people diagnoses with psychosis secondary to substance abuse will go on to be diagnosed with other schizophrenia at a later health care contact (89).

The diagnostic categories for psychosis secondary to other medical illness could contribute information relevant to health services planning, but is probably best captured through other systems. While collecting these cases could be of value for both service planning and epidemiological purposes, this is not directly relevant to planning health services for those with a primary psychotic illness. The assumption of aetiology in this diagnosis also makes it not necessary to include in a database that could be used for etiological research into schizophrenia. The diagnostic category for psychosis secondary to a medical condition could provide information relevant to health services planning, although simple case identification would need to be supplemented with considerable

clinical detail in order for this to be useful. Two examples of medical conditions that might lead to psychosis among other symptoms are multiple sclerosis and Huntington's disease. In both these cases the psychotic symptoms might be persistent and require ongoing treatment through mental health services, and thus be relevant to planning for that sector. On the other hand many other conditions that might include psychosis as a symptom would be best treated through other health services and aimed at the underlying medical cause of psychosis. The need for ongoing psychiatric treatment of individuals suffering from psychosis due to other medical causes should be captured for the purposes of specialized health services planning, possibly through periodic sample surveys of users of psychiatric services. However, this diagnostic category is probably not appropriate for inclusion in a surveillance system for schizophrenia.

'Psychotic disorder not otherwise specified' is included in DSM-IV for situations where the criteria for specific psychotic disorders are not met but psychotic symptoms are present. The criteria may not be met for other disorders due to the clinical presentation, or due to lack of information available to the clinician (for example the duration of illness or level of functioning before the onset of psychotic symptoms, or whether there has been a history of mood symptoms). There is some evidence this might differentially affect immigrants with psychotic symptoms, where language or cultural barriers may delay the sharing of collateral information from family members (89). As successful surveillance for schizophrenia may depend on inclusion of cases encountered in settings outside the usual locations of clinical practice, such as shelters and social service agencies where historical and collateral information may not be available, 'psychosis not otherwise specified' may be the best diagnosis available for some individuals encountered in those

settings. 'Psychosis not otherwise specified' should be included in schizophrenia surveillance as a separate category to capture these cases as well as the cases of unclear presentation. Cases should be coded separately in order to retain information about clearly defined schizophrenia versus other disorders.

Schizotypal personality disorder is included in the DSM separately from the psychotic disorders. The ICD classification system does, however, include this in its section of psychotic disorders. While there would be value in recording this diagnosis in surveillance in order to build a longitudinal picture in cases of diagnostic instability and for studies of schizophrenia and psychosis spectrum disorders, any data gathered about schizotypal personality disorder from a surveillance system based mostly on treatment contacts would be biased towards more severe cases, as the definition suggests a lesser degree of impairment associated with this disorder compared to the DSM psychotic disorders. This should be included under separate coding, and resulting data used with caution. Community surveys suggest that there are people who experience psychotic symptoms who are not in contact with the health care system and who function reasonably well (76).

2.2 The population under surveillance

The ideal population under surveillance can be defined using the Statistics Canada approach of 'usual resident'. According to the 2006 census results, this was 12 160 282 for Ontario (90). A 'usual resident' is a person whose main place of residence is in Ontario, and includes institutional residents. It also includes people who are away at school but return to a family home in the province when not studying, as well as people travelling who usually reside in Ontario.

The choice of data sources will affect how closely the surveillance coverage approximates or represents this population under surveillance. The relationship of the population covered by a data source for surveillance to the true census of usual residents must be known or estimated to avoid inaccuracies in the denominator when calculating rates.

The term 'contact prevalence' will be used in this thesis, as the most accurate description of what can be derived from administrative databases or community surveys. The authors of a study of schizophrenia in administrative databases in BC make the point that people with schizophrenia who are in contact with the health system do not always receive ongoing treatment, even when they do receive a diagnosis of schizophrenia resulting from the contact (91). The authors prefer the term 'contact prevalence' to describe a prevalence rate derived from administrative data, rather than the term 'treated prevalence' which is sometimes used for a prevalence derived from medical records. A person seen for involuntary assessment under the Mental Health Act, who declines treatment, and who does not meet criteria under the Act for involuntary committal is an example of how a person could have health system contact, receive an appropriate diagnosis of schizophrenia and not receive treatment. An approximation of true prevalence using contact prevalence is the aim of the proposed surveillance system and case registry. The relationship of treated prevalence to contact prevalence is an important question of quality and outcomes of psychiatric care in Ontario, but is outside the focus of this thesis (although surveillance and case registry would be useful instruments for measuring and addressing this gap). We can assume that contact prevalence will vary

according to the availability of psychiatric services, creating a gap between true prevalence and its approximation through contact prevalence.

2.3 The cycle of surveillance; sources of data

A surveillance system must have a defined cycle of surveillance that is applied to the population in question, using the case definition. The cycle of surveillance refers to the regular input of information about cases occurring in the population under surveillance, compiling the information and producing reports for dissemination. This information can be gathered from various sources, depending on the condition under surveillance and the nature of the population. Usual sources of information for surveillance of chronic disease include mortality data, community health surveys, administrative databases (gathered for some administrative purpose like funding of health care providers), hospital discharge data, and disease registries often affiliated with specialized hospital units (92). Other sources of data such as notifiable disease reports, sentinel practices and laboratory reporting are more suited to communicable disease surveillance when the need for timely results is more relevant (93).

Examples of large scale community surveys as well as the large discharge and physician billing databases will be considered here for their strengths and weaknesses as possible information sources. Mortality data will not be considered as deaths are not generally attributed directly to schizophrenia.

2.3.1 Community Surveys

Several North American community studies of mental illness that are worth examining for their strengths and weaknesses in order to plan a surveillance system for schizophrenia. The various studies have had as their objective to quantify mental illness in defined geographic regions, but have chosen different ways of defining what they want to measure. The advantage of recording psychiatric symptoms in a community study is that this is not dependent on subjects having direct contact with the health care system, therefore avoiding biases of differential health care use in people with schizophrenia and those without, biases arising from uneven distribution of services, as well as potential biases in health care providers in recording a diagnosis of schizophrenia. Three Canadian surveys, and the large Epidemiologic Catchment Area Study in the U.S. are examined here. Features, strengths and weaknesses of the five community studies considered, as well as a study based on administrative data are summarized later in this chapter in Table 2.4.

Stirling County Study

The Stirling County Study was a longitudinal study of community occurring mental illness, begun in 1948 in rural Nova Scotia. The study was notable for attempting to quantify what the investigators called 'total reportable lifetime prevalence' of mental illness, rather than a treated prevalence. The study used a structured face to face interview with study subjects, followed up with an interview with a general physician working in the region familiar with the study subject. The results of these two interviews were then compiled and reviewed by two psychiatrists who agreed on whether or not each study subject met a threshold to be identified as a 'case'. The structured interviews

with study subjects focused on symptoms of depression and dysthymia, anxiety, cognitive dysfunction and alcohol abuse. The study used DSM-I for defining diagnoses. The study design supported identification of cases of mental illness more than identification of discrete diagnostic categories, perhaps reflecting the theoretical orientation of the times. The total reportable lifetime rate of mental disorder was found to be 20% in Stirling County, which was considered high at the time of first publication of results in the 1960s, but which has since been replicated in other community studies (94).

An interesting feature of the Stirling County Study was the use of the psychiatrists to decide on whether a subject was named as a case, because the initial interviews provided a picture of a continuum of pathology, or at least a continuum of certainty of pathology. This method included an evaluation of whether an identified case was a person with functional impairment and required access to health services, which considerably reduced the reported prevalence of people identified as having some symptoms to the 20% prevalence reported in the study (95). A strength of this study was its consideration of true prevalence instead of treatment or contact prevalence, and its building of longitudinal profiles of the residents of the area. However, its methods were extremely labour intensive, and are not suitable for large scale surveillance.

The Epidemiologic Catchment Area Study (ECA)

The ECA study was conducted for the National Institute of Mental Health (NIMH) in the early 1980s, at five sites in the USA. The objective of the study was to determine 'the prevalence of mental disorders in both treated and untreated populations' (76) (pg 7), as well as to explore factors affecting access to mental health services. The study used a structured interview, designed for and used by lay interviewers, to interview

randomly selected community and institutional residents in five locations. The research team at each location was to interview at least 3 000 community and 500 institutional residents, with a total number sampled of over 19 000. The requirement for sample size was calculated using an assumption that schizophrenia would be the rarest of the mental illnesses included in the survey and that it has a prevalence of 1%. Institutional residents, certain minority groups and those over age 60 were all over-sampled. Surveys were conducted in five cities in the USA.

The interview was developed for the survey, based on several existing tools. The NIMH Diagnostic Interview Schedule or DIS was created to cover many of the DSM-III diagnoses, and to be administered by a lay interviewer who did not have to make clinical judgments on the presence or absence of illness, but simply asked questions in the order directed by an algorithm. Although the interview is based on DSM-III, the study did not rank diagnoses in a hierarchical way and allowed subjects to have coexisting disorders (with the exception of cognitive impairment). Schizophrenia and schizophreniform disorder were included in the DIS and are referred to as 'schizophrenic disorders' in the ECA study.

By using a structured interview tool on community subjects, the ECA study captured both treated and untreated illness. Although subjects may have chosen to not answer honestly if they experienced symptoms for fear of being considered mentally ill, the nature of the interviews meant that people were not labelled with a mental illness or asked to report if they had a given diagnosis. The study found a one-year prevalence of 1% and lifetime prevalence of 1.4% for schizophrenic disorders. The study was also designed to give a proportion of treated to untreated illness by asking about use of health

services, and thus challenged the belief that people with schizophrenia inevitably end up in contact with either the medical or the justice system. This is relevant to understanding the possible bias of a surveillance system for mental illness based on physician and hospital contact data (a treated or contact prevalence). The survey found that within the community samples 42% of subjects reported receiving no medical services in the previous year. Table 2.1 summarizes treated and untreated illness for those meeting criteria for schizophrenia, adapted from Robins and Regier (76).

Table 2.1 Recent mental health visits by those with schizophrenia, including inpatient (one year) and outpatient (six months). Data from the ECA study. Adapted from Robins and Regier, 1991.

Mental Health Service Type	**% using services (SE)**
Any MH service	57 (5.1)
Specialty MH service	40 (5.4)
General Medical MH	17 (4.1)
General Medical MH only	12 (3.7)
Other human MH services	14 (3.6)
Other human MH services only	6 (2.8)

The large percentage of people who did not access either medical or mental health services in this survey suggests that administrative data based on physician contact could exclude significant parts of the population, at least in the USA at the time of this survey. The proportion of untreated subjects in the ECA cannot be applied directly in the very different health care environment of Ontario 25 years later, but the study clearly

demonstrated the assumption that all people with schizophrenia end up in contact with the health system to be false, at least in a one year cross-section.

The ECA study was based on place of residence for sampling frame, and included residents of the community as well as institutional residents. It did not include the homeless of the chosen sites. The institutional population included residents of long term care facilities, prisons, and psychiatric hospitals. Overall institutional one-year prevalence was 4.5%, and lifetime prevalence in institutional residents was 5.6%. In fact, a larger percentage of people met some but not all of the criteria for schizophrenia or schizophreniform disorder, supporting the idea of a continuum of psychotic states in the population[4]. This does raise a question of how cases identified in a surveillance system for schizophrenia should be handled if they have an extended period without symptoms.

The ECA study, although 25 years old, is a valuable source of benchmark information to refer to in planning a surveillance system for Ontario. Because it attempted to measure untreated as well as treated illness, it provides a rough estimate of prevalence against which we can compare any estimate based on health care contact. The study demonstrated that institutional populations should be included in a surveillance system for schizophrenia, and that contact or treated prevalence should not be equated with true prevalence of schizophrenia. It also contributed to the understanding of the illness by showing that there is a significant part of the population that experiences

[4] The prevalence of people meeting criterion A, that is, experiencing psychotic symptoms such as delusions or hallucinations, was 3 3% in the community sample If a subject endorsed psychotic symptoms, but did not meet the criterion of decline in functioning, or age of onset less than 45 years, or no organic brain condition, they would not be considered as a case It is worth noting that the age of onset criterion was removed in DSM-IV, so a small percentage of those who did not meet the DSM-III case criteria at the time of the survey would now be considered cases, slightly raising the estimated prevalence DSM-III required symptoms to be current in order for a diagnosis of schizophrenia to be made, which is reflected in the DIS by a question asking whether the person has been free from symptoms for one year This criterion was not used in the ECA study of schizophrenia and the requirement was subsequently dropped in the revised DSM-III-R (76)

symptoms of psychosis without meeting threshold criteria for diagnosable illness, supporting a spectrum rather than a binary understanding of psychotic illness. The study took full advantage of the increasing reliability of the DSM diagnoses with the introduction of DSM-III, by using a structured interview based on DSM-III. The study was fairly labour intensive, and relied on careful sampling technique and analysis to provide results that were generalizable.

Edmonton Epidemiologic Study

A study of the epidemiology of psychiatric disorders in Edmonton was conducted by Bland et al. in the 1980s, using methods similar to the ECA study described above (96,97). The study was based on interviews of over 3 000 community residents in Edmonton, Alberta. Residents were randomly sampled and interviewed by trained lay interviewers, using the DIS, as in the ECA study. The Edmonton study, like the ECA, was generating a prevalence rate based on occurrence of symptoms in the community, not a treated prevalence, but the prevalence identified in Edmonton was lower than the ECA identified rate, with a 1 year prevalence of 0.4% and a lifetime prevalence of 0.6% for schizophrenia, (0.7% including schizophreniform disorder). The Edmonton study recorded a 'one-year recovery rate', by asking people who met criteria for ever having a mental illness whether they had experienced any symptoms in the previous year. For schizophrenia this was found to be 39.3%. This would presumably include those who had met criteria for schizophrenia at the time of a first episode psychosis but who had a full recovery, and some of those who have an episodic course with good functioning in between episodes. The question did not exclude people who were symptom free while receiving active treatment. Two important lessons can be drawn from this survey relevant

to surveillance for schizophrenia. First, the difference in prevalence rates in the Edmonton and ECA studies, which used roughly the same methods, suggest that prevalence is not uniform and should be determined locally rather than relying on studies from other countries. Second, the fairly high rate of one-year remission in the Edmonton study underlines the need for a surveillance system that captures the episodic course of the illness.

The Ontario Health Survey, Mental Health Supplement

The Ontario Health Survey was undertaken in 1990-91 as an assessment of population health in Ontario. The mental health supplement was a survey focusing on psychiatric illness and resulting disability. It was administered to approximately 10 000 residents of Ontario aged 15 and over, using trained lay interviewers and a structured interview tool called the Composite International Diagnostic Interview (CIDI). The investigators identified five concepts of interest: determinants, correlates, psychiatric disorder, disability, and utilization. In their paper explaining the survey methods, the investigators do not list schizophrenia and related disorders among the disorders they wished to identify. They state that the selected disorders 'were deemed important to include because of their anticipated high prevalence, severity, and cost to society for treatment, rehabilitation and lost productivity' (98) (pg 554). However, in another publication on one-year prevalence of psychiatric disorders as identified by the supplement, the investigators state that schizophrenia and related disorders were included in the supplement, but there were only 6 respondents that met the diagnostic criteria and therefore there were no results reported for schizophrenia (giving a prevalence of less than 0.1%). The authors suggest that this may have been a limitation of the lay

interviewers (99). Clearly there were limitations in the sampling, the lay interviewers or the interview tool for recognizing schizophrenia as there are no other Canadian surveys suggesting such a low prevalence. The attempt to identify true prevalence and consider utilization in an Ontario population sample is a strength of the study.

Canadian Community Health Surveys

The Canadian Community Health Survey, version 1.2, was a community survey conducted by Statistics Canada, with supplementary funding and support from Health Canada and the Canadian Institute for Health Information (CIHI). Using a structured interview administered by trained lay interviewers, the survey included interviews with over 37 000 Canadian residents over 15 years of age, in 2002. The survey aimed to determine prevalence of mental disorders in each province and nationally, and to examine demographic and socioeconomic correlates of illness, access to care and disability (100). The investigators chose not to include schizophrenia in the structured interview portion of the survey due to concerns about sensitivity of the questions for that illness, but asked only whether the subject had been diagnosed with schizophrenia or other psychotic illness by a health professional (101). Using this approach, the survey estimated the prevalence of self-reported schizophrenia at 0.25%. This figure would be subject to possible biases of sampling, of access to care as it is based on a report of physician diagnosis, as well as a possible bias of low self-report due to fear of stigma. A reanalysis of the CCHS data including self reported schizophrenia and other psychotic illnesses yielded a prevalence of 0.9% (102).

The CCHS did show that prevalence for the disorders targeted by the structured interview varied considerably from province to province. For example, the ratio of the

highest provincial rate to the lowest for mania was 7.9 (this was the highest rate ratio). The lowest ratios of high to low provincial prevalence were for depression and phobias, at just over 2 (103). Although schizophrenia is not included in these disorders, the variable provincial rates for other disorders support the usefulness of provincial or even regional level surveillance for service planning purposes as there is significant geographical variation in prevalence.

2.3.2 Administrative Databases in Ontario

The major administrative databases in Ontario that could provide information on cases of schizophrenia are physician billing claims to the Ontario Health Insurance Plan (OHIP), the discharge abstract database (DAD) held by CIHI, which contains discharge diagnoses for hospital separations from acute beds in the province, and the Ontario Mental Health Reporting System (OMHRS) which contains information on admissions and discharges from adult psychiatric beds. Results from the 2000 and 2003 CCHS studies suggest that about 82% of Canadians aged 18-64 consulted a physician (general practitioner, specialist, or both) in the previous 12 months (104), meaning there will be at least one entry in the OHIP database for up to 82% of the ideal population under surveillance of Ontario residents per year. The actual figure may, however, be lower owing to physicians working in Community Health Centres or other locations that use block funding, if these do not require individual shadow-billing. Individuals who have no contact with a physician during the course of a year will not appear in the billing database for that year. The same surveys suggest that about 8% of adult Canadians reported an admission to hospital over the previous 12 months. Figure 2.1 shows the presumed distribution of schizophrenia in the population of usual residents, if assumed to

be a proportional distribution of cases through the Ontario population. Schizophrenia in regions with very sparse population can only be guessed at, and the possible effects of factors like concentration of immigrants or urban conglomerations cannot be examined.

Figure 2.1 Presumed distribution of schizophrenia in Ontario residents

OMHRS is a database of fairly detailed demographic and clinical information on each admission to and discharge from an adult mental health bed in the province. The information is gathered using a standardized assessment tool called the Resident Assessment Instrument-Mental Health (RAI-MH). Use of this instrument and submission of data became mandatory in 2007. While OMHRS would capture most of the separations for patients with mental illness, in 2007-08 over 15 000 separations were

included in the DAD (meaning separations from an acute care bed) listing a primary diagnosis of mental illness, compared to over 51 000 in the OMHRS (105). Therefore the DAD clearly remains an important supplementary source of information on discharges of people with mental illness as it contained 23% of the total separations for mental illness in 2007-08.

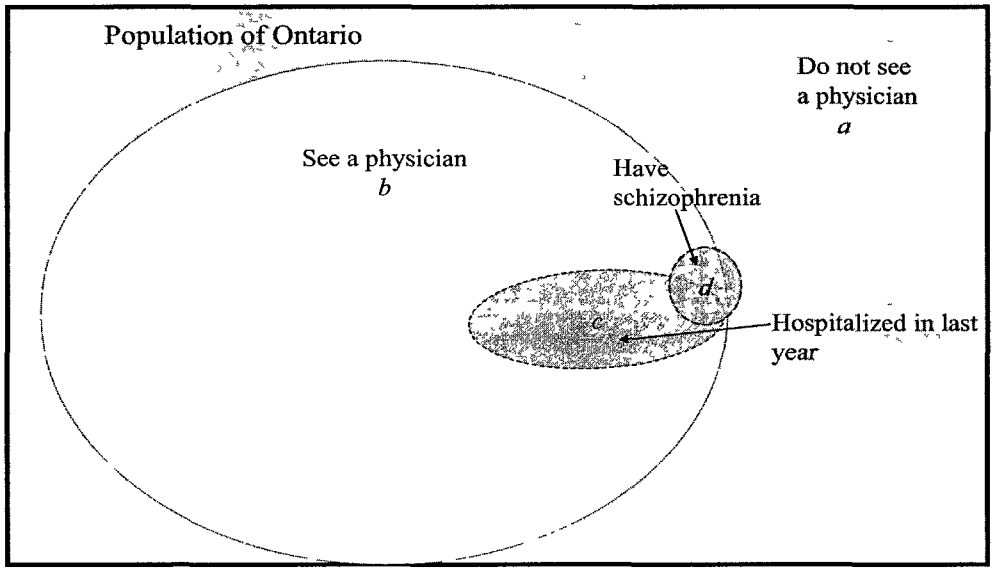

Figure 2.2 Health care contacts of Ontario residents

There are three possible ways that people who have schizophrenia could be excluded from a count of cases and prevalence rate based on a combination of physician billing and hospital discharge information. Such cases would be, first, those who do not see a physician (excluded from the numerator and the denominator of all people who saw a physician that year), and second, people who see a physician but whose associated billing code does not reflect their illness (excluded from the numerator). Third, a smaller

subset of people see a physician but that physician does not bill directly for services so they are not part of the database (excluded from the numerator and the denominator). The second and third groups, people who are in contact with the health system but for some reason do not appear in the databases with the appropriate diagnostic coding, will be considered in Chapter 3. The first group, people not in contact with the health system will be considered here as this represents a fundamental limitation to the use of administrative data that must be understood and mitigated in order to make use of these large databases. Figure 2.2 sketches the possibilities of how cases and non-cases come in contact with the health care system; it indicates that the majority of people with schizophrenia will be seen by a physician, often in a hospital setting, but that some will not see a physician within a year.

2.3.3 Administrative databases and potentially excluded cases

The ECA study estimated the one-year prevalence of treated and untreated schizophrenia as approximately 1% of the population, with a lifetime prevalence of 1.3% (76) and the CCHS 1.2 yielded a one-year prevalence of 0.9% using a broad question regarding previous diagnosis of a psychotic disorder for analysis (102). This is more than twice the one-year contact prevalence of 0.45% obtained using administrative data in British Columbia (91). To what extent this twofold difference in rates reflects the method of using administrative data versus a true rate difference in BC from an overall Canadian rate, or the rate in the American locations of the ECA is an important question.

Not consulting a physician during the course of the year could be due to a lack of access or to a lack of need (or perceived need). In the CCHS surveys for 2000, 2003 and

2005 the rate of consultation with a physician increased with the presence and number of self reported chronic conditions. People who reported fair or poor physical or mental health were more likely to have consulted a physician than people whose self reported physical or mental health was excellent or very good. However, this trend was less pronounced for those with self perceived fair or poor mental health than for those with fair or poor physical health. Self perceived fair or poor mental health was actually associated with a lower use of specialist physician care compared to those with excellent mental health. This trend was the opposite for those with fair or poor physical health, which was associated with increased specialist use compared to those reporting excellent physical health. Fair or poor mental health was not broken down into diagnostic categories. Several factors are associated with not contacting a physician, including not having a regular family doctor, having lower income, being younger and living in a rural area (104,106). All of these factors except rural residence are associated with increased prevalence of schizophrenia, rural residence being associated with a lower prevalence than urban residence. The 18% of people who did not consult a physician over the previous 12 months would be excluded from the denominator of a prevalence estimate. Whether the rate of exclusion of cases from the numerator can be assumed to be 18% is unknown, but the effect of different assumptions about the rate of health care contact for people with schizophrenia can be tested.

The Goldner et al. study of schizophrenia prevalence in BC using administrative data states the assumption that at least 90% of people with schizophrenia have contact with the health system in the course of a year (91) (contrary to the ECA study (76)). The authors calculate a prevalence of 0.45%, using the number of unique individuals with

health care contacts coded for a schizophrenia diagnosis appearing in the various provincial administrative databases as the numerator. They use the census figure for the province's adult population for the denominator (suggesting that 100% of the people with schizophrenia in the province have had a physician contact that year). However, if we assume that 82% of the BC population made a physician visit in the previous year (104), and that people with schizophrenia and people without visit the doctor at the same rate, then the Goldner data can be reanalysed using the appropriate denominator of 82% of the census figure, as shown in Table 2.2.

This simple reanalysis shows that the choice of denominator, based on assumptions about yearly rates of service use, will make a difference to a reported prevalence. If surveillance based on administrative data on a one year cycle, the number of people not appearing in the data (both cases and non-cases) could bias results up to 22% as in the example shown. Using linked year over year data as a mitigation strategy for this potential bias, will be discussed below.

Table 2.2 Sensitivity of one-year prevalence rate to changes in the denominator

Reported prevalence = z/y
Adjusted prevalence = z/y_{adj}
z = 12087 (91)
y = 2703588
And $y_{adj} = y \times 0.82$
Reported prevalence = 12087 / 2703588 = 0.45%
Adjusted prevalence = 12087 / 2216942 = 0.55%
Using the population who saw a physician as the denominator rather than the full census population gives a prevalence of 0.55%, or 22% higher than the reported 0.45%

A sensitivity analysis of the possible effect of different true prevalence rates, and of different assumptions about the rate of service use of those with schizophrenia, is shown in Table 2.3 below. This table also includes rates calculated using a population denominator, and a denominator adjusted for the overall annual rate of contact with a physician, assumed to be 82%. The table shows that where health care contact for both cases and non-cases is high (82-90%), the use of a population denominator is reasonable. If the contact rate in cases is assumed to be very different from the general rate (as shown in the far right column), the bias could be could be considerable. In this example the estimate is more than 40% lower than the true prevalence.

Table 2.3 Sensitivity analysis for one-year prevalence of schizophrenia based on administrative data. The percentages show estimated prevalence, varying according to the true population one-year prevalence, and percentage of cases accessing services in a year.

% of true cases who see a physician in a year	**82% (equal distribution)**		**90% (assumption in BC study)**		**58% (ECA)**	
Prevalence of schizophrenia in population	Population denominator	Adjusted denominator (82%)	Population denominator	Adjusted denominator (82%)	Population denominator	Adjusted denominator (82%)
1% (ECA)	0.82%	1%	0.9%	1.1%	0.58%	0.71%
0.45% (Edmonton)	0.37%	0.45%	0.41%	0.50%	0.26%	0.32%
0.25% (CCHS)	0.21%	0.25%	0.23%	0.27%	0.15%	0.18%

It is important to note Table 2.3 above is based on an assumption that if a person is included in the database and has schizophrenia, she or he will be identified in the database as having the illness. However, this cannot be assumed. True cases who see a physician but do not have coding submitted that accurately describes their condition are a type of error which will be considered in Chapter 3.

In the absence of certainty on the rate of service use of people with schizophrenia, a way to mitigate this uncertainty is to consider unique individuals (cases and non-cases) seen over several years. This is shown in Figure 2.3. We can assume, for example, that the 18% of people who did not see a physician within a given year are not the same 18% year after year. If one half of the 18% saw a physician in the next year, the coverage over 2 years would be 91% of all individuals. Thus the population under surveillance would closely approximate the ideal census population over a period of years of accumulating records. In this way, a case register simply made up of deposited (linked) surveillance

records year over year, becomes not only an additional health services tool, but an improvement in data quality over a simple surveillance of successive one-year prevalence rates.

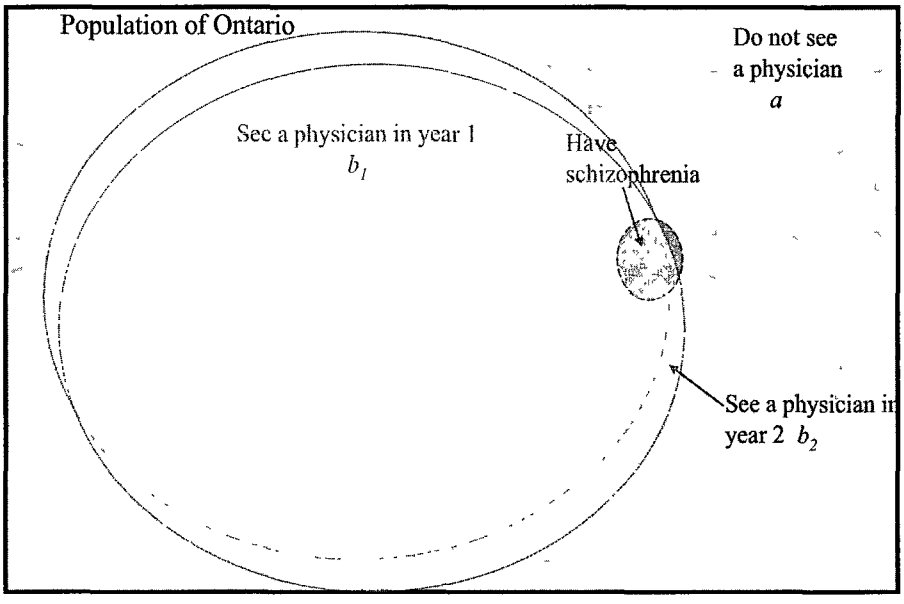

Figure 2.3 Coverage of the Ontario population by OHIP billing over two years

2.3.4 Summary of surveys and data sources

Table 2.4 below summarizes the various community surveys reviewed as well as the administrative data survey from BC. Clearly the administrative data study is low in cost compared to some of the more comprehensive community studies, although estimates derived from administrative data could be improved upon by considering data over a period of several years. The CCHS 1.2 cycle took the interesting approach of abandoning the structured clinical interview favoured from the 1980s on, and enquiring

about schizophrenia using the same type of questioning used for other (non-psychiatric) chronic conditions in other CCHS cycles. While the CCHS is a large scale survey, simply including a question on schizophrenia along with other chronic conditions would not substantially change the cost.

All of the studies considered provide a cross sectional picture of prevalence of illness, with the exception of the Stirling County study. Including questions about lifetime history of symptoms, and remission of symptoms in some of the community questionnaires can give a more detailed picture but none of these examples are equivalent to ongoing surveillance which captures time trends and regional variations and course of illness data. The CCHS does occur at regular intervals however the focus of each cycle changes. The possibility of including schizophrenia and related disorders in the CCHS monitoring of chronic illness is intriguing, but the validity of self report for schizophrenia would have to be explored for this to be useful (102). The lack of institutional residents among the respondents is another limitation to this approach.

Table 2.4 Summary of major studies of prevalence of mental illness relevant to schizophrenia surveillance in Ontario

Study and location	Date	Case definition	Data source/case finding method	Population sampled	Prevalence estimate (range)	Strengths	Weakness
Stirling county Nova Scotia	1948 on	Mental illness defined by DSM-I (not dx specific)	a) structured interview b) physician interview c) review by two psychiatrists	All residents of a county	20% 'total reportable lifetime prevalence' of mental disorders	Long-term follow-up of subjects Careful ascertainment	Very labour intensive ascertainment
Epidemiological Catchment Area Five regions in USA	1980s	DSM-III	Structured interview	Stratified sample of five regions including institutional residents	1% one year 1.4% lifetime prevalence of schizophrenic disorders	Stratified sampling including institutional, residents Attempt to identify true prevalence	Labour intensive Lifetime prevalence of 1.4 at high end of estimates
Edmonton Epidemiologic Study Edmonton AB	1980s	DSM-III	Structured interview	Sample of household residents	0.4% one year schizophrenia 0.7% lifetime including schizophreniform	Attempt to identify true prevalence	No institutional residents sampled, limited non-English sampling
Ontario Health Survey	1990/91	DSM-III	Structured interview	Sample of household residents	< 0.1%	Attempt to identify true prevalence	Structured interview used probably not adequate for schizophrenia

Canadian Community Health Survey	2002	Diagnosis from a health professional	Structured questions asking whether the person has received a dx of schizophrenia or other psychotic disorder from a health professional	Community sample	.25% for schizophrenia only 0.9% using schizophrenia or other psychotic disorder	Large sample size Interesting use of self-report question similar to CCHS approach for other chronic conditions	No institutional residents Self-report approach for psychotic illness needs further validation
BC administrative data	1997/98	Diagnosis as coded in administrative data	Presence of relevant dx in one of three administrative databases	All BC residents appearing in the health administrative databases	0.45% one year prevalence schizophrenia disorders	Population approach (not a sample) Ability to combine/link databases Relatively low cost	Those with no health services contact excluded

2.3.5 Proceeding with surveillance using administrative data

The community surveys demonstrate the conundrum of case definition and diagnosis in psychiatric epidemiology. By attempting to detect untreated illness, they have methods built into them that replace the usual treatment milieu process of the 'competent clinician interview' which often requires multiple interviews over time in the clinical setting, carried out by specialized care providers. The more elaborate these survey methods become, the more costly and labour intensive the survey, as the process essentially approximates the diagnostic process in a clinical setting (for example the Stirling County study where a psychiatrist reviewed all interviews and subjects were interviewed twice, including once by a physician familiar with the individual). While admirable for a single survey, these methods are not practical for ongoing surveillance. At the other extreme, the Ontario Mental Health Supplement streamlined the process to use only lay interviewers and a structured tool, but was unable to detect schizophrenia at a reasonable level. Although many structured interview tools followed the introduction of reliable diagnostic categories in DSM-III, they have proven less useful for schizophrenia when used alone (101,102,107).

Administrative data comes with their own limitations, such as exclusion of cases with no health care contact, and questionable predictive values of a schizophrenia diagnosis recorded in the databases. However, their availability and large scale coverage of the Ontario population offer unmatched advantages for surveillance. The complex process of diagnosing psychotic illness occurs every day in clinical settings, and this is translated (imperfectly) into entries in the administrative databases. To recreate this process separately for surveillance purposes would be an inefficient use of resources.

By building the surveillance system year over year by linking records from one year to the next, the problem of cases and non-cases with no health care contact will be reduced, so that coverage of the population under surveillance should reach 90% within several years. Quantifying the accuracy of the diagnosis in the administrative databases will be considered in Chapter 3, as a practical implication of proceeding with surveillance and linked case registry of schizophrenia based on administrative data.

2.4 Plans for analysis and dissemination of results

Analysis and dissemination of the results of surveillance ensure that the resources dedicated to the activity are justified, and the benefit to those with the illness and society in general are maximized. Analysis of data for schizophrenia surveillance should be issued by the holder of the data (such as CIHI) in a provincial-level report including provincial and regional level incidence, prevalence and trends. Incidence and prevalence should also be shared with the Local Health Integration Networks (LHINs) so they can evaluate their allocation of resources as prevalence can be expected to vary widely (91,103). Further analysis of data from surveillance and a linked longitudinal case registry would provide information such as the ratio of people with the diagnosis to the people with the illness who are receiving adequate treatment (or at least regular contact with the health care system) for purposes of evaluation of care at a regional level. This should be shared with clinicians regionally as well, as data quality will depend on the submissions of clinicians and administrators to the database (108). Follow-up of individual cases, while an interesting possibility if a person receives the diagnosis but does not seem to be receiving adequate treatment, is not the usual practice with surveillance of other chronic disease and would be an invasive use of the data and a

singling out of people with this diagnosis that does not occur with other non-communicable diagnoses.

Further analysis of de-identified data should be available to qualified researchers, in the way data from the CCHS surveys is available, through a vetting process by the data holder.

2.5 Confidentiality and other ethical issues

2.5.1 Privacy of health information

The use of administrative data for surveillance is already an established practice for example in the National Diabetes Surveillance System. Use of aggregate level data generated by health service contacts does not require individual consent for inclusion in surveillance. A case registry represents a slightly more invasive use of personal health information, as it would allow longitudinal study of individual cases based on their contacts with the health system. However, registries are specifically mentioned in the MOHLTC Statement of Information Practices which states 'the Ministry may... disclose personal health information for ... purposes such as facilitating the provision of healthcare (and) improving the provision of healthcare through registries' (109).

The storage of personal health information that is gathered and kept for any purpose must be secure, whether in electronic or paper form. Practical and operational issues of who should hold data and how will be discussed further in Chapter 3, but data should be held securely, with access controlled, and any unnecessary identifying information removed in order for a surveillance system and case registry to operate within current legislated requirements.

2.5.2 Stigma

The stigma associated with mental illness, and especially with schizophrenia, is relevant to any plan to implement surveillance for schizophrenia. Stigma could introduce bias through under-reporting in surveillance based on self-report. Stigma within medical and health care provider communities may contribute to an under reporting bias in a system based on physician diagnosis potentially greater than that of surveillance of other types of illness. Perhaps the most important reason to consider stigma is to acknowledge and understand the risks to people with schizophrenia and their families that might be associated with disclosure so that those risks can be mitigated. The well documented stigma associated with schizophrenia is an argument for concerted population level measures to support research into the illness, although in the short term the perception of potential harm that could result from the misuse of surveillance data could generate some opposition from advocacy groups.

Research from the middle of the 20th century onwards has shown that the response to people with schizophrenia is a desire for greater social distance. Higher educational level has not been consistently shown to improve attitudes toward people with mental illness. A study from the 1950s in Alberta (110) showed that when two small towns were selected, one for a program of education about mental illness and one as a control, the town receiving the experimental intervention did not show significant positive changes in social distance or other measures of stigma. There was even some suspicion in the 'experimental' town that there were hidden motives for the educational program, such as opening a new psychiatric facility close by.

The World Psychiatric Association (WPA) has a multi-centre campaign to combat the stigma of schizophrenia (111). As part of this campaign, surveys were conducted in Alberta in 1997 and 1998 of the general population, medical students, and members of the Schizophrenia Society to assess understanding of and attitudes towards schizophrenia. The study showed that the general population did have an understanding of schizophrenia as an illness, as amenable to treatment, and voiced a level of acceptance for people with the illness. However, people continued to want to keep social distance from people with schizophrenia, and became less accepting in scenarios of less social distance. The concern over level of danger posed by people with schizophrenia was voiced by respondents. One interpretation the authors offer is that an anti-stigma campaign may not need to reach a broad sector of society, as some knowledge is already present, and there may be a limit to how much it is possible to change behaviour towards people with mental illness through simple education and awareness campaigns. The authors suggest that the perception of dangerousness of people with schizophrenia, which was voiced in this survey, may be a factor that limits the level of acceptance and desire for interaction. Although untreated schizophrenia is associated with a risk of violence towards others, particularly when occurring with substance abuse (27), many studies show that this risk is modest and that the victims of violence from someone with schizophrenia are most often family members such as parents, not strangers. In the Alberta survey, the perception of danger was higher in the general population sample than in the Schizophrenia Society sample (which would be made up mostly of family members, who are more at risk than the general population).

Some research has shown more concrete effects of stigma such as the response of landlords to people disclosing a past history of psychiatric illness, making rental accommodations harder to find for those with mental illness. People suffering from mental illness, as well as their families and health professionals may share some of the attitudes of the general population. Patients may use social withdrawal or secrecy about their condition, believing that they will encounter rejection, discrimination or other effects of stigma. This in turn can negatively impact the effect of treatment, or long-term compliance with treatment (110). The availability of basic epidemiological information about schizophrenia at a regional or provincial level will support informed discussion about the health problem, at least within the health system.

A survey of psychiatrists in Turkey, about their own attitudes towards people with schizophrenia and about the psychiatrists' perception of lay opinion found that the diagnosis of schizophrenia is not always shared with the patient by the responding psychiatrists, or on official documents, and that the psychiatrists believed the lay public uses the term schizophrenia in a pejorative way (112). Although the results cannot be generalized without further evidence, the possibility remains that psychiatrists' use of the diagnosis of schizophrenia is influenced by a belief about public perception and stigma in this setting as well, thus biasing data collected from physician diagnoses. Dissemination of surveillance results to care providers will help those providers recognize the value of having accurate data, and will form part of any effort to engage care providers in improving data quality.

The intervention required to reduce stigma surrounding schizophrenia may be more complex than the current awareness efforts that stress the biological nature of the

illness, referring to it as a 'brain disease'. The attempt to publicly describe schizophrenia in these terms is an effort to reinforce the fact that the illness does not amount to a failure of will or discipline, and to overcome the earlier views that schizophrenia was likely a result of the family environment, particularly of parenting. However, the emphasis on genetics can simply transform the burden of guilt on families from their parenting style to their family history and genetic make-up. It can also support a view of the illness that emphasizes 'chronicity, helplessness, and genetic difference or inferiority' (110) (pg 113). The view of schizophrenia as invariably chronic and debilitating is one that also has a long tradition within psychiatry itself (and which Wallace calls 'a long-enduring therapeutic nihilism toward such patients' (74)). The objective of surveillance and dissemination of information must be accompanied by a commitment to accessible treatment, and measures to reduce stigma.

2.5.3 Potential Community Stakeholders

Any plan to commence surveillance and a case registry of schizophrenia should proceed with active engagement of community stakeholders. Stakeholder groups have different interests in administrative and scientific advancement of understanding of schizophrenia. At the simplest level, every resident of Ontario has an interest in surveillance for schizophrenia as an actual or potential consumer of mental health services. People without a personal interest in schizophrenia care may still identify with the advancement of knowledge in the area on humanitarian grounds, or on economic grounds as a taxpayer.

The Schizophrenia Society of Ontario (SSO) is the best known diagnosis specific community organization with an interest in schizophrenia. The SSO states that their mission is 'to improve the quality of life for those affected by schizophrenia & psychosis through education, support programs, public policy & research' (113). Surveillance of schizophrenia would be consistent both with their interest in research and their advocacy for access to care. The SSO does support research related to schizophrenia through grants, but a list of their current funding recipients does not reveal any research based on population level databases, although genetic epidemiology studies as well as studies of stigma have been funded. The Schizophrenia Society will be an important partner to engage in order to address any concerns around individual and family rights to privacy as well as to advocate for the research and planning possibilities associated with surveillance.

The Psychiatric Survivors of Ottawa (PSO) (and similar other groups throughout the province) is an organization of and for people who have experienced mental illness. PSO describes its mission as '...survivors and consumers of the mental health system, engage in mutual support, empowerment, and information sharing... affirming the dignity and worth of the individual, advocate for alternatives and improvements to the established health care system, services and issues which affect our well-being' (114). PSO's membership is limited to people who have personal experience of the mental health system, in contrast to the Schizophrenia Society's focus on support of family members as well as people with a diagnosis of schizophrenia. It is possible that organizations like PSO might have a sceptical view of the benefit of a surveillance system versus its potential for harm. Concerns could be focused on the negative effects

of the 'label' of schizophrenia and possible concerns over confidentiality. The opportunity for stakeholders to voice concerns must occur early in the process of surveillance planning in order to hear and address legitimate questions from people with a personal stake in the process.

The long history of stigma associated with the mental illness label, as well as the history of institutionalization and paternalism or worse that has at times characterized the mental health system's treatment of its patients has left a legacy of scepticism in the public and in users of mental health services. This is expressed in the healthy questioning of psychiatric practice and public policy by organizations such as SSO and PSO as well as by their advocacy efforts. There is, however, a more extreme 'antipsychiatry' movement which views current psychiatric diagnosis and treatment practices as a form of social control. This type of movement will exist whether or not a provincial surveillance system for schizophrenia exists, but it is worth being prepared for the possibility surveillance for mental illness may be more controversial than for example, surveillance for diabetes.

Physicians and other health care providers, hospitals, and LHINs are also stakeholders as service providers and administrators of the public money that is spent on schizophrenia care and other health care. The availability of easily accessible information about the province and its regions will support evidence-based planning of services.

Chapter 3 Implementation of surveillance and case registry for schizophrenia

3.1 Guidelines for the evaluation of a surveillance system

The U.S. Centers for Disease Control and Prevention (CDC) published guidelines for the evaluation of a surveillance system in 1988 (115), and an updated version in 2001(116). Although these guidelines would normally be used to evaluate an established program, it will be useful to consider the CDC's recommended attributes while planning the system. The CDC recommends that evaluation of surveillance should include an assessment of the simplicity, flexibility, data quality, acceptability, sensitivity, positive predictive value, representativeness, timeliness, and stability of the system. Each attribute will not have equal importance for each surveillance system. Timeliness for example, is more of a concern for communicable disease surveillance than for chronic conditions. Some attributes may be enhanced at the expense of others: for example, achieving high sensitivity may come at a cost of simplicity. Due to the nature of the condition, a surveillance system for schizophrenia need not rate highly on timeliness; sensitivity, while important, would have to be considered in balance with simplicity, flexibility, and acceptability.

Chapter 3 will consider some of the practical considerations for implementation, and will assess the CDC recommended attributes for the proposed surveillance system.

3.2 Use of billing and hospital discharge information for surveillance

Within the limitations in sensitivity and specificity of diagnostic coding, physician billing has the capacity to identify cases of schizophrenia from over 80% of the population of Ontario per year. No other database has a comparable coverage of Ontario residents. The Ontario Mental Health Reporting System (OMHRS) and discharge abstract database (DAD), if linked to the billing database, will improve accuracy for a schizophrenia diagnosis in the subset of around 8% of the population who are hospitalized over the course of a year (104), therefore making the combination of these databases worthwhile in terms of benefit at minimal cost. In the ECA study, 13% of the community sample meeting the criteria for schizophrenia reported being hospitalized within the previous year (76). A prospective Canadian study of stable outpatients with schizophrenia showed a hospitalization rate of 14% after a year from baseline measurement, and 20% at two years (26). It is likely that people with the diagnosis are over represented in the 8% of Ontarians hospitalized. If we assume a 14% annual hospitalization rate for people with schizophrenia in Ontario, the subset of cases covered by the OMHRS and DAD annually would be 14%. These three databases should form the basis of surveillance and case registry for schizophrenia in Ontario. Data linkage must be established to allow duplicate entries to be removed for counting purposes, and the compilation of a longitudinal record of health system contacts for each case file. This can be refined through correction for the known limitations of the administrative data to get the most useful picture possible from data not originally collected for the purposes of clinical or health services research.

Table 3.1 shows which administrative records exist for each type of health care contact. Inpatient stays will generate a diagnostic code at discharge in either the OMHRS or the DAD, and most outpatient contacts will be captured in the OHIP billing data.

Table 3.1 Administrative records of health care contacts

Type of contact with health care	Type of record available		
	Billing claims	OMHRS	DAD
Ambulatory	Probable*	No	No
Inpatient psychiatry	Possible*	Yes	No
Inpatient non-psychiatry	Probable*	No	Yes
* depending on whether physician is on fee for service			

Most ambulatory visits will generate a diagnostic code in billing data. However, about 5% of physicians in Ontario receive alternate funding such as salary or sessionals, and therefore do not bill directly for services and visits paid in that way are not in the database (117,118). If we assume that health care visits are randomly distributed across physicians who direct bill and those who don't then we can assume that approximately 5% of visits to a physician in Ontario are not captured in the database because the physician does not bill directly for services. Included in this group are physicians (psychiatrists) who work at some of the former Provincial Psychiatric Hospitals (PPH), some physicians serving community mental health teams such as Assertive Community Treatment Teams (ACTT), GPs linked to Community Health Centres and others. It is possible there is an over-representation of physicians likely to encounter people with severe mental illness but many of those visits would be in an inpatient setting (for

example physician contact while admitted to a former PPH), so the person's diagnostic code would be captured in a discharge abstract. For the case counting purposes of surveillance, the impact of the excluded visits will be minimal, but could have some impact on a linked case registry.

Surveillance based on diagnostic coding in administrative data can be considered fairly simple in design, as it will not rely on additional diagnostic procedures or follow up for cases. Flexibility is a desirable attribute of surveillance that is linked to simplicity, allowing an existing surveillance system to be adapted to changing needs such as changing diagnostic definitions. Surveillance based on administrative data would be flexible enough to adapt to changing diagnostic definitions and coding simply by changing the parameters of what triggers identification of a case. However a major change in the structure of health care in the province such as a large number of physicians moving to salaried positions would have a significant impact on data gathering, and would make redesign of the system necessary. This suggests the proposed system for schizophrenia surveillance would receive a mixed or moderate rating for flexibility. The CDC guidelines suggest that flexibility is best evaluated after the fact of a required adaptation.

3.3 Data linkage and case registers

Last defines a register as a 'file of data concerning all cases of a particular disease or other health-relevant condition in a defined population such that the cases can be related to the population base' (3). By linking administrative databases over time using a unique identifier, a case register can be compiled of people receiving a diagnosis of

schizophrenia. In Ontario linkage would be through the unique identifier of the OHIP number.

A case register can be built by accumulating linkable data from inpatient and ambulatory contacts. Typically in a psychiatric case registry these contacts would be linked to basic demographic information such as date and place of birth, and psychiatric diagnoses (8,119). Through use of a unique identifier such as the OHIP number, Ontario data will also be linkable with prescription profiles for those individuals covered by provincial drug plans, as well as with other registers tracking physical co-morbidities such as diabetes.

Case registries often begin with groups of cases treated at a particular hospital or group of hospitals. Such smaller scale registries provide useful information, for example they can contain some detailed clinical information and can be a source of cases for case-control studies. There are biases in hospital based registries, however, due to selection of patients for treatment at a hospital based on duration of illness and difficulty in managing symptoms. A hospital based registry of schizophrenia cases would present a picture of people with chronic illness, or people transported to hospital under the Mental Health Act (generally for involuntary admission based on a clinician or police assessment of danger to self or others). The relationship of such a hospital based registry to its catchment area population base can be difficult to determine. While providing cases with demographic and valuable clinical details it is not an unbiased sample of people with the illness in the catchment area, so true prevalence and course of illness cannot be determined using this source alone. A registry casting a wider net that can be related to the population base can provide invaluable data for etiological research by including an

unbiased group of cases. The issue of physicians who do not bill for service will create some gaps in some of the case files compiled from successive contacts. For example, a person with repeated contacts and admissions for schizophrenia will have these contacts added to their case file. But if that person is then referred to ACTT as the appropriate level of care, and the ACTT psychiatrist is not on fee for service, that person may see a psychiatrist biweekly for a year, and be receiving other resource intensive support from ACTT, but have no entries in the various databases for a year. However, the case file will remain and have occasional contacts recorded if the person has contact with other physicians, or is admitted to hospital.

A case register for schizophrenia in Ontario based on administrative data would provide information on the great majority of the population and include a wide range of cases. It would also inform the use in planning and research of smaller scale samples and registries such as those based on hospital chart reviews, by providing population level data for comparison. The goals of surveillance and case registry should be to capture information on all prevalent cases, not just treated ones. Use of the large administrative databases, while always imperfect, can approach the true picture.

3.4 Linkage of cases in a registry system

Decisions about linkage of cases in a registry system occur each time a record is added. There is a decision about linkage of a contact record with a given case, based on the degree of agreement of identifying information such as unique number or date of birth.

It is inevitable that a system based on administrative data will contain occasional errors in the basic identifying data such as alternate spellings of a surname, or incorrect date of birth. Names, date of birth and health card number are generally available for health care contacts. Probabilistic methods of defining linkage between cases have been developed by Statistics Canada and remain in wide usage (120), and would be suitable for use for schizophrenia surveillance and case registry. The method developed by Statistics Canada uses a weighted probability that records are in fact a match depending on degree of agreement in key identifiers such as first seven characters of the surname. The method takes into account reasonable alternate spellings of surnames and the frequency of each of the identifiers within the file (for example frequency of surname 'Smith' versus surname 'Middlebro' within the data file). An acceptable threshold of probability of a match is set for case linkage. This method is often applied to linkage with death records, when there can be only one 'right link'. However it can also be applied to find groups of links within a file or several files (121).

3.5 The accuracy of administrative data on schizophrenia

In order to make use of administrative data, the types of inaccuracy that can make their way into the various administrative databases should be considered. Inaccuracies in the discharge databases (the DAD for non-psychiatric beds and OMHRS for psychiatric bed separations) can occur at the time of coding or entering information into an administrative database from the individual patient chart. These would be coding errors such as transposition of numbers or misreading of handwritten discharge diagnoses during coding by health records staff. Similar types of errors can occur when physician

billing claims for inpatient or ambulatory visits are submitted and compiled based on the physician diagnosis.

Inaccuracy can also be a result of the discharge diagnosis not reflecting the condition of the patient. Diagnostic errors could be due to the physician not recognizing the illness or due to a decision not to record the suspected diagnosis on the claim. Although these are referred to as diagnostic errors for the current purpose, this is not an assessment of physicians' diagnostic ability. It is an assessment of the usefulness of the diagnostic codes in the claims database for epidemiological purposes. Therefore these are diagnostic errors in the database regardless of whether arising from mistaken or intentional non-entry (a false negative) of a schizophrenia diagnosis in the claims data for a contact with a person with schizophrenia. This type of error does not include the issue of the evolution of a patient's clinical presentation over time. The possibility of change of diagnosis over time should not be considered a type of error, but rather a clinical complexity that must be incorporated into the use of data generated from medical contacts. This will be considered separately.

Inaccuracies can also make their way into the demographic information about the case, such as date of birth, sex and place of residence. This can occur through data entry errors, or changes in the information such as a change of address.

Data quality assessment includes evaluation of the demographic and diagnostic information contained in the surveillance system and registry. Assessment of diagnostic information in a surveillance system can be quantified using positive predictive value and sensitivity, as recommended by the CDC guidelines.

3.5.1 Demographic accuracy

Administrative data from Saskatchewan has been extensively reviewed to judge the reliability of basic demographic information as well as diagnostic information, including several psychiatric diagnoses (122). Saskatchewan retains records from physician billing claims, from computerized hospital admission and discharge data, and from its 'mental health branch' services, which includes the specialized psychiatric service providers (psychiatric hospitals and related services), as well as inpatient psychiatric services located in general hospitals. Basic demographic information was found to have a concordance rate between 85% and 100% between the three administrative data sources. This suggests that a high level of data quality could be expected from Ontario administrative data as well.

A Manitoba study found basic demographic data from administrative health databases to be highly reliable with the exception of the postal code, which had a rate of agreement of only 59%. The investigators report that the postal code errors were usually an accurate record of a previous address. The investigators conclude that the Manitoba data are reliable enough to be used for research purposes and to form a psychiatric case register based on compiled contacts recorded in the provincial level databases (123). These two Canadian studies suggest that data quality is fairly good for demographic information in administrative data.

3.5.2 Diagnostic validity

Validity of diagnostic data collected for administrative purposes is more difficult to quantify. The complexity of case definition in the absence of useful diagnostic biomarkers was described in Chapter 2.

Diagnostic information from the Saskatchewan databases including billing, discharge, and specialized provider records was compared for reliability between the three types of record, for schizophrenia and for depression. Agreement between the discharge diagnosis of schizophrenia on the chart and the hospital records coded for ICD number was 94% for three digit ICD coding. Agreement for depression was considerably lower. The agreement between hospital discharge data and mental health branch data was 75%, which may reflect the higher rate of specialist contact for patients seen in the mental health branch services, or possibly a clearer diagnostic picture was provided for patients who have moved on to specialized mental health care (122).

The Manitoba study of administrative data for mental health services found a rate of agreement between the chart diagnosis and the information held in the provincial database of 83%, at the three digit ICD coding level for primary diagnosis, and 72% for all psychiatric diagnoses listed (123). Different psychiatric diagnoses were not considered separately although the Saskatchewan study did find schizophrenia to be a more reliably coded diagnosis than depression. Both the Manitoba and Saskatchewan data were less reliable for ICD psychiatric diagnoses coded at higher than three digits. This suggests that sub-classifications of schizophrenia such as 'paranoid' or 'residual' are less reliably used.

If we consider the physician recorded discharge diagnosis on the individual record to be the gold standard in the case of inpatient treatment, then the studies cited above support validity as well as reliability in the administrative records of inpatient care. They also suggest that discharge abstracts are a good source of reliable data for that subgroup of the population that is hospitalized, and that data from specialist providers give a more reliable diagnosis.

A study of discharge diagnoses of schizophrenia in Ontario by the Institute for Clinical and Evaluative Sciences (ICES) is currently underway (in 2010). It is expected that a diagnosis made at discharge from an inpatient stay would reflect a thorough assessment and that diagnostic accuracy would be high, particularly in the OMHRS data. The OMHRS data, similar to the mental health branch data studied in Saskatchewan, is generated more often by specialist providers (psychiatrists), and on a selected, more severely ill group of patients than other administrative data.

For people not admitted to hospital, physician billing claims remain the broadest available record for ambulatory contact with the health care system. Billing claims have been examined in a few studies for reliability and validity of psychiatric diagnoses. The Saskatchewan study cited above found physician billing to be the least accurate source of diagnostic information of the administrative data studied, with 62% agreement between the diagnosis recorded in physician billing for service to inpatients and the discharge diagnosis of schizophrenia as recorded in the clinical record of the same patients.

The reasons for not coding a visit for schizophrenia for someone who does have the disease fall into two categories. The physician may not classify the presence of the illness as a reason for the visit, or the physician may recognize it but have other reasons

not to cite the diagnosis. In Ontario as in other Canadian provinces the payment of physicians depends on the service code, not the diagnostic code, so provincial fee structure should not be a source of bias, but the concerns about stigma and labelling of patients discussed in Chapter 2 could cause under-use of the schizophrenia diagnosis in billing data and elsewhere. The reluctance of physicians to assign a diagnosis of schizophrenia to cases where there is any diagnostic doubt was mentioned but not quantified in a BC study of schizophrenia in administrative data (91).

The CDC guidelines for evaluation of surveillance propose using sensitivity and positive predictive value as measures of the performance of a surveillance system. Sensitivity and specificity are common measures of validity and positive and negative predictive value are measures of the usefulness of a test or case definition (124). Table 3.2 shows the two-by-two table used for calculating these measures for schizophrenia surveillance.

Table 3.2 Two by two table for assessing validity

Schizophrenia status in surveillance data	Schizophrenia present		
	Yes	**No**	**Total**
Yes	A true positive	B false positive	A+B
No	C false negative	D true negative	C+D
Total	A+C	B+D	Total A+B+C+D

Sensitivity measures the probability that a person with the illness is correctly identified as having the illness. Using the two-by-two table above, this is A / (A+C),

where A is the number people with the illness who are so identified by the surveillance system, and A+C is the total number of people with the illness, whether or not they were identified by surveillance. Positive predictive value (PPV) is the probability that a person identified as having the illness, truly has it. PPV is calculated as A / (A+B), or the number of people correctly identified as having the illness divided by the total number of people identified as having the illness. This measure will be affected by the number of false positive results generated.

Iron and Manuel suggest that indicators of the quality of administrative data should be defined by the user as these measures will depend on the uses of the data (125). There will not be a single measure of sensitivity or PPV for schizophrenia in billing data in Ontario, as this will depend on how the data are used. For example, if the data are used to ask a question about the incidence of all psychotic illness in Ontario, the PPV will likely be higher than if the data is used to look at schizoaffective disorder. Cases of schizophrenia may be defined using a single incidence of the diagnosis in any of the databases, or could require a second appearance in one of the databases with the same diagnosis to be considered a certain case, depending on the question being asked, and so the assessment of data quality will change from one situation to the next.

A study of mental health administrative data in the USA showed that PPV and NPV (predictive value of a negative surveillance record, or of not being identified as a case) can be optimized using different criteria for case identification. In that study NPV was optimized to 0.98 for schizophrenia and related illness by using a wider range of ICD codes for psychosis and combining two administrative data sources. PPV was optimized for schizophrenia and related illness at 0.78 by using a more restricted set of ICD codes

(126). The independent confirmation of presence or absence of disease in the study (the 'gold standard' against which the PPV and NPV of the administrative data were measured) was self report of the illness in a community based survey, so PPV for schizophrenia was likely higher than 0.78 if self report of previously diagnosed schizophrenia was less than 100% in the survey. The authors suggest that researchers using administrative data include a sensitivity analysis in their results, considering alternative case definition algorithms applied to the data. An earlier study of American Medicaid claims showed that 86.8% of the claims with a schizophrenia diagnosis were for patients whose history on review showed definite or probable schizophrenia (assessed by two clinicians based on DSM III-R criteria), and that 27.5% of charts associated with claims for other mental illnesses also showed definite or probable schizophrenia (127). This study included only claims for mental illness. This gives a PPV of 87% or 0.87. Sensitivity can be calculated from the results given in the study, at 86.5%, and specificity at 72.9%. Because this study looked at a group with a high prevalence of schizophrenia, this affects the specificity measure, which would be higher in a general population sample.

A review of cases in an Australian registry found that of cases with one or more entries for a diagnosis of schizophrenia, 82.8% had a lifetime schizophrenia diagnosis based on an independent structured interview (the SCID) (119). This gives a PPV of 0.83 for a single diagnosis of schizophrenia in the case registry.

A study of billing claims for a variety of chronic conditions including 'mental health problems' in the U.S. showed that the claims had a sensitivity of 0.71 using a review of the patient chart as the standard, and specificity of 0.97 (128). The study also

considered self report of the same chronic conditions against the patient record, and found that sensitivity was 0.25 and specificity was 1.00 for mental health problems.

From these studies we can predict a PPV of over 80% for a diagnosis of schizophrenia appearing in one of the databases, and possibly higher if a case requires more than one appearance of the diagnosis in the OHIP data. Sensitivity is harder to estimate from these studies. A calculation of sensitivity requires an estimate of the false negatives, which means sampling the population not identified as having schizophrenia in any of the administrative databases. The difficulty of identifying cases that were not included is clearly more challenging than measuring PPV with a low-prevalence illness. Sensitivity should be over 70% and quite possibly higher, based on the concordance rates found in Manitoba and Saskatchewan provincial data, and the 1992 study of Medicaid claims (and depending on the case definition used). These results support the view that billing data may provide an underestimate of schizophrenia, but that people with schizophrenia may be coded with other significant mental illness. Some of these will be captured by including the related psychotic illness codes in surveillance.

3.6 Capturing clinical changes in a case registry based on administrative data

As discussed in Chapter 2, the term 'schizophrenia' as it appears in Ontario administrative data can be assumed to refer to the illness as defined in the later DSM editions. Due to the inclusion of duration and functional impairment criteria along with symptom combinations in the DSM definition for schizophrenia, there are people with psychotic symptoms who are encountered in the health care system but do not meet the threshold for a diagnosis of schizophrenia. Some of these would be captured by the other

psychotic illness diagnoses as discussed in Chapter 2. For example, schizophreniform disorder can be applied when the duration of symptoms is less than six months, and other diagnostic labels if functional impairment is less marked. It is possible for a person to present features more consistent with a primary mood disorder, and over a period of months or years to show evolving symptoms resulting in a diagnosis of schizophrenia (129). For people who present to care with psychotic symptoms among their presenting symptoms it is more likely for a non-schizophrenia diagnosis to be changed to schizophrenia than for change to occur in the other direction. In a population based study that followed a cohort of incident cases of psychotic illness, including mood disorders with psychotic features, 91% of those initially diagnosed with schizophrenia received the same diagnosis 2.5 years later in a blinded interview. About 50% of those who had initially received other diagnoses received a diagnosis of schizophrenia 2.5 years later (89).

It is possible for a person to have comorbid conditions such as substance abuse along with schizophrenia. Therefore it is to be expected that someone who receives a diagnosis of schizophrenia may also have some health care contacts that generate other DSM diagnoses. If health care contacts associated with schizophrenia and related diagnoses are collected to compile a case record this will provide a picture of the onset and evolution of illness.

Table 3.3 below shows the increasingly detailed information that can be gathered from simple annual surveillance, surveillance with a linked case registry made up of administrative data, and more detailed clinical case registry and record keeping linked to surveillance. More complex systems generate information that is more detailed and can

answer more research questions, but a system based solely on administrative data has the advantages of being cost effective and feasible based on current practices.

Table 3.3 Stepwise use and linkage of administrative data

Type of information gathering on schizophrenia	**Type of question that can be answered using information**	**Limitations**
Cross sectional surveillance of one-year prevalence	One-year prevalence of schizophrenia. Location of clusters of prevalence (not of incidence)	Limited by annual contact rate of cases and non-cases, and by sensitivity and PPV of a single diagnostic record. Cannot tell new cases from old ones
Linked multi-year surveillance based on administrative data	One year prevalence of disease. Location of clusters (incidence and prevalence). Course of illness- limited information. Some epidemiologic studies possible, especially if linked with other data.	Would take several years of data before incident and prevalent cases can be distinguished. Course of illness information limited by lack of in-depth clinical information including outcome measures
Hospital based registry drawn from clinical contacts	Cases for case-control studies, with detailed clinical information available. Long term follow-up and outcomes for some cases	Relationship with population unknown. Losses to follow-up
Multi-year surveillance linked with clinical information such as provincial drug plan or e-health record	Detailed epidemiologic studies. Case-control, population studies and linkage to clinical interventions and to outcome measures	Barriers of cost and complexity

An interesting issue in the course of illness is the possibility of remission or even recovery from schizophrenia. A surveillance system or case registry for a condition considered 'irreversible' can be fairly simple to compile. For example, the NDSS identifies new cases of diabetes each year but does not remove old cases identified through billing in previous years (except for deaths), as the assumption for that system is that a diagnosis for diabetes cannot be reversed (130). The situation is less clear for schizophrenia, as there is at present no explicit rule about whether the diagnosis of schizophrenia should be considered 'permanent'.

Longitudinal studies have shown over the years that a minority of people (less than 30%, although some studies suggest as low as 8%) who meet the criteria for schizophrenia at one time, do have sustained periods of recovery and good functional outcomes (28). Such studies have been carried out in North America and Europe, as well as the WHO multi-site studies, but diagnostic criteria, outcome criteria and measurement and loss to follow-up have all been limiting factors in comparing studies. The majority of those diagnosed with schizophrenia have either an episodic course with periods of variable duration and degrees of remission between episodes, or a more chronic and sometimes deteriorating course with ongoing symptoms and functional impairment. Surveillance should capture all three of these groups, although which group an individual will fall into is not known at the time of initial diagnosis, and is not usually reflected in diagnostic codes (although the DSM IV-TR does allow a descriptor of 'in remission' to be added to a diagnosis of schizophrenia). Individuals who are diagnosed with schizophrenia but who go on to recover and not be functionally impaired are of great interest to researchers for what they may illustrate about prognostic factors and about the

value of early interventions for schizophrenia. For this reason it is important to retain records of cases identified with a diagnosis of schizophrenia in one year but with subsequent health care contacts for other reasons and no further schizophrenia diagnoses appearing in the record. A clinical reason for retaining a category of such cases is the evaluation of any proximal preventive interventions that might come out of research, aimed firstly at people who have been diagnosed at one time with schizophrenia or other psychotic condition, (as this is the strongest predictor of further episodes).

The idea of remission in schizophrenia is becoming more accepted and proposed standard criteria for remission in schizophrenia were published in 2005 by an American working group (131). They recommended that the term 'remission' apply when someone who had previously been diagnosed using accepted criteria achieves a low and stable level of symptoms for a period of at least six months. The low level of symptoms are defined by the scores on one of three well known and validated measurement scales for psychiatric symptoms, the Positive and Negative Syndrome Scale (PANSS), the Brief Psychiatric Rating Scale (BPRS), or the Scale for Negative Symptoms/Scale for Positive Symptoms (SANS/SAPS). Of note, use of the proposed state of remission does not depend on whether the improvement was spontaneous or followed treatment (132). This is an important part of the definition with implications for planning health services based on surveillance. Cases in remission should by definition require less intervention and not require hospital bed days, but they may continue to be users of outpatient, community psychiatric, or primary health care services, as they may be maintained on medication that requires regular monitoring for medical complications or side effects as well as monitoring for psychiatric stability. The authors also refer to recovery in schizophrenia,

which forms a more ambitious goal for treatment of patients, and the threshold between remission and recovery remains undefined. The value of defining and using the concept of remission in schizophrenia is seen by the originators and others as identifying a goal that patients and families can hope to achieve even though all my not achieve it, as supporting the identification and understanding of the heterogeneity of schizophrenia, and also as a way of improving the measures used in clinical trials for pharmacologic treatments of schizophrenia. These traditionally use a measurement of improvement from baseline for each study subject, rather than an actual sustained return to reasonable functional status as a result of intervention (30,131,133).

Whether or not these criteria come into widespread use, the importance of this literature is that it underlines the need to not simply add cases each year to a case list compiled from administrative data, but to try to understand more from the data in order for it to be truly useful in 'completing the clinical picture'. Unless and until qualifiers such as 'in remission' routinely appear in administrative data, this would have to be done by tracking whether cases identified in one year continue to appear with a diagnosis of schizophrenia in the database in subsequent years, or appear in the database without the diagnosis, or do not appear further in the database. An algorithm of how cases once identified should be classified based on subsequent contacts would have to be applied when using the administrative data to look at long term outcomes. Data quality could be expected to improve with the increasing use of qualifiers on the schizophrenia diagnosis, but some general categories for schizophrenia and related illnesses could still be captured without this information. An example of such an algorithm is shown in Figure 3.1. This is an example only as the precise algorithm applied to the registry data to define cases as

active or in remission would vary with the question being considered. The ability to capture evolution and possible remission of the illness would be of great interest in the Ontario setting, as the WHO studies finding a different course of illness in different geocultural settings could be further explored for separate influences of geography and culture in the large immigrant communities of urban Ontario.

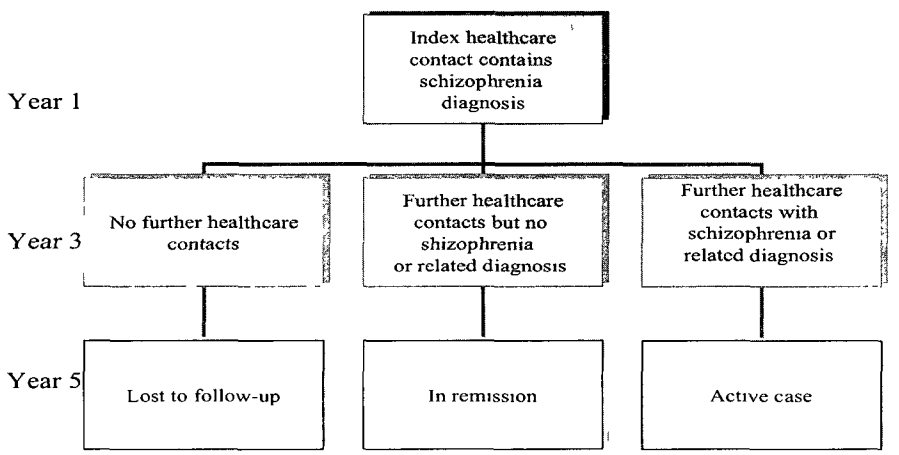

Figure 3.1 Algorithm for classifying cases as active or in remission

Surveillance can be introduced without a case registry, but the suggested case registry based on administrative records will mitigate some of the limitations and uncertainties in annual surveillance based on administrative data at minimal extra cost, as the suggested registry is really a compilation and linkage of the surveillance records. This is quite different from a case registry based on clinical records which may contain

detailed clinical and outcome information, but which typically represents a non-random sample of treated cases, often with an unknown relationship to the population from which they are drawn.

3.7 Construction of the case registry and surveillance system

Construction of a surveillance and case registry system will start with a year of data from the three sources. Each recorded contact in any of the databases that includes a first appearance of a diagnostic code for schizophrenia or related disorders will trigger a case record. Subsequent contacts will be grouped into entries related to a single case record based on the probabilistic record linking described earlier. For people who appear with a diagnosis of schizophrenia or related disorder and do not have subsequent contacts recorded for that year, a grouping of one will be created. This will give an estimate of prevalent cases, by grouping linked contacts and thus counting unique individuals. The annual grouping and counting of these records will be the means for the surveillance of schizophrenia. Retention and linkage of these cross-sectional annual pictures will form the longitudinal case registry. In each successive year, some prevalent cases will be removed through death or termination of OHIP coverage due to moving away. This event (death or termination of coverage) will be recorded on the case registry through linkage. New cases will be added each year as they appear in the administrative databases and the surveillance system will generate a case record for each unique individual at their first appearance, or 'index contact' in any one of the three databases with one of the relevant diagnoses. Subsequent health system contacts for those cases will be added to the case register, including the associated diagnosis for that contact. Figure 3.2 shows a simple algorithm for creation of a case record.

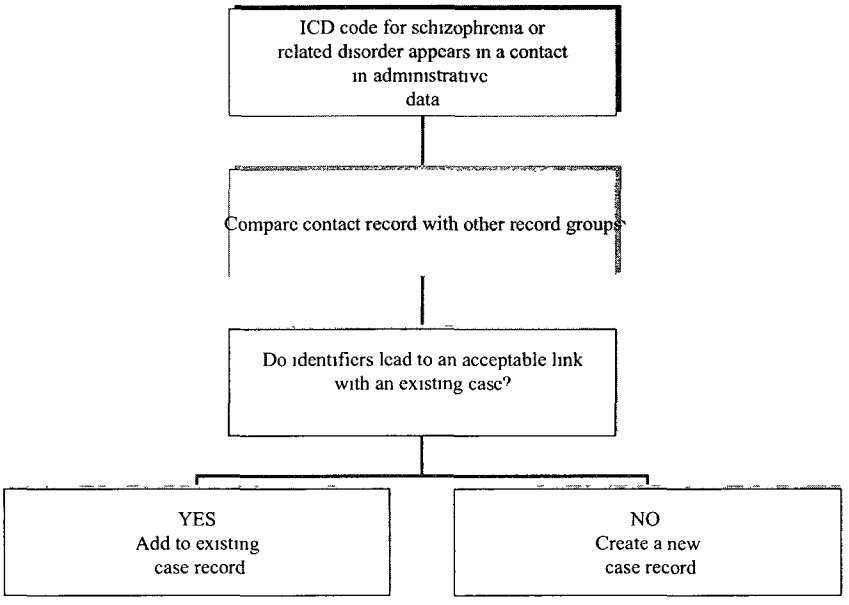

Figure 3.2 Algorithm for creation of case records of schizophrenia

A diagnosis of schizophrenia or related disorder anywhere on either billing data or a discharge abstract for the year will ' trigger' creation of a case record given the evidence reviewed that the diagnosis is more likely underused than overused. As discussed in the Case Definition section in Chapter 2, diagnoses of schizophreniform disorder, schizoaffective disorder, delusional disorder, psychosis secondary to substance use, and psychosis not otherwise specified should also be captured for the registry and considered cases in their own categories for surveillance, as this will complete the picture of schizophrenia and related disorders.

Although inclusion based on a single diagnosis may lead to the counting of a

small number of non-cases who are identified through coding or other administrative errors, on the whole the evidence supports that the diagnosis of schizophrenia is used cautiously and is not often reversed (89,119).

Surveillance alone will give a picture in cross section of the prevalence of schizophrenia, based on a decision about case criteria. For example criteria could be a single appearance in any of the databases with the diagnosis of interest, or could be defined as a single appearance in either DAD or OMHRS or two or more appearances in the OHIP data. The limitations of this approach are firstly that it will likely lead to a slight underestimation of prevalence due to the incomplete coverage of the population by the databases in the course of a year, and secondly that it will not really complete the picture by telling us anything about the cases counted. Although the imposition of an algorithm that arrives at a 'case or not case' decision is attractive for its simplicity, Kirkby et al. argue that a case registry compiled of longitudinal records of contacts including inconsistent diagnoses allows the epidemiological researcher to define caseness by looking at the proportion of schizophrenia diagnoses out of total diagnoses In their study of data held in an Australian mental health case register the authors use the term 'diagnostic dominance' to describe the distribution of all the diagnoses attributed to a single case. Schizophrenia was found to have a high diagnostic dominance compared with mood disorders, with 60.2% of people with one or more diagnoses of schizophrenia having a 'schizophrenia diagnostic dominance' of 60% or greater (60% or more of all their recorded diagnoses were schizophrenia) and 42.1% of patients with one or more diagnoses of schizophrenia had a schizophrenia diagnostic dominance of 90% or greater (119).

A case registry generated from administrative records of contacts will be most useful if it casts a wide net and leaves the algorithm regarding case definition to the individual user, depending on the purpose of the enquiry. Using different algorithms for case definition will lead to different results, and the most appropriate algorithm will vary with the aims of the study. Having multiple entries for each case in the registry would support a research approach that considers degree of certainty. Cases could be considered possible, probable or certain and weighted based on the probability of being a true case. This would depend on the diagnostic dominance of schizophrenia, or depend on the source of the contact information (for example a discharge diagnosis might be considered equivalent to several billing claims diagnoses for the degree of certainty it brings). The level of diagnostic certainty required may vary according to the purpose of the surveillance. Research into risk factors for schizophrenia, for example, might want to restrict cases to those with diagnostic certainty, whereas health services planning questions would be better answered by looking at cases with multiple contacts regardless of diagnostic dominance, as these would likely indicate people with severe mental illness and high service needs, regardless of exact diagnosis.

A different approach would be used in a longitudinal study of an incidence cohort. This type of study will define incident cases of schizophrenia and related psychosis as anyone having a first appearance in the databases with one of the relevant diagnoses within a defined timeframe, and then follow further contacts. Such a study would include cases with single or few contacts, as exclusion of people lost to follow-up could bias results, as these usually include people who have had a remission or recovery (28). A sample case record is shown in Figure 3.2.

Unique identifier (OHIP)_____

Name

Date of birth (yyyy/mm/dd) Place of birth (province of Canada, or International region)

Sex F M

Index contact generating a diagnostic code for psychotic illness:

Type of contact	Diagnostic code	Date of contact yyyy/mm/dd	Postal code at contact

Further healthcare contacts

Type of contact	Diagnostic code	Date of contact yyyy/mm/dd	Postal code at contact
Physician billing ambulatory			
Physician billing inpatient			
Hospital OMHRS			
Hospital DAD			

(add to list as new entries generated)

Clozapine status

Termination of OHIP coverage (yyyy/mm/dd)

Deceased (yyyy/mm/dd)

Figure 3.3 Sample case registry record

3.8 Addition of clozapine status to the register

Clozapine is an antipsychotic medication prescribed in Ontario and the rest of Canada for symptoms of schizophrenia that have not responded to other antipsychotic medications. It has been shown to be superior to usual treatment both for symptom reduction and for overall reduction in mortality in people with schizophrenia (134).

Along with other potential side effects common to antipsychotic medications, clozapine is associated with a potentially fatal hematologic side effect, agranulocytosis. Because of this possible side effect, the drug can only be prescribed and dispensed under monitoring rules set by Health Canada. The patient, the prescribing physician and the dispensing pharmacy must all be registered, and the patients' white blood count monitored weekly or monthly depending on risk factors present. The drug manufacturer maintains a database of the patients' lab results as they are forwarded to the manufacturer, and alerts the physician if the lab results are outside normal parameters. Until 2003 this was maintained by a single pharmaceutical company which was the only supplier of the drug in Canada. Since 2003 two generic manufacturers have joined the market, and patient information is now held in three different registries, depending on which drug is used (135). The essential piece of information that can get lost with this system is whether a patient is considered 'non-rechallengeable'. This means that the person has had a potential agranulocytosis, the drug has been withdrawn, and possibly tried a second time under controlled conditions, and the patient is considered at high risk if exposed to the drug again. Because of the possibility of a patient who is a poor historian receiving treatment in an unfamiliar clinical setting, this is information that should be held in a single location and outside of the privately held databases where it currently resides. At present, the patient must sign consent for the three companies to share information regarding hematologic status, in order to start the drug. The issue of how to address the fragmented state of clozapine monitoring in Canada is outside the scope of this paper, but the mandatory reporting of a patient being started on the drug and of a non-rechallengeable status to a central registry of schizophrenia cases is a sensible start.

Under Health Canada regulations the reporting is already mandatory, but the report goes to whichever data bank belongs to the company manufacturing the drug dispensed to the patient.

3.9 Introduction and maintenance of surveillance and case registry

The introduction of surveillance and case registry to Ontario is consistent with a population approach to recognition and treatment of psychotic illness in the province. Mental health services are notoriously fragmented in Ontario, and the patchwork of providers and routes to care makes it difficult to collect basic epidemiological data. The introduction of surveillance through counting of cases identified in administrative data is a relatively straightforward way to begin a stepped introduction. The example of the NDSS for diabetes, the CJRR for joint replacements, and cancer surveillance are all established systems in Canada. Although these examples are national, introduction of surveillance for schizophrenia can be planned and executed at the provincial level, which may then lead to national reporting as other provinces adopt similar systems. Case definition issues will be similar across provinces, but different patterns of physician payment and data collection from ambulatory and hospital care mean that each province will have some unique biases in reporting and data quality concerns. Sampling of high prevalence groups should follow shortly after so the quality of data generated by the administrative records can be assessed and missed cases added. Introduction of the case registry will be the next step, with data submitted to the registry from the large administrative databases. With the introduction of the case registry, there will have to be dedicated resources in place for maintenance, data quality checks, and integration of different data sources. The resources required would be one or more full time staff

supporting the system, in an environment providing access to expertise in data management, epidemiology and academic and clinical psychiatry. CIHI already holds much of the surveillance data collected in Canada, and is an excellent source of data management, methodology, and epidemiology expertise. If the surveillance and case registry of schizophrenia were held and managed at CIHI in Ottawa, then academic and clinical psychiatry support would be available from the Royal Ottawa Health Care Group (ROHCG). The ROHCG provides specialized mental health care at a regional level, and is a teaching hospital affiliated with the University of Ottawa. It is also the recipient of funding for clozapine dispensing at all of Ontario's participating hospitals (this funding flows through the ROHCG budget and out to the other organizations). The possibility of adding the clozapine status as a mandatory reporting element to a case registry makes the ROHCG an ideal clinical partner. CIHI also maintains the OMHRS data. OMHRS contains fairly detailed information on inpatients treated in adult psychiatric beds, and the ability to link some of this with surveillance data or registered cases would provide important detail on a subset of identified cases (those having been in an inpatient bed).

Conclusion

Why consider surveillance and a registry of schizophrenia in Ontario?

Surveillance of chronic diseases of public health importance through the use of health administrative data is practiced and accepted in Canada and elsewhere. This is often linked to case registry so outcomes can be measured as in the CJRR. Although there are Canadian examples of surveillance and registry of chronic disease, this has not so far extended to mental illnesses, despite the significant burden associated with these conditions.

Schizophrenia clearly meets the criteria for introduction of surveillance. It is the most debilitating of the major mental disorders and, due to the early age of onset, causes many years of disability. Suicide is the cause of death for around 10% of people with the illness, and elevated rates of accidental death, diabetes, respiratory and cardiac illness contribute to a standardized mortality rate of 2.5. The prevalence of schizophrenia and related illnesses in Canada is probably close to 1%. Costs associated with the illness are high because of the high rate of hospitalization and because of the heavy indirect costs of an illness that causes significant disability starting at a time when people are often finishing education or entering the workforce. Most cost estimates in developed countries find the cost to be between 1.5% and 3% of national health care expenditures. Some of this burden and cost can be averted by secondary prevention and treatment. This means early intervention at the onset of psychosis, and adequate treatment for people with established illness. At this time there are no confirmed primary prevention interventions, but the known risk factors suggest that there could be distal interventions

during the prenatal period or in the social milieu in early life that might hold promise. Because many known risk factors are associated with pre- and perinatal conditions, evaluation of any future primary prevention efforts will rely on population surveillance due to the long period between risk exposures and development of disease. Dissemination of surveillance and case registry based trends and rates at the provincial and the LHIN level would support evaluation of early interventions and ongoing treatment and support of people with psychotic illness. Adequate secondary and tertiary prevention occurs at the individual clinical level, but this will only occur consistently in a health system that is designed to meet these needs based on adequate information, and the surveillance system will enable evaluation of its performance.

A number of the known risk factors for schizophrenia are of particular interest in Ontario. Urban exposure in early life and migration are both associated with an increased risk for developing schizophrenia. These factors have been shown to operate independently, but often occur together, with migrants often moving to the large urban centres of the province. Ontario has one of the highest rates of residents born in another country of any jurisdiction in the world, and has become an increasingly urban province. The population concentration in urban centres is higher in Ontario than the Canadian national average. The importance of these risk factors as measured in the Ontario setting underlines the need for surveillance in the province rather than the current reliance on data from elsewhere when estimating service needs. This also provides an opportunity for research on these factors in this province.

What is required for a surveillance system for schizophrenia?

Each of the required elements of a surveillance system must be adapted to the illness under surveillance, or the environment in which surveillance takes place. The absence of accepted biomarkers for schizophrenia means that case definition of schizophrenia (and other mental illnesses) depends on the 'competent clinician interview' resulting in a DSM diagnosis of schizophrenia as the gold standard. Due to the possibility of changes to the definitions in future editions of the DSM, and also to the issue of changing clinical presentation and diagnosis, information about schizophrenia will be best collected along with information about related diagnoses in the DSM, such as other psychotic disorders. Although a diagnosis of schizophrenia is fairly reliable, some other psychotic illness diagnoses have less stability. These diagnoses grouped together probably represent a spectrum of illness and so will give a better picture of the population incidence than data on schizophrenia alone. Including this range of diagnoses under separate codes will give the data user flexibility to define cases as needed depending on their purpose.

The use of combined OHIP, DAD and OMHRS data will give excellent coverage of the Ontario population. Using these data year over year to capture users of the health care system over a period of several years and to build a case registry will give coverage of over 90% of the population of 'usual residents', approximating the census population. As these are already existing databases they will provide a cost-effective way to introduce surveillance of schizophrenia.

The CDC guidelines for the evaluation of surveillance state that the purpose of evaluating a surveillance system is to ensure the efficient and effective monitoring of conditions of public health concern. The application of these guidelines to the proposed

system (as far as possible for a system not yet in existence) shows that the combination of the three databases is relatively simple in the sense that it will be built on existing structures, is flexible in the sense of leaving case definition algorithms to the data user, and will supply data of good quality with acceptable PPV. Sensitivity of the data should be acceptable, but will require review after the system is developed to confirm sensitivity. The data will be representative as it will be drawn the pool of people accessing health care over a period of years, which represents the vast majority of usual residents.

The surveillance system proposed here will provide valuable information for planning and evaluation of health services as well as supporting research into the causes and outcomes of schizophrenia in Ontario. The dissemination of reports from surveillance data, not only to health planners but to clinicians, and to consumer and family advocacy groups will support the continued maintenance of the system and will ensure that schizophrenia will enter and remain in public consciousness as a condition of public health concern.

List of Abbreviations and Acronyms

ACT Assertive Community Treatment

AFP Alternate Funding Plan

BC British Columbia

BPRS Brief Psychiatric Rating Scale

CAMH Centre for Addiction and Mental Health

CCHS Canadian Community Health Survey

CIDI Composite International Diagnostic Interview

CIHI Canadian Institute for Health Information

CJRR Canadian Joint Replacement Registry

DAD Discharge Abstract Database

DALY Disability Adjusted Life Year

DIS Diagnostic Interview Schedule

DSM Diagnostic and Statistical Manual of Mental Disorders (followed by a roman numeral indicating the edition. The current edition is DSM IV-TR or DSM fourth edition with text revision)

ECA Epidemiologic Catchment Area

GP General Practitioner

ICD International Classification of Diseases

ICES Institute for Clinical and Evaluative Sciences

MHA Mental Health Act of Ontario

NDSS National Diabetes Surveillance System

NIMH National Institutes of Mental Health

NJRR National Joint Replacement Registry

NPV Negative predictive value

OHIP Ontario Health Insurance Plan

OHS Ontario Health Survey

OMHRS Ontario Mental Health Reporting System

PANSS Positive and Negative Syndrome Scale

PHIPA Personal Health Information Protection Act

PPH Provincial Psychiatric Hospital

PPV Positive predictive value

PSO Psychiatric Survivors of Ottawa

ROHCG Royal Ottawa Health Care Group

SANS/SAPS Scale for Negative Symptoms/Scale for Positive Symptoms

SSO Schizophrenia Society of Ontario

USA United States of America

WHO World Health Organization

WPA World Psychiatric Association

YLD Years Lived with Disability

References

(1) Bland RC. Demographic aspects of functional psychoses in Canada. Acta Psychiatrica Scandinavica 1977;55(5):369-380.

(2) Cardno A, Murray RM. The 'classical' genetic epidemiology of schizophrenia. In: Murray RM, Jones PB, Susser E, van Os J, Cannon M, editors. The Epidemiology of Schizophrenia. first ed. Cambridge: Cambridge University Press; 2003. p. 194.

(3) Last JM editor. A Dictionary of Epidemiology. fourth ed. New York: Oxford University Press; 2001.

(4) Paquette D, Lowry RB, Sauvé R. Two to three percent of infants are born with a congenital anomaly, but who's counting? A national survey of congenital anomalies surveillance in Canada. Chronic Dis.Can. 2006;27(1):36-38.

(5) Buehler JW. Surveillance. Modern Epidemiology. second ed. Philadelphia: Lippincott Williams and Wilkins; 1998. p. 435.

(6) Parkin DM. The evolution of the population-based cancer registry. Nature Reviews Cancer 2006;6(8):603-612.

(7) Canadian Institute for Health Information. www.cihi.ca/cjrr. Accessed July 10, 2009.

(8) Hafner H, An Der Heiden W. The contribution of European case registers to research on schizophrenia. Schizophr.Bull. 1986;12(1):26-51.

(9) Tansella M. Do we still need psychiatric case registers? Acta Psychiatr.Scand. 2000;101(4):253-255.

(10) Thacker SB, Stroup DF, Rothenberg RB, Brownson RC. Public health surveillance for chronic conditions: A scientific basis for decisions. Stat.Med. 1995;14(5-7):629-641.

(11) Teutsch SM. Considerations in planning a surveillance system. In: Teutsch SM, Churchill RE, editors. Principles and Practice of Public Health Surveillance Oxford, New York: Oxford University Press; 2000. p. 17.

(12) Koné Péfoyo AJ, Rivard M, Laurier C. Public health surveillance and role of administrative data. Rev.Epidemiol.Sante Publique 2009;57(2):99-111.

(13) Health Canada. A Report on Mental Illness in Canada. Ottawa: Health Canada; 2002.

(14) McGrath J, Saha S, Welham J, El Saadi O, MacCauley C, Chant D. A systematic review of the incidence of schizophrenia: The distribution of rates and the influence of sex, urbanicity, migrant status and methodology. BMC Med. 2004;2.

(15) Mortensen PB, Pedersen CB, Westergaard T, Wohlfahrt J, Ewald H, Mors O, et al. Effects of family history and place and season of birth on the risk of schizophrenia. N.Engl.J.Med. 1999;340(8):603-608.

(16) Mortensen PB. Urban-Rural Differences in the Risk for Schizophrenia. Int. J. Ment. Health 2000;29(3):101-110.

(17) Cantor-Graae E, Pedersen CB, McNeil TF, Mortensen PB. Migration as a risk factor for schizophrenia: A Danish population-based cohort study. Br. J. Psychiatry 2003;182(FEB.):117-122.

(18) Pinikahana J, Happell B, Keks NA. Suicide and schizophrenia: A review of literature for the decade (1990-1999) and implications for mental health nursing. Issues Ment. Health Nurs. 2003;24(1):27-43.

(19) Saha S, Chant D, McGrath J. A systematic review of mortality in schizophrenia: Is the differential mortality gap worsening over time? Arch. Gen. Psychiatry 2007;64(10):1123-1131.

(20) Bland RC, Stebelsky G, Orn H, Newman SC. Psychiatric disorders and unemployment in Edmonton. Acta Psychiatr.Scand. 1988;77(SUPPL. 338):72-80.

(21) Roberts L, Roalfe A, Wilson S, Lester H. Physical health care of patients with schizophrenia in primary care: A comparative study. Fam. Pract. 2007;24(1):34-40.

(22) Ro□ssler W, Joachim Salize H, Van Os J, Riecher-Ro□ssler A. Size of burden of schizophrenia and psychotic disorders. European Neuropsychopharmacology 2005;15(4):399-409.

(23) Ustun TB, Saxena S, Rehm J, Bickenbach J. Are disability weights universal? [10]. Lancet 1999;354(9186):1306.

(24) Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. Lancet 2006;367(9524):1747-1757.

(25) Bottlender R, Strauß A, Möller H-. Social disability in schizophrenic, schizoaffective and affective disorders 15 years after first admission. Schizophr.Res. 2010;116(1):9-15.

(26) Williams R, Kopala L, Malla A, Smith G, Love L, Balshaw R. Medication decisions and clinical outcomes in the Canadian National Outcomes Measurement Study in Schizophrenia. Acta Psychiatr.Scand. 2006;113(SUPPL. 430):12-21.

(27) Walsh E, Buchanan A. Criminal and violent behaviour in schizophrenia. In: Murray RM, Jones PB, Susser E, van Os J, Cannon M, editors. The Epidemiology of Schizophrenia; 2003. p. 343.

(28) Jobe TH, Harrow M. Long-term outcome of patients with schizophrenia: A review. Can. J. Psychiatry 2005;50(14):892-900.

(29) Jablensky A. Epidemiology of schizophrenia: The global burden of disease and disability. European Archives of Psychiatry and Clinical Neuroscience 2000;250(6):274-285.

(30) Andreasen NC. Standardized remission criteria in schizophrenia. Acta Psychiatr.Scand. 2006;113(2):81.

(31) Lamarre-Cliche M, Castilloux AM, LeLorier J. Association between the burden of disease and research funding by the Medical Research Council of Canada and the National Institutes of Health. A cross-sectional study. Clinical and Investigative Medicine 2001;24(2):83-89.

(32) Knapp M, Mangalore R, Simon J. The global costs of Schizophrenia. Schizophr.Bull. 2004;30(2):279-293.

(33) Goeree R, O'Brien BJ, Goering P, Blackhouse G, Agro K, Rhodes A, et al. The economic burden of schizophrenia in Canada. Can. J. Psychiatry 1999;44(5):464-472.

(34) Goeree R, Farahati F, Burke N, Blackhouse G, O'Reilly D, Pyne J, et al. The economic burden of schizophrenia in Canada in 2004. Curr. Med. Res. Opin. 2005; 21(12):2017-2028.

(35) Carr VJ, Lewin TJ, Neil AL. What is the value of treating schizophrenia? Australian and New Zealand Journal of Psychiatry 2006;40(11-12):963-971.

(36) McGrath J. Prevention of schizophrenia- not an impossible dream. In: Murray RM, Jones PB, Susser E, van Os J, Cannon M, editors. The Epidemiology of Schizophrenia; 2003. p. 427.

(37) Romaguera PA, German RR, Klaucke DN. Evaluating public health surveillance. In: Teutsch SM, Churchill RE, editors. Principles and Practice of Public Health Surveillance Oxford, New York: Oxford University Press; 2000. p. 176.

(38) Mojtabai R, Malaspina D, Susser E. The Concept of Population Prevention: Application to Schizophrenia. Schizophr.Bull. 2003;29(4):791-801.

(39) McGrath J. Editorial: Is it time to trial vitamin D supplements for the prevention of schizophrenia? Acta Psychiatr.Scand. 2010;121(5):321-324.

(40) Hafner H. Prodrome, onset and early course of schizophrenia. In: Murray RM, Jones PB, Susser E, van Os J, Cannon M, editors. The Epidemiology of Schizophrenia; 2003. p. 124.

(41) Norman RMG, Malla AK, Verdi MB, Hassall LD, Fazekas C. Understanding delay in treatment for first-episode psychosis. Psychological Medicine 2004;34(2):255-266.

(42) Addington J, Van Mastrigt S, Addington D. Duration of untreated psychosis: Impact on 2-years outcome. Psychol.Med. 2004;34(2):277-284.

(43) Malla A, Norman R, Bechard-Evans L, Schmitz N, Manchanda R, Cassidy C. Factors influencing relapse during a 2-year follow-up of first-episode psychosis in a specialized early intervention service. Psychol.Med. 2008;38(11):1585-1593.

(44) Whitty P, Clarke M, McTigue O, Browne S, Kamali M, Kinsella A, et al. Predictors of outcome in first-episode schizophrenia over the first 4 years of illness. Psychol.Med. 2008;38(8):1141-1146.

(45) McGrath JJ. Myths and plain truths about schizophrenia epidemiology - The NAPE lecture 2004. Acta Psychiatr. Scand. 2005;111(1):4-11.

(46) Mueser KT, McGurk SR. Schizophrenia. Lancet 2004;363(9426):2063-2072.

(47) Clarke M, O'Callaghan E. The value of first-episode studies in schizophrenia. In: Murray RM, Jones PB, Susser E, van Os J, Cannon M, editors. The Epidemiology of Schizophrenia; 2003. p. 148.

(48) Jablensky A. Prevalence and incidence of schizophrenia spectrum disorders: Implications for prevention. Australian and New Zealand Journal of Psychiatry 2000;34(SUPPL. 1):S26-S34.

(49) Boydell J, Murray RM. Urbanization, migration and risk of schizophrenia. In: Murray RM, Jones PB, Susser E, van Os J, Cannon M, editors. The Epidemiology of Schizophrenia; 2003. p. 49.

(50) Jablensky A. The 100-year epidemiology of schizophrenia. Schizophrenia Research 1997;28(2-3):111-125.

(51) Cannon M, Kendell R, Susser E, Jones PB. Prenatal and perinatal risk factors for schizophrenia. In: Murray RM, Jones PB, Susser E, van Os J, Cannon M, editors. The Epidemiology of Schizophrenia; 2003. p. 74.

(52) Malaspina D, Harlap S, Fennig S, Heiman D, Nahon D, Feldman D, et al. Advancing paternal age and the risk of schizophrenia. Arch.Gen.Psychiatry 2001;58(4):361-367.

(53) Milan A. One Hundred Years of Families. 2000;no. 56.

(54) Pedersen CB, Mortensen PB. Evidence of a dose-response relationship between urbanicity during upbringing and schizophrenia risk. Arch.Gen.Psychiatry 2001;58(11):1039-1046.

(55) Statistics Canada. Available at: www.statcan.ca/health-sante. Accessed September 30, 2009.

(56) Geddes JR, Black RJ, Whalley LJ, Eagles JM. Persistence of the decline in the diagnosis of schizophrenia among first admissions to Scottish Hospitals from 1969 to 1988. British Journal of Psychiatry 1993;163(NOV.):620-626.

(57) Harrison G, Mason P. Schizophrenia - Falling incidence and better outcome? British Journal of Psychiatry 1993;163(OCT.):535-541.

(58) Gregory I. An analysis of family data on 1000 patients admitted to a Canadian mental hospital. Acta Genet.Stat.Med. 1959;9(1):54-96.

(59) Statistics Canada. Number and share of the foreign-born population in Canada, 1901 to 2006. Available at: http://www12.statcan.gc.ca/census-recensement/2006/as-sa/97-557/figures/c1-eng.cfm. Accessed October 1, 2009.

(60) Statistics Canada. Immigration in Canada: A Portrait of the Foreign-born Population, 2006 Census: Driver of population growth. Available at: http://www12.statcan.gc.ca/census-recensement/2006/as-sa/97-557/p3-eng.cfm. Accessed September 30, 2009.

(61) Jarvis GE. Rethinking social causes of psychosis. Canadian Journal of Psychiatry 2007;52(5):275-276.

(62) Selten J-, Cantor-Graae E, Kahn RS. Migration and schizophrenia. Current Opinion in Psychiatry 2007;20(2):111-115.

(63) Greenland S. Applications of Stratified Analysis Methods. In: Rothman KJ, Greenland S, editors. Modern Epidemiology. second ed.; 1998. p. 281.

(64) Cantor-Graae E. The contribution of social factors to the development of schizophrenia: A review of recent findings. Canadian Journal of Psychiatry 2007;52(5):277-286.

(65) Bresnahan M, Susser E. Investigating the socioenvironmental influences in schizophrenia; conceptual and design issues. In: Murray RM, Jones PB, Susser E, van Os

J, Cannon M, editors. The Epidemiology of Schizophrenia. first ed. Cambridge: Cambridge University Press; 2003. p. 5.

(66) Ontario. Ministry of Health. Making it happen : implementation plan for mental health reform. Toronto: Queen's Printer for Ontario; 1999.

(67) Ontario. Ministry of Health. Making it happen: operational framework for the delivery of mental health services and supports. Toronto: Queen's Printer of Ontario; 1999.

(68) Prince M editor. A Practical Psychiatric Epidemiology. Oxford New York: Oxford University Press; 2003.

(69) First MB, Frances A, Pincus HA. DSM-IV-TR Guidebook. first ed.: American Psychiatric Pub.; 2004.

(70) Chandarana P, Pellizzari JR. Canadian perspectives on undergraduate education in psychiatry. In: Rae-Grant Q, editor. Psychiatry in Canada: 50 years (1951 to 2001). first ed. Ottawa: Canadian Psychiatric Association; 2001. p. 149.

(71) Greenland C, Griffin JD, Hoffman BF. Psychiatry in Canada from 1951 to 2001. In: Rae-Grant Q, editor. Psychiatry in Canada: 50 years (1951 to 2001). first ed. Ottawa: Canadian Psychiatric Association; 2001. p. 1.

(72) Leverette JS, Persad E. Postgraduate education in psychiatry: a climate of rapid change. In: Rae-Grant Q, editor. Psychiatry in Canada: 50 years (1951 to 2001). first ed. Ottawa: Canadian Psychiatric Association; 2001. p. 163.

(73) Allardyce J, Gaebel W, Zielasek J, van Os J. Deconstructing psychosis conference February 2006. In: Tamminga CA, Sirovatka PJ, Regier DA, van Os J, editors. Deconstructing Psychosis; Refining the Research Agenda for DSM-V. first ed. Arlinton Virginia: American Psychiatric Association; 2010. p. 1.

(74) Wallace ER. Psychiatry and its nosology: a historico-philosophical overview. In: Sadler JZ, Wiggins OP, Schwartz MA, editors. Philosophical Perspectives on Psychiatric Diagnostic Classification Baltimore: The Johns Hopkins University Press; 1994. p. 16.

(75) Jablensky A. The conflict of the nosologists: Views on schizophrenia and manic-depressive illness in the early part of the 20th century. Schizophrenia Research 1999;39(2):95-100.

(76) Robins LN, Regier DA editors. Psychiatric Disorders in America; The Epidemiologic Catchment Area Study. New York: The Free Press; 1991.

(77) Houts AC. Discovery, invention and the expansion of the modern diagnostic and statistical manuals of mental disorders. In: Beutler LE, Malik ML, editors. Rethinking the

DSM: A Psychological Perspective. first ed. Washington DC: American Psychological Association; 2002. p. 17.

(78) Kendell RE. Relationship between the DSM-IV and the ICD-10. Journal of Abnormal Psychology 1991;100(3):297-301.

(79) Goldbloom DS, Garfinkel PE. The next 50 years. In: Rae-Grant Q, editor. Psychiatry in Canada: 50 years (1951 to 2001). first ed. Ottawa: Canadian Psychiatric Association; 2001. p. 255.

(80) Rose G, Barker DJP. What a case? Dichotomy or continuum? Br.Med.J. 1978;2(6141):873-874.

(81) Van Os J, Hanssen M, Bijl RV, Ravelli A. Strauss (1969) revisited: A psychosis continuum in the general population? Schizophr. Res. 2000;45(1-2):11-20.

(82) Jablensky A. Categories, dimensions and prototypes: Critical issues for psychiatric classification. Psychopathology 2005;38(4):201-205.

(83) van Os J, Verdoux H. Diagnosis and classification of schizophrenia:categories versus dimensions, distributions versus disease. In: Murray RM, Jones PB, Susser E, van Os J, Cannon M, editors. The Epidemiology of Schizophrenia; 2003. p. 364.

(84) Crow TJ. A continuum of psychosis, one human gene, and not much else - The case for homogeneity. Schizophrenia Research 1995;17(2):135-145.

(85) Baldwin P, Browne D, Scully PJ, Quinn JF, Morgan MG, Kinsella A, et al. Epidemiology of first-episode psychosis: Illustrating the challenges across diagnostic boundaries through the Cavan-Monaghan study at 8 years. Schizophr. Bull. 2005;31(3):624-638.

(86) Kempf L, Hussain N, Potash JB. Mood disorder with psychotic features, schizoaffective disorder, and schizophrenia with mood features: Trouble at the borders. Int. Rev. Psychiatry 2005;17(1):9-19.

(87) Lichtermann D, Karbe E, Maier W. The genetic epidemiology of schizophrenia and of schizophrenia spectrum disorders. European Archives of Psychiatry and Clinical Neuroscience 2000;250(6):304-310.

(88) Murray RM, Grech A, Phillips P, Johnson S. What is the relationship between substance abuse and schizophrenia. In: Murray RM, Jones PB, Susser E, van Os J, Cannon M, editors. The Epidemiology of Schizophrenia; 2003. p. 317.

(89) Veen ND, Selten J-, Schols D, Laan W, Hoek HW, Van Der Tweel I, et al. Diagnostic stability in a Dutch psychosis incidence cohort. British Journal of Psychiatry 2004;185(DEC.):460-464.

(90) Statistics Canada. Available at: www12.statcan.gc.ca/census-recensement/2006/dp-pd. Accessed October 1, 2009.

(91) Goldner EM, Jones W, Waraich P. Using administrative data to analyze the prevalence and distribution of schizophrenic disorders. Psychiatr. Serv. 2003;54(7):1017-1021.

(92) Garbe PL, Blount SB. Chronic Disease Surveillance. In: Halperin W, Baker EL, editors. Public Health Surveillance New York: Van Nostrand Reinhold; 1992. p. 130.

(93) Istre GR. Disease surveillance at the state and local levels. In: Halperin W, Baker EL, editors. Public health surveillance New York, N. Y.: Van Nostrand Reinhold; 1992. p. 42.

(94) Murphy JM. The Stirling County Study: Then and now. International Review of Psychiatry 1994;6(4):329-348.

(95) Blazer D, George L, Winfield I. Epidemiologic data and planning mental health services. A tale of two surveys. Social Psychiatry and Psychiatric Epidemiology 1991;26(1):21-27.

(96) Bland RC, Newman SC, Orn H. Period prevalence of psychiatric disorders in Edmonton. Acta Psychiatrica Scandinavica 1988;77(SUPPL. 338):33-42.

(97) Bland RC, Orn H, Newman SC. Lifetime prevalence of psychiatric disorders in Edmonton. Acta Psychiatrica Scandinavica 1988;77(SUPPL. 338):24-32.

(98) Boyle MH, Offord DR, Campbell D, Catlin G, Goering P, Lin E, et al. Mental health supplement to the Ontario health survey: Methodology. Canadian Journal of Psychiatry 1996;41(9):549-558.

(99) Offord DR, Boyle MH, Campbell D, Goering P, Lin E, Wong M, et al. One-year prevalence of psychiatric disorder in Ontarians 15 to 64 years of age. Canadian Journal of Psychiatry 1996;41(9):559-563.

(100) Gravel R, Béland Y. The Canadian community health survey: Mental health and well-being. Canadian Journal of Psychiatry 2005;50(10):573-579.

(101) Beck CA, Williams JVA, Jian LW, Kassam A, El-Guebaly N, Currie SR, et al. Psychotropic medication use in Canada. Canadian Journal of Psychiatry 2005;50(10):605-613.

(102) Supina AL, Patten SB. Self-reported diagnoses of schizophrenia and psychotic disorders may be valuable for monitoring and surveillance. Canadian Journal of Psychiatry 2006;51(4):256-259.

(103) Thompson AH. Variations in the prevalence of psychiatric disorders and social problems across Canadian provinces. Canadian Journal of Psychiatry 2005;50(10):637-642.

(104) Curtis LJ, MacMinn WJ. Health care utilization in Canada: Twenty-five years of evidence. Canadian Public Policy 2008;34(1):65-87.

(105) Canadian Institute for Health Information. Exploring hospital mental health service use in Ontario, 2007-2008. Available at: http://secure.cihi.ca/cihiweb/dispPage.jsp?cw_page=AR_2813_E&cw_topic=2813.

(106) Nabalamba A, Millar WJ. Going to the doctor. Health reports / Statistics Canada, Canadian Centre for Health Information = Rapports sur la santé / Statistique Canada, Centre canadien d'information sur la santé 2007;18(1):23-35.

(107) Eaton WW, Romanoski A, Anthony JC, Nestadt G. Screening for psychosis in the general population with a self-report interview. J. NERV. MENT. DIS. 1991;179(11):689-693.

(108) Snider DE, Stroup DF. Ethical issues. In: Teutsch SM, Churchill RE, editors. Principles and Practice of Public Health Surveillance Oxford, New York: Oxford University Press; 2000. p. 194.

(109) Ontario Ministry of Health and Long Term Care. Collection, use and disclosure of personal health information by the Ministry of Health and Long Term Care. 2004; Available at: http://www.health.gov.on.ca/english/public/legislation/bill_31/collection_use_disclosure.pdf.

(110) Hinshaw SP. The Mark of Shame: Stigma of Mental Illness and an Agenda for Change. Oxford, New York: Oxford University Press; 2007.

(111) Thompson AH, Stuart H, Bland RC, Arboleda-Florez J, Warner R, Dickson RA. Attitudes about schizophrenia from the pilot site of the WPA worldwide campaign against the stigma of schizophrenia. Social Psychiatry and Psychiatric Epidemiology 2002;37(10):475-482.

(112) U□c□ok A, Polat A, Sartorius N, Erkoc□ S, Atakli C. Attitudes of psychiatrists toward patients with schizophrenia. Psychiatry and Clinical Neurosciences 2004;58(1):89-91.

(113) Schizophrenia Society of Ontario. Vision, Mission and Mandate. Available at: http://www.schizophrenia.on.ca/about-sso/6-about-the-organization/14-vision-mission-a-mandate.html?active=1. Accessed February, 2009.

(114) Psychiatric Survivors of Ottawa. Mission Statement. Available at: http://www.psychiatricsurvivors.org/. Accessed February, 2009.

(115) Centers for Disease Control. Guidelines for evaluating surveillance systems. MMWR.Morbidity and mortality weekly report 1988;37 Suppl 5:1-18.

(116) Centres for Disease Control and Prevention. Updated guidelines for evaluating public health surveillance systems. Morb.Mortal.Weekly Rep. 2001;50(13):1-29.

(117) Canadian Institute for Health Information. Alternative payments and the national physician database (NPDB). Ottawa; 2002.

(118) Iron KS, Manuel DG, Williams J. Using a linked data set to determine the factors associated with utilization and costs of family physician services in Ontario: Effects of self-reported chronic conditions. Chronic Dis.Can. 2003;24(4):124-132.

(119) Kirkby KC, Hay DA, Daniels BA, Jones IH, Mowry BJ. Comparison between register and structured interview diagnoses of schizophrenia: A case for longitudinal diagnostic profiles. Aust.N.Z.J.Psychiatry 1998;32(3):410-414.

(120) Fair M, Cyr M, Allen AC, Shi Wu Wen, Guyon G, MacDonald RC. An assessment of the validity of a computer system for probabilistic record linkage of birth and infant death records in Canada. Chronic Dis.Can. 2000;21(1):8-13.

(121) Howe GR, Lindsay J. A generalized iterative record linkage computer system for use in medical follow-up studies. Computers and Biomedical Research 1981;14(4):327-340.

(122) Rawson NSB, Malcolm E, D'Arcy C. Reliability of the recording of schizophrenia and depressive disorder in the Saskatchewan health care datafiles. Soc.Psychiatry Psychiatr.Epidemiol. 1997;32(4):191-199.

(123) Robinson JR, Tataryn DJ. Reliability of the Manitoba Mental Health Management Information System for research. Canadian Journal of Psychiatry 1997;42(7):744-749.

(124) Aschengrau A, Seage GRI. Essential of Epidemiology in Public Health. Sudbury Massachusetts: Jones and Bartlett Publishers; 2003.

(125) Iron K, Manuel D. Quality assessment of administrative data (QuAAD): An opportunity for enhancing Ontario's health data. Toronto: Institute for Clinical Evaluative Sciences; 2007.

(126) Frayne SM, Miller DR, Sharkansky EJ, Jackson VW, Wang F, Halanych JH, et al. Using administrative data to identify mental illness: What approach is best? American Journal of Medical Quality 2010;25(1):42-50.

(127) Lurie N, Popkin M, Dysken M, Moscovice I, Finch M. Accuracy of diagnoses of schizophrenia in Medicaid claims. HOSP. COMMUNITY PSYCHIATRY 1992;43(1):69-71.

(128) Fowles JB, Fowler EJ, Craft C. Validation of claims diagnoses and self-reported conditions compared with medical records for selected chronic diseases. Journal of Ambulatory Care Management 1998;21(1):24-34.

(129) Canadian Institute for Health Information. Depression in Ontario: What predicts a first mental health re-hospitalization? 2010.

(130) Manuel D. Presentation to the Department of Epidemiology and Community Medicine, University of Ottawa. 2008.

(131) Andreasen NC, Carpenter Jr. WT, Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in schizophrenia: Proposed criteria and rationale for consensus. American Journal of Psychiatry 2005;162(3):441-449.

(132) Van Os J, Burns T, Cavallaro R, Leucht S, Peuskens J, Helldin L, et al. Standardized remission criteria in schizophrenia. Acta Psychiatrica Scandinavica 2006;113(2):91-95.

(133) Van Os J, Drukker M, Campo JÀ, Meijer J, Bak M, Delespaul P. Validation of remission criteria for schizophrenia. American Journal of Psychiatry 2006;163(11):2000-2002.

(134) Tiihonen J, Wahlbeck K, Lo□nnqvist J, Klaukka T, Ioannidis JPA, Volavka J, et al. Effectiveness of antipsychotic treatments in a nationwide cohort of patients in community care after first hospitalisation due to schizophrenia and schizoaffective disorder: Observational follow-up study. Br. Med. J. 2006;333(7561):224-227.

(135) Health Canada. Advisories, Clozapine. Available at: www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis. Accessed March, 2010.

(136) Smith GN, Boydell J, Murray RM, Flynn S, McKay K, Sherwood M, et al. The incidence of schizophrenia in European immigrants to Canada. Schizophrenia Research 2006;87(1-3):205-211.

(137) Centre for Addiction and Mental Health. History of the Queen St site. Available at: http://www.camh.net/News_events/Redeveloping_the_Queen_Street_site/History%20of%20the%20Queen%20Street%20Site/history_of_the_queen_street_site.html. Accessed January 28, 2010.