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Chronic Diseases in Canada (CDIC) is a quarterly scientific journal focussing on current evidence relevant to the control and prevention of chronic (i.e. non-communicable) diseases and injuries in Canada. Since 1980 the journal has published a unique blend of peer-reviewed feature articles by authors from the public and private sectors and which may include research from such fields as epidemiology, public/community health, biostatistics, the behavioural sciences, and health services or economics. Only feature articles are peer reviewed. Authors retain responsibility for the content of their articles; the opinions expressed are not necessarily those of the CDIC editorial committee nor of the Public Health Agency of Canada.

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Preface to the Canadian Health Measures Survey results Oral health statistics, 2007–2009[1]

Dr. P. Cooney, Chief Dental Officer, Health Canada

While the eyes are the window to the soul, the mouth is a mirror to the body.[2]

Both dental professionals and the general public increasingly understand that oral health is connected to overall health and that oral diseases are chronic diseases in their own right. According to the World Health Organization (WHO), "oral diseases share common risk factors with the four leading chronic diseases—cardiovascular diseases, cancer, chronic respiratory diseases and diabetes—including unhealthy diet, tobacco use, and harmful alcohol use. Poor oral hygiene is also a risk factor."[3]

Chronic disease is defined as disease that is long-lasting or recurring; systemic disease refers to disease that affects the whole body. With these definitions in mind, we can classify the two major oral health conditions—periodontal (gum) disease and dental caries (tooth decay)—as both chronic and systemic diseases. Oral diseases can be recurring and long-lasting, and impact overall health, as in the case of painful tooth decay that affects eating and hence nutritional intake. According to WHO, "oral health means being free of chronic mouth and facial pain, oral and throat cancer, oral sores, birth defects such as cleft lip and palate, periodontal (gum) disease, tooth decay and tooth loss, and other diseases and disorders that affect the mouth and oral cavity."[3]

Periodontal diseases and dental caries are the most prevalent chronic diseases, affecting children, adolescents, adults and the elderly.[4,5] In fact, dental caries affects 60% to 90% of schoolchildren and the vast majority of adults in most industrialized countries.[6] Among 5-to 17-year-olds, dental decay is five times as common as asthma and seven times as common as hay fever.[7] Research points to a connection between poor oral health and diabetes as well as respiratory diseases; poor oral health may also contribute to heart disease, stroke, and the risk of having premature, low birth-weight babies.[7]

Results of systemic disorders, for example, loss of saliva due to radiation treatment or medications, affect conditions in the mouth. Oral signs and symptoms can also be precursors of systemic diseases such as leukoplakia, a white spot or patch on soft tissues in the mouth that may become cancerous.[8] Many other systemic conditions and illnesses play a role in oral health. Significant examples include malnutrition, osteoporosis, eating disorders, anemia, HIV/AIDS, thyroid disorders and even stress.

The Office of the Chief Dental Officer (OCDO) was created in October 2004 to increase awareness about ways to prevent oral diseases and to improve the oral health status of Canadians. One of OCDO's top priorities is to collect current statistical information. The Canadian Health Measures Survey (CHMS) was developed in collaboration with Statistics Canada, Health Canada, and the National Department of Defence to collect baseline information on a number of health factors, including oral health; with no national oral health assessment since 1972, there was a great need for this baseline data. The CHMS collected health measures from almost 6000 people, representing 97% of the Canadian population aged 6 to 79, from March 2007 to November 2009. Following the design of the CHMS, four sub-group surveys (First Nations on-reserve, Inuit, seniors, and the homeless in Toronto) have been or are in the process of being completed.

The results from the oral health component of the CHMS, along with the results expected from the other sub-group surveys on oral health, means that public health dental professionals now have a real understanding of the current status of oral health in Canada. This information will allow us to develop informed policies to address the true oral health needs of Canadians. I hope that you as readers will use this information and research to better understand the connections between oral health and other health issues, and to explore these connections with the goal of improving the oral health and hence the overall health of Canadians.

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Canadian Health Measures Survey results – Oral health statistics, 2007-2009

The highlights presented below are taken from Health Canada's *Summary Report on the Findings of the Oral Health Component of the Canadian Health Measures Survey, 2007–2009.*[1] The accompanying technical report provides in-depth analysis of the survey results. Both documents can be found at www.fptdwg.ca/English/e-documents.html.

Oral health statistics, 2007-2009

Oral health refers to the health of one's mouth and teeth. Good oral health is more than just a nice smile—it is an important part of being healthy. Poor oral health and poor oral hygiene affect more than just the mouth and teeth: there is a demonstrated connection between poor oral health and systemic disease such as diabetes in people of all ages and respiratory diseases particularly among older adults. Research also points to possible connections between poor oral health and certain systemic conditions such as heart disease and the risk of having premature, low birth-weight babies. Due to these connections, the significance of maintaining the health of one's mouth and teeth throughout life takes on greater importance.

The results from the Oral Health Component of the CHMS demonstrate that, overall, Canadians pay attention to and have very good oral health:

- Three of every four Canadians visit a dental professional every year;
- Two out of every three Canadians with natural teeth do not need dental treatment.

In terms of Canadians' preventive behaviours:

- 73% report brushing twice a day;
- 28% floss at least 5 times a week.

Canadians were asked how they felt about their oral health:

- 84% report that they have good or excellent oral health;
- 12% avoid certain foods because of problems with their teeth or mouth; and
- 12% report that they have had ongoing pain in their mouth in the past year.

Canadians were asked about mouth pain:

- 16% from the lower income group report that they had pain in their mouth in the past year;
- 17% of current smokers report that they had pain in their mouth in the past year; and
- 18% of those who are publicly insured report that they had pain in their mouth in the past year.

Some of the other highlights from the Oral Health Component of the CHMS are as follows:

- 57% of 6 to 11 year olds have or have had a cavity;
- 59% of 12 to 19 year olds have or have had a cavity;
- The average number of teeth affected by decay in children aged 6 to 19 years old is 2.5;
- 6% of adult Canadians no longer have any natural teeth;
- Although cavities are largely preventable, 96% of adults have had a history of cavities;
- 21% of adults with natural teeth have or have had a moderate or a severe periodontal (gum) problem;
- 34% of Canadians 6 to 79 years of age (who have teeth) had some sort of treatment need identified by the dentists;
- So few children have moderate or severe fluorosis that, even combined, the prevalence is too low to permit reporting. This shows that dental fluorosis remains of low concern in Canada.

The oral health care system in Canada is mostly privately operated, which means the majority of dental practices are owned and operated by dental professionals. Most Canadians pay for their oral health services themselves or through insurance from their place of employment. Some dental services are paid through the public health system, including those covered under the Canada Health Act, or by federal government departments (e.g. dental coverage for First Nations and Inuit) or through provincial/territorial or municipal dental programs across Canada. Studies show that having dental insurance is one of the main factors that determine whether or not Canadians go to see a dental professional for dental care. Results from the CHMS indicate that 17% of Canadians avoided going to a dental professional in the previous year and 16% avoided getting all their recommended treatment done in the same period due to the cost.

The Oral Health Component of the CHMS asked all respondents whether they had insurance or a government program that covered all or part of their dental expenses.

- 62% of Canadians have private dental insurance (usually an employee benefit), 6% have public insurance, and 32% have no dental insurance;
- 78% of respondents from the higher income bracket have private insurance coverage;

- 53% of adults between 60 and 79 years of age do not have any dental insurance; and

- 50% of respondents from the lower income bracket do not have any dental insurance.

For more information see
www.healthcanada.gc.ca/ocdo

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The public health implications of assisted reproductive technologies

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Abstract

Objective: The public health implications of Assisted Reproductive Technologies (ART) are largely unknown by researchers and policy makers alike. Outcomes need to be considered, not just as clinical issues, but in terms of effect on public health.

Methods: Using a qualitative key informant process involving interviews with selected professionals and a review of the medical literature, eight general themes of public health issues associated with ART were identified, and are discussed.

Recommendations: Short and long-term health outcomes of women undergoing ART procedures, and of their offspring, need to be considered, as do the epidemiological risks associated with donated gametes and the effect on health services of multiple and preterm births, both produced in higher rates by ART. A national surveillance system and greater inter-jurisdictional communication are important strategies for addressing these evolving concerns.

Keywords: *public health, reproductive medicine, review literature, infant, IVF, ART, in vitro fertilization*

Introduction

In 2004, the parliament of Canada enacted the *Assisted Human Reproduction Act* to provide health and safety oversight of assisted reproduction procedures, which the Act defines as controlled technological activities performed for the purpose of creating a human being, specifically in vitro fertilization (IVF), its related technologies, such as intracytoplasmic sperm injection (ICSI), and activities relating to the handling of gametes and embryos.[1] In the arena of public discourse, issues concerning assisted reproductive technologies (ART) tend to be contextualized in terms of specific clinical outcomes; ethical concerns regarding, among other things, the extension of fertility into old age; and the rapid commercialization of the sector, resulting in evolving relationships between government, commercial medical practices and various public health insurance models. Less discussed, but no less important, are the public health implications of ART.

In Canada, ART remains among the few categories of medicine that exists outside many of the provincial public health insurance systems. Most ART services are provided by commercial clinics that deal directly with patients. This is particularly true for the more advanced ART procedures such as ICSI and embryo cryopreservation. As a result, discussions about the effects and societal role of ART are more commonly replaced by the more politically sanguine topics of business management and the role of health insurance.

ART, and in particular IVF, exists within a delicate sociopolitical context along with eugenic philosophies, gender selection, congenital screening, equity and access. These are issues with a far greater societal reach that transcend the intimate relationship between the ART patient and practitioner, and extend into the mandate of government.

Objectives

The objectives of this study are to explore the population health implications of the growing group of medical interventions that constitute ART. The goal is to enumerate potential and observed beneficial and potentially deleterious public health effects of ART on Canadian society, and to suggest ways of ameliorating the negative effects. The intent is to introduce and explore ART as an area of potential policy interest, rather than conduct an exhaustive systematic review of the evidence surrounding ART and public health.

Methods

Public health issues associated with ART were identified using two methods: (1) a qualitative key informant process involving input from the author and other selected professionals, who were questioned through one-on-one unstructured interviews; and (2) a parallel review of medical literature from the National

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Library of Medicine's PubMed* database, using the following search terms: public health, assisted reproduction, artificial reproduction, in vitro fertilization and its initialism IVF, and intracytoplasmic sperm injection and its initialism ICSI. The author paid special attention to topics deemed most relevant to Canada and only examined studies published in English. Once general themes were identified through this dual process, the author undertook a broader Google and PubMed search to find examples of these themes in practice in both peer-reviewed and lay media.

Results

The research and interviews identified eight general themes of public health issues associated with ART. Four of these themes can be considered outcomes typically expected from ART procedures (general biological outcomes, psychosocial outcomes, multiple pregnancies and births, and premature births), a fifth theme concerns ICSI, and three additional themes are neither ART outcomes nor procedures but concepts of public health concern (gametes as disease vectors, consanguinity and cross-border reproductive care). Lastly, both the key informants and the literature noted that ART may present many positive public health, demographic and economic impacts, besides those deemed deleterious.

Discussion

General biological outcomes

The most obvious impact on public health is the as yet poorly understood long-term outcomes associated with various ART procedures. Some outcomes affect the mother, and others, the child. In a public health context, we must also consider outcomes affecting whole families and their support structures.

IVF, the flagship procedure within the panoply of ART technologies, has been with us for over 30 years; as such, we are now able to assess its long-term effects. Most studies of short-term biological outcomes suggest that congenital malformations and aberrations, childhood cancers, acquired medical conditions, chronic illness, physical growth, and cognitive and socio-emotional development are within the expected range for naturally conceived pregnancies.[2] Comprehensive studies looking at effects beyond early childhood are few, largely due to difficulties with data linkage and long-term longitudinal follow-up. One attempt to perform such a linkage concluded that "long-term morbidity among children conceived by IVF is higher than among naturally conceived infants."[3] In what is a recurring theme in the literature examining morbidities associated with ART, Kallen et al. suggest that the elevated risk of morbidity has much to do with the tendency of ART to produce multiple and preterm births.[3]

Psychosocial outcomes

Some studies suggest that the mothers of ART-conceived children view their offspring as more vulnerable, see themselves as less competent, have higher levels of anxiety about parenting and less satisfaction with family functioning.[4-6] Moreover, the parents of these children may have lower self-esteem and marital satisfaction.[6,7] Several studies have found that ART-conceived children are more temperamental as babies, have more negative behaviours in response to stress, have more behavioural problems and adjust more poorly at school, and are more aggressive, anxious and depressed.[4,7,8,9] A recent cross-sectional evaluation of the first cohort of IVF-conceived young adults in the USA found that psychological health problems were preponderant.[10] Depending upon the extent of these effects, as ART becomes more widely used, these trends will affect a variety of our institutions, particularly public education and public health.

A dimension of psychosocial health associated with ART that is underrepresented in the literature is the negative emotional impact on patients who fail to produce a child, even after lengthy, invasive and expensive ART treatments. Since the IVF failure rate outstrips the success rate,[11] the management of expectations must be a priority. Ironically, it seems that women with high anticipatory anxiety may also have lower pregnancy rates[12] and, not surprisingly, women undergoing IVF show much higher levels of anxiety than do those in the general population.[13] Moreover, at least one study suggests that among women undergoing IVF, it is the experience of receiving a negative pregnancy test that is the greatest predictor of depression.[14]

As our population ages and the demand for ART services increases, the mental health profile of our community will also change. Our public mental health system must be able to respond to this change.

More immediate public health concerns for parents undergoing ART interventions are the adverse effects associated with fertility drugs, including the reported association with an increased risk of breast, uterine and ovarian cancer. Though these associations have not been proven,[15] since older women tend to be the ones seeking ART services, there is some concern that health risks associated with ageing (such as certain cancers) may still be exacerbated by the hormone-altering effects of fertility drugs.[15,16]

Despite the evidence to the contrary described earlier, the overall evidence suggests that ART-conceived children are not psychosocially significantly different from naturally conceived children. It seems that pre-existing "personality factors" that are already present in the family seeking ART are more important predictors of psychosocial issues reflected by an ART-conceived child than are any treatment-related factors.[17]

Multiple pregnancies and multiple births

Perhaps the single most important impact of ART remains the high rate of multiple pregnancy: about a fifth to a third of all ART pregnancies are twins, who outnumber ART triplets and higher order multiples by a factor of between four and ten.[18,19] Multifetal gestations face greater problems than singletons at every stage of pregnancy and labour; each additional fetus leads to curtailment of both fetal growth and the duration of gestation, two of the most

* http://www.ncbi.nlm.nih.gov/pubmed

important predictors of fetal and neonatal health.[20]

Twins are at an increased risk for cerebral palsy, developmental delay, learning disability, sensory impairment, language delay, and attention and behavioural problems.[21] The cerebral palsy rate for triplets is 47 times that of singletons.[22] Overall, 1 in 10 women pregnant with twins and 1 in 5 women pregnant with triplets, regardless of mode of conception, who reach 20 weeks of gestation, will experience at least one of the following: a stillbirth, an infant death or a child with cerebral palsy.[22] A recent review of the literature concluded that there does appear to be an association of ART with a heightened risk of cerebral palsy, owing, it is suggested, to ART's tendency to produce preterm births.[23]

These effects constitute a burden on the public health of a community, both in terms of their direct health costs, and in terms of their effect on the psychosocial and economic well-being of the parents. Indeed, families with children afflicted with cerebral palsy face an increased chance of marital breakdown.[24] The impact on a community, in terms of service demand and overall cost, are difficult to quantify.

However, any association between IVF and cognitive impairment or development issues may be confounded by intervening technologies. For instance, a Danish study of 957 singletons born after frozen embryo implantation found that using frozen embryos resulted in a lesser chance of cerebral palsy than using fresh embryos, but still presented a higher risk than in the non-ART group.[25]

Many patients undergoing ART may see a multiple pregnancy as a positive outcome, as it represents an increased chance of producing a live child. But it also represents an increased chance of producing a multiple birth which, as has been discussed, is susceptible to a host of deleterious consequences. Indeed, in instances of co-twin death in pregnancies of over 20 weeks, there is an eight-fold increase in the risk of cerebral palsy for the surviving twin compared with the risk for twins when both survive.[22] As such, we need a more robust counselling strategy to better manage expectations and offer a more thorough patient education package.[26]

A 2008 review of published evidence surrounding the long-term health of ART-conceived children concluded that "the main risks for the future well-being of ART children remain multiple pregnancies and low birth weight. Evidence regarding the outcome of singletons born at term following ART is generally reassuring."[27]

Premature births

There is strong evidence that IVF is associated with an increased chance of both preterm birth and low birth weight (LBW), often in association with multiple pregnancies and multiple births. In 2003, Tough et al. found that IVF accounted for 17.8% of the rise in LBW and 10.5% of the rise in preterm birth rates in 1994–96 in Alberta.[28] Note that preterm birth has been identified as one of the most important perinatal health problems in industrialized nations,[29] typically accounting for 75% to 85% of all perinatal mortality (stillbirths plus deaths to infants less than 7 days old) in Canada.[30,31] And, as mentioned above, the increased risk of preterm birth may explain the observed increased risk in cerebral palsy.[23]

The extent to which ART contributes to the heightened mortality and morbidity rates among infants and to the economic costs of caring for preterm deliveries needs to be considered when formulating the public health profile of a community. Factors such as an increased demand for neonatal care services, despite a national reduction in birth rate, may be pertinent to policy makers.

Intracytoplasmic sperm injection

ICSI is a procedure that in many ways bypasses natural selection by forcing the union of gametes that are otherwise biologically impeded from fertilizing. In 1995, In't Veld et al. suggested that there may be an increased risk of fetal sex chromosome anomalies following ICSI conception.[32] Seven years later, another study found that, of 1437 ICSI-conceived fetuses, 2.9% had chromosomal anomalies;[33] other studies since have found similar and slightly higher rates, such as a Belgian review of ICSI cycles between 1994 and 2000, which reported a total malformation rate of 6.5%.[34] Kurinczuk argued that ICSI enables the inheritance of y-chromosome linked microdeletions,[26] thus increasing the population prevalence of otherwise rare genetic disorders; however, there is a comparatively low risk of y-linked inheritance of abnormalities. It is possible that the more subtle of these disorders will not emerge until well into adolescence, and are thus presently unnoticeable.

The role of ICSI as a treatment for male-factor infertility, in coordination with IVF, makes it both important and prevalent among ART services. To better gauge its public health implications, longer term longitudinal studies need to be undertaken to identify and quantify putative adverse effects into adolescence and young adulthood.

Gametes as disease vectors

A public health issue that is unlikely to present a crisis, but nonetheless deserves attention, is the risk of infectious disease transmission via donated gametes. Fertility clinics diligently test all reproductive fluids for major infections such as HIV, and disease testing for sperm and other donated tissues in Canada is quite robust. But given that no test is 100% effective, and that a typical testing panel will only cover the most likely infections, it is possible that sperm banks, for instance, could act like disease vectors.

The risk is not restricted to infectious disease: inherited diseases, such as hypertropic cardiomyopathy, can be transmitted through the gamete donation process.[35] In 2007, the Los Angeles Times reported on an American woman who had donated her eggs to at least four infertile couples, only to learn later that she was a carrier of the gene for Tay-Sachs disease. At least one of the offspring generated from her donations has the disease, which is typically fatal.[36] Her case illustrates the potential for gamete donation to blossom into unforeseen public health challenges, and the need for both superior disease screening and donation tracking, through either a donor registry or large-scale surveillance system.

While it is true that natural conception (i.e. unprotected sexual intercourse) presents

risks of disease transmission of greater overall relevance to Canadian public health needs, gamete donation represents a unique disease vector modality that may need to be considered within the scope of public health policy by virtue of its ability to produce clusters of offspring in the scores and potentially hundreds.

Consanguinity

A related risk is the potential for offspring produced from gametes from the same donor, unaware of their genetic bonds, to create a family together. The public health implications are obvious, as offspring of consanguine unions have greater risk for a host of inherited ailments. Given the dearth of sperm donors in Canada, and thus the wide spread of each donor's genetic material, this risk may not be as small as would otherwise be expected. For example, the media reported on one such donor in 2007, a man who may have as many as 50 children in the United States alone.[37]

Possible strategies for mitigating the risk of consanguinity include surveillance of donation clusters, better access by offspring to their status as products of donation, and the conscious limiting of the number of offspring permissible per donor.

Cross-border reproductive care

An emerging issue with respect to ART is the trend of infertile couples to seek services beyond their countries of residence. Couples typically use "cross-border reproductive care" or "reproductive tourism" either to obtain the services they require more cheaply abroad, or because these services are not offered in their home country. A caveat to the latter reason is that often cross-border services are sought to bypass legal restrictions at home, for example, to acquire a paid surrogate mother, to buy sperm from a paid donor or to select the sex of one's child—all illegal in Canada.

The public health implications of seeking cross-border care are manifold, but can be reduced to two requirements: the need to protect such couples from poor quality services abroad, and the need to protect disadvantaged individuals from being exploited for their reproductive tissues or capabilities. An international effort is needed to put in place ethical and health and safety guidelines for the management of cross-border care and the avoidance of undue suffering or exploitation.

While most regard the phenomenon of cross-border reproductive care as involving the movement of people (those seeking care or those providing services, such as surrogate mothers or gamete donors), a separate category involves the movement of reproductive tissues, such as gametes and embryos. The concerns in this case involve the inability to ensure that procedures for the extraction, creation, preservation, transportation and sharing of these tissues meet the standards set within Canadian borders. Efforts to itemize and monitor quality control indicators may help assuage such concerns.

Positive public health impacts

ART presents us with several positive societal outcomes: first and foremost, of course, is the potential to treat the chronic disease of infertility, and hence benefit from the positive psychosocial effects of successful treatment.

Additionally, in some circles the West's declining birth rate is considered a demographic crisis, threatening to reduce our tax base and cultural longevity; ART represents an avenue to quell that trend. Older individuals' ability to conceive has also effectively lengthened the available time for education, self-exploration and unfettered economic activity, arguably resulting in improved and more productive human capital. Older, childless couples also typically enjoy higher standards of living, and are thus better able to afford the resources for caring for a child that they produce through ART.

Of possibly significant demographic relevance is the Rand Corporation finding that "an IVF-conceived child, average in every respect (for example, future earnings, healthcare consumption, and life expectancy), represents a net positive [financial] return to the government."[38] In other words, the application of ART may ultimately result in economic advantages to certain societies, barring any deleterious health characteristics of ART-produced individuals who may represent exceptional costs to the health care system.

Recommendations

Policy concerning the impacts of ART must be informed by reliable data. Research in this field has been predominantly in the scientific arena, focusing on maximizing the probability of pregnancies and live births and on minimizing invasiveness and cost. Non-clinical research has explored the economic dimensions of IVF and related procedures, well known as costly endeavours that must co-exist with traditional medical care within a socialized medical system. Less common are population health studies exploring the extent of demand of fertility services, and the long-term health consequences of ART interventions for both mother and child.

Clearly, surveillance is the ideal instrument for monitoring a variety of important factors associated with ART-related public health, including donated gametes as disease vectors, potential consanguinity, deleterious short-term health consequences for women undergoing ART procedures, deleterious long-term impacts on both mothers and offspring, and longitudinal factors related to infertility, such as whether infertility can (ironically) be passed on from parent to child. Surveillance would also provide data important for long-term social planning, as it provides a basis for estimating demographic change resulting from ART-generated modifications to population birth rates and health service demands.

Additional policy directions may include limiting the number of offspring that can be produced from a single gamete donor, thus controlling for the risk of inadvertent consanguine couplings and, again, better surveillance of gamete usage and the risk factors of donors. For the improved safety and quality control of cross-border reproductive care, international cooperation is required to both determine the true extent of the phenomenon and to establish universally acceptable standards of care, both clinically and socially. This, too, would be helped by improved surveillance of the use of ART.

The pursuit of an ART surveillance strategy in any nation is a large undertaking. In Canada, it is complicated by federal-provincial jurisdictional issues, data compatibility issues, anonymity/confidentiality concerns, migratory forces and the specific nature of ART as a privately funded endeavour within a publicly funded socialized medicine milieu. But progress down this path begins with an appreciation of the importance—from the societal and public health standpoint—of ART, beyond the personal and intimate relationship between patient and doctor.

Conclusion

As the populations of Canada and similar Western nations age, and the trend of deferring reproduction into the later stages of life continues, the demand for ART services will increase. Short-term biological outcomes of IVF, ICSI and other reproductive technologies have been studied to some extent, but the opportunities for examining long-term outcomes are only now arising. Such outcomes need to be considered, not just as clinical issues, but in terms of public health impacts.

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Autism spectrum disorders, maternal characteristics and obstetric complications among singletons born in Alberta, Canada

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Abstract

Objective: To determine whether certain maternal characteristics and obstetric complications are associated with increased risk of autism spectrum disorders (ASD) in children.

Methods: Provincial delivery records identified the cohort of 218 890 singleton live births in Alberta, Canada, between January 1, 1998, and December 31, 2004. These were followed-up for ASD via ICD-9 diagnostic codes assigned by physician billing until March 31, 2008. Maternal and obstetric risk factors were also extracted from PDR.

Results: Prevalence and incidence of ASD in Alberta are in line with those reported elsewhere and suggest recent increases in rate of diagnosis and/or incidence. Boys have 5-fold higher prevalence than girls. The peak age of diagnosis occurs at age 3 years. Relative risk modelling indicates that the risk of ASD is elevated among children of older mothers and those who experience specific pregnancy and birth complications.

Conclusion: Certain maternal characteristics and obstetric complications are associated with ASD in children. We identified lower rates of ASD and later age at diagnosis among children of Aboriginal mothers that requires further research.

Keywords: *autism spectrum disorders, epidemiology, cohort studies, Alberta*

Introduction

The autism spectrum disorders (ASD) are a group of neurodevelopmental conditions that typically manifest before 3 years of age and are associated with impaired verbal and non-verbal communication and social interaction, and restricted and repetitive patterns of behaviour.[1] ASD reduces quality of life in affected children and their parents, and leads to extraordinary economic costs for society.[2] There have been relatively few population-based studies of ASD prevalence in Canada. A 2006 Montreal-based study of 27 749 children born between 1987 and 1998 suggests an ASD prevalence of 6.5 per 1000,[3] consistent with the prevalence estimates from the US and UK over the past several years;[4-7] estimates from service-based agencies in Manitoba and Prince Edward Island in 2002 put the prevalence among 5- to 9-year-olds at 3.8 to 4.1 per 1000;[8] and an educational database in British Columbia identifies the prevalence of ASD among 9-year-olds as 4.3 per 1000 in 2004.[9] (However, service-based databases are vulnerable to bias from diagnostic substitution.[9,10]) In general, there is a tendency for the prevalence of ASD to increase in more recent birth cohorts[7] and for diagnoses to be made at earlier ages. However, recent estimates from the US Centers of Disease Control and Prevention based on population-based data from 14 states place the median age of diagnosis at 4 to 5 years.[11]

The etiology of ASD is poorly understood, but genetic and environmental factors are believed to contribute. While some genetic risk factors are clearly established,[12] determining the contribution of the environment remains elusive. A recent review limited to only seven epidemiological studies suggests that advanced parental age, fetal growth restriction, and fetal or newborn hypoxia are associated with increased risk of developing ASD.[13] Based on the meta-analysis of 40 relevant studies, others concluded that, while it is premature to implicate specific pregnancy complications in the etiology of ASD, there is an excess of prenatal complications among children with ASD.[14]

Given the paucity of Canadian data on the epidemiology of ASD and the importance of replicating findings on maternal and obstetrics risk factors in large, representative and diverse populations,[13] our goals are (1) to estimate incidence and prevalence of ASD in a population-based birth cohort of residents in Alberta, Canada, and (2) to assess whether maternal characteristics and obstetric complications are associated with ASD in this population.

Methods

Record linkage

Delivery records held by the Alberta Perinatal Health Program (APHP) identified the

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cohort of singleton live births in the province of Alberta, Canada, between January 1, 1998, and December 31, 2004. The APHP provided information regarding relevant ante- and perinatal risk factors. Information on the risk factors was collected on admission to hospital for delivery, as part of routine clinical care. These are considered to be accurate and any internal inconsistency in the records is scrutinized by APHP; if an apparent error in the delivery records cannot be resolved, APHP records a missing value for a given variable. Maternal weight and height cut-offs were imposed by the data captured in the delivery records: actual values were not available to us.

The unique Personal Health Number of mother and child along with each child's gender and date of birth as recorded in each APHP file were used to follow-up the cohort through the records held by Alberta Health and Wellness (AHW). In the universal health care insurance system of Alberta, all residents are served by physicians and hospitals that bill the government for their services, with the fee linked to specific diagnostic codes from the *International Statistical Classification of Diseases and Related Health Problems, 9th revision* (ICD-9). Only children who were unambiguously matched in the APHP files to AHW records were followed-up by AHW until March 31, 2008, for (1) any of the two diagnostic codes listed with the physician billing record indicating ASD: ICD-9 codes 299.0, 299.8; (2) date of each ASD "service"; (3) specialty of the physician; (4) child's residency and mortality (in a given fiscal year ending on March 31) and (5) mothers' socioeconomic (SES) or Aboriginal status (available data did not allow us to distinguish Aboriginal mother from different economic statuses).

Study protocol was approved by the University of Alberta Health Ethics Research Board and the participating data custodians. Personal identifying data were not released to the investigators.

Statistical analyses

Four different case definitions were used in estimating the prevalence of ASD, which varied in stringency from "any claim by one physician" to "at least 2 ASD-linked billings from a pediatrician or psychiatrist." Incident cases of ASD were identified as the first physician service associated with an ASD diagnostic code (that is, the date of first filing was used as a proxy for age at diagnosis). Annual incidence was estimated separately for each sub-cohort defined by year of birth and gender. We recognize that this definition of incidence does not capture the true timing of the onset of ASD and hence, strictly speaking, our measure of incident case is rather akin to "recognized or diagnosed" case. Therefore, the notion of incidence (nearly impossible to estimate for psychiatric/chronic conditions from administrative data) is used in this paper with the above caveat in mind, accepting that it merely approximates true (un-measurable) incidence. After calculating crude ASD prevalence rate for strata of each risk factor, the relative risks (RR) and associated 95% confidence intervals (CI) were obtained in log-binomial regression that considered all covariates simultaneously. To reflect potential clustering of risk among children born to the same mother, we introduced random "mother effect" via generalized estimating equations assuming a compound symmetry covariance structure. We conducted a number of sensitivity analyses to explore the possible biases from outcome misclassification, uncontrolled confounding by parity, short follow-up for births after 2002, causal pathway from 1 to 5 minute Apgar scores, and uncertainty about causal pathway associated with cigarette smoking. All analyses were undertaken in SAS version 9.1 (SAS Institute, Cary, NC).

Results

There were 273 343 singleton live births in Alberta between 1998 and 2004. Of these, 25 970 children could not be unambiguously identified by AHW and 28 421 either died or lost residence during follow-up; a further 62 had missing gender, leaving 218 890 children for analysis of prevalence and incidence. The 28 421 children excluded from the study because of incomplete follow-up had similar distribution of all studied risk factors to those retained (details not shown).

The impact of varying case definitions on estimates of prevalence of ASD is illustrated in Table 1. The prevalence for both genders combined varied by a factor of 1.7, from 3 per 1000 (two services by any combination of psychiatrist or pediatrician) to 5.2 per 1000 (one claim by any physician). Regardless of the case definition, boys had approximately 5-fold higher prevalence than girls. Subsequent analyses first defined ASD based on "one claim by any physician," and were then repeated using the most stringent case definition. Estimate of prevalence were precise with standard errors in the order of 0.1 to 0.3 per 1000.

Time and gender trends in annual incidence show that peak age of diagnosis is between ages of 3 and 4 for both genders (Table 2). There was a 4- to 5-fold increase in annual incidence in more recent birth cohorts among 3-year-olds (0.52 per 1000 in 1998 to 2.32 per 1000 in 2004 for both genders). The patterns of results seen in Table 2 are also shown in Figure 1 for boys and Figure 2 for girls. There was an overall tendency for higher annual incidence among more recent birth cohorts across all age groups. Because the estimates of annual birth-cohort incidence were based on small numbers, each estimate was imprecise, with standard error of the rate as high as 70% to 100% of the rate estimate for younger ages (< 2 years) and females, decreasing to 10% to 20% for older age groups and more recent birth cohorts. All the numbers required to perform these calculations are presented in Table 2. Imprecision of these estimates precluded their further modelling, except that the effects of gender and birth cohort were examined in more detail below, after controlling for prenatal and perinatal factors (Table 4).

We examined trends by age of diagnosis, focusing on 1998 to 2002 birth cohorts (with at least 5 years of follow-up). Consistent with results shown in Table 2, both boys and girls were diagnosed at an earlier age, with median age of diagnosis 2 years earlier for boys and almost 3 years earlier for girls in 2002 compared to 1998 birth cohorts. Boys born in 1998 were diagnosed at a median (m) age of 69 months (inter-quartile range [IQR] 48-90), but girls

born in the same birth year were diagnosed at an older age (m = 74 months, IQR 40-104). In the 2002 birth cohort, on the other hand, both genders were diagnosed much younger (boys: m = 45, IQR 35-54; girls: m = 40, IQR 32-51). There was no indication of gender-by-birth-cohort interaction (details not shown).

Children who had missing information on maternal/obstetric covariates (n = 3673) were excluded from analyses of these risk factors. Excluded children were evenly distributed among birth years and had ASD rates similar to the rest of the cohort (16 cases, 4.4 per 1000). The maternal characteristics that were statistically associated with increased risk of ASD in a child included advanced maternal age (> 35 years versus ≤ 25 years: RR = 1.57, 95% CI = 1.25-1.97) with the bulk of excess risk in the women older than 25 (note: all groups with age greater than the reference category appeared to be at an increased risk); low maternal pre-pregnancy weight (RR = 2.15, 95% CI = 1.20-3.85); pre-pregnancy (not gestational) diabetes (RR = 1.65, 95% CI = 1.01-2.71); bleeding at less than 20 weeks of gestation (RR = 1.34, 95% CI = 1.08-1.67) and being nulliparous (Table 3).

Notably, children born to an Aboriginal mother appeared to have *reduced* rates of ASD (RR = 0.58, 95% CI = 0.40-0.84) and the median age at diagnosis was almost 2 years later than the rest of the cohort (m = 59.5 months, IQR 38-74 versus m = 36 months, IQR 47-65). Boys born to Aboriginal mothers (n = 26, m = 64.5 months, IQR 40-77) were diagnosed at much older age than girls (n = 8, m = 40 months, IQR 38-58). These numbers stand in stark contrast to ages of diagnoses of children born to mothers without any indications of SES disadvantage of marginalization ("Other" in Table 3): there is a much smaller overall differential in age of diagnosis among boys (n = 767, m = 47 months, IQR 37-66) and girls (n = 132, m = 44 months, IQR 32-62). Further, boys born to Aboriginal mothers appear to have been diagnosed on average 17 months later, while there does not appear to be a difference in age of diagnosis for Aboriginal and "other" girls.

TABLE 1
Prevalence of autism spectrum disorders[a] among Alberta singletons born 1998–2004

Case definition	Both genders N = 218 890		Male N = 111 960		Female N = 106 930	
	Count	Rate per 1000 (SE)[b]	Count	Rate per 1000 (SE)[b]	Count	Rate per 1000 (SE)[b]
One claim						
By any physician	1 138	5.2 (0.2)	952	8.5 (0.3)	186	1.7 (0.1)
By pediatrician or psychiatrist	1 016	4.6 (0.2)	849	7.6 (0.3)	167	1.6 (0.1)
Two claims						
By any physician	743	3.4 (0.1)	638	5.7 (0.2)	105	1.0 (0.1)
By psychiatrist or pediatrician	663	3.0 (0.1)	566	5.1 (0.2)	97	0.9 (0.1)

Abbreviations: N, overall sample size; SE, standard error.

[a] Relevant ICD-9 codes in any of the 3 diagnostic fields associated with physician billing, follow-up till March 31, 2008.

[b] Standard error of the rate calculated as $1000 \times (\text{rate}/1000)(1-\text{rate}/1000)/N)^{0.5}$.

Obstetric complications that significantly correlated with risk of ASD were pre-eclampsia (RR = 1.49, 95% CI = 1.00-2.23); breech or shoulder presentation in labour (RR = 1.31, 95% CI = 1.02-1.69); planned Caesarian section (RR = 1.23, 95% CI = 1.01-1.49); birth weight less than 2.5 kg (RR = 1.33, 95% CI = 1.01-1.75) and 1-minute Apgar of less than 7 (RR = 1.34, 95% CI = 1.15-1.55) (Table 4).

We conducted a number of sensitivity analyses. Using the most stringent ASD case definition and restricting the sample to nulliparous women (to correct for women altering their likelihood of having more children as a result of their firstborn being affected) and to 1998–2002 birth cohorts (ensuring longer follow-up) did not alter the pattern of results in Tables 3 and 4. Next, because Apgar score at 1 and 5 minutes post-partum are expected to be causally related, we examined the risk associated with trends in Apgar scores from 1 to 5 minutes. The excess risk was associated with low Apgar score at 1 minute, regardless of whether the score improved; the other risk estimates in Tables 3 and 4 did not change. Finally, smoking during pregnancy is an established risk factor for many of the covariates included in the multivariable regression model along with maternal smoking (e.g. low birth weight, prematurity, pre-eclampsia). Therefore, we restricted the analysis to children born to self-reported never-smokers (931 ASD cases, 169 372 births). The results are not materially different from those presented in Tables 3 and 4, except that among non-smokers there is a statistically significant excess of risk among larger women, that is, those with pre-pregnancy weight exceeded 91 kg (adjusted RR = 1.26, 95% CI = 1.01-1.57) and height equal to or over 152 cm (adjusted RR = 1.82, 95% CI = 1.02-3.23). There were too few observed ASD cases (191) to repeat the analysis only among children born to smokers. When risk factors that can be intermediate between smoking and ASD risk (low birth weight, prematurity, pre-eclampsia) were removed from the analyses, the estimated effect of smoking was unchanged.

Discussion

The prevalence and incidence of ASD in the birth cohort of children born in Alberta in 1998–2004 is in line with that observed in other jurisdictions. Not surprisingly, absolute rates of ASD vary by criteria used for case identification. However, time trends and associations with obstetric risk factors were robust to the ASD case definition. Our results also confirm that the risk of ASD is elevated among children of older mothers and those who experience complicated pregnancy and birth. Importantly, we identified lower rates of ASD and diagnosis

TABLE 2

Number of autism spectrum disorder cases[a] and incidence rate[b] by year of birth, age of diagnosis and gender among singletons born in Alberta, 1998–2004, followed up till March 31, 2008

Age (years)[c]		1		2		3		4		5		6		7		8		9	
Year of birth	Cohort size	n	Rate per 1000	n	Rate per 1000	n	Rate per 1000	n	Rate per 1000	n	Rate per 1000	n	Rate per 1000	n	Rate per 1000	n	Rate per 1000	n	Rate per 1000
Both genders																			
1998	28 953	3	0.10	4	0.14	15	0.52	37	1.28	21	0.73	22	0.76	24	0.83	21	0.73	27	0.94
1999	29 466	4	0.14	9	0.31	29	0.98	34	1.16	29	0.99	33	1.12	21	0.72	36	1.23		
2000	29 222	1	0.03	22	0.75	28	0.96	40	1.37	32	1.10	22	0.76	29	1.00				
2001	30 127	2	0.07	11	0.37	46	1.53	40	1.33	29	0.97	35	1.17						
2002	31 775	1	0.03	21	0.66	52	1.64	48	1.51	51	1.61								
2003	33 917	2	0.06	31	0.91	54	1.59	59	1.74										
2004	35 430	3	0.08	28	0.79	82	2.32												
TOTAL	218 890	16	0.07	126	0.58	306	1.40	258	1.18	162	0.74	112	0.51	74	0.34	57	0.26	27	0.12
Males																			
1998	14 874	1	0.07	2	0.13	14	0.94	34	2.29	21	1.42	19	1.28	23	1.56	18	1.22	21	1.42
1999	15 059	3	0.20	8	0.53	25	1.66	27	1.80	26	1.73	23	1.54	20	1.34	31	2.08		
2000	14 858	1	0.07	17	1.14	25	1.68	36	2.43	29	1.96	20	1.36	24	1.63				
2001	15 489	2	0.13	10	0.65	36	2.33	37	2.40	22	1.43	32	2.08						
2002	16 224	0	0.00	15	0.92	39	2.41	38	2.35	41	2.54								
2003	17 325	1	0.06	22	1.27	47	2.72	52	3.01										
2004	18 131	3	0.17	17	0.94	70	3.87												
TOTAL	111 960	11	0.10	91	0.81	256	2.29	224	2.01	139	1.25	94	0.85	67	0.60	49	0.44	21	0.19
Females																			
1998	14 079	2	0.14	2	0.14	1	0.07	3	0.21	7	0.50	3	0.21	1	0.07	3	0.21	6	0.43
1999	14 407	1	0.07	1	0.07	4	0.28	3	0.21	3	0.21	10	0.69	1	0.07	5	0.35		
2000	14 364	0	0.00	5	0.35	1	0.07	4	0.28	3	0.21	2	0.14	5	0.35				
2001	14 638	0	0.00	0	0.00	10	0.68	3	0.21	7	0.48	5	0.34						
2002	15 551	1	0.06	6	0.39	13	0.84	10	0.64	9	0.58								
2003	16 592	1	0.06	9	0.54	7	0.42	8	0.48										
2004	17 299	0	0.00	11	0.64	10	0.58												
TOTAL	106 930	5	0.05	34	0.32	46	0.43	31	0.29	29	0.27	20	0.19	7	0.07	8	0.07	6	0.06

Abbreviations: n, number.

[a] Number of autism spectrum disorder cases, using one physician claim rule.

[b] Per 1000 members of the birth cohort (prevalent cases excluded from denominator).

[c] Approximated by year of diagnosis since birth.

FIGURE 1
Rate of autism spectrum disorders per 1000 in males by birth cohorts (1998–2004) in Alberta

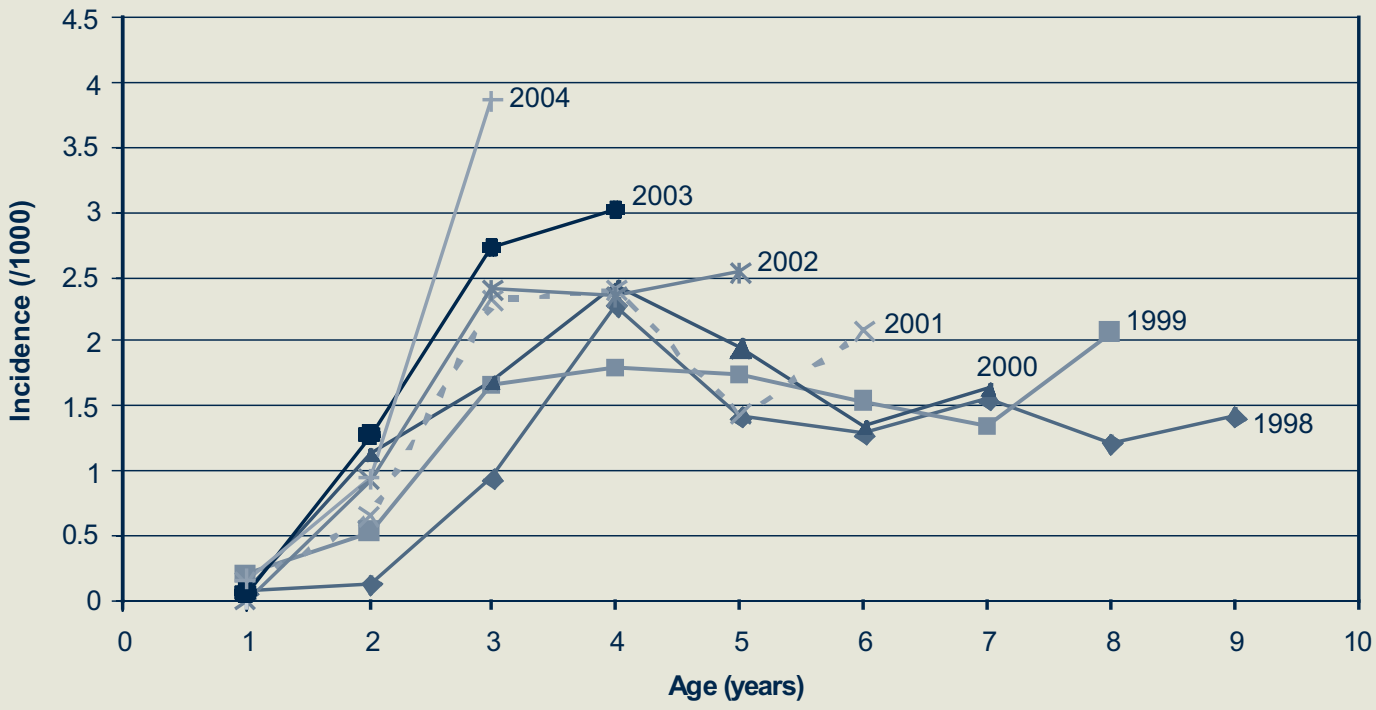

FIGURE 2
Rate of autism spectrum disorders per 1000 in females by birth cohorts (1998–2004) in Alberta

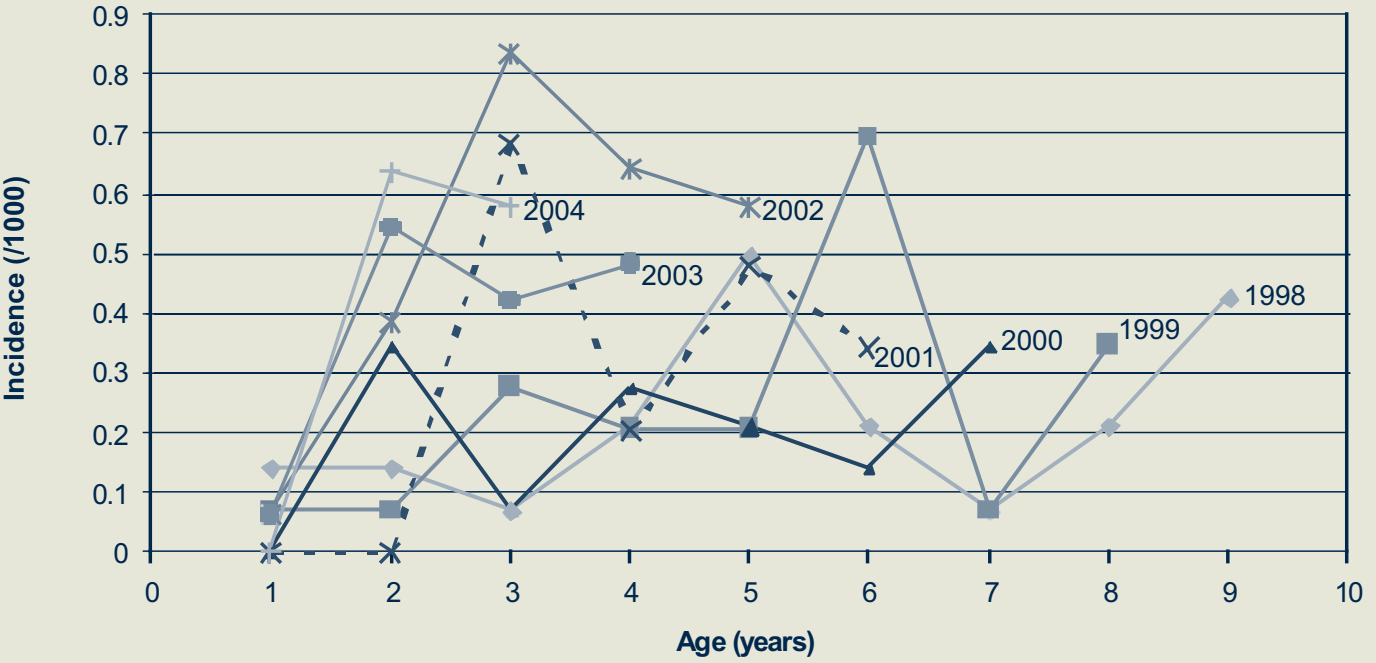

TABLE 3

Autism spectrum disorders and ante- or perinatal risk factors among singleton live births in Alberta, 1998–2004 (relative risk model spans Tables 3 and 4)

Risk factor		Number of ASD cases	Number of singleton live births	Crude rate (per 1000)[a]	RR[b]	95% CI
Maternal age (years)	≤ 25	276	66 736	4.1	1.00	—
	25 ≤ 30	372	70 256	5.3	1.31	1.11 - 1.56
	30 ≤ 35	339	56 369	6.0	1.51	1.26 - 1.80
	> 35	149	24 573	6.1	1.57	1.25 - 1.97
	Unknown	2	956	2.1	0.56	0.14 - 2.27
Maternal weight > 91 kg	Yes	109	17 417	6.3	1.18	0.96 - 1.44
	No	1013	197 800	5.1	1.00	—
	Unknown	16	3673	4.4	[c]	
Maternal weight < 45 kg	Yes	11	1097	10.0	2.15	1.20 - 3.85
	No	1111	214 120	5.2	1.00	—
	Unknown	16	3673	4.4	[c]	
Maternal height < 152 cm	Yes	16	3941	4.1	0.64	0.39 - 1.05
	No	1106	211 279	5.2	1.0	—
	Unknown	16	3670	4.4	[c]	
Pre-pregnancy diabetes	Yes	16	1645	9.7	1.65	1.01 - 2.71
	No	1106	213 575	5.2	1.00	—
	Unknown	16	3670	4.4	[c]	
Gestational diabetes	Yes	54	7453	7.2	1.24	0.94 - 1.65
	No	1068	207 767	5.1	1.00	—
	Unknown	16	3670	4.4	[c]	
Bleeding < 20 weeks	Yes	90	12 323	7.3	1.34	1.08 - 1.67
	No	1032	202 897	5.1	1.00	—
	Unknown	16	3670	4.4	[c]	
Bleeding ≥ 20 weeks	Yes	45	7046	6.4	1.05	0.78 - 1.43
	No	1077	208 174	5.2	1.00	—
	Unknown	16	3670	4.4	[c]	
Cigarette smoking (any)	Yes	191	45 846	4.2	0.86	0.72 - 1.02
	No	931	169 374	5.5	1.00	—
	Unknown	16	3670	4.4	[c]	
Poor weight gain (26-36 weeks < 0.5 kg/week)	Yes	15	3095	4.8	0.95	0.57 - 1.59
	No	1107	212 125	5.2	1.00	—
	Unknown	16	3670	4.4	[c]	
Parity	0	535	90 431	5.9	1.00	—
	1	416	75 519	5.5	0.91	0.79 - 1.04
	2	119	31 962	3.7	0.61	0.49 - 0.76
	3	39	11 493	3.4	0.54	0.38 - 0.75
	≥ 4	24	8174	2.9	0.50	0.32 - 0.76
	Unknown	5	1311	3.8	0.79	0.33 - 1.92
Socio-economic status of mother	Aboriginal group[d]	34	14 486	2.3	0.58	0.40 - 0.84
	Low income[e]	149	28 605	5.2	1.12	0.93 - 1.34
	Welfare	41	7601	5.4	1.26	0.91 - 1.75
	Other	899	164 940	5.5	1.00	—
	Unknown	15	3258	4.6	0.88	0.80 - 0.97

Abbreviations: CI, confidence interval; N, overall sample size; n, subsample size; RR, relative risk.

[a] N = 218 890.

[b] n = 215 217; adjuster relative risks (RR) for factors in Tables 3 and 4 and 95% confidence intervals (CI), corrected for clustering of births with mother.

[c] 3673 subjects excluded from the RR model because of missing covariates (see text for details).

[d] Treaty Aboriginal status, qualifying for subsidies from the federal government regardless of family income.

[e] Completely or partially subsidized health insurance premiums.

TABLE 4

Autism spectrum disorders and at-birth or delivery risk factors, child's gender and birth year among singleton live births in Alberta, 1998–2004 (relative risk model spans Tables 3 and 4)

Risk factor		Number of ASD cases	Number of singleton live births	Crude rate (per 1000)[a]	RR[b]	95% CI
Pre-eclampsia	Yes	27	2747	9.8	1.49	1.00 - 2.23
	No	1095	212 473	5.2	1.00	—
	Unknown	16	3670	4.4		
Presentation	Cephalic	1049	206 590	5.1	1.00	—
	Breech/Shoulder	79	10 557	7.5	1.31	1.02 - 1.69
	Unknown/Other	10	1743	5.7	1.22	0.63 - 2.35
Type of labour	Spontaneous	597	123 434	4.8	1.00	
	Induced	337	60 930	5.5	1.07	0.93 - 1.23
	No labour[3,c]	149	22 185	6.7	1.23	1.01 - 1.49
	Unknown	55	12 341	4.5	0.79	0.57 - 1.08
Delivery by Caesarian section	Yes	304	49 152	6.2	1.04	0.88 - 1.22
	No	834	169 738	4.9	1.00	—
Gestational age	< 37 weeks	125	17 889	7.0	0.97	0.75 - 1.25
	≥ 37 weeks	1011	200 557	5.0	1.00	—
	Unknown	2	444	4.5	0.94	0.24 - 3.72
Birth weight (kg)	< 2.5	100	13 130	7.6	1.33	1.01 - 1.75
	2.5-4.5	1012	201 598	5.0	1.00	—
	> 4.5	26	4125	6.3	1.00	0.67 - 1.49
	Unknown	0	37	0.0		
Apgar at 1 min	< 7	248	34 275	7.2	1.34	1.15 - 1.55
	7-10	888	184 301	4.8	1.00	—
	Unknown	2	314	6.4	2.08	0.53 - 8.26
Apgar at 5 min	< 7	34	4094	8.3	1.03	0.71 - 1.49
	7-10	1107	214 795	5.2	1.00	—
Female child		186	106 930	1.7	0.20	0.17 - 0.24
Birth year	1998	174	28 953	6.0	1.95	1.53 - 2.47
	1999	195	29 466	6.6	2.09	1.65 - 2.63
	2000	173	29 222	5.9	1.89	1.49 - 2.39
	2001	164	30 127	5.4	1.69	1.33 - 2.15
	2002	172	31 775	5.4	1.69	1.33 - 2.14
	2003	146	33 917	4.3	1.32	1.04 - 1.69
	2004	114	35 430	3.2	1.00	—

Abbreviations: CI, confidence interval; N, overall sample size; n, subsample size; RR, relative risk.

[a] N = 218 890.

[b] n = 215 217; adjuster relative risks (RR) for factors in Tables 3 and 4 and 95% confidence intervals corrected for clustering of births with mother.

[c] Caesarian-section delivery without labour (likely planned Caesarian section; other Caesarian section deliveries may have been preceded by spontaneous or induced labour).

at later age among children of Aboriginal mothers, which, to our knowledge, has not previously been reported. It should be noted that our results were obtained in the context of the health care system that exists in the Canadian province of Alberta and our findings may reflect peculiarities to this context (especially trends in time period and age at diagnosis, as well as the SES gradients).

Our study is one of the few epidemiological studies of pre- and perinatal risk factors for ASD that meet the stringent quality criteria of Kolevzon et al.,[13] namely, a large and well-defined population-based sample with prospective standardized risk factors and outcome assessments. Among studies addressing association of ASD with pre- and perinatal factors, ours is the second largest study in terms of number of ASD cases, after Croen et al.,[15] and is among the first Canadian reports.[16] Consistent with previous literature, we observed that risk of ASD was related to increased maternal age and obstetric complications. We observed that low birth weight, but not preterm birth (gestational age < 37 weeks), was associated with risk of ASD. Other studies, which have used non-standard definitions of prematurity (ranging from less than 28 to 35 weeks of gestation), have reported varying evidence of association with ASD.[17-19] Preliminary analysis suggests that the relationship between gestational age and risk of ASD is not straightforward in the Alberta birth cohort, with some evidence that more severely premature births are associated with higher risk of ASD. We will examine the relationship between gestational age and birth weight (across the continuum) and risk of ASD in a future study. We replicated the well-known gender difference in ASD risk.[20] Our study did not confirm association of ASD with maternal smoking, although the association was reported with daily, not ever-smokers in pregnancy.[21] Our work adds evidence in support of association of ASD with breech presentation,[17] pre-pregnancy diabetes[21,22] and pre-eclampsia.[17] However, it should be noted that Gardener et al.[14] observed that the effect of pre-eclampsia on risk of ASD meta-analysis was heterogeneous among studies, concluding that it is unlikely that it is associated with risk of ASD.

A novel finding, which should be treated with caution, is elevated risk among children of mothers with lower pre-pregnancy weight. In this regard, it is noteworthy that Wentz et al.[23] reported excess of ASD among patients with severe eating disorders. If it were true that such conditions have a genetic component, then low pre-pregnancy weight of the ASD case's mother may simply be a marker for a genetic risk factor common to both eating disorders and ASD. The observation that among non-smoking mothers the risk of ASD in children was confined to those with greater weight and height is new but congruent with a previous report.[16] It must be noted that these associations with crude anthropometric measures can be the result of confounding by racial differences (and the underlying genetics) or differences in nutritional habits/acculturation.

The most significant and unexpected association is that of reduced rates and later diagnosis of ASD among children, especially boys, of Aboriginal mothers. It may point to poor access to diagnostic and treatment facilities in remote areas (note that children of mothers who were on welfare—perhaps similarly economically disadvantaged, but more likely to reside in urban areas—were not at increased risk), but a difference in genetic vulnerability cannot be ruled out. A two-fold increase in ASD risk was previously associated with urbanization (regarding place of birth) in Denmark;[24] therefore, if it were true that rural/reserve lifestyle is protective for ASD, then our observation of protective effect of having an Aboriginal mother may also reflect the associated level of "urbanization." Shattuck et al.[25] observed that the nature or trajectory of ASD can affect age of diagnosis, which suggests that our observation of later diagnosis among boys born to Aboriginal mothers may be attributed to variation in the course of the disease in this sub-population compared to the rest of the population. Close scrutiny of ASD trajectory (the nature and age of onset of specific symptoms), not feasible within the context of this study, is needed to address this possibility. It would also be important to determine whether children born to Aboriginal mothers are also diagnosed with other psychiatric disorders at a later age to check whether our findings are specific to ASD. Our findings are generally in agreement with those of Leonard et al.[22] who reported decreased risk of autism with mental retardation among Australian Aboriginal children relative to Caucasians, pointing out to apparent differences in risk of ASD among Aboriginal people living in industrialized countries compared to the rest of the population.

There is no uniform ASD case ascertainment methodology in the health care system of Alberta. Because of universal health care in Canada, most children and families have a community physician who provides primary health care. In Alberta, there is no systematic screening for ASD, although a universal community health centre visit for vaccination at age 18 months and 4 to 5 years includes developmental surveillance. In general, ASD diagnosis is provided by a specialized multi-disciplinary team at a small number of regional developmental assessment centers. However, for some children, a community pediatrician may be the first to diagnose ASD and record this in the billing records. A detailed analysis of access to specialized assessment services is beyond the scope of this paper, but is certainly of interest, particularly given that our results suggest that it may be different for different SES or ethnic groups (e.g. Aboriginal families).

According to Shattuck et al., boys tend to be diagnosed with ASD at a younger age than girls,[25] which is supported by our data in the older (e.g. 1998) but not the younger (e.g. 2002) birth cohorts. The more recent birth cohorts showed either no difference in age of diagnosis by gender or a slightly younger age of diagnosis among girls. This difference in patterns of diagnosis can be attributed either to real changes in diagnostic practices over time and between US and Alberta, or differences in information on ASD diagnosis between our studies. Shattuck et al.[25] used both health (broadly defined) and educational records, while we were limited to diagnoses made by physicians. Therefore, Shattuck et al.[25] were likely to miss fewer cases and perhaps had their sample enriched by cases with less severe or pronounced disease trajectory, which would also account for later

expected age of diagnosis—5 years versus 3 to 4 years in our cohorts. Differences in our studies can also be attributed to more complete case ascertainment by Shattuck et al.[25] as witnessed by the high prevalence observed in their work.

The most obvious shortcoming of our work is lack of independent verification of ASD diagnosis by direct clinical assessment using gold standard measures, which would certainly affect estimates of incidence and prevalence. However, it appears that risk factor profiles are independent of variation in the case definitions considered here, thus our main conclusions appear to be robust to diagnostic misclassification. The case ascertainment method most comparable to our methodology (one physician claim) had reasonable sensitivity (59.7%) and specificity (85.2%) in another Canadian province and was not materially inferior to the diagnostic rule that also considered outpatient databases and/or multiple physician claims; both measures were independent of risk factors (e.g. gender).[26] Data from the Alberta delivery records on risk factors may have contained errors, but these would be independent of outcome definition, resulting in attenuation of risk estimates.[27] The available data did not allow us to consider either presence of birth defects or fathers' age (an established risk factor[13]). It should be noted that maternal and paternal age both appear to contribute to risk of ASD independently.[28,29] We were not able to explicitly control for genetic risk factors[12] beyond modelling correlation in risk of ASD due to clustering of children within their mother.

In conclusion, we confirmed in a large population-based study that maternal characteristics and obstetric complications are associated with the risk of ASD in the Canadian province of Alberta. We obtained the first estimates of prevalence and incidence of ASD in Alberta that are in line with those reported in other jurisdictions and suggest recent increases in the rate of diagnosis and/or incidence. The *apparently* reduced risk of ASD in Aboriginal populations requires further research. Although our epidemiological ASD definition appears to be useful, it has to be validated to provide more precise picture of burden of ASD, not just to detect trends. Population-level surveillance to monitor trends in ASD with adjustment for diagnostic biases and with special focus on socio-economically marginalized and rural populations remains a priority for public health research. Accurate estimates of ASD rates are essential to health service planning for the many individuals and families affected by ASD, and understanding its antecedents at a population-level may provide important new insights into the etiology of ASD.

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An investigation of cancer incidence in a First Nations community in Alberta, Canada, 1995–2006

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Abstract

Objective: To determine colorectal and overall cancer incidence as part of a three-pronged investigation in response to the concerns of a First Nations community in Alberta, Canada, located close to sulfur-rich natural gas installations, and to determine whether the incidence of cancers observed in this reserve was higher than expected.

Methods: A population dataset with information identifying First Nations status and band affiliation was linked to the Alberta Cancer Registry to determine cancer incidence cases between 1995 and 2006 for on- and off-reserve study populations. Using indirect standardized incidence ratios, observed cancer incidence cases for the study populations were compared with cases expected based on three separate reference populations.

Results: Observed colorectal and overall cancer incidence cases within the First Nations community were not higher than expected. Cervical cancer incidence cases, however, were higher than expected for on- and off-reserve populations; public health measures designed to address this risk have been implemented and on-going surveillance of cancer incidence in the community will be maintained.

Keywords: *neoplasms; Alberta; Indians, North American; epidemiological methods; First Nations*

Introduction

Hydrogen sulfide (H_2S) is a colourless gas with a distinctive rotten egg smell. It occurs naturally in geothermal environments such as volcanoes and hot springs, and is emitted by pulp and paper installations, sewage treatment plants, and natural gas and petroleum operations.[1] Oil and gas fields in Alberta contain a high concentration of sulfur-rich natural gas, known as sour gas.[1,2]

While low-level frequent or persistent exposures to H_2S have been shown to cause headache, sleep disturbance or nausea,[3,4] no long-term adverse health effects, including increased risk of cancer, have been documented.[2,3,5-7] In addition, H_2S has not been identified as a carcinogen by any internationally recognized cancer, environmental or occupational health agency; the carcinogenicity of H_2S has not been reviewed by the International Agency of Research on Cancer;[8,9] and H_2S has not been assigned a carcinogenicity designation by the American Conference of Governmental Industrial Hygienists.[9] Further, in response to southern Alberta residents' concerns about chronic exposure to sour gas emissions, Spitzer et al.[10] evaluated multiple health measures such as mortality rate, reproductive problems, respiratory function and incidence of cancer; the study found that the residents did not experience significantly more adverse health outcomes compared to an unexposed population.[10] A simultaneous cohort study of these residents examining the rates of all cancer and specific cancer sites found no statistically significant differences compared to the reference populations.[11]

The band leadership and administration of a First Nations community in Alberta, Canada, reported concerns about the health effects of sulfur-rich natural gas installations located near their reserve. One of the concerns was a perceived increase in cancer incidence within the community; specifically, it was reported that six of seven children within one family (all under 30 years of age) had been diagnosed with colorectal cancer. As a result, First Nations and Inuit Health (FNIH), Health Canada, Alberta Region launched a three-pronged field investigation that focused on the potential familial colorectal cancer cluster—defined as a greater than expected number of cancer cases in a group of people, geographic area and time.[12] This included a familial cancer cluster investigation by a Field Epidemiologist from the Public Health Agency of Canada, an environmental risk assessment by Environmental Health Officers with Health Canada and a cancer incidence investigation by the Surveillance Department of the Alberta Cancer Board.

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The objectives of this study are to contribute to the three-pronged colorectal cancer cluster investigation by identifying the number of colorectal cancer cases (colon, rectum and rectosigmoid) diagnosed within this particular First Nations on-reserve community located close to sulfur-rich natural gas installations, and to address community concerns about overall cancer incidence in the area by determining whether the incidence of cancers observed in this First Nations reserve was higher than expected.

Methods

To maintain anonymity, as part of a publication agreement, the First Nations community involved in this study is referred to as "X" and the Regional Health Authority (RHA) within which the X First Nations reserve is located is referred to as "Y." Further measures have been taken throughout this report to prevent the identification of both the First Nations community and individuals.

Data sources and population

An Alberta Cancer Board representative accompanied a Field Epidemiologist (from the Public Health Agency of Canada) and Environmental Health Officers (from Health Canada) to the X First Nations community as part of the three-pronged approach to the investigation. The X First Nations leadership and administration were consulted about the selection of the study population and analysis plan; in support of the analytic process, a letter was sent to Alberta Health and Wellness (AHW) by an X First Nations band council member permitting the release of information identifying First Nations individuals to the Alberta Cancer Board. This Alberta Health Care Insurance Plan (AHCIP) administrative data contained First Nations status indicators and population estimates for all study and reference groups up until 2007; the dataset did not contain easily decipherable X First Nations band membership identifiers prior to 1995, limiting the timeframe that X First Nations individuals could be identified to 1995 to 2007.

Two study populations and three reference populations were used; the first study population included all X First Nations band members living in the province of Alberta, and the second restricted the X First Nations band member population to those living on-reserve. The reference populations included all First Nations in Alberta, the residents of the Regional Health Authority in which the X First Nations reserve is located (RHA Y) and the overall Alberta population. All persons living in the province of Alberta, including all First Nations individuals, were identified by age, sex, year and residential postal code information from Alberta Health and Wellness data. The associated Regional Health Authority was defined by the RHA designation within the population dataset. All First Nations individuals were identified by First Nations status; band affiliation was established through X First Nations band number designation within the population dataset. Those X First Nations individuals living on-reserve were identified by X First Nations band number and one of two residence postal codes covering an area around the reserve.

For each study and reference population (all X First Nations, on-reserve X First Nations, all First Nations in Alberta, Regional Health Authority Y and all of Alberta), yearly estimates were averaged over a 12-year period between 1995 and 2006. Population averages within each group were used to calculate indirect standardized incidence ratios (ISIR). In addition, we calculated the proportion of the averaged study and reference populations within three age groups (0-19, 20-54 and 55 + years) and by sex, and determined the proportion of the total population distributed across three age groups (0-19, 20-54 and 55 + years) for each year between 1995 and 2006 for the overall X First Nations population in Alberta, as well as the population of X First Nations individuals living on-reserve.

Cancer case counts

Population estimates from the AHCIP dataset and cancer incidence data from the Alberta Cancer Registry (ACR) were used to identify the number and type of cancer cases diagnosed in X First Nations band members. At the time of the study, 2006 was the last complete year for data entry of cancer cases housed within the ACR and therefore marked the most recent boundary for the study period. The healthcare numbers (obtained from the AHCIP dataset) of all individuals identified as X First Nations at any point between 1995 and 2007 were linked with the ACR. On- or off-reserve designation for cancer cases was based on postal code within the ACR at the time of diagnosis. Cases diagnosed in individuals living in RHA Y were identified in the ACR by RHA designation at the time of diagnosis.

To identify the number of colorectal cancer cases accounted for in the familial cancer cluster investigation, we extracted colorectal cancer cases (ICD-O-3* topography codes C18, colon; C19, rectosigmoid; and C20, rectum) diagnosed in identified X First Nations individuals during any year in the ACR (not restricted to the study period) and all other invasive cancer incident cases, excluding non-melanoma skin cancer, diagnosed between 1995 and 2006 in identified X First Nations individuals from the ACR.

Indirect standardized incidence ratios

To determine whether or not cancer incidence was higher than expected in the X First Nations reserve, the number of observed cancer cases in this population was compared to the expected number of cancer cases for all cancer cases combined and for specific cancer types observed over the study time period (1995 to 2006). The number of cancer cases observed between 1995 and 2006 in all X First Nations band members in Alberta and X First Nations band members living on-reserve were compared with an expected number of cases that were adjusted by age (by five-year age group), sex and year using incidence data from two different reference populations for all X First Nations (all First Nations in Alberta and the general Alberta population) and from three different reference populations for on-reserve X First Nations

* *International Classification of Diseases for Oncology, 3rd Edition*

(all First Nations in Alberta, RHA Y and the general Alberta population). The X First Nations study population was excluded in all calculations of the expected number of cases based on any reference population. In order to determine whether the results were statistically significant, we calculated a 95% confidence interval (CI) for each ISIR using methods described by Liddell.[13]

Results

Population

The average population distribution between 1995 and 2006 for all X First Nations band members in Alberta, on-reserve X First Nations band members, all First Nations in Alberta and the general Alberta population is shown in Table 1. To protect confidentiality, only inexact population numbers for all and on-reserve X First Nations are shown and the population of Regional Health Authority (RHA) Y was omitted. For each population group, the sex distribution was approximately 1:1. The percentage of the total population aged 55 years and over was 20.1% and 18.6% for RHA Y and Alberta general populations, respectively. First Nations populations had a lower proportion of those over the age of 55: 4.8%, 6.0% and 6.5% for all X First Nations band members, on-reserve X First Nations band members and all First Nations in Alberta, respectively.

Further analysis of the population distribution between 1995 and 2006 in on-reserve and all X First Nations revealed that the proportion of people within the youngest age group, 0 to 19 years, decreased over the study period while the proportion between 20 and 54 years old increased (not shown). For on-reserve X First Nations, the proportion of the population over 55 years of age increased from 4.5% in 1995 to 7.1% in 2006; a similar increase was noted in the percent of X First Nations people in this age group across the province, rising from 3.6% to 6.0% over the same time period.

Cancer case counts

The extraction of all colorectal cancer cases from the Alberta Cancer Registry (ACR) for individuals identified as X First Nations in the AHCIP administrative dataset at any point between 1995 and 2007 revealed fewer than five colorectal cancer cases, all diagnosed in individuals over the age of 25 years; only one of the observed colorectal cancer cases corresponded to the original six cases reported. All six incident cases, however, were followed-up as part of the familial cancer cluster investigation and will be reported on separately.

The total number of X First Nations cancer cases diagnosed between 1995 and 2006 was 25: 14 on-reserve and 11 off-reserve. There were 11 cases of cervical cancer diagnosed in X First Nations women between 1995 and 2006; for all other cancer types, there were fewer than five cases diagnosed over the study period. A list of cancer sites observed in the study population between 1995 and 2006 is shown in Table 2.

TABLE 1
Population distribution by age group and sex for various populations, Alberta, 1995–2006

Population category	Average population[a]	Age group (%)			Sex (%)	
		0-19 years	20-54 years	55+ years	F	M
X First Nations all Alberta	< 2 000	52.5	42.7	4.8	49.9	50.1
X First Nations on reserve[b]	< 1 000	53.4	40.6	6.0	49.8	50.2
All First Nations Alberta	138 079	43.9	49.6	6.5	49.9	50.1
Regional Health Authority Y	—	30.4	49.5	20.1	50.1	49.9
Alberta general population	2 993 731	28.5	52.9	18.6	50.1	49.9

Abbreviations: F, female; M, male.

[a] Average population over the 12-year study period is based on administrative data provided by Alberta Health and Wellness. To protect confidentiality, inexact population numbers for all X First Nation and on-reserve X First Nation individuals are provided, and the population of Regional Health Authority Y was omitted.

[b] On-reserve is based on postal codes that cover a larger area than the reserve and, therefore, might include individuals living in the postal code area but not on-reserve.

Indirect standardized incidence ratios

All X First Nations in Alberta. The observed number of colorectal cancer cases for both men and women in all X First Nations in Alberta were slightly lower than the number expected based on all First Nations in Alberta (ISIR = 0.77, 95% CI: 0.02-4.31) and the general Alberta reference populations (ISIR = 0.72, 95% CI: 0.02-4.01), though neither observation was statistically significant (Table 2). However, a significantly higher number of cervical cancer cases was observed in X First Nations women compared to all First Nations women in Alberta (ISIR = 11.43, 95% CI: 5.71-20.45) and the general female population of Alberta (ISIR = 20.03, 95% CI: 10.00-35.85).

A higher number of retroperitoneal and peritoneal cancers was also noted for men and women of X First Nations (ISIR = 24.44, 95% CI: 2.96-88.28 compared with all First Nations; ISIR = 20.42, 95% CI: 2.47-73.75 compared with the general population of Alberta). Upon review, the cancer cases observed within this category included cases of cyst adenocarcinoma (cancer of the glandular tissue) and of sarcoma (cancer of the soft/connective tissue), and varied by location of residence; they were diagnosed in individuals living on-reserve and off-reserve.

A higher number of overall cancer cases was observed in all X First Nations men and women in Alberta compared to the number of cases expected based on all First Nations in the province (ISIR = 1.36, 95% CI: 0.88-2.01) and the general population of Alberta (ISIR = 1.06, 95% CI: 0.69-1.57); however, these results were not statistically significant.

On-Reserve X First Nations. The number of colorectal cancer cases observed between 1995 and 2006 for on-reserve X First Nations men and women was slightly higher than expected based on all First Nations (ISIR = 1.08, 95% CI: 0.03-6.01), but slightly lower than expected based on RHA Y (ISIR = 0.94; 95% CI: 0.02-5.25) and all of Alberta (ISIR = 0.98, 95% CI: 0.02-5.45); none were statistically significant (Table 3).

There was a statistically significant higher number of observed cervical cancer cases

TABLE 2

Indirect standardized incidence ratio[a] (ISIR) for all X First Nation band members using all First Nations in Alberta and the general Alberta population as reference populations, Alberta, 1995–2006

	All First Nations in Alberta		General Alberta population	
Cancer site	ISIR	95% CI	ISIR	95% CI
Mouth, other and unspecified	23.01	0.58 - 128.21	28.46	0.72 - 158.55
Colorectal	0.77	0.02 - 4.31	0.72	0.02 - 4.01
Biliary tract, other and unspecified	7.68	0.19 - 42.77	14.39	0.36 - 80.18
Bronchus/lung	0.86	0.10 - 3.09	0.86	0.10 - 3.10
Retroperitoneum & peritoneum	24.44	2.96 - 88.28	20.42	2.47 - 73.75
Cervix uteri	11.43	5.71 - 20.45	20.03	10.00 - 35.85
Ovary	2.92	0.07 - 16.29	2.33	0.06 - 13.00
Prostate gland	1.13	0.14 - 4.08	0.72	0.09 - 2.60
Meninges & CNS	5.17	0.63 - 18.67	2.69	0.33 - 9.73
Leukemia	1.20	0.03 - 6.71	0.93	0.02 - 5.16
Multiple myeloma & plasmacytoma	4.48	0.11 - 24.95	4.87	0.12 - 27.12
All cancer excluding NMSC	1.36	0.88 - 2.01	1.06	0.69 - 1.57

Abbreviations: CI, confidence interval; CNS, central nervous system; ISIR, indirect standardized incidence ratio; NMSC, non-melanoma skin cancer.

[a] Adjusted by age, sex and year. Excludes non-melanoma skin cancer (NMSC). The number of observed and expected cases has been removed to maintain confidentiality; there were a total of 25 cases combined, 11 cases of cervical cancer, and fewer than 5 cases of every other cancer type over the study period.

TABLE 3

Indirect standardized incidence ratio[a] (ISIR) for on-reserve X First Nation band members[b] using all First Nations in Alberta, Regional Health Authority Y and the general Alberta population as reference populations, Alberta, 1995–2006

	All First Nations in Alberta		Regional Health Authority Y		General Alberta population	
Cancer site	ISIR	95% CI	ISIR	95% CI	ISIR	95% CI
Mouth, other and unspecified	0.00	-	0.00	-	0.00	-
Colorectal	1.08	0.03 - 6.01	0.94	0.02 - 5.25	0.98	0.02 - 5.45
Biliary tract, other and unspecified	10.89	0.28 - 60.69	24.07	0.61 - 134.13	19.79	0.50 - 110.26
Bronchus/lung	1.14	0.14 - 4.12	1.18	0.14 - 4.24	1.16	0.14 - 4.18
Retroperitoneum & peritoneum	17.79	0.45 - 99.10	11.92	0.30 - 66.41	14.70	0.37 - 81.89
Cervix uteri	6.68	1.82 - 17.11	9.90	2.70 - 25.35	12.17	3.32 - 31.16
Ovary	4.20	0.11 - 23.39	3.14	0.08 - 17.50	3.46	0.09 - 19.25
Prostate gland	1.61	0.19 - 5.80	1.07	0.13 - 3.85	0.99	0.12 - 3.58
Meninges & CNS	4.40	0.11 - 24.54	1.93	0.05 - 10.77	2.10	0.05 - 11.70
Leukemia	0.00	—	0.00	—	0.00	—
Multiple myeloma & plasmacytoma	6.00	0.15 - 33.43	8.24	0.21 - 45.89	6.55	0.17 - 36.48
All cancer excluding NMSC	1.09	0.60 - 1.83	0.85	0.47 - 1.43	0.86	0.47 - 1.44

Abbreviations: CI, confidence interval; CNS, central nervous system; ISIR, indirect standardized incidence ratio; NMSC, non-melanoma skin cancer.

[a] Adjusted by age, sex and year. Excludes non-melanoma skin cancer (NMSC). The number of observed and expected cases has been removed to maintain confidentiality; for the on-reserve population there were a total of 14 cases combined, and fewer than 5 cases of every cancer type over the study period.

[b] On-reserve is based on postal codes that cover a larger area than the reserve and, therefore, might include individuals living in the postal code area, but not on-reserve.

diagnosed in X First Nations women living on-reserve compared to the expected number of cases calculated using all reference populations: all First Nations in Alberta (ISIR = 6.68, 95% CI: 1.82-17.11), RHA Y (ISIR = 9.90, 95% CI: 2.70-25.35) and the general Alberta population (ISIR = 12.17, 95% CI: 3.32-31.16). A statistically significant increase in cancers classified as "biliary tract, other and unspecified" in women (not shown) was also noted when all three reference populations were used: all First Nations (ISIR = 40.58, 95% CI: 1.03-226.10), RHA Y (ISIR = 61.82, 95% CI: 1.57-344.43) and the general Alberta population (ISIR = 44.73, 95% CI: 1.13-249.22).

Using all First Nations in Alberta as the reference population, the number of observed cancer cases between 1995 and 2006 for X First Nations men and women identified as living on-reserve were slightly higher than expected; however, this elevation was not statistically significant (ISIR = 1.09, 95% CI: 0.60-1.83). Comparisons between the overall observed number of cancer cases and the expected number of cases that were calculated based on the remaining two reference populations, RHA Y (ISIR = 0.85, 95% CI: 0.47-1.43) and all Alberta (ISIR = 0.86, 95% CI: 0.47-1.44), revealed that the observed overall cancer case numbers were lower than expected, though not statistically significant.

The magnitude of the ISIR results differ between the cancer site-specific values and the overall ISIRs calculated. Major cancer sites such as "lung" and "prostate" have relatively small ISIRs compared to less common cancer sites such as "biliary tract, other and unspecified." Additionally, the ISIRs for each cancer site observed were based on a comparison of the numbers of cancer site-specific cases observed in the study populations versus the number of site-specific cases expected based on the reference populations. For all cancers combined, however, this comparison was between all cancers observed in the study populations (comprising 11 different cancer sites) and the number of overall cancers expected based on the reference populations; the overall cancer sites expected

would be based on more than the 11 cancer sites observed in the study populations.

Discussion

In response to concerns expressed by the X First Nations band leadership and administration, a three-pronged investigation was launched by FNIH, Health Canada, Alberta Region. This included a follow-up of the six incident cases through a familial cancer cluster investigation by the Public Health Agency of Canada and an environmental risk assessment by Health Canada; the results of these two investigations will be reported separately (Tustin J et al., Drobina MW et al.; submitted manuscripts). The objectives of the third investigation, a cancer incidence investigation, were to support the three-pronged investigation through the identification of the number of colorectal cancer cases diagnosed within the on- and off-reserve X First Nations and to address general community concerns through the evaluation of cancer incidence in the X First Nations population.

A search of the entire Alberta Cancer Registry revealed fewer than five cases of colorectal cancer cases diagnosed in identified X First Nations individuals; only one observed colorectal cancer case matched the original six cases reported. We also compared the number of observed cancer cases diagnosed in X First Nations individuals between 1995 and 2006 and the number of cases that would be expected in this period derived from calculations using all First Nations in Alberta, Regional Health Authority Y and the Alberta general population as reference populations. There were no statistically significant differences between the number of colorectal or overall cancer cases observed in either all X First Nations people across Alberta or the on-reserve population compared to the number of colorectal or overall cancer cases expected. Postal codes included in the X First Nations population cover a larger area than the reserve and would be expected to overestimate the detection of the cluster. The results of this investigation, therefore, did not support a colorectal cancer cluster in the X First Nations population.

Because Canadian cancer registries do not collect information on ethnicity, it is difficult to identify First Nations study populations to investigate cancer incidence in these groups. In this study, administrative data containing registered First Nations individual identifiers was linked with the Alberta Cancer Registry. The administrative dataset containing First Nations identifiers does not distinguish between registration through heredity or marriage. In addition, First Nations populations tend to be relatively small, leading to considerable random variation and calculations that yield low statistical power. This was apparent in the current study through seemingly statistically significant elevations in specific cancer sites that were based on fewer than five cases. The uncertainty in interpreting statistical findings based on small numbers is one of the reasons why, despite many requests for cancer cluster investigations throughout North America, few lead to further study.[14,15]

Although there was no evidence of a higher than expected number of colorectal cancer cases in the X First Nations population, the 11 cervical cancer cases observed in all X First Nations women in Alberta was 11 times higher than the number expected based on other First Nations women in the province and 20 times higher than expected based on the general population of Alberta, a statistically significant elevation. As a result of this investigation, this important public health issue is being addressed by the FNIH Medical Officer of Health and Nursing Unit in collaboration with public health officials within RHA Y. Preventative interventions include the introduction of the Human Papilloma Virus (HPV) vaccination program to school-aged girls and increasing access to Pap smear screening services for women in the X First Nations community.

This study also revealed that the proportion of all and on-reserve X First Nations people within the 20 to 54 years and the 55 years and over age groups increased between 1995 and 2006, while the proportion within the youngest age group (0-19 years) decreased. The risk of an individual developing cancer increases with age; consequently, increases in cancer diagnoses can be expected. It has also been noted that First Nations peoples throughout North America are experiencing an epidemiologic transition where the rates of chronic disease are increasing as infectious disease occurrence is decreasing.[16-18] A recent study in First Nations men and women in Ontario, Canada, found that although current incidence rates of all cancers combined and for colorectal cancer were significantly lower than the general population, First Nations groups experienced different distribution of cancer types and faster increases in cancer incidence rates for all cancers combined and for colorectal cancers and lung cancer compared to the general population, possibly as a result of lifestyle risk factors such as high obesity rates and changes in diet and physical activity levels, as well as sociocultural or genetic factors.[19] Differences between the cancer rates in First Nations and non-First Nations in Alberta have also been observed. An investigation into cancer incidence in Fort Chipewyan, Alberta, noted that although the rates of lung and colon cancer were not different, Alberta First Nations had a significantly lower rate for all cancers combined, breast cancer and leukemia and a higher rate of cholangiocarcinoma compared to non-First Nations peoples across the province.[20] Our study attempted to adjust for potential differences in cancer risk in First Nations peoples by comparing cancer cases observed in X First Nations individuals to those expected based on other First Nations in the province.

The results, conclusions and recommendations from each of the three prongs of the investigation were presented in-person to the X First Nations band leadership and administration and followed by a question and discussion period. As part of the collaborative process, the Surveillance Department of the Alberta Cancer Board (recently renamed Cancer Surveillance, Surveillance and Health Status Assessment, Population and Public Health – Alberta Health Services) arranged for follow-up with community leadership and administration in one year's time. On-going examination of cancer incidence within the X

First Nations population will ensure that potential increases in rates are monitored, evaluated and managed.

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Myocardial infarction and the validation of physician billing and hospitalization data using electronic medical records

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Abstract

Objective: Population-based identification of patients with a myocardial infarction is limited to patients presenting to hospital with an acute event. We set out to determine if adding physician billing data to hospital discharge data would result in an accurate capture of patients who have had a myocardial infarction.

Methods: We performed a retrospective chart abstraction of 969 randomly selected adult patients using data abstracted from primary care physicians on an electronic medical record in Ontario, Canada, as the reference standard.

Results: An algorithm of 3 physician billings in a one-year period with at least one being by a specialist or within a hospital or emergency room plus one hospital discharge abstract performed with a sensitivity of 80.4% (95% CI: 69.5-91.3), specificity of 98.0% (95% CI: 97.1-98.9), positive predictive value of 69.5% (95% CI: 57.7-81.2), negative predictive value of 98.9% (95% CI: 98.2% to 99.6%) and kappa statistic of 0.73 (95% CI: 0.63-0.83).

Conclusion: Using a combination of hospital discharge abstracts and physician billing data may be the best way of assessing trends of MI occurrence over time since it increases the capture of MI beyond those patients who have been hospitalized.

Keywords: *myocardial infarction, medical care costs, electronic health records, patient discharge, validation studies, Ontario*

Introduction

The validity of using hospital claims data to identify myocardial infarction (MI) patients compared to hospital records varies depending on where the validation took place, what hospital code was assessed and how the patient population was selected.[1-5] Similarly, the validity of hospital claims data compared to registry data varies widely.[6-11] Regardless, estimates indicate that at least a quarter of all MIs are silent or unrecognized.[12-15] Some patients have MIs out of country or province that, as a result, are not captured in a provincial hospital discharge abstract database. Since the prognosis of silent or unrecognized MIs is worse than that of recognized MIs of similar severity, this has very important clinical implications.[14,16,17] Previous administrative data validation studies have neither looked at using outpatient clinic data in a primary care or family practice setting nor assessed the use of outpatient physician billing claims data to identify patients with MIs. As a result, when we report on the occurrence of MIs within a province or across the country, we are restricted to methods for reporting acute MIs that present to hospital or that are in mortality records.

All provinces in Canada keep a record of both hospitalization data and physician billing data. However, physician billing data only require recording of one diagnostic code with each patient visit despite that patients often present with multiple reasons for a visit and often have multiple medical conditions. Validated algorithms using both physician billing data and hospital discharge abstracts have been successfully used to identify patients with chronic disease conditions who do not necessarily require hospitalization, such as hypertension[18] and diabetes.[19]

Using data from primary care physician electronic medical records (EMRs) as a reference standard, we set out to determine if the addition of physician billing data to hospital discharge abstracts could accurately identify patients who have had an MI, which could then be applied to determine the occurrence of MI at a population level.

Methods

We collected data from 17 physicians who had been using Practice Solutions® EMR for at least 2 years; this ensured that their EMRs were populated with a full practice of patients. Data from the EMR were extracted from June to December of 2007, de-identified, encrypted and then transferred electronically to the Institute for Clinical Evaluative Sciences (ICES) in a secure fashion. ICES is a prescribed entity under the *Personal Health Information Protection Act,*[20] and the data were handled

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as per ICES's standard operating procedures to preserve patient privacy and confidentiality.[21]

Our convenience sample of 17 physicians was 29.4% female, 41.7% in rural practice, and all but one in a group practice. The average number of years in practice was 20.5 years (standard deviation [SD] = 10.2) and the average length of time using the EMR was 7.4 years (SD = 7.3). The average age of our patient cohort was 49.0 years (SD = 17.2) and 53.7% were female.

We took a 5% random sample of the EMR patients aged 20 years and over as of Dec 31, 2006, with valid health card numbers and with at least two progress note entries in the three years prior to the date the data were downloaded. Three trained chart abstractors reviewed all of the 969 patient records in this random sample up to March 31, 2007, and each entry was scored to indicate a definite MI, a possible MI, a family history of MI, or not an MI. A definite MI was defined as having an MI recorded in the cumulative patient profile, in a progress note, on an electrocardiogram (ECG), in a diagnostic test or procedure, or in a hospital discharge summary, emergency record, consultation letter or operative note. The resulting abstraction classification for each patient was tabulated; patients were classified as having had an MI if there were one or more entries denoting definite MI and as a possible MI if there were only entries scored as possible MI and no entries scored as definite MI. Intra-observer reliability testing resulted in kappa statistic values exceeding 0.80, indicating very good agreement; inter-observer reliability testing resulted in kappa statistic values exceeding 0.85 for all comparisons between the three abstractors, also indicating very good agreement.

Next, all the MIs that were classified as definite or possible were reviewed by a physician expert on the research team and classified according to the level of evidence for MI: 1) solid MI evidence—a hospital discharge summary, or a consultation letter describing an MI or listing an MI in the past medical history, or a catheterization report describing complete occlusion of a coronary artery; 2) MIs that were only recorded in the cumulative patient profile entered in the family physician office; 3) weaker MI evidence—MIs that were described in a diagnostic test such as an echocardiogram ("wall motion abnormality in keeping with infarct") or a sestamibi cardiac scan, but not interpreted as depicting an MI as reported in a consultation letter; and 4) ECG evidence of an MI with no other supporting documentation. The aim of this classification was to assess the quality of MI evidence in the EMR; sensitivity analysis was performed using differing levels of evidence for MI as the reference standard.

Patient health card numbers were replaced with a unique identification number and anonymously linked to the Ontario administrative data holdings housed at ICES. The data holdings include the Canadian Institute for Health Information hospital discharge abstract database (CIHI DAD) that records the diagnosis most responsible for a hospital admission and up to 15 comorbid conditions using the *International Classification of Diseases and Related Health Problems, 9th* and *10th Revisions* (ICD-9 codes 410 and 412 prior to fiscal year 2002 and ICD-10 codes I21, I22, I25.2 after fiscal year 2002). We used the most responsible diagnostic codes or any of the secondary diagnostic codes to indicate that a patient had had an MI, and CIHI data from 1988 until fiscal 2006.

The random sample of 969 patients became the reference standard against which we compared various case definitions using combinations of data from CIHI, the Ontario Health Insurance Plan (OHIP), the National Ambulatory Care Reporting System (NACRS) and the Same Day Surgery (SDS) databases. OHIP physician billing claims data records over 95% of the out-patient visits for the residents of Ontario,[22] as well as the type of physician billing a claim (e.g. type 00 = general practitioner or family physician) and the location of the encounter (i.e. hospital, emergency room, out-patient clinic, nursing home); OHIP data are available from mid-1991 until the most recent quarter. NACRS is a data collection tool that is used to capture information on patient visits to hospital and community-based ambulatory care, out-patient clinics and emergency departments from July 2000 to March 2007. NACRS also includes same day surgery procedures as of April 2003; prior to this the SDS database captured this information.

We also assessed whether restricting the physician billing claim to only those billed by a specialist or by a general practitioner/family physician in a hospital or emergency room affected the results.

We calculated the sensitivity of the administrative data as the proportion of MI patients identified according to the reference standard of manual EMR abstraction compared to those identified by the administrative algorithm. Specificity was calculated in the same manner except that it was based on individuals without an MI. Positive predictive value (PPV) was defined as the proportion of MI patients identified by the administrative algorithm that was confirmed by the reference standard, and negative predictive value (NPV) was defined similarly for patients who did *not* have an MI according to the manual EMR abstraction. Since both data sources have limitations, we calculated kappa between the EMR data and the administrative data. All proportions were calculated with 95% confidence intervals (CI) using the binomial approximation method in SAS version 9.1.* All analyses were conducted using SAS version 9.1.

This study received ethics approval from the Sunnybrook Health Sciences Centre Research Ethics Board.

Results

Of the 969 patients included in our study, 51 had solid evidence of an MI documented in the EMR and 918 did not. On examining the strength of the evidence for MI, excluding patients with only ECG evidence or weaker evidence resulted in the highest sensitivity (60.8%, 95% CI: 47.4-74.2) with the least sacrifice of PPV (88.6%, 95% CI: 78.0-99.1) (see Table 1). Accordingly,

* http://www.sas.com/

we adopted this level of EMR evidence to identify patients who have had an MI to compare with the accuracy of other administrative data sources to identify such patients (see Table 2). Generally, we found that using hospital discharge abstracts alone to identify patients who have had an MI was not sensitive enough and likely underestimates the true population occurrence of MIs. For instance, only 31 of the 51 patients in our reference group who had an MI had a discharge abstract that mentioned the MI.

The results of accuracy tests using secondary administrative data sources plus hospital discharge data are presented in Table 3. The small gain in sensitivity with the addition of NACRS or SDS (62.7%, 95% CI: 49.5-76.0) was reflected in a similar drop in PPV (84.2%, 95% CI: 72.6-95.8), indicating that using these administrative databases did not contribute to the accuracy of the calculations.

Adding a single physician billing claim to the hospital discharge abstract substantially increased the sensitivity (86.3%, 95% CI: 76.8-95.7) but decreased the PPV to an unacceptably low rate (41.5%, 95% CI: 32.1-50.9). Requiring two physician billing claims for MI increased the sensitivity by 20 percentile points (82.4%, 95% CI: 71.9-92.8) but dropped the PPV by more than 25 percentile points (60.9%, 95% CI: 49.4-72.4) compared to using the hospital discharge abstract alone. Adding an additional year for the second MI physician billing claim to meet the case definition did not improve sensitivity (82.4%, 95% CI: 71.9-92.8) and slightly decreased PPV (59.2%, 95% CI: 47.7-70.6) compared to using 2 physician billing claims within one year. Requiring a third physician billing claim dropped the sensitivity by 2 percentile points (80.4%, 95% CI: 69.5-91.3) but increased the PPV by 6 percentile points (66.1%; 95% CI: 54.3-77.9) compared to using only 2 physician billing claims in a one-year period or a hospital discharge abstract (see Table 4).

Requiring the physician billing claims to be from a specialist or a general practitioner/family physician with an encounter in a hospital or an emergency room slightly dropped the sensitivity (84.3%, 95% CI: 74.3-94.3) but increased the PPV slightly more (48.9%, 95% CI: 38.4-59.3) compared to using physician billing claims without regard to location of encounter or type of physician. Only requiring one of the physician billing claims to meet this criteria increased the PPV slightly more (65.6%, 95% CI: 54.0-77.3) with less of a sacrifice of sensitivity (82.4%, 95% CI: 71.9-92.8). Three physician billing claims in one year with at least one of the claims from an encounter in a hospital or an emergency room or by a specialist resulted in the largest increase in sensitivity (80.4%, 95% CI: 69.5-91.3) combined with the least sacrifice of specificity (98.0%, 95% CI: 97.1-98.9) and PPV (69.5%, 95% CI: 57.7-81.2) compared to using a hospital discharge abstract alone to identify patients who have had an MI (see Table 4).

Discussion

Similar to other chronic disease conditions such as diabetes[19] and hypertension,[18] this validation study shows that physician billing data help identify patients who have

TABLE 1
Tests of various levels of EMR evidence of MI for use as a reference standard for hospital discharge abstract data

Levels of EMR evidence	Number	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)
Patients with any evidence of an MI	58	53.4 (40.6 - 66.3)	99.6 (99.1 - 100.0)	88.6 (78.0 - 99.1)	97.1 (96.0 - 98.2)
Patients with an MI excluding people with only ECG evidence	56	55.4 (42.3 - 68.4)	99.6 (99.1 - 100.0)	88.6 (78.0 - 99.1)	97.3 (96.3 - 98.4)
Patients with an MI excluding people with only ECG evidence or weaker evidence	51	60.8 (47.4 - 74.2)	99.6 (99.1 - 100.0)	88.6 (78.0 - 99.1)	97.9 (96.9 - 98.8)
Patients with an MI excluding people with only ECG evidence, weaker evidence, or MI only recorded in the cumulative patient profile	45	62.2 (48.1 - 76.4)	99.2 (98.7 - 99.8)	80.0 (66.7 - 93.3)	98.2 (97.3 - 99.0)

Abbreviations: CI, confidence interval; ECG, electrocardiogram; EMR, electronic medical record; MI, myocardial infarction; N, sample size; NPV, negative predictive value; PPV, positive predictive value.

Note: N = 969 (reference sample).

TABLE 2
Patients with an MI excluding people with only ECG evidence or weaker evidence versus patients identified by one hospital discharge abstract for MI.

		Patients with an MI according to EMR chart abstraction excluding people with only ECG evidence or weaker evidence		
		Positive	Negative	
Patients with an MI identified by a hospital discharge abstract	Positive	31	4	88.6% PPV
	Negative	20	914	97.9% NPV
		60.8% Sensitivity	99.6% Specificity	

Abbreviations: ECG, electrocardiogram; EMR, electronic medical record; MI, myocardial infarction; N, sample size; NPV, negative predictive value; PPV, positive predictive value.

Note: N = 969 (reference sample).

TABLE 3
Tests of accuracy adding a claim from NACRS or SDS to a hospital discharge abstract[a]

Administrative data algorithm	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Kappa statistic (95% CI)
Hospital discharge abstract or NACRS	62.7 (49.5 - 76.0)	99.3 (98.8 - 99.9)	84.2 (72.6 - 95.8)	98.0 (97.1 - 98.9)	0.71 (0.60 - 0.82)
Hospital discharge abstract or SDS	60.8 (47.4 - 74.2)	99.6 (99.1 - 100.0)	88.6 (78.0 - 99.1)	97.9 (96.9 - 98.8)	0.71 (0.60 - 0.82)
Hospital discharge abstract or NACRS or SDS	62.7 (49.5 - 76.0)	99.3 (98.8 - 99.9)	84.2 (72.6 - 95.8)	98.0 (97.1 - 98.9)	0.71 (0.60 - 0.82)

Abbreviations: CI, confidence interval; MI, myocardial infarction; NACRS, National Ambulatory Care Reporting System; NPV, negative predictive value; SDS, Same Day Surgery; PPV, positive predictive value.

[a] Evidence for MI as documented in a cardiac specialist note or hospital discharge summary, or recorded in the cumulative patient profile (prevalence = 5.3%) as the reference standard.

TABLE 4
Tests of accuracy for physician billing claims added to hospital discharge abstracts[a]

Administrative data algorithm	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Kappa statistic (95% CI)	Prevalence estimate (%)
1 hospital discharge abstract[a]	60.8 (47.4 - 74.2)	99.6 (99.1 - 100.0)	88.6 (78.0 - 99.1)	97.9 (96.9 - 98.8)	0.71 (0.60 - 0.82)	5.3
1 physician billing claim or a hospital discharge abstract	86.3 (76.8 - 95.7)	93.2 (91.6 - 94.9)	41.5 (32.1 - 50.9)	99.2 (98.6 - 99.8)	0.53 (0.43 - 0.62)	10.9
2 physician billing claims in 1 year or a hospital discharge abstract	82.4 (71.9 - 92.8)	97.1 (96.0 - 98.2)	60.9 (49.4 - 72.4)	99.0 (98.3 - 99.7)	0.68 (0.58 - 0.78)	7.1
2 physician billing claims in 2 years or a hospital discharge abstract	82.4 (71.9 - 92.8)	96.8 (95.7 - 98.0)	59.2 (47.7 - 70.6)	99.0 (98.3 - 99.6)	0.67 (0.57 - 0.77)	7.3
3 physician billing claims in 1 year or a hospital discharge abstract	80.4 (69.5 - 91.3)	97.7 (96.7 - 98.7)	66.1 (54.3 - 77.9)	98.9 (98.2 - 99.6)	0.71 (0.61 - 0.81)	6.6
1 physician billing claim in a hospital or emergency room or by a specialist or a hospital discharge abstract	84.3 (74.3 - 94.3)	95.1 (93.7 - 96.5)	48.9 (38.4 - 59.3)	99.1 (98.5 - 99.7)	0.59 (0.49 - 0.69)	9.1
2 physician billing claims in 1 year in a hospital or emergency room or by a specialist or a hospital discharge abstract	80.4 (69.5 - 91.3)	97.6 (96.6 - 98.6)	65.1 (53.3 - 76.9)	98.9 (98.2 - 99.6)	0.70 (0.60 - 0.80)	6.5
2 physician billing claims in 1 year with at least one being in a hospital or emergency room or by a specialist or a hospital discharge abstract	82.4 (71.9 - 92.8)	97.6 (96.6 - 98.6)	65.6 (54.0 - 77.3)	99.0 (98.4 - 99.7)	0.71 (0.62 - 0.81)	6.6
3 physician billing claims in 1 year in a hospital or emergency room or by a specialist or a hospital discharge abstract	78.4 (67.1 - 89.7)	98.1 (97.3 - 99.0)	70.2 (58.3 - 82.1)	98.8 (98.1 - 99.5)	0.73 (0.63 - 0.82)	5.9
3 physician billing claims in 1 year with at least one being in a hospital or emergency room or by a specialist or a hospital discharge abstract	80.4 (69.5 - 91.3)	98.0 (97.1 - 98.9)	69.5 (57.7 - 81.2)	98.9 (98.2 - 99.6)	0.73 (0.63 - 0.83)	6.1

Abbreviations: CI, confidence interval; MI, myocardial infarction; NPV, negative predictive value; PPV, positive predictive value.

[a] Evidence for MI as documented in a cardiac-related specialist note or hospital discharge summary, or recorded in the cumulative patient profile (prevalence = 5.3%) as the reference standard.

had a silent or unrecognized MI or an MI not recorded in the hospital discharge data that would not otherwise be captured. Given the detrimental effect of unrecognized MIs on long-term mortality and major cardiac events,[14,16,17] knowing the occurrence of these events in a population has important implications for health service planning and for assessment of secondary treatment and prevention strategies and quality measurement. Our findings also show that the addition of emergency room records does not improve the accuracy of identifying patients with an MI; thus provinces without such records would not be at a disadvantage in identifying MI patients through their administrative data.

Administrative data have the potential to facilitate the assessment of MI occurrence in a population. Note that the PPV in the administrative data algorithms using physician billing claims may not be high enough to avoid the accumulation of false positives and therefore these may overestimate the true occurrence of MI in a population. However, given that the sensitivity of these algorithms is in the 80% range—suggesting that not all cases are picked up—the possible over-reporting may not be that high. Further, administrative data are confined to patients who have come in contact with the medical system; it is possible that there are patients in the general population who have had an unrecognized MI but who have never sought medical attention or had their MI diagnosed by a physician.

It is difficult to compare our findings with previous validation studies as they used a reference standard derived from either hospital charts or clinical patient registries based upon hospitalization, and none have looked at using physician billing claims to identify MIs that did not result in hospitalization. Another Ontario-based validation study looked for ICD-10 code I21 for acute MI as the most responsible and secondary diagnoses and found a sensitivity of 89% and PPV of 87% for the most responsible diagnosis, but a sensitivity of 78% and PPV of 76% when using the hospital chart as the reference standard. These results are higher than ours since the data sources were restricted to patients who were hospitalized for their MI.[1] Our results, which used physician claims data plus hospital discharge abstracts compared to family physician charts, performed similarly to a study in Australia that used registry data as the reference standard and showed a sensitivity of 79% and PPV of 66% for acute MI using hospital diagnostic codes.[10] Our study also had similar results to one in the US that compared hospital coding to hospital discharge records as a reference standard with a sensitivity of 81% and a PPV of 55%.[5]

Limitations

We only used data from a convenience sample of physicians who were on one particular EMR. We do not know if physicians on this particular EMR code differently to physicians who are not on an EMR or are on a different one. However, it is unlikely that the patient population or disease occurrence is different for physicians who are on an EMR compared to those who are not.

Second, it is possible that some of the weaker evidence for MI or the ECG-only evidence may, with time, turn out to be real or silent MIs; capture of MIs in the EMR may depend on the length of time the patient has been on the EMR, how well the physician captured historic patient medical information in the EMR, or when the abnormalities were captured in relation to the date the EMR data were downloaded.

Third, we were unable to fully apply WHO criteria for MI as only the interpretation of ECG wave forms are typically captured in the EMR; troponin values are also generally not captured in the EMR. Fourth, data were only available from CIHI as of 1988 and from OHIP as of 1991. Thus patients who had an MI before then may not be captured in the administrative data.

Last, our analysis did not take into account the 52.1 per 100 000 people who die of an MI on the way to the hospital[23] as our data were confined to patients registered on the physician EMR; patients who died may have been taken out of the physician EMR.

Nonetheless, data contained within an EMR appear to be rich and reasonably comprehensive and can be used to validate case ascertainment algorithms using administrative data. Using a combination of hospital discharge abstracts and physician billing data increases the capture of MI beyond patients who have been hospitalized and may best be used for assessing trends of MI occurrence over time.

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Executive Summary

Meals and snacks consumed by young Quebecers

In June 2010, the Institut de la statistique du Québec, in collaboration with Brigitte Bédard and Lise Dubois of the University of Ottawa's Institute of Population Health published *Les jeunes québécois à table : regard sur les repas et collations*,[1] its second report based on analysis of the data from Statistics Canada's 2004 *Canadian Community Health Survey – Nutrition*. This publication looks at important facets of the diet of Quebec children and adolescents (1 to 18 years old): meals, snacks and consumption of food prepared outside the home.

The results point to several problems with the young people's diet. The report reveals, among other things, that approximately 14% of Quebec children and adolescents (nearly 20% of the 9-18 year-olds) skipped at least one meal during the day. Skipping a meal is not without nutritional consequences. Lower average intakes of several nutrients were observed in young people who skipped at least one meal during the day, compared with those who ate three meals. This was the case, for example, for proteins, carbohydrates, fibre, calcium and vitamins C and D in girls 14 to 18 years old. Such results suggest that, when a meal is skipped, it is more difficult to obtain a level of nutritional intake equivalent to that obtained by eating three meals, even if snacks are eaten. Thus, young people who skip a meal may have more difficulty meeting their needs for certain nutrients.

That said, consuming food or beverages between meals is a very popular practice among young Quebecers. Depending on age and sex, between 54% and 73% of children and adolescents consumed at least three snacks during the day. Dietary intakes between meals contributes to over one fifth or even one quarter of the daily energy intake, i.e. slightly more than breakfast, which accounts for between 17% and 21% of energy intake.

In terms of content, the analyses reveal that the snacks consumed are often foods that are less nutritious and that are higher in sugar, fat or salt, particularly among 14-18 year-olds. The "Other foods" category (not belonging to the four *Food Guide* groups) accounts for as much as 48% of the energy intake from snacks in this age group.

A relatively large proportion of Quebec children and adolescents consume food prepared outside the home: 39% of 4-8 year-olds, 45% of 9-13 year-olds and 57% of 14-18 year-olds, for a given day. Moreover, foods from fast food restaurants were consumed by 11% of 4-8-year-olds, 16% of 9-13 year-olds and 28% of 14-18 year-olds. Nutritionally, consuming fast food was associated with a lower-quality diet. For example, among boys 14 to 18 years old, the results reveal that having consumed foods from fast food restaurants, compared to foods prepared exclusively at home, is associated with higher average intakes of energy, fat and saturated fats.

At a time when the vision for healthy eating[2] proposed by the Ministère de la Santé et des Services sociaux du Québec is emphasizing the overall food environment, these results confirm the importance of taking action on the food supply to which young people are exposed.

The publication *Les jeunes québécois à table: regard sur les repas et collations* is available on the Web site of the Institut de la statistique du Québec. It complements the dietary and nutritional portrait of young people, *L'alimentation des jeunes québécois: un premier tour de table*,[3] published in 2008.

The *Canadian Community Health Survey (CCHS) – Nutrition* is a large national survey with two separate and complementary components: a general health component and a dietary component. The dietary data were collected by means of a complete questionnaire on foods and drinks consumed during a 24-hour period, the day before the interview (24-hour dietary recall). The results presented in the ISQ publications are based on 2014 respondents 1 to 18 years old.

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Book review

Culture and Health: Applying Medical Anthropology

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Culture and Health: Applying Medical Anthropology compares and contrasts models of health around the world with the Western biomedical model. The text goes beyond individual factors affecting health care and explores macrolevel effects on health, such as government policies and economic issues. While the book is written for those with a health sciences background, scientific jargon is kept to a minimum, and the author aims to broaden the reader's understanding of health from different ethnocultural perspectives.

The self-assessment questions included at the end of each chapter highlight the focus on students as readers. However, these questions encourage all readers to reflect on their own experiences and critically evaluate their own cultural competence in comparison to the information in the chapters. The most interesting aspect of the text, however, are the practitioner profiles, case studies and examples of cultural concepts in health that supplement and illustrate the information provided.

The ten chapters of the book can be grouped into two categories: the first five chapters provide an introduction to medical anthropology, while the remainder focus on applying these concepts to explain the complex cultural, ecological, political and psychological factors affecting physiological responses and health.

In the first two chapters, the author compares and contrasts cultural concepts of health and illness, highlighting how these can be affected by the physical and cultural environment. While our understanding of health is effective in certain situations, these chapters illustrate how the biomedical definition of disease is extremely limited and can be complimented by the Cultural Systems Model, where a person's cultural milieu is also considered. This is illustrated in the book with the example of increased prevalence of cardiovascular disease among African Americans compared to their Hispanic American counterparts.

The author investigates the implications of cultural competency in health care, advocacy, research and administration in Chapters 3 and 4. He also discusses guidelines for developing culturally sensitive policies and programs, as well as how communities can act to support treatment and assist with the healing process.

Introducing ethnomedical systems in health care in the fifth chapter, the author discusses how various cultures have different interpretations of symptoms, and analyzes folk and alternative medicine. He points out how the professional sector of medicine can be considered a culture by itself because of the traditions it adheres to. The author uses transcultural psychiatry in Chapter 6 as an example of how there are different ethnomedical views of psychology and psychiatry, and how "normal" behaviour should be considered in the cultural context. The in-depth example used to highlight this was particularly interesting given the policies being currently developed in Canada to help combat stigma associated with mental illness.

Chapters 7 and 8 delve into the ecological factors affecting health, such as race, ethnicity and social contexts. The argument used in this discussion is the analysis of alcoholism from a critical medical anthropology perspective. Oftentimes, the focus is on the individual, using terminology such as "their drinking problem"; historical and societal values that may cause the individual to be more susceptible to alcoholism are not considered by health care professionals. The author raises a compelling argument in favour of this approach when designing interventions and programs.

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Chapter 9 discusses psychobiological dynamics of health, focusing specifically on how religion, rituals and symbolic healing can affect our bodily processes. In this chapter, the physiological response to various symbols is discussed alongside the effects of placebos and other non-prescription medications. Lastly, the author introduces the field of psychoneuroimmunology, a relatively new area focusing on how symbols, personal expectations and social relations can affect our immune systems.

The book concludes with a discussion of shamanism, a relatively foreign concept in Western medicine. The author demystifies the practices of shamans by explaining how they achieve their altered state of consciousness. At the end of the chapter, he highlights the benefits shamanism has for current psychotherapy practices, including highlighting specific aspects of shamanism that are currently used.

The author's purpose for writing this book is to advocate that many issues affecting multicultural communities have social, economic and cultural origins. Established clinical or pharmacological solutions provide a "band-aid" solution and, in order for the issues to be resolved completely, we need to manage the social and cultural conditions affecting health. His analysis provides an alternative way of conceptualizing the etiology of a disease, and he uses literature to support his arguments.

As medical students and researchers, we found the examples of cultural concepts in health, health care and expressions of illness and the biocultural interactions most applicable to our work. This approach is not emphasized in Western medical education and should be considered as a potential alternative to current medical practices. Using this approach could lead to novel interdisciplinary research approaches to existing healthcare problems.

The main limitation of the book was the lack of diversity in the health practitioner profiles. While they may be applicable to students of anthropology, the significant focus on successful academic researchers does not offer concrete methods that could be used by non-anthropologists while developing interventions or research programs. In future editions of the book, the author may want to consider expanding the profiles to include front-line health care professionals discussing the cultural issues they have faced in their careers.

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